Analysis of neovascular membrane activity changes in age-related macular degeneration (AMD) patients undergoing intravitreal injections before and after cataract surgery

Purpose
To evaluate macular fluid before and after cataract surgery in patients undergoing treatment for age-related macular degeneration. Setting/Venue: Urban Tertiary hospital. Hospital Universitario de la Princesa. Madrid

Methods
We conducted a retrospective study of 550 patients undergoing phacoemulsification cataract surgery in the macula section of an Urban Tertiary hospital, Hospital Universitario de la Princesa, Madrid (Spain). 83 of those initial participants were also AMD patients treated with intravitreal injections. Demographic and clinical data of these patients were collected: age, gender, operated eye, presence of risk factors for surgery (mature cataract, pseudoexfoliation syndrome, poor dilatation and posterior subcapsular cataract), the experience of the surgeon (less or more than 5 years), presence of intra-surgical complications (posterior capsule rupture, zonular disinsertion or dislocation of the lens to the vitreous nucleus), time phacoemulsification surgery took place (whether it was in the first 6 months after the beginning of the intravitreal injections, or in a later period of their lives), number of injections received prior to cataract surgery (10 or more), visual acuity (VA) (Logmar) before and 6 months after de surgery and neovascular membrane activity status. This activity was determined by the presence of intraretinal fluid (IRF) and/or subretinal fluid (SRF) through structural OCT images before and at least 4 weeks after the surgery.

Results
83 patients (15%) had received prior intravitreal injections. 57 were women (68%) and 26 men (31.3%). The average age was 84.5 years. 39 were right eyes (47%) and 44 were left eyes (53%). There was an increase between preoperative and 6 months postoperative visual acuity (logmar VA: 0.73, logmar VA: 0.38). 80% of the surgeries were performed by expert surgeons and the majority of patients (88%) had received more than 10 intravitreal injections before the cataract surgery was performed. 45.8% of the patients had no activity one month before surgery but 54.2% had either SRF (15.7%) or IRF (28.9%) or both (9.6%). In the group of patients in which the membrane was no active before surgery (38), 9.6% (9) suffered a reactivation. One month after surgery, 62.7% of the patients had neovascular membrane activity, being those patients with both types of activity (SRF and SRF) who increased more (9.6% versus 18.1%). In the subanalysis of the type of macular fluid, 6 out of the 13 patients with SRF (46.15%) presented an increase in fluid quantity.

Conclusions
Cataract surgery is one of the most frequent procedures performed in industrialized countries and intravitreal treatment for AMD has increased exponentially in recent years. Both are bound to be found more and more prevalent in the future, even more so taking into account the aging of the population, as our study shows, where the mean age of the patients was 85 years. More than half of our patients presented neovascular membrane activity before cataract surgery, included those who had been with intravitreal treatment longer than 6 months. There were no significant differences in final postoperative VA between patients with or without reactivation, probably due to an increase in SRF that would less affect the visual acuity than the presence of IRF. Patients with preoperative macular fluid in OCT should be considered for cataract surgery, since these patients visually evolved well despite the presence of fluid, avoiding lengthening the number of intravitreal injections with the risk of future complications in cataract surgery.

Financial Disclosure
None
Spontaneous regression of subretinal choroidal neovascularisation in a patient with AMD

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Purpose
To present a case of spontaneous regression of choroidal neovascularisation after interruption of anti-VEGF treatment

Setting/Venue
The patient was reviewed at the Athens Eye Center

Methods
A 69-year-old presented in 2019 with bilateral choroidal neovascularization caused by age related macular degeneration (AMD). Visual acuity was 6/18 in both eyes. He underwent treatment with intravitreal Lucentis injections in both eyes and cataract surgery.

Results
Subretinal and intravitreal fluid resolved and best corrected visual acuity improved to 6/12 in both eyes. The subretinal tissue remain unchanged throughout the treatment with Lucentis. The patient was seen in March 2020 and planned for further anti-VEGF treatment because of new fluid accumulation. He was lost to follow up because of the pandemic and resurfaced in April 2021. At that time the subretinal tissue had completely regressed in the right eye and remained unchanged in the left eye.

Conclusions
It is unclear whether this was an automatic regression of choroidal neovascularization or different pathology was at play.

Financial Disclosure
None
Results of surgical complications after cataract surgery in patients treated with intravitreal injections for age-related macular degeneration (AMD)

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Purpose
To evaluate intraoperative complications during cataract surgery in patients undergoing treatment for age-related macular degeneration.

Setting/Venue
Urban Tertiary hospital. Hospital Universitario de la Princesa, Madrid.

Methods
We conducted a retrospective review of adult patients undergoing phacoemulsification cataract surgery in the macula section of an urban tertiary hospital in Madrid (Spain). Clinical data was anonymized and extracted, including prior administration of intravitreal injections. The variables studied were age, gender, operated eye, presence of risk factors for surgery complication, duration of intravitreal treatment (≤ 6 or >6 months) and number of intravitreal injections prior to surgery (≤ 10 or >10). Experience of the surgeon (≤ 5 or >5 years) and initial and final visual acuity were also included for univariate analysis. All patients previously injected with anti-VEGF due to AMD were analyzed. The main inclusion criterion was phacoemulsification cataract surgery during the study period. We excluded those patients who underwent non-phacoemulsification cataract extraction and those with evidence of posterior capsule rupture before cataract surgery. The primary outcome measure was posterior capsule rupture (PCR) during cataract surgery. The statistical analysis was carried out using the SPSS 25.0 data processing programme. Categorical variables were analyzed using the chi-square test and continuous variables were compared using the t-Student test. To determine the strength of association, the odds ratio (OR) was used with a confidence interval (CI) of 95%. P-value ≤0.05 was deemed statistically significant.

Results
Data was available for 550 cataract surgeries. Of these, a total of 83 eyes (15.09%) had received prior intravitreal injections. 57 were women (68.67%) and 26 (31.33%) men. Mean age was 84.52 ± 6.68 years being the 81.90% (n=68) of the sample over 80 years. Focusing on risk factors for surgery complication, we found 20 eyes with posterior subcapsular cataract (24.10%), 3 eyes (3.60%) with poor dilatation, 2 eyes (2.40%) with mature cataract and 1 eye (1.20%) with pseudoexfoliation syndrome. Patients with posterior subcapsular cataract presented an OR=5.67 (CI 95% [5.67-5.67]; p <0.05) for suffering a complication during the surgery. On examining the complication rate, we observed that 10 eyes (12.05%) presented complications during cataract surgery. The most frequent cause was dislocation of nucleus to the vitreous (n=5, 6%), followed by PCR (n=3, 3.60%) and zonular disinsertion (n=2, 2.40%). In the univariate analysis, we found an increase between preoperative and postoperative visual acuity at 6 months (preoperative Logmar VA: 0.75, postoperative Logmar VA: 0.32) with a mean gain of 0.43 lines (CI 95% [0.28-0.59]; P = 000). Within this study, surgeon experience and number of prior intravitreal injections were not found to be statistically significant risk factors for PCR.

Conclusions
Cataract surgery is the most frequent surgical operation in industrialized countries and intravitreal treatment for AMD has increased exponentially in recent years. These two pathologies are bound to be found more and more in the future, even more so taking into account the aging of the population, as our study shows, where the mean age of the patients was 85 years. The female gender is also more frequent (67%) and thus an elderly woman is the typical patient who receives injections for AMD. Posterior capsule rupture occurs more frequently during cataract surgery in patients who have received previous intravitreal injections and especially those with a posterior subcapsular cataract, probably caused by the needle induced trauma to the posterior capsule during injection. We must therefore insist on a good exploration of the cataract prior to surgery in these patients. A large majority of the complications had to be solved by vitrectomy, so this eventuality must be included in the informed consents and in the information given to the patient.

Financial Disclosure
No financial conflicts
### Title

Structural and vascular features in non-responder neovascular age-related macular degeneration after Brolucizumab injection: An optical coherence tomography angiography study

### Purpose

To evaluate pigment epithelium detachment (PED) variation and vascular morphological changes after Brolucizumab intravitreal injection in non-responder neovascular age-related macular degeneration (nAMD) patients using Optical Coherence Tomography (OCT) and OCT angiography (OCTA).

### Setting/Venue

Retina 3000 Eye Clinic, Milan

### Methods

This is a prospective observational case series. Patients diagnosed with nAMD with a non-responder PED to previous treatment with anti-VEGF agents and switched to Brolucizumab were enrolled in this study. In order to be classified as non-responders, patients had to have persistent PED associated with intraretinal/subretinal fluid after at least 3 additional consecutive anti-VEGF injections. All patients underwent structural OCT and OCTA at the same retinal location at the time of the first Brolucizumab injection and fifteen, thirty, and sixty days after treatment. Greatest PED height was measured using the in-built measure distance tool at each visit. Moreover, a qualitative assessment of the macular neovascularization (MNV) was performed during the study period. A paired t-test was used to calculate the variation of the greatest PED height.

### Results

Ten eyes of ten patients (mean age 73 SD± 8 years) were enrolled in this study. The mean number of anti-VEGF treatments was 12.6 (SD± 3) during a mean follow-up period of 3 years from the first diagnosis to the last injection before switching. One month after Brolucizumab administration, no activity signs were detected by SD-OCT in all patients. We also found a statistically significant reduction of the greatest PED height after 15 days from the Brolucizumab injection (P<0.05) and a subsequent further decrease after a 1-month follow-up. Greatest PED height was then preserved up to month two (P>0.05). OCTA showed a shrinking of the neovascular network with reduction of peripheral branching vessels and anastomotic arches and appearance of a pruned tree appearance of the vascular loops in 70% of the patients. In 20% no evident morphological changes of the neovascular network were present despite the improvement appreciated from the structural scans while in the last 10% there were an initial decrease of intraretinal fluid, but it was subsequently followed by a structural worsening with persistence of activity signs one month after the injection.

### Conclusions

In non-responder patients, Brolucizumab could represent a valid treatment option promoting a reduction of the neovascular exudation. Moreover, we found a significant reduction of chronic PED. Further randomized control studies are necessary to confirm our findings.

### Financial Disclosure

The authors do not have any financial relations.
Risk of intraocular pressure spike after intravitreal aflibercept using vial-prepared vs. the novel prefilled syringe formulation

Purpose
To compare the risk of severe intraocular pressure spike (IOPS) with transient central retinal artery occlusion after intravitreal aflibercept application using the novel prefilled syringe (PFS) vs. the old vial system.

Setting/Venue
Intravitreal injection service of the Ludwig Maximilians-University Munich and Technical University Munich, Departments of Ophthalmology

Methods
The databases of the Ludwig Maximilians-University Munich and the Technical University Munich, Germany, were screened for patients with IOPS after intravitreal injection of aflibercept. The observation period included two full months prior to the introduction of the novel PFS and two months afterwards. IOPS was defined as loss of perception of hand movement for a duration of more than 30 seconds.

Results
Over a period of four months, 1720 intravitreal injections of aflibercept were administered in 672 patients. There were 842 injections with the old vial system, and 878 injections using the novel PFS. Using the vial system, IOPS was noted during two injections (0.24 %) in two patients, as compared to 11 cases of IOPS (1.25%) in 10 patients with the PFS (p=0.015). Using the PFS, patients had a 5.3-fold risk of IOPS as compared to the vial system (OR: 5.33; 95 % CI: 1.2 – 24.1; p=0.0298).

Conclusions
There was a more than five-fold risk of severe intraocular pressure spike using the novel pre-filled aflibercept syringe as compared to the established vial system. This study adds evidence to the data recently communicated by the European Medicines Agency (EMA).

Financial Disclosure
No financial interests relevant to this study.
**Title**
Choroidal vascularity index is associated with geographic atrophy progression

**Purpose**
To investigate the correlation between choroidal vascularity index (CVI) and the enlargement of geographic atrophy (GA) lesion secondary to age-related macular degeneration (AMD) during a 2-year follow-up.

**Setting/Venue**
This was a longitudinal observational study, including consecutive patients affected by GA secondary to dAMD presenting at the Medical Retina & Imaging Unit of the Department of Ophthalmology of University Vita-Salute San Raffaele in Milan, Italy. Patients presenting between January 2018 and October 2018 and followed for 2 years (until October 2020) were included. This study was conducted in agreement with the Declaration of Helsinki for research involving human subjects. All patients signed a written consent to participate in observational studies that was approved by the Local Ethics Committee.

**Methods**
In this longitudinal observational study, 26 eyes of 26 patients (mean age 75.7±8.8 years) affected by GA secondary to AMD were included. All patients underwent structural optical coherence tomography (OCT) and fundus autofluorescence (FAF) at baseline and 2-year follow-up. CVI (the ratio between the luminal choroidal area and the total choroidal area) was calculated in the subfoveal 3000 μm area. The main outcome measure included correlation analysis between baseline CVI and the rate of GA enlargement.

**Results**
During the 2-year follow-up, visual acuity significantly decreased from 0.32±0.18 to 0.39±0.18 LogMAR (p<0.001), and mean GA area increased from 6.99±5.28 mm² to 10.69±6.61 mm² (p<0.001), accounting for a growth rate of 0.33±0.17 mm/year after the square root transformation. Stromal choroidal area (SCA) significantly decreased during the 2-year follow-up (p<0.001). Interestingly, there was a significant correlation between the baseline CVI and the rate of GA enlargement (r=-0.432, p=0.027), and between SCA and the rate of GA enlargement (r=0.422, p=0.032). No other significant relationship was disclosed among choroidal parameters with the rate of GA enlargement.

**Conclusions**
CVI impairment is strictly related to the rate of enlargement during the 2-year follow-up in patients affected by GA. For this reason, CVI could be considered as a predictor of GA progression in the clinical setting, and it could be considered as a new potential biomarker in the efficacy evaluation of new GA interventions.

**Financial Disclosure**
Riccardo Sacconi is a consultant for: Novartis (Basel, Switzerland), and Zeiss (Dublin, USA). Enrico Borrelli is a consultant for: Novartis (Basel, Switzerland), and Zeiss (Dublin, USA). Francesco Bandello is a consultant for Alcon (Fort Worth, Texas, USA), Alimera Sciences (Alpharetta, Georgia, USA), Allergan Inc (Irvine, California, USA), Farmila-Thea (Clermont-Ferrand, France), Bayer Shering-Pharma (Berlin, Germany), Bausch And Lomb (Rochester, New York, USA), and Theraclion (Bordeaux, France). Francesco Bandello is a speaker for: Novartis (Basel, Switzerland), Allergan Inc (Irvine, California, USA), Alimera Sciences (Alpharetta, Georgia, USA), and Zeiss (Dublin, USA). Giuseppe Querques is a consultant for: Zeiss (Dublin, USA), Bayer Shering-Pharma (Berlin, Germany), Allergan Inc (Irvine, California, USA), Farmila-Thea (Clermont-Ferrand, France), and Novartis (Basel, Switzerland).
Purpose
There are gaps in understanding causes of non-adherence (NA) to anti-vascular endothelial growth factor (VEGF) therapy and subsequent undertreatment in patients with neovascular age-related macular degeneration (nAMD). The aim of the ANDROMEDA study is to assess treatment adherence over a period of 24 months during intravitreal aflibercept (IVT-AFL) therapy for nAMD, and to identify the impact of patient- and/or physician-related factors on adherence.

Setting/Venue
ANDROMEDA (NCT03714308) is a 24-month, prospective, observational cohort study in treatment-naïve as well as pre-treated patients with nAMD receiving IVT-AFL injections across 41 centers in Germany. All treatment decisions, including the decision to treat with IVT-AFL, were made by the treating physician.

Methods
A 4-month interim analysis was performed for the total study cohort as well as for treatment-naïve and pre-treated patients. The date of data cut-off for the 4-month analysis was May 31, 2021. Primary endpoints are the time to first occurrence of NA, defined as relevant deviation from on-label use of IVT-AFL, and reasons for missing a scheduled injection visit asked directly in telephone interviews. Secondary endpoints include best-corrected visual acuity (BCVA), health-related and vision-related quality of life, treatment satisfaction, and patient-reported barriers to adherence. Health-related and vision-related quality of life, treatment satisfaction, and treatment adherence barriers were assessed via telephone interviews using the 5-level EuroQol 5-Dimension (EQ-5D-5L) health questionnaire, the National Eye Institute Visual Function Questionnaire 25 (NEI-VFQ-25), the Macular Disease Treatment Satisfaction Questionnaire (MacTSQ), and the Patient Questionnaire for Longitudinal Assessment of Adherence Factors to Intravitreal (anti-vascular endothelial growth factor therapy) Therapy (LAF-IVT). Cox models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for time to first occurrence of NA for defined baseline risk factors, which was visualized using Kaplan–Meier plots.

Results
Of a total of 554 patients enrolled in the study, 511 were valid for analysis of study endpoints. BCVA of naïve patients (58.6 ±18.55, n=224) was worse than that of pretreated patients (IVT-AFL pretreated 66.8 ±15.34, n=118; other pretreatment 64.8 ±15.78, n=169) and increased after 4 months to 63.3 ±17.47 in the naïve patient group and 66.8 ±15.34 and 64.8 ±15.78 in IVT-AFL pretreated and other pretreatment group respectively. Telephone interviews were documented for 91.2% of the total cohort at baseline and 89.2% at 4 months. The EQ-5D-5L and NEI-VFQ-25 scores were 0.8 (±0.20) and 79.2 (±13.32) at baseline and 0.8 (±0.23) and 79.7 (±13.72) at 4 months, respectively. The mean (± SD) MacTSQ (first applied at 4 months) score was 59.7 (±9.89). During the first 4 months, 45 (8.8%) patients reported missed injection visits in the LAF-IVT questionnaire. Patients reported "other diseases" as the most common reason (n=26, 57.8%) for a missed injection appointment during this observation period. The COVID-19 pandemic coincided to varying degrees with the enrolment and/or observation of 85% of the study population.

Conclusions
NAMD patients showed a high rate of non-adherence, even higher than anticipated before start of the study. Thus, not only the successful recruitment of comparable groups with and without IVT-AFL pretreatment promises insights into which phenomena are actually vs. patient perceived to be relevant for off-label treatment intervals. Pertinent risk factors will be identified in the analysis of the 12- and 24-month data and furthermore the impact of the COVID-19 pandemic on treatment adherence will be considered.

Financial Disclosure
**Title**
Comparison of switching treatment from Ranibizumab to Afibercept and Afibercept to Ranibizumab on serous pigment epithelial detachments due to age-related macular degeneration

**Co-Author 1**
Fatma Savur

**Purpose**
To compare the efficacy and treatment switch response of two intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents, ranibizumab and afibercept, for the treatment of large serous pigment epithelium detachment (sPED) due to age-related macular degeneration (AMD).

**Setting/Venue**
We included 38 AMD patients (38 eyes) having sPED ≥200 μm in fovea that is measured manually with optic coherence tomography (OCT). All patients were treatment naive before anti-VEGF therapy. Patients received a serial of three monthly Ranibizumab (0.5 mg/0.05 ml) or Afibercept (2.0 mg/0.05 ml) followed by pro re nata (PRN) schedule. The treatment protocol after switched consisted of a fixed dosing regimen comprising of monthly injections for first 3 months, followed by PRN injections in last visit of treatment.

**Methods**
In this retrospective study, cases were divided into 2 groups. Group 1 (22 eyes) treated initially with intravitreal Ranibizumab (0.5 mg/0.05 ml) and later switched to Afibercept (2.0 mg/0.05 ml) and later switched to Ranibizumab (0.5 mg/0.05 ml). The outcome measures of this study were best corrected visual acuity (BCVA), PED height, PED width, the presence of subretinal fluid (SRF), intraretinal fluid (IRF), number of injections and and follow up time. Examination findings were recorded at baseline, month 3, month 6 and at time point of switch, 3 month, 6 months and at last follow up visit post-switch. Student’s t test and repeated measurements ANOVA were calculated to analyze variables at baseline, at switch and change in variables at last visit.

**Results**
There was not a significant difference in BCVA, PED height, PED width between the two groups at pre-switch, at-switch and after-switch visits (p<0.05). All patients had SRF and IRF at baseline two groups. At switch point, 22(%100) eyes in Group 1, 16(%100) eyes in Group 2 had SRF. In Group 1, 11(%50) eyes showed SRF and 8(%50) eyes in Group 2 had SRF at last visit after switching which was insignificant (p=1.00). Thirteen eyes(%59) eyes in Group 1 and 5(%31) eyes in Group 2 had IRF at baseline. At switch point, 1(%4.5) eye in Group 1 and 1(%6) eye in Group 2 had IRF. One (%4.5) eye in Group 1 and 1 eye(%6) in Group 2 had IRF at last visit after switching (p=0.816). sPED complete resolved in 8 eyes(%36) in Group 1 and 5(%31) eyes in Group 2, whose sPED height was less than 350 microns. The mean number of injections of both groups at the time of the switch and at the last visit after the switch were found to be similar (p=0.995, p=0.384, respectively). The follow-up periods of both groups at the time of the switch and at the last visit after the switch were found to be similar (p=0.404, p=0.884 respectively). In Group 1, retinal pigment epithelial collapse was observed in one case before switch.

**Conclusions**
There is no clear consensus on which anti-VEGF and which treatment regimen should be used in patients with sPED due to AMD. We aimed to treatment once visual acuity and sPED have stabilized and SRF or IRF have resolved. Our study found that both anti-VEGF treatment showed similar anatomical effectiveness with significant reduction in PED height and resolution rate of SRF, IRF. The other finding in our study was complete resolved sPED in eyes with below 350 microns sPED height.

**Financial Disclosure**
I do not have financial relations.
External limiting membrane disruption predicts long-term outcome in strict Treat-and-Extend regimen in neovascular age-related macular degeneration

To determine long-term outcomes in visual acuity and outcome predicting factors in patients with neovascular age-related macular degeneration (nAMD) applying a strict treat-and-extend regimen (TER).

Setting/Venue
Retrospective study at Vista Eye Clinic Binningen, Switzerland.

Methods
Up to eight-year retrospective follow-up of treatment-naïve subjects with nAMD starting treatment with either ranibizumab or aflibercept in a strict TER without loading dose but with predefined exit criteria.

Results
Two hundred-eleven (211) eyes of 187 patients with a mean follow-up of 60.3±20.9 months were included. Mean BCVA increased from initially 63.9±15.5 ETDRS letters (20/55) to 70.0±14.7 (20/40) after one year (+6.1 letters, p<0.001) and to 68.5±18.1 (20/43) (+4.6 letters, p=0.028) at 5 years. During follow-up 30.3% of eyes reached exit criteria. A worse BCVA (p=0.001) and a better external limiting membrane (ELM) disruption score at baseline predicted (p=0.019) BCVA gain at 5 years. The probability of reaching the exit criteria was significantly associated with a low central retinal thickness (CRT) (p=0.025), a better ELM disruption score (p=0.044) and the absence of a central pigment epithelial detachment (PED) (p=0.05) at baseline.

Conclusions
Significant visual gains were sustained after 5 years of follow-up in a TER in a real-world setting. Integrity of ELM at baseline predicted BCVA gain and anatomic disease stability at 5 years of treatment.

Financial Disclosure
Dr Hoffmann has no conflicts of interests to disclose; PD Dr Hatz has received financial compensation from Novartis Switzerland, Bayer Switzerland, Alcon, Allergan and Roche for consultancies and contract research.
### Title

Pachychoroid neovasculopathy can mimic wet age-related macular degeneration

### Purpose

To determine the percentage of patients with pachychoroid neovasculopathy (PNV) among patients who have been misdiagnosed and treated with wet age-related macular degeneration (AMD)

### Setting/Venue

For doing this retrospective cross-sectional study, patients over 60 years old, who were diagnosed with wet AMD, were re-evaluated. All patients were recalled for examination and imaging.

### Methods

The present retrospective study was carried out on patients over 60 years of age, who were diagnosed with type I AMD-CNV (including new cases and cases treated with anti–vascular endothelial growth factor therapy (anti-VEGF). All patients were recalled for examination and imaging. Pachychoroid neovasculopathy was diagnosed if all of the following criteria were met: (1) Pigment epithelium detachment named “doublelayer” sign or CNV below the RPE. (2) Subfoveal choroidal thickness (SFCT) 300 µm or more in both eyes. (3) Presence of drusen-like deposits (total area < 125 µm circle or hard drusen < 63 µm findings corresponding to Age-Related Eye Disease Study Level 1) in both eyes or presence of pachydrusen which presented as a singular lesion, larger than 125 µm, with a scattered outer border. (4) Presence of central serous chorioretinopathy (CSCR), or pachychoroid pigment epitheliopathy (PPE) (included RPE abnormality regardless of CNV lesion, the presence of dilated choroidal vessels, or choroidal thickening below the type 1 CNV, or thinning of the choriocapillaris can be noted over the pachyvessel area or a history of CSCR) in each eye

### Results

120 patients (137 eyes) were recorded with wet AMD in the clinic. Finally, after complete re-evaluation, 94 (106 eyes) and 26 patients (31 eyes) were assigned to the AMD and the PNV group, respectively. Thus, a total of 20% of patients with primary mistake diagnosis of wet AMD, actually had PNV. The mean sub field choroidal thickness (SFCT) in the AMD and PNV groups was 173.89 ± 69 µm and 342 ± 27 µm, respectively, which the difference was statistically significant (p-value 0.001). Also, drusen was found in 69.9% and 24% of the cases with AMD and PNV, respectively. (p-value 0.001) The average number of intravitreal injections of anti-VEGF (vascular endothelial growth factor) required in the AMD and PNV groups was about 5 and 3, respectively, which was statistically significant (p-value 0.02)

### Conclusions

About a one-fifth of wet AMD patients are actually due to PNV and often are misdiagnosed. Thus the disorder must be considered as important differential diagnosis of wet AMD.

### Financial Disclosure

The authors have no conflicts of interest to declare.
Real world data on prognostic factors for visual acuity LogMAR 0.10 or better in eyes with choroidal neovascularization treated with intravitreal vascular endothelial growth factors inhibitors

Purpose
Clinical trials proved intravitreal vascular endothelial growth factor inhibitors (anti-VEGF agents) to be able to stabilise or even improve visual acuity outcomes in various types of choroidal neovascularization. The purpose of the study is to identify prognostic factors and number of injections needed to obtain high visual acuity (equal or better than LogMAR 0.10) in eyes with neovascular age-related macular degeneration (nAMD) treated with anti-VEGF agents.

Setting/Venue
Department of Ophthalmology, General Hospital of Lamia, Lamia, Greece

Methods
retrospective chart review of medical records of 85 patients with nAMD treated with anti-VEGF agents in General Hospital of Lamia. 42 elsewhere treatment-naive patients (42 eyes) with more than one year follow up were identified. Age, gender, pseudophakia, baseline visual acuity, subretinal or intraretinal fluid at baseline, being the second eye affected, number of injections needed to achieve the best vision and achievement of visual acuity (VA) logMAR 0.10 or better were recorded. Fundus auto fluorescence imaging (FAF) was performed in 20/42 patients. Data were analysed with aparametric methods (Fischer’s exact test and Wilcoxon-Mann-Whitney test).

Results
Baseline VA 0.30 logMAR or better was identified as the only prognostic factor for the achievement of VA logMAR 0.10 or better (p=0.001). The best VA was achieved with 2 to 7 injections (median 3). All patients with VA=0.10 logMAR or better who were tested with FAF (6/12) showed minimal or no pathology.

Conclusions
patients at risk for nAMD should be followed up closely in order to diagnose the disease at the earliest possible stage and thus gain superior results with antiVEGF treatment. All available technology should be dedicated in this purpose.

Financial Disclosure
no financial relation with any company
Title
Relative ellipsoid zone reflectivity and age-related macular degeneration severity in the MACUSTAR study

Purpose
Quantification of the relative ellipsoid zone reflectivity (rEZR) on spectral-domain optical coherence tomography (SD-OCT) is assumed to be an in-vivo surrogate for photoreceptor integrity, potentially representing a candidate biomarker for disease progression in age-related macular degeneration (AMD). The purpose of this study was to compare the rEZR between different AMD disease stages.

Setting/Venue
Cross-sectional analysis of data collected for the observational natural history MACUSTAR study, which aims in developing and validating new methods to study disease progression in intermediate AMD

Methods
SD-OCT volume scans (241 B-scans, field size 30°x25°) of participants with early, intermediate, and late-stage AMD as well as age-similar controls were assessed at baseline. Using an automatic rEZR determination approach, the average rEZR [arbitrary units, AU] of each volume scan, after exclusion of drusen area, was analysed cross-sectionally. Linear mixed-effects models with the rEZR as response variable, adjusted for age, sex and the eccentricity within the volume raster scan, were applied to evaluate the association between AMD staging and the rEZR.

Results
A total of 301 eyes of 301 participants (mean age: 71.2 ± 7.2 years) classified as early AMD (n=34), intermediate AMD (n=168) and late-stage AMD (n=56) as well as controls (n=56) were analyzed. The mean rEZR differed across disease stages with a mean (± standard deviation, SD) of 42.08 (± 33.41) AT (median [interquartile range]: 33.0 [19.1 – 55.4] AU) in the early AMD group, a mean of 37.57 (± 29.76) AU (median: 29.9 [16.8 – 50.0] AU) in the intermediate AMD group and a mean of 19.1 (± 19.39) AU (median: 14.2 [5.9 – 26.4] AU) in the late AMD group compared to controls exhibiting a mean rEZR of 47.91 (± 35.89) AU (median: 38.3 [23.1 – 60.7] AU). The linear mixed-effects model shows a significant decrease of the rEZR of -8.05 in individuals with intermediate AMD (p=0.0011) and of -22.35 in late-stage AMD (p<0.0001) as well as a significant association of the rEZR with age (coefficient estimate: -86.93; p<0.0001) and eccentricity (fitted as a B-spline of degree 2, p<0.0001).

Conclusions
The rEZR correlates with AMD severity, being decreased with more advancing disease stages that are characterized by progressing photoreceptor degeneration. The results of this study warrant further longitudinal analyses to characterize the rEZR as an innovative biomarker and its prognostic value for AMD progression.

Financial Disclosure
Heidelberg Engineering, Carl Zeiss Meditec, Optos, CenterVue provides imaging devices and device for probing retinal function in research activities
**Purpose**

Polypoidal choroidal vasculopathy (PCV) is an exudative maculopathy, currently recognised as a phenotype of neovascular age-related macular degeneration (n-AMD) with higher prevalence in Asian and African descent than in Caucasians. The treatment of choice for PCV is controversial. Intraocular injection of anti-vascular endothelial growth factor (VEGF) has been the predominant treatment for all subtypes of n-AMD including PCV. Photodynamic therapy with verteporfin (PDT) is shown to cause regression of polypoidal lesions. Previous trials demonstrated superior outcomes of combination therapy with anti-VEGF injection and PDT in treatment-naive patients. In practice, the fundoscopic features of n-AMD and PCV may be indistinguishable, OCT and OCT-Angiography can also be of limited value in discerning the two pathologies, indocyanine-green angiography (ICGA-A) remains the gold standard imaging modality to confirm definite diagnosis of PCV. But due to the relatively lower incidence of PCV in the Western world, ICG-A is only performed in eyes refractory to anti-VEGF injections and PDT considered as a treatment option. While most previous studies demonstrated efficacy of combination therapy in treatment-naive eyes, this retrospective analysis aims to evaluate the real-world outcomes of PDT for PCV pre-treated with anti-VEGF injections.

**Methods**

We reviewed all consecutive cases of PCV treated with PDT from 1st Jan 2016 to 31st Dec 2019 to enable a minimum 12 months of follow-up after PDT. Data was extracted from the Medisoft electronic patient record system and paper-based records. Eyes with pre-existing non-macular visually-impairing pathology such as glaucoma or cataracts were excluded. Each eye was analysed individually, irrespective of the status and treatment received in the other eye. OCT and OCT-A, but not ICG-A, were routinely performed in all patients at initial consultation. ICG-A was only performed when clinical suspicion of PCV aroused due to sub-optimal response to Anti-VEGF therapy. Baseline data including demographic information, age of onset, initial diagnosis, time to correct identification of polypoidal lesions (diagnostic delay), location of polyps, baseline best corrected visual acuity (BCVA, in EDTRS letter score) at presentation and on the day of PDT and number of anti-VEGF injections per year before PDT were collected. Anti-VEGF injections received by patients included 2.0mg of aflibercept and/or 0.5mg of ranibizumab. Patients were followed-up for at least 12 months after PDT. Outcome measures include BCVA and the numbers of anti-VEGF injections required per year after PDT, disease activity (as assessed by visual acuity and OCT parameters) and anti-VEGF injection regimen. All statistical analyses were performed using SPSS.

**Results**

61 cases were identified, 5 cases were excluded due to pre-existing visually impairing pathology. Initial diagnosis at presentation included n-AMD (n=39, 69.6%) and CSCR (n=2, 3.6%). The mean (SD) diagnostic delay in these 41 patients (Delayed group) from initial presentation to correct identification of polypoidal lesions was 24.6 months (±21.5). 26.8% (n=15) were however diagnosed as PCV at presentation (Treatment-Naïve group). The mean post-PDT follow-up was 33.9 months (Range: 12 - 81 months). Overall, mean (SD) BCVA letter-score significantly improved from 59.4 (±19.2) letters before PDT to 64.6 (±18.0) at final follow-up visit (p=0.035). In the Delayed group, mean BCVA significantly dropped from 62.2 (±13.4) letters at first presentation to 56.6 (±18.2) letters on the day of PDT, despite anti-VEGF injections (p=0.015), but improved to 62.5 (±17.5) at final follow-up post-PDT (p=0.037); in Treatment-naïve group, mean BCVA before PDT was 74.4 (±18.3) and 75.2 (±17.7) at final visit (p=0.803). There was no significant difference in final BCVA between Delayed and Treatment-naïve groups (p=0.074). The mean change of BCVA 12-months after PDT was a gain of 6.2 (±12.2) letters. In the Delayed group, the mean (SD) number of anti-VEGF injection administered per year prior to PDT was 10.4 (±6.7), compared to 6.6 (3.9) injections per year after PDT (p=0.002); In Treatment-naïve group, the mean number of anti-VEGF injections received per year after PDT was 2.39 (2.45), which was significantly less.

**Conclusions**

There is limited evidence on the efficacy of PDT in treating patients with PCV already receiving regular anti-VEGF injections, as most existing studies focus on assessing the efficacy of PDT in treatment-naïve patients. Our study demonstrates that in eyes with PCV receiving anti-VEGF injections, PDT was able to improve BCVA and reduce the injection burden, even after a period of diagnostic delay. It also highlights that in case of strong clinical suspicion, if ICGA performed at the outset and PDT performed, the number of anti-VEGF injections required can be significantly reduced. Our experience provides real-world evidence that supports the use of combination treatment with ICGA guided PDT in association with anti-VEGF in PCV.

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**Financial Disclosure**

None
Title

Histological characterization of sodium iodate-induced pathology in rats as a useful model for assessing therapeutic efficacy in age-related macular degeneration

Purpose

Age-related macular degeneration (AMD) is a degenerative retinal disease and the leading cause of blindness in the elderly. The late stage of dry AMD, or geographic atrophy (GA), is characterized by extensive retinal pigment epithelium (RPE) degeneration. The use of sodium iodate (NaIO3), a relatively specific oxidant for the RPE, has extensively been used as a pre-clinical model of RPE atrophy. The severe retinal changes in the mouse NaIO3 model have been broadly described in literature, whereas the rat NaIO3 model is less well documented. This study aimed to characterize the retinal histopathological changes of rats injected with NaIO3.

Setting/Venue

The rodent NaIO3 model has emerged as an acute valuable model to study RPE degeneration in GA in a compact time-frame. Characterization of the histopathologic changes in the retina are necessary to understand and validate the NaIO3 model for further drug testing for dry AMD.

Methods

Animals were divided into two groups (n=5-11/group): PBS-injected control rats and NaIO3-injected rats. NaIO3 (40 mg/kg) was administered via the sublingual vein in 9-11-week-old male Brown Norway rats at day 0. At day 7, retinal inflammation (CD11b), gliosis (Glial fibrillary acidic protein: GFAP), RPE (RPE65) and rod bipolar cell (PKC alpha) changes were quantified using immunohistochemistry on 9µm paraffin sections. Positive area of the histological markers in the NaIO3-treated retinas was measured over the total retinal area and presented relative towards the control. RPE/choroidal flat mounts were analyzed after a phalloidin staining for RPE intactness in the peripheral, middle and central area, using a scoring system from 0 (intact cells), 1 (intact and elongated cells), 2 (elongated cells), 3 (elongated cells and atrophy) to 4 (atrophy). Comparisons between the two groups were performed using unpaired Student’s t-tests.

Results

Key markers of retinal inflammation and gliosis were significantly increased after NaIO3 by respectively 2.5-fold (%CD11b+ area in NaIO3: 100 ± 5.47 vs. control: 40.4 ± 6.87, p-value smaller than 0.01) and 3.1-fold (%GFAP+ area in NaIO3: 100 ± 8.8 vs. control: 32.5 ± 4.05, p-value smaller than 0.0001). Increased PKC alpha signal in the rod bipolar cells, indicative of a rewiring process, was also observed in the group treated with NaIO3, as compared to the control group. Analysis of the RPE staining revealed that NaIO3 induced complete RPE damage/loss (score : 3 to 4) in the central/middle areas whereas the periphery remained relatively intact (score : 0 to 2, p-value smaller than 0.0001).

Conclusions

This study demonstrated that sublingual injection of NaIO3 (40 mg/kg) in the rat induced retinal inflammation and gliosis which was consistently accompanied with RPE loss and disruption in the central/middle retinal area whereas the periphery remained relatively intact. As such, the rat NaIO3 model might be a suitable acute model for testing and developing drugs for dry AMD.

Financial Disclosure

Direct financial relationship for Oxurion
A qualitative survey to understand disease awareness, diagnostic challenges and perspective of anti-VEGF therapy in patients with neovascular age related macular degeneration in India

Purpose
Age-related macular degeneration (AMD) is a major socioeconomic challenge worldwide, affecting 10% to 13% of adults >65 years of age. Individuals with AMD mostly mistake the disease symptoms for a normal sign of ageing which leads to conditions such as neovascular AMD (nAMD). It is the leading cause of vision loss in people aged >60 years worldwide. Key symptoms of nAMD include sudden blurred/distorted vision, blind spots developing in the line of sight, difficulty distinguishing between the colors, and difficulty carrying out daily routine activities. Anti-vascular endothelial growth factor (anti-VEGF) therapy is the standard of care for nAMD. Evidently, better treatment outcomes can be achieved with an early diagnosis of nAMD. However, numerous global clinical and real-world studies on patients with nAMD highlight the fact that ocular lesions are usually detected when there is already a considerable visual loss. Therefore, awareness must be increased among individuals aged 50 years and older, to save them from the potentially sight-damaging delays occurring from the symptom onset to diagnosis. The present patient-based survey was conducted to determine the symptoms experienced, challenges encountered from symptom onset to diagnosis of nAMD, and fear/concerns associated with the intravitreal anti-VEGF therapy.

Setting/Venue
Patient-based survey conducted across 6 metro cities in India (Mumbai, Delhi, Kolkata, Chennai, Bangalore, Hyderabad) in real-world settings.

Methods
This was a cross-sectional, questionnaire-based qualitative survey conducted between December 2020 and March 2021. The inclusion criteria were adult patients (≥50 years old, either gender) diagnosed with nAMD in the previous 3 years, who either received anti-VEGF therapy in a year prior in the private clinical settings or were recommended but rejected the anti-VEGF therapy. The inclusion of patients was verified through their previous medical and prescription records. The survey interviews were conducted telephonically for the duration of 45 to 60 minutes using a validated questionnaire. The survey evaluated general patient related information, the symptoms of nAMD experienced, referral to eye specialists (ophthalmologist/retina specialist), time taken to seek the help, challenges faced during the diagnosis process of nAMD, as well as fears or doubts regarding the initiation of intravitreal anti-VEGF therapy. The interviews were audio-recorded, and the responses were transcribed, segregated, and analyzed to check for common themes and trends.

Results
Total 30 patients with nAMD were included, 18 received anti-VEGF therapy and 12 rejected the therapy. Majority patients were >60 years old (n=22). Most patients experienced watery eyes as the first symptom of nAMD, which gradually progressed to vision disturbances (unclear/blurred vision with distorted images), followed by gradual loss of central vision (few black spots developing into central vision loss). There was a delay of few days to few months from the patients before consulting either the optometrist/family physician. All patients visited an eye specialist (ophthalmologist/retina specialist), either on their own or post referral from family physician/optometrist. Diagnosis procedure at ophthalmologist included checking the history, current symptoms, routine eye check-up, eye scan using optical coherence tomography, and necessary blood tests. Few patients were further referred to the retina specialist for final diagnosis. Majority patients experienced discomfort during diagnostic work-up and found tests to be expensive, time-consuming, and difficult to manage. During the first consultation with specialist post nAMD diagnosis, patients were apprised that it is a common age-related eye disease, and the intravitreal anti-VEGF injection was the only effective treatment. All patients expressed a sense of fear about eye injections (fear of the process/administering procedure/recovery process/possible complications and side-effects).

Conclusions
The survey offered a unique insight into the patient awareness, diagnostic challenges, as well as treatment comprehensions from patient’s perspective, providing important implications for clinical practice. It concluded that there is a need to create awareness about certain distinguishing symptoms of nAMD versus general eye fatigue or other eye diseases. Awareness/alertness about the condition will ensure that the patients accept and discuss the symptoms earlier and more readily with their family, to seek timely medical help. A structured program at primary-care physician level for individuals ≥60 years of age can help identify early symptoms of nAMD. This will avoid the diagnostic delays by shortening the timeframe of symptom onset to diagnosis of nAMD (watery eyes + visual disturbance=suspect nAMD in the elderly). Lastly, the surveyed patients expressed fear of injection and concerns about the anti-VEGF therapy due to its ocular administration. Since the patients are already in an emotionally vulnerable position due to the symptoms and the condition, any patient support program and educational initiative can be of help to alleviate their fears and resolve their concerns about the therapy.
Maximum consecutive fluid free months and its association with visual and anatomical outcomes in nAMD: A post-hoc analysis of the 96-week data from HAWK and HARRIER

Purpose
Retinal fluid is an important biomarker of disease activity in neovascular age-related macular degeneration (nAMD). Resolving retinal fluid and maintaining a dry retina is a common clinical goal of anti-vascular endothelial growth factor (VEGF) therapy. Here we assess the impact of absolute retinal fluid-free duration and its association with visual and anatomic outcomes of nAMD patients in HAWK and HARRIER.

Setting/Venue
HAWK and HARRIER were two 96-week, Phase 3, prospective, randomized, double-masked, multicenter studies comparing efficacy and safety of brolucizumab 3 mg (HAWK only) and 6 mg with aflibercept 2 mg in eyes with nAMD.

Methods
In HAWK, patients were randomized 1:1:1 to brolucizumab 3 mg (n=358), brolucizumab 6 mg (n=360) or aflibercept 2 mg (n=360). In HARRIER, patients were randomized 1:1 to brolucizumab 6 mg (n=370) or aflibercept 2 mg (n=369). After three loading doses, brolucizumab patients received 12-weekly (q12w) dosing with an option to adjust to 8-weekly dosing (q8w) if disease activity (as identified by a masked investigator) was present; aflibercept was dosed q8w as per the label. 96-week data from the brolucizumab 6 mg and aflibercept 2 mg groups of the Phase III HAWK and HARRIER studies were pooled for the current treatment agnostic analysis. Patients were categorized based on the maximum consecutive number of months they remained fluid free after the anti-VEGF loading phase (from Week 12 to 96), with a fluid-free month (FFM) defined as the absence of sub-retinal fluid and intraretinal fluid. The categories were as follows: category 1: 0 FFMs (‘never dry’); category 2: 1-3 FFMs; category 3: 4-9 FFMs; category 4: 10-21 FFMs (‘dry for a long period of time’); category 5: 22 FFMs (‘always dry’), with category 1 used as a reference for statistical comparison purposes.

Results
At Week 96, patients in categories 4 and 5 had a least square mean (95% CI) best corrected visual acuity (BCVA) gain of 7.8 (4.5, 11.2) letters and 8.0 (4.3, 11.7) letters, respectively, compared with patients in category 1 (‘never dry’ [who gained 0.2 (-2.88, 3.30) letters from baseline]). At Week 96, the least square mean (95% CI) central subfield thickness (CSFT) of patients in categories 4 and 5 was -121.8 µm (-143.7, -99.8) and -127.8 µm (-152.2, -103.4) lower, respectively, compared with patients in category 1 (‘never dry’ [whose CSFT decreased by -86.2 µm (-106.0, -66.0] from baseline]).

Conclusions
In comparison with patients who were ‘never dry’ after anti-VEGF loading, nAMD patients in HAWK and HARRIER who were ‘always dry’ or ‘dry for a long period of time’ had better visual and anatomic outcomes at study end, and greater reduction of CSFT throughout. These findings suggest that longer absolute fluid-free periods have a positive impact on visual and anatomic outcomes in nAMD patients.

Financial Disclosure
Novartis, Alcon, Bayer, Allergan, Roche, Zeiss
High reflectivity and low reflectivity properties on OCTA influence the detection of macular neovascularization in AMD

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Purpose
Optical coherence tomography (OCT) angiography (OCTA) has changed the approach to AMD patient and its staging thanks to the capacity to detect MNV without intravenous dye. The vessels morphology visible with OCTA is not a fully structural reconstruction of the neovascularization and usually appears smaller than the ones seen by fluorescein angiography (FA) and indocyanine green angiography (ICGA). In this study, we aimed to discriminate high reflectivity and low reflectivity macular neovascularization (MNV) lesions secondary to age-related macular degeneration (AMD) and to assess the influence of blood flow features on the amount of MNV detected by optical coherence tomography angiography (OCTA).

Setting/Venue
The study is designed as a cross-sectional, observational case series. It was totally placed in at the Department of Ophthalmology of IRCCS San Raffaele Hospital, Milan, Italy. Each patient signed an informed consent approved by the ethical committee of IRCCS Scientific Institute San Raffaele Hospital.

Methods
Pseudophakic patients affected by type-1 or type-2 naïve MNV were recruited from January 2018 to January 2019. Polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP), whose pattern are hardly detectable by OCTA, such as media opacities, ophthalmologic surgery within the last six months and any ophthalmologic or systemic condition potentially affecting the analyses were considered as exclusion criteria. The analysis starts from the most superficial portion of the MNV lesion obtained from one segmentation, modifying the boundaries in order to underline the deepest portion of the MNV. Using the mean reflectivity value as a threshold for each MNV we divided them into low and high flow vessels respectively for the ones with poor and the elevated reflectivity. Then we compared OCTA highlights (degree, size and quantitative reflectivity) to dye angiography features.

Results
Fifty eyes from 50 patients were included into the study. We classify MNV as follows: 35 (70%) type 1 and 15 (30%) type 2. The mean OCTA reflectivity values were 100±15 for type 1 MNV and 120±10 for type 2 MNV (p<0.01). Taking these values as thresholds, we found that 85±5% of the type 2 MNV was distinguished by highly detected flow, whereas the proportion was just 56±12% in type 1 MNV (p=0.01) (Fig. 4). In both cases, the poorly detected flow signal was distributed mainly in the peripheral MNV region. We found a good agreement between early ICGA size and OCTA size for type 1 MNV (2.10±1.91mm² vs 2.09±1.87mm²; p>0.05), whereas MNV lesions turned out to be remarkably bigger on late ICGA phase (3.41±2.87mm²; p<0.01). Interestingly, OCTA well-matched with FA in terms of MNV size for type 2 lesions (2.36±2.15mm² vs 2.37±2.25mm²). MNV reflectivity was higher in type 2 MNV and it was strongly associated with the OCTA ability to reconstruct the neovascular network.

Conclusions
MNV size appears larger on FA/ICGA than on OCTA, corroborating the findings of previous investigations. In particular, the type 1 MNV plaque can be visualized in its entirety in the late stages of the ICGA examination, proving to be significantly larger than the corresponding OCTA reconstruction. On the other hand, type 2 MNV showed unvaried size in both early and late stages of FA/ICGA examination and offered an excellent match with the corresponding OCTA reconstruction. In our cohort of patients, type 2 MNV lesions turned out to be significantly more detected on OCTA than type 1 MNV, as assessed by the mean reflectivity intensity calculated from OCTA reconstructions. Furthermore we found the highly detected flow signal to be more evenly distributed in type 2 MNV than in type 1 MNV. The type 1 MNV filling signal, which is slower and less intense in perfusion in periphery, smaller new vessels proved to be poorly detected by OCTA or not detected at all, probably because of the limits of current OCTA devices which cannot detect a blood flow signal under a speed cut-off.

Financial Disclosure
none
**Title**
Drusen ooze: Predictor for progression of dry age-related macular degeneration

**Purpose**
To evaluate natural history of drusen ooze and its role as a predictor for progression of dry age-related macular degeneration (AMD) longitudinally.

**Setting/Venue**
Multi-centric retrospective observational case series of 72 eyes (72 patients) with dry AMD with a minimum follow-up of 4 years.

**Methods**
Multi-centric retrospective observational case series of 72 eyes (72 patients) with dry AMD with a minimum follow-up of 4 years. Drusen types were identified on volume scans on optical coherence tomography (OCT) and were characterized for occurrence of drusen ooze at baseline till last visit. Drusen ooze was defined as hyperreflective dots overlying a collapsing drusen or pseudodrusen, or hyperreflective RPE above drusen or isoreflective dots at the level of outer nuclear layer. The consequent incidence of incomplete retinal pigment epithelium and outer retinal atrophy (iRORA), complete retinal pigment epithelium and outer retinal atrophy (cRORA) and neovascular AMD (nAMD) were evaluated statistically.

**Results**
Total 72 eyes with a mean follow-up of 68.89 (± 25.57 months) were studied. At presentation, 11 eyes (15.3%) had a single drusen type, whereas 61 eyes (84.7%) had mixed drusen. Reticular pseudodrusen were most common (84.7%) followed by soft drusen (66.6%). Drusen ooze was seen in 47 eyes (65.2%) at presentation. Presence of drusen ooze at baseline (p <0.01) and baseline best corrected visual acuity (BCVA) (p =0.04) significantly correlated with iRORA and cRORA. Total 14 eyes progressed from iRORA to cRORA over a mean follow up of 29.14 (±24.33) months. Odds of progression to iRORA or cRORA were 20.3 times greater for eyes with drusen ooze at baseline (95% C.I., 4.4-94.2).

**Conclusions**
In dry AMD, drusen ooze is a useful sign for predicting progression to iRORA and cRORA over time.

**Financial Disclosure**
No relevant financial disclosures.
Investigating barriers to long-term anti-vascular endothelial growth-factor (anti-VEGF) treatment adherence in neovascular age-related macular degeneration: A multicenter study

Purpose
Real-world evidence demonstrates that adherence to the recommended treatment regimens of anti vascular endothelial growth factor agents (anti-VEGFs) in retinal diseases such as neovascular age-related macular degeneration (nAMD) is suboptimal, particularly beyond 12 months’ treatment. Suboptimal adherence can result in poor treatment outcomes. A prior systematic review (Okada et al, Ophthalmology 2021;128:234–247) demonstrated that behavioral, environmental, and logistical barriers may impact patient adherence to treatment regimens. This study sought to further evaluate behavioral and environmental influences that may impact adherence (according to definitions previously specified [Okada et al, 11th COPHy EU Congress, 2020]) to recommended anti-VEGF regimens, specifically in patients with nAMD. The outputs from this study will be used to generate hypotheses for interventions to support improved adherence for patients with nAMD.

Setting/Venue
The study was conducted in three centers (in France, Germany, and the UK) to provide insights from a range of different healthcare settings. A qualitative study design was employed to understand the holistic reasons for patient-driven non-adherence to treatment. The first patient interview was conducted in October 2020.

Methods
Patients (up to 10 per country) were identified and recruited via participating clinicians. The goal was to recruit patients representing diverse treatment durations and personal circumstances. Clinicians completed a brief online survey for each patient regarding disease characteristics and co-morbidities, and the clinician’s perception of the patient’s anti VEGF treatment knowledge and ability to manage their disease. Individual in-depth semi-structured interviews with patients were conducted by phone. The patient interview included questions on the patient’s nAMD history, knowledge, attitude towards nAMD, and the relationship with the clinician. Transcripts of patient interviews were used to develop a coding system, specifying key themes and sub-themes, which was refined throughout the analysis phase. Patients also completed the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) and a health status scale (0-100).

Results
Fifteen patients were included in the interim analysis (mean age 77 years; France: n=5, Germany: n=4, UK: n=6; seven ‘fully adherent’, four ‘adherent’, and four ‘non-adherent’). A challenge in recruiting non-adherent patients was noted and recruitment targets were relaxed due to a disruption of usual services caused by the coronavirus pandemic. Site-related factors that supported adherence included transparent communication between the patient and specialist/practice team, sufficient time to fully inform the patient, consistency in the treating physicians and practice team over the course of the treatment, and additional healthcare professional support (such as a psychologist within the ophthalmologist department). Regular scheduled appointments such as consistent injection days, having the next two appointments planned, and sharing information about the next appointment with the patient’s accompanying person or as a calendar entry were also found to support adherence. Patient-related factors that supported adherence included history of nAMD in the family, an awareness of the disease and importance of treatment, a younger age (approximately 70 years), limited/no requirement for caregiver support, recent diagnosis and treatment initiation, and a good early response to treatment. Easy transport to and from appointments and accessible/adequate site parking were also identified as supporting adherence.

Conclusions
Published evidence has shown that the effective treatment of nAMD is hindered by poor adherence and persistence to recommended anti-VEGF treatment regimens. In this study, we determined that provision of information explaining that nAMD is a chronic disease requiring long-term treatment is key to supporting adherence. We found that treatment itself is not a driver of non-adherence (besides fear of getting a first injection). Access to transportation was a common issue for both adherent and non-adherent patients. Challenges in study recruitment, aside from those associated with the COVID-19 pandemic, suggests that non-adherent patients may have been reticent to participate due to perceived criticism of their behavior, or a desire not to complain about the service or perceived lack of treatment benefit.

Understanding the drivers of low adherence to anti-VEGF treatment is the first step towards developing relevant and meaningful interventions to support improved adherence and outcomes for patients with nAMD.
**Title**

HAWK and HARRIER 48-week data: potential for treatment interval extension in patients with nAMD disease activity at week 16

**Purpose**

The Phase 3 HAWK (NCT02307682) and HARRIER (NCT02434328) studies evaluated the efficacy and safety of brolucizumab versus aflibercept in previously untreated patients with neovascular age-related macular degeneration. All patients received three monthly loading injections for both drugs, then brolucizumab was injected q12w unless disease activity (DA) was identified resulting in permanent adjustment to q8w, while aflibercept was dosed q8w throughout the study, as per label at study initiation. Due to the study design, brolucizumab patients adjusted to a q8w regimen at the end of the matched loading phase at Week 16 owing to DA could not subsequently extend to a q12w interval. The aim of this post-hoc analysis is to assess subsequent DA in patients with DA at Week 16 to determine the potential for interval extensions during the first year of treatment if the protocol had allowed it.

**Setting/Venue**

HAWK and HARRIER were 2-year, randomized, double-masked, multicenter active-controlled trials conducted at 408 sites in North, Central, and South America; Europe; Asia; Australia; and Japan.

**Methods**

In Year 1 of HAWK and HARRIER, disease activity assessments (DAA) were conducted at Weeks 16, 20, 32, and 44 in both studies for all brolucizumab and aflibercept patients regardless of whether DA was detected at earlier visits or not; presence of DA was determined at the discretion of the masked investigator. This post-hoc analysis evaluated subsequent DA, and thus potential for interval extension, in the matched cohort of brolucizumab and aflibercept patients with DA at Week 16 using pooled data from brolucizumab 6 mg and aflibercept arms of both studies.

**Results**

At the first DAA at Week 16, fewer brolucizumab vs aflibercept patients had investigator-identified DA (22.8% [n=161/730] vs 32.2% [n=226/729]). In the subgroup of patients with DA at Week 16, fewer brolucizumab-treated patients had DA at subsequent visits in Year 1 compared with aflibercept-treated patients: 31.8% vs 39.2% (OR 0.72; 95%CI: 0.47, 1.12); 27.3 vs 43.5 (OR 0.49; 95%CI: 0.31, 0.76) and 17.4 vs 31.2 (OR 0.47; 95%CI: 0.28, 0.78) during DAA at Weeks 20, 32, and 44, respectively.

**Conclusions**

In HAWK and HARRIER, fewer brolucizumab than aflibercept-treated patients had DA at the first DAA at Week 16. Of patients with DA at Week 16, fewer brolucizumab vs aflibercept-treated patients had DA at subsequent visits in Year 1. These findings indicate a higher potential for treatment interval extension with brolucizumab within the first year of treatment.

**Financial Disclosure**

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### Title
Cross sectional survey to assess the treatment goals and therapy-related attributes influencing selection of anti-VEGF therapy for management of neovascular age-related macular degeneration among Indian general ophthalmologists and retina specialists

### Purpose
Neovascular age-related macular degeneration (nAMD) is a rapidly progressing and potentially blinding degenerative eye disease in population ≥60 years of age, affecting over 17 million people worldwide. Although anti-vascular endothelial growth factor (anti-VEGF) therapy is the standard of care, there are still significant gaps and challenges faced by the healthcare professionals (HCPs) while managing patients with nAMD, including but not limited to diagnosis, treatment, choice of regimen, financial considerations, and lack of treatment compliance. Evidently, aging is the most important risk factor for nAMD. Thus, in developing countries like India, increasing geriatric population is yet another concern for HCPs. In addition, treatment affordability and overall financial burden imposed on the patients with anti-VEGF treatment (due to out-of-pocket expenses, insufficient insurance coverage), as well as scarcity of healthcare infrastructure (tertiary-care centres located primarily in metro and tier-1 cities) further contribute to the treatment challenges faced by Indian HCPs. Thus, exploring the aforesaid factors can help HCPs to build effective strategies for nAMD management. The present survey sheds a light on the nAMD patient load in India, along with treatment goals and therapy-related drivers considered important while initiating any anti-VEGF therapy as well as extensive clinical evidence, and frequency of dosing as equally important attributes for selection.

### Methods
This nationwide cross-sectional, quantitative survey was conducted between August 2020 and October 2020. The HCPs (N=222) included were retina specialists (RET: n=122 with ≥70% retina practice) and general ophthalmologists (OPH: n=100 with ≥40% retina practice), who manage patients with nAMD and administer intravitreal anti-VEGF injections (RET: ≥20 injections/month, GEN-OPH: ≥10 injections/month). The survey was conducted using a mix of computer-assisted personal interviews (75%) and computer assisted web-based or telephonic interviews (25%) for 30-35 minutes using a validated questionnaire. The survey evaluated patient load of nAMD patients with anti-VEGF therapy per month. Key treatment goals most HCPs considered during therapy initiation were improvement in vision (67%), reduction/drying of fluid (51%), and anatomical improvement (37%). To measure achievement of treatment goals, gain in visual acuity was rated ‘extremely important’ by 75% HCPs (OPH: 73%, RET: 77%). Retinal fluid drying was second-most chosen ‘extremely important’ marker by OPH (63%); RET (65%) chose better penetration to retina and choroid. Within fluid types, reduction in sub-retinal fluid was key priority and most critical attribute (ranked number 1 by 55% HCPs). While choosing anti-VEGF therapy, ~25% HCPs considered gain in visual acuity, reduction in fluid, and reduction in central retinal thickness (CRT) as key attributes of therapy. Gain in visual acuity was relatively higher among RET (28%) vs OPH (19%), reduction in CRT was relatively higher among OPH (29%) vs RET (19%). Cost of therapy/affordability was another most critical attribute while choosing anti-VEGF therapy as per OPH (ranked number 1 by 42%); RET gave equal emphasis (~25%) to cost/longer duration of action/extensive clinical evidence/dosing frequency.

### Financial Disclosure
Maulik Bhavsar and Nitin Maksane are employees of Novartis India Limited

### Results
Patients with nAMD accounted for 13% of total patient-pool per HCP per month (OPH: 12%, RET: 14%). Each HCP on average initiated 15 new nAMD patients with anti-VEGF therapy per month. Key treatment goals most HCPs considered during therapy initiation were improvement in vision (67%), reduction/drying of fluid (51%), and anatomical improvement (37%). To measure achievement of treatment goals, gain in visual acuity was rated ‘extremely important’ by 75% HCPs (OPH: 73%, RET: 77%). Retinal fluid drying was second-most chosen ‘extremely important’ marker by OPH (63%); RET (65%) chose better penetration to retina and choroid. Within fluid types, reduction in sub-retinal fluid was key priority and most critical attribute (ranked number 1 by 55% HCPs). While choosing anti-VEGF therapy, ~25% HCPs considered gain in visual acuity, reduction in fluid, and reduction in central retinal thickness (CRT) as key attributes of therapy. Gain in visual acuity was relatively higher among RET (28%) vs OPH (19%), reduction in CRT was relatively higher among OPH (29%) vs RET (19%). Cost of therapy/affordability was another most critical attribute while choosing anti-VEGF therapy as per OPH (ranked number 1 by 42%); RET gave equal emphasis (~25%) to cost/longer duration of action/extensive clinical evidence/dosing frequency.

### Conclusions
The survey offered constructive insights from the HCPs perspective while managing and initiating the anti-VEGF therapy in Indian patients with nAMD. The factors and attributes considered by the OPH and RET were on similar lines for determining the treatment goals, assessing the key markers/indicators to measure treatment progress, as well as factors accounted while selecting a particular anti-VEGF therapy. Of note, there was a difference in opinion among the HCPs for the non-therapy related attributes of anti-VEGF therapy: OPH considered cost of therapy/affordability as an important attribute for selection of anti-VEGF therapy, while RET considered the cost, longer duration of action, extensive clinical evidence, and frequency of dosing as equally important attributes for selection.
Baseline Sattler layer-choriocapillaris complex thickness cutoffs associated with age-related macular degeneration progression

**Purpose**
So far, little is known about the factors that influence the natural history of Age-Related Macular Degeneration (AMD). This study aims to assess the relationship between choroidal overall and sublayer thickness and AMD stage progression.

**Setting/Venue**
The study was designed as a prospective, observational case series. Patients affected by AMD at different stages were recruited at the Department of Ophthalmology of IRCCS San Raffaele Hospital, Milan, Italy. Written informed consent was obtained from all the study subjects. The study was approved by the ethical committee of IRCCS Scientific Institute San Raffaele Hospital, which verified its conduction in accordance with Helsinki declaration.

**Methods**
A prospective, observational case series was performed. 262 eyes of 262 patients with different stages of AMD were imaged by Optical Coherence Tomography (OCT). AMD stage, choroidal thickness (CT), Sattler layer-choriocapillaris complex thickness (SLCCT) and Haller layer thickness (HLT) were determined at the baseline visit, at a 1-year follow-up visit, at a 2-year follow up visit and at a final 3-year follow-up visit.

**Results**
Baseline AMD stages were distributed as follows: early AMD (30 eyes; 12%), intermediate AMD (97 eyes; 39%) and late AMD (126 eyes; 49%). At the final follow-up, AMD stages were so distributed: early AMD (15 eyes; 6%), intermediate AMD (83 eyes; 33%) and late AMD (156 eyes; 61%). Each group showed a statistically significant decrease in CT values over the entire follow-up ($p < 0.01$) and SLCCT reduction was associated with AMD progression ($p < 0.01$). Moreover, SLCCT quantitative cutoffs $< 20.50 \, \mu m$ and $< 10.5 \, \mu m$ were associated with a moderate and high probability of AMD progression, respectively, and SLCCT quantitative cutoffs $< 18.50 \, \mu m$ and $< 8.50 \, \mu m$ implied a moderate and high probability of MNV onset, respectively.

**Conclusions**
Progressive choroidal impairment contributes to AMD progression. Among choroidal layers, a reduced SLCCT is a promising biomarker of disease worsening and its quantitative evaluation could help to identify patients at higher risk of stage advancement.

**Financial Disclosure**
None.
Patients wearing face masks during intravitreal injections and endophthalmitis: A real world experience

**Purpose**
To analyse the impact of wearing face masks during intravitreal injections in endophthalmitis rate.

**Setting/Venue**
Retina Departament of La Princesa University Hospital in Madrid, Spain

**Methods**
A retrospective, comparative analysis of the rate of endophthalmitis in patients undergoing intravitreal injections before (January 1, 2016 - October 31, 2018) and after (November 1, 2018 - April 31, 2021) initiation of wearing patient face masks. The electronic health record data for all study eyes were analyzed.

**Results**
In the present study, the incidence rate of endophthalmitis during patient face mask protocol was 0.014% (3/20786) whereas during previous no patient mask protocol was 0.037% (6/21755) (P=0.3513)

**Conclusions**
Notwithstanding the limitations of real-life studies and the very low incidence of this complication, we have obtained a reduction of endophthalmitis rate in our more than two-year practical experience using face masks in patients undergoing intravitreal injections in comparison with previous protocol and published data.

**Financial Disclosure**
No financial disclosures
Title
Characteristics features of age-related macular degeneration (AMD) in UK Biobank (UKBB) based on human grading results

Purpose
UK Biobank is a biomedical database comprising lifestyle, biomedical and genetic data from over 500,000 UK participants aged 40-69. Close to 70,000 participants had ophthalmic imaging of colour fundus photography and optical coherence tomography (OCT) at baseline. The purpose of this current abstract is to provide human grading results in order to describe the most common characteristic features of AMD on both colour and OCT imaging in UKBB. Imaging took place undilated during the participant’s baseline visit at the UKBB site. Altogether, 68527 participants’ image sets were available for grading by the NetwORC UK’s trained and accredited graders.

Setting/Venue
A single colour photograph of the optic disc and the macula were acquired using Topcon 3D OCT-1000 Mark II system, with a field angle of 45°, a digital zoom (2X, 4X), scanning range 6×6 mm, 4.5×4.5 mm, 3×3 mm and scanning speed of 18,000 A-scans per second. The horizontal and longitudinal (depth) resolutions were ≤20 µm and 5–6 µm, respectively. The same equipment obtained the spectral domain 3-dimensional OCT using a 3D macular volume scan (512 horizontal A-scans/B-scan; 128 B-scans in a 6×6 mm raster pattern).

Methods
Colour and OCT images were analysed by trained and certified NetwORC UK reading centre graders answering pre-determined questions to capture relevant AMD features visible on the images. These data were captured in a study specific grading form linked to the study database. Image sets of each participant were graded independently by one grader; the grader scrutinized both image modalities for features characteristic of AMD. If the images required second review, the grader requested adjudication of the encounter by a senior grader or clinician. Quality assurance (QA) was carried out by provision of rigorous training and certification of all graders, senior graders and clinicians before grading began; by double grading a subset of images; providing regular clinician review sessions and training exercises. In addition, quality assurance grading was undertaken on 1:20 randomly selected images that were re-introduced into the grading queue without any prior warning so exact agreement, intra- and intergrader reliability could be calculated. The UK Macula Society grant enabled this project.

Results
Approximately 99% of colour images and 99% of OCTs were available for the right eye and left eye. Of these available images, 90% of colour and 99% of OCT images were of gradable quality. Grading revealed approximately 10% of right eyes and 9% of left eyes had drusen only phenotype; an additional 0.5% of right eyes and 0.4% left eyes had drusen with pigmentary changes. Within these two categories, approx. 0.1% of right eyes and 0.13% of left eyes had reticular drusen identified on colour imaging. End-stage disease (geographic atrophy and late AMD - active or inactive) was seen in approximately 0.06% of right eyes and 0.07% of left eyes. In addition, 5% of right eyes and 6% of left eyes, with no apparent AMD features on colour imaging, were found to have at least one druse and/or sub-retinal drusenoid deposits on OCT imaging. The prevalence of features characteristic of AMD was less than 0.05% in both eyes.

Conclusions
The cohorts identified with characteristic changes for age related macular disease will form the basis of further analysis for its genetic and lifestyle determinants. The importance of the grading results presented here is that over 69000 participants’ image sets have been graded in details for characteristics of age related macular degeneration. As the UKBB reaches more subjects for follow-up and linkage, this set of grading will become an important dataset for research purposes, and might provide ground-truth for further analysis. The dataset provides an unparalleled opportunity to examine eye disease in this cohort and will provide the much needed baseline data for the follow-up studies that are to be conducted by UKBB.

Financial Disclosure
None relevant to current abstract. We thank the Macula Society for the grant that enabled this grading activity.
## Purpose
To investigate choroidal vascularity index in eyes with adult-onset foveomacular vitelliform dystrophy (AOFVD), early age-related macular degeneration and age-matched controls

## Methods
Eyes with AOFVD of any stage and early AMD according to the Beckman classification were consecutively enrolled. Age-matched healthy controls served as the control group. Eyes with concomitant ophthalmic disorders, diabetes, prior intraocular surgery, and the presence of subretinal drusenoid deposits (SDD) alone were considered as exclusion criteria. Spectral-domain optical coherence tomography with RTVue XR (RTVue XR Avanti, Optovue, Inc., Fremont, CA; software version 2017.1.0.151) was performed in all cases using a grid pattern. Choroidal thickness (CT) was measured manually using a digital caliper at the fovea, 500 and 1500 µm nasally and temporally to the fovea. The subfoveal horizontal b-scan was imported into Fiji software (version 2.1.0/1.53c, available at http://fiji.sc) and the central 3 mm was selected and cropped for choroidal vascularity index (CVI) calculation. A polygonal selection was drawn delineating the choroid from the outer retinal pigment epithelium border and the choriocapillaris junction. After binarization using the Niblack method, the image was converted to RGB color, and the luminal area was calculated using the threshold tool.

## Results
Of 54 patients initially screened, 16 patients (29.6%) were excluded from the analysis for the presence of SSD, macular complications, or not acceptable image quality. A total of 38 eyes of 38 patients, 19 eyes with AOFVD and 19 eyes with conventional drusen (CD), and 16 healthy subjects (16 eyes) were included in the study. The subgroups appeared homogenous for gender (p=0.06) and age (p=0.80). CVI was significantly different among subgroups (ANOVA, p=0.006). On post-hoc Bonferroni analysis, eyes with AOFVD presented a higher CVI (+0.03 ± 0.01, p=0.005) than eyes with CD. No differences in CVI were detected in CD (p=0.81) and AOFVD (p=0.13) when compared with controls. On further analysis, AOFVD eyes accounted for the greatest luminal area, particularly significant in comparison with healthy controls (+0.27 ± 0.11, p=0.04). CT at various locations did not significantly differ among subgroups.

## Conclusions
AOFVD eyes present a greater CVI than eyes with CD. The major choroidal involvement is on the luminal component, further corroborating a possible role of the choroidal vasculature in the pathological manifestations of AOFVD disease. It may be hypothesized that choroidal vessels enlarge in the efforts to clear the vitelliform material leading to a secondary choriocapillaris impairment with the development of late-stage complications and the atrophic stage. Further studies with a larger sample would be desirable to understand the cascade of events characterizing the different pathological stages preceding the development of macular complications.

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### Setting/Venue
Academic medical center - Retina Centre, Ophthalmology Unit, NESMOS Department, University of Rome Sapienza, St. Andrea Hospital, Rome
Rate of misdiagnosis and clinical usefulness of the correct diagnosis in exudative neovascular maculopathy secondary to AMD versus pachychoroid disease

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Purpose
The aim of this study was to explore the relative prevalence and clinical differences between age-related macular degeneration (AMD) and pachychoroid disease in patients older than 50 years with newly diagnosed exudative neovascular maculopathy, and also assess the rate of misdiagnosis between these two disorders.

Setting/Venue
Retrospective study at San Raffaele Scientific Institute, Milan, Italy

Methods
In this retrospective observational study, we reviewed data from patients 50 years of age and older with newly diagnosed treatment-naive exudative macular neovascularization (MNV) secondary to AMD or pachychoroid disease.

Results
Of the 139 patients (139 eyes) who fulfilled the inclusion criteria, 35 patients were graded as being affected by pachychoroid disease complicated by exudative MNV and 104 subjects had neovascular AMD. Therefore, prevalence of pachychoroid disease complicated by exudative MNV was 25.2% (confidence interval-CI 18.2-33.2%). Mean ± SD age was 67.0 ± 8.8 years in the pachychoroid disease group and 80.6 ± 6.6 years in the neovascular AMD group (P < 0.0001). At baseline, BCVA was better in patients with pachychoroid disease complicated by exudative MNV (0.4 ± 0.3 LogMAR vs. 0.7 ± 0.5 LogMAR, P = 0.003). At the 1-year follow-up visit, BCVA was still better in patients with pachychoroid-associated MNV (0.34 ± 0.32 LogMAR vs. 0.59 ± 0.52 LogMAR, P = 0.005). In our study cohort, 19 patients were graded to be affected by pachychoroid disease complicated by exudative MNV even though a diagnosis of neovascular AMD was erroneously reported in their medical records at baseline.

Conclusions
In conclusion, pachychoroid disease is a frequent cause of exudative MNV in aged patients with a high rate of misdiagnosis. A correct diagnosis may be important as these two disorders differ in terms of clinical characteristics and prognosis.

Financial Disclosure
None
The importance of monitoring wet age-related macular degeneration patients during coronavirus disease 2019 pandemic: A retrospective study of assessment of functional and structural outcomes

**Purpose**

Intravitreal anti-Vascular Endothelial Growth Factor (VEGF) injections are the gold standard treatment for neovascular Age-related Macular Degeneration (nAMD, also known as wet AMD). Coronavirus disease 2019 (COVID-19) and the resulting confinement, led to a change in the clinical practice as many patients did not attend their programmed injection visits. Our purpose is to compare the functional and structural visual outcomes of patients that did not respect their intervals (group 1) and those who did (group 2).

**Setting/Venue**

Swiss Visio Montchoisi (Lausanne, Switzerland) and RétinElysée Ophthalmology Center (Lausanne, Switzerland).

**Methods**

Patients diagnosed with nAMD of any type (I, II, or III), that had intravitreal anti-VEGF injections, both before and after the period of confinement due to the COVID-19 pandemic, regardless if the programmed injection interval was respected or not, were included in the study, after signing an informed consent form. Best-corrected visual acuity (BCVA) changes between the first post- and last pre-confinement visit were assessed for each patient. An unfavorable functional or BCVA outcome was established if the post-confinement visit showed a ≥ 5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters BCVA loss compared to pre-confinement. Structural or optical coherence tomography (OCT) outcomes were assessed by OCT changes between the first post- and last pre-confinement visits. Reduction or stability of the intraretinal fluid (IRF), subretinal fluid (SRF), and pigment epithelium detachment (PED) post-confinement established a favorable structural outcome while an increase of the aforementioned values established an unfavorable structural outcome. The statistical significance level was set to 0.05.

**Results**

Patients that lost at least one scheduled injection (group 1, n=89, 109 eyes, favorable/unfavorable BCVA, and OCT outcomes: 64/45 and 53/56, respectively) of intravitreal anti-VEGF during confinement, had a 13.41% greater rate of unfavorable BCVA change and 38.27% greater rate of unfavorable OCT change than patients who respected their assigned interval (group 2, n=96, 122 eyes, favorable/unfavorable BCVA, and OCT outcomes: 88/34 and 106/16 respectively) (P = 0.04, P <0.0001, respectively). The rates of PED and IRF increase in the first post-confinement visit were significantly higher in group 1 than in group 2 (P = 0.0004 and 0.0374, respectively) with a relative increase of unfavorable OCT outcome of 200% and 66.67%, respectively. Multivariate analysis showed that a) intervals followed by patients (which differed from their assigned interval in some cases) and their b) BCVA pre-confinement were predictive factors for unfavorable BCVA changes. The more the patients deviated from their programmed injections, the higher the rate of unfavorable BCVA change (P = 0.03). The higher the BCVA pre-confinement, the higher the rate of unfavorable BCVA change (P = 0.02). Multivariate analysis failed to identify predictive factors for unfavorable OCT changes.

**Conclusions**

COVID-19 pandemic was a unique circumstance to analyze the importance of designated individualized injection intervals in wet AMD patients. It also allowed us to confirm the crucial role of maintaining continuity in the treatment with intravitreal anti-VEGF injections, in order to ensure the best functional and structural outcome for each patient. During a next confinement due to COVID-19, or circumstances similar to it, ophthalmologists need to ensure the continuity of injections for their patients.

**Financial Disclosure**

None
Evaluation of the effects of intravitreal Aflibercept and Ranibizumab on systemic inflammatory and cardiovascular biomarkers in patients with neovascular age-related macular degeneration

**Purpose**
To investigate the effects of intravitreal ranibizumab (IVR) and intravitreal aflibercept (IVA) on systemic inflammatory and cardiovascular biomarkers in treatment-naive patients with neovascular age-related macular degeneration (nAMD)

**Methods**
This study included 24 eyes of 24 patients treated with 0.5 mg ranibizumab (IVR group) and 25 eyes of 25 patients treated with 2.0 mg aflibercept (IVA group). Complete blood count, C-reactive protein (CRP), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), uric acid (UA), albumin, fibrinogen levels were measured in blood samples before and after the three-monthly loading dose treatment. Neutrophil/lymphocyte ratio (NLR), monocyte/HDL-c ratio (MHR), CRP/albumin ratio (CAR), monocyte/lymphocyte ratio (MLR), platelet/lymphocyte ratio (PLR) were also calculated.

**Results**
A statistically significant decline was determined in post-treatment CRP (P=0.002), LDL-c (P=0.001) levels, white blood cell (WBC, P=0.001), neutrophil (P=0.001), monocyte (P=0.019) counts and NLR (P=0.020), MHR (P=0.042), CAR (P=0.010) ratios comparing with pre-treatment values in the IVA group. No statistically significant change was found in any of the parameters evaluated in the study in the IVR group. Also, there was no significant change in fibrinogen, lymphocyte count, MLR, HDL-c, UA, PLR, and platelet count values in both groups.

**Conclusions**
Compared to IVR, IVA treatment had a small but significant effect on systemic inflammatory and cardiovascular biomarkers.

**Financial Disclosure**
No funding was received for this research. Authors have no financial or proprietary interest in any product mentioned in the article. No author has any possible conflict of interest. The authors alone are responsible for the content and preparation of the paper.
The structure-function relationship of eyes with age-related macular degeneration as measured with OCT and microperimetry

Purpose
Both structural and functional changes that occur in age-related macular degeneration (AMD) are important to understand disease progression and response to therapy. However, structural changes may not always correlate to functional changes. While visual acuity (VA) is used as a gold standard outcome measure to define visual function, previous studies have shown that microperimetry may be more sensitive in detecting functional changes in the macula and also provide the added benefit of a direct structure-function correlation of various pathological optical coherence tomography (OCT) features associated with AMD. Hence, our study aims to assess the overall visual function losses in eyes with AMD compared to normal controls using microperimetry (MP); and to then correlate this with the pathological OCT structural changes associated with AMD.

Setting/Venue
This was a prospective, observational study that involved 65 eyes of 40 patients with intermediate to advanced AMD and visual acuity worse than 6/15, compared to the right eye of 19 eyes of 19 normal controls without disease recruited from a single tertiary center.

Methods
Enface and cross-sectional OCT (Heidelberg HRA-2) imaging and MP (Nidek MP-3) were performed for all eyes. Cross-sectional OCT images were graded for pathological lesions by 2 independent graders with adjudication from a senior grader. Boundaries of pathological lesions identified on cross-sectional OCT were marked out on the corresponding en-face infra-red fundus (IRF) images. MP was performed by first taking a reference color fundus photo (CFP) with retinal sensitivity (RS) taken at multiple pre-determined protocolized points with fixation area and stability analysis. Using rotating multi-scale template matching, retinal vasculature masks of IRF images are superimposed onto MP-CFP with RS points and the resulting overlay is used to correlate OCT pathological structural changes to zonal functional changes detected on MP such as mean retinal sensitivity (MRS), fixation area and stability (Figure 1). Further analysis was done to identify OCT areas with overlapping pathological structures and areas with only one pathological structure.

Results
The mean age and gender of AMD patients compared to controls was 71.8 versus 66.7 years (p<0.05); and 52.5% versus 52.6% male (p=1.00). The overall average MRS of eyes with AMD was significantly worse than normal controls (16.00dB;SD=7.94 versus 25.02dB;SD=2.24 (p < 0.001)). Majority of eyes with AMD (67.5%) had unstable fixation, compared to a third of normal eyes (36.8%) (p=0.0185). Pathological structural changes associated with AMD identified on OCT in a subset of 65 eyes in 40 patients were correlated to MP. The mean total lesion area in these eyes was 16.51mm2, compared to that without any lesions, was 120.39mm2. The average MRS of total lesion area (11.86dB;SD=8.00) was lower than the average MRS of the surrounding anatomically normal areas of the retina with no notable apparent pathological lesions (MRS=16.81dB;SD=8.03) (p<0.001). However, these areas still had a lower average MRS when compared with the MRS of normal control eyes (p<0.001). The analysis of the various pathological structures imaged with OCT showed the average MRS in various areas of ascending order was (1) fibrosis (3.27dB;SD=3.84), (2) atrophy (3.92dB;SD=4.45), (3) intra-retinal fluid (IRF) (8.19dB;SD=8.18), (4) subretinal fluid (SRF) (8.88dB;SD=6.73) and (5) pigment epithelial detachment (PED) represented areas of highest MRS (13.26dB;SD=7.57).

Conclusions
Eyes with advanced AMD compared to normal controls have a significantly worse overall visual function as measured by lower MRS and more unstable fixation. In eyes with AMD, even the seemingly anatomical normal areas seen on OCT of retina had lower average MRS than normal controls, suggesting that visual function may be impaired even in areas where there are no clinically evident pathological structural changes. End stage pathological changes such as fibrosis and atrophy had the lowest average MRS. Although, areas of IRF had a lower average MRS when compared with the MRS of normal control eyes (p<0.001). Further study is required to better understand the implications of these findings in clinical practice.

Financial Disclosure
Anna CS Tan receives speaks and receives grant funding from Nidek, Zeiss, Novartis, Bayer and Allergan.
Purpose
To define the morphological characteristics of pigment epithelial detachments (PEDs) associated with acquired vitelliform lesions (AVLs) in dry age-related macular degeneration (AMD).

Methods
The patients presenting with AVLs associated with dry-AMD were included (Group 1, 21 eyes). An intermediate dry AMD group without AVL (Group 2, 21 eyes) and a healthy control group were (Group 3, 23 eyes) also selected to compare the morphological differences. Greatest basal diameter (GBD) and maximum height (MH) of the largest PED on spectral domain optical coherence tomography were measured using the manual caliper tool. Internal reflectivity of PEDs were measured using ImageJ software. To eliminate the effect of interindividual variation in signal strength and scan intensities, reflectivity measurements of vitreous and retinal nerve fiber layer were performed for standardization. The choroidal area (CA) was binarized to the luminal area (LA) and stromal area (SA). Then, the choroidal vascularity index (CVI), which was defined as the proportion of the LA to the total CA, was assessed.

Results
The mean age of the patients was 68.7±8.5 years in group 1, 70.0±6.9 years in group 2, and 68.1±6.7 years in group 3 (p=0.281). Subfoveal choroidal thickness was 290.3±86.8 µm in group 1, 215.6±85.0 µm in group 2, and 238.3±51.7 µm in group 3 (p=0.016). Regarding binarized measurements, CA and LA measurements were significantly higher in group 1 (0.840±0.302 mm², 0.602±0.227 mm²) than group 2 (0.594±0.183 mm², 0.429±0.139 mm²) in pairwise comparisons (p=0.017, p=0.020, respectively). CVI was 71.43% in group 1, 72.08% in group 2, and 76.8% in group 3 (p=0.000). The mean GBD and MH of the largest PED was significantly higher in group 1 (1443±595 µm, 188±86 µm) than group 2 (851±368 µm, 119±38µm) (p=0.001, p=0.001, respectively). Internal PED reflectivity was significantly lower in group 1 (0.44±0.21) than group 2 (0.66±0.17) (p=0.001). Internal PED reflectivity showed significant negative correlation with GDB and MH of the largest PED in group 1 (r=-0.587 p= 0.005; rho= -0.448 p=0.042, respectively). In group 2, internal PED reflectivity had significant negative correlation with MH of the largest PED (rho= -0.511, p= 0.018).

Conclusions
Dry AMD patients with AVL are more prone to have thick choroid and large and hyporeflective PEDs compared to the ones without AVL.

Financial Disclosure
Lecturer and Consultant (Bayer, Novartis, Alcon, Allergan, Bausch & Lomb)
Title
Efficacy of half-dose photodynamic therapy versus high-density subthreshold micropulse laser for treating pigment epithelial detachments in chronic central serous chorioretinopathy: PLACE trial report No. 5

Purpose
To compare the effect of half-dose photodynamic therapy (PDT) and high-density subthreshold micropulse laser (HSML) treatment on retinal pigment epithelial detachments (PEDs) in chronic central serous chorioretinopathy (cCSC).

Setting/Venue
This study included data from the PLACE trial, a prospective randomized controlled trial comparing half-dose PDT and HSML treatment in cCSC. Data of patients from 5 different academic medical centers located in Leiden (The Netherlands), Nijmegen (The Netherlands), Cologne (Germany), Paris (France) and Oxford (United Kingdom) were included in this study.

Methods
Main outcome measurements were changes in both the foveal PED and highest PED within the macula on optical coherence tomography at baseline compared to first evaluation visit (at 6-8 weeks) and final evaluation visit (at 7-8 months).

Results
At baseline, a macular PED was detected in 76.9% (123/160) of patients, and a PED within 1500 µm from the foveal center in 37.5% (60/160) of patients. In the half-dose PDT arm (61 patients), there was a significantly higher decrease in the highest macular PED compared to the HSML treatment arm (62 patients), both at first and final evaluation visit (p<0.001 and p=0.012, respectively). The decrease of highest foveal PED was significant at first visit (p=0.025).

Conclusions
Half-dose PDT is superior to HSML treatment with regard to a statistically significant reduction in the height of macular PEDs in active cCSC. These findings may also have implications for other diseases within the pachychoroid disease spectrum that can present with PEDs.

Financial Disclosure
Financial Disclosure: Sascha Fauser: Employee (Hoffman-La Roche, Basel, Switzerland). No financial disclosures exist for any of the other authors.
**Title**
Structural and functional effects of delay in anti-vascular endothelial growth factor intravitreal injections in neovascular age-related macular degeneration

**Purpose**
To assess the impact of COVID-19 related delay in intravitreal injection timing on macular structure and visual acuity among patients treated for neovascular age-related macular degeneration (nvAMD).

**Setting/Venue**
This retrospective study included consecutive patients who received appointments with one retina specialist at the Shaare Zedek Medical Center, a tertiary ophthalmology center, for anti-VEGF injection from March to April 2020 – the “first wave of COVID-19”.

**Methods**
We reviewed demographic and clinical data as well as macular OCT images of 34 patients (48 eyes, group A) who departed from their original injection schedule during the first wave of COVID-19 and compared them to 46 patients (71 eyes, group B) who, during the same period, followed the original treatment plan. Functional worsening was defined as a loss of at least 0.1 in decimal visual acuity. Anatomic worsening was defined as new or worsening of subretinal/intraretinal fluids or new hemorrhage.

**Results**
The planned interval period between intravitreal injections were 5.7±2.7 and 5.5±2.4 weeks in group A and group B, respectively (p=0.60). The mean actual interval period between intravitreal injections was 13.6±6.8 (delay of 7.9±5.2 weeks;) and 5.3±2.4 weeks (0 weeks delay) in group A and group B, respectively (p <0.001). The best corrected visual acuity worsened in 23 eyes (47.9%) and in 6 eyes (8.5%) in group A and group B, respectively (OR 9.97, p <0.001). Anatomic features indicating worsening of the disease were detected in 31 eyes (64.6%) and 16 eyes (22.5%) in group A and in group B, respectively (OR=5.73, p <0.001). A new macular hemorrhage was observed in 4 eyes (8.3%) in group A, while no new bleeding was observed in group B (p=0.09).

**Conclusions**
In nvAMD patients, delay in retinal care during the Covid-19 restrictions period results in negative short-term outcomes, including macular bleeding.

**Financial Disclosure**
N/A
Choroidal modifications preceding the onset of macular neovascularization in age-related macular degeneration

Purpose
The pathogenesis of the MNV in AMD is a consequence of a multifactorial elements such as the suffering of the retinal pigment epithelium (RPE), the inflammatory cytokines and metabolic alteration among the deep layers of the retina which leads to the release of VEGF. Even if the role of choroid and choriocapillaris modifications in geographic atrophy’s evolution is demonstrated, it is still unknown and debated their contribution in the onset, progression and staging of the neovascular form. The aim of our study is to analyze choroidal and choriocapillaris changes occurring before the onset of macular neovascularization (MNV) in patients affected by age-related macular degeneration (AMD) by quantitative optical coherence tomography (OCT) and OCT angiography (OCTA) trying to discover a way to predict the MNV formation.

Setting/Venue
The study was designed as retrospective case series. It was totally placed in at the Department of Ophthalmology of IRCCS San Raffaele Hospital, Milan, Italy after the signature of informed consent from all the patients and under the approval of the ethical committee of IRCCS Scientific Institute San Raffaele Hospital.

Methods
Patients affected by AMD, categorized in eyes complicated by MNV and eyes not developing MNV, was retrospectively analyzed for 1-year of follow-up. Exclusion criteria were the diagnosis of other ocular diseases, ophthalmic surgery in the last six months before the inclusion, high media opacities, and systemic diseases potentially affecting the results of the study. All the ophthalmological data, including best-corrected visual acuity (BCVA), anterior and posterior slit-lamp examination, tonometry, Choroidal thickness (CT), Sattler layer thickness (SLT) and Haller layer thickness (HLT) were measured on structural OCT scans. CT and HLT were calculated from the mean value of five samples (subfoveal, 750µm (right-left) and 1500µm (right-left)), measured in a horizontal high-resolution structural OCT foveal scan. Vessel density (VD) and choriocapillaris (CC) porosity were quantified on OCTA reconstructions obtained from the automatic segmentations of Topcon software, manually corrected by two independent expert graders to minimize potential artifacts. Furthermore we calculated choroidal hyperreflective foci (HF) and CC porosity, a new parameter for the measurement of flow voids in the CC, starting from OCTA CC binarized reconstructions and using the ImageJ porosity pipeline to analyze percentage CC porosity. Main outcome measure was the relationship between choroidal and CC parameters, and MNV onset.

Results
We included 50 eyes of 50 AMD patients (28 males; mean age 74±5 years). Over the 1-year follow-up, 15/50 eyes developed MNV (9 type 1; 3 type 2; 3 mixed type 1-2). Mean best-corrected visual acuity (BCVA) was 0.15±0.15 LogMAR at baseline, resulting stable in eyes not developing MNV (0.15±0.12 LogMAR; p > 0.05), and worsening to 0.38±0.20 LogMAR in eyes developing MNV (p<0.01). VD values were similar between eyes developing MNV and eyes not complicated by MNV at baseline, with significant worsening detected only in MNV eyes. CC porosity was significantly higher in MNV eyes already before the onset of MNV. Furthermore, SLT resulted significantly lower in eyes developing MNV. The onset of MNV was preceded by significant increasing of intraretinal HF, whereas choroidal HF showed no evident changes.

Conclusions
Our study underline how vessel density reduction and choriocapillaris porosity increase, both expression of choriocapillaris degeneration, together with the Sattler layer thinning indicate early signs of macular neovascularization onset in age-related macular degeneration. Furthermore intraretinal HF progressively increased before and during the development of MNV. Our correlation analysis, proving to be statistically significant when comparing the intraretinal HF increase and the progression of vascular impairment (SLT and CC porosity), further reinforces the hypothesis of a primary impairment of the RPE, prompting the later cascade of events leading to MNV development. It may be hypothesized that the functional impairment of the blood supply of CC is an early pathogenic mechanism leading to a RPE distress which bring to the development of MNV. The degeneration of CC and the SLT thinning represent early biomarker of MNV onset in AMD. Small number of patients, the retrospective design and the lack of histopathology are the major limitations of the study but the results obtained may identify the OCT-A such as a useful first step in staging AMD patients.
Prevalence of subclinical macular neovascularization in fellow eyes of unilateral exudative age-related macular degeneration on OCT-angiography

Purpose
To investigate the prevalence of subclinical macular neovascularization (MNV) in fellow eyes of patients with unilateral neovascular age-related macular degeneration (AMD) using optical coherence tomography angiography (OCT-A) and to quantify choriocapillaris non-perfusion adjacent to MNV.

Setting/Venue
An observational monocentric retrospective study conducted in the Department of Ophthalmology in the Military Hospital of Tunis, Tunisia.

Methods
We conducted an observational monocentric retrospective study consisting in reviewing all patients with AMD who underwent OCT-A between February 2019 and January 2021 in our Department. Patients with unilateral exudative AMD were included. We determined the presence of subclinical MNV on en-face macular OCT-A sections of the outer retina and choriocapillaris. The choriocapillaris non-perfusion area (CCNPA) has been quantified in proportion to the entire choriocapillaris layer as well as to the 250 µm surrounding subclinical and exudative MNV.

Results
Among the 84 AMD patients who underwent OCT-A, twenty-one had unilateral exudative AMD and thus met our inclusion criteria. The mean age was 69.05 ± 9.74 years. Subclinical MNV was present in two of the 21 fellow eyes (9.5%). The proportion of CCNPA to the 250 µm surrounding area was significantly higher than to the entire choriocapillaris layer (15.5±6.5% versus 10.5±4.5%, p < 0.001). No statistically significant difference has been found between CCNPA in exudative MNV eyes and fellow subclinical MNV eyes (p= 0.09).

Conclusions
Subclinical MNV in fellow eyes with unilateral exudative MNV should be investigated. Choriocapillaris non-perfusion seems to be more extensive adjacent to all MNV lesions.

Financial Disclosure
The authors declare no conflict of interest.
Purpose
Age-related macular degeneration (AMD) is the leading cause of blindness in the United Kingdom (UK), with the number of new cases and associated costs to the UK economy continuing to rise alongside an increase in life expectancy and an ageing population. In the UK, the standard therapy for treatment of neovascular AMD (nAMD) is intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) therapy. Prompt intervention with anti-VEGF treatment and continued maintenance of therapy following early diagnosis of nAMD is paramount to providing disease control and preserving the vision of patients, with treatment delays likely to lead to irreversible visual loss and subsequent higher social support costs. There has, however, been limited research investigating anti-VEGF treatment patterns and associated clinical outcomes within real-world clinical practice in the UK. The objective of this retrospective non-interventional study was to describe the current management landscape for patients with nAMD treated with anti-VEGF therapy in the UK and associated clinical outcomes during the first 24 months after initiating treatment.

Setting/Venue
The RATE study for nAMD involved the collection of pseudonymised patient and service-level data about current treatment practices and outcomes for patients newly initiated on licensed anti-VEGF therapy at eighteen hospitals within the UK National Health Service. Participating centres were from a diverse setting of teaching and district general hospitals spread geographically across England and Wales. Data were collected using a mixed-methodology approach that involved the retrospective review of patient medical records, additional independent interpretation of medical imaging results and a service mapping survey with healthcare professionals: early results from the medical record review are presented here.

Methods
Patients were sequentially included if they had been initiated on a licensed anti-VEGF therapy (aflibercept or ranibizumab) for nAMD and received ≥1 intravitreal injection between 01/01/2017 and 31/12/2017. (The date of the first injection is the ‘index date’; the eye that received first injection is the ‘index eye’). Patients were required to be aged ≥50 years at index, have a first diagnosis of nAMD on or within 60 days prior to the index date, and be anti-VEGF treatment naive in both eyes. Data were analysed using descriptive statistics (analyses included data on the index eye only). Key treatment and clinical outcomes during the 12 months post-index are presented here. For the purpose of this analysis, disease control was defined as the absence of retinal fluid (no intra-retinal [IRF] and no sub-retinal fluid [SRF]), as documented in medical records by the treating physician in relation to the most recent optical coherence tomography (OCT) result at Month 12 (±2 months). OCT scans were also independently assessed by a central reading centre and these data will form the basis of further analyses. Change in visual acuity (VA) from baseline (the closest pre-index measurement) was assessed in Early Treatment Diabetic Retinopathy Study (ETDRS) letters.

Results
Of the 331 patients included in this analysis, the median (interquartile range [IQR]) age at index was 79 (74–84) years and 200 (60%) patients were female. The median (IQR) duration from nAMD diagnosis until first anti-VEGF injection was 2 (0–11.5) days. All patients received a NICE-approved anti-VEGF therapy for nAMD: 194 (59%) patients received aflibercept and 137 (41%) received ranibizumab. 313 (95%) patients received at least three anti-VEGF injections within 90 days after the index date, with patients receiving a mean (standard deviation [SD]) of 7.3 (2.0) injections during the 12 months post-index. Of 256 patients with available information on IRF and SRF status and at least 12 months follow-up, 117 (46%) were documented to have achieved disease control in the index eye at Month 12. The median (IQR) VA at baseline (n=304) was 55.0 (45.0 – 65.0) ETDRS letters. There was a median (IQR) increase in VA from baseline of 6.5 (0.0–15.0) letters at Month 3 (n=300), 7.0 (0.0–16.0) letters at Month 6 (n=286), 9.0 (0.2–16.0) letters at Month 9 (n=270) and 7.0 (0.0–18.0) letters at Month 12 (n=253 [all p<0.001]).

Conclusions
Early results from the RATE study indicated that at month 12, disease control was achieved in approximately half of patients initiated on a licensed anti-VEGF therapy, with VA improving by a median of 7 letters. Within UK clinical practice, there was prompt access to anti-VEGF treatment (within 2 days on average of diagnosis) and 95% of patients received ≥3 anti-VEGF injections within 90 days, in alignment with recommendations that a loading phase of three injections at monthly intervals is completed for patients newly initiated on treatment. Patients received a mean of 7.3 injections in total within the first year, suggesting that centres are opting to extend the intervals between injections after completion of the loading phase (the service mapping analysis completed as part of this study will further clarify treatment protocols used within these centres). It will also be important to understand the extent to which service capacity issues, treatment protocols and VA outcomes influence treatment interval decisions. Further planned analyses will consider wider aspects of the management and visual outcomes of patients with nAMD during the first 24 months of treatment, including anti-VEGF regimens and treatment patterns and the wider structure of UK retinal services.
**Purpose**
Age-related macular degeneration (AMD) is characterized by progressive mitochondrial dysfunction in retinal pigment epithelial cells, resulting in higher reactive oxygen species (ROS) levels and leading to apoptosis. Elamipretide binds to cardiolipin to stabilize mitochondrial structure and reduce ROS emission, thereby slowing and reversing effects of oxidative stress.

**Setting/Venue**
The ReCLAIM program consists of two clinical trials to evaluate the safety and efficacy of elamipretide for the treatment of non-central geographic atrophy (NCGA) secondary to age-related macular degeneration (AMD). ReCLAIM-1 was performed at a single center in the US; ReCLAIM-2 is ongoing at 42 locations in the US.

**Methods**
ReCLAIM-1 was an open-label, Phase I trial in which dry AMD patients with non-central geographic atrophy (NCGA) or high-risk drusen were treated with 40 mg subcutaneous elamipretide daily for 24 weeks. Safety and visual function were assessed from baseline to week 24. Outcomes were assessed separately in pre-defined NCGA and high-risk drusen (HRD) subgroups, and the NCGA results are presented here. Best corrected visual acuity (BCVA) and low-luminance visual acuity (LLVA) were assessed. Area of NCGA was measured by fundus autofluorescence (FAF). ReCLAIM-2 is an ongoing, randomized, placebo-controlled Phase-2 trial of subcutaneous elamipretide for treatment of NCGA. Patients are being randomized 2:1 to receive subcutaneous elamipretide (40 mg daily) or placebo for 48 weeks, with a primary endpoint of LLVA at 48 weeks. BCVA and low-luminance reading visual acuity (LLVA) as well as change in GA area measured by FAF and OCT will also be assessed.

**Results**
In ReCLAIM-1, subcutaneous elamipretide was well tolerated. Injection site reactions were observed; however, there were no serious ocular or non-ocular safety concerns. Mean distance BCVA and LLVA in the NCGA subgroup (n = 19) improved significantly at week 24 compared to baseline (4.6 ± 5.1 and 5.4 ± 7.9 letters, respectively; P < 0.05). At week 24, LLVA improved > 5 letters in 53.3% of patients, > 10 letters in 33.3%, and > 15 letters in 6.7%. Using the square root area of NCGA, the mean (SD) at baseline was 1.690 (0.9773) mm² by FAF, increasing by 0.136 (0.0831) mm² at week 24 (P < 0.05). These results led to the initiation of ReCLAIM-2 (N = 180) in which the primary endpoint is mean change in LLVA. Mean baseline age (SD) for all patients is 77.0 (8.5) years, and 61.2% (n = 101) are female. Entering mean (SD) BCVA and LLVA are 76.0 (8.7) letters and 55.0 (14.6) letters, respectively. Mean (SD) baseline NCGA area on FAF is 2.7 (2.5) mm². The trial is currently underway.

**Conclusions**
Subcutaneous elamipretide appeared safe in the ReCLAIM-1 trial. BCVA and LLVA in NCGA patients improved significantly at 24 weeks. Mean NCGA growth at 24 weeks appeared reduced compared to natural history studies, and further investigation is ongoing in the ReCLAIM-2 study.

**Financial Disclosure**
Consultant for: NGMB Biopharma, Apellis Pharmaceuticals, Boehringer-Ingelheim Pharmaceuticals, Genentech, Roche, Galmedix Therapeutics, Oxurion, Palatin Technologies, Inc., Iveric bio
Title
Statin use and the incidence of age-related macular degeneration: A meta-analysis

Purpose
Age-related macular degeneration (AMD) shares many of the same risk factors with atherosclerosis. As such, there is a postulated role for lipid-lowering agents in preventing AMD. This meta-analysis investigates the possible role for statins in the prevention of AMD onset and progression.

Setting/Venue
Meta-analysis.

Methods
MEDLINE, EMBASE, Cochrane CENTRAL, and the reference lists of included studies were systematically searched from inception to September 2020. Studies were included if they measured the risk of AMD development or progression with statin use. Two reviewers independently assessed study eligibility and risk of bias. The primary outcomes assessed were AMD incidence and progression. Secondary outcomes were the incidence of early AMD, late AMD, choroidal neovascularization, and geographic atrophy. Meta-analysis was conducted in R using a random effects model with a Paule-Mandel estimator, with pooled risk ratios and 95% confidence intervals reported for all outcomes. A p-value of 0.05 was considered statistically significant for all analyses.

Results
Twenty-one articles (1 randomized controlled trial, 20 observational studies) collectively reporting on 1,460,989 participants were included. The mean age was 67, 54.8% of participants were Caucasian, and 53.2% were female. The pooled risk ratios [95% CI] for statin use on any, early and late AMD incidence were 1.05 [0.85, 1.29] (p = 0.44), 0.99 [0.88, 1.11] (p = 0.86), and 1.15 [0.90, 1.47] (p = 0.27), respectively. In patients with existing AMD, the respective risk ratios for statin use on incidence of AMD progression, choroidal neovascularization, and geographic atrophy were 1.04 [0.70, 1.53] (p = 0.85), 0.99 [0.66, 1.48] (p = 0.95), and 0.84 [0.58, 1.22] (p = 0.36). Subgroup analysis revealed no significant effect of follow-up duration for any outcome. Performing leave-one-out sensitivity analyses did not significantly change the magnitude and direction of effect for any outcome.

Conclusions
This meta-analysis found that there was no significant difference in the incidence or progression of AMD based on statin use. However, in the prevention of cardiovascular disease, statin therapy produces the most noticeable therapeutic effect in patients with strong risk factors, with a smaller effect in those with a low risk profile. A similar effect may exist in patients at risk for AMD, yet none of the included studies conducted such a subgroup analysis. Future studies should therefore aim to investigate the effect of statin use on AMD incidence in patients with high baseline risk profiles to see if the same conclusions hold true.

Financial Disclosure
MMP: Financial support (to institution) – PSI Foundation. PJK: Advisory board – Roche, Novartis, Alcon, Bayer, Novelty Nobility; Financial support (to institution) – Allergan, Bayer, Roche, Novartis; Financial support – Novartis, Bayer; Equity owner – ArcticDx. RHM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis.
Semantic analysis of patient voice in wet AMD and diabetic retinal disease: Patients' journey and healthcare experience

**Purpose**
The purpose of the study is to analyze Patient Voice (messages from patients with wet age-related macular degeneration (wAMD) and diabetic retinal disease (DRD), or their caregivers) from open Internet resources in the Russian Federation, using artificial intelligence (AI) methods: technologies for automated analysis of unstructured natural language texts, incl. semantic technologies. The study provides valuable information, not only on patients’ characteristics and treatment patterns in real-world management of retinal diseases, but also on patients’ attitude to the disease, diagnostic and treatment-related procedures, their needs and barriers to treatment. The need for such data is explained by the fact that there are no available comprehensive reviews of country-specific patients’ ‘journeys’ assessed from patients’ perspective and analyzed by extracting insights from ‘big data’. Moreover, recent publications show that the healthcare system is ready to recognize such information as an important source of real-world data (RWD). The intensive development of the virtual environment boosted by COVID-19 pandemic also highlighted the responsibility of healthcare stakeholders to develop digital solutions for different groups of patients (apps, remote monitoring tools, web-based platforms, etc.), and it is not achievable without understanding patients’ preferences, needs, and barriers to treatment.

**Setting/Venue**
Real-life anonymized patient stories from Russian-language open Internet-sources (forums, social networks) were processed with the technologies of natural language understanding (NLU). Patients and caregivers (mainly, relatives) provide direct insights on their journey in diagnostics and treatment in an open and ‘uncensored’ way while looking for a second opinion or exchanging their experience and supporting each other. They use social networks (e.g., Facebook, Instagram, and country-specific networks), disease-related forums, and Q&A portals. There were 73,098 DRD/wAMD-related posts identified including 13,138 posts by 844 DRD patients and 358 posts by 212 wAMD patients.

**Methods**
The key concept was ‘Patient Voice’ - a source of the patients ‘reality’ which is applied by regulatory bodies (e.g., FDA), pharmaceutical companies, patient advocacy groups, etc. It was analyzed in several steps with semantic technologies aimed at processing large volumes of unstructured information (text semantic analysis considering not keywords, but the whole structure of the natural language and its meaning): 1. Crawling: gathering unstructured data (user posts) from open Web 2.0 sources. After additional filtering based on the system of heuristics (selecting only ‘target’ discussions), plain text data were converted into XML representation. Anonymized patient stories matching the criteria of the ‘diseases of interest’ were selected. 2. Extracting information from each post by NLU algorithms based on hybrid approach to text mining, including pattern-based approach similar to expert systems and machine learning by the Semantic Hub platform. It was driven by the formal domain models called ‘ontologies’ i.e. semantic networks or directed graphs showing the domain concepts and relations between them. Output results were structured in a JSON format, then merged with intelligent algorithms and loaded into a ‘knowledge base’. 3. After unstructured ‘big text data’ were transformed into structured base, traditional biostatistics methods and visualization tools were applied.

**Results**
Low ‘digital’ awareness and activity of wAMD and DRD patients was detected compared with the diseases with lower prevalence (breast cancer, multiple sclerosis, etc.). The majority of content for DRD was produced by relatives (82.6% of messages), in wAMD - by patients themselves (65%). The key focus for DRD patients was diabetic microvascular manifestations (over 42,000 posts for ‘diabetic foot’ and only 681 for ‘diabetic retinopathy’). Quality of life (QoL) was shown to be significantly affected with inability to work as a major burden for 30% of wAMD patients, and diabetes-associated comorbidities as a key factor compromising QoL in 20% of DRD patients. In wAMD patients mean time-to-diagnosis after disease manifestation was 1 year, in DRD more than a half mentioned 1-2 months. Key reasons for visiting the clinics included in-depth eye exams (CCT mentioned by 27.6% of wAMD patients) and treatment (24.1%) visits. The proportion of DRD patients seeking primary advice of ophthalmologist was higher compared to wAMD (23.3% vs 8.6%). Only 33.2% of wAMD patients and 7% of DRD patients noted that they received anti-VEGFs with affordability as a key barrier mentioned. Patients demonstrated the lack of clear understanding of prognosis and effective treatment options.

**Conclusions**
The study revealed low activity and awareness in wAMD and DRD patients compared to other ophthalmological and systemic conditions. The awareness on other microvascular diabetic complications in DRD was obviously higher in comparison to other eye disease. This justifies a need for increasing ‘digital’ literacy and awareness not only of patients (it may be challenging due to the age of wAMD patients and their access to digital environment in general) but of their younger relatives as well. The results confirm that vision-related quality of life is compromised among the studied population that could be used for the justification of the appropriate resources allocation in negotiations with health authorities. Based on healthcare experience reported by patients with two vision-threatening retinal diseases it has been demonstrated that there is a need for improvement in at least several points in their ‘journey’ - time-to-diagnosis, treatment choice and availability of effective treatment options. There is also a need to improve patients’ awareness on effective therapeutic options, and efficacy criteria in parallel with improving the access to anti-VEGF therapy.

**Financial Disclosure**
No
Pharmacokinetic profile of the port delivery system with Ranibizumab in the phase 3 Archway trial

Purpose
The Port Delivery System with ranibizumab (PDS) is an investigational drug delivery system that includes a pars plana implant for continuous delivery of ranibizumab into the vitreous. In the phase 3 Archway trial in patients with neovascular age-related macular degeneration (nAMD), serum and aqueous humor samples were collected to characterize the pharmacokinetic profile of ranibizumab delivered via the PDS with fixed refill-exchanges every 24 weeks (PDS Q24W).

Setting/Venue
Archway (NCT03677934) was a phase 3, randomized, active treatment–controlled trial for the treatment of nAMD, conducted at 77 study locations in the United States (N = 415).

Methods
In the PDS with ranibizumab 100 mg/mL Q24W and intravitreal ranibizumab 0.5 mg injections every 4 weeks (Q4W; monthly ranibizumab) arms, serum pharmacokinetic samples were collected at randomization and at weeks 4, 24, 36, and 96 from all patients. At selected sites, samples were taken at days 2 and 7 and at weeks 12, 48, and 72 in the PDS Q24W arm, and 1–5 days after an injection in the monthly ranibizumab arm. Optional aqueous humor samples were collected from patients in either arm at randomization and at weeks 24, 28, 48, 52, 72, 76, and 96; serum samples were also collected at this time. The pharmacokinetic-evaluable population included patients who did not receive ranibizumab as supplemental treatment in the study eye after implant insertion or in the fellow eye, or patients with prior intravitreal bevacizumab treatment. Ranibizumab concentrations were measured using a validated enzyme-linked immunosorbent assay with lower limits of quantitation of 15 pg/mL for serum and 20,000 pg/mL for aqueous humor. Vitreous concentrations were predicted using a population pharmacokinetic model with a compartmental structure, including compartments for the implant, vitreous, and serum, where the dose was either administered into the vitreous or into the implant.

Results
In the PDS Q24W arm (n = 94), geometric mean (CV%) serum ranibizumab concentrations ranged from 419 (54%) pg/mL at week 4 to 340 (94%) pg/mL at week 24. In the monthly ranibizumab arm (n = 79), the geometric mean serum ranibizumab concentrations ranged from 1880 (57%) pg/mL at 1–5 days after injection (Cmax) to 58.1 (171%) pg/mL at week 4 (Ctrough). The aqueous humor pharmacokinetic profile reflected the same trends seen in serum, with PDS Q24W (n = 42) maintaining concentrations above monthly ranibizumab Ctrough (n = 46). Using a population pharmacokinetic model, in both serum and vitreous, the total ranibizumab exposure (as summarized by area under the concentration curve) with PDS 100 mg/mL Q24W was predicted to be ~40% of the total ranibizumab exposure with intravitreal ranibizumab 0.5 mg Q4W injections. The predicted vitreous humor concentrations of ranibizumab were estimated to decrease by half by 170 days after a refill-exchange procedure.

Conclusions
The PDS continuously released ranibizumab over the Q24W refill-exchange interval, achieving steady concentrations. Ranibizumab concentrations with PDS Q24W were within the range experienced with monthly ranibizumab injections. The aqueous humor pharmacokinetic profile was consistent with the serum pharmacokinetic profile.
### Purpose
The presence of retinal fluid on optical coherence tomography (OCT) scans is the main morphological biomarker of disease activity influencing a clinician's re-treatment decisions when treating neovascular age-related macular degeneration (nAMD) with anti-vascular endothelial growth factor (VEGF) intravitreal injections (IVI). However, recent evidence on the impact of residual fluid in different retinal compartments suggests that differentiation of fluid location is required to best guide individualized treatment protocols.

### Setting/Venue
Selected members of the Vision Academy met to review the influence of fluid on treatment outcomes in nAMD, with a particular focus on the criteria for re-treatment with anti-VEGF IVI according to fluid status. The Vision Academy comprises over 90 international retinal experts who collaborate to provide collective recommendations on clinical challenges in areas where there is a lack of conclusive evidence. Vision Academy recommendations are subject to a validation process to ensure there is consensus and endorsement from the entire group.

### Methods
Existing data on the use of residual fluid to guide decision-making in nAMD were identified by literature searches performed using the MEDLINE/PubMed database; the cut-off date was January 2021 and searches were restricted to English-language publications only. These insights were used to develop an algorithm to guide treatment decisions for patients with nAMD according to residual fluid status.

### Results
At baseline, macular neovascularization type, size, and location in relation to the fovea should be recorded. Disease activity should be monitored by best corrected visual acuity (BCVA), examination for retinal hemorrhage, and OCT. Fluid status should be assessed in each retinal compartment. Monthly anti-VEGF IVI should be administered during the induction phase and until maximal anatomical effect is achieved. If intraretinal fluid (IRF) and/or subretinal fluid (SRF) amounts are reducing, treatment should be continued without interval extension until resolution/stability is reached. During the maintenance phase, the treatment interval should be individually adjusted. In cases of disease inactivity (i.e., absence of IRF and SRF, no new retinal hemorrhage, and no decrease in BCVA attributable to disease reactivation), intervals can be extended by 2 weeks if using a treat-and-extend regimen. Disease stability/control is compatible with stable persistent residual SRF despite at least 3 monthly IVI. In the absence of any other signs of disease activity, treatment intervals may be maintained or cautiously increased. Persistent stable IRF can result from atrophic degeneration and often has other OCT signs to determine its origin. IRF due to persistent VEGF activity is considered a risk factor for continued vision loss and should not be tolerated.

### Conclusions
The suggested treatment algorithm for those on a treat-and-extend regimen reflects recent data, taking into consideration the impact of residual fluid in different retinal compartments on visual acuity and our increased understanding of how to interpret fluid within the retina in patients with nAMD treated with anti-VEGF IVI. It hereby offers a more individualized approach which allows tolerance of stable amounts of residual SRF.
Perceptions of COVID-19 in patients with macular disease during the third national lockdown in England

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**Purpose**
A year has passed since the initial outbreak and this study aims to investigate if the perceived risk of contracting COVID-19 is still a factor that could influence patients’ willingness to attend hospital appointments. Further, we aim to identify the groups of patients that have higher level of COVID-19 anxiety and to pinpoint factors that increase the likelihood of clinic non-attendance.

**Setting/Venue**
This non-interventional survey study was conducted at the Macular Treatment Centre (MTC), Manchester Royal Eye Hospital. MTC is a tertiary ‘one-stop’ centre for diagnosing and treating macular diseases in the North West of England and it’s consisted of one large central clinic and 3 smaller peripheral units. Patients attending MTC typically have macular disorders that require regular monitoring or treatment in the form of intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection. The study was carried out during the second wave of COVID-19 after the third national lockdown was announced in England.

**Methods**
All patients who had missed their scheduled MTC appointment in the study period were invited to participate in this survey over the telephone. Eligible patients were those older than 18 years old diagnosed with macular disorders requiring intravitreal anti-VEGF injection. Exclusion criteria included pre-existing mental health issues such as general anxiety disorder and depression, dementia, and hearing problems or language barriers that prevent the patients from understanding the survey questions. Patients who could not be reached after three separate attempts, and who declined to participate were also excluded. Verbal informed consent was obtained from all participants and all data were anonymized. Demographic information and clinical data were collected from electronic health records. The two-parts telephone survey consisted of a non-validated 23-items questionnaire and the COVID-19 Anxiety Syndrome Scale (C-19ASS). Statistical analysis was performed using SPSS.

**Results**
DNA rate in January 2021 was significantly higher than that in February 2020 (8.7% vs 6.3%, p<0.001), the month before the first national lockdown, but lower than April 2020 (8.7% vs 21.5%, p<0.001). Although the majority of the respondents had received COVID-19 vaccination (84.6%), only 26.1% of the vaccinated patients believed the jab had influenced their willingness in attending hospital appointments. The majority of patients (68.3%) adhered to government guidance and only go out for shopping for essential items and attending hospital appointments, and 15.9% of respondents decided not to leave home at all, while a small number of individuals (3.8%) confessed that they were going out as usual. Around half of the respondents felt concerned about contracting COVID-19 during their journey to/from hospital (49.0%) and spreading the virus to other people (52.9%), while most patients (60.6%) were also worried about catching COVID-19 inside hospital facilities. The C-19ASS was significantly higher in female patients compared to male (19.3±8.2 vs. 14.4±8.2, p=0.005), in patients older than 70 years old (18.9±7.8 vs. 13.9±7.8, p=0.002), and in patients with mobility issues (20.9±8.0 vs. 14.6±8.0, p<0.001). C-19ASS scores, age, personally knowing someone who had contracted COVID-19, living alone, were predictors of clinic non-attendance.

**Conclusions**
This survey study demonstrated that COVID-19-anxiety and fear of viral exposure could adversely affect patient adherence to clinic appointments during the national lockdown. Special attention should be provided to older patients, those who lives alone and patients with impaired mobility, as these groups were more prone to have higher C-19ASS scores and a greater likelihood of missing appointments. If the issue with poor clinic attendance is not addressed urgently, a sustained high rate of non-attendance will add to the existing healthcare burden created by reduced clinic capacity during the first lockdown. In time of uncertainty, firm public health messages should be conveyed to address the unwarranted fear of COVID-19 infection e.g. eyecare professionals should ensure patients appreciate that the material risk of irreversible visual impairments needs to be weighed against the risk of COVID-19 transmission. This is particularly relevant as hospital eye services across the country are in the process of restarting.

**Financial Disclosure**
None
**Title**
Assessment of Choriocapillaris/Sattler and Haller layer changes after intravitreal injection in eyes with age-related macular degeneration: Aflibercept vs Ranibizumab

**Purpose**
To evaluate the changes in Choriocapillaris (CC)/Sattler and Haller layer thicknesses as a treatment response in eyes with neovascular age-related macular degeneration (nAMD) after aflibercept or ranibizumab injections and to describe the role of individual choroidal layers in the pathophysiology of nAMD.

**Setting/Venue**
A prospective, controlled case series, comparative study, Kütahya Health Science University Hospital

**Methods**
This study included a total of 70 eyes of 70 patients with treatment-naive exudative nAMD (type 1 and 2) treated with three consecutive injections of aflibercept or ranibizumab. The patients were randomize divided into two groups: aflibercept group (34 eyes) who received intravitreal aflibercept (IVA) and ranibizumab group (36 eyes) who received intravitreal ranibizumab (IVR). Only one eye of each patient was included. Three consecutive aflibercept or ranibizumab injections at intervals of 1 month were applied to all patients. CC/Sattler and Haller layer thicknesses were measured by enhanced-depth imaging optical coherence tomography at nasal and temporal regions of 1000 µm from the center of the fovea at baseline and after three monthly intravitreal injections. Also, choroidal neovascularization (CNV) size was measured as the largest horizontally diameter of the hyperfluorescence region from the baseline fluorescein angiography (FA) image and from FA image taken after three loading dose injections.

**Results**
After three consecutive injections, the mean reduction of nasal/temporal CC/Sattler layer thickness in the IVR and IVA groups were -10.1±2.3/-8.5±1.8 and -25.2±15.2/-19.4±12.8 µm, respectively. Also, the mean reduction of nasal/temporal Haller layer thickness in the IVR and IVA groups were -6.5±3.6/-7.2±7.9 and -9.5±8.0/-7.0±6.2 µm, respectively. Changes in CC/Sattler layer thickness of the IVA group were greater than that of the IVR group (p<0.001); however, changes in Haller layer thickness were similar between groups (p>0.05). At nasal and temporal region, the decrease in both the amount and proportion of CC/Sattler layer thickness (for IVR 12.3% and 10.2%, for IVA 34.1% and 24.4%) was more prominent compared with Haller layer thickness (for IVR 4.9% and 5.2%, for IVA 7.1% and 5.1%) in both groups. After three injections, mean change in CNV size of the IVA group was greater than that of the IVR group (for IVR -46.1±34.5 µm and for IVA -177.8±145.5 µm, p<0.001). After loading doses, 19 eyes (55%) in the IVA group and 14 eyes (38%) in the IVR group is showed intraretinal and subretinal fluid regression (dry macula) (p = 0.04). Also, the visual gain was significantly higher in IVA group versus IVR group (p=0.04).

**Conclusions**
In current study, after three injections of aflibercept and ranibizumab treatment, we observed that the decrease in CC/Sattler layer thickness was more prominent compared with Haller layer. However, the decrease in CC/Sattler layer thickness and CNV size was greater in aflibercept-treated eyes. Such results suggest that aflibercept treatment significantly influence the CNV size by reducing choroidal vascular hyperpermeability in especially CC/Sattler layer.

**Financial Disclosure**
o no have financial relations
Simultaneous angiopoietin-2/vascular endothelial growth factor-a inhibition prevents subretinal fibrosis progression in preclinical mouse models of choroidal neovascularisation (CNV)

Purpose
Faricimab, a bispecific antibody currently in year 2 of phase 3 trials (TENAYA: NCT03823287; LUCERNE: NCT03823300), targets both angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A), which are key drivers of vascular instability. Faricimab demonstrated improvement in best-corrected visual acuity and durability up to every 16 weeks versus anti-VEGF monotherapy in phase 2 and 3 clinical trials in patients with neovascular age-related macular degeneration. We present new preclinical data from 2 mouse models of choroidal neovascularisation (CNV) showing that dual Ang-2/VEGF-A blockade, through its vessel-stabilising potential, significantly reduces fibrosis linked to vision loss versus anti-VEGF monotherapy.

Setting/Venue
Two independent mouse models of CNV were used: laser-induced CNV and spontaneous CNV (JR5558 mice).

Methods
Effect of Ang-2/VEGF-A blockade on subretinal fibrosis was analysed in a laser-induced CNV mouse model by treating 10- to 12-week-old wild-type mice intraperitoneally with mouse cross-reactive tool antibodies against Ang-2, VEGF-A or both (with the bispecific anti–Ang-2/VEGF-A antibody) on days 0, 7 and 21 post laser injury. Untreated or immunoglobulin G (IgG)-treated mice were used as controls. Subretinal fibrosis was characterised by fibronectin immunostaining and binding of fluorophore-labelled collagen hybridising peptides (CHPs), which detect collagen remodelling in active fibrotic lesions. Seven-week-old JR5558 mice developing bilateral spontaneous neovascular fibrotic lesions were treated intraperitoneally with mouse cross-reactive tool antibodies against Ang-2, VEGF-A or both (with the bispecific antibody), and IgG (control). Fibronectin immunostaining was performed on retinal pigment epithelium (RPE)/choroid flat mounts to assess fibrosis at 1 (PT1), 3 (PT2) and 5 (PT3) weeks post treatment. CHP binding was assessed 3 weeks post treatment (PT2).

Results
In the laser-induced CNV mouse model, dual inhibition significantly reduced both fibronectin-positive (47%; P < 0.05) and CHP-positive (39%; P < 0.01) areas at 3 weeks; blocking Ang-2 or VEGF-A alone had no significant effect. There was significant reduction in fibronectin-positive area in the RPE/choroid of JR5558 mice with the bispecific antibody (38%; P < 0.01) and anti–Ang-2 (41%; P < 0.001) versus IgG at PT1; effect of anti–VEGF-A alone was not significant. Only dual Ang-2/VEGF-A inhibition maintained significant reduction at PT2 (47%; P < 0.01) and PT3 (54%; P < 0.05). Dual inhibition significantly prevented collagen remodelling, as shown by reduced CHP in RPE/choroid lesions at PT2 (66%; P < 0.01). Anti–Ang-2 or anti–VEGF-A alone showed no significant effect.

Conclusions
We present preclinical data from 2 independent CNV mouse models suggesting sustained prevention of fibrosis with dual Ang-2/VEGF-A pathway inhibition. Our findings support the hypotheses that Ang-2 and VEGF-A contribute to vascular instability and drive subretinal fibrosis. Future studies are underway to determine how dual Ang-2/VEGF-A inhibition limits subretinal fibrosis.

Financial Disclosure
All authors are employees of F. Hoffmann-La Roche Ltd.
10 years of submacular haemorrhage (SMH): 101 cases at a tertiary centre - Outcomes and aetiology

**Purpose**
To describe aetiologies and visual outcome of the largest UK dataset of submacular haemorrhage treated with pneumatic (PD) and pars plana vitrectomy assisted displacement (PPV). We analysed descriptive and outcome differences in various aetiologies for SMH and after PD or PPV.

**Setting/Venue**
Ophthalmology Department, Southend University Hospital, Southend-On-Sea, Essex, UK

**Methods**
Retrospective case analysis of patients treated for SMH between April 2011 and April 2021. Primary outcome was logMAR Best corrected visual acuity (BCVA) change 3 months post treatment. BCVA compared pre-operatively with 3 months post operatively and the difference in BCVA (ΔBCVA) was analysed. We analysed demographic, and ocular features of patients, previous anti Vascular Endothelial Growth Factor (VEGF) treatment and surgical intervention. Surgical intervention included either (a) pneumatic displacement (PD) using tissue plasminogen activator (t-PA) and gas tamponade with or without anti-VEGF intravitreal injections; or (b) Pars Plana Vitrectomy (PPV) using tissue plasminogen activator (t-PA) and gas tamponade with or without anti VEGF subretinal injections.

**Results**
101 cases representing 94 eyes were identified. 5 were re-operated due to insufficient displacement and 2 were re-operated due to a subsequent re-SMH. Median age was 81.5 years with 59 (62.8%) female patients. Aetiologies included neovascular age-related macular degeneration (nAMD) (79 (84.0%)), macroaneurysm (11 (11.7%)), trauma (2 (2.1%)), unspecified (2 (2.1%)). 39 (41.5%) were either using antiplatelet or anticoagulant medication. 64 (68.1%) underwent PD; 5 (7.8%) of these subsequently underwent PPV due to insufficient displacement of haemorrhage. The remaining 31.9% underwent primary PPV. 20 (24.7%) of SMH caused by nAMD had had preceding anti-VEGF therapy. Median number of injections prior to SMH was 6 (range 2-28) and median number of weeks since last injection was 13.75 (range 2.5-150). 9 (11.4%) of nAMD eyes had a re-bleed after treatment. 8 (88.9%) of these occurred beyond 8 weeks of their last anti-VEGF injection. Other aetiologies did not re-bleed. Visual acuity analysis was available for 60 eyes. Overall, median ΔBCVA was -0.37 (+1.40 to -2.03) (p< .00001). Median ΔBCVA was -1.10 in macroaneurysm SMH and -0.30 in nAMD SMH (p=0.02). No significant difference in ΔBCVA was found between naïve nAMD and treated (p=0.32) or PD and PPV (p=0.09).

**Conclusions**
87% of SMH were caused by nAMD. 75.3% of these were previously untreated. 2.5% of nAMD SMH subsequently had a further SMH. Displacement of SMH by either PD or PPV significantly improved visual acuity. Visual acuity improvement was similar in eyes previously treated with anti-VEGF with naïve eyes, and between PD and PPV assisted displacement. Macroaneurysm SMH had significantly better visual improvement than nAMD SMH.

**Financial Disclosure**
None to declare
Title
Quantifying risk factors for non-adherence and non-persistence to anti-vascular endothelial growth factor treatments in neovascular age-related macular degeneration: A multi-country patient and clinician survey

Purpose
Long-term outcomes of management of neovascular age-related macular degeneration (nAMD), diabetic retinopathy (DR) and diabetic macular edema (DME) may be impacted by non-adherence and non-persistence to anti-vascular endothelial growth factor (anti-VEGF) injections. This survey, part of the nAMD Barometer programme, aims to better understand the factors for suboptimal adherence and non-persistence from the perspectives of patients, healthcare professionals (HCPs), and clinic staff.

Setting/Venue
A survey of patients, HCPs, and clinic staff with the aim to recruit approximately 100 clinics from more than 20 countries in Europe, North America, South America, the Middle East, Africa, and the Asia Pacific region.

Methods
An online clinic primer questionnaire, completed by responsible administrators (or equivalent) at clinic enrolment, comprised of 21 questions relating to clinic-level data/characteristics, including number of patients treated, average wait times/delays, and patient-support programs. Following the completion of clinic primers, paper-based multiple-choice questionnaires (including 4-point Likert-scale questions) will be completed anonymously by patients receiving/having previously received anti-VEGF injection therapy, HCPs prescribing/administering anti-VEGF treatment, and clinic staff who do not prescribe/administer anti-VEGF treatment, but otherwise interact with patients. Patients will complete a 38-question survey exploring personal characteristics, disease information provided at diagnosis, opportunities and challenges to treatment adherence/persistence, and treatment experiences, expectations, and burden. HCPs will complete a 34-question survey, and clinic staff a 22-question survey; both explore personal and practice characteristics, depth and frequency of discussion with patients, setting of treatment expectations, opportunities for, and challenges to, treatment adherence/persistence, and opportunities for improving outcomes. ‘Non-adherence’ was defined as missing (by ≥2 weeks) two or more visits within 12 months, and ‘non-persistence’ was defined by non-attendance (or equivalent) at clinic enrolment, comprised of 21 questions relating to clinic-level data/characteristics, including number of patients treated, average wait times/delays, and patient-support programs. Following the completion of clinic primers, paper-based multiple-choice questionnaires (including 4-point Likert-scale questions) will be completed anonymously by patients receiving/having previously received anti-VEGF injection therapy, HCPs prescribing/administering anti-VEGF treatment, and clinic staff who do not prescribe/administer anti-VEGF treatment, but otherwise interact with patients. Patients will complete a 38-question survey exploring personal characteristics, disease information provided at diagnosis, opportunities and challenges to treatment adherence/persistence, and treatment experiences, expectations, and burden. HCPs will complete a 34-question survey, and clinic staff a 22-question survey; both explore personal and practice characteristics, depth and frequency of discussion with patients, setting of treatment expectations, opportunities for, and challenges to, treatment adherence/persistence, and opportunities for improving outcomes. ‘Non-adherence’ was defined as missing (by ≥2 weeks) two or more visits within 12 months, and ‘non-persistence’ was defined by non-attendance (or no

Results
By 18 July 2021, 31 clinics had responded to the clinic primer, and this interim analysis of the clinic primer results is based on these clinics. 51.6% of clinics reported they had previously completed audits assessing whether patients adhere to scheduled appointments. Clinics observed and estimated higher rates of adherence in patients with nAMD compared to those with DR and DME. Multiple choice questionnaires will ask patients whether other chronic health conditions make it difficult to manage their appointments, if travelling to the clinic is difficult (because of ability/distance/cost), whether they worry about changes in their vision until their next appointment if they do not receive an injection at a particular visit, or whether it is difficult for the patient’s accompanying person to attend appointments (amongst other questions). HCPs and clinic staff professionals will be asked to assess the extent of non-adherence and non-persistence in their own clinics. They will also be asked to provide their views of patients’ challenges associated with managing their disease, and on different strategies to better support patients with nAMD/DR/DME, such as treating both eyes on the same day for those patients affected bilaterally, or the opportunity for patients to join a peer-to-peer support group.

Conclusions
To our knowledge, this survey is the largest initiative of its kind, and will provide detailed and systematic data on the challenges and opportunities for managing nAMD/DR/DME, including comprehensively evaluating factors for non-adherence and non-persistence to anti-VEGF treatment. There are 61 clinics enrolled, and further data from all primers, and the patient, HCP, and clinic staff questionnaires will be reported when available. The analysis of available clinic primer data, and the full survey results, will inform future nAMD/DR/DME-focussed initiatives designed to improve patients’ experiences of their disease management, including those intended to enhance long-term adherence and persistence to anti-VEGF treatment.
Title
Reticular pseudo-drusen in adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP)

Purpose
Adult onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) is caused by a dominant acting mutation in the CSF1R gene. CSF1R mutations may drive a disruption in brain endothelial cell and microglial/macrophage crosstalk and has been characterized by blood-brain barrier (BBB) disruption in animal models and human subjects. Like the BBB the inner blood retinal barrier (iBRB) has been shown to be dynamic and tightly regulated. Interestingly, CSF-1R signalling has been associated with diseases of the retina, including Age Related Macular Degeneration (AMD). The sub-retinal location of reticular pseudo-drusen (RPD) suggests inner retinal pathology and there is increasing evidence that the inner retina may have a role in the pathogenesis of AMD. We conducted a thorough analysis of retinal and retinal vascular integrity in a patient with a known mutation in the CSF-1R gene.

Setting/Venue
All studies were carried out in the Royal Victoria Eye and Ear Hospital, Dublin 2.

Methods
ETDRS visual acuity was obtained at four metres and was performed by a clinical nurse specialist. Static automated perimetry was performed using the Humphrey Field Analyzer and a central 30-2 threshold test was carried out. NIDEK LM-970 Auto Lensmeter was used to estimate the patient’s glasses prescription. Autorefraction was performed using the NIDEK ARK-530A Keratometer. Intraocular pressure was measured through Goldman applanation tonometry using Minims Proxymetacaine Hydrochloride 0.5% and Minims Fluorescein Sodium 2% eye drops. Fundus fluorescein angiography (FFA), Optical Coherence Tomography (OCT) and fundal autofluorescence were performed using the Heidelberg SPECTRALIS. Pupils were dilated using 1% tropicamide and 2.5% phenylephrine. Intravenous administration of a standard dose of 2 ml of sodium fluorescein (1 mg/mL) was administered and images obtained at 1 minute, 2 minutes, 4 minutes and 5 minutes post injection. FFA and OCT images were obtained with a 30 degree angle of view and 73 line cuts were acquired. Heidelberg Eye Explorer (HEYEX) was used to capture images. FFA analysis was quantified against a threshold determined from the fluorescein signal of n = 33 normal healthy controls (aged 18 -30).

Results
We report the appearance of localised inner retinal vascular leakage and the appearance of reticular pseudo-drusen in the macula of both eyes in a patient with a mutation in the kinase region of CSF-1R. Fundus autofluorescence imaging demonstrated drusenoid deposits in the superior temporal macula of the left eye and in both the superior and inferior macula of the right eye. FFA images showed a significantly increased fluorescein signal in the peri- and para-foveal regions of the macula. Evidence of stage 3 RPD was observed bilaterally in this patient. Areas of stage 3 RPD exhibited a “haloing” effect on FFA, with conical shaped sub-retinal drusen. Areas of hyper-fluorescence on FFA appeared to associate with stage 2 RPD accumulation.

Conclusions
This report suggests a potential association between localised inner retinal vascular leakage and the appearance of reticular pseudo-drusen in a patient with decreased CSF-1R signalling capacity. We now suggest that the early stages of reticular pseudo-drusen accumulation may be associated with disrupted iBRB integrity and a decrease in CSF-1R signalling. These findings suggest a potential role for the inner retina in RPD development. In effect, stabilising the integrity of the iBRB and enhancing the CSF-1R signalling axis may be beneficial in preventing RPD accumulation and AMD development.
Comparison of reduced-duration and standard-duration photodynamic therapy on retinal and choroidal thickness

Purpose
The EVEREST II study reported superior outcomes in polyp closure rates using verteporfin photodynamic therapy (PDT) in combination with intravitreal ranibizumab compared to intravitreal ranibizumab monotherapy. Some authors suggest that reduced-fluence or variable-duration PDT may reduce complications including subretinal, vitreous and suprachoroidal hemorrhage, as well as tears and rips of the retinal pigment epithelium. PDT is also believed to cause choroidal ischemia which may lead to chorio-retinal atrophy. We aimed to evaluate the efficacy of reduced-duration PDT and compare it with standard-duration PDT in the treatment of polypoidal choroidal vasculopathy (PCV).

Setting/Venue
Tertiary ophthalmology referral centre

Methods
Retrospective review of all consecutive PDT-naive patients diagnosed with PCV and treated with PDT from January 2011 to December 2013. Patients treated with reduced (light dose, 50 J/cm²; dose rate, 600 mW/cm²; wavelength, 689 nm; time, 42 seconds) and standard-duration (light dose, 50 J/cm²; dose rate, 600 mW/cm²; wavelength, 689 nm; time, 83 seconds) PDT were recruited for this study. Central foveal thickness (CFT) in the central 1-mm ETDRS subfield and central choroidal thickness (CCT; manual sub-foveal point choroidal thickness using caliper measurement) were generated using spectral domain optical coherence tomography (SD-OCT) for analysis. The changes in CFT and CCT after PDT were used to evaluate the efficacy of treatment. These were compared between standard and reduced-duration PDT.

Results
Thirty-six eyes of 36 patients (23 males and 13 females) with a mean age of 70.2 years (range 50 – 89 years old, S.D. ± 8.7) were included the analysis. They were followed-up for a mean duration of 22.4 months (range 6 – 48 months). Of these, 28 (77.8%) were treated with standard-duration PDT while 8 (22.2%) had reduced-duration PDT. There were no statistically significant differences when comparing mean decrease in CFT between eyes which underwent standard-duration PDT compared to eyes which underwent reduced-duration PDT respectively (3 months: -146.4µm vs. -120.3µm, p=0.62; 6 months: -124.2µm vs. -119.5µm, p=0.94; 12 months: -129.3µm vs. -101.5µm, p=0.62). Similarly, there were no statistically significant differences when comparing mean decrease in CCT between the two groups (3 months: -22.3µm vs. -10.8µm, p=0.46; 6 months: -29.9µm vs. -15.9µm, p=0.43; 12 months: -18.5 vs. -5.6, p=0.56). Recurrence rates (standard-duration vs. reduced-duration: 64.3% vs. 50%, p=0.47) and number of anti-vascular endothelial growth factor (VEGF) injections administered (standard-duration vs. reduced duration: 6.0 vs. 4.8, p=0.45) during the course of the follow-up were similar between the two groups. There were no significant adverse events reported in both groups.

Conclusions
From these results, reduced-duration PDT has similar efficacy when compared to standard-duration PDT in reducing retinal oedema, while having negligible effect on the thickness of the choroid at the end of 1 year. Further studies are needed to further ascertain if reduced-duration PDT results in less chorio-retinal atrophy compared to standard-duration PDT in the longer term.

Financial Disclosure
Novartis - conference support Bayer - conference support
Title
Description of the age-related macular degeneration impact on quality of life from the patients’ perspective: OBJETIVO DMAE study

Purpose
To evaluate the impact of age-related macular degeneration (AMD) on health-related quality of life (QoL) and daily activities from the patients' perspective.

Setting/Venue
Patients diagnosed with AMD (dry AMD [dAMD] or neovascular AMD [nAMD]) who voluntarily decided to contact to participate in a telephone interview, between August 29th, 2019 and February 28th, 2020 in Spain.

Methods
Observational, non-interventional, cross-sectional study in Spain. Patients ≥50 years AMD diagnosed (dAMD or nAMD) who voluntarily contacted to answer to a telephone interview. Patients were informed about the study from patients’ associations, pensioners’ organizations, online advertisements, or informative leaflets available in hospital centers. Six-month data collection period.

Results
181 evaluable patients: 44.9% dAMD and 55.1% nAMD. Mean (standard deviation, SD) age of 72.5 (8.9) years, mainly females (59.1%), living in company (81.2%). 79.0% suffered concomitant diseases: most prevalent osteoarthritis (37.8%), diabetes (30.1%) and hypertension (26.6%). At diagnosis, 11.6% showed poor/very poor vision; 69.6% reported fear of going blind. 63.2% stopped driving and 33.7% reported having less control over their daily routine due to their vision. Mean (SD) time from first complaints to AMD diagnosis was 6.4 (14.5) months and 2.9 (6.8) months from diagnosis to first treatment. Most frequent visual symptoms were blurred vision in the center of the visual field (76.2%) and alteration in the shape of the images (38.7%). Greatest limitations were observed in daily living activities in environments unknown to the patient: use of public transport in new routes (32.0%), mobility in unknown places/paths (31.0%) and attending to a medical appointment (27.6%). Therefore, 48.8% of the patients needed support from a caregiver to perform domestic/housekeeping tasks and accompanying, while 13.9% needed support from domestic employees (mostly payed by patients or their families). AMD showed a great impact on patient’s self-confidence/security (44.2%), in their mood (39.7%) and anxiety/nervousness (36.5%), with greater psychological impact in nAMD patients.

Conclusions
The loss of vision in AMD patients is important, having a relevant impact on health-related QoL in aspects directly associated with the vision loss or psychological affectionation. Furthermore, the dependence of these patients generates significant indirect costs. Preservation of vision is critical to limit the AMD impact on patient’s life.

Financial Disclosure
José María Ruiz-Moreno: Advisory board of Allergan, Bayer, Novartis, and Topcon Luis Arias Barquet: Advisor for Allergan, Bayer, Novartis, Roche, and Topcon Laia Gómez-Baldó: Employee of Novartis José García-Arumí: Advisory board of Novartis, Bayer, and Alcon
Longitudinal characterization of and the impact of established risk factors for AMD progression on the relative ellipsoid zone reflectivity

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Pret much of the relative ellipsoid zone reflectivity (rEZR) on spectral-domain optical coherence tomography (SD-OCT) imaging is a potential indicator for photoreceptor’s health. The purpose of this study was to investigate the natural history of the rEZR in subjects with intermediate age-related macular degeneration (iAMD) and its association with high-risk factors of disease progression including reticular pseudodrusen (RPD) and pigmentary abnormalities (PA).

Setting/Venue
Logitudinal analysis over 3 years on a three-dimensional SD-OCT image data set from an existing natural history cohort of AMD patients with bilateral large drusen

Methods
SD-OCT volume scans (49 B-scans, field size 20°x20°, collected every 6 months for 3 years) from an existing natural history cohort of AMD patients with bilateral large drusen (>125 μm) were used in this study. Using an automatic rEZR determination approach, the average rEZR of each raw SD-OCT volume was determined as the mean ratio of the ellipsoid zone (EZ) to the external limiting membrane (ELM) reflectivity (linear range of grey values: 0-1). The change in rEZR over 3 years was determined using linear regression models, adjusting for baseline age and the presence of RPD and PA.

Results
A total of 145 eyes of 145 iAMD patients (mean age: 69.8 ± 8.1 years) were included, with RPD and PA being present in 30 (21%) and 37 (26%) eyes, respectively. At baseline, the average rEZR was lower in eyes with RPD (28.9 ± 15.5, arbitrary units, AU) compared to eyes without RPD (38.7 ± 17.2 AU, p = 0.005), however, there was no significant difference in rEZR between eyes with (33.6 ± 14.2) and without PA (37.8 ± 18.2, p = 0.208). Longitudinal analysis showed that rEZR was associated with age, the presence of RPD and PA. The rEZR linearly decreased over time and that the rate of change was significantly greater in eyes with RPD (-6.66 ± 2.2 AU per 6 months) compared to eyes without RPD (-0.73 ± 0.06 AU per 6 months, p<0.001), adjusted for age and the presence of PA at baseline.

Conclusions
The rEZR decreases over time and the rate of reduction is greater in eyes with RPD, a high-risk phenotype of progression, compared to eyes without. These findings warrant further studies evaluating the rEZR as a prognostic biomarker for progression to advanced AMD.

Financial Disclosure
Heidelberg Engineering, Carl Zeiss Meditec, Optos and CenterVue provide devices for retinal imaging and functional probing in research activities
Purpose
Age-related macular degeneration (AMD) is the leading cause of blindness in the industrialized countries and the third worldwide after glaucoma and cataract, according to the World Health Organization. Vitamin D may be implicated in the pathophysiology of several ocular diseases, but its role in age-related macular degeneration (AMD) remains uncertain. We sought to review systematically the existing evidence to evaluate the association between serum 25-hydroxyvitamin D 25(OH)D levels and AMD.

Methods
A four-database search (Pubmed, ISI Web of Science, Cochrane, and Scopus) was performed from inception to May 2020 using the MeSH terms: (“Macular Degeneration” OR “Age-related macular degeneration” OR “Retinal degeneration” OR “Macula lutea”) AND (“Vitamin D” OR “Ergocalciferols” OR “Cholecalciferol” OR “25-Hydroxyvitamin D”). Random-effects meta-analysis were performed to compute 1) the standard mean difference in 25(OH)D concentration between AMD and non-AMD patients and 2) the AMD risk according to serum 25(OH)D levels.

Results
Eighteen observational studies enrolling 75,294 patients after a selection process among 375 original abstracts were selected. This review included 11 cross-sectional studies, 4 case-control, 2 cohorts and 1 case series. A total of 75,294 adults were recruited, 9,736 of which presenting AMD. The number of participants ranged from 30 to 17,045, with a range of 15–2359 AMD cases. Both middle-aged and elderly participants were recruited. In the first meta-analysis, the summary standard means difference of −0.13 (95%CI: −0.35; 0.08) indicates a non-significant difference of -13% between the average members of the AMD and the non-AMD groups (P = 0.26). In the second meta-analysis, no significant differences were found, but there appears to exist a trend for late AMD among subjects with serum 25(OH)D below 50 nmol/L (OR 1.8, 95%CI: 1.00–3.24, P = 0.05).

Conclusions
There is no clear evidence of an inverse association between serum 25(OH)D and AMD risk, mainly due to heterogeneity in studies procedures and lack of longitudinal designs. Further longitudinal studies are needed, ideally taking both genetic and environmental factors into account, to clarify the role of serum vitamin D on AMD pathophysiology. If an association between vitamin D deficiency and AMD is proven, this might influence further supplementation strategies that, so far, do not include vitamin D.
Patient perspectives in the management of neovascular age-related macular degeneration: A systematic literature review

**Setting/Venue**
Patients with nAMD managed with anti-VEGF therapy in non-RCT settings.

**Methods**
Electronic searches were conducted in EMBASE and MEDLINE for articles published up to October 2020 according to pre-defined search criteria. Abstracts from key conferences (including EURETINA and ARVO annual meetings) held in the last two years were also searched. Identified articles were manually screened based on the title and abstract, and potentially relevant full-text articles were assessed for eligibility. Articles on real-world clinical practice were eligible if they described the impact of anti-VEGF therapy on QoL of patients/caregivers with nAMD, psychosocial and psychological impact of disease, and treatment burden.

**Results**
QoL was evaluated in 24/63 (38%) studies using various assessment tools; in five studies evaluating the effect of anti-VEGF treatment using the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), QoL improved early (by month 1), with improvements sustained at 1 year in most studies. In addition to visual acuity, age, social support, and marital status appeared to impact QoL; one study (n=142) found depression correlated significantly with NEI VFQ-25, but another (n=51) concluded depression was unrelated to QoL. Prevalence of depression or depressive symptoms in patients treated with anti-VEGFs varied widely (8–42%), but in the absence of longitudinal evidence, a causal relationship cannot be concluded. Only one study evaluated the effect of anti-VEGFs on anxiety and depression, showing treat-and-extend therapy reduces mental burden over 1 (n=40) and 2 (n=25) years. In four studies reporting perspectives of treat-and-extend versus pro re nata dosing, treat-and-extend regimens were associated with reduced patient/caregiver burden. One study highlighted treat-and-extend regimens may allow patients to better prepare mentally for injection appointments. Six studies reported perspectives related to caregiver burden, and despite >60% of patients requiring someone to accompany them to clinic appointments, approximately 75% of caregivers did not necessarily consider this burdensome.

**Conclusions**
In observational studies evaluating the effects of anti-VEGF treatment, patient QoL improved early (by month 1), with some improvements sustained at 1 year. The heterogeneity of how QoL and other patient-relevant concepts, such as mental health, were evaluated highlights the need for a standardized approach. If results from individual studies in patients with nAMD are to be more easily compared. It remains to be established whether sustained improvement in QoL should be a realistic expectation of anti-VEGF treatment (particularly in longer-term treatment). In nAMD, depression and anxiety have complex and nuanced origins rather than being simply related to anti-VEGF injections or poor vision alone. A coordinated, holistic approach to patient care and patient-physician dialogue are therefore key to optimizing the likelihood of patient well-being, as well as visual outcome. As long as anti-VEGF treatment maintains vision, studies indicate that patients prefer a treat-and-extend regimen due to reduced burden and certainty of injection schedule. Overall, few studies evaluate the management of nAMD from the perspective of the patient (or caregiver). The heterogeneity of patient characteristics, and multiple factors impacting patient psychology, should be considered when evaluating patient-reported outcomes in randomized controlled trials (RCTs). Non-interventional observational studies may provide a setting closer to real-world practices to evaluate these perspectives. The aim of this systematic literature review was to describe patient experiences of the management of nAMD in routine clinical practice in terms of quality of life (QoL), psychosocial and psychological impact of disease, and treatment burden.

**Financial Disclosure**
Title
Assessment of a novel OCT classification of age-related macular degeneration severity using dark adaptation data from a large cohort study (Northern Ireland Sensory Aging studies – NISA)

Purpose
Studies have suggested delayed rod-mediated dark adaptation (DA) to be a relevant diagnostic indicator of age-related macular degeneration (AMD) that worsens with disease severity. DA impairment has also been suggested to worsen in people with subretinal drusenoid deposits (SDDs), accretions of material within the retinal pigment epithelium (RPE) that extend through the ellipsoid zone. AMD severity is graded in a range of ways. The majority of published literature on DA relied on the Beckman classification, based on colour fundus photography (CFP), despite reported limitations of the technique. We aim to assess if differences in RIT are more discernible between different grades of AMD severity when a novel Optical Coherence Tomography (OCT) based criteria is used as compared to one using a CFP-based classification. A secondary aim is to investigate if SDD presence is associated with changes in rod-mediated DA at different AMD severity grades, according to an OCT-based severity scale.

Setting/Venue
Centre for Public Health, Queen's University Belfast and Royal Hospital, Belfast, Northern Ireland

Methods
We used prospectively collected data from the case-control Northern Ireland Sensory Aging studies (NISA) and Northern Ireland Sensory Aging-2 (NISA-2) studies conducted at Queen’s University Belfast. Data for participants (≥50-years) with complete rod-intercept time (RIT) data, CFP and spectral domain OCT (SD-OCT) images and had been classified into both the Beckman grading and an OCT-based grading system were extracted, with demographic data. The eye with worse monocular visual acuity was designated the study eye. CFP and SD-OCT images were acquired with the Canon CX-1 Digital Fundus Camera (Canon,USA) and Heidelberg Spectralis SD-OCT (Heidelberg Engineering,Heidelberg,Germany) respectively. CFP and SD-OCT images were evaluated by TN and UC and participants were classified into the Beckman classification and OCT-based classification. SDD presence was identified via OCT. The OCT grading included: participants with no drusen/RPE abnormalities (OCT0), participants with drusen present but no RPE abnormalities (OCT1) and participants with drusen and RPE abnormalities present (OCT2). RIT was measured by the AdaptDx (Maculogix,USA). Time-to-event analysis assessed the magnitude of differences in RIT between groups of participants graded by the different imaging classifications. Simple summary statistics were calculated for RIT but comparisons between groups included age as a

Results
459 eyes (mean [standard deviation; SD] age 66[8] years) were stratified into 338 eyes in Beckman 0 (B0), 29 in Beckman 1 (B1), 20 in Beckman 2 (B2) and 72 in Beckman 3 (B3) Simple mean (SD) RIT for these four groups was 7.5 (5.3), 8.0 (4.3), 7.3 (4.7) and 15.6 (11.9) minutes respectively. The same 459 participants were split into 312 eyes in OCT0, 96 in OCT1 and 51 in OCT2. Simple mean (SD) RIT for these groupings appeared more distinct being 7.4 (5.5), 10.0 (7.2) and 15.3(21.0) minutes respectively. SDDs were detected in 55 eyes in OCT0, 30 in OCT1 and 24 in OCT2. Eyes with intermediate AMD (B3) had significantly longer RITs compared to each of the other Beckman groups (vs B0, B1, B2; p<0.005 all). However, there were no statistically significant differences in RIT between any of the other Beckman groups. Eyes in OCT2 had slower RITs compared to OCT-defined controls (OCT0) (p=0.001) and eyes in OCT1 (p=0.009). There was, however, no statistically significant difference between OCT0 and OCT1 (p=0.195). SDD presence significantly worsened RIT within OCT2 (p=0.002) but not within OCT1 (p=0.285). On the contrary, in OCT0 the presence of SDDs improved the RIT (p=0.012).

Conclusions
Our results provide some evidence of differences in RIT being marginally more apparent between different grades of AMD severity when a novel OCT-based criteria is used rather than a CFP-based classification. An OCT-based classification taking account of SDD presence seems relevant, too. We utilised a novel time-to-event analysis to assess RIT which allowed us to control for the effect of age under the assumption that age is a linear predictor of delayed DA. After controlling for age, the differences in RIT between the OCT grades were much less marked and this is noteworthy. These results are meaningful because RIT is a surrogate of a deficit in measurable loss of visual function (delayed DA) for a person. Our study had other strengths including a large sample size and a large cohort of people with SDDs which is uncommon when compared to recent DA research in people with AMD. An OCT-based classification, while partially mimicking Beckman, could account for structural abnormalities that CFP-based classifications cannot. For example presence of SDDs may be important when defining selection criteria for eyes entering prospective studies.
Title
Evaluation of dosing regimen patterns and treatment adherence to anti-VEGF (vascular endothelial growth factor) therapy in Indian patients with neovascular age related macular degeneration: A healthcare professional-based cross-sectional survey

Presenter
Nitin Maksane - India

Co-Author 1
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Purpose
Age-related macular degeneration (AMD) is a common chronic retinal disease with the global and Indian prevalence of 8.7% and ~3% respectively. The intravitreally administered anti-vascular endothelial growth factor (anti-VEGF) therapy is currently the mainstay treatment. However, there are still significant gaps and challenges in the treatment and management of nAMD, which pose barriers in achieving optimal outcomes for these patients. Few of the many considerations include individual patient characteristics or response to the anti-VEGF therapy, financial considerations, and inadequate patient adherence to the treatment and monitoring. Such factors highlight the substantial logistical, emotional, and financial burdens of the long-term, frequent intravitreal injections. Management of nAMD patients with personalized treatment approach has moderately helped overcome the challenges. For example, reducing the number of anti-VEGF injections per year by using alternative dosing regimens like pro re nata (PRN) or treat-and-extend (T&E) strategies in the specific nAMD patient population. Although there are several studies underlining the treatment burden and mitigation strategies, there is lack of India-specific studies exploring these aspects. Thus, the present survey was conducted to get insights from the Indian HCPs on the anti-VEGF dosing

Setting/Venue
HCP-based survey conducted in 11 cities (metro and non-metro cities) across India in real-world settings.

Methods
This was a nationwide, cross-sectional, questionnaire-based survey conducted between August 2020 to October 2020. Total 222 HCPs comprising of retina specialists (n=122) and ophthalmologists (n=100) who manage patients with nAMD and administer intravitreal anti-VEGF injections were included. The survey was performed using a mix of computer-assisted personal interviews (75%) and computer assisted web-based or telephonic interviews (25%) for a duration of 30 to 35 minutes. The questionnaire used for the survey was checked for validity and reliability, and then used to collect data from the HCPs. The survey evaluated anti-VEGF therapy dosing regimens followed by the HCPs, patient adherence to the therapy, as well as frequency and reasons for the patient dropouts. This information was further analysed to compare the practice patterns among retina specialists and ophthalmologists, as well as across the four zones of India (North, East, West, South)

Results
Each HCP managed 13% nAMD patients (14%: retina specialist; 12 % ophthalmologists) of the total patient pool per month. Most HCPs used PRN regimen (43%) followed by T&E (32%), the usage for PRN was relatively higher among retina specialists (45%) than the ophthalmologists (40%). The PRN regimen scored highest in the East (59%) and T&E scored highest in South (44%). In PRN regimen, ~70% patients were on 4-8 weeks dosing regimen. Similar trend was observed across all the zones, except for the South, where ~66% patients were on 6-12 weeks dosing regimen. In terms of treatment adherence, HCPs opined ~ 35% patients on anti-VEGF therapy dropped out before completing the ideal dosage (as decided after diagnosis based on the patient profile). Overall HCPs observed a slight improvement in vision (74%), affordability (71%), and symptomatic relief (67%) as the top three reasons for patients dropping out of an anti-VEGF therapy. Considering zonal trends, in East affordability (94%); for West a slight improvement in vision (53%) were ranked as the number 1 dropout reason by HCPs. The HCPs from North opined symptomatic relief (74%) to be the topmost dropout reason, while in South all the top three reasons scored equally (~51%).

Conclusions
The survey concluded that most of the HCPs preferred the use of anti-VEGF therapy on PRN basis for 4 to 8 weeks. Treatment dropouts were mainly driven by the patients experiencing slight improvement in vision, affordability of anti-VEGF therapy, and symptomatic relief from the nAMD.

Financial Disclosure
I am an employee of Novartis India Limited
Title
Brolucizumab in wet age related macular degeneration and polypoidal choroidal vasculopathy: Real world evidence

Purpose
To determine the efficacy and safety of intravitreal brolucizumab in wet age related macular degeneration as well as polypoidal choroidal vasculopathy in treatment naive patients and patients requiring switch therapy as experienced in the real world.

Setting/Venue
Institute based practice in India and Europe

Methods
Retrospective, multicentric, observational study conducted across multiple centres in India and Europe. Data collected included demographics, details of the ocular examination, results of special investigations (e.g. fundus fluorescein angiography optical coherence tomography), the characteristics of the neovascular membrane/polyp, past therapy in case of patients requiring switch therapy, the treatment interval prior to switch therapy and complications, if any. All patients received therapy as per the HAWK and HARRIER protocol once they were initiated on brolucizumab therapy. Follow ups were scheduled on post injection days 1, 7 and then monthly. Statistical analysis included assortment of data in absolute and relative frequencies and as per demographics. The paired t-test, Chi-square test and logistic regression analysis were used, wherever appropriate. The primary outcome measure was the determination of change in best corrected visual acuity after initiation of brolucizumab therapy. The secondary outcome measures included: change in central subfield thickness, the number of injections administered, the treatment interval and complications, among others. Statistical significance was set at p<0.05

Results
A total of 133 patients (133 eyes; 58 males; mean age 71.75 years, standard deviation (SD)-5.36 years) were recruited for analysis. 8 patients had polypoidal vasculopathy (all treatment naive) while 6 patients had wet AMD associated with pigment epithelial tear (RPE tear). 34 patients were treatment naive; the rest had received prior therapy with aflibercept and ranibizumab. The mean number of injections prior to switch therapy were 33.4(SD-3.4; range 12-87). The mean treatment interval prior to switch was 6.7 weeks (SD-2.1). 4 patients with RPE tears were treatment naive. The other two had prior therapy with aflibercept (mean 5.3 injections). The mean follow up in wet AMD patients was 10.5 months (SD-3.7 months). The baseline BCVA was 0.72 logMAR (SD-0.14). The final BCVA was 0.42 logMAR (SD-0.16). The mean baseline Central subfield thickness (CST) was 423 microns (SD-78.5 microns). The final CST was 289 microns (SD-42 microns). The mean baseline BCVA in patients with PCV was 0.87 logMAR (SD-0.10) and it improved to 0.64 logMAR (SD-0.12 logMAR). 5/8 PCV patients showed complete resolution after a mean of 4.2 injections. 3 patients required supplemental photodynamic therapy. The mean number of brolucizumab injections to complete resolution of fluid in wet AMD was 6.3 (SD-2.3 injections). One patient developed occlusive vasculitis (reversed) and one patient developed macular hole.

Conclusions
Intravitreal brolucizumab is an effective and largely safe treatment for wet AMD and polypoidal choroidal vasculopathy. One eye developed vascular occlusion that was reversed completely with the use of low molecular weight heparin therapy. The patient who developed macular hole received successful surgery. Intravitreal brolucizumab therapy demonstrates good results in patients resistant to therapy with aflibercept or ranibizumab. The treatment interval could be increased by a mean of 4.2 weeks in all patients who needed 4 weekly injections with either aflibercept or ranibizumab. 5/8 patients with PCV showed resolution of polyps as demonstrated on ICG angiography.

Financial Disclosure
No financial relations
**Title**
Baseline OCT predictors of 3-year visual outcome for type 3 macular neovascularization

**Purpose**
Type 3 macular neovascularization (MNV) is an aggressive and often bilateral form of neovascular age-related macular degeneration (nAMD). Although the anti-vascular endothelial growth factor (VEGF) injections therapy has changed the natural history of nAMD, the treatment of type 3 MNV remains tedious with overall worse functional outcomes. In this way, identifying type 3 patterns featuring less favorable prognosis is of paramount importance. The aim of this study is to identify baseline optical coherence tomography (OCT) predictors of the 3-year visual outcome for type 3 MNV secondary to AMD treated by anti-VEGF therapy.

**Setting/Venue**
This is a longitudinal study of patients enrolled in Medical Retina and Imaging Unit of the Department of Ophthalmology, San Raffaele Scientific Institute in Milan, Italy.

**Methods**
Patients affected by exudative treatment-naïve T3 MNV were enrolled. The following baseline OCT features were analyzed: AMD phenotype (presence of drusen, reticular pseudodrusen, or both), presence of atrophy of retinal pigment epithelium, T3 stage, foveal involvement of exudation, AMD stage in the fellow-eye (dry AMD or nAMD), number of active T3 lesions, central macular thickness (CMT), subfoveal choroidal thickness (ChT), mean ChT, sublesion ChT, presence of hyperreflective dots (HRD), presence of intraretinal fluid (IRF), subretinal fluid (SRF), subretinal hyperreflective material (SHRM), pigment epithelium detachment, and neuroretinal thickness above the lesion. Univariate and multivariate analyses served to identify risk factors associated with the 3-year BCVA. Factors included in the multivariate model needed a p-value<0.3 in the univariate analysis.

**Results**
40 eyes of 30 patients (mean age 79±6 years old) were enrolled. Mean baseline best-corrected visual acuity (BCVA) was 0.34±0.28 LogMAR and significantly decreased to 0.52±0.37 LogMAR at the end of 3-year follow-up (p=0.002). Nineteen eyes were classified as Stage 2 T3 MNV, whereas 21 eyes as Stage 3. All patients displayed HRD and IRF at the baseline. In the univariate analysis, the following baseline features were associated with the 3-year BCVA outcome: baseline BCVA (p=0.007), AMD phenotype (p=0.041), foveal involvement of exudation (p=0.014), and presence of SRF (p=0.019). In the multivariate model, baseline BCVA (B=0.373, p=0.017), CMT (B=-0.363, p=0.045), number of active T3 lesions (B=-0.290, p=0.042), and presence of SRF (B=0.467, p=0.005) were associated with the 3-year BCVA outcome. Interestingly, 3-year BCVA was significantly lower in 19 eyes with SRF at the baseline (0.37±0.24 LogMAR, p=0.004) in comparison to 21 eyes without SRF (0.37±0.24 LogMAR, p=0.004).

**Conclusions**
The identification of biomarkers is of paramount importance in order to predict outcomes. In this study, we identified structural OCT features associated with the BCVA outcome after 3-year treatment with anti-VEGF injections. Differently from previous studies on nAMD, in our series the presence of SRF at the baseline was the most significant independent negative predictor of functional outcomes. Current findings may be employed to identify less favorable T3 patterns potentially deserving a more intensive treatment.

**Financial Disclosure**
None
Switch of anti-VEGF agent from Aflibercept to Bevacizumab: Outcomes in chronic wet AMD

### Purpose
Wet age-related macular degeneration (wet AMD) is the leading cause of severe visual impairment in the elderly population of the western world. Wet AMD is treated with intravitreal injections of anti-VEGF-agents. Currently, there are three anti-VEGF agents approved for treatment of wet AMD: ranibizumab, aflibercept and brolucizumab. In addition, bevacizumab is used off-label at a much lower cost. At the Department of Ophthalmology at the County Hospital of Vastmanland Sweden, treatment for wet AMD is given according to a treat-and-extend protocol using aflibercept, with the aim at increasing treatment intervals up to 14 weeks. However, there is a subset of eyes with chronic severe and highly active wet AMD in need of intense treatment with 4-weekly injections of anti-VEGF agent over several years. In an attempt to reduce drug-related costs at the department, we decided to switch anti-VEGF agent from aflibercept to bevacizumab in this subset of eyes beginning on January 1, 2020. A re-switch back to aflibercept was allowed in case of reduction in visual acuity, increase in macular edema or both. The aim of the present study was to evaluate the clinical outcomes of the switch of anti-VEGF agents and investigate the frequency of re-switch.

### Methods
Data from the Swedish Macular Register (SMR), electronic patient charts and imaging data (optical coherence tomography, OCT) from OCT 2000, Topcon were used. From the SMR, eyes with wet AMD on chronic 4-weekly anti-VEGF treatment for at least 12 months which had been switched from aflibercept to bevacizumab were identified. Follow-up for 12 months after the switch to bevacizumab was required for inclusion in the study. Main outcome measure was frequency of re-switch from bevacizumab to aflibercept over 12 months. The following data were collected: visual acuity (VA; ETDRS letters), central retinal thickness (CRT; µm), presence of intraretinal- (IRF)- subretinal- (SRF) and sub-RPE fluid (proportion of eyes; %) at the time of switch and at 12 months as well as number of anti-VEGF-treatments over 12 months. In case of re-switch to aflibercept, number of bevacizumab injections given at the time of re-switch and reasons for re-switch were collected. Statistical analysis was performed using SPSS (IBM). Mean and standard deviations (SD) are presented.

### Results
In total, 75 eyes were included. Mean age at the time of switch was 78.8 (SD 7.0) and 59% of patients were female. At inclusion, eyes had been on anti-VEGF-treatment for 4.5 (2.7) years. VA was ETDRS 66 (12) at treatment start and 68 (15) at switch. Proportions of eyes with IRF, SRF and sub-RPE fluid were 81%, 63%, and 32%, respectively and CRT was 221 (38) µm at switch. During the 12 months follow-up, a re-switch from bevacizumab to aflibercept was performed in 46 eyes (62%). The re-switch was due to increased macular edema in 34/46 (74%) eyes, reduced VA in 30/46 (65%) eyes or combination of these in 21/46 (46%) eyes. Three eyes were re-switched due to intraocular inflammation. In 22% of eyes, the re-switch was performed at the follow-up after the first bevacizumab injection and in 69% of eyes after a maximum of four bevacizumab injections. At 12-month follow-up, mean VA was ETDRS 66 (18) for all eyes. IRF, SRF and sub-RPE fluid was detected in 80%, 69%, and 37% of eyes, respectively and CRT was 227 (38) µm. Eyes were treated with a total 12 (2) anti-VEGF-injections over 12 months.

### Conclusions
In this study, we found that almost 40% of eyes with chronic, severe, highly active wet AMD on 4-weekly anti-VEGF treatment had stable vision and unchanged macular status on OCT over 12 months following switch from aflibercept to bevacizumab. On the other hand, worsening of the disease occurred in 62% of eyes after the switch to bevacizumab. In a majority of these eyes, the worsening occurred early after switch of anti-VEGF agent. In 2/3 of eyes, the deterioration was detected within four bevacizumab injections. After re-switch to aflibercept, VA and macular edema on OCT recovered. Our findings indicate that a subset of eyes on chronic 4-weekly anti-VEGF treatment remain stable after switch to bevacizumab. In case of worsening of VA and OCT after switch to bevacizumab, we found that it occurred early after change of anti-VEGF agent. If switch from aflibercept to bevacizumab is considered, close surveillance of VA and OCT is necessary, especially during the first 6 months. Re-switch to aflibercept should be performed promptly if deterioration is detected to avoid irreversible visual loss.

### Financial Disclosure
Elisabet Granstam: Novartis (consultant, advisory board), Bayer (advisory board), Allergan (advisory board, lecturing fee) Kersti Sjövall: Novartis (consultant, advisory board), Bayer (advisory board) Sandra Aurell: no financial relations Anna Paul: no financial relations Mats Rosén: no financial relations
Purpose
There have been recent, multiple, post-marketing case reports linking Beovu (brolucizumab) treatment with the findings of retinal vasculitis (RV) and/or retinal vascular occlusion (RO). These findings are typically in the presence of intraocular inflammation and have led to an update of the Beovu prescribing information. The reported cases predominantly occurred in the first several months after treatment initiation; a time of onset consistent with a possible immunologic mechanism. The purpose of the current study was to determine if patients similar to those in the case reports manifested evidence of a systemic immune response directed against brolucizumab.

Setting/Venue
BASICHR0049, a non-interventional study, collected at-home blood samples from patients in the USA who had received marketed Beovu.

Methods
From June to August 2020, blood (sera, plasma, peripheral blood mononuclear cells [PBMCs]) was collected from 11 patients treated with Beovu. Five of these patients had an RV/RO event while on Beovu and were no longer receiving Beovu at the time of blood collection. Six patients were receiving Beovu treatment and had not had an RV/RO event; they were considered controls. Blood was assayed for isotyping and titer determination of anti-drug antibodies (ADAs) against brolucizumab, in vitro T cell proliferation response to brolucizumab, and in vitro whole blood impedance platelet aggregometry.

Results
The RV/RO cases had a higher range of total ADA titer (1004 – 50950) compared to controls (200 – 790) and a higher frequency of neutralizing ADAs compared to controls (80% vs 0%, respectively). The ADAs measured were predominantly IgG isotype and IgG1 and IgG3 subclasses in both cases and controls. Upon in vitro stimulation with brolucizumab, PBMCs from RV/RO cases had a 1.3- to 1.5-fold increase (p=0.03) in total CD4 T cell activation and a 1.4- to 1.7-fold increase (p=0.11) in memory CD4 T cell activation compared to controls. When patient plasma was incubated in the presence of healthy volunteer whole blood and supraphysiologic concentrations of brolucizumab and VEGF-A, platelet aggregation was increased 2.9-fold (p<0.023) in RV/RO cases compared to controls.

Conclusions
Even in the setting of the COVID-19 pandemic, it was possible to obtain at-home collected blood from Beovu-treated nAMD patients. Beovu-associated RV/RO was characterized as a systemic, drug-specific, mature B cell and T cell mediated immune response that included downstream in vitro platelet aggregation.

Financial Disclosure
Employee, Novartis Institutes of BioMedical Research, Cambridge, MA, USA
Multimodal characterization of unaffected fellow eyes in patients with polypoidal choroidal vasculopathy in a caucasian cohort

**Purpose**
Polypoidal choroidal vasculopathy (VPC) is a chorioretinal pathology that is defined by the presence of an anomalous neovascular network associated with aneurysmal dilations, which develops between the choriocapillary and the retinal pigment epithelium (EPR), and which has traditionally been associated with sero-hemorrhagic detachments at the posterior pole. Concomitant choroidal changes, once present, can also affect the fellow eye, lacking characterization especially in Caucasian populations. Thus, this work aims to perform, in a sample of Caucasian patients with unilateral PCV, the multimodal imaging characterization of unaffected fellow eyes.

**Setting/Venue**
Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal (tertiary center, university hospital); Association for Innovation and Biomedical Research on Light and Image (AIBILI), Coimbra, Portugal.

**Methods**
Multicenter retrospective cohort study with a sample of 55 unaffected fellow eyes from patients diagnosed with unilateral PCV confirmed by Indocyanine Green Angiography (AVI). The sample was characterized in the baseline by color fundus photography, spectral domain optical coherence tomography (SD-OCT), fluorescein angiography and with indocyanine green. Morphological characteristics of both the retina and the choroid were evaluated in multimodal scope. The SD-OCT of the last follow-up visit was also evaluated in order to exclude evolution to VPC / choroidal neovascularization.

**Results**
From our initial sample (77 patients), 11.7% of patients had bilateral PCV. The 55 patients included had a median age of 74±15 years. After 15.5±6.4 months of follow-up, only one developed disease (1.9%). Soft drusen were present in 32.7% of the fellow eyes, hard drusen in 27.3%, reticular pseudodrusen in 5.4% and pachydrusen in 23.6%. Pigmentary changes were also present in 29.1% of the cases. The thickness of the central retina was 273.4±37.0um, subfoveal choroid thickness was 238.3±83.0um, with signs of pachychoroid (both focal and diffuse) present in 47.2% of the sample. We identified the double layer sign in 36.4% of the cases, elevation due to detachment of the retinal pigmented epithelium in 5.4%, disruption of the EPR due to epitheliopathy / pigmentary changes in 16.4% and presence of fluid in 9.1% of the cases. EPR atrophy was present in 10.9% of the sample. In AVI, choroidal vascular dilation was present in 63.6% of patients, diffuse hyperfluorescence in 49.1%, punctiform hyperfluorescence in 52.7%, anastomoses in the posterior pole occurred in 18.2% of cases and late geographic hyperfluorescence in 16.4%, Branching vascular network was identified in only 1.8% of cases.

**Conclusions**
The pachychoroid signs in the OCT and AVI were present in more than half of the cases and the double layer sign in more than a third. They are very relevant findings for the better characterization of this pathology and for the understanding of its pathogenesis, being able to translate different phases of its progression.
Purpose
Geographic atrophy (GA) is an advanced form of the non-neovascular (dry) type of age-related macular degeneration (AMD). Late-stage clinical trials suggest that intravitreal injections of novel therapeutics may slow down the rate of GA progression by up to 29% in one year, thus allowing people with GA to preserve central vision for a longer period. While intravitreal injections have become an established treatment modality for neovascular (wet) AMD, it is unknown whether patients with (more gradually progressing) GA would accept regular injections that slow down, but do not stop or reverse, vision loss. Patients are more likely to adhere to treatment recommendations and to benefit from improved clinical outcomes if they consider an intervention acceptable. Therefore, our group has begun to explore whether regular intravitreal injections will be acceptable as treatment for people living with GA, and the factors that may affect treatment acceptability. This work presents learnings from the initial patient involvement phase of the 'AGAIN' study, working with a patient advisory group of eight individuals living with GA who are helping to shape the overall AGAIN study’s design, analysis and dissemination.

Methods
In an initial discussion, we asked each of the eight advisory group members about their knowledge and understanding of GA, and their hopes for what treatment for GA might achieve. On the basis of this initial discussion, we compiled an information pack about GA which was posted out to our patient advisors. This contained general information about emerging intravitreal treatments being investigated in phase 3 clinical trials, their potential benefits and risks, and a brief proposed outline of our study on acceptability of intravitreal injections. We conducted follow-up calls with the patient advisors to discuss their interim thoughts on the information received by post. We tested out a range of structured and semi-structured questions to explore the acceptability of intravitreal injections for people living with GA. Lastly, we explored various methods of communicating reduction in rate of progression of GA lesions. Key points from the discussions were collated using the principles of the framework method of qualitative analysis, and we generated analytic summaries that encapsulated these discussions.

Results
All of the advisors had GA in at least one eye, with total GA area between 1.5mm3–19mm3. Advisors were relatively knowledgeable about dry AMD being gradually progressive compared to wet AMD, although knowledge about GA specifically, including the terminology of ‘geographic atrophy’, was relatively low. In general, improvement of vision or reversal of visual loss was seen as ‘a bonus’, but all hoped that treatment would stop progression and prevent deterioration from current status. There was anxiety about the injection process, particularly among those who were injection-naïve. Advisors were concerned about any potential side-effects of treatment, the long-term effects of potentially lifelong treatment, potential consequences of missing appointments, and how described benefits would translate to their lived experience. They reasoned that personal circumstances (e.g. age; comorbidities; living/family situation; distance from and mode of transport to hospital), as well as individual differences in risk tolerance and in the value attributed to maintaining vision, would influence acceptability. We discussed how they interpreted ‘up to 29%’ slowing down of GA progression; most found this figure understandable but abstract. There was uncertainty regarding whether this rate of slowing would remain constant, and what the 29% slowing meant for likely continuation with vision-related daily activities.

Conclusions
Working with an advisory group of people living with GA has alerted us to the complexities that surround ‘acceptability’, and consequently the likely challenges for real-world adherence to and persistence with potential new intravitreal treatments for GA. Although such treatments are yet to be approved, we believe it is vital to consider prospective acceptability, in order to anticipate issues that could be addressed in advance; for instance, in terms of setting clear expectations, and providing adequate patient education and service delivery planning. This initial phase of patient advisory group discussions has informed the development of an ongoing mixed-methods pilot study, to explore the acceptability of intravitreal injections for GA. We will use a combination of quantitative, Likert-type scale questions, a semi-structured interview, and a patient preference task modelled on discrete choice experiments, to explore the attributes (e.g. injection frequency, time spent in hospital, probability of side-effects, potential benefit) that may influence prospective acceptability of intravitreal injections among people living with GA. Our research is being guided by the Theoretical Framework of Acceptability (Sekhon et al., 2017), and will be used to develop validated, standardised tools to assess acceptability in GA and retinal diseases more broadly.
**Title**
Investigation of choroidal vasculature in non-neovascular age-related macular degeneration patients with reticular pseudodrusen

**Purpose**
Age related macular degeneration is the leading cause of the blindness among older people in developed countries. It was divided into neovascular and non-neovascular age related macular degeneration. The clinical hallmark of the non-neovascular age related macular degeneration is accumulation of the extracellular material under retinal pigment epithelium called drusen. Drusen are subdivided into hard drusen, soft drusen, cuticular drusen, autosomal dominant drusen and reticular pseudodrusen. The aim of this study was to compare choroidal thickness, luminal area, stromal area and choroidal vascularity index in patients with reticular pseudodrusen and drusen.

**Setting/Venue**
The study was conducted at Ege University School of Medicine Department of Ophthalmology. It was approved by local ethic committee of Ege University School of Medicine and adhered to the tenets of the Declaration of Helsinki.

**Methods**
This retrospective analysis was performed among patients with reticular pseudodrusen and drusen who presented at our Retina subdivision. Inclusion criteria were age ≥55 years, the presence of five or more medium-large drusen, reticular pseudodrusen which detected on both infrared imaging and OCT in 2 or more quadrant. Exclusion criteria were neovascular age related macular degeneration, scar, hemorrhage, geographic atrophy, previous treatment including anti vascular endothelial growth factor, photodynamic therapy, or laser photocoagulation. After a detailed ophthalmic examination, infrared reflectance images and optical coherence tomography with enhanced depth imaging mode obtained from all patients. Images were evaluated by 2 independent retina specialist. Image binarization and stromal area, luminal area and choroidal vascularity index were obtained by Image J program. Statistical analysis was performed using SPSS software (version 20; SPSS Inc, Chicago, Illinois, USA). Demographic characteristics were evaluated by chi square test and intergroup evaluations performed by student t test. A p-value less than 0.05 (typically ≤ 0.05) is considered as statistically significant.

**Results**
A total of 100 eyes of 100 patients with non neovascular age related macular degeneration recruited to the study (48 eyes of 48 patients with reticular pseudodrusen (Group 1) and 52 eyes of the 52 patients with drusen (Group 2)). Female/Male ratio was 56/44. The mean age of the Group 1 patients 73.63±6.14 (61-91) years; 69.43±6.97 (59-87) in Group 2 patients. The difference was statistically significant (p=0.005). Choroidal thickness, total choroidal area, stromal area and luminal area was significantly lower in Group 1 patients (p values <0.001 Respectively) and choroidal vascularity index, foveal thicknesses was not statistically significant between groups.(p values 0.214 and 0.384 respectively). Reticular pseudodrusen was detected in 48/48 (100%) of the patients in superior quadrant, in 41/48 (85.4%) of the patients in temporal quadrant in 36/48 (75%) of the patients in nasal quadrant and in 34/48 (70.8%) of the patients in inferior quadrant.

**Conclusions**
Total choroidal area, stromal area and luminal area which reflecting choroidal vasculature were decreased in patients with reticular pseudodrusen. These results may lead to obtain valuable data to detect pathophysiology of the disease.

**Financial Disclosure**
No financial interest for all authors
Multiple clinical vision tests reveal heterogeneous deficits in intermediate AMD

**Purpose**
People classified as having structural signs of intermediate age-related macular degeneration (iAMD) may actually have an assorted profile of visual function loss. For example, individuals with iAMD have been shown to have difficulty in low luminance and low contrast conditions. Establishing evidence for this heterogeneity of visual function (VF) in people classified with iAMD would be useful for future trial design, regulatory purposes and studies of new therapies. We take advantage of cross-sectional data collected from a large multi-centre study (MACUSTAR) with a wide range of clinical visual function assessments, to test the hypothesis that large numbers of people with iAMD have visual function deficits not seen in peers with no signs of AMD.

**Setting/Venue**
MACUSTAR is a prospective multi-centre clinical study with 20 sites across seven European countries comprising cross-sectional and longitudinal arms. Here we present cross-sectional data collected from 18 clinical sites.

**Methods**
All cross-sectional participants classified as having iAMD or no AMD were included. Disease classification was performed according to the Beckman classification by a central reading centre. Clinical VF assessments included: best-corrected visual acuity (BCVA); low luminance visual acuity (LLVA); Moorfields acuity chart (MA); Pelli-Robson contrast sensitivity (CS); International Reading Speed Test (IReST); average threshold from mesopic and scotopic fundus-controlled perimetry (mAT and sAT; Macular Integrity Assessment, CenterVue, Italy) and rod intercept time (RIT) from dark adaptometry (AdaptDx, Maculogix, USA). Measurements from participants with no signs of AMD defined a one-sided normal reference limit (at a 5% level) for each test. Where data were normally distributed, reference limits were defined as the mean of the no AMD group ± 1.64 standard deviation (SD). Where data were not normal, a direct method taking the 5th percentile as the limit was also calculated and the most ‘conservative’ limit used. Proportion of iAMD participants exceeding the 5% reference limit (worse function) on each test was calculated. With eight tests, 33.6% of iAMD participants would be expected to exceed the reference limit on at least one test by chance (binomial probabilities) under the null hypothesis that their VF is equivalent to visually healthy peers.

**Results**
A total of 168 participants with iAMD (63% female, mean [SD] age 71 ± 8 years) and 56 visually healthy peers with no AMD (59% female, mean [SD] age 68 ± 6 years) were used in the analysis. The following reference limits for each test were estimated: BCVA: >0.10 LogMAR; LLVA: >0.28 LogMAR; MA: >0.53 LogMAR; CS: <1.44 LogCS; IReST: <93 wpm; Mes AT: <21.74dB; Sco AT: <17.04 dB and RIT: >6.39 mins. More people with iAMD exceeded the reference limit on low contrast (MA, 25%; CS, 20%) and low luminance tests (LLVA, 33%; mAT, 24%; sAT 24%; RIT, 34%) than high contrast tests (BCVA, 17%; IReST, 11%). We found 116 participants with iAMD (69%) exceeded the reference limits on at least one VF test. Sixty-seven (40%) exceeded the reference limits on at least two VF tests.

**Conclusions**
A large proportion of participants with structurally defined (Beckman) iAMD were estimated to have deficits in clinical tests of VF that fall outside reference limits established in visually healthy peers under the same testing conditions. The estimate was more than two-fold greater than that expected by chance. This evidence of heterogeneity in VF in iAMD is relevant to the design and participant inclusion criteria of planned trials for interventions in iAMD, especially those looking to halt or slow photoreceptor degeneration and loss. It remains to be seen whether participants with iAMD who have VF deficits are more likely to progress to late AMD, or whether these findings are a reflection of various stages of progression within those with iAMD. This will be established in the longitudinal arm of MACUSTAR.
Morphological associations with visual and disease activity in eyes with PCV

To evaluate influence of baseline imaging features on visual and anatomical outcomes in eyes with PCV treated with anti-VEGF monotherapy.

In this prospective clinical study we enrolled participants with treatment-naïve PCV who followed a treat-and-extend protocol using intravitreal aflibercept (IVA) monotherapy. Baseline clinical features evaluated included Best corrected visual acuity (BCVA), traditional features such as lesion size and fluid-related OCT parameters and novel parameters using automated software. This included quantitative and qualitative Pigment epithelium detachment (PED) parameters [height, volume]; and choroidal parameters [choroidal thickness (CT), choroidal volume (CV) and choroidal vascularity index (CVI)]. We evaluated the predictive value of each parameter on visual and anatomical outcome at month 12. We additionally evaluated initial treatment response after 3 monthly injections with respect to month 12 outcomes.

Lower baseline BCVA (p=0.02) and lower baseline CRT (p=0.04) were significantly associated with better vision at month 12. Compared to eyes with persistent disease activity (n=22, 44%), eyes with inactive disease at month 12 had lower baseline CRT (p <0.001), lower baseline PED height (p<0.01), lower baseline PED volume (p<0.01), lower proportion with choroidal hyperpermeability (17.9% vs 46.2%, p=0.02) and lower choroidal vascularity index (CVI) (p<0.02). Larger (per 100nm) decrease in CRT and larger PED volume reduction (per 100nl) at month 3 from baseline were associated with greater BCVA gain and inactive disease.

PED morphology has additional predictive value to traditional biomarkers of disease activity in eyes with PCV undergoing anti-VEGF monotherapy. With increasingly precise quantification, PEDs can be a crucial biomarker in addition to traditional parameters and may aid in retreatment decisions.

no financial conflicts to declare
OCT-A characterization of evolving lesions in fellow eyes of exudative type 3 MNV patients

Purpose
Type 3 macular neovascularization (MNV) is the second most frequent subtype of MNV in neovascular age-related macular degeneration (AMD). Patients diagnosed with unilateral type 3 lesions were reported to develop exudation in the fellow-eye during a 3-year follow-up. However, the diagnosis of a pre-clinical stage (i.e. nascent form) of the neovascularization may guide an early treatment of patients with better outcomes. The aim of the current study is to investigate evolving lesions in fellow eyes of exudative type 3 MNV patients by assessing the presence of a pre-clinical neovascular component.

Setting/Venue
This is a longitudinal study involving 3 retinal referral centers (the Medical Retina and Imaging Unit of the San Raffaele Scientific Institute in Milan, Italy, Department of Ophthalmology, Hospital Intercommunal de Creteil, University Paris Est in Creteil, France and of Bietti Foundation in Rome, Italy).

Methods
Patients affected by unilateral exudative treatment-naïve T3 MNV were enrolled. Fellow-eye was evaluated at the baseline and during 3-year FU using optical coherence tomography angiography (OCTA). Two retinal experts (readers) independently investigated the presence of a preclinical nascent T3 MNV (i.e. non-exudative form) and the development of an active T3 MNV (i.e. exudative form) over time.

Results
Twenty-five patients (mean age 82±9 years old) were enrolled. Among 25 eyes, 9 eyes (36%) displayed the presence of a nascent non-exudative T3 MNV at the baseline, that developed exudation (i.e. active form) after a mean of 9 ± 7 months. Five out of 25 eyes (20%) did not display neovessels at the baseline but showed a nascent non-exudative T3 after a mean of 12 ± 6 months before developing exudation. Five out of 25 eyes (20%) presented with an active exudative T3 MNV with no detectable nascent T3 stage, whereas 6 out of 25 eyes (24%) did not develop MNV during the follow-up. Overall, in the current series, T3 MNV in the fellow eye accounted for 76% (both exudative and non-exudative T3 MNV) over 3 years by combining prevalence and incidence.

Conclusions
The occurrence of a nascent non-exudative form of type 3 MNV is a frequent event in the fellow eye of patients affected by unilateral type 3 MNV and it often precedes the development of an active exudative form of type 3 MNV. OCTA allows better defining prevalence and incidence of T3 MNV in fellow eyes. Such approach may be employed to perform an early diagnosis and treatment of patients affected by type 3 MNV.

Financial Disclosure
None
Clinical and demographic factors associated with loss to follow-up in patients with geographic atrophy secondary to age-related macular degeneration

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Purpose
This observational study used the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) to compare the demographic and clinical characteristics of geographic atrophy (GA) patients with less than 2 years and 2+ years of follow-up. There is a lack of systematic analyses describing clinical care and monitoring of patients with GA, partly due to the absence of a therapy. A previous IRIS Registry study investigating clinical characteristics and outcomes of a GA cohort found that a substantial proportion of patients may be lost to follow up (LTFU) over time. The current study identifies demographic and clinical characteristics that increase risk of LTFU in this sub-group.

Setting/Venue
The IRIS Registry is the world's largest comprehensive eye disease clinical database. It comprises data from electronic health records of more than 66 M patients in the U.S. This retrospective observational study analyzed data from 2,558 practices.

Methods
This analysis first identified patients with a diagnosis of GA between January 1, 2016 and December 31, 2017. The start date was chosen based on availability of an International Classification of Disease (ICD)-10 code for GA and specified laterality, allowing for stratification of patients by disease stage. Patients were excluded from the analysis when any of the following conditions were met: if demographic information was entirely absent from the entry (some subjects were included with partial demographic information); if visual acuity data was incomplete or missing; if the patient had a history of any other retinal condition(s) such as retinal vein occlusion, diabetic retinopathy, or myopic neovascularization; or if the subject was seen at a practice that had contributed to the IRIS Registry for less than 2 years. The study included a bivariate analysis of the less than 2 years and 2+ years of follow-up cohorts. Variables included patient-level demographics and clinical characteristics. Covariates strongly associated with LTFU were included in a backwards stepwise multivariable logistic regression model to estimate the odds of less than 2 years of follow up. An exploratory analysis included the relationship between LTFU and provider type.

Results
Overall, 230,174 patients with documented GA in at least 1 eye during the study period were identified, and 142,474 GA patients met the inclusion criteria. Of these, 40.6% (n=57,788) had less than 2 years of follow-up. The multivariable model identified numerous factors that increased the odds of LTFU, such as: older age (80+ years old), Medicaid or no insurance, management by an optometrist at index, VA worse than 20/40 in the study eye or fellow eye, and increased distance to a provider. Factors contributing to lower risk of LTFU included: younger age (60-80 years old), management by a retinal specialist at index, fellow eye diagnosis of nAMD, and concomitant glaucoma/cataract diagnosis/procedure (i.e. trabeculectomy or pseudophakia). In our exploratory analysis of visit frequency, we found that patients with 2+ years of follow-up were seen more frequently in the first year, particularly by retina specialists, with an average of 4.09 visits (standard deviation (SD) = 3.26) vs. LTFU patients (mean = 2.91 visits; SD = 2.59). This trend held in the second year, as non-LTFU patients were seen at 4.08 visits (SD = 3.18) vs. 2.16 visits (SD = 1.83) in LTFU patients.

Conclusions
An analysis of these US practices demonstrates that a significant number of GA patients are LTFU in a real-world setting. The multivariable analysis revealed patient factors that can inform decision making of both individual providers and the broader healthcare system. Although these results are based entirely on US practices, some of the findings may be generalizable to European practice patterns. For instance, while payer status does not directly translate to the European system, factors like age and visual acuity are likely to remain consistent factors in contributing to LTFU. It will be crucial to understand this patient population as therapeutic options become available for GA.

Financial Disclosure
Verana Health, Consultant
"I’d trade some of my life to stop the scotoma getting bigger": Simulations to elicit health state utility values in progressing geographic atrophy

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Purpose
Geographic atrophy (GA) can manifest as development of an absolute scotoma, an area of absence of function in the central retina. In turn, this can have a serious impact on health-related quality of life. New treatments for GA, which promise to halt or slow the progress of the disease, must be subject to health economic evaluation - these are not trivial exercises to do. Typically, regulatory bodies recommend that the public (not patients) value health states to derive utility values for economic evaluation of new treatments. We demonstrate how a computer-based gaze contingent simulated scotoma can be combined with a time trade-off (TTO) experiment to elicit utility values about severity of progressing scotoma in GA.

Setting/Venue
University based cross sectional study in people with normal vision.

Methods
Adults with normal vision were recruited and instructed to watch four films of everyday scenes shot from a point-of-view camera. Films were incorporated into a computer-based set-up, using an eye tracker, which applies a ‘simulated’ scotoma in correspondence to the user’s gaze. Before each film participants were told to imagine this condition would be their permanent vision. In experiment 1, participants viewed a film with a very large scotoma obscuring most (60%) of the screen followed by a film with a very small scotoma (2% of the screen) in the peripheral visual field. In experiment 2 participants viewed two ‘realistic’ central scotoma calculated from microperimetry measurements taken in GA patients; these conditions were similar but obscured 5% and 8% of the film respectively, with the latter encroaching on the point of regard, mimicking how GA might progress to foveal involvement. After each film, participants were asked to choose between 10 years of life with the condition they just observed versus varying amounts of perfect vision in 1-year decrements from 10 to 0 years. The difference between their choice is the number of years of perfect health they would trade to avoid the condition with the scotoma (TTO value [years]).

Results
Seventy-five young adults (52 female; median [interquartile range] age of 21 [20 to 22] years) with normal or correct-to-normal vision, established by a short optometric examination, completed the study. Each participant session lasted approximately 30-40 minutes. Films/conditions were presented in random order. In experiment 1, mean (SD) TTO value for the very large and very small scotoma was 5.0 (2.7) and 1.9 (1.4) years respectively. This means, for example, for a 10-year period, participants were prepared on average to trade 5.0 (95% confidence interval [CI]: 4.4-5.6) years of perfect health to avoid ten years of life with the very large scotoma. The mean (95%CI) difference of 3.1 (2.6, 3.6) years between the conditions in experiment 1 demonstrates the utility and good understanding of the task. In experiment 2 the mean (SD) TTO value for two realistic scotoma was 2.6 (1.9) and 3.5 (2.1) years respectively; the mean (95%CI) difference of 0.9 (0.5, 1.3) years was clearly different from zero and was statistically significant (P=0.001). This is an important result suggesting that even relatively small differences in GA like scotoma can be quantified as preferred years of perfect vision in a TTO experiment in volunteers with normal vision.

Conclusions
We have shown how a computer based gaze contingent simulated scotoma can be combined with a TTO experiment to elicit utility values about severity of progressing scotoma in GA from people with normal vision. Specifically we have evidence that relatively small differences in GA like scotoma can be quantified as preferred years of perfect vision. In economic evaluation of healthcare interventions, utilities represent the strength of individuals’ preferences for different health states. Conventionally the valuations fall between 0 and 1, with 1 representing the valuation of a state of perfect health. TTO experiments are accepted to be a direct method for calculating a utility and our value for the difference between the progressing GA like scotoma would be considered 0.09; this is a significantly large utility value. Our methodology for eliciting utility values for vision impairment in members of the public may be preferable to previous approaches (e.g. obscuring contact lens) and will be useful in health economic evaluation of promised treatments for slowing progression of GA or other eye diseases that manifest scotoma.

Financial Disclosure
DPC: Allergan, Bayer, Santen, THEA (Honoraria); Allergan, Apellis, Roche, Santen (Unrestricted funding); Centervue, Apellis (Consultant)
Title
The RAP study, report 5: Rediscovering macular neovascularization type 3 - Multimodal imaging of fellow eyes over 24-months

Purpose
To explore the degenerative condition of fellow eyes of patients with newly diagnosed macular neovascularization type 3 (MNV3), and to verify whether the retinal-choroidal anastomosis (RCA), first recognized at the fibrosis stage, develops equally in all MNV types.

Setting/Venue
94 (76 solitary, 18 multifocal) eyes with MNV3 in addition to 96 eyes with MNV2 and 96 eyes with MNV1 as two control groups were included.

Methods
Multimodal imaging including optical coherence tomography, color fundus photography, fluorescein angiography was performed at least at three different visits. The degenerative condition including the development of fibrosis with or without RCA of fellow eyes over 24 months.

Results
In the solitary MNV3 group 32 (42.1%) eyes showed early/intermediate AMD, 25 (33%) eyes showed MNV3, 11 (14.5%) eyes experienced fibrosis, of which 4 (5.2%) had a RCA, 7 (9.2%) eyes had atrophy after resolved MNV3 and 1 (1.3%) eye developed MNV1. In the multifocal MNV3 group 2 (11.1%) eyes showed early/intermediate AMD. 9 (50%) eyes showed 15 MNV3 lesions. 4 (22.2%) eyes showed fibrosis, of which 2 (11.1%) manifested with a RCA. 3 (16.7%) eyes showed atrophy after resolved MNV3. The number of eyes with a RCA accounted for 40% of the total eyes with fibrosis. The count of simultaneous bilateral multifocal MNV3 was 5 (55.6%). No concurrent MNV1 or MNV2 were found. In MNV1 and MNV2 groups the scarring was seen in 11 (11.7%) and 12 (12.8%) eyes, but no eye developed a RCA. The higher incidence of RCA in MNV3 group was statistically significant compared to the control group (p:0.0001).

Conclusions
RCA is an exclusive clinical feature of MNV3 and this type (MNV3) was therefore first described by Oeller in 1904. The development of fibrosis in MNV3 has dramatically decreased after the introduction of anti-angiogenic therapy. Multifocal lesions are frequently bilateral and emerge simultaneously. In bilateral cases the multifocal phenotype in one eye tends to emerge prior to the development of a solitary one in the partner eye. The atrophy seen in treated eyes is related to the angiogenic features rather than coexisting dry AMD.

Financial Disclosure
BHN: Retinsight, unrelated to this study. GD: none. GM: none. SS: Roche, Novartis, Bayer all unrelated to this study, USE: Bayer/Novartis/Boehringer-Ingelheim/Alcon/Kinarus, all unrelated to this study. BG: Novartis/Kinarus/IDx, all unrelated to this study.
Comparative assessment of the maximum thickness of pigment epithelial detachments and sub-RPE fluid in patients treated with Brolucizumab versus Aflibercept in the HAWK & HARRIER studies

**Purpose**
The presence of pigment epithelial detachments (PEDs) and sub-retinal pigment epithelium (sub-RPE) fluid may be indicators of disease activity (DA) in neovascular age-related macular degeneration (nAMD). This post hoc analysis compares the efficacy of brolucizumab and aflibercept treatment in reducing the maximum thickness of PED and sub-RPE fluid in the macula in patients with nAMD in the HAWK & HARRIER studies.

**Setting/Venue**
HAWK (NCT02307682) and HARRIER (NCT02434328) were two 96-week, prospective, randomized, double-masked, active controlled, multicenter studies that enrolled 1,775 patients across 11 countries in HAWK and 1,048 patients across 29 countries in HARRIER.

**Methods**
Patients were randomized 1:1:1 to brolucizumab 3 mg, 6 mg or aflibercept 2 mg in HAWK or 1:1 to brolucizumab 6 mg or aflibercept 2 mg in HARRIER. After three monthly loading doses, brolucizumab patients received q12w dosing with an option to adjust to q8w at predefined DA assessment visits; aflibercept was dosed in a fixed q8w regimen. Here, we present a retrospective analysis of optical coherence tomography images from patients in the pooled HAWK & HARRIER studies treated with brolucizumab 6 mg (n=700) or aflibercept 2 mg (n=696). Images were assessed for the maximum thickness or height of PED (measured from the RPE inner border to the Bruch’s membrane) and sub-RPE fluid (between the RPE and Bruch’s membrane) across the macula at baseline through Week 96. In addition, PED and sub-RPE thickness from baseline to Week 96 were compared in the subgroup of patients in both treatment arms who had DA at Week 16, which was the first DA assessment visit after loading. As brolucizumab patients with DA were adjusted to q8w dosing until the end of the study, these two subgroups were matched in terms of number of injections and treatment interval.

**Results**
In this pooled analysis, least square mean (LSM) (±SE) PED thickness in the brolucizumab group was 202.8, 139.0 (3.7), 122.9 (3.7) and 116.0 (3.7) µm at baseline, Weeks 16, 48, and 96, respectively, whereas in the aflibercept group it was 202.8, 152.5 (3.7), 142.3 (3.8) and 134.0 (3.8) µm. For sub-RPE fluid, LSM thickness in the brolucizumab group was 64.3, 14.0 (2.2), 10.0 (2.1) and 10.8 (2.0) µm at baseline, Weeks 16, 48, and 96, respectively, whereas in the aflibercept group it was 64.3, 22.4 (2.2), 19.5 (2.1) and 15.5 (2.1) µm. The observed better reductions in the pooled analysis were also seen in the individual studies. In patients with DA at Week 16, LSM PED thickness in the brolucizumab arm (n=152) was 234.4, 200.0 (9.3), 173.1 (9.5) and 156.8 (10.0) µm at baseline, Weeks 16, 48 and 96 respectively; in the aflibercept-treated subgroup (n=215), it was 234.4, 208.7 (7.8), 198.3 (8.1) and 180.9 (8.5) µm. LSM sub-RPE thickness in the brolucizumab arm was 76.7, 20.0 (6.1), 8.9 (5.9) and 7.3 (5.0) µm at baseline, Weeks 16, 48 and 96 respectively whereas in the aflibercept-treated subgroup, it was 76.7, 40.2 (5.1), 31.3 (5.0) and 21.0 (4.3) µm.

**Conclusions**
The results of this analysis show that brolucizumab achieved greater reductions in PED and sub-RPE fluid thickness in the macula than aflibercept over the 96-week study period in both the overall pooled treatment arms and in the matched subgroups with DA at Week 16 in HAWK & HARRIER.

**Financial Disclosure**

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Purpose
To investigate the visual and anatomical impact of treatment deferral during the COVID-19 lockdown on patients affected by neovascular age-related macular degeneration (nAMD) in a tertiary clinical setting.

Setting/Venue
Medical Retina Department, Jules Gonin Eye Hospital, Fondation Asile des Aveugles, Lausanne, Switzerland

Methods
A retrospective case series of patients that were scheduled to receive intravitreal (IVT) injections treated according to the Observe-and-Plan (O&P) regimen during the Swiss lockdown (16th March - 26th April). Two groups of patients were included: patients that continued to receive their scheduled IVT treatment without clinical consultation (Group Continue 'C'), and patients for whom the IVT injections were completely deferred until the end of the lockdown (Group Stop, 'S'). Functional and anatomical parameters were collected based on optical coherence tomography (OCT) scans at four different time points, before (T-1, T0) and after (T1, T2) the lockdown.

Results
394 eyes of 314 patients were included, with 215 eyes in group C and 179 eyes in group S. In group C, baseline best available visual acuity (VA) was 0.29 ± 0.32 logMAR (20/40 Snellen equivalent) and it did not change significantly after the lockdown, being 0.30 ± 0.36 logMAR at T1 (20/40, p=.083). In group S, best available VA was respectively 0.32 ± 0.41 (20/40) and 0.40 ± 0.43 logMAR (20/50) at the pre- and post-lockdown visits (p<.001) and slightly improved after the reprise of the treatment (0.39 ± 0.51 logMAR at T2, 20/50) but it did not recover to the values before the lockdown, being significantly worse in comparison to baseline (p<.001). Mean central subfield thickness (CST) remained stable at the pre- and post-lockdown visits in group C (288±89 µm and 294±88 µm respectively, p=.449) while it increased in group S from 278±65 µm to 322±106 µm after the lockdown (p<.001) and it returned to pre-lockdown values after treatment recover (281±78 µm, p=.365).

Conclusions
Our results showed that treating patients with an injection-only approach was effective in managing nAMD patients during the first COVID-19 pandemic lockdown, while patients that deferred their scheduled treatment showed partially irreversible deterioration of visual function. These results could help retina specialists to manage future pandemic scenarios by developing successful management strategies.

Financial Disclosure
None to disclose.
Exploratory investigation of reticular pseudodrusen in Asian patients

Purpose
1) To investigate the feature of AMD patients having reticular pseudodrusen (RPD).  2) To observe the association of RPD with advanced AMD and impact of RPD on visual function

Setting/Venue
Cross sectional study

Methods
Patients having intermediate AMD in any eye were recruited from the patients visiting the clinic. Fundus photography, fundus autofluorescence image, optical coherence tomography (OCT) and OCT angiography (OCTA) were obtained. Visual acuity and microperimetry data were used to assess the visual function. Drusen type was determined in each eye. Participants were divided as to having RPD or not. AMD severity was scored as AREDS severity scale.

Results
Total 626 eyes of 313 patients were recruited. Patients having RPD in any eye was 108 (34.5%). Female was predominant (85%) and average age was 76.5 years. Gender distribution (Female 87.0% vs 83.4%, P = 0.358) and age (average 76.9 vs 76.3, P=0.496) was not different between RPD and non RPD group. Geographic atrophy (GA) was found in 1% of RPD group and 2% of non RPD group (odds ratio 0.4605 (0.0471-2.341)). Choroidal neovascularization (CNV) was observed in 7% of RPD group and 10% of non-RPD group (odds ratio 0.6288 (0.2981-1.2508)). Comparing visual function of intermediate AMD eye, mean retinal sensitivity and visual acuity were not different between RPD and non RPD group. Central retinal sensitivity was significantly lower in RPD group (17.4 ± 5.4 vs 18.0 ± 6.7, P=0.298)

Conclusions
RPD was found in 30% of intermediate AMD. Advanced AMD prevalence including GA and CNV, were not different whether RPD present or not. Central retinal sensitivity was lower in eye having RPD while visual acuity and mean retinal sensitivity was not different.

Financial Disclosure
We have no financial relation with any company.
Comparison of anatomical and functional outcomes of Ranibizumab and Aflibercept treatment in patients with age-related macular degeneration resistant to bevacizumab: a one-year real life study

Purpose
To compare the long term anatomical and functional outcomes of intravitreal ranibizumab versus aflibercept in patients with neovascular age-related macular degeneration resistant to bevacizumab.

Setting/Venue
Retrospective, cohort study, Kütahya Health Science University Hospital

Methods
This study included 63 eyes of 63 patients with nAMD resistant to bevacizumab treatment. In the case of residual intraretinal and subretinal fluid on optical coherence tomography image and/or no improvement visual acuity and/or no more than 100 μm central macular thickness decreases from baseline after a minimum of 4 monthly bevacizumab injections were defined as resistant to bevacizumab treatment. Patients who were switched from bevacizumab to ranibizumab or aflibercept were followed for 12 months. Data were obtained from medical records for retrospectively included patients. The treatment protocol included 3 monthly injections of ranibizumab or aflibercept as a loading phase after bevacizumab treatment and then treat and extent treatment. Primary outcome measures were mean changes in visual acuity, central retinal thickness and pigment epithelial detachment (PED) height at the end of the 12-month follow-up.

Results
Thirty two eyes of 32 patients were received ranibizumab injection, and 31 eyes of 31 patients received the aflibercept injection. Mean number of injections given at the end of the 12 months in aflibercept and ranibizumab groups were 7.6 and 7.8, respectively (p >0.05). Mean central retinal thickness decreased from 421.5 ± 154.8 to 231.4 ± 53.7 μm at 12 months in ranibizumab group (p < 0.001) and from 442.7 ± 152.3 to 224.6 ± 65.1 μm in the aflibercept group (p< 0.001). Also, PED height reduced from 182.4 ± 86.2 to 89.6 ± 32.8 μm in ranibizumab group (p < 0.001) and from 179.5 ± 83.1 to 51.7 ± 26.3 μm in the aflibercept group (p < 0.001). Mean PED height reduction was significantly higher in the aflibercept group (p < 0.05), whereas the changes in central retinal thickness was not statistically significant differences between groups (p>0.05). Visual acuity improved significantly at the 12 months in both groups (0.98 ± 0.35 to 0.62 ± 0.23 logMAR, p<0.001 in the ranibizumab group and 1.1 ± 0.41 to 0.69 ± 0.34 logMAR, p<0.001 in the aflibercept group). However, the increase in mean visual acuity favored the aflibercept group (p < 0.05).

Conclusions
The present study showed that the both of ranibizumab and aflibercept treatment were effective in eyes with nAMD resistant to bevacizumab therapy. However, anatomical and functional results were found to be better in the aflibercept treatment group compared with ranibizumab group in the long term follow-ups.

Financial Disclosure
no have financial relation
### Purpose

Age-related macular degeneration (AMD) is the leading cause of blindness in the United Kingdom (UK) and is associated with a significant cost to the healthcare system. In the UK, standard care for the treatment of neovascular AMD (nAMD) is intravitreal injection of anti–vascular endothelial growth factor inhibitors (anti-VEGF). Treatment success, in terms of the ability to achieve disease control and preserve visual function, relies on early diagnosis of nAMD followed by prompt initiation and continued timely maintenance of therapy. Due to the chronic nature of nAMD, ongoing follow-up and review of treatment requires patients to regularly attend retinal clinics for many years. As such, clinical service-related considerations including capacity, staffing, service structure and operational delivery are key to minimising delays and optimising patient outcomes. There are, however, limited studies describing real-world practices for the management of patients within the UK. The overall aim of the RATE Study in nAMD was to describe the current landscape of nAMD treatments and clinical outcomes during the first 24 months after initiating anti-VEGF treatment. As part of this study, we aimed to understand the structure of current clinical services utilised for the management of nAMD patients treated with anti-VEGF therapy in the UK.

### Setting/Venue

The RATE study involved the collection of pseudonymised patient and service-level data about current treatment practices and outcomes for patients newly initiated on licensed anti-VEGF therapy at eighteen hospitals within the UK National Health Service. Participating centres were from a diverse setting of teaching and district general hospitals known to routinely treat patients with nAMD and were spread geographically across England and Wales. As part of this study, a bespoke cross-sectional survey was completed by nominated healthcare professionals at each centre: initial survey results are reported here.

### Methods

A clinical staff member from each participating study centre was nominated by their principal investigator to complete a survey about the structure of current services used for the management of nAMD patients treated with anti-VEGF therapy at their centre. This person was required to (i) be a healthcare professional who was routinely involved in the treatment and management of patients with nAMD receiving anti-VEGF treatment; (ii) be able to provide accurate information about clinical practice over the past two years at that centre and (iii) give their consent to take part. The completing clinician was asked questions for two timepoints; the end of December 2017 and current service at the time of survey completion. All surveys were completed between November 2020 and February 2021. The self-reported data received for each question were pooled across all study centres and summarised using descriptive statistics (the denominators for the analyses, based on the total number of evaluable responses received for each question, are also provided in the results).

### Results

At the time of survey completion, a median (interquartile range [IQR]) of 1810 (900–2625) patients with nAMD per centre were estimated to be receiving anti-VEGF treatment (based on estimates provided by 16 centres). 71% (n=12/17) of centres used ‘one stop’ clinics for the management of patients while 29% (n=5/17) used a combination of ‘one stop’ and ‘two stop’ clinics. 65% (n=11/17) of centres currently used virtual clinics for the management of patients with nAMD who are receiving anti-VEGF treatment (at the end of 2017, 35% [n=6/17] of centres used virtual clinics). Anti-VEGF injections could currently be administered by non-physicians at all centres (n=17), with a median (IQR) of 1050 (465–1850) patients per centre estimated to receive injections from non-physicians. All respondents (n=17) reported that their centre provided specific guidance about the type of treatment regimen used to administer anti-VEGF (i.e. that their centre had a preference that is communicated to physicians). Specific guidance about fixed treatment regimen was given at 41% (n=7/17) of centres, while 59% (n=10/17) of centres provided guidance on pro re nata (PRN) treatment regimes and 76% (n=13/17) on treat-and-extend (T&E) regimes.

### Conclusions

Early results from the RATE study provide insight into the current structure of nAMD services in the UK, including the adoption of different approaches for improving care delivery which may reflect strategies to alleviate burden in light of high patient caseloads and/or adaptations made in light of the COVID-19 pandemic. At the time of survey completion (which occurred during the pandemic), three quarters of the centres surveyed used one stop clinics for the management of patients and all centres allowed non-physicians to administer injections. Virtual clinics were used for the management of patients with nAMD at approximately two-thirds of centres, with usage appearing to have increased from 2017 when approximately one-third of centres used virtual clinics. Guidance on alternative treatment regimes that allow for longer intervals between injections were available at over half of centres (76% of centres provided guidance on T&E and 59% on PRN regimes, respectively). These data may serve as a benchmark for evaluating future retinal services and for planning for changes to the management of nAMD in the post COVID-19 era.

### Financial Disclosure

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Fiona Glen: Employee of Open Health, who have received...
Patient and retina specialists’ preferences in neovascular age-related macular degeneration treatment: A Discrete Choice Experiment

Purpose
Neovascular age-related macular degeneration (nAMD) leads to severe and permanent visual impairment, significantly impacting patients’ quality of life and functional independence. Although treatment with anti-VEGF prevents and, in some cases, reverses visual damage, the need for frequent monitoring visits and intravitreal injections represents a significant burden on patients, caregivers and retina specialists. The objective of this study was to elicit preferences for nAMD treatment characteristics from the perspectives of patients and retina specialists.

Setting/Venue
Patients diagnosed with nAMD who started treatment with anti-VEGF drugs, indicated for nAMD, between November 1st, 2016 and March 31st, 2017 in 20 tertiary (high complexity) public and private hospitals of all the Spanish regions.

Methods
A discrete choice experiment was conducted. Participants were asked to select one of two hypothetical treatments resulting from the combination of five attributes (effects on visual function, effects on retinal fluid, treatment regimen, monitoring frequency and cost); their levels were identified by reviewing the literature and two focus groups. The relative importance (RI) given to each attribute was estimated using a mixed logit model. The marginal rates of substitution (MRS) were calculated taking cost as the risk attribute.

Results
A total of 110 patients (P) [79.0 (SD:7.4) years; 57.3% women; 2.3 (SD:0.7) years with nAMD; 2.1 years (SD:0.1) in treatment] and 66 retina specialists (RS) participated in the study. Participants gave greater RI to improvements in visual function [60.0% (P); 52.7% (RS)], lower monitoring frequency [20.2% (P); 27.1% (RS)] and reduction in retinal fluid [9.8% (P); 13.0% (RS)]. Patients and retina specialists would agree to an increase in cost by 65.0% and 56.5%, respectively, in exchange for improving visual function; and 25.5% and 43.3% for delaying monitoring frequency by one month.

Conclusions
For patients and retina specialists, treatment election is determined by its ability to improve visual function. Treatment monitoring requirements are also considered, mainly from the retina specialist perspective. These results suggest that the use of more efficacious anti-VEGF agents with a longer duration of action would facilitate better disease management, fulfilling the unmet needs of patients and retina specialists.

Financial Disclosure
Title
Choroidal vascularity index changes characterize different cohorts of dry age-related macular degeneration

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Purpose
To investigate the choroidal vascular index (CVI) among different cohorts of dry age-related macular degeneration (dAMD) compared to healthy subjects.

Setting/Venue
This is a retrospective study of patients enrolled in Medical Retina and Imaging Unit of the Department of Ophthalmology, San Raffaele Scientific Institute in Milan, Italy.

Methods
In this study, four distinct cohorts were collected: three cohorts with different dAMD phenotypes (i.e. drusen, reticular pseudodrusen [RPD], and geographic atrophy [GA] group) and an age-matched cohort of healthy subjects (controls). All patients were investigated using a multimodal imaging approach, including CVI in the subfoveal 1000μm area. CVI was defined as the ratio between the luminal choroidal area (LCA) and the total choroidal area (TCA).

Results
One hundred and twenty eyes (120 patients) were included (30 eyes in each cohort). The mean age was 76.6±7.1 years, and the 4 cohorts of patients did not show statistical differences in terms of age population, axial length, and central macular thickness among study groups. TCA showed a different distribution among the 4 cohorts (p=0.003), mainly due to the changes of LCA (p=0.001). Interestingly, CVI showed a different distribution between the 4 cohorts (p<0.001). In detail, RPD showed a lower CVI in comparison to controls (p=0.040), whereas GA showed a lower CVI in comparison to drusen, RPD, and controls (p=0.001, p=0.046, and p<0.001, respectively).

Conclusions
Different cohorts of dAMD are characterized by different impairments of the choroidal vascular and stromal components (i.e. CVI), reflecting different degrees of AMD severity. CVI provides insights for better understanding the pathogenesis of AMD, and we anticipate a potential role in the prognosis of dAMD patients.

Financial Disclosure
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The Archway phase 3 trial of the port delivery system with Ranibizumab (PDS) for nAMD: Data update and key surgical pearls

### Purpose
The Port Delivery System with ranibizumab (PDS) is an investigational drug delivery system designed for continuous intravitreal ranibizumab release through a surgically implanted, refillable ocular implant. The Archway trial evaluated the safety and efficacy of the PDS for the treatment of neovascular age-related macular degeneration (nAMD). Here, we present results from the Archway September 2020 data cut and report key surgical pearls from the optimization and standardization of the PDS implant insertion procedure.

### Methods
Patients were randomized 3:2 to treatment with the PDS with ranibizumab 100 mg/mL with fixed 24-week (W) refill-exchanges (PDS Q24W) or intravitreal ranibizumab 0.5 mg injections every 4W (monthly ranibizumab). Archway enrolled 418 patients; 251 were randomized to and 248 received treatment with the PDS Q24W, and 167 were randomized to and received treatment with monthly ranibizumab. All patients had received a diagnosis of nAMD within 9 months of screening and were responsive to anti–vascular endothelial growth factor (VEGF) treatment, with ≥3 intravitreal anti-VEGF injections within the previous 6 months. The trial evaluated noninferiority (NI) and equivalence of the PDS Q24W versus monthly ranibizumab on the primary endpoint of best-corrected visual acuity (BCVA) change from baseline averaged over W44/48, with a difference (95% CI) of –0.2 (~1.8, +1.3) letters between arms (equivalence not tested). 98.4% (242/246) and 94.6% (228/241) of PDS Q24W patients assessed for supplemental treatment need did not receive supplemental ranibizumab during the first or second refill-exchange intervals, respectively. The mean total treatment number (initial fill, refill-exchanges, and supplemental injections) through September 2020 was 3.9 (PDS Q24W) versus 19.5 (monthly ranibizumab). PDS implant insertion and refill-exchange procedures were generally well tolerated and the ocular safety profile was generally unchanged from the primary analysis. Systemic safety findings were comparable across arms. Edge-to-edge pars plana laser ablation while maintaining a final incision size of 3.5 mm ensures a secure implant fit and postoperative hemostasis. Delicate/precise handling and dissection of the conjunctiva and Tenon's capsule during peritomy and closure is critical to preserve tissue integrity over the implant. Capturing both the conjunctiva and Tenon's capsule is key when anchoring to the anterior limbus with scleral bites. Meticulous hemostasis ensures optimal visualization and minimizes vitreous hemorrhage risk.

### Results
Change in adjusted mean BCVA score from baseline averaged over W44/48 was 0.0 (PDS Q24W) versus +0.2 (monthly ranibizumab). PDS Q24W was noninferior to monthly ranibizumab at W44/48, with a difference (95% CI) of –0.2 (~1.8, +1.3) letters between arms (equivalence not tested). 98.4% (242/246) and 94.6% (228/241) of PDS Q24W patients assessed for supplemental treatment need did not receive supplemental ranibizumab during the first or second refill-exchange intervals, respectively. The mean total treatment number (initial fill, refill-exchanges, and supplemental injections) through September 2020 was 3.9 (PDS Q24W) versus 19.5 (monthly ranibizumab). PDS implant insertion and refill-exchange procedures were generally well tolerated and the ocular safety profile was generally unchanged from the primary analysis. Systemic safety findings were comparable across arms. Edge-to-edge pars plana laser ablation while maintaining a final incision size of 3.5 mm ensures a secure implant fit and postoperative hemostasis. Delicate/precise handling and dissection of the conjunctiva and Tenon's capsule during peritomy and closure is critical to preserve tissue integrity over the implant. Capturing both the conjunctiva and Tenon's capsule is key when anchoring to the anterior limbus with scleral bites. Meticulous hemostasis ensures optimal visualization and minimizes vitreous hemorrhage risk.

### Conclusions
As previously reported, Archway met its primary endpoint, demonstrating that PDS Q24W treatment resulted in noninferior and equivalent vision outcomes compared with monthly ranibizumab when averaged over W36/40. BCVA results for the average of W44/48 were consistent with the primary analysis, with the PDS Q24W noninferior to monthly ranibizumab treatment. Over 90% of patients did not receive supplemental treatment before each refill-exchange procedure. The PDS was generally well tolerated, with a favorable benefit-risk profile. Attention to laser application, hemostasis control, and proper handling of the conjunctiva and Tenon's capsule during the PDS implant insertion procedure is important to minimize complications. To maximize optimal surgical outcomes, the procedure requires careful attention to elements generally not emphasized in other vitreoretinal procedures. With a view to supporting optimal patient outcomes, the PDS procedures have evolved based on learnings from the trial.
Short-term evaluation of treatment for refractory neovascular age-related macular degeneration

Purpose
Intravitreal injections (IVI) of anti-vascular endothelial growth factor (VEGF) agents is the cornerstone of management of neovascular Age-related Macular Degeneration (nAMD), dramatically improving its prognosis. Some cases remain incomplete responders despite maximal monthly injections. These cases are sometimes referred to as refractory. However, the short term response profile is poorly understood. The goal of the present study was to study their short term response in between monthly IVI and identify factors associated with the short term response profile.

Setting/Venue
Monocentric prospective study conducted in the tertiary referral center of Jules Gonin Eye Hospital, Lausanne, Switzerland.

Methods
Patients were prospectively selected from the regular AMD clinic. Patients with refractory nAMD were recruited, defined by the presence of intraretinal (IRF) and/or subretinal fluid (SRF) at monthly monitoring visits over at least 6 months, despite monthly IVI. Patients with confounding retinal diseases or poor image quality were excluded. A complete ophthalmic exam was performed at baseline (next IVI), and weekly for 4 weeks. In addition, SD-OCT and infrared images were obtained at each visit. A fluorescein angiography (FA), indocyanine green angiography (ICGA), and color fundus photography were also performed at baseline. Fluid metrics were quantified using an artificial intelligence (AI) algorithm. This allowed computations of IRF volumes, SRF volumes, and pigment epithelium detachment (PED) volumes at each visit.

Results
A total of 28 eyes of 26 patients were enrolled. Central retinal thickness (CRT), PED volume, and IRF and SRF volumes all significantly decreased one week after IVI. Maximal fluid reduction was reached on average at 1.93 weeks. At week 4 the values reached levels similar to baseline and the significant difference was lost. Large response variation was observed between the patients: the percentage of fluid resolution showed quartile limits at 36.6%, 70.1%, and 88.6%, respectively. No imaging factor was identified as significantly associated with the relative response. However, the amount of residual fluid was associated with more baseline SRF (r=0.76, p=0.0001) and larger PED (r=0.65, p=0.0001).

Conclusions
A majority of patients with so called refractory nAMD are in fact short term responders to treatment, with a maximum response after approximately two weeks and an early relapse at week four. However, presence of residual fluid was frequent, and an important proportion of patients showed little fluid change in between injections. The size of PED and the amount of SRF was associated with more residual fluid. Further studies are needed to understand the reasons for this truly refractory fluid.
To understand the characteristics, treatment patterns and outcomes in neovascular age related macular degeneration (nAMD): Rationale and design of a multicentre real-world study in India

Purpose
Age-related macular degeneration (AMD) is responsible for 8.7% of global blindness with its impact severe in the developing countries, such as India. The neovascular AMD (nAMD), sub-type accounts for 90% of severe vision impairment cases. The anti-vascular endothelial growth factor (anti-VEGF) agents are mainstay of treatment and have been able to preserve the vision and improve the quality of life (QoL) in nAMD. Despite, clinical trials demonstrating positive visual outcomes with agents over different study durations, the real-world evidences have reported attenuated visual gains. It has been observed that on prolonged use, there is a difference in response to the anti-VEGF therapy at patient level, apart from difference in tolerance level. Moreover, there exists very limited real-world clinical data/ with studies restricted to a few clinics/ institutes or a specific region within the Indian subcontinent. Thus, the objective of this study is to understand real-world data for visual acuity (VA) related outcomes, treatment patterns including injection burden, treatment adherence and monitoring patterns in the real world setting amongst nAMD patients in India. This study aims to gain insights on the overall treatment compliance with follow-up data of at least 2 years.

Setting/Venue
This is a non-interventional, retrospective, non-comparative, non-randomized study across multiple zones (multi-centre) in India. The study will include treatment naïve nAMD, newly diagnosed patients ≥50 years of age (at Index date). Secondary data source i.e., Electronic Medical Record (EMR) database of Retina Clinics/ Hospitals from different zones across India will be used to collect approximately 300 anonymized patients’ data for over a period of at least 24 months of follow-up period to analyze primary, secondary and exploratory objectives.

Methods
The study will aim to enroll approximately 300 patients from approximately 8-10 sites across north, south, east and west zones of India during the study period (01 Mar 2015 and 30 Mar 2020). The study will include newly diagnosed treatment naïve nAMD patients aged ≥ 50 years of age at Index date; who received ranibizumab or aflibercept or bevacizumab or biosimilar ranibizumab between 01 Mar 2015 and 30 Mar 2018 (Index period). The eye will be the unit of analysis in this study; therefore, a patient may have one or two study eyes. Other additional inclusion criteria for this study includes patients with VA/OCT assessments at baseline, Month 12 and Month 24; patients treated with intravitreal injection of anti-VEGF (received at least one anti-VEGF injection during the post-index follow-up period and at least 2 visits with OCT in between Months 0-12); and patients with minimum follow-up period of 24 months. (Received at least one anti-VEGF injection and at least 1 visit with OCT in between Months 13-24) All data extracted from EMR shall be anonymized. The study has been registered on CTRI (Clinical Trials Registry of India) and has been initiated after approval from local ethics committee of selected sites.

Results
Demographic profile and baseline characteristics of nAMD patients would be recorded (age, gender, co-morbidities, findings of fundus fluorescein angiography [FFA], color fundus photography [CFP], OCT, etc.). The data collected will be used to evaluate the effect of anti-VEGF agents on anatomical parameters (CRT, fluid) at months 3, 6, 18 & 24 and study its association with changes in functional outcome from baseline to Months 3, 6, 18 and 24. Also the data would be used to characterize the treatment patterns with anti-VEGF therapy, total number of visits, number of anti-VEGF injections and number of non-injection visits during the first 2 years of treatment after initiation of an anti-VEGF agent (Month 0-12, Month 13-24). Furthermore, the data collected will also be utilized to characterize the number of fluid free visits, treatment compliance and anti-VEGF switch rate. The primary objective is to explore the association between anatomical outcomes (presence/absence) at Month 12 and changes in functional outcome at Month 12. 5. The predictive value of age, baseline VA, proper loading phase (yes/no), number of anti-VEGF injections (maintenance phase), baseline IRF (Intra-retinal fluid) (presence/absence), baseline SRF (Sub-retinal fluid) (presence/absence) on the VA gains at Month 12 would be also studied.

Conclusions
This first of its kind pan-India multi-centre real world study using EMR data analysis will help to understand the patient characteristics and demographics, current treatment patterns with anti-VEGF injections and VA outcomes, association of visual and anatomical outcomes, treatment burden and adherence. The data generated through this study will assist in adapting the real world Anti-VEGF treatment patterns and outcome to take a rationale evidence based decision in clinical practice to better manage nAMD patients in Indian subcontinent.
Title
Optical coherence tomography angiography parameters correlated to the growth of macular neovascularization in age-related macular degeneration

Purpose
Quantitative optical coherence tomography angiography (OCTA) allowed to perform several steps forward in the comprehension of the complex pathogenesis of macular neovascularization (MNV) secondary to age-related macular degeneration. This study investigated the quantitative OCTA parameters associated with size modifications of neovascular network over 1 year of follow-up and treatment. The main aim was to identify the factors involved in the MNV size changes over follow-up, especially pointing out the role of MNV vessel tortuosity (VT), MNV reflectivity and MNV subtypes. Moreover, we evaluated the potential predictive role of these factors regarding the direction of the expansion or reduction of the neovascular lesion over the follow-up.

Methods
The study included patients with type 1, mixed or type 2 MNV diagnosed by structural OCT and by fluorescein angiography (FA) examinations. We excluded all the other MNV lesions because they are not easily detectable on OCTA. All the patients underwent Ranibizumab 0.5 mg intravitreal treatment, including a loading dose with 3 monthly injections, followed by further anti-VEGF administrations according to a treat and extend regimen. In the study, we measured for each eye the vessel tortuosity (VT) considering it as an indirect sign of MNV blood perfusion, higher values corresponding to a higher blood flow. We applied a MNV VT cutoff of 8.40 to obtain Group 1 (MNV VT<8.40) and Group 2 (MNV VT>8.40) at baseline. In addition, we calculated the reflectivity value of the MNV area and we divided it in eight different sectors. In the sectors displaying low reflectivity at baseline, we observed if MNV size changes occurred at the end of the follow-up, considering only cases with at least 20% of size difference during the study. All the measurements were performed at baseline, after the loading dose of 3 anti-VEGF injections and at the end of the 1-year follow-up.

Results
We recruited 28 eyes (28 patients). Mean BCVA was 0.36±0.21 LogMAR, improved to 0.28±0.22 Log-MAR (p<0.01) with a mean of 8±3 injections. 15 eyes showed MNV type 1 (54%), 9 mixed type (32%), 4 type 2 (14%). Eyes belonging to MNV VT>8.40 group (50% of our cases) showed worse outcome in terms of BCVA, OCTA parameters and outer retinal atrophy (46%vs20%; p<0.01). Furthermore, a mean MNV reflectivity value of 101 was associated with high probability of changes in MNV size (larger or smaller). MNV growth was directly related to MNV VT values. In particular, MNV VT>8.40 was associated with higher increases in MNV size (p<0.01). Moreover, MNV growth was influenced by the type, with type 2 and mixed type lesions being related with greater expansions in MNV size (p<0.01). Remarkably, the association of MNV type + MNV VT>8.40 was associated with higher MNV enlargement rate (p<0.01). MNV sectors showing low reflectivity values resulted prone to greater neovascular growth (p<0.01). MNV type 2 (or mixed type) combined with MNV VT>8.40 and low MNV reflectivity showed cumulative effect in determining MNV expansion (p<0.01). Conversely, MNV lesions with low VT values might experience size reductions (34 % of cases).

Conclusions
The study highlighted quantitative OCTA parameters associated with changes of MNV lesions. These metrics lead to the identification of highly perfused MNV lesions, to the assessment of MNV size modifications and of the direction of the expansion. In particular, higher MNV VT values were correlated with more aggressive lesions and with greater MNV growing during the follow-up. Furthermore, we found a cumulative effect of type 2 or mixed MNV associated with MNV VT>8.40 and low MNV reflectivity values on MNV size increase. The lower MNV reflectivity might be correlated with immature and unstable neovascular structures which can undergo more size changes with respect to neovascular network mainly characterized by higher MNV reflectivity values. In our investigation, the number of intravitreal injections was not significantly associated with modifications of the quantitative OCTA parameters. In conclusion, the proposed OCTA-based approach provided a way to quantitatively characterize the dynamic changes occurring in AMD-related MNV.
Title
Prevalence and area of retinal pigment epithelium and outer retinal atrophy in eyes with non-exudative macular neovascularization

Purpose
To assess the prevalence of complete Retinal pigment epithelium (RPE) and outer retinal atrophy (cRORA) in patients with unilateral exudative Age-Related Macular Degeneration (AMD) of the fellow eye and establish if the presence of non-exudative macular neovascularization (NE-MNV) influences the prevalence of RPE and outer retinal atrophy in eyes with AMD.

Setting/Venue
Retrospective single-center study that took place in Centro Hospitalar Universitário S. João (Porto, Portugal), a tertiary university hospital.

Methods
Observational cross-sectional study of 69 patients with unilateral exudative AMD. Demographic and clinical data were collected and multimodal retinal imaging was performed in all patients. Two groups of patients were defined according to the presence (NE-MNV) or absence (No NE-MNV) of NE-MNV in the study eye. We compared the prevalence of cRORA and differences in cRORA area between groups.

Results
The prevalence of cRORA in eyes of patients with unilateral exudative AMD of the fellow eye was 14.7% (10 eyes) and the overall mean area of cRORA was 9.25 ± 7.50 mm². The prevalence of NE-MNV in these eyes was 14.7% (10 eyes). Eyes with NE-MNV and eyes without NE-MNV had a similar prevalence of cRORA (20% (2 eyes) and 14% (8 eyes), respectively; p=0.64). Eyes with NE-MNV had a significantly lower mean area of cRORA (2.07±0.24 mm² vs. 11.05±7.34 mm²; p=0.01) compared with the No NE-MNV group.

Conclusions
There were no significant differences in the prevalence of complete RPE and outer retinal atrophy between eyes with or without NE-MNV. Nevertheless, eyes with NE-MNV presented significantly lower cRORA areas, which suggests that this type of neovascularization may prevent the progression of RPE and outer retinal atrophy. Longitudinal studies are required to confirm these preliminary results.

Financial Disclosure
No financial disclosures.
Title
Short-term OCT-angiography changes of type 1 macular neovascularization in exudative AMD treated with intravitreal Afibercept

Purpose
To assess short-term OCT-Angiography changes in type 1 macular neovascularisation (MNV) secondary to exudative Age-related Macular Degeneration (AMD) after intravitreal Afibercept treatment.

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
In a prospective monocentric study conducted in the Department of Ophthalmology of the Military Hospital of Tunis from October 2020 to February 2021, we included seven eyes of seven patients with type 1 MNV treated with intravitreal Afibercept. All patients underwent OCT-Angiography (Optovue RTVue XR Avanti, AngioVue) before and 3 days after intravitreal treatment. OCT-A 6 mm × 6 mm metrics of the MNV area, the superficial (SCP) and deep capillary plexus (DCP) as well as the foveal avascular zone (FAZ) area were analyzed in all eyes.

Results
We enrolled seven patients (3 males and 4 females). The mean age was 69.7 ± 8.3 years. MNV mean area decreased significantly 3 days after intravitreal Afibercept (p<0.001). Cystoid macular edema initially present in two eyes decreased. Serous retinal detachment (6 eyes) decreased in 5 cases (83.3%). The qualitative evaluation showed that narrow MNV vessels density tended to decreased, even so larger MNV vessels remained steady. Flow signal from the choriocapillaris layer decreased in all cases. Vessel density in the SCP and the DCP remained unchanged as well as the FAZ area (all p>0.05).

Conclusions
OCT-Angiography is a non-invasive valuable tool, able to assess short-terms changes of type 1 MNV structure after intravitreal Afibercept therapy.

Financial Disclosure
NO
Short-term efficacy and safety outcomes of Brolucizumab in the real-life clinical practice

**Purpose**
To report the early efficacy and safety outcomes of treatment with intravitreal injections of brolucizumab (IVT-B) in patients presenting neovascular age-related macular degeneration (nAMD) in a tertiary clinical setting

**Setting/Venue**
Medical Retina Department, Jules Gonin Eye Hospital, Lausanne, Switzerland

**Methods**
A retrospective case series of patients that received IVT-B with a minimum of two injections performed and at least four weeks of follow-up

**Results**
Nineteen eyes of 19 patients were included. The total number of IVT-B performed was 58 (mean 3.0 ± 1.0; range 2 - 6) injections per patient and an average follow-up time of 14.4 ± 9.0 (range 4.0 - 35.8) weeks. Mean baseline best-corrected visual acuity was 0.4 ± 0.4 logMAR and at the last follow-up was 0.4 ± 0.6 logMAR (p=0.774). All eyes showed a reduction in retinal thickness, with the central subfield thickness being 477 ± 153 µm at baseline and 373 ± 149 µm at the last follow-up (p=0.041). Intra-retinal fluid was present at baseline in 12 eyes (63%) and in three eyes (16%) at the last follow-up (p=0.065). Sub-retinal fluid was present at baseline in 17 eyes (89%) and at the last follow-up in three eyes (16%, p=0.011). Pigment epithelium detachment was apparent in the 16 eyes (84%) at baseline and was still present in 14 eyes (73%, p=0.811). One adverse event of intraocular inflammation was noted.

**Conclusions**
In our short-term experience, brolucizumab was highly effective in restoring the anatomy and in stabilizing the visual acuity of eyes with nAMD. Its safety profile should be evaluated carefully and needs further investigations.

**Financial Disclosure**
None to disclose
Title
Patient-reported low-luminance impairment in intermediate age-related macular degeneration corresponds with visual function in the MACUSTAR study

Purpose
Individuals with intermediate age-related macular degeneration (iAMD) have visual function (VF) impairments which are most prominent in low-luminance and low-contrast surroundings. The Vision Impairment in Low Luminance (VILL) questionnaire has been specifically developed to capture the impact of these functional deficits on vision-related quality of life. The relationship between measurable impairment in functional tests and patient-reported outcome (PRO) measures has been sparsely studied but represents an important prerequisite to understand how the visual deficit impacts people with iAMD in their daily lives. We investigated associations between VILL-based self-report and visual function in the MACUSTAR study.

Setting/Venue
Multi-centre cohort study in 20 ophthalmologic referral centres from seven European countries.

Methods
All participants of the iAMD and no AMD groups within the cross-sectional part of the MACUSTAR study were included. PRO measures included the reading and mobility subscales of the VILL questionnaire (Rasch person measures). Function assessments included best-corrected visual acuity (BCVA), low-luminance visual acuity (LLVA), Moorfields acuity chart test (MA), Pelli-Robson contrast sensitivity (CS), average threshold of mean sensitivity in mesopic and scotopic fundus-controlled perimetry (mAT and sAT; Macular Integrity Assessment), rod intercept time in dark adaptometry (AdaptDx) and International Reading Speed Texts reading speed (IReST). AMD was categorized according to the Beckman classification. Participants who reported difficulties on the subscales of the VILL and poor performers of VF assessments were defined based on test performance within the no AMD group. The threshold was set per individual assessment, at a test result worse than the no AMD group’s mean ± 1.64 standard deviations (SD) for normally distributed parameters or the 5th percentile for non-normally distributed parameters. Overlaps between individuals with poor VILL scores and poor performers in function tests were compared. In iAMD participants, linear regression controlled for age, sex and number of comorbidities, were used to perform the associations. Overlaps between individuals with poor VILL scores and poor performers in at least two function tests. The relationship between PRO measures and overall VF. Thus, considering more than one functional measure seems necessary to capture the patient-relevant VF deficit in iAMD. The functional tests most associated with low VILL person measures were LLVA (overlap with low VILL person measures in 15 individuals, 44%) sAT (overlap with low VILL person measures in 14 individuals, 41%), CS and MA (overlap in 13 individuals, 38%, respectively). In multivariable regression models across all participants with iAMD, the VF assessments BCVA, CS, sAT and IReST were significantly associated with the VILL reading subscale (ps0.043). BCVA, mAT and sAT were significantly associated with the VILL mobility subscale (ps0.014) in all iAMD participants.

Results
A total of 168 participants with iAMD (63% female, mean age 71±8 years) and 56 people with no AMD (comparator group; 59% female, mean age 68±6 years) were included in the analysis. Thirty-four individuals with iAMD (20%) reported impairment outside the defined limits in at least one subscale and 16 (10%) reported impairment in both subscales. 116 participants with iAMD (69%) were poor performers in at least one function test, 67 (40%) were poor performers in at least two function tests. 31 (86%) people with low VILL scores also performed poorly in at least 1 functional test, 18 (53%) people with low VILL scores also performed poorly in at least 2 functional tests. The relationship between PRO measures and overall VF. Thus, considering more than one functional measure seems necessary to capture the patient-relevant VF deficit in iAMD. The functional tests most associated with low VILL person measures were LLVA (overlap with low VILL person measures in 15 individuals, 44%) sAT (overlap with low VILL person measures in 14 individuals, 41%), CS and MA (overlap in 13 individuals, 38%, respectively). In multivariable regression models across all participants with iAMD, the VF assessments BCVA, CS, sAT and IReST were significantly associated with the VILL reading subscale (ps0.043). BCVA, mAT and sAT were significantly associated with the VILL mobility subscale (ps0.014) in all iAMD participants.

Conclusions
Self-reported visual functioning and vision-related quality of life under challenging light conditions including low luminance and low contrast situations corresponds to VF measures in iAMD in the MACUSTAR study. The function measures LLVA, CS, MA, sAT, mAT, BCVA and IReST were most strongly with the reading and mobility subscales of the VILL. However, no single VF assessment alone could explain this relationship between PRO measures and overall VF. Thus, considering more than one functional measure seems necessary to capture the patient-relevant VF deficit in iAMD. The reliability of the chosen thresholds and the association between functional assessments and structural biomarkers in the context of a structurally-defined disease classification (Beckman classification) remain to be investigated.

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**Title**
Influence of fibrosis on visual outcomes in eyes with neovascular age-related macular degeneration

**Purpose**
To describe the rate of development of fibrosis over 10 years and its relationship with visual outcome in eyes with neovascular age-related macular degeneration (nAMD)

**Setting/Venue**
Moorfields Eye Hospital, London, UK

**Methods**
Single centre, non-interventional cohort study of nAMD patients initiated on intravitreal anti-VEGF injections in 2008-2009 with follow-up for at least 10 years. All participants were treated according to standard of care. Visual acuity (VA) in Early Diabetic Retinopathy Study (ETDRS) letters, injection records, spectral-domain optical coherence tomography (SD-OCT) scans, colour fundus photos (CFP) and fundus fluorescein angiography (FA) were analysed. The images were graded by 2 retinal physicians and fibrosis was determined based on multimodal imaging. Main outcome measure was incidence of fibrosis and its impact on visual outcome over 10 years.

**Results**
We included 142 eyes (142 patients) of which 19 (13.4%) had fibrosis at baseline, 72 (50.7%) developed new fibrosis by 10 years and 51 (35.9%) never had fibrosis. The incidence of new fibrosis at 1st, 2nd, 5th, 7th and 10th year of follow up was 9 (7.3%), 19 (16.7%), 32 (33.7%), 7 (11.1%) and 5 (8.9%). The mean (SD) gain in VA in the 1st year was 7.8 (±3.1) in baseline fibrosis group, 8.9 (±3.8) in new fibrosis group versus 12.3 (±2.8) in no fibrosis group (p<0.001). Mean VA change at 10 years was -3.1, -1.1 and 0 letters in baseline fibrosis, new fibrosis and no fibrosis group respectively (p<0.05). The prevalence of macular atrophy at 10 years was 26.3%, 72.2% and 31.4% in the 3 groups respectively. Presence of intraretinal fluid (p<0.05), persistent pigment epithelial detachment (p<0.01) and classic choroidal neovascularization (p<0.01) were significantly associated with fibrosis. There was no statistically significant difference in the number of injections received among all groups. Mean central retinal thickness was significantly less in eyes with no fibrosis 198.5 (±74.1) microns versus eyes with baseline fibrosis 216.3 (±41.1) and new fibrosis 224.9 (±55.6) (p<0.05).

**Conclusions**
We describe the incidence of fibrosis over long term follow up of eyes with nAMD. The incidence of new fibrosis declines after 5 years and significantly determines VA outcomes at 1 year and 10 year of follow-up as well. Eyes with new fibrosis had the highest prevalence of macular atrophy indicating common factors for development of both morphological outcomes. Intraretinal fluid and persistent pigment epithelial detachment were significant factors determining fibrosis whereas injection frequency had no role. These results emphasize the need for use of antifibrotic agents along with anti-vascular endothelial growth factors for treatment of nAMD.

**Financial Disclosure**
None
Title
Genetic characterization and progression of age-related macular degeneration in the Coimbra Eye Study: Common, rare risk variants analysis and Genetic Risk Score

Purpose
The heritable component in AMD is estimated to be as high as 70% and to date, 52 variants at 34 genomic regions are known to be associated with increased risk of disease development and progression. Strategies such as calculating the genetic risk score (GRS) can also be useful if integrating the genetic information with environmental and demographic factors when assessing individual risk. The Coimbra Eye Study (CES) is an epidemiologic study for the estimation of prevalence and 6.5-year incidence of AMD in a Portuguese population (NCT01298674, NCT02748824). This report aims to explore the effect of common and rare genetic risk variants in the development of AMD in the CES population and to calculate the GRS.

Methods
Participants in the CES underwent standardized interviews, ophthalmologic examination, and imaging in both visits. AMD staging was performed with Rotterdam classification in a centralized reading center. Two analyses for common variants were performed, a case-control analysis and a progression to AMD analysis. In the first, cases were AMD patients (stage 2,3 or4) and non-AMD cases were participants staged 0 (>60years-old) or 1 (>70years-old) at the follow-up visit. In the progression analysis, non-progressors were participants that remained in stage 0 or 1 through follow-up. Genomic DNA was isolated from blood samples. The genotyping assay was based on single-molecule molecular inversion probes for target selection and used next-generation sequencing to sequence 87 single nucleotide polymorphisms (SNPs),(EyeRisk Project,E3 Consortium). Successfully genotyped SNPs were tested for association under an additive model with presence/absence of AMD in the follow-up visit as a binary outcome, and progression/no progression in the longitudinal analysis. Logistic regression analysis was performed to assess allelic odds ratio at 95%CI for each variant, adjusted for age and sex, significance level at 0.05. The GRS for common AMD risk variants was calculated. For the rare variant analysis, we performed logistic regression analyses to assess the cumulative effect of rare variants with AMD.

Results
Samples from 237 AMD cases and 638 non-AMD controls were successfully genotyped for a total of 69 SNPs in the cohort of the follow-up Incidence CES. The risk-variants associated to increased risk of AMD presence were: ARMS2 rs10490924, ARMS2_HTRA1 rs3750846, CFH rs35292876, SLC16A8 rs8135665 and TGFBR1 rs1626340. As for a protective effect we identified the variants: C2_CFB_SKIV2L rs429608, CFH rs10922109 and rs1410996, CNN2 rs10422209, CETP rs5817082, CB rs6411153 and RDBP_CFBrs760070. When considering progression from no-AMD to AMD through the 6.5-year follow-up time of the complete epidemiological study, we obtained 630 samples from non-progressors and 137 from progressors. Variants associated to risk of progression were: ARMS2 rs10490924, ARMS2_HTRA1 rs3750846 and CFH rs35292876; and variants protective of progression were again C2_CFB.SKIV2L rs429608, CFH rs10922109 and rs1410996, CNN2 rs10422209, but also CFBHR5 rs10922153, SYV3/TIMP3 rs5754227 and COL10A1 rs3812111. The GRS was significantly different between AMD vs non-AMD cases(0.535±1.47 vs 0.034±1.36,p<0.001), and between progressors vs non-progressors(0.647±1.48 vs 0.042±1.38,p<0.001). The rare variants analysis included 218 cases and 597 controls. For the CFH gene, a total of 78 rare variants were included with a known Polyphen score. Damaging rare variants in the CFH were significantly more present in AMD patients.

Conclusions
Several variants were found to be associated with the presence and progression to AMD in our epidemiological longitudinal study, while others were protective. The genes associated with AMD act in different pathophysiologic pathways, sustaining the multifactorial etiology of AMD. Their effects on our population agree with major reports, including large GWAS studies. The GRS was significantly different between AMD and non-AMD cases and between progressors, confirming its utility in more complex multifactorial analysis when assessing individual risk. Furthermore, we also found that rare variants in the CFH gene with damaging effects were significantly associated with AMD in our cohort. This is the first genetic study in AMD in a Portuguese population, and in the future, we will also explore the correlation between genetics, phenotypic and environmental features in risk assessment. Genetic characterization is important to pursue in different populations, as the identification of potential genetic therapeutic targets is of major interest.
**Title**
Addressing COVID-19 fear to improve clinic attendance for patients with wet age-related macular degeneration

**Presenter**
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**Purpose**
In line with recommendations from the Royal College of Ophthalmologists and the American Academy of Ophthalmology, only urgent and emergent care was provided for in our department during the peak of the COVID-19 pandemic. Despite implementing precautions to reduce transmission, we noticed a sharp fall in attendance for patients with sight-threatening conditions, such as wet age-related macular degeneration (wAMD). We evaluated the effect of COVID-19 on clinic attendance rate for patients with wAMD, and whether non-attendance could be improved by addressing patients’ fears of contracting COVID-19.

**Setting/Venue**
Department of Ophthalmology, Royal Derby Hospital, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK.

**Methods**
All patients with wAMD scheduled for an intravitreal injection clinic, from 27 April 2020 to 1 May 2020, were invited to a survey assessing their perception of personal safety in clinic during the pandemic. Patients who did not attend their appointment received a telephone survey, whilst those who attended received a self-completion survey. For all patients, the survey asked about awareness of clinic precautions in place to minimise infection. For patients who did not attend, the survey also asked the reasons for non-attendance and if they would have attended if informed beforehand of the precautions taken. For patients who attended, the survey also asked whether they felt fearful attending, and if they would have been less fearful had they been informed of the clinic precautions.

**Results**
Overall 253 patients completed the survey; 123 patients did not attend their appointment (49%) whilst 130 patients did attend (51%). For patients who did not attend, 85% stated the reason was because they felt fearful of contracting COVID-19. 98% of patients who did not attend were not aware of the precautions in place minimising infection, whilst 71% stated that they would have attended had they been informed of these precautions. For patients who attended, 51% were fearful of contracting COVID-19, 62% were unaware of the clinic precautions put in place, and 53% stated that they would have been less fearful had they been informed beforehand of these precautions.

**Conclusions**
During the COVID-19 pandemic there has been a significant problem with poor clinic attendance for patients with wAMD, associated with a fear that it is not safe enough to attend. Ophthalmology departments should take steps to inform patients beforehand about the local precautions in place to prevent infection in order to make patients feel safer and reduce non-attendance. Crucially this may minimise sight loss for those with wAMD and other sight-threatening conditions. Not only is this of importance during the COVID-19 pandemic but it is also of great relevance in the coming months as more ophthalmology care is restored.

**Financial Disclosure**
I do not have any financial relations with any company.
Intravitreal Brolucizumab for treatment of refractory macula edema due to neovascular age-related macular degeneration (real life data)

### Purpose
To assess the morphological and functional outcome of intravitreal brolucizumab for treatment of refractory macula edema due to neovascular age-related macular degeneration.

### Setting/Venue
This retrospective study included 20 eyes from 18 patients with refractory macula edema due to neovascular age-related macular degeneration.

### Methods
All patients were switched to brolucizumab after treatment with at least 2 other anti-VEGFs. All eyes received 3 brolucizumab 6 mg/0.05 ml intravitreal injections IVIs monthly as upload phase. Then eyes received an injection every 12 weeks and were interval adjusted to every 8 weeks if disease activity was present. Main outcome measures included: best corrected visual acuity (BCVA) and central macular thickness (CMT). In addition, we reported the adverse event rate.

### Results
Patients age was 78±8 years on average. The number of previous anti-VEGF IVIs was 36±22 in the affected eyes before switching to brolucizumab. 100 brolucizumab IVIs (5 IVIs/eye) were carried out during the first seven months of treatment. BCVA (ETDRS) was 49±14 before treatment and improved to 58±17 at week 4 (p=0.1), to 64±17 at week 8 (p=0.04), to 64±26 at week 16 (p=0.03), to 65±18 at week 20 (p=0.01), to 60±20 at week 24 (p=0.02) and to 59±19 at week 28 (p=0.05). CMT was 335±78 μm before treatment and decreased to 317±106 μm at week 4 (p=0.2), to 307±42 μm at week 8 (p=0.4), to 324±37 μm at week 16 (p=0.9), to 309±40 μm at week 20 (p=0.6), to 333±39 μm at week 24 (p=0.9) and to 299±40 μm at week 28 (p=0.2). Finally, two cases of intraocular inflammation were diagnosed as adverse events.

### Conclusions
Patients treated with intravitreal brolucizumab achieved statistically significant visual acuity improvement in the first seven months of treatment. Two cases of intraocular inflammation were reported during the first seven months of treatment.

### Financial Disclosure
No financial disclosure.
Purpose
To report on the morphological characteristics and regional distribution of multifocal macular neovascularization type 3 (mMNV3).

Setting/Venue
22 consecutive eyes of 21 patients with mMNV3 were included using multimodal imaging.

Methods
The count and stage of lesions of all MNV types and the existence of exudate and hemorrhage were determined. Also, we addressed the regional distribution of MNV3 lesions between the superior-inferior and the nasal-temporal halves of the macula, and the range of the distance of the lesions from the central fovea. Furthermore, we explored the number of feeding vessels including the cilioretinal artery.

Results
We found 51 lesions in 22 eyes of 21 patients. They were bifocal in 16 (73%) eyes, trifocal in 5 (23%) and quadrifocal in one (4%). No lesion of MNV1 or 2 was found. 15 (68%), 2 (9%) and 16 (73%) eyes were associated with retinal hard exudate, sub retinal pigment epithelium exudate and intraretinal hemorrhage, respectively. 30 (59%) lesions were located in the temporal half of the macula, whereas 21 (41%) were located nasally (p=0.07). One (2%) lesion was closer than 500µm, 49 (96%) between 500 and 1500µm and one (2%) between 1500 and 3000µm. The lesions were supplied by one arteriole in one (4%) eye, two arterioles in 16 (73%) eyes and 3 arterioles in 5 (23%) eyes. The CRA contributed as a feeding vessel in 5 (23%) eyes.

Conclusions
The multifocal variant of MNV3 has specific morphological and topographical characteristics. Multimodal imaging allows to understand the pathomorphological condition in more detail.
Effect of COVID induced delay in treatment in a cohort of patients with exudative age related macular degeneration type 3

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Consecutive observational case series of patients diagnosed with eAMD type 3 in our Hospital whose follow-up and treatment was interrupted by COVID pandemic. Best corrected visual acuity (BCVA) in ETDRS letters, Heidelberg Spectralis OCT image and antiVEGF used were included for analysis in the visit before the onset of COVID pandemia in Spain (named covid-1), the visit before covid-1 (covid-2) and the visit when follow-up was resumed (covid-0). For each patient, real delay in days (from scheduled visit to actual visit after COVID onset) was calculated. Year of diagnosis of eAMD and number of antiVEGF injections received the year prior to COVID lockdown was 5,1 (SD 1,7) and the year before was 3,7 (SD 2,8). Mean real delay was 107,8 days (SD 57,3; range 28-298). BCVA at diagnosis was 60,5 letters (SD 18,1), at covid-2 was 60,7 (SD 16,6), at covid-1 was 59,9 (SD 16,8) and at covid-0 was 55,5 (SD 19,2). The difference of 4.4 letters in BCVA before and after COVID were statistically significant (p=0.01) whereas difference of 0,9 letters between covid-2 and covid-1 were not (p=0,44) Structural OCT was described as active in covid-2 in 35 eyes (62,5%), in covid-1 in 35 eyes (62,5%) and in covid-0 in 44 eyes (78,6%, difference statistically significant, p=0.04). Mean central retinal thickness (CRT) in covid-2 was 294,9 (SD 141,5), in covid-1 was 295,9 (SD 161,5) and in covid-0 was 347,5 (SD 210; difference 51,6 microns, p=0.001) with an increase of eyes with both intra and subretinal fluid compared to before COVID lockdown.

In eAMD type 3 eyes, delay imposed by COVID pandemic resulted in visual loss not attributable to natural history of the disease, an increased percentage of active OCT, increase in mean CRT and reappearance of subretinal fluid added to intraretinal fluid. Further studies are warranted to measure how much of that visual loss will be reversible with proper continuous follow-up and treatment.

Alicia Valverde-Megías and Juan Donate López: Novartis medical lectures
**Title**

Intravitreal Aflibercept for the treatment of patients with neovascular age-related macular degeneration in routine clinical practice in Latin America: The AQUILA study

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**Purpose**

The purpose of AQUILA was to evaluate the clinical effectiveness (functional and anatomic outcomes) and safety of intravitreal aflibercept (IVT-AFL) in patients with neovascular age related degeneration (nAMD) and with diabetic macular edema (DME) in routine clinical practice in Latin America. The study was also designed to understand how patients with nAMD and DME are treated with IVT-AFL in Latin America, including treatment regimens utilized and the reasons for changes in treatment regimens or treatment discontinuation. The results for the patients with nAMD are presented here.

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**Setting/Venue**

AQUILA (NCT03470103) was a prospective, multicenter, observational, 12-month study evaluating the effectiveness of IVT-AFL in patients with nAMD or DME. The data below summarize the outcomes for the patients with nAMD.

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**Methods**

Treatment-naïve and pre-treated patients with nAMD (aged ≥55 years) were enrolled from April 2018 to September 2019. Patients became eligible for the study once the decision was made to treat with IVT-AFL according to routine clinical practice and local prescribing information. Decisions regarding IVT-AFL treatment were made at the discretion of the prescribing physician, according to their medical practice. The primary efficacy endpoint was change in best-corrected visual acuity (BCVA; Early Treatment Diabetic Retinopathy Study [ETDRS] letters) from baseline to Month [M] 12 in treatment-naïve and pre-treated patients. Secondary endpoints included the change in central retinal thickness (CRT) from baseline, number of visits and IVT-AFL injections, mean duration of treatment intervals, and the proportions of patients with no fluid on optical coherence tomography, a Snellen equivalent of 20/40 or better (~70 ETDRS letters), and ≥15 ETDRS letter gain. Patients who received at least one IVT-AFL injection and had a BCVA assessment in the study eye at both baseline and at least one follow-up visit were included in the full analysis set (FAS: Argentina, n=196; Mexico, n=41; Colombia, n=19; Costa Rica, n=18).

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**Results**

Of 324 patients with nAMD, 274 (201 treatment-naïve; 73 pre-treated) were included in the FAS (mean age: 77 years; male: 35%) and 215/324 patients (66%) completed 12 months’ follow-up. Median duration from diagnosis to IVT-AFL treatment was 1.2 months (treatment-naïve) and 19.5 months (pre-treated) and the mean±SD number of IVT-AFL injections by M12 was 4.2±1.9 (treatment-naïve) and 5.2±2.7 (pre-treated). Overall, 170/274 patients (62%) received ≥3 initial monthly IVT-AFL injections (127/201 treatment-naïve; 43/73 pre-treated) and 47/274 patients (17%) received ≥7 injections by M12 (24/201 treatment-naïve; 23/73 pre-treated). Mean BCVA improved from baseline to M12 by +5.2±18.3 (treatment-naïve; baseline: 48.2±23.5) and +3.1±15.3 letters (pre-treated; baseline: 47.7±21.4). BCVA change from baseline to M12 was +5.5±15.1 (treatment-naïve) and +7.0±15.1 (pre-treated) in patients who received ≥3 initial monthly doses and ≥4.6±6.2 (treatment-naïve) and –2.5±14.1 (pre-treated) in patients who received <3 initial monthly injections. By M12, 25% of patients (both groups) had BCVA improvements of ≥15 letters and 36% of patients had a BCVA ≥70 letters (treatment-naïve: 37% [from 21% at baseline]; pre-treated: 32% [from 19% at baseline]). By M12, mean CRT decreased by -106.7±143.0 μm (treatment-naïve; baseline: 377.9±136.6) and -80.9±154.8 μm (pre-treated; baseline: 400.2±136.8). No new safety signals were observed.

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**Conclusions**

AQUILA is the first study to assess the use of IVT-AFL in routine clinical practice in Latin America. In AQUILA, >60% of patients with nAMD received ≥3 initial monthly doses of IVT-AFL, but <20% received ≥7 injections in the first year of treatment. Functional and anatomic outcomes improved during 12 months’ treatment with IVT-AFL. Improvements in BCVA were numerically greater in treatment-naïve patients than pre-treated patients and in patients who received ≥3 initial monthly injections than those who did not. Thus, in real-world studies, patients treated regularly and proactively with IVT-AFL have the potential to achieve outcomes consistent with those observed in interventional studies. The safety profile of IVT-AFL was consistent with previous studies.
Imaging biomarkers of 1-year activity in type 1 macular neovascularization

**Purpose**
To explore the influence of optical coherence tomography (OCT) and OCT angiography (OCTA) parameters on the final lesion’s activity, in treatment-naïve type 1 macular neovascularization (MNV) eyes treated with a 1-year fixed regimen of intravitreal aflibercept injections (q8IAI).

**Setting/Venue**
This observational study was conducted at IRCCS-Fondazione Bietti of Rome, Italy.

**Methods**
Patients received a complete ophthalmological examination, which included the measurement of best corrected visual acuity (BCVA), intraocular pressure, and dilated fundus examination. All patients were imaged by Spectral Domain (SD-)OCT to evaluate central macular thickness (CMT), subretinal fluid (SRF), subretinal hyperreflective material (SHRM), intraretinal fluid (IRF) and intraretinal hyperreflective dots (HRD) and by Swept Source (SS-)OCTA to measure baseline MNV area, perfusion density (PD), vessel length density (VLD) and vessel diameter index (VDI) in the retinal pigment epithelium (RPE)-RPE fit scan. At the end of q8IAI, patients were classified in two groups: active-MNV (A-MNV) and inactive-MNV (I-MNV), considering the OCT signs of activity. SD-OCT and SS-OCTA parameters at baseline and their influence on lesion’s activity 1 month after the end of q8IAI, were analyzed. Three binary logistic regression models were developed: 1) OCT-based, 2) OCTA-based, 3) OCT/OCTA-based model. The models’ performance to distinguish between active and inactive groups was measured by the receiver operating characteristic (ROC) analysis with the area under the curve (AUC).

**Results**
Thirty-one treatment-naïve type 1 MNV were enrolled (13 A-MNV and 18 I-MNV). No differences were observed in baseline OCT and OCTA characteristics between A-MNV and I-MNV. In the first model we explored the combination of OCT parameters (CMT, SRF, IRF, HRD and SHRM) as predictive factors for final lesion activity. In a second model we explored the combination of OCTA parameters (MNV Area, PD and VLD), excluding the VDI for a potential collinearity problem. In a third model we combined parameters of models 1 and 2 (OCT+OCTA). The model 1 and 3 showed a significant AUC (p = 0.013 for model 1 and p <0.001 for model 3), in the model 2 the AUC was not statistically significant p=0.088. Combining OCT and OCTA parameters a significant improvement of model performance was observed. The A-MNV group showed at baseline the presence of SRF, greater CMT, wider area of MNV on OCTA scans and lower PD and VLD compared to I-MNV.

**Conclusions**
In this study we analyzed the predictive value of baseline OCT and OCTA parameters in treatment-naïve type 1 MNV treated with q8IAI, using statistical logistic regression models. Our study demonstrated that the combination of baseline OCT and OCTA parameters allowed to achieve a good models’ performance in the prediction of MNV activity permitting to correctly classifying the active lesions at the end of follow-up period, with excellent sensitivity. By the analysis of the models, the presence of SRF, great CMT, large MNV area and low PD and VLD represent predictive baseline biomarkers for lesion’s activity after 1-year treatment in type 1 MNV.
Patients' opinion on the monitoring of their wet age-related macular degeneration during coronavirus disease 2019 pandemic and on the importance of telemedicine

Purpose
The purpose of this study is to present the patients’ subjective view concerning the monitoring of their wet Age-related Macular Degeneration (wet AMD) during Coronavirus disease 2019 (COVID-19) pandemic, as well as the impact that the techniques of telemedicine could have on it. Two questionnaires were completed by each patient for the fulfillment of this purpose.

Setting/Venue
Swiss Visio Montchoisi (Lausanne, Switzerland) and RétinElysée Ophthalmology Center (Lausanne, Switzerland).

Methods
 Patients diagnosed with neovascular AMD (nAMD) of any type (I, II, or III), that had intravitreal anti-Vascular Endothelial Growth Factor (anti-VEGF) injections both before and after the period of confinement due to the COVID-19 pandemic, regardless if the programmed injection interval was respected or not, were included in the study, after signing an informed consent form. Two questionnaires were given to each patient. Our research team explained to each patient how to complete the questionnaires. The patients completed the questionnaires without any time restrictions either in the clinic or in their homes, alone or with the help of their families. The first questionnaire aimed to evaluate the patients’ subjective opinion concerning their adherence to their programmed intravitreal anti-VEGF injections during the period of confinement and to assess their opinion on the future use of telemedicine. The second questionnaire was a visual function questionnaire adapted from National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ25) and focused on the patients’ opinion regarding the change of their visual function during or after the confinement, compared to their visual function before the confinement. The statistical significance level was set to 0.05.

Results
130 of 185 patients (70.2%) responded to the questionnaires. 8.4% responded that they did not respect their assigned injection interval during the confinement (group 1), while the other 91.5% responded that they respected it (group 2). The majority of group 1 (37.5%) responded they did not attend their programmed injection visit to avoid using public transportation. The majority of group 2 (78.7%) considered the continuation of their treatment more important than the risk of contracting COVID-19. Before the lockdown, patients of group 2 were more worried about their vision than patients of group 1 (P=0.0579) and had more need for help from others (P=0.0225). During the lockdown, patients’ NEI-VFQ25 visual function was similar between the two groups. In the event of a future lockdown, 36.3% of group 1 and 8.7% of group 2 would prefer remote monitoring of their wet AMD using telemedicine (P = 0.0204), 54.5% of group 1 and 86.9% of group 2 would prefer to visit the clinic, while 9.0% of group 1 and 4.3% of group 2 would completely avoid the visit. 70% of group 1 and 33.6% of group 2 would rather use the telemedicine application in their home than visiting a telemedicine center (P=0.0367).

Conclusions
COVID-19 pandemic and the resulting confinement was a unique circumstance, in which a large proportion of wet AMD patients did not receive their scheduled treatment, despite the availability of our clinic to provide continuous intravitreal anti-VEGF injections. Our results suggest that during a next confinement due to COVID-19, or circumstances similar to it, the majority of the patients would still prefer to visit the clinic. The patients that missed their intravitreal anti-VEGF injection would prefer remote monitoring of their AMD using telemedicine at a much higher rate than the patients that followed their scheduled injections during the confinement due to COVID-19.

Financial Disclosure
None
The effect of intravitreal Bevacizumab treatment on ciliary muscle thickness in neovascular type age-related macular degeneration

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Purpose
The current treatment modalities of Neovascular Type Age-Related Macular Degeneration base on anti-vascular endothelial growth inhibitor agents. Bevacizumab is one of these agents. These agents are given into the vitreous space through the pars plana. Ciliary muscles may be affected by both trauma during injection and may be affected by the effect of anti-vascular endothelial growth inhibitor agent. In the current study, we aimed to investigate the effect of intravitreal bevacizumab on ciliary muscle thickness in Neovascular Type Age-Related Macular Degeneration using ultrasonic biomicroscopy.

Methods
This study conducted in the Department of Ophthalmology. 15 eyes of 15 patients who were diagnosed with Neovascular Type Age-Related Macular Degeneration, who had not received any treatment before, and who received 3 doses of intravitreal bevacizumab were taken. Before bevacizumab treatment, patients underwent complete ophthalmological examination, optical coherence tomography, ultrasonic biomicroscopy, and fundus fluorescein angiography. All patients received 3 doses of bevacizumab injections one month apart. Ciliary muscle thickness measurements were performed using ultrasonic biomicroscopy before the treatment and one month after the 3rd dose bevacizumab treatment. The best-corrected visual acuities (BCVA), central macular thickness (CMT), and temporal ciliary muscle thickness were compared before and after the treatment in the 4th month.

Results
Fifteen patients, 8 males (53.3%) and 7 females (46.7%), with a mean age of 72.2 years, participated in the study. While the pre-treatment BCVA was 1.09 ± 0.62logMAR, it was 0.63 ± 0.06logMAR at the 4th month (p: 0.008). The mean pre-treatment CMT value was 367.53 ± 48.02 μm, while the mean CMT value at the 4th month was 308.87 ± 71.49 μm (p 0.001). Ciliary muscle thicknesses 1mm (M1), 2mm (M2) and 3mm (M3) from the scleral spur before treatment and at the 4th month, respectively 1.02mm and 0.90mm (p: 0.002) for M1, 0.69mm for M2 It was 0.61mm (p: 0.003), 0.41 and 0.36mm (p 0.001) for M3 (Figure 1 and Figure 2). No complications were observed in any of the cases.

Conclusions
This study is an important study investigating the effect of bevacizumab treatment on ciliary muscle thickness, and a significant decrease in ciliary muscle thickness measurements was found in the study. Changes in ciliary muscle anatomy after bevacizumab treatment may cause impairment in the accommodation mechanism. In addition, the ciliary body is likely to be affected and may cause deterioration of the aqueous humor production.

Financial Disclosure
none
The impact of fluid compartments on functional outcomes for patients with neovascular age-related macular degeneration: A systematic literature review

Understanding the impact of fluid in different retinal compartments is critical to developing treatment paradigms that optimize visual acuity (VA) and reduce treatment burden for patients with neovascular age-related macular degeneration (nAMD). This systematic literature review aimed to determine the impact of persistent and/or new subretinal fluid (SRF), intraretinal fluid (IRF), and sub-retinal pigment epithelial (RPE) fluid on VA over a 1-year treatment course with anti-vascular endothelial growth factor (anti-VEGF) treatment in patients with nAMD.

This review was conducted in accordance with the principles set out in the Cochrane Handbook for Systematic Reviews of Interventions. EMBASE, PubMed, and CENTRAL databases, as well as conference websites and clinical trial registries were searched between 1 January 2006 and 1 August 2020 with restrictions on language (English language only).

The primary objective was to determine the impact of SRF, IRF, and sub-RPE fluid (both at baseline and throughout the course of treatment) on VA during 1 year of anti-VEGF treatment in patients with nAMD. Secondary objectives were to determine the impact of SRF, IRF, and sub-RPE fluid on VA at other timepoints, morphologic outcomes, treatment burden, and safety (data availability permitting). Outcomes in patients with nAMD undergoing intravitreal anti-VEGF treatment, stratified by SRF or IRF, were included. Studies were excluded if they did not report outcomes, did not report SRF or IRF, included a mixed-disease study population (e.g. nAMD and diabetic macular edema) unless an nAMD subgroup of patients was reported separately, reported a mixed-disease study population (e.g. photodynamic therapy and anti-VEGF) unless the anti-VEGF group was reported separately, or if they consisted of individual case studies. Publication eligibility and data extraction were conducted according to Cochrane methods. Risk of bias was assessed using the Cochrane RoB-2 and ROBINS-I tools. Of the 1797 records screened, 188 articles were assessed in full and 27 met the inclusion criteria.

Baseline and persistent/new IRF negatively impacted VA throughout the course of treatment and the strength of the association increased from Years 1 and 2 to Year 5. Additionally, the location of fluid relative to the foveal center influenced VA – foveal IRF was generally associated with worse VA compared with extrafoveal IRF or absence of IRF. Data on the role of SRF were not as clear. Most studies suggested that SRF did not negatively affect VA at baseline or throughout the first year of treatment. At Year 2, one study corroborated the Year 1 findings, and another found that SRF (particularly foveal SRF) was associated with improved VA. In the study exploring long-term effects of SRF on VA, patients with foveal SRF at any timepoint had better vision at Year 5 than those without SRF, with the effect being more pronounced that at Year 2. Data on the effects of sub-RPE fluid were scarce and a consensus could not be reached. Few studies reported the number of injections associated with fluid status; a difference according to IRF and SRF status was not apparent, and it was not possible to draw any clinically meaningful conclusions.

To optimally manage patients with nAMD with anti-VEGF drugs, clinicians should understand the impact of fluid compartment changes on VA. Current evidence suggests that after an initial course of treatment, anti-VEGF regimens that tolerate stable, persistent SRF (on the condition that VA is stable or improved) but not IRF may enable patients to achieve their best possible VA and minimize treatment burden. The location of the fluid relative to the foveal center should also be considered when making retreatment decisions. Confirmatory, prospective studies are required to validate the effects of different fluid compartments on VA.

Financial Disclosure
Varun Chaudhary: Personal fees from Alcon Inc., Bayer Healthcare AG, and Novartis AG; Grants from Bayer Healthcare AG, and Novartis AG Frédéric Matonti: Personal fees from AbbVie, Bayer, Horus Pharma, and Novartis Javier Zarranz-Ventura: Personal fees from Alcon, Alimera Sciences, Allergan, Bayer, Brill Pharma, Dorc, Novartis, and Roche; grants from Allergan, and Novartis; Non-financial support from Alcon, Alimera Sciences, Allergan, Bausch and
Title
Switching to Brolucizumab in eyes incompletely responsive to Ranibizumab or Aflibercept: Real-life 6-month outcomes

Purpose
To evaluate the effect of switching treatment to brolucizumab with regard to morphological and functional outcomes in eyes with neovascular age-related macular degeneration (nAMD) and treatment intervals of six weeks due to high treatment demand under ranibizumab and aflibercept.

Setting/Venue
In this ongoing prospective single-center cohort study eyes with persisting retinal fluid indicating active nAMD under aflibercept or ranibizumab, not exceeding treatment intervals of six weeks in a treat-and-extend (T&E) protocol were switched to brolucizumab.

Methods
Treatment intervals were adjusted according to optical coherence tomography (OCT) imaging and T&E standard of care. Best corrected visual acuity (BCVA), reading acuity treatment intervals, central subfield thickness (CST) and the presence of intra- and subretinal fluid were recorded. We report preliminary 6-months outcomes.

Results
Seven of twelve eyes completed the 6-month follow-up and received 4.3±0.8 brolucizumab injections within 28±2.8 weeks. The treatment interval increased from 5.3±0.9 weeks to 9.0±2.8 (95% confidence interval (CI) -5.9 to -1.6) weeks. BCVA improved from 67.8±7.2 to 72.2±7.5 (95% CI -0.3 to 9.1) ETDRS letters, RA from 0.48±0.15 to 0.31±0.17 LogRAD (95% CI 0.03 to 0.25) and CST from 422.1±97.3 to 353.6±100.9 (95% CI -19.9 to 157.1) µm. Treatment was early terminated in five eyes (45%: twice (18%) for intraocular inflammation and vascular occlusion without vision loss, once (9%) due to transient ischemic attack, twice (18%) changes in treatment.

Conclusions
Our preliminary 6-month data show improvement in RA and longer treatment intervals after switching to brolucizumab in eyes with incomplete response despite intensive treatment with other anti-VEGF our series. Brolucizumab may thus reduce treatment burden for patients with nAMD, but should be used prudently, with a high degree of awareness and patient education to avoid delayed detection and treatment of possible side effects.

Financial Disclosure
Conflicts of Interest: The authors declare no conflicts of interest. (Commercial relationships dis-closures: Isabelle B. Pfister, None; Justus G. Garweg, AbbVe, Allergan, Chengdu Kbanghong, Bayer, Novartis, all without connection to this work).
**Title**
Simultaneous combined intravitreal Bevacizumab and dexamethasone implant treatment for vascularized serous retinal pigment epithelial detachment

**Purpose**
To report the efficacy of intravitreal bevacizumab and dexamethasone for vascularized serous retinal pigment epithelial detachments (PEDs) secondary to neovascular age-related macular degeneration (nAMD).

**Setting/Venue**
Retrospective and case-control series

**Methods**
In this single-centered, retrospective and case-control series; we reviewed the medical records of 20 patients who had neovascular serous PEDs secondary to nAMD between January 2019 and June 2020. Inclusion criteria are as follows; 1- Patients with a diagnosis of vascularized serous PED secondary to nAMD based on clinical, FFA and OCT findings, 2- Patients treated with 3 monthly consecutive intravitreal bevacizumab injections due to this diagnose, 3- Despite this treatment, the presence of new or persistant cystoid macular edema, intraretinal or subretinal fluid on optical coherence tomography (OCT), the presence of at least 250μm PED height or <10% decrease in PED height or greatest linear diameter, presence of active CNVM findings in FFA (the presence of dotted and slightly hypo-fluorescent “notch” at the border of the serous PED indicative of CNVM with serous PED), new or persistant hemorrhage or exudates and loss of 5 letters or more. Exclusion criteria were; patients with nAMD without neovascular PEDs, patients with fibrovascular PED or hemorrhagic PED, polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP) in indocyanine green angiography (IGA), patients with glaucoma, uveitis, diabetes, vitreous hemorrhage, foveal hard exudate, epiretinal membrane, juxtafoveal telangiectasia, macular scar, ischemia shown in the FFA, cerebrovascular...
**Title**
Characterization of macular neovascularization in geographic atrophy

**Purpose**
To characterize macular neovascularization (MNV) developing in eyes affected by geographic atrophy (GA).

**Setting/Venue**
This is a multicentric longitudinal study involving 3 retina referral centers (the Medical Retina and Imaging Unit of the San Raffaele Scientific Institute in Milan, Italy, Department of Ophthalmology, Hospital Intercommunal de Creteil, University Paris Est in Creteil, France and of and Bietti Foundation in Rome, Italy).

**Methods**
In this multicentric longitudinal study involving 3 retina referral centers, patients previously affected by GA that developed an active MNV were included. Patients were investigated using structural optical coherence tomography (OCT), fundus autofluorescence, OCT-angiography, and dye angiographies. Patients were treated with ProReNata (PRN) anti-vascular endothelial growth factor (VEGF) injections and were revaluated after treatment.

**Results**
Among 512 patients previously diagnosed with GA, 40 eyes of 40 patients (mean age 80.8±7.9 years, mean GA area 8.73±7.39 mm²) presented with treatment-naïve exudative MNV (accounting for an estimated prevalence of 7.81%; 5.49 - 10.13, 95% confidence intervals) and thus were included in the analysis. 67.5% of MNVs were classified as type 2 MNV, 25% as type 1, 2.5% as type 3, and 5% as mixed phenotype. In 92.5% of cases, active MNV in GA showed subretinal hyperreflective material (SHRM) with or without evidence of sub-/intra-retinal hyporeflective exudation. During a mean follow-up of 28±25 months, patients were treated with 6.6±0.3 anti-VEGF injections, with 2.9±1.4 injections in the first year of treatment. No patient developed GA enlargement in the area of MNV.

**Conclusions**
MNVs in GA showed different features and therapeutic response in comparison to previously reported features of MNV in age-related macular degeneration (AMD) without GA. For these reasons, the combined phenotype (i.e. GA with neovascular AMD) should be considered as a distinct entity in the research and clinical setting.

**Financial Disclosure**
none
Presence of retinal fluid following over 1 year treatment with anti-VEGF in Korean nAMD patients: PROOF study

**Purpose**
To evaluate presence of retinal fluid and the association of fluid-free period with visual outcome in patients with neovascular age-related macular degeneration (nAMD) who were treated with anti-vascular endothelial growth factor (VEGF)

**Setting/Venue**
Retrospective, multi-institutional study

**Methods**
This study included nAMD patients who were treated with ranibizumab, aflibercept, or bevacizumab at least 12 months after diagnosis. The presence of any retinal fluid, intraretinal fluid(IRF), subretinal fluid(SRF), and sub-retinal pigment epithelial(RPE) fluid at diagnosis and at 12 months was evaluated. Patients were divided into quartiles based on time with absence of fluid over 12 months and difference in the improvement in visual acuity (VA) was compared among the following three quartile groups: Q1 vs Q2-Q3 vs Q4.

**Results**
A total of 600 patients were included. During the 12 months, mean 5.54 anti-VEGF injections were administered. The mean baseline VA and central subfield thickness (CST) was 54.14 ± 20.69 (SD) ETDRS (Early Treatment of Diabetic Retinopathy Study) letters and 379.75 ± 135.15 (SD) µm. At 12 months, mean 8.91 ± 17.22(SD) letters of improvement in VA and mean 106.9 ± 136.68(SD) µm of decrease in CST was noted. At diagnosis, the incidence of any retinal fluid, IRF, SRF, and sub-RPE fluid was 97.16%, 39.97%, 90.13%, and 32.44%, respectively. At 12 months, the incidence was decreased to 58.1%, 24.66%, 37.59%, and 21.21%, respectively. The mean fluid-free period was 67.30 ± 92.54(SD) days. When divided into quartiles based on time with absence of fluid, the mean improvement in VA was +10.93 ± 17.96 (SD) letters in Q4 (25% of the patients with the longest fluid-free time), +10.10 ± 17.24 (SD) letters in Q2-Q3, and +5.56 ± 16.17 (SD) letters in Q1 (25% of the patients with the shortest fluid-free period). When compared to Q1, greater improvement in VA was noted in Q2-Q3(P=0.0038) and Q4(P=0.0004).

**Conclusions**
Result of the present study suggests that appropriate fluid control is important to achieve good visual outcomes. However, retinal fluid was noted in approximately two-thirds of the nAMD patients even after anti-VEGF therapy, suggesting the unmet needs in clinical practice.

**Financial Disclosure**
This study was supported by Novartis Korea, Ltd.
AI algorithm assisted anti-VEGF therapy in neovascular AMD

**Purpose**
Anti-VEGF treatment in neovascular AMD (nAMD) has been established as "gold standard" reducing visual loss significantly. Therefore this therapy is widely introduced in the care of these patients. Especially in Germany cooperative therapeutical system including general ophthalmologists and retina specialists have been develop. To support general ophthalmologists to refer and monitor AMD patients during this ongoing cooperative treatment, AI algorithm and assistance may of important. Also AI may support counseling of patients in respect to the prediction of clinical relevant parameters like length and intensity of treatment.

**Setting/Venue**
SD-OCT and clinical data of an unselected consecutive real-life cohort of 1347 AMD patients, treated between 2014-20 (IVAN therapy strategy) and with longterm follow-up were analysed.

**Methods**
To support referral for treatment and monitoring retreatment indications on SD-OCTs a novel deep learning network (DLN) based on SD-OCT volume scans (49 scans) was developed differentiating between early/intermediate vs nAMD (referral) and between stabilized vs retreatment nAMD SD-OCT. In addition improved image processing and mixed data analysis were used to predict the individual treatment intensity (number of treatment IVAN cycles) in the first 12 mo after upload included the initial SD-OCT volume scans and the time until the first visit with renewed lesion activity. With this experimental structure an AUC of 0.71 (10-fold CV-AUC) was achieved with an AUC of 0.84 only including eyes with a trust-filter >0.6.

**Results**
The DLN algorithm to differentiate between early/intermediate vs nAMD SD-OCT achieved an AUC of 0.932 (10-fold CV-AUC) and between stabilized vs retreatment nAMD SD-OCT an AUC of 0.865 (10-fold CV-AUC). The best DLN algorithm to predict the number of future injection cycle (1 vs 3 IVAN-cycle) in the next 365 days after upload included the initial SD-OCT volume scans and the time until the first visit with renewed lesion activity. With this experimental structure an AUC of 0.71 (10-fold CV-AUC) was achieved with an AUC of 0.84 only including eyes with a trust-filter >0.6.

**Conclusions**
Assistance by the new developed AI algorithms can support ophthalmologists at first in their initial decision to refer AMD patients to retina specialists for anti-VEGF therapy, but secondly to monitor patients during the course of the therapy. For both the developed AI algorithm demonstrated a very high AUC and accuracy. In addition further AI algorithm may help to predict the future intensity of anti-VEGF-therapy. Saliency maps of the individual SD-OCT volume scans may help ophthalmologists and patients to understand the individual decisions of the AI algorithm.

**Financial Disclosure**
The study was supported by a grant of Novartis
Retinal layer thickness alterations in early age related macular degeneration in eyes with subretinal drusenoid deposits or conventional drusen

Purpose
The aim of this study was to evaluate inner and outer retinal layer thickness in early age related macular degeneration (AMD) in patients with subretinal drusenoid deposits (SDD) or conventional drusen (CD).

Setting/Venue
Academic medical centre: Retina Centre, Ophthalmology Unit, NESMOS Department, University of Rome Sapienza, St. Andrea Hospital, Rome

Methods
This investigation was an observational cross-sectional study including participants with eyes with SDD only, CD only, and healthy age-matched subjects. Participants underwent comprehensive ophthalmoscopic examination. Evidence of SDD or CD was evaluated through the simultaneous evaluation of near infrared reflectance and spectral domain optical coherence tomography images. Macular thicknesses measurements were obtained from generated maps over the central circles with 1 mm, 3 mm, and 5 mm diameter for the full, inner, and outer retinal thicknesses. Continuous variables were compared by Student t-test for independent samples or by the analysis of variance (ANOVA). A p value ≤ 0.05 was considered statistically significant.

Results
Fifty-five patients were included in the study. The sample included 18 eyes with SDD alone, 19 eyes with CD alone, and 18 eyes of healthy age-matched subjects (control group). The groups were homogenous for gender, best corrected visual acuity, and spherical equivalent. In the SDD group, 8 of 18 eyes had subfoveal lesions (44%), while in the CD group, 13 of 19 eyes had subfoveal lesions (68%). There was a significant reduction (p ≤ 0.05) in the macular inner layer thickness in the central 1mm area in the SDD group (69.83 ± 6.14 mm) and in the CD group (69.21± 9.72 mm) compared to controls (78.22 ± 11.31 mm), no difference was detected between the SDD and the CD group. A significant reduction of inner retinal thickness was detected in the superior and nasal sector of the 3 mm area, in the SDD and CD group compared to controls (p = 0.001). There was a trend of generalized outer retinal thinning in patients with SDD and CD compared to controls that did not reach statistical significance. Globally, outer, inner, and total retinal thickness in the SDD group was always lower than the CD group, although not statistically significant.

Conclusions
There are inner retinal layers alterations in early AMD in eyes with both CD and SDD. The presence of SDD causes thinning of the inner retinal layers where deposits are anatomically distributed, including the central 1mm area. Evaluation of the difference in thickness between eyes with SDD and CD requires further study on larger patient populations.

Financial Disclosure
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Role of intraretinal and subretinal fluid on clinical and anatomical outcomes in patients with neovascular age-related macular degeneration treated with bimonthly, treat-and-extend and as-needed ranibizumab in the In-Eye study

**Purpose**
To assess the effect of fluid status at baseline (BL) and at the end of the loading phase (ELP) of three different ranibizumab regimens: treat-and-extend (T&E), fixed bimonthly (FBM) injections and pro re nata (PRN); on visual and anatomical outcomes of patients with neovascular age-related macular degeneration (nAMD).

**Setting/Venue**
This was a post hoc analysis conducted using data obtained from the In-Eye study (EudraCT trial number 2012-003431-37), a prospective 12-month, three-armed, multicenter (31 sites in Spain), randomized phase IV clinical trial.

**Methods**
Patients were randomized 1:1:1 to receive one of the three study regimens: T&E, FBM or PRN. Following a mandatory loading phase of three monthly injections, patients in the PRN treatment regimen underwent monthly follow-up assessments and received treatment when activity criteria were met. In the T&E regimen, the treatment and follow-up visits were extended by periods of 2 weeks, if appropriate, up to a maximum of 10 weeks. Disease activity was determined by loss of ≥5 ETDRS letters and/or one of the following criteria: new haemorrhages on fundus examination, persistent or recurrent IRF or SRF on spectral-domain OCT (SD-OCT), and leakage from CNV on fluorescein angiography (FA; mandatory at the beginning and at the end of the study). The study included 14 or 15 visits, depending on the treatment regimen. Best-corrected visual acuity (BCVA), the mean change from baseline BCVA (BL BCVA), and the proportion of eyes gaining more than 15 letters or losing more than 5 letters were analysed. Morphological characteristics including the subtype of choroidal neovascular membrane and the development of atrophy and fibrosis were also evaluated.

**Results**
A total of 270 patients (88.5%) completed the study. Throughout the study, patients with persistent SRF only and those with a dry macula at had significantly higher BCVA than patients with IRF (alone or in combination with SRF). The presence and localization of fluid provided different visual outcomes depending on the treatment regimen. In patients with a dry macula or SRF, there were no significant differences in the mean change in BCVA among the treatment regimens. In contrast, among patients with persistent IRF, the mean change in BCVA was significantly lower in the BM group. The presence of IRF at BL was significantly associated with the development of fibrosis (OR, 2.43; CI 95%: 1.26–4.66, p = 0.006). Moreover, persistent IRF at ELP also conferred a higher risk fibrosis (odds ratio 1.899, 95% CI 1.02–3.53, p = 0.045). In contrast, the presence of SRF at BL significantly decreased the risk of developing fibrosis (OR, 0.369; CI 95%: 0.185–0.738, p = 0.007). The presence of SRF did not have a significant effect in the risk of developing atrophy, while persistence of IRF at BL showed a tendency to increase this risk (OR, 1.80; CI 95%: 0.93–3.46, p = 0.08).

**Conclusions**
While persistence of SRF is compatible with good visual and anatomical outcomes, IRF leads to worse results in patients with nAMD. Our results suggest that patients with IRF may have better visual outcomes when individualized treatment regimens are used (PRN or T&E) in contrast with a fixed bimonthly regimen.

**Financial Disclosure**
None to disclose
Is retinal microvasculature affected in adult offspring of patients with nAMD

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Purpose
The pathogenesis responsible for age-related macular degeneration (AMD) involves environmental factors and varying susceptibilities to these external factors based upon different genetic backgrounds. There has been compelling documented evidence that heredity plays a role in AMD. The tendency for familial aggregation in AMD cases further points to a genetic background for the disease. Approximately 20% of AMD patients have a positive family history. The aim of this prospective cross-sectional study was to investigate the retinal microvasculature in adult offspring of patients with neovascular AMD (nAMD) who have no clinical evidence of retinopathy and to compare these with non-nAMD offspring.

Setting/Venue
Ulucanlar Eye Training and Research Hospital

Methods
Seventy-one adult offspring of patients with nAMD (41 males and 30 females, mean age 51.23 ± 7.39 years) and 81 age- and sex-matched healthy control subjects were included in the study. Data regarding age, gender and parenteral nAMD subtypes were recorded. Patients with smoking habits and systemic diseases including diabetes mellitus, systemic hypertension, pulmonary hypertension, heart failure and rheumatological disease were excluded. Exclusion criteria also encompassed the presence of retinal diseases, severe cataract, nystagmus, poor eye fixation, significant media opacity and refractive spherical and cylindrical error ≥2 D that could possibly confound the observation. After complete ophthalmological examination, all patients underwent optical coherence tomography angiography (OCTA) measurement (Optovue Inc., Fremont, California, USA) to assess the foveal avascular zone (FAZ) area; FAZ perimeter; acircularity index of FAZ; foveal density-300; superficial and deep capillary plexus vessel densities; and choriocapillaris flow area at 1mm radius. Three-dimensional OCTA scans were acquired over 6 mm × 6 mm regions. The data from the right eyes of all participants were used for statistical analysis.

Results
There was no significant difference between offspring of patients with nAMD and control groups in terms of age, gender distribution, spherical equivalent of refraction, and intraocular pressure (p = NS for all). The superficial capillary plexus vessel density of the whole image, fovea and perifovea were significantly lower than those in healthy control subjects (p= 0.025, p= 0.034, p= 0.046). The deep capillary plexus vessel density of the whole image, fovea and perifovea were significantly lower than those in healthy control subjects (p= 0.037, p= 0.044, p= 0.041). No significant difference was found in the FAZ area, FAZ perimeter, acircularity index of FAZ, foveal density-300 and choriocapillaris flow area measurements between the offspring and controls (p= NS for all).

Conclusions
Non-invasive quantitative analysis of retinal perfusion using OCTA in adult offspring of patients with nAMD demonstrated that macular vessel density was significantly lower in the study group compared to healthy controls. The results of our study supported the existence of hereditary factors in the pathogenesis of AMD and provided evidence which may explain the underlying mechanism of familial aggregation in AMD.

Financial Disclosure
The authors report no conflicts of interest. The authors received no financial support for the research.
**Title**
Treat-and-extend dosing of intravitreal anti-VEGF agents in neovascular age-related macular degeneration: A meta-analysis of 1697 eyes

**Purpose**
Intravitreal injections (IVI) of antiangiogenic agents are pivotal in treating neovascular age-related macular degeneration (nAMD). Treat-and-extend (T&E) dosing aims to maintain and maximize visual gains while reducing the burden of ongoing injections. This meta-analysis aims to elucidate the comparative efficacy and safety of anti-vascular endothelial growth factor (VEGF) IVIs via T&E versus bimonthly, monthly, and pro re nata (PRN) dosing regimens.

**Setting/Venue**
Systematic review and meta-analysis.

**Methods**
We conducted a systematic literature search of Ovid MEDLINE, EMBASE, and Cochrane CENTRAL to September 2020. English-language RCTs reporting on efficacy and/or safety outcomes of T&E in comparison to bimonthly, monthly, and/or PRN dosing regimens of anti-VEGF IVIs in nAMD patients were included. Critical appraisal was performed using Cochrane bias assessment and GRADE guidelines. The primary outcome was improvement in best corrected visual acuity (BCVA); secondary outcomes included changes in central subfield thickness (CSFT), mean number of injections administered, and incidence of adverse events. All outcomes were collected at last follow-up. Meta-analyses were conducted using a random effects model; weighted mean differences (WMD) and risk ratios (RR) were calculated.

**Results**
Across six included RCTs, 781 eyes were treated with a T&E IVI dosing regimen, 663 received monthly, 130 PRN, and 123 bimonthly IVIs. There was a low risk of bias across the trials. Mean changes in BCVA and CSFT at last follow-up were similar between T&E versus monthly (WMD, –0.62; 95%CI, –2.12 to 0.87; P=0.41; and WMD, 5.30; 95%CI, –10.67 to 21.26; P=0.52, respectively), bimonthly (WMD, 0.30; 95%CI, –3.49 to 4.09; P=0.88; and WMD, –18.91; 95%CI, –46.41 to 8.60; P=0.18, respectively), and PRN (BCVA WMD, 0.05; 95%CI, –3.55 to 3.66; P=0.98) dosing regimens. T&E was associated with a significantly reduced injection burden versus monthly (WMD, –4.52; 95%CI, –6.66 to 2.39; P<0.001) but higher injection burden versus PRN (WMD, –1.81; 95%CI, 1.12 to 2.51; P<0.001) dosing at final follow-up. There was no significant difference in safety outcomes amongst comparators.

**Conclusions**
The efficacy and safety outcomes of T&E, bimonthly, monthly, and PRN dosing were non-significantly different. However, T&E eyes had significantly fewer injections and clinic visits compared to monthly and PRN, respectively. Future assessment of patient satisfaction, treatment adherence, and cost savings with T&E regimens is recommended.

**Financial Disclosure**
Conflicts of Interest: PN: None. MMP: PSI Foundation (RI). ASD: None. AP: None. RHM: Allergan (C), Bayer (C, RI), Novartis (C, RI), Roche (C). PJK: Alcon (C), Allergan (RI), ArcticDx (E), Bayer (C, RI, RP), Novartis (C, RI, RP), Novelty Nobility (C), Roche (RI). Legend: C – consultant/consulting fees; E – equity owner; S – speaker honoraria; RI – research grant/financial support (to institution); RP – research grant/financial support (personal).
Purpose
This retrospective study aimed to analyze the clinical outcomes of two regimens of intravitreal injections of conbercept [1+pro re nata (PRN) and 3 + Q3M] for the therapy of exudative age-related macular degeneration (AMD).

Methods
In total, 105 eyes diagnosed with exudative AMD were enrolled. The eyes in the 1+PRN group (n = 51) received intravitreal injection of conbercept one time, followed by PRN retreatment. The eyes in the 3 + Q3M group (n = 54) received intravitreal injection of conbercept on three consecutive monthly, subsequently, once every three months for three times. After treatment, patients were followed up for 12 months.

Results
The best-corrected visual acuity (BCVA), central retinal thickness (CRT), and choroidal neovascularization (CNV) leakage area were compared before and after treatment. Moreover, the number of injections and adverse reactions were recorded. Compared with the 1+PRN group, BCVA was significantly improved and CRT was remarkably decreased in the 3 + Q3M group at 3, 6 and 12 months after operation. The disappeared or reduced CNV leakage area (93%) of the 3 + Q3M group was higher than that of the 1 + PRN group at the last follow-up. Moreover, the mean numbers of conbercept injections of the 1 + PRN group were less than the 3 + Q3M group. During the follow-up, there were no serious adverse reactions or ocular complications.

Conclusions
This study reveals that intravitreal injection of conbercept using 3 + Q3M regimen has certain advantages than 1 + PRN regimen in extending drug delivery interval, improving patient’s vision, and reducing CRT.
Early experience of Brolucizumab use in a tertiary hospital setting for neovascular age-related macular degeneration (nAMD)

Co-Authors

Purpose
Brolucizumab was recently approved in the UK for the treatment of nAMD. HAWK and HARRIER trials have suggested that following the loading phase, Brolucizumab 8 or 12-weekly administration is non-inferior to Aflibercept, administered every 8 weeks. BREW study demonstrated that Brolucizumab was safe and effective in stabilizing visual acuity (VA) in patients previously treated with anti-VEGFs agents. The potential for 12-weekly dosing is expected to help reduce the number of patient visits and injections. This is particularly important during the recovery phase of the COVID19 pandemic when capacity is limited by the need to maintain social distancing. To assess the efficacy and the risk profile of Broucizumab, an anti-Vascular Endothelial Growth Factor (anti-VEGF) intravitreal injections (IVT) in patients with an inadequate prior response to Aflibercept. This was defined as persistent disease activity / unstable visual acuity despite frequent therapy or disease control but a heavy treatment burden. A preliminary protocol has been published here: http://yorkshireretinasociety.com/pdfs/yobro%20suggested%20pathway.pdf.

Setting/Venue
Outpatient Consultant-led Medical Retina clinics in a tertiary hospital setting within Leeds Teaching Hospitals NHS Trust

Methods
In this retrospective observational study, medical charts of 35 patients with nAMD treated with Brolucizumab IVT between April 2020 to April 2021 were reviewed. Each patient underwent VA measured on EDTRS letter chart, central retinal thickness with spectral-domain optical coherence tomography and intraocular pressure measurement, and complete ophthalmic examination at baseline and at follow-up after Brolucizumab injection.

Results
35 patients had 102 IVT’s of Brolucizumab. The age range was 66 - 93 years (Median 80 years) of whom 51% were females. The number of prior Aflibercept injections ranged between 3-62 (Median 17). Their median injection interval when on Aflibercept was 6 weeks (Range 4-10). The first review interval after switching to Brolucizumab was the same as the last interval on Aflibercept. 28 (80%) of the patients had their first follow-up. Median VA was 57 EDTRS letters before and 67.5 after. The median CRT was 337 microns before and 436 after. The treatment was well tolerated by patients and no adverse events were observed.

Conclusions
The median improvement of VA after the first injections was 10.5 letters despite the median CRT increasing by 112.5 microns after the first dose of Brolucizumab. The treatment was well tolerated by the patients and no adverse events were observed, especially there was no intraocular inflammation or vascular retinitis detected in this case series. This case series has limitations, as it is a retrospective data collection predominantly of the first follow-up and therefore long-term results cannot be determined.

Financial Disclosure
NA
Purpose
To evaluate presence of retinal fluid and the association of fluid-free period with visual outcome in patients with neovascular age-related macular degeneration (nAMD) who were treated with anti-vascular endothelial growth factor (VEGF).

Methods
This study included nAMD patients who were treated with ranibizumab, aflibercept, or bevacizumab at least 12 months after diagnosis. The presence of any retinal fluid, intraretinal fluid (IRF), subretinal fluid (SRF), and sub-retinal pigment epithelial (RPE) fluid at diagnosis and at 12 months was evaluated. Patients were divided into quartiles based on time with absence of fluid over 12 months and difference in the improvement in visual acuity (VA) was compared among the following three quartile groups: Q1 vs Q2-Q3 vs Q4.

Results
A total of 600 patients were included. During the 12 months, mean 5.54 anti-VEGF injections were administered. The mean baseline VA and central subfield thickness (CST) was 54.14 ± 20.69 (SD) ETDRS (Early Treatment of Diabetic Retinopathy Study) letters and 379.75 ± 135.15 (SD) µm. At 12 months, mean 8.91 ± 17.22 (SD) letters of improvement in VA and mean 106.9 ± 136.68 (SD) µm of decrease in CST was noted. At diagnosis, the incidence of any retinal fluid, IRF, SRF, and sub-RPE fluid was 97.16%, 39.97%, 90.13%, and 32.44%, respectively. At 12 months, the incidence was decreased to 58.1%, 24.66%, 37.59%, and 21.21%, respectively. The mean fluid-free period was 67.30 ± 92.54 (SD) days. When divided into quartiles based on time with absence of fluid, the mean improvement in VA was +10.93 ± 17.96 (SD) letters in Q4 (25% of the patients with the longest fluid-free time), +10.10 ± 17.24 (SD) letters in Q2-Q3, and +5.56 ± 16.17 (SD) letters in Q1 (25% of the patients with the shortest fluid-free period). When compared to Q1, greater improvement in VA was noted in Q2-Q3 (P=0.0038) and Q4 (P=0.0004).

Conclusions
Result of the present study suggests that appropriate fluid control is important to achieve good visual outcomes. However, retinal fluid was noted in approximately two-thirds of the nAMD patients even after anti-VEGF therapy, suggesting the unmet needs in clinical practice.
The morphology of retinal pigment epithelium in age-related macular degeneration, a histologic comparison to unaffected cells

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Purpose

Altered retinal pigment epithelium (RPE) is a hallmark of age-related macular degeneration (AMD) [PMID: 31173079]. Morphology and function are closely intertwined and pathological RPE phenotypes may not be able to preserve important functions for outer retinal health [PMID: 31714897]. In this study, we quantified differences in RPE morphology between donors with unaffected macula and AMD. Further, we characterized differences in RPE morphology dependent on donor’s age and the respective retinal location.

Setting/Venue

Globes were collected from the Advancing Sight Network Birmingham, AL, USA. Microscopic imaging was achieved at the Leibniz Institute of Photonic Technology, Jena. Cell analyses were carried out at the University Hospital of Bonn. Data analyses were performed at the Department of Ophthalmology, Birmingham, AL, and statistical analyses were performed at the Hausdorff Center for Mathematics, Bonn.

Methods

Seven AMD-affected human RPE flatmounts (early: 3, late dry: 1; neovascular: 3) and 15 human RPE flatmounts from all two age-groups (≤51 years, n = 8; >80 years, n = 7) were imaged at three locations (fovea, perifovea, near periphery) using a laser scanning confocal fluorescence microscope (excitation 488 nm; emission: 500-750 nm; z-stack step size 390 nm). Using FIJI, RPE cell bodies were manually marked and extracted. Shape descriptors for each cell (e.g., cell area, length of the major and minor axes, eccentricity, solidity, perimeter, aspect ratio, form factor) were calculated with the help of customized software and a principal component analyses (PCA) was calculated.

Results

Of 4404 cells analysed (fovea 927; perifovea: 1430; near-periphery 2047), 626 were from AMD affected and 3778 were from healthy donors. The first principal component was able to explain 47% of variability (first two: 79%). AMD RPE cells were greatly enlarged with altered morphology and PCA identified area as the most important followed by the perimeter and the form factor (ratio between area of the block and the area of the circumscribed hull) as the shape descriptors that were strongly discriminatory. Differences between AMD affected and unremarkable maculae were most pronounced at the fovea.

Conclusions

We were able to accurately quantify RPE morphology with the presence of AMD. Enlarged and deformed cells in AMD are indicative of a dysfunctional RPE. Interestingly, RPE alterations were most pronounced at the fovea, an area typically affected by accumulation of soft drusen in AMD as well as preservation of cone-mediated visual acuity. The results of this study may help guide the interpretation of RPE morphology in vivo studies utilizing adaptive optics-assisted imaging. Further, the results of this study could be applied to characterize stem cell derived RPE cell cultures.

Financial Disclosure

Von der Emde, Vaisband, Hasenauer, Sloan: none. Curcio: Genentech (f), Heidelberg Engineering (F), Rgeneron (F), MacRegen Inc (I) Ach: Roche (C), Novartis (F,R), MacRegen Inc (I) Funding: NIH/NEI 1R01EY027948-01 (TA, CAC), R01EY029595 (CAC), R01EY024738 (CAC)
A global non-interventional study investigating real-world proactive dosing regimens with intravitreal aflibercept in patients with neovascular age-related macular degeneration: Interim analysis of first 12-month completers from XTEND

Purpose
The objective of the 36-month XTEND (evaluation of an eXtended and proactive dosing regimen in treatment-naive patients with neovascular age-related macular Degeneration [nAMD]) study is to examine the outcomes of real-world proactive treatment regimens of intravitreal aflibercept (IVT-AFL) in routine clinical practice in patients with nAMD. The study involved centers from countries with European Medicines Agency (EMA)-aligned labels (Argentina, Belgium, China, Columbia, Denmark, France, Ireland, Italy, Norway, South Korea, Spain, Sweden, Thailand, and the UK), and three other countries without EMA-aligned labels (Australia, Canada, and Switzerland). Enrollment was planned to include ≥1200 patients from countries reflecting the EMA-aligned IVT-AFL label and ≥250 patients from Australia, Canada, or Switzerland. This prespecified interim analysis was to be conducted after ≥500 patients had a 12-month follow-up assessment of visual acuity, including ≥300 patients from those countries with the EMA-aligned label (data cut-off date was February 4, 2021).

Methods
Treatment-naive patients aged ≥50 years with nAMD were eligible for enrollment if the physician planned to initiate 2 mg IVT-AFL in a proactive regimen and according to local marketing authorization as part of routine clinical practice. Depending on the country, one of two different regimens are specified in the label: a minimum treatment interval of 8 weeks following three initial monthly injections in Year 1 (per the EMA-aligned label), or a minimum treatment interval of 4 weeks following three initial monthly injections in Year 1 (in countries without an EMA-aligned label). Treatment intervals could be extended in 2- or 4-weekly increments up to a maximum of 12 or 16 weeks according to the local label. The primary endpoint was to describe the effectiveness of flexible proactive treatment approaches with IVT-AFL in treatment-naive nAMD patients (stratified by regimen type) by evaluating the mean change in best-corrected visual acuity (BCVA; Early Treatment Diabetes Retinopathy Study [ETDRS] letters) from baseline at Month 12 (M12). Statistics were descriptive only, and no formal hypothesis testing was planned. Secondary endpoints included change in central retinal thickness (CRT) from baseline to M12 and the distribution of intervals between injections. Safety was also assessed throughout the study.

Results
XTEND enrollment is complete (n=1563 patients enrolled). Overall, 742 patients (mean age 79 years; 63% female) completing 12 months’ follow-up (enrolled May 2019–March 2020) were included in the interim analysis: n=565 from countries with EMA-aligned labels (UK, n=310; France, n=60; Belgium, n=54; Denmark, n=35; and <25 patients each from other countries); n=177 from countries without EMA-aligned labels (Canada, n=120; Switzerland, n=32; Australia, n=25). Most patients (90%) were scheduled to be treated according to a treat-and-extend dosing regimen; however, because of the COVID-19 pandemic (beginning after study initiation), planned treatment interval extensions were not performed in all countries. Overall, mean±SD change in BCVA from baseline to M12 was +5.1±16.5 letters (baseline: 55.6±18.6). Mean change in CRT from baseline to M12 was -109.0±127.5 μm (baseline: 372.8±123.4). There were no differences in improvements in BCVA or CRT between patients in countries with the EMA-aligned label and in the other three countries. By M12, the mean number of IVT-AFL injections was 7.8±2.1 overall and the last completed injection interval was ≥8 weeks in 73% of patients (≥10 weeks in 44%; ≥12 weeks in 24%; ≥16 weeks in 8%). No new safety concerns were identified; two cases of endophthalmitis were reported.

Conclusions
Despite the impact of the COVID-19 pandemic, patients with treatment-naive nAMD achieved robust vision gains over the first year. Improvements in both BCVA and CRT were similar in countries with the EMA-aligned label (minimum treatment interval of 8 weeks after three initial monthly injections) and in countries where the label allows for a minimum treatment interval of 4 weeks after three initial monthly injections. The safety profile of IVT-AFL in XTEND was consistent with previous studies. Follow-up in XTEND is ongoing; based on data availability, presentation of the primary endpoint evaluation in the full analysis population is planned for 2022.

Financial Disclosure
The contribution of fluoroangiography in the evaluation of persistent neovascular network in quiescent (non-leaking) choroidal neovascularization in eyes with age related macular degeneration

**Purpose**
To examine the clinical value of fluoroangiography (FA) in the evaluation of persistent neovascular network (NV) in quiescent (non-leaking) choroidal neovascularization in eyes with age related macular degeneration (nAMD).

**Setting/Venue**
Department of Ophthalmology, General Hospital of Lamia, Lamia, Greece

**Methods**
Prospective study of 12 eyes (12 patients) with nAMD and quiescent (not leaking as identified in structural OCT) persisting NV network in eyes with AMD, on anti-VEGF. After three months of no leakage in structural OCT, patients underwent FA and OCT angiography. Follow up for 4 to 6 months. Angio OCT was performed every 2 months. Leakage in FA and time to recurrence were recorded. Intravitreal anti-VEGF was given according to the presence of retinal fluid in structural OCT (PRN treatment protocol).

**Results**
Two patients (2/12 eyes) showed leakage in FA in the absence of retinal fluid (RF) in structural OCT. Both (2/2) developed retinal fluid and required anti-VEGF treatment within 1 month of FA. The persisting vascular network was visible in all angio OCT images of all patients but differed in shape and extend from one examination to another. The extent of area affected was larger in FA than the area corresponding to the neovascular formation in angio OCT.

**Conclusions**
In quiescent neovascular network in nAMD patients, leakage may be present in the absence of subretinal (SRF) or intraretinal (IRF) fluid in structural OCT. This should be considered as a sign of disease activity and these patients should be followed up with structural OCT to allow early diagnosis of the presence of SRF or IRF and treated accordingly.

**Financial Disclosure**
No financial relations to any company
Title
Evaluation of a calculation model to estimate the impact of the COVID-19 pandemic lockdown on visual acuity in neovascular AMD

Purpose
To evaluate a calculation model performed during the Austrian coronavirus disease 2019 (COVID-19) pandemic lockdown to estimate the effect of short-term treatment interruption due to health care restrictions on visual acuity (VA) in exudative neovascular age-related macular degeneration (nAMD).

Setting/Venue
Retrospective data collection of 142 eyes in 142 patients receiving repeated intravitreal injections with anti-vascular endothelial growth factor at the Medical Retina Unit service (Rudolf Foundation Hospital, Vienna) in a personalized pro re nata regimen prior to the COVID-19 associated lockdown, when treatment was deferred between March 16 and May 4, 2020.

Methods
During the lockdown, the preliminary data was integrated into pre-existing formulae based on the natural course of the disease in the long term. Patients were re-scheduled and treated after gradually opening operating rooms. The calculation model was compared to the effective VA change.

Results
The model calculated an overall VA loss of 3.5±0.8 letters early treatment diabetes retinopathy study (ETDRS) (p<0.001 [95% CI:3.3;3.6]) on average compared to 2.5±6 letters ETDRS (p<0.001 [95% CI:1.5;3.5]) as measured after re-opening the doors with a mean treatment delay of 61±14 days. The total difference between the model exercise and the real-life outcomes accounted for 1±5.9 letters ETDRS (p=0.051 [95% CI:0;2]).

Conclusions
The herein presented calculation model might not be suitable to estimate the effective VA loss correctly. Untreated eyes and eyes under previous therapy behave differently after short-term treatment interruption. However, this study demonstrated the potentially negative impact of the COVID-19 pandemic lockdown on patients compromised by nAMD.

Financial Disclosure
No financial disclosure
Purpose
To analyze the inter-session and the inter-reader reliability of structural biomarkers for inter-mediate age-related macular degeneration (iAMD) based on the European multi-center, natural history study MACUSTAR (ClinicalTrials.gov Identifier: NCT03349801).

Setting/Venue
Cross-sectional analysis of the observational natural history MACUSTAR study in eyes with early, intermediate (i) and late AMD.

Methods
For the analysis of the inter-session variability gradings on the presence of pigment epithelium detachment (PED), reticular pseudodrusen (RPD), vitelliform lesions and maximum drusen size classification (>125 µm; >63 µm; ≤63 µm) were performed. For assessing the inter-reader variability, RPD en-face size assessment and retinal multilayer segmentation were performed by up to three independent readers (R1/R2/R3). Repeatability of gradings between sessions and readers was assessed with Cohen's kappa and intraclass-correlation coefficients. For the retinal layer segmentation, the overlap (Dice similarity coefficient [DSC]) was further compared between manual gradings and a deep-learning (DL) based segmentation model. Mixed-effects models were fitted to data from each retinal layer with the DSC as dependent variable and patient as random intercept term in order to compare the different pairings (R1-vs.-R2; R1-vs.-DL; R2-vs.-DL), which were included as independent variable.

Results
Between sessions, good agreement was found for the maximum drusen size classification with Cohen's kappa = 0.817 [95% confidence interval 0.70 – 0.94] based on 195 study eyes of 195 patients with early and iAMD. Within the iAMD group (168 study eyes of 168 patients), there was a high agreement between sessions for the presence of PED 0.869 [0.69 – 1.0] and RPD 0.752 [0.63 – 0.87], while repeatability was less for the presence of vitelliform lesions 0.649 [0.39 – 0.91]. Further almost perfect agreement was observed for the en-face size assessment of areas with RPD (161 study eyes of 161 patients with early, i- or late AMD) between readers (kappa = 0.958 [0.94 – 0.97] for R1-vs.-R2; 0.947 [0.93 – 0.96] for R1-vs.-R3 and 0.945 [0.93 – 0.96] for R2-vs.-R3). For the multilayer segmentation, the inter-reader-overlap and the reader-vs.-algorithm-overlap were equivalent for the retinal-nerve fiber layer (RNFL) (DSC estimate [95% CI] of 0.86 [0.83 – 0.88]), the outer nuclear layer (ONL) (0.88, [0.83 – 0.94]), the inner photoreceptor segments (IS) (0.82 [0.77 – 0.87]) and the choroidal layer (0.92 [0.91 – 0.94]).

Conclusions
For qualitative and quantitative retinal imaging biomarkers high agreement was exhibited be-tween session and readers. Further, fully-automated DL-based image segmentation provides highly comparable results in terms of multilayer segmentation of the retina and will be helpful for establishing robust and reliable structural endpoints for future interventional clinical trials in early and intermediate AMD disease.
Brolucizumab q16w/q12w dosing allocation in nAMD: a post hoc evaluation of data from the HAWK and HARRIER studies

**Purpose**

HAWK (NCT02307682) and HARRIER (NCT02434328) evaluated the efficacy and safety of brolucizumab versus aflibercept in previously untreated patients with neovascular age-related macular degeneration (nAMD). An adaptive study design was applied to the brolucizumab treatment arms, whereby all patients received three monthly loading injections, then brolucizumab was injected q12w unless disease activity (DA) was identified at pre-specified disease activity assessments (DAA) resulting in switching to q8w for the remainder of the study. With this design, the percentage of patients on brolucizumab 6 mg maintained on q12w until the primary analysis at Week 48 was 56% in HAWK and 51% in HARRIER. This design represents a conservative approach to evaluating durability of a new anti-vascular endothelial growth factor (anti-VEGF) therapy and reflects the treatment landscape for nAMD at the time the studies were initiated. In more recent studies, allocation to fixed dosing (q16w, q12w, and q8w) until Week 48, following the initial loading phase, has been reported. The aim of this post hoc analysis is to examine the percentage of brolucizumab patients in HAWK and HARRIER that would be assigned to q16w, q12w, and q8w fixed dosing had different treatment allocation criteria been used.

**Setting/Venue**

HAWK and HARRIER were 2-year, randomized, double-masked, multicenter active-controlled Phase 3 trials conducted at 408 sites in North, Central, and South America; Europe; Asia; Australia; and Japan.

**Methods**

In the HAWK and HARRIER studies, the first DAAs were conducted at Weeks 16 and 20, following three loading doses at Weeks 0, 4, and 8. In this post hoc analysis, the following criteria were applied for hypothetical allocation of patients from the brolucizumab 6 mg treatment arms of HAWK or HARRIER to q8w, q12w, and q16w fixed dosing: patients with DA at Week 16 were allocated to q8w dosing; patients without DA at Week 16 but with DA at Week 20 were allocated to q12w dosing; and patients without DA at Weeks 16 and 20 were allocated to q16w dosing. Patients that did not meet the DA criteria at Week 16 but received an injection at the visit were excluded from the analysis. DA was defined, as per recent clinical trials, as best-corrected visual acuity (BCVA) loss ≥10 Early Treatment Diabetic Retinopathy Study (ETDRS) letters from the maximum of the last two visits or BCVA loss ≥5 ETDRS letters from the average of the last two visits or central subfield thickness (CST) increase ≥75 µm from the minimum of the last two visits or CST increase ≥50 µm from the average of the last two visits.

**Results**

Based on the applied DA criteria, the percentage of brolucizumab patients assigned to fixed q8w, q12w, and q16w dosing regimens following three loading doses was as follows: HAWK q8w=20.9% (n=63/301), q12w=20.6% (n=62/301), q16w=58.5% (n=176/301); HARRIER q8w=22.7% (n=73/321), q12w=24.0% (n=77/321), q16w=53.3% (n=171/321). With this alternative design applied, the percentage of patients on a fixed dosing regimen of q12w or longer until the primary endpoint at Week 48 would be 79.1% in HAWK and 77.3% in HARRIER.

**Conclusions**

The HAWK and HARRIER studies applied a conservative approach to brolucizumab dosing with adjustment to q8w dosing based on DA at multiple points throughout the study. If fixed dosing allocation criteria had been applied following the loading phase, similar to more recent development studies, and initial treatment allocations had not been rechallenged at multiple DAA visits, approximately 55% of patients would have been allocated to q16w dosing and approximately 78% of patients would be allocated to q12w dosing or longer through Year 1. Further clinical studies with brolucizumab would be needed to study the visual and anatomic outcomes with these dosing allocation criteria.

**Financial Disclosure**

Consulting fees: Aerie, Allegro, Allergan, Eyepoint, Genentech, Kodiak, Novartis, Regeneron, Santen; Speakers bureau: Allergan, Genentech, Mallinckrodt, Novartis, Regeneron, Spark; Contracted research: Aerie, Allegro, Allergan, DRCR, Genentech, Icon, Ionis, Kalvista, Kodiak, Novartis, Opthea, Optos, Regeneron, Santen, Senju, Sydneaxis, Ribomic; Equity: Aviceda, Nanoscope, Inflamasome
Intraocular intraocular implants for low vision: A new kind of visual perception?

Purpose
Some of the patients with retinal diseases end up in low vision. Most of them have problems in carrying their conventional LVA (low vision aids). The developments in nanotechnology and computer sciences has great impact on innovations. So for low vision patients there are some new intraocular lenses and intraocular telescopes. The aim of this review is to highlight their advantages and disadvantages.

Setting/Venue
Review of the literature about intraocular lenses with special design in the central area and intraocular telescopes.

Methods
Intraocular lenses with special design in the central area and intraocular telescopes which are on the market are reviewed and compared to each other in respect of optical effects and induced visual perception.

Results
The problem of carrying relatively heavy LVA devices are solved with the new implants for low vision patients. The optical problems are solved to some extent. Extraocular LVA’s are dependent from the distance to corneal apex. They can make the image bigger, but they cannot shift the image with prisms because of the compensatory movements of the eye. The fixation of the implants in the eye eliminates the change with the location of the LVA and with the eye movements because prisms in the eye can shift the image to the desired location with the better vision capacity. The resulting effect area of the implants can be foreseen to some extent. The higher illumination needs are still there with the implants, because of the magnifying effect of the implants. The use of the peripheral retina for peripheral vision of the non-implanted eye may be limited by the fact that for the central and peripheral part there is a big aniseikonia.

Conclusions
For some low vision patients the new developments in implants may be of benefit. However the restrictions of the optical systems should be known in advance. Intraocular lenses with special design in the central area and intraocular telescopes may be a good option for low vision patients especially with little mobility and low level of compliance.

Financial Disclosure
None
Purpose
To report 4 cases of acute serous retinal detachment (ASRD) after the same operating session of uncomplicated cataract surgeries.

Methods
In this case series, data of patients who developed an ASRD after an uncomplicated phacoemulsification with IOL implantation during the same operating session were collected. Diagnosis was made at the first post-operative day, when all patients had a very low best corrected visual acuity (BCVA) despite of a good aspect of the anterior segment, without significant keratopathy and with only trace cells in the anterior chamber. Spectral domain optic coherence tomography (SD-OCT) revealed a serous retinal detachment with subretinal fluid accumulation in the macular area. Patients received parabulbar injection of 40 mg/ml triamcinolone in addition to usual post-operative topical treatment of 0.1% dexamethasone and 0.3% netilmicin eyedrops. Patients were examined postoperatively at day 1, 3, 7, and 1 month. BCVA and central foveal thickness (CFT) measured by a SD-OCT were evaluated at each visit. A relationship between demographics, preoperative ocular conditions, systemic diseases, parameters of surgery and the development of ASRD was analysed.

Results
After a single operating session of 10 uneventful cataract surgeries, operated by the same expert surgeon, at day 1 post-operative an ASRD was detected in 4 patients (3 male, 1 female; mean age 71 ± 4.1 years). Pre-operatively, mean BCVA was 0.6 ± 0.1 decimals and mean CFT was 191.3 ± 13.7 micron. At the first post-operative day, mean BCVA was 0.01 ± 0.1 decimals, and all eyes had serous retinal detachment, with a mean CFT of 682.0 ± 97.4 microns. At the following controls, BCVA improved and CFT reduced significantly. At day 7, BCVA was at least 0.7 decimals in all eyes, with complete reabsorption of subretinal fluid. At 1 month, mean BCVA was 1.0 ± 0.0 decimals and no eye had recurrence of serous retinal detachment, with a mean CFT of 202.3 ± 26.7 microns. No relevant data were found on other parameters investigated.

Conclusions
Acute serous retinal detachment is a rare event that can occur after uncomplicated phacoemulsification, that in our cases resolved in a few days without recurrence.
Purpose

Recently, optical coherence tomography (OCT) based indicators have been used and assessed for the ability to predict both functional and structural outcome after macular hole surgery. This has advanced the role of OCT from just diagnosing FTMH towards predicting outcome. This application of different FTMH parameters based on pre-operative OCT can give us further insight into the pathogenesis of FTMH and effectiveness of varying surgical techniques in yielding better surgical outcomes. Researchers have used Diameter Hole Index (DHI), Tractional Hole Index (THI), Hole Form Factor (HFF), minimum hole diameter, hole base diameter, maximum hole diameter, apex diameter, macular hole height, hole arm length and Macular Hole Index (MHI) as OCT based indicators to predict structural and functional outcome of FTMH surgery.

Similarly, other OCT based findings may correlate with the functional outcome of macular hole surgery like the integrity of External Limiting Membrane (ELM) and Inner Segment/Outer Segment (IS/OS) line. We aim to study these OCT based parameters in our population in predicting the functional outcome of FTMH surgery and compare the results with international literature to explore the utility of this information in our population of FTMH.

Setting/Venue

This study was designed as retrospective chart review of 30 eyes diagnosed to have FTMH and then proceeded with surgical management. The cases reviewed in this study were from January 2016 to March 2020. All of these cases presented at The Aga Khan University Hospital, Karachi, Pakistan.

Methods

These cases were diagnosed clinically on slit lamp examination by an experienced vitreoretinal surgeon. Further macular hole staging and parameter measurement was done using Spectral Domain Optical Coherence Tomography (SD-OCT – Spectralis® Heidelberg Engineering Inc. Franklin, USA). This parameter measurement was done using caliber function of OCT machine in all pre-operative OCT scans by two independent operators and then verified by an experienced vitreoretinal surgeon. Patients who had other concurrent diseases that may impair the functional outcome of surgery were excluded from the study (glaucoma, retinal detachment, vascular retinopathy, proliferative vitreoretinopathy, high myopia > -6.00 DS). Secondary macular holes were also excluded from the study (trauma, high myopia, secondary epiretinal membrane associated macular hole). Patients with a history of symptoms of more than 6 months were not included in this study. The Ethical Review Committee (ERC) of The Aga Khan University Hospital gave approval of this study. The reference number of ERC is 2020-5158-11463. Various OCT based ratios were calculated using following formulas:

- Diameter Hole Index (DHI) = MD/BD
- Tractional Hole Index (THI) = H/MD
- Hole Form Factor (HFF) = (RAL + LAL)/BD
- Macular Hole Index (MHI) = H/BD

Results

We analyzed the data of 28 out of 30 patients. The mean age was 61.5 ± 6.2 years. The female to male ratio was 2.11:1. Mean Minimum Diameter (MD) was 448.3 ± 189.9 μm. Mean hole height was 456.2 ± 112.6 μm. Hole base diameter was 888.9 ± 277.1 μm. Table 1 shows pre-operative and 6 months post-operative BCVA in LogMAR with a p-value <0.001 which is statistically significant. Indices of various OCT cut points derived from ROC curve analysis that predict favorable outcomes (BCVA equal to or better than 0.4 logMAR at 6 months post-operative) was: 0.454, 1.086, 0.854, and 0.501 for Diameter hole index (DHI), Tractional hole index (THI), Hole form factor (HFF) and Macular hole index (MHI) respectively. Area under the curve and 95% confidence interval) of 0.827, 69, 100 for HFF; 0.846 (0.660 to 0.954), [0.827 (0.637 to 0.943)] for THI, HFF, and MHI respectively. Specificity was 100% for each indices and sensitivity was high for HFF (84.6%) and lowest for DHI (64.29%).

Conclusions

The cut off values for MHI, DHI, HFF and THI in our study were 0.501, 1.086, 0.854 and 1.086 respectively. These cut off values showed a predicted LogMAR vision gain of 0.4 or better at 6 months post-operative time. These cut offs were associated with area under curve (AUC with 95% confidence interval), sensitivity (with 95% confidence interval) and specificity (with 95% confidence interval) of 0.827, 69, 100 for MHI; 0.75, 64, 100 for THI; 0.846, 84, 100 for HFF; 0.827, 73, 100 for DHI. This result is in comparison with Geng et al where cut off values for MHI and HFF were 0.427 and 1.02 with comparable sensitivities and specificities. The difference was the BCVA at 6 months post-operative BCVA in LogMAR with a p-value <0.001 which is statistically significant. Indices of various OCT cut points derived from ROC curve analysis that predict favorable outcomes (BCVA equal to or better than 0.4 logMAR at 6 months post-operative) was: 0.454, 1.086, 0.854, and 0.501 for Diameter hole index (DHI), Tractional hole index (THI), Hole form factor (HFF) and Macular hole index (MHI) respectively. Area under the curve and 95% confidence interval) of 0.827, 69, 100 for HFF; 0.846 (0.660 to 0.954), [0.827 (0.637 to 0.943)] for THI, HFF, and MHI respectively. Specificity was 100% for each indices and sensitivity was high for HFF (84.6%) and lowest for DHI (64.29%).
Effect of cataract surgery on the macula in eyes with epiretinal membrane and vitreomacular traction

Ahmet Altun

Purpose
To investigate the macular anatomical and functional changes induced by cataract surgery in eyes with vitreomacular traction (VMT) and epiretinal membrane (ERM).

Setting/Venue
The eyes of patients that underwent cataract surgery for the phacoemulsification technique were included in this prospective and controlled study.

Methods
Eyes with and without ERM and VMT were included in the study (Group 1) and control (Group 2) groups, respectively. Changes in the macular before and after the operation were monitored by optical coherence tomography for 6 months postoperatively. Characteristics, systemic diseases and ophthalmologic examination findings of the groups were investigated and compared.

Results
A total of 56 eyes of 56 patients were included in the study. There were 28 eyes of 28 patients in both groups. There was no significant difference between the groups in terms of age, gender and cataract level. In Group 1, VMT spontaneous released in 5 eyes, cystoid macular edema in 6 and full-thickness macular hole developed in 2 eyes in Group 1 during the six-month follow-up period. In Group 2, only spontaneous posterior vitreous detachment developed without complications in 3 eyes. The average best corrected visual acuity in Group 2 improved statistically significantly better than in Group 1.

Conclusions
During cataract surgery, changes in intraocular dynamics and vitromacular traction may affect the macula negatively.

Financial Disclosure
The authors declare that they have no financial or non-financial relationship or commercial interest with any of the materials discussed in this manuscript.
Post-operative complications in scleral versus limbic incision in Artisan® aphakia IOL

**Purpose**
Aphakic IOL (intraocular lens) are used when there is no support for a bag IOL. Artisan® is one of the options for implantation. They can be performed either by corneal or scleral incision with known advantages in each option. This study aims to evaluate post-operative complications and outcomes relative to the type of the 6 mm incision performed (limbic versus scleral) for Artisan® insertion in aphakic patients.

**Setting/Venue**
Department of Ophthalmology, Hospital de Braga, Braga, Portugal

**Methods**
This retrospective cohort study includes all aphakic IOL implantation at a tertiary care center in Portugal between January 2017 and December 2019. The case files were retrieved from the electronic medical records using the ICD-9 3619 coding – posterior dislocation of lens, mechanical complication of intraocular lens or other complications due to cataract surgery. All eyes with a minimum follow-up of 12 months were included in the study. Patients over 18 years-old and with the following diagnosis were included: aphakia, traumatic cataract, posterior dislocation of lens, decreased corneal endothelium cell count, intracapsular cataract extraction, dislocated IOL, IOL exchange, posterior capsule rupture. Excluded criteria were: other ophthalmic or systemic pathology which interfere with visual acuity, phakic IOL, Nd:yag laser codification, insufficient data or follow-up. Collected data included: age, gender, laterality, baseline and postoperative best-corrected visual acuity (BCVA), spherical equivalent (SE), and intra-ocular pressure (IOP), type of incision (corneal versus scleral), concomitant surgery, date of diagnosis and surgery, ocular and systemic concomitant pathologies, and intraoperative and postoperative complications. BCVA was recorded based on Snellen decimal scale. All data were verified before and 3, 6 and 12 months after surgery.

**Results**
After all data collection, 404 eyes were included in statistical analysis. According to the chosen criteria, 106 eyes were included. In 69.8% (n=74) eyes a corneal incision was made – C group – and in 30.2% (n=32) eyes the IOL was inserted via scleral incision – S group. No significant differences between groups were found regarding gender, age, ocular laterality or concomitant ocular pathology (p-values>0.05). The most common primary diagnoses were IOL complication or posterior dislocated lens fragments in both groups. Combined surgery was mostly done in S group (p-value=0.001). Regarding visual and refractive outcomes, there was a significant improvement of BCVA and SE in both groups from baseline to the end of follow-up period (p-values<0.05), without significant difference between groups (p-value>0.05). Intracocular pressure was also similar between groups. Complications were divided according to the affected segment in anterior, posterior or both segments, with all categories showing no significant difference between groups (p-value=0.44, 0.55, and 0.85, respectively). The only reported anterior complications in group S were corectopia and corneal pigmentation. No complications were reported in 60.8% (n=45) and 68.8% (n=22) eyes in group C and S, respectively.

**Conclusions**
This study reported good and similar visual and refractive outcomes for Artisan® aphakia lens implantation either via scleral or limbic incision. Complications were also reported with a non-significant difference between both groups, concluding that Artisan® aphakia lens implantation is an effective procedure regardless the type of incision (scleral or limbic) with no outcome differences between the two techniques. Although anterior complications are statistically similar between groups, they have a tendency to be more varied and serious in group C. Since group S has a significant smaller sample size, a further study with a larger sample is needed in order to confirm or refute this tendency for better anterior segment outcomes in group S. The wide range of complications and different primary and associated diagnosis, and the statistically significative greater number of combined surgeries in group S, increases the likelihood of a confounding factor(s).

**Financial Disclosure**
This research received no financial support. The authors declare no financial, institutional nor commercial interests related to the research.
### Title
Pars plana vitrectomy and scleral fixation of Akreos AO60 Intraocular Lens using GORE-TEX suture: Focus on complications

### Purpose
"In-the-bag" placement of an IOL is the holy grail for any cataract surgeon. However, in the absence of capsular integrity, alternative surgical options to place the IOL must be sought. We aim to report the visual results and safety profile of ab externo scleral-fixed Akreos AO60 intraocular lens implantation using Gore-Tex suture, with particular attention to postoperative retinal outcomes.

### Setting/Venue
Department of Ophthalmology, Centro Hospitalar e Universitário de São João, Porto, Portugal.

### Methods
Single-center, Retrospective case series. Electronic clinical records of all patients submitted to pars plana vitrectomy and scleral fixation of a Bausch and Lomb Akreos AO60 IOL were reviewed. Data concerning age, sex, laterality, pre- and postoperative best-available visual acuity, surgical indication and postoperative complications were collected. Considered outcomes were difference in best-available visual acuity and frequency of postoperative complications.

### Results
A total of 22 eyes from 21 patients were included. 45.5% (n=10) of patients were females. The mean age at time of surgery was 73.41 ± 13.55 years. The mean follow-up period was 705.64 days (range 30-1431 days). Globally, the mean best available logMAR visual acuity improved from 1.42 preoperatively (0.22 decimal correspondent) to 0.46 postoperatively (0.55 decimal correspondent), this difference being statistically significant (P<0.001). Postoperative complications included ocular hypertension (27.3%; n=6), transient cornea edema (27.3%; n=6), cystoid macular edema (18.2%, n=4), self-limited hemovitreous (4.5%, n=1), self-limited hypotension (4.5%, n=1), and one case of late retinal detachment (4.5%). No suture related complications were observed namely IOL displacements.

### Conclusions
Visual acuity significantly improved after pars plana vitrectomy and scleral fixation of Akreos AO60 intraocular lens using Gore-Tex suture. There was a low ratio of relevant early postoperative complications but a late retinal detachment occurred. No suture related problems were recorded. As so, this seems to be a valuable alternative when "in-the-bag" placement of an IOL is not possible.

### Financial Disclosure
No financial disclosures to report
**Title**
Influence of underlying retinal pathology in refractive outcomes in combined phacovitrectomy

**Purpose**
To investigate the influence of underlying retinal pathology on the refractive outcome in combined phacovitrectomy.

**Setting/Venue**
Retrospective case-control study

**Methods**
Eyes that underwent combined small-incision cataract surgery and small-gauge vitrectomy for age-related cataract and epiretinal membrane (ERM), macular hole (MH) or retinal detachment (RD) were included. Eyes that underwent uneventful phacoemulsification and in the bag implantation of the same IOL (CT Asphina 409M) served as controls. Prerequisites for enrollment were uneventful surgery with in-the-bag implantation of the same IOL, absence of intra- or postoperative complications, preoperative swept-source OCT-based biometry (IOLMaster700) with successful integrated check, follow-up period of eight to twelve weeks after surgery, postoperative CDVA ≤0.4 Logmar and corneal astigmatism ≤2D. After constant optimization for the control group biometric formulas Haigis, SRKT and HofferQ were evaluated.

**Results**
A total of 448 eyes from 448 patients were included in the study. The cataract control group comprised 101 eyes, the ERM group 137, the MH group 93 and the RD group 117 (63 with attached and 54 with detached macula). Preoperative mean axial length was 24.3±1.64mm (range 20.6 to 32.59mm), preoperative spherical equivalent -0.75±3.79 (range -20.63 to 10.38D). Refractive prediction error (PE) was zeroed out for the cataract group for all three formulas after a-constant optimization. PE was then calculated for ERM, MH and RRD group and was -0.16D, -0.26D and -0.16D with Haigis, -0.13D, -0.26D and -0.13D with SRKT, -0.12D, -0.24D and -0.09D with HofferQ, respectively. Absolute error for ERM, MH and RRD was 0.38D, 0.49D and 0.89D with Haigis, 0.42D, 0.51D, 0.89D with SRKT and 0.40D, 0.49D and 0.89D with HofferQ, respectively.

**Conclusions**
In terms of combined phacovitrectomy a myopic shift seems to occur postoperatively, when compared to phacoemulsification only. Refractive deviations seem to be strongly affected by the underlying macular pathology and should be taken into account for optimizing outcomes.

**Financial Disclosure**
No financial disclosures
Inverted ILM flap technique for idiopathic small, medium and large macular holes

**Purpose**
To study the functional and morphological results of the inverted internal limiting membrane (ILM) flap technique for idiopathic small (<250µm), medium (250-400µm), and large (>400µm) macular holes (MHs).

**Setting/Venue**
We are a group of Munich-based retinal specialists associated with Herzog Carl Theodor eye clinic. Since 2014, we have been using the inverted flap technique, initially for the treatment of large MHs. Convinced by the results, we also started to use it for small and medium-sized MHs.

**Methods**
Retrospective, nonrandomized interventional study of 70 eyes in 65 patients with primary idiopathic MHs ranging from 69 to 709µm in minimum diameter who underwent pars plana vitrectomy (PPV) with the 360° inverted ILM flap technique between March 2015 and January 2018. Closure rate, best-corrected visual acuity (BCVA) and integrity of external limiting membrane (ELM) as well as ellipsoid zone (EZ) were analyzed by optical coherence tomography (OCT).

**Results**
Total closure rate was 97.1% (68/70 eyes) with 100% (15/15 eyes) in the <250µm group, 100% (29/29 eyes) in the 250-400µm group, and 92.3% (24/26 eyes) in the >400µm group. We found that mean BCVA significantly improved after treatment: from 0.18 decimal (0.7 LogMAR) preoperatively to 0.49 decimal (0.3 LogMAR) postoperatively in the <250µm group (n=15, p= <0.001), from 0.11 decimal (0.9 LogMAR) preoperatively to 0.4 decimal (0.4 LogMAR) postoperatively in the 250-400µm group (n=29, p= <0.001) and from 0.1 decimal (1.0 LogMAR) preoperatively to 0.3 decimal (0.5 LogMAR) postoperatively in the >400µm group (n=26, p= <0.001). In 17 patients (mean MH diameter: 318µm) follow-up over a period of 14 months was possible. BCVA increased from 0.39 decimal (0.4 LogMAR) after 1 month to 0.49 decimal (0.3 LogMAR) after eight months and 0.52 decimal (0.2 LogMAR) after 14 months (p=0.00122, t-test). In this subgroup a recovered ELM could be observed in 58.8% (10/17 eyes) after one month, in 82.4% (14/17) after eight months and in 88.2 % (15/17 eyes) after 14 months A recovered EZ could be observed in 23.5% (4/17 eyes) after one month, in 52.9% (9/17) after eight months and in 70.6 % (12/17 eyes) after 14 months.

**Conclusions**
In addition to its importance as a treatment option for large MHs, the inverted ILM flap technique also appears to be an effective and safe procedure for the treatment of small and medium-sized MHs.

**Financial Disclosure**
none
That really flows?! - A closer look at the cutting process of a newly developed laser vitrectomy system

**Purpose**
The movement of the duty-cycle of existing mechanical vitrectomy cutters causes traction through the vitreous body. This force is transmitted to the retina and can lead to tears. Replacing this mechanical movement with a laser-induced plasma to cut the vitreous, these tractions could be minimised and allow continuous flow at the vitrectomy tip.

**Setting/Venue**
ultraslowmotion videos show the dutycycle of a mechanical and laser vitrectomy-cutter removing porcine vitreous and visualized balanced salty solution (BSS). Laser source is a diode-pumped Q-switched Nd:YAG laser, $\lambda = 1064$ nm, pulse duration 4 ns.

**Methods**
The dutycycle and vitreous removal are described with video recordings and physical calculations; what is the duration of the cutter opening and cutter closure, how exactly do the cutting process and the flow interact?

**Results**
Video recordings show an almost continuous flow of tissue at the laser-vitrectomy-tip and present the differences to mechanical cutting systems.

**Conclusions**
The use of a laser cutter allows less traction within the vitreous body, a reduction in iatrogenic complications during vitrectomy is therefore conceivable.

**Financial Disclosure**
I don't have any financial relations to a company
## Title
Outcomes and complications of pneumatic retinopexy: Moroccan experience

## Purpose
The purpose of this study is to evaluate anatomic and visual outcomes after pneumatic retinopexy (PR) for treatment of primary rhegmatogenous retinal detachment repair. Additionally, we analyze the preoperative factors predicting the anatomic failure.

## Setting/Venue
Department of ophthalmology, University Hospital Hassan II of Fez, Morocco.

## Methods
In this interventional case series consecutive patients with new on set primary rhegmatogenous retinal detachments were treated with pneumatic retinopexy and followed prospectively. The primary outcome measure was anatomic and visual outcomes at minimum 3 months. The following were analyzed: epidemiological data, initial visual acuity, anatomical characteristics of the RD, surgical technique, complications, and procedures for surgical recovery.

## Results
60 eyes were recruited between June 2016 and November 2018. The anatomical success after a single surgical procedure was achieved in is 69.4% and visual acuity improved significantly (1.26 LogMAR +/- 0.773 VS 0.42 LogMAR +/- 0.3; p<0.001). (8.17 +/- 6.14 LogMAR lines; p<0.001). The factors associated with anatomic failure are vitreoretinal proliferation (PVR) greater than or equal to stage B (p = 0.015) and the size of detached area (p = 0.015). A new or missed breaks were identified in 3 patients, subretinal gas in one patient and choroidal detachment in one patient. At final follow-up, the retina was fully attached in 97.95% of eyes.

## Conclusions
The anatomical and functional results of this study confirm that PR remains a reasonably successful option in the management of primary retinal detachment. Its benefit / risk ratio is positive when its indications are respected and its technical features are mastered.
Title
Refractive outcomes after combined phacoemulsification cataract and vitrectomy surgeries

Purpose
To evaluate refractive accuracy and factors influencing refractive outcomes after combined phacoemulsification cataract and vitrectomy surgeries

Setting/Venue
Single surgeon, private practice setting, Adelaide, Australia

Methods
Eighty-nine consecutive patients (89 eyes) who had phacoemulsification, intraocular lens (IOL) implantation and pars plana vitrectomy (PPV) between 2016 and 2019 were enrolled in a retrospective study. The final spherical equivalent refractive outcomes were measured using an autorefractor 3 months postoperatively. The refractive accuracy and factors influencing the postoperative refractive outcomes were analyzed.

Results
The mean final refractive outcome in spherical equivalent (postoperative refraction minus predicted refractive outcome) was -0.02 ± 0.607 diopters (D). The vast majority of patients (n=82, 92.1%) achieved final refractive outcomes within ± 1.00 D. Among those who achieved good refractive outcomes, the study found final refractive outcome of within ± 0.25 D, ± 0.50 D and ± 0.75 D were 44 patients (49.4%), 64 patients (71.9%) and 77 patients (86.5%) respectively.

Conclusions
Combined phacoemulsification cataract and vitrectomy surgeries produce good refractive outcomes which are comparable to cataract surgery alone in a variety of vitreoretinal pathologies. There were no specific pre-operative factors that influenced the final refractive outcomes.

Financial Disclosure
Nil
Digitally assisted 3D surgery: Beyond vitreous

Shilpi Narnaware
India

Prashant Bawankule

Purpose
To evaluate the application and safety of 3D visualization system in varied anterior segment procedures and Scleral Buckle.

Setting/Venue
Sarakshi Netralaya, Nagpur, Maharashtra, India

Methods
A prospective observational study of 313 eyes. Patients undergoing phacoemulsification (PE) with Intra Ocular Lens (IOL), Trabeculectomies, Glaucoma triple procedure (GTP), Scleral Fixated (SF) IOL and Scleral buckle (SB) were included. Cases were randomly distributed in 3D visualization system (Learning and post-learning phase) and conventional Microscope group. Parameters studied were complications (intra-operative and early post-operative), surgical outcomes, and surgeon's perspective on various parameters (through a validated questionnaire) like surgical time, time lag, learning curve, ease of doing various steps and its value as an educational tool, for both groups.

Results
Complications rate were not different in 2 groups. Surgical outcomes (anatomical and physiological) were similar in both the groups. Mean duration of surgery in PE+IOL, Trabeculectomy, GTP in learning stage by 3D was significantly higher than Microscope, which became insignificant in post learning stage. For, SB and SF IOL, duration between 2 groups were insignificantly different. There was significant learning struggle in PE+IOL, SB and Trabeculectomy. Image resolution, depth perception, illumination and postural comfort was graded higher for 3D surgery across the stages. Time lag, poor color contrast and field of view was appreciated during the learning stage. Educational relevance of 3D was higher, as appreciated by resident and nurses.

Conclusions
3D surgery is as safe, faster and predictable after initial learning struggle. Even in anterior segment procedure, no apparent lag was appreciated after learning curve.

Financial Disclosure
No financial relations
Results in comparison between 30 gauge ultrathin wall and 27 gauge needle in sutureless intraocular lens flanged technique in diabetic patients: 24-month follow-up study

**Purpose**
Intraoperative complications in cataract surgery are more common in diabetic patients. Solving aphakia in these circumstances remains a challenge, as the scleral structure has been shown to be different in diabetes. This study aims to analyze the role of a secondary sutureless scleral intraocular lens (IOL) flanged fixation in diabetic patients without capsular support and to compare the anatomical and functional outcomes using a 30 gauge (G) ultrathin wall needle vs. a 27G needle.

**Setting/Venue**
1) Retina Private Office, University of Buenos Aires, 525  2) Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel Ophthalmology Division, Tel Aviv Medical Center, Sackler  3) Diagnostic Ophthalmology Center, Buenos Aires, Argentina  4) Ophthalmology Department, University of Leipzig, Leipzig, Germany

**Methods**
multicenter international study. 105 eyes (105 patients) who underwent PPV with secondary IOL fixation using a sutureless 27G (n = 51) or a 30G ultrathin wall (UTW) needle technique (n = 54) and had a 24 months postoperative follow up. Consecutive patients’ records were reviewed for lens stability and centration parameters, intra- and postoperative complications at 7 days, 1, 3, 6, 12, and 24 months after surgery. Correlations between outcome measures and needle size (27G vs. 30G UTW) were analyzed.

**Results**
IOL displacement occurred in 30 patients (41.2%) in the 27G group and did not occur in the 30G UTW needle group (p < 0.001). Mean time until IOL displacement was 10.5 ± 7.0 months (range: 7 days–24 months). IOL centricity was significantly better in the 30G ultrathin wall needle group compared to 27G (p = 0.001). Additional surgical interventions were necessary only in the 27G group (n = 14).

**Conclusions**
Sutureless IOL flanged technique using a 30G UTW needle is more predictable and has less complications in aphakic diabetic patients, compared to a 27G needle technique.

**Financial Disclosure**
Title
Complications and management of Carlavale lens implantation in patients with insufficient capsular support

Purpose
To evaluate the safety profile of Carlavale intraocular lens (IOL) implantation.

Setting/Venue
Institut Català de Retina, Barcelona, Spain

Methods
Prospective, consecutive case series of patients with insufficient capsular support undergoing 25-gauge pars plana vitrectomy (PPV) with Carlavale IOL implantation in a single procedure. The main outcome measures were intra- and postoperative complications during at least 3-month follow-up.

Results
Thirty-two patients were included, 22 were male. Mean age, follow-up and axial length were 68.5 ± 11 years, 6 ± 4.4 months and 25.2 ± 1.7 mm, respectively. Twenty-four eyes had IOL/bag dislocation, 1 lens subluxation, 5 aphakia, and 2 uveitis-glaucoma-hyphema syndrome. Previous PPV, pseudoexfoliation syndrome and ocular trauma were diagnosed in 15, 6, and 5 patients. Median corrected-distance visual acuity (CDVA) improved from 0.4 to 0.2 logMAR; however, when previous ocular comorbidities affecting VA were excluded, this improved to 0.11 logMAR. CDVA increased in 17 and decreased in 3 eyes. Hyphema (n=2, 6.3%), vitreous haemorrhage (VH, n=2, 6.3%), retinal tears (n=2, 6.3%) and IOL transient opacification (n=1, 1.1%) were observed intraoperatively. Mild, transient corneal edema (n=12, 37.5%) and cystic macular edema on OCT (CME, n=7, 21.9%) were the most frequent early (<1 month) and late complications, respectively. CME was associated with an epiretinal membrane in 2 cases. Complications were managed with observation and topical treatment mostly. In 2 cases sub-Tenon’s triamcinolone and in 2 intravitreal dexamethasone were used. One Nd-YAG-laser vitreolysis for pupil dyscoria, 1 IOL plug extrusion repositioning and 1 IOL exchange for IOL opacification were required. No retinal detachment, endophthalmitis or IOL subluxation was observed.

Conclusions
Carlavale IOL implantation provides excellent visual and refractive results. The safety profile of this technique for patients with insufficient capsular support is at least as good as previous procedures. The management of complications is not challenging. This IOL should be considered as the first option for patients without capsular support, especially as it is specifically designed and approved for sulcus fixation.

Financial Disclosure
Neither author has a financial or proprietary interest in any material or method mentioned.
Prospective in vivo analysis of 0.6% Povidone-Iodine eye drops as antiseptic procedure for intravitreal injections

Marco Pastore
Italy

Purpose
To assess the antimicrobial activity of the antiseptic ophthalmic solution with preservative-free 0.6% povidone-iodine as a prophylactic treatment in eyes scheduled for intravitreal treatments, and to compare its efficacy to the untreated fellow eye used as the control group.

Setting/Venue
Eye Clinic, Department of Medical, Surgical Sciences and Health, University of Trieste, and Microbiology Unit, University Hospital of Trieste.

Methods
Prospective cohort analysis in which 208 patients received preservative-free 0.6% povidone-iodine eye drops (IODIM®, Medivis, Catania, Italy) three times a day for three days before the intravitreal injection. Before and after the prophylactic treatment, a conjunctival swab was collected from both the study eye and the untreated contralateral eye, used as control. The swab was inoculated on different culture media and the colony-forming units were counted. Bacteria and fungi were identified by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-ToF-MS, VITEK® MS Plus).

Results
A statistically significant decrease (p<0.001) of the bacterial growth from conjunctival swab cultures was found in the study group, with an eradication rate of 82%. The most commonly isolated pathogen at each time point and in both groups was coagulase-negative Staphylococci, isolated in 84% of the positive cultures. Other bacteria identified in order of frequency were staphylococci aureus and other gram-positive bacteria. 8 (3.9%) out of 208 patients who underwent 0.6% PI eye drops treatment experienced conjunctival hyperemia with light serous conjunctival discharge in 3 eyes (1.4%).

Conclusions
This large independent study conducted on two-hundred and eight eyes provides evidence about the effectiveness of 0.6% povidone-iodine eye drops in reducing the conjunctival bacterial load in eyes scheduled for intravitreal treatment while also showing a good safety profile.

Financial Disclosure
None
Title
Posterior capsular rupture during cataract surgery in eyes treated previously with intravitreal injections

Purpose
To evaluate the risk of posterior capsular rupture (PCR) during cataract surgery in eyes treated previously with intravitreal antivascular endothelial growth factor (anti-VEGF) and/or steroids injections.

Setting/Venue
Centro Hospitalar Universitário do Porto, Oporto, Portugal.

Methods
Retrospective, observational study that included consecutive eyes submitted to phacoemulsification cataract surgery (PCS), between November of 2019 and October of 2020. Combination surgeries with pars plana vitrectomy or glaucoma surgery were excluded from the analysis. The primary outcome was the rate of occurrence of PCR during surgery in eyes with or without previous treatment with intravitreal injections. Other variables including age, the presence of ocular comorbidities, diabetes, mature cataract, primary surgeon, injection frequency and type, and date of most recent injection were also recorded.

Results
A total of 2227 cataract surgeries were included in this study and 100 (4.5%) of these eyes had received previous treatment with intravitreal injections (IVI) for diabetic macular edema (62.0%), age-related macular degeneration (19.0%), vascular occlusion (11.0%) and other causes (8.0%). These eyes were treated with anti-VEGF alone (75.0%), an association between anti-VEGF and steroids (20.0%) or with steroids alone (5.0%). Globally, the rate of PCR during PCS was 1.6% (n=35): in patients with previous treatment with IVI the rate was 8.0% (n=8) and 1.2% (n=27) in the eyes without previous treatment with IVI (OR = 6.8, 95% CI: 3.0-15.3, p<0.001). Analyzing the group with previous IVI, the majority of the PCR occurred in eyes with ≥ 10 previous IVI (87.5%), with a time interval between the date of the last IVI and the surgery <6 months (in 87.5%) and without ocular comorbidities (in 75%). There was no significant relationship between PCR and age (p=0.288 and p=0.855), diabetes (p=0.623 and p=0.318), mature cataract (p=0.280 and p=0.036) and the relationship between the degree of training of the surgeon and the rate of PCR (p=0.613 and p=0.406) in both groups (with prior IVI history and globally).

Conclusions
Our study, conducted in a central service with a high formative vocation, shows that eyes with previous treatment with IVI have a higher risk of PCR during cataract surgery and highlights the need for careful preoperative evaluation of the posterior capsule in these eyes.

Financial Disclosure
NO
Assessment of choroidal thickness after alpha-lytic therapy withdrawal

**Purpose**
To detect the impact of alpha-lytic therapy discontinuation on choroidal thickness (CT) changes that could help in the cataract surgery timing decision.

**Setting/Venue**
University eye clinic, Salerno

**Methods**
In this case-control study 36 eyes of 36 patients with mean age of 75±7 years, under alpha-lytic therapy, and 36 eyes of 36 healthy subjects (HS) with mean age of 74±7 years, were examined. Both groups were scheduled for cataract surgery. All patients underwent Heidelberg Spectralis EDI-OCT at the first pre-operative visit and approximately one month after alpha-lytic therapy withdrawal. For the HS group, the OCT was performed at pre-operative visit and approximately one month after the first examination. In both groups, the fellow non operated eyes were examined, the operated eyes were excluded. CT evaluation was performed at sub-foveal level and at 1.5 mm nasally and temporally from the fovea for each arm. The data normal distribution was assessed with Kolmogorov-Smirnov test and the data were tested with a two-tailed T-test. The statistical analysis was performed using SPSS Software (IBM SPSS Statistics version 25).

**Results**
The mean subfoveal CT was 214 ± 79.9 µm during therapy and 206 ± 80.1 µm one month after withdrawal, 1.5 mm nasally from the fovea CT was 185 ± 80.0 µm and 179 ± 79.1 µm respectively, 1.5 mm temporally from the fovea CT was 211 ± 59.0 µm and 200 ± 58.1 µm respectively. Measurements showed a statistically significant reduction in subfoveal (p=0.002), nasally (p=0.01) and temporally (p=0.008) from the foveal CT. No significant changes were found in the HS.

**Conclusions**
CT decrease could be an important sign for deciding the timing of cataract surgery in these patients.

**Financial Disclosure**
None
Management of rhegmatogenous retinal detachment in time of COVID-19 epidemic

**Purpose**
The optimal surgical approach in the treatment of rhegmatogenous retinal detachment during the period of the epidemic rise of COVID-19 should presuppose obtaining the maximum anatomical and functional result, which is possible only when performing a surgical operation by an experienced surgeon.

**Setting/Venue**
Indications for urgent surgery in patients with retinal detachment (RD) are: rhegmatogenous retinal detachment (RRD), tractional RD, RD with undetected retinal breaks, RD in the only seeing eye. RRD in patients with no light perception are not indicated for surgery in difficult epidemic situation. Purpose: to evaluate the management of RRD in patients have undergone surgical treatment on the basis of a non-ophtalmological department by surgeons of the Department of Ophthalmology of BelMAPE in "first wave" of COVID-19.

**Methods**
Main goals in management of RRD during “first wave” of COVID-19 were: 1) urgency of surgery; 2) protection during treatment to preserve doctor’s and patient’s health; 3) selection of operation room for surgery: “clean” ophthalmic operating room or operating room for patients infected with COVID-19; 4) selection of optimal surgical approach; 5) selection of surgeon - an experienced surgeon will shorten the surgery time and reduce the risks of intraoperative complications; 6) selection anesthethia type depends on patient’s health status, including severity of patient’s pneumonia associated with SARS COV-2, and recovery time. During the COVID-19 "first wave" (100 days), 52 surgeries were performed for RRD treatment.

**Results**
The final decision for RRD surgery indications was determined in each case individually. Our decision was based on RRD type (macula on, macula off), visual acuity of affected eye and general condition of the patient (age, comorbidity). Diagnosis and surgery were perfomed with the use of protective masks (for both the doctor and the patient), respirators, protective glasses and shields, maintaining physical distance. Direct ophthalmoscopy was excluded. Before surgery PCR test for COVID-19 was performed. Patients underwent following procedures: scleral buckling (SB) (88%), combined surgery (SB and pars plana vitrectomy (12%). There were 23% of surgeries that were performed after previous unsuccessful surgery of RRD, complicated with PVR. Anatomical and functional success were achieved in 90% of cases.

**Conclusions**
The optimal management of RRD during the COVID-19 epidemic period should have high rates of anatomical and functional success. We consider that it’s possible only when treatment perfomed by experienced surgeon.

**Financial Disclosure**
no financial interest
Title
Scleral fixated versus anterior chamber intraocular lens implantation: A meta-analysis

Purpose
We aim to compare the efficacy and safety outcomes following scleral fixated (SF) versus anterior chamber (AC) intraocular lens (IOL) implantation in adults.

Setting/Venue
A systematic literature search was performed on Ovid MEDLINE, EMBASE, and Cochrane CENTRAL from 2005-2020.

Methods
Inclusion criteria were the following: adult patients, comparison of SFLIOI and ACIOL implantation, sample size of at least 5 eyes per group, and English-language articles. Studies reporting on concurrent surgery were excluded. Outcomes included corrected distance visual acuity (CDVA), endothelial cell density (ECD), and incidence of complications. Meta-analysis was conducted using a random effects model in which weighted mean differences (WMD) and risk ratios (RR) with 95% confidence intervals (95%CI) were computed. The Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) tool was completed for all studies. Certainty of evidence for outcomes was evaluated via the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool.

Results
411 eyes from 5 studies were included. Mean follow-up was 27±21 months. There was no significant difference between techniques for mean CDVA from 1 month to 1 year postoperatively (P=0.13) or at final follow-up (P=0.13). ACIOL implantation was significantly more likely to result in a higher proportion of patients achieving final CDVA 20/40 or better (RR=0.76,95%CI=[0.61,0.95],P=0.01). There was no significant difference in final ECD (P=0.60). Techniques were not significantly different in the incidence of perioperative (P=0.18) or early postoperative (P=0.31) complications. SFLIOI implantation was significantly more likely to lead to late postoperative complications (RR=1.57,95%CI=[1.11,2.22],P=0.010) and vitreous hemorrhage (RR=2.33,95%CI=[1.13,4.81],P=0.02).

Conclusions
There was no significant difference between ACIOL and SFLIOI implantation for mean CDVA, but when analyzed as a categorical variable, a significantly greater proportion of patients achieved final CDVA 20/40 or better following ACIOL implantation. SFLIOI implantation was associated with a higher incidence of late postoperative complications and vitreous hemorrhage relative to ACIOLs. Overall, the quality of evidence in this setting is limited, and future prospective studies are needed to confirm these findings.

Financial Disclosure
PK: Advisory board – Novartis, Alcon, Bayer; Financial support (to institution) – Allergan, Bayer, Roche, Novartis; Financial support – Novartis, Bayer, Novelty Nobility; Equity owner – ArctiDx. RM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis.
Deep-learning based automated quantification of critical OCT features in neovascular age-related macular degeneration

**Purpose**
Exudative neovascular age-related macular degeneration (AMD) represents a leading cause of vision loss in older populations. This disease may be characterized by the egression of fluid into the sub-retinal pigment epithelium (RPE), subretinal and intraretinal locations. Indeed, the presence and amount of intra- (IRF) and sub-retinal (SRF) fluids were demonstrated to be associated with visual prognosis in these patients. Neovascular pigment epithelium detachment (nPED) measurements have additionally been associated with visual outcomes in exudative neovascular AMD, but manual quantification using structural optical coherence tomography (OCT) is extremely time consuming with variable interpretation. Deep learning–based segmentation of volumetric OCT data may, however, represent a reliable and fast approach to automatically detect and quantify such anatomic features. The aim of this study was to validate a deep learning algorithm for automated IRF, SRF and nPED segmentations in eyes with exudative neovascular AMD and understand its performance relative to different graders.

**Setting/Venue**
Retrospective study at San Raffaele Scientific Institute, Milan, Italy.

**Methods**
This IRB-approved retrospective analysis used OCT data from 50 patients with exudative neovascular AMD collected using a Heidelberg Spectralis HRA+OCT device (Heidelberg Engineering, Heidelberg, Germany). Each OCT volume was separately labeled by two masked readers, R1 and R2, to delineate and quantify the amount of IRF, SRF and nPED. This cohort of 50 volumes was randomly divided into two subgroups: 35 for model training and 15 for evaluation. Two models, A1 and A2, were created based on gradings from readers R1 and R2, respectively. Area under the curve (AUC) values gauged detection performance, and quantification between readers and models was evaluated using Dice and correlation (R2) coefficients.

**Results**
The deep learning–based algorithms had high accuracies for all fluid types between all models and readers: per B-scan IRF AUCs were 0.953, 0.932, 0.990, 0.942 for comparisons A1-R1, A1-R2, A2-R1 and A2-R2, respectively; SRF AUCs were 0.984, 0.974, 0.987, 0.979; and nPED AUCs were 0.963, 0.969, 0.961 and 0.966. Similarly, and for the same comparisons, the R2 coefficients for IRF were 0.973, 0.974, 0.889 and 0.973; SRF were 0.928, 0.964, 0.965 and 0.998; and nPED were 0.908, 0.952, 0.839 and 0.905. The Dice coefficients for IRF averaged 0.702, 0.667, 0.649 and 0.631 again for comparisons A1-R1, A1-R2, A2-R1 and A2-R2, respectively; for SRF were 0.699, 0.651, 0.692 and 0.701; and for nPED were 0.636, 0.703, 0.719 and 0.775. In an inter-observer comparison between manual readers R1 and R2, the R2 coefficient was 0.968 for IRF, 0.960 for SRF, and 0.906 for nPED, with Dice coefficients of 0.692, 0.660 and 0.784 for the same features. Taken together, this uniformly demonstrates that the deep learning models were accurate in segmenting anatomic features in neovascular AMD eyes with performance akin to the human graders.

**Conclusions**
Our deep learning-based method applied on patients with exudative neovascular AMD can volumetrically segment structural metrics on OCT scans with human levels of performance. Our models also showed high accuracy when compared to gradings performed by a different reader to that used to build the model, further underlining the method’s validity and consistency. Once replicated in future, larger studies, our approach may prove to be a useful tool for evaluating eyes with neovascular exudative AMD.

**Financial Disclosure**
None
Deep learning model for automated screening of moderately severe and severe non-proliferative diabetic retinopathy from 7-field colour fundus photographs

Purpose
Artificial intelligence models could optimise screening of patients with diabetic retinopathy at risk of disease progression for participation in clinical trials as well as support clinical decision making to improve patient outcomes. Here we assess the performance of deep learning (DL) employing 7-field colour fundus photographs (7F-CFP) in automated identification of eyes with moderately severe and severe non-proliferative diabetic retinopathy (NPDR) among patients with diabetes.

Setting/Venue
Primary care centres in the United States.

Methods
The eyes of 37,358 patients with diabetes were analysed using data (including images) collected between 1999 and 2016 (Source: Inoveon Corporation, Oklahoma City, OK). Professional graders at a centralised reading centre assessed DR severity and the presence of clinically significant macular edema from 7F-CFP. DR severity was graded using the Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale (DRSS). Prevalence of moderately severe or severe NPDR (DRSS 47–53), considering the worst DRSS score at the patient level, was 2.2% in this cohort. The dataset was split into 80% for model training, 10% for tuning and 10% for testing, for a total of 29,890, 3732 and 3736 patients with 1,430,046, 180,534 and 180,135 images, respectively. A DL Inception-v3 model with transfer learning was trained at the image level on all 7 fields of view (including stereoscopy) for being either DRSS 47–53 or not. Predictions were averaged over all fields of view to provide a prediction at the eye level. Model performance metrics in terms of area under the receiver operating characteristic (AUROC) curve, specificity, sensitivity and positive predictive value are reported.

Results
The best model was selected based on performance on the tuning set, as well as the optimal cutoff for specificity and sensitivity maximising the Youden index. The model performed well on the testing set, as shown by an AUROC of 0.988 (95% CI, 0.9872, 0.9879), sensitivity of 96.39% (95% CI, 96.28%, 96.55%), specificity of 96.24% (95% CI, 96.21%, 96.25%) and positive predictive value of 0.368 (95% CI, 0.366, 0.370).

Conclusions
Our findings demonstrate that DL can support automated identification of eyes with DRSS 47–53. The model can optimise screening of patients at risk of disease progression for participation in clinical trials before vision threatening presentations occur, as well in clinical practice. Future research will further refine this proof-of-concept algorithm, with validation conducted on other independent diverse datasets and in a real-world setting.

Financial Disclosure
Fethallah Benmansour, Dimitrios Damopoulos, Ales Neubert, Jelena Novosel and Beatriz Garcia Armendariz are employees of F. Hoffmann-La Roche Ltd., Basel, Switzerland. Qi Yang, Neha Anegondi and Daniela Ferrara are employees of Genentech Inc., South San Francisco, CA
Prediction of geographic atrophy lesion area and growth rate from multimodal imaging using deep learning

**Purpose**

Geographic atrophy (GA) is a major cause of severe visual impairment. Disease heterogeneity, particularly the widely variable GA lesion growth rate, poses a challenge for the clinical development and evaluation of new therapies for GA. Artificial intelligence-based models have the potential to predict disease progression from images. The study aimed to predict baseline GA lesion area and annualised lesion growth rate from baseline fundus autofluorescence (FAF) and/or spectral-domain optical coherence tomography (OCT) images using a multimodal multitask deep learning (DL) approach.

**Setting/Venue**

Retrospective analysis of baseline imaging data (macular Spectralis [Heidelberg Engineering, Inc., Heidelberg, Germany] OCT volumes [496×1024×49 voxels]; macular 30-degree FAF images [768×768 pixels]) from study eyes of patients with bilateral GA enrolled in natural history and lampalizumab clinical trials (NCT02247479, NCT02247531, NCT02479386).

**Methods**

For OCT volumes, each B-scan was flattened along Bruch’s membrane (BM), and en face maps averaged over full, sub-BM and above-BM depths were combined as a 3-channel input. GA lesion growth rate (mm2/year) was estimated as slope of a linear fit on all the available measurements of lesion area (mm2, graded by an independent reading centre). The full dataset was split into development (1279 patients/eyes) and holdout (443 patients/eyes) sets. The development set was further split into 5 outer folds. Baseline characteristics were balanced across splits. Three multitask convolutional neural network models were used to simultaneously predict lesion area and growth rate: OCT only, FAF only and multimodal (OCT+FAF). For each, nested cross-validation (CV) was performed on the development set; inner and outer folds were used for hyperparameter tuning/selection and performance estimation, respectively. The models were re-trained on the entire development set using the best hyperparameters from each inner fold, generating 5 models per type. An ensemble of the 5 models was performed to generate holdout set predictions for each type. Performance was evaluated by calculating the in-sample coefficient of determination (R2), defined as the square of Pearson correlation coefficient between true and predicted lesion area and growth rate.

**Results**

On the development set, the multimodal model had the best CV performance, with mean (SD) R2 of 0.93 (0.03) and 0.52 (0.05) for GA lesion area and GA lesion growth rate predictions, respectively. On the holdout set, the same model showed R2 (bootstrap 95% CI) of 0.94 (0.92, 0.96) for GA lesion area prediction and 0.47 (0.40, 0.54) for GA lesion growth rate prediction. Respective development set mean R2 values for GA lesion area and GA lesion growth rate predictions were 0.91 (0.03) and 0.42 (0.05) for the OCT-only model, and 0.93 (0.03) and 0.48 (0.05) for the model based on FAF images only. On the holdout set, the respective R2 values for GA lesion area and GA lesion growth rate predictions were 0.91 (0.87, 0.95) and 0.36 (0.29, 0.43) for the OCT-only model, and 0.96 (0.95, 0.97) and 0.48 (0.41, 0.55) for the FAF-only model. For comparison, applying a previously developed benchmark model using a simple linear function based on baseline GA lesion area, lesion distance to fovea, lesion contiguity and low-luminance deficit on the same holdout set showed an R2 value of 0.16 (0.10, 0.24) for GA lesion growth rate predictions.

**Conclusions**

These findings show the feasibility of using baseline FAF and/or OCT images to predict individual GA baseline lesion area and annualised lesion growth rate with a multitask DL approach. The multimodal approach showed slightly improved performance in the development set. However, the performance was comparable with the FAF-only model in the holdout set. Artificial-intelligence-based predictions could be used to inform clinical trial design, implementation, and analysis. Further validation in additional datasets is required to confirm robust performance.

**Financial Disclosure**

All authors are employees of Genentech, Inc.
Towards automated imaging analysis: assessing accuracy and reliability of lesion segmentation by multimodal deep learning networks in patients with geographic atrophy in the Proxima A and Proxima natural history studies

**Purpose**
Fundus autofluorescence (FAF) and near-infrared (NIR) imaging are commonly used for diagnosis and monitoring of geographic atrophy (GA) secondary to age-related macular degeneration (AMD), a leading cause of irreversible loss of visual function. Use of artificial intelligence–based models to automate segmentation and extract features of GA lesions could support patient monitoring in clinical trials and clinical practice, and may facilitate predictions of GA lesion growth over time. The aim of this study was to examine deep learning–based segmentation of GA lesions and the reliability of derived features.

**Setting/Venue**
Retrospective analysis of imaging data from the Proxima A (NCT02479386) and Proxima B (NCT02399072) natural history studies of patients with GA.

**Methods**
A total of 194 patients provided 940 pairs of images, with each pair comprising a FAF and NIR image from 1 eye (Proxima B). A grader annotated lesions on FAF images, and the data were split at the patient level into training (n = 155) and validation (n = 39) sets. A test set comprising 90 FAF-NIR pairs from 90 patients (Proxima A) was annotated by 2 graders (G1 and G2). Two multimodal deep learning networks, YNet and UNet, were trained on the training set and tuned on the validation set. The final network was applied to the test set. The lesion area, perimeter, circularity, Feret diameters and number of lesions were extracted for each segmentation mask. As a numerical proxy for the FAF pattern, the excess rim intensity (ERI), equal to the mean FAF intensity in a 0.5-mm rim around the lesion minus the mean FAF intensity in a 0.5- to 1-mm rim around the lesion, was also extracted. The relevant metric was computed for the whole segmented area without separating it into different components for all measures except for number of lesions.

**Results**
The average Dice score between the YNet and G1 on the test set was 0.92. The Pearson correlation (r) values between the YNet and G1 were 0.98 for area, 0.93 for perimeter, 0.86 for circularity, 0.87 for major Feret diameters, 0.93 for minor Feret diameters, 1.00 for ERI and 0.46 for number of lesions. The average Dice scores on the test set were 0.90 between the UNet and G1. The Pearson r values for the UNet and G1 were 0.96 for area; 0.86 for perimeter; 0.81 for each of circularity, major Feret diameters and minor Feret diameters; 1.00 for ERI; and 0.45 for number of lesions. YNet-G2 and UNet-G2 values were similar to their respective G1 values. Between G1 and G2, the average Dice score on the test set was 0.93. The Pearson r values were 0.97 for area, 0.95 for perimeter, 0.96 for circularity, 0.98 for major Feret diameters, 0.97 for Feret minor diameters, 0.99 for ERI and 0.94 for number of lesions.

**Conclusions**
The results showed that networks trained to segment GA lesions could produce accurate segmentations. The agreement between the networks and human graders was comparable with the agreement between 2 graders when the segmentations were used to obtain the values of area and ERI. Despite similar Dice scores, inferred values of perimeter, circularity and Feret diameters were less similar and often varied between models. The inferred number of lesions matched human grading poorly. This suggests that the variable accuracy of the examined features could be an important factor for their use in predictive models of GA growth. This methodology can enable deep learning–based tools that may support clinical development in GA, bringing efficiency and reliability to clinical trials of this major cause of visual loss.

**Financial Disclosure**
All authors are employees of Genentech, Inc.
Presenter

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Title

Structural changes of retina and choroid in Crimean-Congo hemorrhagic fever

Purpose

Crimean-Congo hemorrhagic fever (CCHF) is an acute viral hemorrhagic fever with a high mortality rate. The disease could lead to a mild form of ocular disease consist of subconjunctival and retinal hemorrhages. In this study, we aimed to evaluate the retinal and choroidal structural changes in Crimean-Congo hemorrhagic fever (CCHF).

Setting/Venue

Sivas Cumhuriyet University, Departments of Ophthalmology and Infectious Disease

Methods

This prospective and observational study included 38 eyes of 19 patients over 17 years of age diagnosed with CCHF and 76 eyes of 38 age and sex-matched healthy controls. After a complete ophthalmologic examination, central foveal thickness (CFT), retinal nerve fiber layer (RNFL) analysis, were evaluated from the images obtained via spectral domain optical coherence tomography. Also, choroidal thickness was measured at 5 different points (750 and 1500 μm from the foveal center in the temporal and nasal quadrants and beneath the fovea) by using choroidal mode. Total choroidal area (TCA), luminal area (LA) and choroidal vascularity index (CVI) were calculated using the binarization method in ImageJ image analysis software. CVI was defined as the proportion of LA to the TCA. The disease severity classification was made according to the systemic findings and laboratory parameters of the patients. All ophthalmic examinations and measurements were performed during the active phase of CCHF.

Results

The mean age of 19 patients was 34,3 ± 14,7 years of whom 7 (36,8%) were female. There was no significant difference between groups regarding CFT (p=0.2). The mean RNFL thickness in all quadrants and choroidal thickness at 5 points were significantly higher in CCHF patients compared to the control group (p<0.05, for all). TCA and LA were 1,12 ± 0,26 mm² and 0,75 ± 0,17 mm² in CCHF patients and 1.02±0.22 mm² and 0.68±0.14mm² in the control group respectively (p<0.05). Even though TCA and LA were statistically higher in the CCHF group, there was no significant difference in terms of CVI between groups (p=0.7). There was no significant association between TCA, LA and CVI and disease severity in patients with CCHF.

Conclusions

Crimean-Congo hemorrhagic fever may cause an increase in choroidal and RNFL thickness due to endothelial dysfunction, increased capillary permeability and increased systemic inflammatory response. Despite a significant increase in TCA and LA without an increase in CVI may be explained by the fact that the inflammatory changes in the CCHF cause dilation not only in the luminal area but also in the stromal area.

Financial Disclosure

None
The change in optical coherence tomography biomarkers in patients with idiopathic epiretinal membrane after a long-time follow-up

Purpose
To describe the changes in central macular thickness (CMT) and central macular volume (CMV) values in patients with idiopathic epiretinal membrane (ERM) along follow-up time.

Setting/Venue
University of Health Sciences, Ulucanlar Eye Research and Education Hospital.

Methods
A cross-sectional case study includes 115 Caucasian subjects with idiopathic ERM who had no underwent vitreoretinal surgery. The baseline and final spectral domain optical coherence tomography (Spectralis, Heidelberg, Germany) biomarkers including CMT and CMV were investigated. The change in CMT and CMV along follow-up time were calculated.

Results
The mean age of the subjects was 64.9 ± 7.9 years (54-77). The male to female ratio was 51/64. The mean baseline CMT and CMV values were 322.8 ± 86.6 μm (204-633) and 9.2 ± 1.2 μm³ (6.6-14.3). The mean follow-up time was 44.4 ± 30.1 months (6-132). The mean final CMT and CMV values were 339.9 ± 120.1 μm (207-957) and 8.7 ± 1.1 μm³ (5.6-11.7). The mean change in CMT and CMV values were 17.3 ± 128.4 μm (-216-687) and -0.4 ± 1.3 μm³ (-4.7-1.9).

Conclusions
After a long-time follow-up, CMT is tend to increase despite of being CMV is tend to decrease in patients with idiopathic ERM.

Financial Disclosure
none
A comparative study of choroidal vascular and structural characteristics of typical polypoidal choroidal vasculopathy and polypoidal choroidal neovascularization cases.

**Setting/Venue**
A retrospective cross-sectional study

**Methods**
Thirty-five eyes of 33 PCV cases, proven with indocyanine green angiography (ICGA), were included in this study. The PCV cases were divided into a T-PCV group (n = 23) and a P-CNV group (n = 12). The total choroidal area (CA), luminal area (LA), and stromal area (SA) were measured with ImageJ software and Niblack threshold method. The CVI, the proportion of the luminal area to the total choroidal area, was assessed. ICGA images were evaluated for anastomoses between vortex vein systems.

**Results**
The mean age was 71.4 years in T-PCV and 69.8 years in P-CNV groups (p=0.657). T-PCV cases had significantly higher mean subfoveal choroidal thickness (356.0±168.0 vs 267.8±68.7 µm), lumen area (0.647±0.301 vs 0.502±0.122 mm²) and CVI values (73.9±3.7 vs 70.8±4.5%) comparing to P-CNV cases (p=0.036, p=0.052, p=0.039, respectively). Intervortex venous anastomoses was observed in 69.6% of T-PCV eyes and in 50.0% of P-CNV cases (p=0.292). Regarding T-PCV group, in eyes with intervortex venous anastomoses, mean CA (0.986±0.383 vs 0.613±0.290 mm²), and LA (0.734±0.297 vs 0.449±0.212 mm²) values were significantly higher than cases without venous anastomoses (p=0.012, p=0.022, respectively). In P-CNV group, eyes with and without intervortex venous anastomoses did not show significant difference in choroidal measurements (p>0.05).

**Conclusions**
T-PCV and P-CNV differs especially in terms of choroidal vascular characteristics. The presence of the higher CVI values and higher frequency of intervortex venous anastomoses in T-PCV cases may ensure distinct vascular pathogenesis of these two PCV subgroup.
Title
Alterations of retinal layer thicknesses in the macula at pathological myopia

Purpose
Myopia is a growing major public health problem around the world. High myopia (HM) has conventionally been defined as a spherical equivalent refractive error exceeding -6.0 diopter (D) and/or an axial length longer than 26.5 mm. HM is the primary cause of uncorrected visual acuity loss and the main cause of low vision and blindness worldwide. Pathological myopia (PM) is different from other types of myopia in that it causes not only uncorrected visual acuity loss but also loss of best-corrected visual acuity. PM was firstly defined as the presence of structural changes that cause vision loss in the context of PM. However, although axial elongation is generally believed to play a key role in degenerative changes, axial elongation is not the only marker of PM. However, beyond the cut-off value in PM, the prevalence of PM increases exponentially. PM is commonly defined as myopia with posterior segment complications due to progressive and excessive elongation of the eyeball. The aim of this study is to investigate thickness alterations of each macular retinal layers in pathological myopic eyes and understand retinal perfusion by comparing the thickness of each retinal layer in eyes with PM and control group.

Methods
The patients were divided into the following two subgroups: The first group is the ‘myopic group’ with a spherical equivalent between -6.00 and -10.00 D and an axial length between 26.5 and 28.5 mm, the second group is the ‘control group’ with a spherical equivalent between -1.00 D and +1.00 D and axial length between 22.00 mm and 24.00 mm. In this study, the META-analysis for Pathologic Myopia Study Group classification was used and the cases included in the study and accepted as pathological myopia were with the unaffected macular area and additional degenerative chorioretinal findings. Moreover, the cases had additional chorioretinal degenerative findings except for the macular region. Fifty-one eyes of 34 patients in the myopia group and 51 eyes of 26 patients in the control group were included in the study. Total retinal thickness and each retinal layer thickness in the macular region was measured by using spectral domain optical coherence tomography (HRFA2-Heidelberg Retina Angiography - Optical Coherence Tomography, Heidelberg Engineering, Germany) device. The densities of radial peripapillary capillary plexus (RPCP), superficial capillary plexus (SCP), and deep capillary plexus (DCP) were obtained by optical coherence tomography angiography (OCTA) instrument (RTVue XR Avanti, version 2017.1.0.151; Optovue, Inc., Fremont, USA).

Results
There was no significant difference between the pathological myopic group and the control group in terms of age, gender, and intraocular pressure (p = 0.087, p = 1.000, and p = 0.960, respectively). However, compared with the control group, patients with PM had more refractive errors, worse best corrected visual acuity, and longer axial lengths (p <0.001, p <0.001, and p = 0.009, respectively). A summary of demographic data and comparative statistical analysis for the PM group and the control group are given in Table 1. The thicknesses of each retinal layer were measured with retinal segmentation analysis and the results are shown in Tables 2 and 3. Based on the OCTA images, RPCP density was found 46.89 ± 2.42% in the myopic group, 49.44 ± 2.83% in the control group, and there was no statistically significant difference between the groups (p= 0.381). SCP density was 41.18 ± 0.68%, DCP density was 42.90 ± 1.36% in the myopic group, while SCP density was 48.03 ± 1.33% and DCP density was 49.33 ± 2.51% in the control group. It was observed that the density was less in both SCP and DCP in the myopic group (p= 0.003 and p= 0.040, respectively).

Conclusions
This study shows that there is a thinning in total retinal thickness in PM. This thinning is predominantly in the outer retina in the fovea, whereas it is in both of the inner and the outer retinal layers in extrafoveal regions. Although there is thinning in the inner retinal layers, the absence of the decrease in retinal nerve fiber layer thickness can be interpreted as RPCP is less affected than other SVP and DVP areas in high myopia. We think that any evidence demonstrating a vascular insufficiency environment in certain sublayers of the retina in PM may be indicative of vascular diseases affecting retinal and choroidal circulation. In this connection, it may be illuminative for researchers to investigate each retinal layer separately in their future studies. Changes in retinal layer thicknesses and capillary plexus densities are observed in PM. Accordingly, evaluating the thickness of each retinal layer separately may be a marker in vascular diseases affecting the retinal and choroidal circulation.

Financial Disclosure
The authors received no grants and funds in support of the study.
Retinitis pigmentosa (RP) is the most common form of hereditary retinal dystrophy characterized by progressive impairment and death of the retinal photoreceptors. Previous RP studies have reported that the earliest histopathological change is a shortening of the photoreceptor outer segments. This change begins in the mid-periphery and progresses to the central retina; therefore, morphological and functional assessments of retinal changes may be useful in predicting disease progression and remaining retinal function in RP patients. Optical coherence tomography (OCT) in vivo quantitatively tracks these morphological changes in retinal tissue by in vivo segmentation. The new OCT device software enables easier and more accurate automatic differentiation and thickness measurement for each retinal layer. The information provided by optical OCT-angiography (OCT-A) about the vascular densities of retinal vessels has been a guide for researchers especially about RP patients. Evaluating the retinal layers one by one and obtaining information about vascular densities in RP can help us to understand the course of the disease and its clinical reflections. This study analyzes the retinal layers in macular regions of RP eyes one by one to examine their retinal vascular plexus densities and to evaluate the effect of the pathophysiological process on the disease and its clinical reflections. This study analyzes the retinal layers in macular regions of RP eyes one by one to examine their retinal vascular plexus densities and to evaluate the effect of the pathophysiological process on the RP patients.

### Methods

Thirty-six eyes from 20 patients showing the classic triad for RP who had undergone retinal segment analysis and OCT-A were included; a control group of 36 eyes from 18 patients was also included in the study. Patients with systemic diseases such as diabetes mellitus or hypertension; ocular diseases that require chronic medication use such as uveitis, glaucoma, dry eye; an ocular history of intraocular surgery or trauma; and patients with additional findings affecting the macular area, such as cystoid macular edema, vitreomacular adhesion/traction, epiretinal membrane, or macular atrophy, were excluded from the study. The eyes of RP patients with additional pathology affecting the macular region were not included in the study. Besides, cases with artifacts in measurements and those whose retinal segmentation analysis could not be performed were also excluded from the study. Total retinal thickness and retinal layer thickness in the macular region were measured using spectral domain OCT (HRA2-Heidelberg Retina Angiography, Optical Coherence Tomography, Heidelberg Engineering, Heidelberg, Germany). OCT-A imaging of the cases was performed using AngioVue OCT-A (RTVue XR Avanti, version 2017.1.0.151; Optovue, Inc., Fremont, CA, USA).

Radial peripapillary capillary plexus (RPCP), superficial capillary plexus (SCP), and deep capillary plexus (DCP) density values were obtained.

### Results

RP and control groups had similar characteristics in terms of age and gender (p = 0.323 and p = 0.092, respectively) (Table 1). Analyzes were performed in the central 1 mm foveal area and 4 regions (superior, inferior, temporal, nasal) in the parafoveal and perifoveal region. Retinal layers were evaluated with retinal segmentation analysis and the results are shown in Tables 2 and 3. The density of RPCP detected by OCT-A was 45.57 ± 1.82% in the RP group and 49.46 ± 2.78% in the control group. SCP density was 42.62 ± 3.18%, DCP density was 41.33 ± 1.33% in the RP group, while SCP density was 48.02% ± 1.34% and DCP density was 49.34 ± 2.51% in the control group. The density of RPCP, SCP, and DCP were less in the RP group (P: 0.044, P: <0.001, and P: 0.016, respectively).

### Conclusions

The weakening of the retinal vessels occurs long before the bone specular pigment formation in RP. The migration of RPE cells around the inner retinal vessels stimulates the accumulation of extracellular matrix (ECM) which is similar to the ectopic Bruch membrane, and this perivascular ECM gradually thickens and occludes the lumen of the vessels. Inner and outer retinal segments feed from different vascular structures, so different retinal segments may be affected in circulatory disorders. Since retina is rich in terms of vascular tissues, there are vascular pathologies in many retinal diseases. In this study we examined how much retinal perfusion and retinal layers are affected in patients with RP, which may have a complex genetic structure. According to this study, while there was no significant difference in retinal layer thickness in RP patients in the central fovea, RNFL, GCL, IPL, and ONL were thinner in both parafoveal and perifoveal regions. As an OCT-A finding, patients with RP had less vascular densities in the RCP, SCP, and DCP layers. When the retinal layers are examined, it is revealed that in addition to the genetic pathophysiologic process of RP, retinal vascular perfusion is also affected by this process and/or affects the process.
Occult neovascular membrane in central serous chorioretinopathy

**Presenter**
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**Purpose**
To highlight the importance of OCT-A imaging in patients with acute vision loss diagnosed with central serous chorioretinopathy (CSC).

**Setting/Venue**
A case report of a young male patient diagnosed with CSC reporting acute vision loss and treated with aflibercept intravitreal injections is presented.

**Methods**
A 39-year-old male patient attended our Ophthalmology Clinic due to subacute vision loss in his right eye. He had been diagnosed with central serous chorioretinopathy in another ophthalmological centre but had received no treatment. Visual acuity was 0.8/1.0 according to Snellen's visual acuity chart. Anterior segment slit lamp examination showed no pathological findings. Fundus examination showed retinal pigment epithelium changes. Structural OCT showed pigment epithelium detachment (PED) associated with subretinal fluid in his right eye. Central macular thickness (CMT) was 288. OCT angiography (OCT-A) was performed and an occult neovascular membrane (NVM) in the inner surface of the PED was observed. Central serous chorioretinopathy with complicated NV diagnosis was made. Aflibercept injections were administered.

**Results**
After the first aflibercept injection, an improvement in right eye's visual acuity (visual acuity went from 0.8 to 1.0) and CMT were observed (from 288 to 241).

**Conclusions**
Various conclusions can be drawn from this case. Aflibercept has been shown to be effective in NVM secondary to CSC. In addition, this case highlights the importance of implementing OCT-A imaging in diagnostic protocols involving CSC, especially when patients refer vision loss, in order to reveal occult NVM and be able to administer an effective treatment as early as possible avoiding chronic vision loss in these patients.

**Financial Disclosure**
None
Are there quantitative changes in peripapillary capillaries, optic disc capillaries, and retinal nerve fiber layer (RNFL) thickness in fellow eyes of patients with unilateral chronic central serous chorioretinopathy?

**Purpose**
Quantitative evaluation of peripapillary capillaries, optic disc capillaries, and retinal nerve fiber layer (RNFL) thickness in fellow eyes of patients with unilateral chronic central serous chorioretinopathy (CSCR).

**Setting/Venue**
Prospective cross-sectional, case-control study / Health Sciences University, Antalya Training and Research Hospital, Ophthalmology Clinic

**Methods**
The study was conducted between March 2020 and March 2021. Group 1 consisted of 28 patients with unilateral chronic CSCR and no choroidal neovascularization. Fellow eyes of these patients formed Group 2. One hundred and 2 eyes of 102 healthy control included in the study as Group 3. Patient and control groups were matched in terms of age and gender. Peripapillary and macular microvascular structures were imagined with OCT-A (RTVue XR100-2 Avanti; Optovue, Inc., Fremont, CA, USA). The quantitative comparison was performed between groups.

**Results**
There was no difference in peripapillary and inside disc area vessel densities (VD) between eyes with chronic CSCR, fellow eyes, and healthy control eyes. Similarly, there was no difference in RNFL thickness between the three groups. However, except for the foveal areas, we found that both the superficial macular and deep macular VD were lower in group 1 and group 2 compared to group 3. In addition, we found that the choriocapillaris flow area decreased in group 1 and group 2 compared to group 3 while the subfoveal choroidal thickness was thickened only in group 1 compared to group 3.

**Conclusions**
The patient with chronic CSCR in one eye had similar quantitative changes in macular vascular structures in the fellow eye compared to the control group, as well as in peripapillary vascular, optic disc vascular, and RNFL thickness. Briefly, there was no quantitative difference in peripapillary vascular structures, optic disc vascular structures, and RNFL thickness in both eyes of patients with chronic CSCR compared to the control group.

**Financial Disclosure**
Financial disclosure: The authors have no financial or ownership rights over a product, method, or material mentioned herein. Declaration of interest: The authors reported no conflict of interest. They are solely responsible for the content and writing of the article. Funding: The authors declare that they did not receive financial support from any foundation, public or private source for this study.
Correlation of sectoral choroidal vascularity with angiographic leakage in central serous chorioretinopathy

Purpose
To correlate sectoral choroidal vascularity with angiographic leakage in eyes with central serous chorioretinopathy (CSCR).

Setting/Venue
The current study was a multicentric, retrospective, cross-sectional study and included eyes with active CSCR. This was defined as subretinal fluid (SRF) on optical coherence tomography (OCT) and/or leakage on fundus fluorescein angiography (FFA).

Methods
Multimodal imaging including fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) were performed to identify leakage site and obtain choroidal measurements, respectively. An automated algorithm was used to perform shadow compensation, choroidal boundary localization and binarization, three (3-D) dimensional mapping, and early treatment of diabetic retinopathy study (ETDRS) grid based choroidal quantification i.e., choroidal thickness (CT) and choroidal vascularity index (CVI). Nested analysis of variance (ANOVA) was performed to compare CT and CVI in different sectors.

Results
Thirty-two eyes with active CSCR were analyzed. CT values varied significantly among the sectors (range, 450.27 to 482.63µm; p=0.005) and rings (range, 459.71 to 480.45µm; p <0.001), however, CVI failed to show significant variation among various segments (sectors, rings, and quadrants; range, 0.53-0.54; all p values >0.05). Among 25 leaking spots in 25 different sectors, 12 (48%) had an increased CT compared to the overall CT whereas only 24% had increased CVI compared to overall CVI. Mean CT and CVI of the sectors with leakage (427.1±81.1µm; 0.51±0.05) and remaining sectors without leakage (411.3±73.9µm; 0.53±0.04) were not statistically different (p=0.48; p=0.12 respectively).

Conclusions
Though CT varied in different segments and increased CT corresponded to leakage points on FFA in 48% of eyes, CVI changes were more diffusely spread and local changes in CVI were not predictive of leakage location in eyes with active CSCR.

Financial Disclosure
None
Comparing measurements of vascular diameter using adaptive optics imaging and conventional fundus imaging

**Purpose**
To compare retinal vascular diameter measurements taken from standard fundus images and adaptive optics (AO) images.

**Setting/Venue**
Prospective comparative study.

**Methods**
We analyzed retinal images of 20 healthy participants with 45-degree funduscopic color photographs (CR-2 Canon fundus camera, Canon™) and adaptive optics (AO) fundus images (rtx1 camera, Imagine Eyes®). Diameters were measured using three software applications: the VAMPIRE® (Vessel Assessment and Measurement Platform for Images of the Retina) Annotation Tool, IVAN (Interactive Vessel Analyzer) for funduscopic color photographs, and AO_Detect_Artery™ for AO images.

**Results**
For the arterial diameters, the mean difference between AO_Detect_Artery™ and IVAN measurements was 9.1 µm (-27.4–9.2 µm, p=0.005) with a significant correlation between measurements (r=0.79). The mean difference between the AO_Detect_Artery™ and VAMPIRE™ Annotation Tool measurements was 3.8 µm (-34.4–26.8 µm, p=0.16) with a weak correlation between measurements (r=0.12). For the venous diameters, the mean difference between the AO_Detect_Artery™ and IVAN measurements was 3.9 µm (-40.9–41.9 µm, p=0.35) with a strong correlation between measurements (r=0.83). The mean difference between the AO_Detect_Artery™ and VAMPIRE™ Annotation Tool measurements was 0.4 µm (-17.44–25.3 µm, p=0.91), and the correlation was moderate (r=0.41).

**Conclusions**
Taking AO imaging as a reference, we found that the VAMPIRE Annotation Tool, an entirely manual software, provides accurate measurements of the arterial and venular diameters, but the correlation is weak. By contrast, IVAN, a semi-automatic software tool, has slightly higher differences in measurements compared with AO imaging, but the correlation is stronger.

**Financial Disclosure**
Imagine eyes for Nicolas CHATEAU
Automated measurement of iris surface smoothness using anterior segment optical coherence tomography

**Purpose**
To present an automated method in a observational case control series to measure the smoothness index (SI) of iris surface in anterior segment optical coherence tomography (AS-OCT) images.

**Setting/Venue**
a observational case control series

**Methods**
The ratio of the length of the straight line connecting the most peripheral and central points of the anterior iris border (in nasal and temporal sides) to the actual length of this border on AS-OCT images, was defined as SI. In a uveitis referral center twenty-two eyes of 11 patients with unilateral Fuchs uveitis (FU) (7 female) and 22 eyes of 11 healthy control subjects underwent AS-OCT imaging. Image J and a newly developed MATLAB algorithm were used for manual and automated SI measurements, respectively. Agreement between manual and automated measurements was evaluated with Bland-Altman analysis and interclass correlation coefficient. The inter-eye difference of SI was compared between FU group and control group.

**Results**
Automated mean overall SI was 0.868 ± 0.037 and 0.840 ± 0.039 in FU and healthy fellow eyes, respectively (estimated mean difference = -0.028, 95% CI [-0.038, -0.018], p<0.001). Bland- Altman plots showed good agreement between two methods in both healthy and FU eyes. Interclass correlation coefficient between the manual and automated measurements in the FU and healthy fellow eyes was 0.958 and 0.964, respectively. Inter-eye difference of overall SI was 0.029 ± 0.015 and 0.012 ± 0.008 in FU group and control group, respectively (p=0.01).

**Conclusions**
We concluded that the automated algorithm can rapidly and conveniently measure SI with results comparable to manual method.

**Financial Disclosure**
No financial interest to declare
Influence of retinal and choroidal perfusion times measured using dye angiography on quantitative analysis of OCT-angiography

**Purpose**
To study the impact of preocular and ocular circulatory dynamics on measurements of vascular density (VD) of superficial capillary plexus (SCP), deep capillary plexus (DCP) and of the choriocapillaris (CC), as well as choroidal blood flow (BF) in optical coherence tomography-angiography (OCTA) in patients without (Group 1) and with (Group 2) cardiovascular risk factors.

**Setting/Venue**
RétinElysée Ophthalmology Center (Lausanne, Switzerland).

**Methods**
Monocentric retrospective observational study where medical records from patients were analyzed. Patients were divided into two groups based on their cardiovascular risk factors: diabetes type I and II, hypertension, and hypercholesteremia. Dynamic film of early phases of fluorescein angiography (FA) and indocyanine green angiography (ICGA, Spectralis OCT, Heidelberg Inc®) data were used for the measurement of the respective arterial times and correlated respectively with SCP, DCP, and CC VD. OCTA (6.0 x 6.0 mm scan size; Optovue, Angiovue®, RTVue XrPAR, Version 2017.1.0.150) data were used for the extraction of the following measurements: SCP and DCP VD of the fovea and of the whole image; and choroidal blood flow data that were subsequently imported for binarization and calculated with the Fiji software available online.

**Results**
177 patients were analyzed. Group 1 consisted of 85 patients (41 female, 44 male) (48.02% of total) with a mean age of 60.7 ± 17.1 years. Group 2 consisted of 92 patients (47 female, 45 male) (51.98% of total) with a mean age of 69.2 ± 13.7 years. Group 1 showed a significant correlation between the SCP VD of the fovea and of the whole image with both the FA arterial perfusion time (AT) and laminar flow (LF) parameters (P = 0.0007, 0.0023, respectively; Spearman' Rho correlation). This group also showed significant correlations between the CC VD and ICGA arterial time (P = 0.0472; Spearman' Rho correlation). In Group 2, DCP VD of the fovea and of the whole image was significantly correlated with AT (P = 0.0477; Spearman' Rho correlation) and showed a trend towards statistical significance with LF (P = 0.0980, Spearman' Rho correlation). In this group, CC VD was correlated with a trend towards statistical significance with ICGA arterial time (P = 0.0843; Spearman' Rho correlation). On univariate analysis, FA and ICG AT were respectively significant on the parameter VD (deep and superficial; P=0.0043, P=0.0012) and CC VD (P=0.0048).

**Conclusions**
OCTA is widely used in clinical practice to diagnose and monitor retinal and choroidal vascular diseases. Our study demonstrated a significant influence of preocular blood flow dynamics and intraocular transit time on VD values in retinal capillary plexus and CC in OCTA. The influence seems to differ among groups with or without cardiovascular risk factors. Results of OCTA should be interpreted considering the influence of the pre- and intra-ocular blood flow dynamics.

**Financial Disclosure**
None
The choroid after half-dose photodynamic therapy in chronic central serous chorioretinopathy: A study using enhanced depth imaging optical coherence tomography (EDI-OCT) and optical coherence tomography angiography (OCT-A)

**Purpose**
The purpose of the study was to evaluate the choroidal structural and vascular changes after half-dose photodynamic therapy (hd-PDT) in eyes with chronic central serous chorioretinopathy (CSC) using Enhanced Depth Imaging Optical Coherence Tomography (EDI-OCT) and Optical Coherence Tomography Angiography (OCT-A).

**Methods**
This prospective case-control study included 10 eyes with chronic CSC (10 patients). The choroidal layer was examined before applying hd-PDT (at baseline) and at 1 month following treatment. Binarization process and analysis by ImageJ were applied at EDI-OCT and OCT-A images. We investigated the changes of the mean choroidal thickness (CT) at the subfoveal area and at areas 750 µm to the nasal and temporal side of the fovea. The thickness of the Haller and choriocapillaris (CC)/Sattler layers were measured independently. The binarization method was applied to separately measure the whole area (WA), the luminal area (LA) and the interstitial area (IA) at EDI-OCT and the perfusion density (PD) at OCT-A. The ratio of LA to WA at EDI-OCT corresponded to the choroidal vascularity index (CVI). Visual acuity (VA) was measured. The unaffected fellow eyes were used for comparisons.

**Results**
The mean CT at the subfoveal area and the areas located 750 µm to the nasal and temporal sides of the fovea were all significantly lower at 1 month after hd-PDT than the baseline (all p<0.001). The mean values of the Haller and CC/Sattler layers were significantly lower at 1 month after treatment than at baseline (all p<0.001). The values of WA, LA and IA were significantly reduced at 1 month post-treatment compared to the baseline values (all p<0.001). A statistically significant increase of PD was observed at 1 month after hd-PDT compared to baseline (p<0.001). CVI did not differ significantly before and after treatment (p=0.148). Correlation analysis revealed that there was a statistically significant (p<0.05) negative correlation (ρ=-0.658) between PD and post-treatment logMAR VA. None of the analyzed parameters reached the values of the unaffected fellow eye at 1 month after hd-PDT.

**Conclusions**
Following hd-PDT, the choroidal thickness at the subfoveal area as well as the thickness of the Haller and CC/Sattler layers significantly declined, with both luminal and interstitial components becoming markedly smaller. Based on OCT-A findings, the perfusion of choriocapillaris improved after treatment.
**Title**
Optical coherence tomography angiography in unilateral Purtscher retinopathy

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**Purpose**
To describe a case of Purtscher retinopathy in multimodal imaging including swept-source optical coherence tomography (SS-OCT) and optical coherence tomography angiography (OCT-A).

**Setting/Venue**
Department B, Hedi Raies Institute.

**Co-Author 7**

**Methods**
A case report of a patient of Purtscher retinopathy

**Results**
A 31-year-old man, who underwent a motor vehicle accident resulting in head trauma with cerebral hemorrhage was admitted to the intensive care unit for 30 days. He complained of decreased vision of his right eye after leaving intensive care. His best-corrected visual acuity was positive light perceptions and 10/10 in the right eye and the left eye respectively. Biomicroscopic examination of the anterior segment of eyes was unremarkable, fundus examination revealed retinopathy with multiple cotton wool spots and flame hemorrhages in the posterior pole in intermaculo-papillary. Swept-source OCT showed macular atrophy. Optical coherence tomography angiography revealed extensive non-perfusion in the macular area in both the superficial and the deep capillary plexus of the right eye with normal capillary plexus in the left eye.

**Conclusions**
Purtscher retinopathy is a rare condition that was first described by Purtscher in 1910 in patients with a history of trauma distant from the eyes with typical findings of cotton wool spots of varying sizes or Purtscher flecken, retinal hemorrhages, and optic disk swelling, are confined to the posterior pole, it is often bilateral but can be unilateral, OCT-A is non-invasive and useful in the detection of retinal vascular damage. The prognosis is generally poor and the visual acuity may remain decreased particularly in the case of foveal photoreceptor atrophy as the case of our patient.

**Financial Disclosure**
None
Evaluation of macular microvasculature by optical coherence tomography angiography in children with amblyopia

Purpose
To assess retinal microvascular changes in children with amblyopia using Optical Coherence Tomography Angiography (OCTA).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
We conducted an observational study including 24 amblyopic eyes of 20 children (age <18 years) and 40 control eyes of 20 age-matched healthy subjects. All included individuals underwent a complete ophthalmic examination including visual acuity, refraction, ocular motility tests, anterior and posterior segment examination as well as OCT-A. The study enrollment was led between September 2020 and February 2021. Amblyopia was defined as best-corrected visual acuity (BCVA) between 20/40 and 20/200 in one or both eyes without organic cause for the decreased vision. OCTA was performed using Optovue RTVue XR Avanti, AngioVue. 6 mm x 6 mm macular scans with measurement of the foveal avascular zone (FAZ) and vessel densities (VD) in both superficial (SCP) and deep (DCP) capillary plexus were analyzed.

Results
The mean age was 8.6 years ± 4.4 in the study group and 10.4 years ± 3.6 in healthy control group. The mean logMAR BCVA was 0.51 (0.33-0.82) in the amblyopia group and was −0.03 (−0.12 -0.00) in the control group (p < 0.001). No significant refractive difference in spherical equivalent was found between the 2 groups (p=0.08). The macular vessel densities were significantly lower in the amblyopic group than in the control in the SCP (48.2% ±4.1 and 52.1%±2.8; p=0.02) and the DCP (53.3% ±4.8 and 60.1% ±3.3; p= 0.002). Compared to the control group, the FAZ was significantly larger in amblyopic eyes than in normal eyes (0.47 ± 0.02 mm2 and 0.38 ± 0.01 mm2 respectively; p=0.01).

Conclusions
Amblyopia is the most common cause of visual impairment in childhood. We found that OCTA reveals microvascular alterations in eyes with amblyopia. However, further studies are warranted to confirm the mechanism underlying these findings.

Financial Disclosure
The authors declare no conflict of interest.
Pathologic myopia and severe pathologic myopia: Clinical characteristics and its correlation with ATN grading system

Purpose
Our study's aims were to analyse axial length (AL), age and best-corrected visual acuity in high myopic patients and its correlation with the different ATN components.

Setting/Venue
Puerta de Hierro-Majadahonda University Hospital.

Methods
Cross-sectional, non-interventional study. A series of 656 eyes from 352 highly myopic patients with spherical equivalent (SE) > -6.0 D and/or >26 mm of Axial Length (AL) were included. All patients underwent complete ophthalmologic examination, ATN grading and multimodal imaging.

Results
The eyes were graded on the ATN system and classified as PM (≥A2) or severe PM (≥A3, ≥T3, and/or N2). Significant between-group (PM vs. severe PM) differences (p<0.05) were observed on the individual ATN components (atrophic [A], tractional [T] and neovascular [N]). AL was linearly correlated with the A, T and N components (r=0.53, p<0.00; r=0.24, p<0.00; r=0.20, p<0.00; respectively). Age was linearly correlated with the A score (r=0.31, p<0.00), but wasn’t correlated with AL (r=0.09, p=0.053). Patients classified with severe PM were older, had longer AL, and worse BCVA (p<0.05). The Cohen’s kappa coefficients between graders by component (A, T, N) were as follows A: 0.97 (p<0.00); T: 0.97 (p<0.00); and N: 0.99 (p<0.00).

Conclusions
The findings of this study conclude that axial length is the main variable associated with myopic maculopathy. AL was positively correlated with all three components of the ATN classification system. Eyes classified as PM or severe PM differed significantly in terms of patient age, AL, and BCVA.

Financial Disclosure
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# Choroidal vascularity index in thyroid-associated ophthalmopathy: A cross-sectional study

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## Purpose
Hemodynamic changes have been observed in patients with Graves’ disease. The aim of our study was to evaluate choroidal vasculature change using the choroidal vascularity index (CVI) in patients with thyroid-associated ophthalmopathy (TAO) and to compare the results with age- and sex-matched healthy controls. CVI was obtained by binarization of optical coherence tomography images and was defined as the proportion of luminal area (LA) to total cross-sectional choroidal area (TCA). An additional objective was to evaluate the relation between CVI and clinical activity score, exophthalmometric value, diplopia status, gender and age.

## Setting/Venue
In this cross-sectional single center study, we included 40 patients affected by TAO referred to Ophthalmology Unit by the Endocrinology Department of Pisa University Hospital. Forty healthy individuals, matched for age and sex, served as controls.

## Methods
The following data were collected: age, gender, visual acuity, intraocular pressure (IOP) (Goldmann applanation tonometry), biomicroscopy findings, clinical activity score (CAS), concomitant and previous therapy, exophthalmometric values and motility status. The presence of subjective diplopia in primary gaze position was graduated using Gorman score. Inclusion criteria were diagnosis of Graves’s Disease in the last 12 months; first episode of TAO; age between 25 and 45 years; euthyroidism in treatment with anti-thyroid drugs; refractive value (spherical equivalent) within the range −3 diopters (D) to +3 D. We excluded patients with a history of radiotherapy or thyroidectomy; previous treatment with corticosteroids in the 3 months before enrolment; any ocular or systemic disease that could interfere with the measurements. The control group comprised of 40 healthy subjects with the same age range (25–45 years) and the same male:female proportion (4:1) vs. the study group. They had no history of ocular or systemic disease and minimal refractive error. Ocular proptosis was measured by a Hertel exophthalmometer. Spectral-domain optical coherence tomography (SD-OCT) was performed in all subjects using the enhanced-deep image (EDI) mode. Binarization of images was processed using the open-source software ImageJ. TCA, LA, stromal area (SA) and CVI were calculated.

## Results
Both eyes of 80 patients, 21 males and 59 females, were included in this study. Forty cases were diagnosed with TAO and 40 subjects served as controls. Since there was a strong correlation between right and left eye variables, only data of the right eyes were included in the statistical analysis. No significant differences were observed in SFCT, TCA and SA comparing patients with TAO and healthy controls (all P>0.05). LA was significantly higher in TAO subjects when compared with controls (P=0.045). Mean CVI significantly differed between TAO patients (64.78 ± 3.28%, range: 52.60-72.13%) and healthy controls (62.19 ± 4.44%, range: 51.89 – 70.23%) (P=0.004). In subgroup analysis considering only patients with CAS ≥3 (28 subjects, 23 females), no significant differences were observed between patients with active TAO and controls in TCA, SA and SFCT (all P>0.05). LA (P=0.046) and CVI (P=0.011) were significantly higher in patients with active TAO. Univariate linear regression analysis was performed for age, gender, presence or absence of diplopia, CAS, degree of exophthalmos, Inami, TCA, LA and SA and their impact on SFCT and CVI.

## Conclusions
In this study, we found that CVI was higher in eyes with TAO than in healthy controls, despite similar SFCT. CVI was significantly associated with TCA, LA and SFCT in univariate analysis and with TCA and LA in multivariable linear regression analysis. No association was found between either CVI or SFCT and age, gender, presence of diplopia, CAS, exophthalmometry and Inami. This is the first study that has compared CVI in eyes with TAO and healthy controls and has assessed its association with clinical features; it can, therefore, serve as a starting point for further prospective research.

## Financial Disclosure
Not appliable
Bilateral anterior optic neuropathy secondary to covid-19: Report of a case

Haishel Sierra Colombia

Purpose
To describe a case of bilateral optic neuropathy in a young woman during her covid-19 infection.

Setting/Venue
Villavicencio, Meta, Colombia.

Methods
case report.

Results
A case of a 34-year-old woman with the presence of covi-19 infection is described and on the third day of infection she presents sudden loss of visual acuity, she comes after the 10th day of isolation and there are signs of anterior optic neuropathy with vascular congestion of the optic disc, treatment is given after 20 days of the infectious process with topical and intravenous corticosteroids, with slow recovery of vision and subsequent improvement of the anatomical state of the optic disc.

Conclusions
covid-19 could be related to optic nerve disorders.

Financial Disclosure
I have no conflicts of interest
To shade or not to shade, that is the question

Paolo Milani
Italy

To evaluate the sensitivity of a spectral-domain optical coherence tomography (SD-OCT) biomarker, the choroidal shadowing, in active myopic choroidal neovascularization (mCNV). This finding is typically caused by the tissue density of the neovascular complex that leads to the tomographic hypo-transmission from the retina toward the choroid.

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Setting/Venue
This retrospective, cross-sectional study was based in IRCCS Istituto Auxologico Italiano, Milan, Italy.

Methods
The clinical and imaging parameters of eyes with high myopia (spherical equivalent of -6D or less) with naïve or recurrent mCNV were reviewed independently by two investigators. A control group with inactive mCNV was included, too. The presence of mCNV was based on multimodal imaging that included fluorescein angiography and SD-OCT findings. When available, OCT angiography was also used. Presence of choroidal hypo-transmission was defined as the shadowing of the retinal lesion projected toward the underlying choroid on SD-OCT. The shadowing enables distinction of the adjacent, unaffected choroid from the underneath choroid masked by the lesion.

Results
Eighty-three eyes (27 men, 56 women) with active mCNV were included in the study. The mean patient age was 67.69 years (range, 39–89 years) with a mean of -10.02 diopters (range -6, -24). In the control group 30 eyes (10 men, 20 women) with fibrotic mCNV were included. The mean patient age was 65.06 years (range 44-89) with a mean of -11.7 (range -6,-20). Fifty-two eyes with active mCNV presented choroidal shadowing in correspondence of the lesion resulting in a sensitivity of 63%. Twelve eyes with fibrotic mCNV presented choroidal shadowing too, thus resulting in a specificity of 60%. The concordance between the investigators was good (Cohen’s k factor = 0.80).

Conclusions
In active mCNV, choroidal shadowing is a tomographic biomarker with a limited positive and negative predictive value.

Financial Disclosure
No financial relations to disclose.
**Title**
Retinal alterations in Niemann Pick type C

**Purpose**
Retinal layer changes in common neurological diseases are well studied. Retinal neurodegeneration in the ultra-rare inherited neuro-visceral disease Niemann Pick type C (NPC), with an estimated incidence of 1/120,000 live births, receives little attention. NPC is a progressive lysosomal lipid storage disorder with a broad spectrum of neurological signs, such as vertical supranuclear gaze palsy, cataplexy, ataxia, dysarthria, and progressive cognitive impairment. The present study aims to analyze quantitative retinal layer measurements of the macular area and the optic disc by use of Spectral-Domain (SD) Optical Coherence Tomography (OCT) in NPC patients, which seem reasonable to expect in neurodegenerative disorders.

**Setting/Venue**
Monocentric cross-sectional study of NPC patients and controls, recruited in the University Medical Center Mainz.

**Methods**
Fourteen eyes of 8 NPC1 patients, and 180 eyes of 94 healthy controls were included. All patients underwent ophthalmologic examination including non-cycloplegic auto-refraction measurements, best corrected visual acuity, slit lamp biomicroscopy of the anterior segments, and fundoscopy. Peripapillary OCT (pOCT), and macular OCT (mOCT) with 49 horizontal single scans were acquired. Blind quality control of each examination was conducted after semi-automated segmentation. We compared global pOCT measurements and sectorial data with the controls. Mean macular thickness values of the fovea, the inner ring, and the outer ring of each retinal layer were analyzed. We used linear mixed models to control for the inclusion of one and two eyes of a study participant, and an adjustment for age, sex, and spherical equivalent was included. Spearman’s rank correlation was computed between outer nuclear layer (ONL) and clinical parameters.

**Results**
The mOCT analysis revealed significant thinning of the total retinal thickness in the fovea (256.1 µm SD 21.1 in NPC vs. 278.3 µm SD 19.2 in controls, p = 0.003). Specifically outer nuclear layer (ONL) and outer retinal layer (ORL) (external limiting membrane to Bruch’s membrane), forming the main parts in the fovea, were thinned (ONL: 80.4 µm SD 8.5 vs. 92.5 µm SD 10.3, p = 0.002; ORL: 87.6 µm SD 4.6 vs. 90.6 µm SD 4.1, p = 0.027). The results remained significant after adjusting for age, sex, and spherical equivalent (p = 0.001, 0.007, and 0.010 respectively). No correlation was found between foveal ONL and clinical features (NPC-disability score: r= -0.06, p= 0.25, and horizontal peak velocity of reflexive saccades: r= 0.3, p= 0.25). Peripapillary RNFL thickness was not significantly different in NPC compared to healthy controls (99.9 µm SD 8.1 in NPC vs. 96.7 µm SD 9.8 in controls, p = 0.37 (0.28 after adjustment).

**Conclusions**
Foveal retinal thinning, specifically of the ONL, and ORL (photoreceptors) was demonstrated in NPC for the first time. In contrast to our initial hypothesis, GCL/IPL and nerve fibre layers were normal.

**Financial Disclosure**
none
Changes in the retinal and choroidal microvasculature during menstrual cycle

Purpose
To evaluate the retinal and choroidal microvascular changes during the menstrual cycle using swept-source optical coherence tomography angiography (SS-OCTA)

Setting/Venue
University of Health Sciences, Beyoglu Eye Training and Research Hospital, Istanbul, Turkey

Methods
Twenty-one healthy women with regular menstrual cycles were recruited and one eye per participant was randomly selected. Subjects underwent complete ophthalmologic examination including SS-OCTA imaging in the follicular phase (3rd day of the cycle), ovulatory (14th day of the cycle), and mid-luteal phase (21st day of the cycle). Macular microvasculature was evaluated using a 6x6 volume angiography scan pattern centered on the fovea. Measurements were performed within the same menstrual cycle. Vessel density of the superficial capillary plexus (SCP), deep capillary plexus (DCP), and choriocapillaris (CC) were automatically calculated using the built-in software of the device. The foveal avascular zone (FAZ) area of the SCP and DCP were manually calculated by delineating the border using the device's built-in measurement tool.

Results
The mean age was 27.3±3.9 years of the subjects. There was no significant difference in terms of systemic blood pressure, refractive error, and central corneal thickness measurements among the three menstrual phases (p>0.05). The FAZ area of SCP and DCP did not significantly differ during the menstrual cycle (p>0.05). The mean SCP vessel density of the superior, temporal, inferior, and nasal parafoveal quadrant was slightly higher in the ovulatory phase compared to the follicular and mid-luteal phases (p>0.05). The vessel density of the SCP, DCP, and CC in the foveal region showed no significant difference during the menstrual cycle (p>0.05). There was a significant difference in average parafoveal vessel density values of SCP and CC among the menstrual phases (p=0.037, p<0.001 respectively). A posthoc analysis revealed ovulatory phase vessel density measurements were significantly higher compared to the follicular and mid-luteal phases.

Conclusions
Hormonal fluctuations during the menstrual cycle may affect both retinal and choroidal microvasculature. Our findings indicate that clinicians should take into consideration of the menstrual phase during the interpretation of OCTA parameters in young reproductive women.

Financial Disclosure
The authors declare that there is no conflict of interest.
**Title**
Evaluation of the choroidal vascularity index after subthreshold yellow laser photocoagulation in the patients with central serous chorioretinopathy

**Purpose**
To evaluate the choroidal vascularity index (CVI) after subthreshold yellow laser photocoagulation in the patients with central serous chorioretinopathy (CSR) and to compare with non-treated patients with CSR.

**Setting/Venue**
Mugla Sitki Kocman University

**Methods**
This study analyzed enhanced depth imaging-optical coherence tomography (EDI-OCT) and optical coherence tomography angiography (OCTA) scans of 21 eyes of 21 patients with CSR (≥4 months of duration). The patients were divided into two groups according to whether they received laser treatment or not. Group1 consisted of 8 eyes of 8 patients with persistent CSR were treated with the PASCAL (Streamline) at 577-nm wavelength, using 200-mm retinal spot sizes. Group 2 consisted of 13 eyes of 13 CSR patients without laser treatment. Using Endpoint Management Software, the laser power was first titrated for a barely visible burn with 15-ms pulses, which was defined as 100% pulse energy. Then treatment was applied over the area of serous retinal detachment, using 30% pulse energy with the spot spacing of 0.25 beam diameter. The CVI were measured by binarization of EDI-OCT images. The image binarization was performed using a public domain software (Image J). Choriocapillaris (CCP) flow area were measured by OCTA. Changes in subretinal fluid height (SFH), best-corrected visual acuity (BCVA), and central macular thickness (CMT), subfoveal choroidal thickness (SCT), CVI, and CCP flow area were evaluated over 3 months. BCVA, SCT, CVI, and CCP flow area were compared between the groups.

**Results**
There was no significant difference between groups in terms of BCVA, CMT, SCT, CVI and CCP flow area at baseline. (For all p > 0.05) Compared to the baseline values in group 1, a significant decrease was observed in CMT, SCT, SCF, and CVI at the 3rd month. (Respectively; p=0.02, p<0.001, p=0.03, p=0.017) The BCVA and CCP flow area values were increased at 3 months after laser treatment in group1. (p=0.002, p=0.04) The CMT was significantly decreased and the BCVA was increased in group 2 over follow-up time. (p=0.01, p=0.04) However, there was no significant difference in terms of SCT, SCF, CVI and CCP flow area in group2 over time. (p= 0.228, p=0.891, p=0.06, p=0.102) At third month, the CMT, SFH and CVI was significantly lower in group1 than group2. (p=0.003, p=0.02, p=0.013) The BCVA was higher in group 1 than group2 at the 3 months. (p=0.03)

**Conclusions**
Decreased CVI was noted in patients with CSR after subthreshold yellow laser. The CVI and CCP flow area could be a useful index to assess the treatment response after subthreshold yellow laser photocoagulation in CSR.

**Financial Disclosure**
no financial disclosure
Structural changes of choroid via binarization method in children with attention deficit hyperactivity disorder

**Purpose**
To compare the structural changes of the choroid and the choroidal vascularity index (CVI) alterations in the eyes of the children with attention deficit hyperactivity disorder (ADHD) receiving methylphenidate, children with newly diagnosed ADHD not receiving any medication and with the healthy controls.

**Setting/Venue**
Sivas Cumhuriyet University School of Medicine, Department of Ophthalmology, Sivas, TURKEY

**Methods**
This study consisted of 33 right eyes of 33 children who received methylphenidate treatment for at least 6 months, 25 right eyes of 25 patients who were diagnosed with ADHD but not receiving methylphenidate treatment, and 25 right eyes of 25 healthy controls. Demographic data of the patients were evaluated. Subfoveal choroidal thickness was measured in all groups via the images obtained by optical coherence tomography in choroidal mode. Also, calculations of the luminal area (LA) and total choroidal area (TCA) and choroidal vascularity index (CVI) using the binarization method in the ImageJ image analysis software were compared between three groups.

**Results**
The mean age of 83 patients was 10.1±2.5 (6-17) of whom 59 (71%) were male; 24 (29%) were female. No statistically significant difference was found between groups in terms of age and gender (p=0.08 for age, p=0.8 for gender). The mean duration of methylphenidate use was 10.4±3.3 (6-19) months in the methylphenidate group. The subfoveal choroidal thickness was 301.3±26.9 µm in the ADHD group not receiving medication, 295.6±30.7 µm in the methylphenidate group and 297.9±27.3 µm in the control group. There was no statistically significant difference between the groups regarding subfoveal choroidal thickness (p=0.7). LA and TCA were 0.43±0.07 mm² and 0.65±1.0 mm² in the group not receiving medication; 0.37±0.08 mm² and 0.53±0.11 mm² in the methylphenidate group; and 0.4±0.06 mm² and 0.58±0.1 mm² in the control group respectively. CVI was 0.66±0.02 in the group not receiving medication; 0.68±0.02 in the methylphenidate group, and 0.68±0.02 in the control group. Although LA and TCA were statistically higher in the ADHD group not receiving medication (p=0.002 for LA and p=0.001 for TCA), CVI was found to be statistically lower (p=0.001).

**Conclusions**
TCA and LA were higher in the eyes of children with ADHD not receiving medication compared to healthy controls. The use of methylphenidate may cause decrease in both LA and TCA. However, the lower CVI in the group not receiving medication can be explained by the fact that methylphenidate use causes a greater reduction in the total choroid area compared to the luminal area. It would be beneficial to design future studies with the correlation of pre-medication, post-medication measurements in the same patient group diagnosed with ADHD and duration of medication use.
**Title**
Optical coherence tomography and color fundus photography in the screening of age-related macular degeneration: A comparative, population-based study

**Purpose**
to analyze the individual value and the contribution of optical coherence tomography (OCT) added to color fundus photography in the screening of age-related macular degeneration (AMD) of an unselected population.

**Setting/Venue**
this was an observational retrospective study.

**Methods**
15957 fundus photos and OCT images of 8069 subjects older than 55 years, obtained during during a population-based screening for AMD, were analyzed. The screening campaign used a hi-tech unit, equipped with a single diagnostic imaging device to obtain both fundus photos and OCT scans. All photos and OCT images were separately, and randomly classified by a blinded examiner. The two techniques were preliminary analyzed, considering the dichotomous parameter gradable/ungradable. Gradable images were then classified. Fundus photos were graded according to the clinical classification of AMD; the presence of other retinal diseases was also recorded. OCT images were categorized considering the presence of signs of early/intermediate AMD, late AMD, or other retinal diseases. 1978 randomly selected images (for both fundus photos and OCT scans) were separately graded by another, blinded operator, to assess test reproducibility.

**Results**
Of the 15957 images, 8356 fundus photos (52.4%) and 15594 (97.7%) OCT scans were gradable. Moreover, 96.6% of eyes with ungradable fundus photos were gradable with OCT. AMD signs were detected in 7.4% gradable photos (1.2% late AMD) and in 10.4% gradable OCT images (1.8% late AMD). Signs of AMD were identified at OCT in 1110 (6.9%) eyes where fundus photos were ungradable (847 eyes) or without signs of AMD (263 eyes). The inter-graders agreement was good for gradable vs ungradable, and optimal for the grading parameter, in the fundus photos analysis. It was optimal for all parameters in the OCT analysis.

**Conclusions**
OCT provided gradable images in almost all examined eyes, compared to poor fundus photos efficiency. Moreover, OCT images allowed to detect more AMD eyes compared to gradable photos. OCT imaging appears to significantly improve, compared to fundus photos alone, the power of AMD screening in a general, unselect population, thus proving its primary and undisputable role in the screening of AMD.

**Financial Disclosure**
None
Concordance of SIVA, IVAN and VAMPIRE software tools for semi-automated analysis of retinal vessel caliber

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Purpose
Retinal vascular diameter can be measured from retinal photographs using semi-automated software tools. We aim to compare the measurements from three most used packages in the literature: SIVA (Singapore I Vessel Assessment), VAMPIRE (Vascular Assessment and Measurement Platform for Images of the Retina) and IVAN (Integrative Vessel Analysis) and to generate conversion algorithms for CRAE and CRVE measurements, between SIVA and IVAN and between SIVA and VAMPIRE.

Setting/Venue
We analyzed 223 retinal photographs from 133 human subjects (CR-2 Canon fundus camera, Canon™) with each software tool, computing vessel widths measurements and the central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE) and arteriole-to-venule ratio (AVR).

Methods
The agreement was assessed using Bland-Altman plots and intra-class correlation coefficients. We propose a transformation between measurements from different system using linear regression, and validated it using bootstrapping and root-mean-square-error (RMSE).

Results
The agreement between VAMPIRE (version 3.1, 2017 and IVAN was poor to moderate: the mean difference was 20.2 µm (95% LOA, -12.2 to 52.6 µm) for CRAE, 21.0 µm (95% LOA, -17.5 to 59.5 µm) for CRVE, and 0.023 (95% LOA, -0.12 to 0.16) for AVR. The agreement between VAMPIRE and SIVA was also poor to moderate: the mean difference was 36.6 µm (95% LOA, -12.8 to 60.4 µm) for CRAE, 40.3 µm (95% LOA, 5.6 to 75.0 µm) for CRVE, and 0.037 (95% LOA, -0.071 to 0.15) for AVR. The agreement between IVAN and SIVA was good to excellent: the mean difference was 16.4 µm (95% LOA, -4.25 to 37.0 µm) for CRAE, 19.3 µm (95% LOA, 0.09 to 38.6 µm) for CRVE, and 0.015 (95% LOA, -0.09 to 0.11) for AVR. Using the conversion algorithm, the agreement was higher between SIVA measurements and IVAN-derivate SIVA approximates (RMSE was 4.88 µm for CRAE and 5.19 µm for CRVE) than between SIVA measurements and VAMPIRE-derivate SIVA approximates (RMSE was 7.27 µm for CRAE and 9.69 µm for CRVE).

Conclusions
Comparing CRAE, CRVE and AVR estimates from three widely used retinal vessel measurement software tools, we found an excellent agreement between SIVA and IVAN, a poor to moderate agreement between VAMPIRE (version 3.1, 2017) and the two other software tools. We propose an algorithm converting IVAN and VAMPIRE measurements into SIVA estimated measurements, that could be used to homogenize sets of vascular measurements obtained with different packages.

Financial Disclosure
none
Title
Sensitivity and specificity of MultiColor imaging in detecting proliferative diabetic retinopathy

Purpose
Fluorescein angiography (FA) has been regarded as the gold standard for proliferative diabetic retinopathy (PDR) assessment, despite the development of other noninvasive imaging modalities, such as MultiColor imaging (MC). This study intended to appraise the accuracy of MC compared to FA in detecting PDR and its features.

Setting/Venue
Department of Ophthalmology, Hospital de Santa Maria, Lisboa, Portugal.

Methods
Fifty-nine eyes from 38 PDR patients were selected. MC images were evaluated by 2 independent masked graders. A qualitative analysis based on the following features was performed: neovascular complexes (NVC), disc neovascularization (NVD), neovascularization elsewhere (NVE), microaneurysm (MA), intraretinal hemorrhage (IRH), vitreous hemorrhage (VH), preretal hemorrhage (PRH), fibrosis, hard exudates (HE), epiretinal membrane (ERM), diabetic macular edema (DME), ischemia and laser spots (LS). Measures of diagnostic accuracy compared to FA were determined.

Results
The sensitivity for the detection of NVC using MC was 95.1%, with a specificity of 40.0%, a positive predictive value (PPV) of 92.9% and a negative predictive value (NPV) of 50.0%. NVD detection presented higher sensitivity and specificity values (88.9% and 76.9%) while NVE registered higher PPV (88.9%). MC was highly sensitive in detecting IRH, HE, ERM and LS (100%), MA (98.0%) and fibrosis (95.5%). However, the highest specificity value was found in detection of VH (100.0%), DME (100.0%), PRH (98.1%) and LS (89.5%). The area under the receiver-operating characteristic analysis of MC was excellent in NVD (0.83, 95% confidence interval (CI), 0.71-0.95, p<0.001), IRH (0.89, 95% CI 0.74-1.00, p=0.005) and PRH (0.89, 95% CI 0.68-1.00, p=0.004) and outstanding in LS detection (0.95, 95% CI 0.87-1.00, p<0.001). The contrast and quality of the MC probably account for these results, as the green wavelength enables better discrimination. The level of interrater reliability for the MC features appraised was almost perfect with an 0.86 weighted kappa (standard error: 0.02, 95% CI: 0.82–0.88).

Conclusions
MC was more accurate than FA in detecting some PDR features, namely NVD, VH, PRH, IRH and laser spots. These findings validate MC as a useful imaging test not only for the diagnosis but also for the follow-up assessment of PDR, enhancing the noninvasive imaging of this disease. The obtention of more information with less testing and without moving patients to different machines and/or rooms has grown even more pressing with the SARS-CoV-2 pandemic.

Financial Disclosure
Tiago Morais Sarmento has no financial interests to disclose; Gabriella de Salvo reports consultant fees from Allergan, Bayer, Heidelberg Engineering and Novartis; Sara Vaz-Pereira reports consultant fees from Bayer, Novartis, Alimera Sciences and Roche.
**Title**
Structural retinal changes and neuronal measures in schizophrenia

**Purpose**
Schizophrenia is a neurodegenerative disease of the brain. In literature, there are studies suggesting reduced retinal nerve fiber layer (RNFL) thickness and macular thickness. The aim of this study is to evaluate the outer retinal layer thickness (ORL) and retinal nerve fiber layer changes in patients with schizophrenia and to compare them with the healthy controls.

**Setting/Venue**
Sivas Cumhuriyet University School of Medicine, Department of Ophthalmology, Sivas, TURKEY

**Methods**
This study consisted of 114 eyes of 57 patients diagnosed with schizophrenia and 114 eyes of 57 healthy controls. Demographic data of the patients were evaluated. Central foveal thickness (CFT), central subfield thickness (CST) and, ORL thickness were measured in both groups via the images obtained by spectral-domain optical coherence tomography (OCT). RNFL was also assessed in four quadrants (inferior, superior, temporal, nasal). CST measurements were presented as the average thickness of the macula in the central 1 mm area on the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. The ORL thickness was defined as the distance between external limiting membrane and retinal pigment epithelium at the center of the foveal pit.

**Results**
The mean age of 57 patients was 37.2±9.9 of whom 34 (59.6%) were male; 23 (40.4%) were female. No statistically significant difference was found between groups in terms of age and gender (p=0.8 for age, p=0.9 for gender). The mean CST in two groups was 255.5±25.8 and 262.2±17.6 µm respectively (p=0.1). ORL thickness was 98.2±14.6 in the patient group and 103.7±6.2 µm in the control group. The difference between groups regarding ORL thickness was statistically significant (p=0.011). Also, RNFL analysis demonstrated a significant thinning in the inferior and superior quadrants compared to healthy controls (p<0.001 and p=0.017 respectively).

**Conclusions**
The retina consists of neuronal cells therefore neurodegenerative disorders may affect retinal structures. Our findings reveal noteworthy retinal layer changes. Consequently, OCT may help facilitate the clinical diagnosis of schizophrenia and substantially may be considered as a potential early biomarker for monitoring the progressive neurodegeneration in schizophrenia.

**Financial Disclosure**
None
Title
Evolution of macular Bruch Membrane Defects (BMD) of patchy chorioretinal atrophy in pathologic myopia based on a recent classification system (ATN)

Purpose
To analyze the progression of macular Bruch Membrane Defects (BMD) in highly myopic patients with Patchy Atrophy (PA) and study its correlation with the enlargement of PA and ATN grading.

Setting/Venue
Puerta de Hierro-Majadahonda University Hospital, Madrid, Spain.

Methods
Cross-sectional, non-interventional study. A series of 451 highly myopic eyes with spherical equivalent (SE) > -6.0 D and/or >26 mm of Axial Length (AL) were included. All patients underwent a complete ophthalmological examination and swept-source optical coherence tomography (SS-OCT), and were graded using the ATN system by two masked retina experts that assessed the atrophic (A), tractional (T) and neovascular (N) components. SS-OCT b-scans were employed to study PA and macular BMD at baseline in a masked fashion by two investigators. At one-year follow-up patients with good foveal fixation, PA and BMD size was again measured.

Results
Out of the total 451 eyes, 126 eyes (27.9%) had PA (53 patients; 75.4% women). Mean T and N in eyes with PA was 1.1±1.3 and 0.08±0.2 respectively. 68 of them had >1-year follow-up, good foveal fixation and enough image quality. From them, BMD were found in 44 eyes (64.7%) at baseline and increased to 59 eyes (86.7%) at 1-year follow-up. The mean great linear dimension of PA and macular BMD increased a median of 384.5±462.5 µm (IR 68.0-660.2) and 265.6±418.1 µm (IR 0-331.7), respectively. At one-year, PA and BMD size increase, were statistically significant (p<0.001). There was a positive correlation between the growth of macular BMD and the growth of PA (r=0.490, p<0.001). T grading correlated significantly with PA growth (p<0.05).

Conclusions
In conclusion, macular BMD is a hallmark of PA in high myopic patients, with an increasing prevalence and size over time. There is a positive correlation between BMD and PA area growth. New studies with larger series, longer follow-up and correlated with AL are necessary to corroborate our findings.

Financial Disclosure
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Visualization of type-1 choroidal neovascularization secondary to pachychoroid spectrum diseases: A comparative study for sensitivity and specificity of indocyanine green angiography and optical coherence tomography angiography

Purpose
To investigate optical coherence tomography angiography (OCTA) in detecting choroidal neovascularization (CNV) compared to indocyanine green angiography (ICGA) in eyes with pachychoroid characteristics and flat irregular pigment epithelial detachment (PED).

Setting/Venue
Retrospective, cross-sectional.

Methods
Patients having pachychoroid spectrum disease characteristics such as hyperpermeability on ICGA and dilated outer choroidal vessels with flat irregular PED, who had undergone ICGA and OCTA imaging at the same visit, were recruited in this study. The diagnosis of CNV has been made by using multimodal imaging techniques under supervision of a senior retinal specialist (FS). After that, both ICGA and OCTA images were separately reviewed by a masked-independent senior retina specialist (SD) in regard to the presence of CNV. The specificity, sensitivity, positive and negative predictive values of the techniques were analyzed.

Results
Fifty-four eyes of 50 consecutive patients with a mean age of 55.5±9.1 years were included. OCTA was able to detect CNV with 97.2% sensitivity, failing to detect CNV only in one eye. The sensitivity of ICGA to detect CNV was 66.7%. The specificity of both techniques was 100%. For all eyes which CNV were negative according to the multimodal imaging, OCTA confirmed absence of CNV with 94.7% accuracy; but this value was 60% for ICGA (negative predictive value).

Conclusions
OCTA demonstrated greater sensitivity in detecting CNV than ICGA in cases with pachychoroid spectrum disease.

Financial Disclosure
Lecturer and Consultant fee (Bayer, Novartis, Allergan, Alcon and Bausch & Lomb)
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Purpose
Hemifacial spasm (HFS) is a chronic peripheral movement disorder characterized by unilateral, involuntary contractions of the muscles innervated by the facial nerve leading to clonic and tonic episodes of squeezing eyelids. This study aimed to investigate choroidal vascular and structural changes in HFS patients using enhanced depth imaging optical coherence tomography (EDI-OCT) with automatic binarization by ImageJ software.

Setting/Venue
Kayseri City Training and Research Hospital Ophthalmology and Neurology clinics

Methods
This cross-sectional study included 138 eyes of 92 patients. Chronic unilateral HFS patients with a minimum follow-up of 12 months were included. The eyes were divided into three groups: (1) 46 affected eyes of patients with clinically unilateral chronic HFS; (2) 46 unaffected fellow eyes; and (3) 46 control eyes of healthy sex and age-matched participants. EDI-OCT scans of the macula were acquired (Heidelberg Engineering, Heidelberg, Germany). Choroidal thickness (CT) analysis was performed from the subfoveal region. Choroidal Images were binarized using ImageJ software (National Institutes of Health, Bethesda, USA). The choroidal vascularity index (CVI), the proportion of the luminal choroidal area to the total choroidal area, was evaluated.

Results
The mean subfoveal CT values of the affected eyes were lower compared with fellow-eyes of the HFS patients (212.63 vs. 252.00, P= 0.013) and controlled eyes (212.63 vs. 247.91 P= 0.034). The macular CVI values of the affected eyes were lower compared with fellow-eyes of the HFS patients (65.94 vs. 68.19, P=0.011) and control eyes (65.94 vs 67.23, P= 0.044). No significant difference was found between the subfoveal CT of the unaffected fellow and control eyes (252.00 vs. 247.91, P= 0.826) and between the CVI of the unaffected fellow and control eyes (68.19 vs. 67.23, P= 0.111).

Conclusions
This study's outcomes show that chronic HFS is associated with decreased subfoveal choroidal vascularity and central choroidal thickness. These results suggest that the pressure generated during periods of orbicular contractions can cause choroidal vascular and structural changes over time.

Financial Disclosure
No authors have a financial or proprietary interest in any material or method mentioned in the present study
**Title**
Short term effects of half-fluence photodynamic therapy on retinal and choroidal vascular parameters in chronic central serous chorioretinopathy patients

**Purpose**
To evaluate the short-term effects of half-fluence photodynamic therapy on retinal and choroidal vascular parameters obtained by optical coherence tomography angiography. As primary pathology in CSC was supposed to be in the choroid, previous studies mainly focused on OCT-A imaging of choroid in patients who underwent PDT. However, verteporfin reaches the retinal vessels and PDT laser beam is also applied to the retinal vessels. To our best knowledge, very short-term effects of half fluence PDT on retinal vessel densities in OCT-A imaging for foveal, parafoveal and perifoveal regions have not been studied before. Therefore, retinal vessels may also be affected by PDT and should be analyzed in this manner.

**Setting/Venue**
Tertiary referral university hospital, retrospective study

**Methods**
Fifteen patients who underwent photodynamic therapy (PDT) for chronic central serous chorioretinopathy (CSC) between 2018-2020 were included in the study retrospectively. The electronic charts of patients evaluated for ophthalmologic examination including best-corrected visual acuity (BCVA), anterior segment examination with slit-lamp, retinal examination with indirect binocular retinoscopy, fundus fluorescein angiography and OCT. Subretinal fluid was followed up with spectral-domain OCT (Spectralis, Heidelberg Engineering Inc., Heidelberg, Germany). Hyperfluorescent spots in FFA indicating active lesions in the choroid, subretinal serous fluid and increased choroidal thickness in enhanced depth imaging mode OCT (subfoveal choroidal thickness ≥300µm) were used as diagnostic criteria for CSC. The subretinal fluid which persisted for more than six months was accepted for chronic CSC. Patients with systemic hypertension, refractive errors ≥±6.0 diopters of spherical equivalent, ocular trauma, intraocular surgery, glaucoma, uveitis and previous PDT or PDT for other choroidal lesions in the electronic charts were excluded from the study. Images with a quality score lower than 6/10 and with eye movement artifacts were excluded from the study. Half fluence photodynamic therapy was performed with a diode laser at 689 nm (Visulas 690S; Carl Zeiss Meditec Inc., Dublin, CA, USA) after infusion of verteporfin.

**Results**
Nineteen patients (10 male and 5 female) who underwent PDT for chronic CSC were included in the study. The mean age was 42 ± 7 years. The first OCT-A images were obtained within 3 days before PDT. The following OCT-A images were performed mean 6.3 days (min 2 – max 21) after PDT. Visual acuity, FAZ area, acircularity index, foveal density 300, outer retinal flow and choriocapillaris flow values were not significantly different before and short term after PDT. The vessel density of the superficial foveal capillary plexus was significantly decreased after PDT (p=0.044). However whole area, parafoveal and perifoveal vessel densities of superficial capillary plexus were not significantly different before and after PDT. The vessel density of the deep parafoveal capillary plexus was significantly increased after PDT (p=0.027). The vessel density of the deep parafoveal capillary plexus was not significantly different before and after PDT. There was no significant correlation between time duration after PDT and superficial foveal vessel density (p=0.49) and deep parafoveal vessel density (p=0.20).

**Conclusions**
In conclusion, this study showed that vessel density of superficial foveal capillary plexus was decreased and vessel density of deep parafoveal capillary plexus was increased in short term after half fluence PDT. However, the foveal avascular zone area, choroidal flow, choroidal signal voids and vascular densities of other remaining macular vascular areas were not changed.
Ganglion cell layer as a novel biomarker for adverse outcome in high-risk pregnancy

Joel Hanhart, Israel

Purpose
To determine whether specific retinal layers are associated with adverse outcome in high-risk pregnancies.

Setting/Venue
This prospective study was conducted between January 9 2017 and May 14 2018 at Shaare Zedek Medical Center, a tertiary hospital. Included were women followed in the maternal fetal medicine unit at Shaare Zedek Medical Center. All participants were between 18-45-years of age, over 24 weeks of gestation, with a singleton pregnancy and without a history of chronic hypertension.

Methods
We performed swept-source OCT macular examinations and measured selective layers at different regions of the macula on 32 pregnant women. Adverse obstetrical outcome was defined as any of the following: preterm delivery, pre-eclampsia, pregnancy induced hypertension, elevated liver function tests, thrombocytopenia and need for magnesium to treat severe pre-eclampsia.

Results
In the group defined by any adverse outcome, that comprised 17 patients (34 eyes, 53%), the inner superior ganglion cell layer was found to be thinner than in patients without adverse outcome (83.9±6.9 vs. 88.6±6.1 μm; P=0.04) This association was retrieved when considering all inner superior (287.5±39.1 vs. 300.8±12.7 μm; P=0.03) and inferior retinal layers (287.8±13.9 vs. 297.7±17.1 μm; P=0.03) as well as total macular volume (7.58±0.30 vs. 7.75±0.30 mm3; P=0.02).

Conclusions
The macular ganglion cell layer can be used as a biomarker in pregnancy: specific thinning of this layer is associated with adverse pregnancy outcome.

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Financial Disclosure
N/A
Analysis of external retinal layers reflectivity in patients treated with hydroxychloroquine using a medical image-processing software

**Purpose**
Spectral domain optical coherence tomography (SD-OCT) allows visualization of structural changes in the retinal layers of patients treated with hydroxychloroquine who developed retinal toxicity. For that reason, is one of the screening methods recommended by American Academy of Ophthalmology. Previous studies in patients with diabetic retinopathy and diabetic macular edema, associated the decrease in the reflectivity of the retinal layers with functional deterioration. Thus, it is possible that the evaluation of the reflectivity of external retinal layers by SD-OCT could provide information about the early degeneration of the photoreceptors in patients receiving hydroxychloroquine, before retinal anatomical changes occurred. Our purpose is to determine changes in retinal pigment epithelium (RPE), photoreceptor inner ellipsoid layer (Elip) and external limiting membrane (MLE) reflectivity using SD-OCT image analysis in patients treated with hydroxychloroquine without any evidence of macular structural damage.

**Methods**
Retrospective, single-centre and controlled clinical study including 39 eyes from 39 patients treated with hydroxychloroquine (400mg/day for more than 5 years) and 37 eyes from 37 age- and sex-matched healthy subjects (control group). Subjects were excluded if they had retinopathy or any evidence of macular structural damage, previous history of ocular disease; surgical or laser treatments; any condition that precluded good quality SD-OCT and inability to consent. The reflectivity of the retinal layers: EPR, Elip and MLE was quantified using a medical image-processing software (ImageJ v1.47®) based on greyscale SD-OCT images. The differences in the reflectivity values between cohort study and control groups were analyzed. The reliability of the sample size was tested at 95% power and 0,05 significance level (95% CI) using statistical software Stata/MP version 14.1. Continues variables (age and reflectivity) were evaluated with t-Student test.

**Results**
The study cohort comprised 36 females and 3 males with a mean age of 46,9±7,15 years and the control group consisted of 33 females and 4 males with a mean age of 46,1±7,63 years. All patients and control subjects had a corrected visual acuity of 20/20 Snellen equivalent. In the study group, the EPR, Elip and MLE layers reflectivity was significantly lower (86,92±2,45; 147,85±3,93 and 205,64±2,53 arbitrary units respectively) when compared with that of the control group (104,37±2,23; 177,39±3,94 and 223,08±2,66 arbitrary units respectively) (p<0,005).

**Conclusions**
Previous neurophysiologic studies showed that decreased retinal layer reflectivity on OCT was associated with structural and/or functional damage. This study demonstrated a significant decrease in the 3 layers reflectivity in eyes treated with hydroxychloroquine, especially the photoreceptor inner ellipsoid layer, reflecting early photoreceptors degeneration before any other manifestation of retinal toxicity. In this way it may become an important tool for screening retinal toxicity in patients treated with hydroxychloroquine.

**Financial Disclosure**
The authors have no financial interest to disclose.
OCT risk factors for 3-year development of macular complications in eyes with “resolved” chronic central serous chorioretinopathy

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Purpose
To assess the relationship between demographics, clinical characteristics, and structural optical coherence tomography (OCT) findings and the development of sight-threatening macular complications (choroidal neovascularization [CNV], large areas of retinal pigment epithelium [RPE] atrophy, and cystoid macular degeneration [CMD]) in a cohort of eyes with “resolved” chronic central serous chorioretinopathy (CSC) at study baseline.

Setting/Venue
San Raffaele Hospital, Milan, Italy.

Methods
In this study, a total of 71 eyes with “resolved” (absence of subretinal fluid) chronic CSC at baseline and 36 months of regular follow-up examinations were retrospectively enrolled. Structural OCT scans were reviewed. Baseline OCT qualitative features reflecting distress of the neuroretina, RPE, or choroid were assessed and included ellipsoid zone discontinuity, outer nuclear layer (ONL) thinning; presence of hyper-reflective intraretinal foci; dome-shaped pigment epithelium detachment (PED); hyper-reflective flat, irregular PED; hyporeflective flat, irregular PED; and inner choroidal attenuation. OCT images obtained at follow-up visits were also reviewed for development of macular complications (CNV, large areas of RPE atrophy [at least 250 μm in diameter], and CMD). Main outcome measurements included incidence of macular complications and hazard ratio (HR) for demographics, clinical characteristics, and OCT risk factors.

Results
At month 36, 20 eyes (28.2%) developed macular complications. Nine eyes (12.7%) displayed CNV, 9 eyes (12.7%) had large areas of RPE atrophy, and 2 eyes (2.8%) developed cystoid macular degeneration. The following factors were associated with an increased risk of development of CNV: intraretinal hyper-reflective foci had an HR of 11.58 (95% confidence interval [CI]: 1.10-37.24; P = .040); inner choroidal attenuation had an HR of 9.66 (95% CI: 1.07-22.34; P = .043); and the presence of macular complications in the fellow eye had an HR of 20.17 (95% CI: 1.34-39.41; P = .030). Factors associated with the development of RPE atrophy were also identified: ONL thinning had an HR of 13.47 (95% CI: 1.10-39.86; P = .042); dome-shaped PED had an HR of 21.40 (95% CI: 1.50-41.10; P = .031); and inner choroidal attenuation had an HR of 13.20 (95% CI: 1.07-39.32; P = .044).

Conclusions
OCT risk factors were identified for the development of macular complications in eyes with chronic CSC. Findings may help in the identification of high-risk patients.

Financial Disclosure
None
Title
A comparative study of short-term vascular and stromal alterations of the choroid following half-fluence photodynamic therapy in pachychoroid neovasculopathy and chronic central serous chorioretinopathy

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Purpose
To compare the effect of half-fluence photodynamic therapy (hf-PDT) on choroidal structure in chronic central serous chorioretinopathy (CSCR) and pachychoroid neovasculopathy (PNV).

Setting/Venue
A retrospective cross-sectional comparative study.

Methods
This retrospective study included 35 patients with chronic CSCR and 18 patients with PNV. The hf-PDT protocol was applied to all eyes. The applied light dose was 25 J/cm² with an intensity of 300 mW/cm². Before and 3 months after hf-PDT, enhanced-depth optical coherence tomography images were analyzed. The total choroidal area (CA), luminal area (LA), and stromal area (SA) were measured using ImageJ software and the Niblack thresholding method. The choroidal vascularity index (CVI), which was defined as the proportion of the LA to the total CA, was assessed.

Results
Comparing to baseline values, 3 months after hf-PDT, the total CA reduced to 1.197 mm² from 1.398 mm² (p < 0.001), LA reduced to 0.896 mm² from 1.041 mm² (p < 0.001), and SA reduced to 0.301 mm² from 0.357 mm² (p < 0.001) in CSCR group. Total CA reduced to 1.000 mm² from 1.050 mm² (p=0.021), LA reduced to 0.737 mm² from 0.770 mm² (p=0.031), and SA reduced to 0.263 mm² from 0.280 mm² (p=0.073) in the PNV group. To compare the rate of changes between the PNV and chronic CSCR groups after hf-PDT, the percentages of changes in choroidal parameters were calculated. The mean percentage changes in CA, LA, and SA values were statistically higher in the chronic CSCR group (13.86%, 13.53%, 14.11%) than the mean percentage changes in the PNV group (4.61%, 4.02%, 5.74%; p=0.001, p=0.002, p=0.031, respectively).

Conclusions
CSCR and PNV are assumed to be located in the same pachychoroid spectrum diseases. However, they differ in choroidal morphological response after hf-PDT, which might be secondary to how severely the choroid is affected by the disease. Also, different structural characteristics of the PNV lesions may have an impact on the response behavior.

Financial Disclosure
None
**Title**
Discerning between macular hemorrhages due to macular neovascularization or due to spontaneous Bruch’s membrane rupture in high myopia: A comparative analysis between OCTA and fluorescein angiography

**Purpose**
To evaluate the sensitivity and specificity of optical coherence tomography angiography (OCTA) in comparison to fluorescein angiography (FA) in discerning between macular hemorrhages due to myopic macular neovascularization (m-MNV) and idiopathic macular hemorrhage (IMH) in high myopic (HM) patients.

**Setting/Venue**
All patients were identified from the medical records of the Medical Retina and Imaging Unit at the San Raffaele Scientific Institute, Milan, Italy.

**Methods**
In this longitudinal study, 13 eyes of 13 patients (mean age 60±17 years) affected by macular hemorrhage due to HM were included. All patients underwent OCTA and FA at the time of macular hemorrhage (i.e. baseline) and were followed for a 3-month follow-up. The main outcome measure included the sensitivity and specificity of OCTA in discerning between m-MNV and IMH.

**Results**
By means of FA, 7 out of 13 eyes with macular hemorrhage (54%) were diagnosed as type 2 m-MNV, whereas 6 eyes (46%) as IMH. Interestingly, OCTA displayed the presence of a neovascular network in all cases previously diagnosed as m-MNV using FA, and also excluded the presence of anomalous flow in all IMH eyes. This accounted for 100% of the sensibility and specificity of OCTA for m-MNV detection in HM cases with macular hemorrhage. After 3-month follow-up, BCVA improved from 0.39±0.16 to 0.21±0.15 LogMAR (p=0.017) in patients with m-MNV treated by a mean of 2.4±0.8 intravitreal anti-VEGF injections. Conversely, BCVA improved without treatment (from 0.55±0.48 to 0.17±0.08 LogMAR, p=0.112) in IMH patients.

**Conclusions**
OCTA is able to discern with excellent reliability between the presence of m-MNV in HM patients presenting with a new macular hemorrhage and a IMH. This could be of paramount relevance in the clinical setting for the diagnosis and treatment of HM patients.

**Financial Disclosure**
none
Vitreoretinal adhesion is a risk factor for pseudophakic cystoid macular edema

Purpose
To evaluate the changes in thickness of central retina, thickness of choroidal layers before and after cataract surgery and determine the impact of vitreoretinal surface status on these parameters

Setting/Venue
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Methods
Retrospective study included 64 patients (64 eyes) with no macular disorder who underwent phacoemulsification, and had stored spectral domain optical coherence tomography (OCT) imagings within 1 week preoperatively as well as at 1 and 3 months postoperatively. The evaluated SD-OCT parameters were central foveal thickness (CFT), subfoveal choroidal thickness (SFCT), the large choroidal vessel layer thickness (LCVL) and the Sattler's layer/choriocapillaris thickness (SCVL), vitreoretinal status including “vitreomacular adhesion” (VMA), “no vitreoretinal contact visible”, and pseudophakic cystoid macular edema (PCME).

Results
Seventeen eyes (26.6%) had VMA. The preoperative SD-OCT parameters of the two groups were not statistically significant (p>0.05). The mean CFT values at post operative first month were statistically significantly higher in VMA group (p=0.01). Pseudophakic cystoid macular edema was observed in the postoperative first month in two eyes (3.1%) which also had VMA. No statistically significant difference was found between preoperative and postoperative SFCT values (p=0.1, 0.2, 0.5, respectively).

Conclusions
Pre-surgical vitreomacular adhesion may be a risk factor for development of PCME after uncomplicated cataract surgery. Choroidal expansion response after cataract surgery was not associated with pseudophakic cystoid edema.

Financial Disclosure
I have no financial relationship with any company.
Retinal layer thickness changes in hypothyroidism

**Purpose**
To investigate whether retinal layer thicknesses change in hypothyroidism

**Setting/Venue**
Ophthalmology department in a tertiary referral center

**Methods**
Seven-teen patients with hypothyroidism and 20 healthy controls were included in the study. Optical coherence tomography imaging of the macula region was performed by Spectralis OCT (Heidelberg Engineering, Germany). Followed by the image acquisition automatic intra-retinal layer segmentation was performed by the inbuilt software. The automatic segmentation of retinal layers included retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), retina pigment epithelium (RPE), inner retinal layers (IRL), outer retinal layers (ORL) and total retina thickness (TRT). The intra-retinal layer thicknesses were obtained for each ETDRS subfields which were central 1 mm circle, superior, temporal, inferior and nasal subfields between 1 mm and 3 mm circles in Spectralis software. ETDRS grid was centered on the fovea manually in the software panel if it was not positioned correctly and images that were not automatically segmented correctly were excluded from the study.

**Results**
Seventeen patients with hypothyroidism (13 female, 4 male) and 20 healthy controls (14 female and 6 male) were included in the study. There was no significant difference between groups for gender distribution (p=0.72). The mean age was 36.5 ± 11.1 in the hypothyroidism group and 36.2 ± 10.1 in the control group and there was no statistical difference (p=0.84). Temporal 1-3 mm RNFL, central 1 mm INL, superior 1-3 mm INL, temporal 1-3 mm INL, nasal 1-3 mm INL, superior 1-3 mm OPL, temporal 1-3 mm OPL, nasal 1-3 mm OPL thicknesses were significantly higher in hypothyroidism group compared to the control group (p=0.02, p<0.001, p=0.02, p=0.002, p<0.001, p=0.004, p=0.01, p<0.001, respectively). Central 1 mm ONL, superior 1-3 mm ONL, nasal 1-3 mm ONL, superior 1-3 mm RPE, inferior 1-3 mm RPE, nasal 1-3 mm RPE, central 1 mm ORL, superior 1-3 mm ORL and nasal 1-3 mm ORL thicknesses were significantly decreased in hypothyroidism group compared to control group (p<0.001, p=0.01, p=0.001, p=0.03, p=0.005, p=0.001, p=0.002, p=0.04 and p=0.01, respectively).

**Conclusions**
Retinal fiber layer, inner nuclear layer, outer plexiform layer thicknesses in some segments were significantly increased and outer nuclear layer, retina pigment epithelium layer and outer retinal layer thicknesses in some segments were significantly decreased in patients with hypothyroidism compared to healthy controls.

**Financial Disclosure**
No conflict of interest.
Angiometric progression in foveal avascular zone (FAZ) over one year in diabetics using optical coherence tomography angiography (OCTA) and fundus fluorescein angiography (FFA)

Purpose
To evaluate and compare the changes in microcirculation in diabetic eyes between OCTA (both, SCP (superficial capillary plexus) & DCP (Deep Capillary Plexus)) and FFA over one year and to correlate these with the progression of diabetic retinopathy.

Setting/Venue
A prospective, non-randomized, non-interventional study done in the outpatient department of regional referral center.

Methods
Three groups of diabetics (30 patients in each group) were studied over 12 months with exams at 0, 6, and 12 months. Group 1 (diabetics with no diabetic retinopathy), group 2 diabetics with diabetic retinopathy but no diabetic macular edema (DME), group 3 diabetics with diabetic retinopathy (DR), and DME. All patients underwent detailed eye exam and A) FFA with Zeiss Visucam 524 at 0, 6 and 12 months and B) OCT +OCTA with Zeiss Angioplex OCT (Carl Zeiss Meditec, Dublin, CA): SD-OCT macular cube scan, 3x3 OCTA scan. OCTA images of DCP were marked using IMAGE J software after setting the scale to 1024x1024 pixels in a 3x3 mm scan area. OCTA images of SCP were marked using in-built Zeiss Angiometric of Angioplex OCT. The FAZ on FFA was manually outlined using the in-built Visupac freehand measuring tool.

Results
A) FFA FAZ area: Group1: baseline 0.48 +/- 0.11; 6 months 0.49 +/- 0.12; 1 year 0.50 +/- 0.12sq.mm. Group 2: baseline 0.56 +/- 0.0; 6 months 0.57 +/- 0.11, 12 months 0.58 +/- 0.11sq.mm. Group 3: at baseline 0.63 +/- 0.11, 6 months 0.64 +/- 0.11, 12 months 0.65 +/- 0.12sq.mm. FAZ values were significant on comparing group 1 and group 3, at all points. B) OCTA (SCP) FAZ area: Group 1: baseline 0.397 +/- 0.044; 6 months 0.401 +/- 0.044; 12 months 0.405 +/- 0.045sq.mm. Group 2: baseline 0.373 +/- 0.050sq.mm; 6 months 0.377 +/- 0.053sq.mm; 12 months 0.381 +/- 0.053sq.mm. Group 3: baseline 0.468 +/- 0.063sq.mm; 6 months 0.474 +/- 0.065sq.mm; 12 months 0.477 +/- 0.066sq.mm. C) OCTA (DCP) FAZ area: Group 1: baseline 0.60 +/- 0.07; 6 months 0.61 +/- 0.08; 12 months 0.61 +/- 0.08 sq.mm. Group 2: baseline was 0.61 +/- 0.07; 6 months 0.63 +/- 0.08; 12 months 0.64 +/- 0.08 sq.mm. Group 3: baseline 0.72 +/- 0.11, 6 months 0.75 +/- 0.12, 12 months 0.77 +/- 0.13sq.mm. Significance was noted at baseline, 6 months, and 12 months, on comparing group 2 with group 3, and group 1 and group 3 for both SCP and DCP.

Conclusions
There was a significant increase in the FAZ area on FFA in all 3 groups at 12 months and the FAZ area was greater with more severe diabetic retinopathy (groups 2&3) at both 6 and 12 months. There was a progressive significant increase in the FAZ at SCP and DCP in all three groups at 6 and 12 months and the worsening was significant when group 3 was compared with 1 and 2. It is possible that with increasing disease and a corresponding increase in the FAZ, there comes a point when DME sets in. To understand this, one would need a longer follow-up, which is a limitation of this study.

Financial Disclosure
None
Early alterations in retinal microvasculature on swept-source optical coherence tomography angiography in acute central serous chorioretinopathy

The purpose of the study was to evaluate the retinal blood flow in patients with acute central serous chorioretinopathy (CSC) over an observational period of six months using swept-source optical coherence tomography (SS-OCTA) and to correlate these findings with conventional indocyanine green angiography (ICGA). ICGA and SS-OCTA images were collected and analyzed of 12 eyes of 12 patients at month 1 and of 9 eyes of 9 patients at month 6.

Patients with the diagnosis of acute central serous chorioretinopathy, who presented in 2017 and 2018 to the outpatient clinic at the Department of Ophthalmology, Kepler University Clinic Linz (Linz, Austria) were included in this retrospective analysis.

All patients underwent at baseline an ophthalmological examination including best corrected visual acuity (BCVA), and detailed slit-lamp biomicroscopy including pupil dilatation and fundoscopy. The subretinal fluid (SRF) was annotated in the overlay en-face images using ICG and FA angiography images to identify the leakage point(s). The area with SRF was defined as the area of interest (A-SRF). A qualitative analysis of choriocapillaris, the vessel density (VD) and perfusion density (PD) of the retinal superficial capillary plexus (SCP) and the deep capillary plexus (DCP) were performed in A-SRF and the unaffected remaining area (RA).

ICGA and SS-OCTA images were collected and analyzed of 12 eyes of 12 patients at month 1 and of 9 eyes of 9 patients at month 6. The VD and PD in the DCP were statistically significantly lower in A-SRF than in the RA at baseline. (VD: p=0.014; PD: p=0.036). After one month, there was a statistically significant difference in the VD and PD of the DCP (VD: p=0.015; PD: p=0.014), and for the PD of the SCP between the A-SRF and the RA (p=0.015), with lower values in the A-SRF. Results for comparison between baseline and month 6 will be presented at the conference. We found low perfused areas in choriocapillaris corresponding to hypofluorescent areas on ICGA.

In conclusion, we demonstrated the changes in retinal perfusion in patients with acute CSC using a SS-OCTA device. The perfusion and vessel density in the deep capillary were statistically lower in the deep capillary plexus within the area of the SRF at baseline and after one month. Changes in the superficial capillary plexus in the area of the SRF found at one month suggest that the duration of the SRF impacts the superficial capillary plexus. The choriocapillaris on SS-OCTA showed changes in perfusion at the leakage point. It can be hypothesized that even in the acute phase damages in perfusion on the level of choriocapillaris are present. These alterations may lead to a chronic change in the microvasculature and potentially to morphological changes.
Title
Optical coherence tomography (OCT) and OCT angiography evaluation of morphology and vascular structures in the retina in recovered pediatric patients with novel coronavirus disease 2019 (COVID-19)

Purpose
Using optical coherence tomography (OCT) and OCT angiography (OCTA), we aimed to determine whether novel coronavirus disease 2019 (COVID-19) induces pathological changes in morphology and vascular structures in the pediatric retina.

Setting/Venue
Prospective, cross-sectional, observational clinical study.

Methods
The current study included recovered pediatric patients with COVID-19 evaluated between May 2020 and June 2020. Retinal morphology (retinal, choroidal, peripapillary retinal nerve fiber, and ganglion cell layer thickness) and vascular structures (superficial, deep, and radial peripapillary capillary plexus vessel densities) in the macular and optic disc regions were quantitively assessed using OCT and OCTA. Data were compared between patients and age-matched healthy controls.

Results
The study included 64 eyes of 32 participants (COVID-19 group, 32 eyes; control group, 32 eyes). Biomicroscopic and fundus examinations revealed no signs of pathology in the COVID-19 group. However, OCT revealed a few vitritis-like hyper-reflective dots in the posterior vitreous in five female patients (31.2%) with COVID-19. Mean choroidal, peripapillary retinal nerve fiber, and ganglion cell layer thickness values were significantly greater in the COVID-19 group than in the control group (p<0.05). OCTA indicated that mean superficial/deep capillary plexus vessel densities and choriocapillaris flow area values were significantly lower in the COVID-19 group than in the control group, whereas mean radial peripapillary capillary plexus vessel density values were significantly higher (p<0.05).

Conclusions
Even if fundus examination results appear normal in pediatric patients with COVID-19, morphological and vascular changes may be observed in the retina. Further studies are required to elucidate the clinical significance of structural and vascular changes in this population.

Financial Disclosure
None
Multimodal imaging in a case of bilateral acute macular neuroretinopathy: The role of structural OCT and angio-OCT

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**Purpose**
INTRODUCTION Acute macular neuroretinopathy (AMN) is an infrequent macular disease characterized by sudden onset of visual acuity loss and paracentral scotoma in one or both eyes. It presents with intraretinal reddish-brown, wedge-shaped lesions aiming towards the fovea and is thought to be ischemic in origin involving the deep retinal capillary plexus (DCP) thus affecting specially the outer nuclear layer. PURPOSE To present a case of bilateral AMN in a young healthy patient, describe its features in multimodal imaging and analyze the retinal microvasculature alterations demonstrated with Optical coherence tomography angiography (OCTA) as well as to compare it to healthy subjects.

**Setting/Venue**
The case was conducted at the Joan XXIII University Hospital in Tarragona (Spain) from octuber 2019 to february 2021.

**Methods**
METHODS Multimodal imaging, including fundus photography autofluorescence (FA), Swept-source OCT and OCTA was performed on the patient and control subjects. Vessel density of superficial capillary plexus (SCP), DCP and choroid, as well as the area of foveal avascular zone (FAZ) were automatically measured. We also assessed the overall vascular structure of SCP and DCP and compared with the same parameters in age-sex-matched healthy controls. CASE REPORT A 26-year-old woman presented with a 6 months’ history of decreased visual acuity and parafoveal scotomas in both eyes. The patient described the onset of symptoms to be acute, more marked in her right eye and having remained stable almost since presentation. There was no history of disease or trauma. The clinical interrogation being only remarkable for the use of oral contraceptives. The patient was referred to the retina department after extensive investigation by the neuro-ophthalmology unit.

**Results**
RESULTS Best-corrected visual acuity was 0.9 in the right eye (RE) and 0.8 in the left eye (LE). Slit lamp examination was unremarkable. Dilated fundus examinations was normal in both eyes except for persistence of myelin fibers in the upper temporal arch of the RE. Swept-Source OCT showed a decrease of retinal thickness temporal to the fovea, located at the nuclear and outer plexiform layers. OCTA showed structural changes in the vessels, especially in DCP with a diffuse decrease in density. The vessel density of the DCP at the FAZ was found to be lower compared to control eyes (11.94% RE; 11.45 % LE vs 15.93-25.71 % in control eyes). The vessel density of the SCP showed similar changes while being more markedly affected in the RE (5.83 % RE; 11.30 % LE vs 16.77-26.81 % in control eyes). Total area of FAZ was larger in both patient’s eyes: 1.012.852 µm2 at SCP and 1.105.049 µm2 at DCP in RE and 645.293 µm2 at SCP and 850.693 at DCP in LE vs control eyes 153,721-331.260 µm2 at SCP and 131,972-341.279 µm2 at DCP. The visual field test, FA, magnetic-resonance imaging as well as visual-evoked potential testing were unremarkable.

**Conclusions**
CONCLUSIONS Although rare, AMN can present bilaterally. It must be considered in young patients complaining of central visual acuity loss with seemingly unremarkable exploration. The level of detail of newer OCT technologies is able to discriminate the changes occurring within different retinal layers. In our case, OCTA demonstrated a decrease in the vessel density of both the DCP and SCP while structural OCT showed a thinning of the outer layers.

**Financial Disclosure**
No financial interest
Choroidal vascularity index changes with Valsalva maneuver in healthy volunteers

Purpose
To evaluate the effects of the Valsalva maneuver (VM) on choroidal vascularity index (CVI) in healthy volunteers.

Setting/Venue
Medical Retina Unit, Ophthalmology Department, Marmara University Pendik Training and Research Hospital, Istanbul, Turkey.

Methods
This prospective, cross-sectional study included 60 eyes of 30 healthy volunteers aged 18-50 years. Participants with any ocular or systemic disease, high hyperopia or myopia (spherical equivalent [SE] ≤−6.00 or ≥+3.00 diopters [D]), and history of resting intraocular pressure (IOP) ≥21 mmHg were excluded from the study. Enhanced depth optical coherence tomography (Spectralis, Heidelberg Eng., Heidelberg, Germany) scans of both eyes involving fovea were taken, and subfoveal choroidal area with a width of 1500 μm was selected for image binarization with open-access Fiji software. Binarized image of the subfoveal choroidal area was segmented into the stromal area (SA, light pixels) and luminal area (LA, dark pixels), then CVI calculated as the ratio (%) of LA to the total choroidal area (TCA). SA, LA, TCA, CVI, subfoveal choroidal thickness (SFCT), IOP, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were evaluated at rest and fifteen seconds after the participant began to perform VM. For VM, each participant was asked to take a deep breath while squeezing their nose with their index finger and thumb and then blow forcefully against their closed glottis. Ten minutes resting period was given to the participants for the examination of consecutive eyes.

Results
The mean age of the volunteers was 31.1±6.1 years, and the mean SE of the eyes of the volunteers was -1.05±0.95 D. During VM, LA (1.02±0.19 vs. 1.05±0.20, p<0.001) and CVI (62.19±4.56 vs. 63.92±5.00, p<0.001) were significantly increased; whereas SA (0.63±0.20 vs. 0.61±0.20, p<0.001) was significantly decreased compared to measurements at rest. There was no statistically significant difference in TCA (1.66±0.37 vs. 1.66±0.37, p=0.547); however, SFCT was significantly increased with VM (366.93±84.70 vs. 374.73±89.64, p<0.001). There was a statistically significant, moderate positive correlation between SE and SCFT at rest and during VM (r[58]=0.49, p<0.0005; and r[58]=0.48, p<0.0005, respectively); however, there was no such correlation between SE and CVI at rest and during VM (r[58]=-0.21, p=0.105; and r[58]=-0.24, p=0.58, respectively). There was no statistically significant correlation between any of the age, IOP, SBP, DBP values, and any of the SCFT, LA, SA, TCA, CVI values both at rest and during VM.

Conclusions
CVI is a new quantitative marker to evaluate the vascular status of the choroid, and it is more commonly used in many recent studies as an indicator of the vascular status of the choroid. We found that VM increases CVI by causing choroidal vascular dilation indicated by an increase in LA and a decrease in SA; therefore, researchers should be careful about patients holding their breath during the examination. The moderate positive correlation found between SE with SFCT but not with CVI may indicate that CVI is more valuable than SCFT when assessing the vascular status of the choroid considering refractive error in the normal population.

Financial Disclosure
The authors have no conflicts of interest to declare.
Evaluation of retinal vessel diameters and retinal layers in patients with severe obstructive sleep apnea syndrome

Purpose
To compare retinal vessel diameters and retinal segmentation analyzes of patients with severe obstructive sleep apnea syndrome (OSAS) with healthy controls.

Methods
Thirty-three eyes of 33 patients with OSAS and 26 eyes of 26 healthy controls were included in the study. Right eyes of all patients were included in the study. Detailed ophthalmological examinations and optical coherence tomography (OCT) (Heidelberg Engineering, Heidelberg, Germany) examinations of the patients were performed. Retinal artery and vein diameters were measured in 4 quadrants (superotemporal-inferotemporal-superonasal-inferonasal) from retinal nerve fiber analysis sections measured by OCT. Retinal layers were evaluated by central macular thickness (CMT) and automatic segmentation analysis.

Results
The mean age was 36.9 ± 6.96 and 37 ± 6.43 years in the OSAS group and control group, respectively (p = 0.959). In retinal segmentation analysis, there was no difference between the two groups in terms of retinal layers and CMT (p > 0.05, all). There was only a difference between inferonasal vein diameters in terms of retinal vein diameters (p = 0.007). The difference in retinal artery diameters in 4 quadrants was significantly lower in the OSAS group than in healthy controls (p < 0.001, all).

Conclusions
Retinal artery diameters were found to be significantly lower in individuals with severe OSAS compared to healthy controls. This may be a hemodynamic response due to hypoxia in OSAS patients. Our study is a static study in terms of retinal blood supply, and studies that can evaluate it at a dynamic level (Doppler USG, etc.) are needed.

Financial Disclosure
NO
Absolute retinal blood flow in healthy eyes and in eyes with retinal vein occlusion

Purpose
To non-invasively measure retinal venous blood flow (RBF) in healthy subjects and patients with retinal venous occlusion (RVO).

Setting/Venue
The prototype named AO-LDV (Adaptive Optics Laser Doppler Velocimeter), which combines a new absolute laser Doppler velocimeter with an adaptive optics fundus camera (rtx1, Imagine Eyes®, Orsay, France), allows for the measurement of absolute RBF as a function of retinal vessel diameters and simultaneous measurement of red blood cell velocity.

Methods
A total of 15 healthy subjects and six RVO patients were included. For healthy subjects, all the retinal veins in one eye were measured to obtain the total RBF. For RVO patients, only the temporal veins were measured in both eyes.

Results
In healthy subjects, the total RBF was 37.8 ± 6.8 µl/min. Our results suggests an inversely proportional relationship between total RBF and intra-ocular pressure (r = -0.57) or central subretinal thickness (r = -0.48). No significant relationship was found between total RBF and systolic blood pressure, diastolic blood pressure, ocular perfusion pressure, heart rate, or hematocrit. In RVO patients, a decrease in RBF was noted in occluded veins compared with the contralateral healthy eye.

Conclusions
The new AO-LDV prototype allowed RBF to be measured in healthy and RVO patients. The main limitation at this time is the parallax phenomenon, which could be avoided using the optical path of the rtx1 for the LDV part of the system. The prototype was improved with a fixation system for both eyes and a laser projection system to reduce the parallax phenomenon.

Financial Disclosure
Bayer : financial support of this study
Title
Evaluation of the Cat-PROM 5 visual function questionnaire in epiretinal membrane surgery outcomes

Purpose
To investigate the effect of epiretinal membrane (ERM) peel on subjective visual function measured by the Cat-PROM 5 questionnaire, and its relationship to anatomical and visual acuity (VA) response.

Setting/Venue
Maidstone and Tunbridge Wells Hospitals NHS trust

Methods
Retrospective observational case series comparing consecutive cases of ERM peel +/- phacoemulsification and intraocular lens insertion in 56 eyes from 56 patients between 1st August 2018 and 1st August 2019. Pre-operative and post-operative data was collated including VA, central retinal thickness (CRT), evidence of ellipsoid zone disruption, lens status, and complications. All patients were asked to participate in a survey questionnaire about their visual function before and after surgery including the Cat-PROM 5 questionnaire.

Results
Pre-operative median VA was 62.5 ETDRS letters (range 35-78) and increased to 69.0 (range 35-80) post operatively (p=0.003). Median pre-operative CRT was 433µm (range 293-670), improving to 385µm (range 308-531) post-operatively (p<0.001). Responses to the survey were received in 45 (80.4%) patients, and results of the pre-operative Cat-PROM 5 questionnaire revealed a median Rasch measure of -2.29 logits (range -9.18-4.23), improving to 0.18 logits (range -9.18-17.0) post operatively (p=0.001). Change in Cat-PROM 5 score was negatively correlated with pre-operative score (<0.001), but it was not significantly correlated with pre-operative or change in VA or CRT. Of the 20 patients who underwent vitrectomy without phaco + IOL, 15 (75%) responded to the survey. Median Rasch measure pre operatively was -2.29 logits (range -6.8-3.56) improving to 0.18 logits (range -9.18-17.0) post operatively (p=0.09).

Conclusions
The Cat-PROM 5 questionnaire may be able to assess subjective change in functional vision after ERM peel. Patients with worse Cat-PROM 5 scores pre-operatively may see greater subjective benefit post operatively.

Financial Disclosure
No
Title
Alterations in central macular thickness after uncomplicated phacoemulsification cataract surgery and intraocular lens implantation

Purpose
The aim of this study was to evaluate the changes in central macular thickness using spectral-domain optical coherence tomography (SD-OCT) in subjects who underwent uncomplicated phacoemulsification cataract surgery and intraocular lens implantation.

Setting/Venue
This prospective study was conducted at the Department of Ophthalmology, Necmettin Erbakan University Meram Medical Faculty Hospital, Konya, Turkey.

Methods
Forty-four eyes of 30 subjects (30 male and 14 female) who underwent uncomplicated phacoemulsification cataract surgery and intraocular lens implantation were enrolled in this study. Patients with any other systemic and ocular disease that could potentially confound results, such as diabetes mellitus, uveitis, or any retinal pathology, were excluded. Central macular thickness was analyzed preoperatively and 2, 4, and 12 weeks postoperatively using an SD-OCT device (Spectralis OCT, Heidelberg, Germany). The macular scans were performed at a 6x6 mm area centered on the fovea, consisting of 25 horizontal axial scans. Central macular thickness was defined as the average thickness at the central 1-mm-diameter zone. The preoperative macular OCT scans were set as reference for the follow-up measurements.

Results
The mean age of the subjects was 66.7 ± 8.7 years. The mean best corrected visual acuity (BCVA) significantly improved at all postoperative visits compared to the preoperative examination (P < 0.001 for all). The mean central macular thickness preoperatively and 2, 4, and 12 weeks postoperatively was 268.6 ± 29.9 µm, 269.3 ± 25.7 µm, 275.9 ± 33.8 µm, and 274.9 ± 37.0 µm, respectively. There was no statistically significant difference in central macular thickness at the postoperative 2 weeks visit compared to the preoperative measurements (P = 0.536), however, significant increases were observed at the 4 weeks and 12 weeks visits (P < 0.001 for both). No significant difference was observed in the central macular thickness change among male and female subjects. There were no statistically significant correlations between the change in central macular thickness and age of the subjects or the change in BCVA.

Conclusions
This study demonstrated an increase in central macular thickness 4 and 12 weeks after uncomplicated cataract surgery in otherwise healthy subjects. Nevertheless, these changes were asymptomatic and did not correlate with BCVA change.

Financial Disclosure
No financial relations
Cystic phenotypes in diabetic macular edema influencing anatomical response after dexamethasone implant

Purpose
To analyze anatomical response in diabetic macular edema (DME) characterized by suspended scattering particles in motion (SSPiM) after intravitreal dexamethasone implant. Further, to characterize the clinical response of other cystic subtypes to treatment.

Setting/Venue
Tertiary referral center at Department of Ophthalmology, IRCCS-Fondazione Bietti, Rome.

Methods
A retrospective review of type 2 diabetic patients suffering from DME treated with a single intravitreal injection of dexamethasone (DEX) implant 0.7 mg (Ozurdex; Allergan, Inc, Irvine, CA) was performed for those with complete medical records and multimodal imaging at 2- and 4- months after injection. Swept-source optical coherence tomography angiography (OCTA, PLEX Elite 9000, Carl Zeiss Meditec, Inc, Dublin, CA) with a 3 mm x 3 mm volume cube were performed in all the cases. After checking the segmentation, OCTA slabs from superficial vascular complex (SVC) and deep capillary plexus (DCP) were analyzed using OCTA b scans as reference. Cystic phenotypes were classified in: cysts with SSPiM with variably hyperreflective decorrelation signal on OCTA, hyperreflective corpuscular cysts without a detectable decorrelation signal on OCTA, and optical empty or pure hyporeflective cysts. The area occupied by the different cystic subtypes and SSPiM was quantified in the entire 3 mm OCTA slabs for SVC and DCP using Fiji software (version 2.1.0/1.53.c, available at http://fiji.sc). The definition for ‘improvement’ was set for a central macular thickness (CMT) reduction of at least 10% and ‘no improvement’ for a CMT +/- <10% since baseline visit.

Results
A total of 18 eyes of 18 patients (69.1 ± 8.5 years) were consecutively enrolled, of whom 6/18 eyes (33.3%) were treatment naïve. In the SVC, the area of hyporeflective cyst occupied 40.7% (0.13 mm2 ± 0.18) of the total cystic area, followed by corpuscular cysts (36.9%, 0.15 mm2 ± 0.18) and SSPiM (22.4%, 0.07 mm2 ± 0.14). In the DVC, the area occupied by the corpuscular component was 38.5% (0.20 mm2 ± 0.4) of the total, followed by hyporeflective (34.1%, 0.26 mm2 ± 0.3) and SSPiM (27.3%, 0.18 mm2 ± 0.27). Eyes with SSPiM presented an older age (p=0.03) and a history of previous intravitreal treatment (75% of cases, r=0.53, p=0.02). Qualitative and quantitative evaluation of the different cystic area demonstrated substantial reabsorption of the hyporeflective component in the SVC (-95.4% at 2- and -84.4% at 4-months, P=0.001) and DVC (-84.4% at 2 months), with a less critical decrease of the corpuscular component in the SVC (-41.9% 2 months, p=0.001 and -1.8% at 4 months, P=0.73), and not significant in the DVC. SSPiM did not significantly change in both the SVC and DVC neither at 2- and 4-months (P>0.05, for all).

Conclusions
The present work analyzed longitudinal anatomical changes in various cystic phenotypes in DME after dexamethasone implant. On morphometric analysis, SSPiM tended to accumulate with a pyramidal stratification from the outer to the inner retinal layers. The association of SSPiM with older age may indicate an easier blood-retinal barrier (BRB) rupture for a physiologic aging process. After a single dexamethasone implant, the clearance of different cystic phenotypes proceeds with resorption of hyporeflective fluid component, followed by a corpuscular component without decorrelation signal on OCTA, starting from the innermost retinal layers. SSPiM persisted despite treatment, representing a factor of a severe BRB breakdown that may require repeated treatment to reach a satisfactory anatomical response.
**Title**  
Functional and anatomical prognostic biomarkers by swept source optical coherence tomography after epiretinal membrane surgery

**Purpose**  
To determine the visual and anatomical prognostic biomarkers in patients with epiretinal (ERM) treated surgically.

**Setting/Venue**  
International FOSCAL, Floridablanca, Colombia.

**Methods**  
Retrospective analytical cohort study. In patients treated with PPV and ERM removal, a correlation was established between the preoperative visual acuity (VA) and preoperative swept-source optical coherence tomography (SS-OCT) variables with the best-corrected VA change (BCVA) and the reduction in average macular thickness (AMT) post-operatively.

**Results**  
A total of 168 eyes of 138 patients with ERM were evaluated, 71 eyes were treated with PPV and ERM removal. The mean follow-up time was 5.25 months (SD ± 7.8) and the mean age was 71.9 years (SD ± 7.2). The preoperative BCVA was LogMAR 0.57 (Snellen: 20/70), with a postoperative BCVA of LogMAR 0.39 (Snellen: 20/50). The EMP was reduced from 326.3 μm (SD ± 161.2) to 307.2 μm (SD ± 153.45). The variable with the highest correlation with the change in BCVA was preoperative BCVA (p <0.05). The variables that showed a positive correlation with the reduction of AMT were preoperative BCVA (p <0.05), ERM stage 1 (p = 0.022) and the presence of internal foveal ectopic layers (EIFLs) (p = 0.007).

**Conclusions**  
Preoperative BCVA, ERM stage 1 and the presence of EIFLs were correlated with a change in BCVA and EMP reduction after surgical management in patients with ERM.

**Financial Disclosure**  
Juan D. Arias: Topcon consultant
Title
The utility of single-capture ultra-widefield imaging with integrated guided swept-source optical coherence tomography in the management of peripheral vitreous and retinal pathology

Purpose
The diagnosis of peripheral vitreoretinal pathology has to date almost completely relied on peripheral retinal examination with the binocular indirect ophthalmoscope with scleral depression, performed by vitreoretinal specialists. Understanding the intraretinal features of peripheral pathology and the potentially complex characteristics of the vitreoretinal interface in vivo, that would otherwise not be visible, can provide significant advantages to vitreoretinal specialists in terms of diagnosis and management decisions. In this study we assess the clinical utility of a commercially available single-capture ultra-widefield confocal scanning laser ophthalmoscope with an integrated guided widefield swept-source OCT (UWF-SS-OCT) for the diagnosis and management of peripheral vitreoretinal pathology.

Setting/Venue
This is a retrospective cohort study carried out at a single vitreoretinal practice in Toronto, Canada between December 2020 and February 2021.

Methods
Consecutive patients with peripheral retinal pathology who underwent UWF-SS-OCT were included. All patients underwent a detailed dilated fundus examination with slit lamp biomicroscopy and indirect ophthalmoscopy with 360 degrees scleral indentation by a single experienced vitreoretinal surgeon. After the clinical examination, those patients with peripheral retinal pathology underwent imaging with UWF-SS-OCT. The imaging was performed by a single photographer to obtain the ultra-widefield 200 degree fundus photograph. The UWF image was then used to identify the lesion of interest and navigate the built-in 100kHz UWF-SS-OCT to image the pathology. Imaging of the lesion of interest was acquired with a high definition (HD) single line scan or volume scan depending on the location and nature of the retinal pathology. Patients with active disease were followed longitudinally with serial imaging. This included patients who underwent laser retinopexy or cryopexy to the peripheral retina during the study period. Retinal imaging was typically acquired at baseline and on the same day immediately following laser retinopexy and for cryopexy at post-procedure day 1. Subsequently, serial imaging was generally performed at post-procedure day 3-4 and 6-7, week 2 and month 1.

Results
138 eyes of 101 patients with peripheral retinal pathology were imaged with UWF-SS-OCT with interpretable images. Of the eyes imaged, 56.5%(78/138) eyes had rhegmatogenous retinal detachment (RRD) (5 eyes had combined retinoschisis detachment), 31.1%(43/138) had retinal tears/holes and 14.5% (20/138) had lattice degeneration. Other retinal findings imaged included chorioretinal atrophy, white without pressure, vortex veins and other ocular manifestations of systemic diseases. All UWF-SS-OCT features were described in details. UWF-SS-OCT enabled novel findings such as in vivo visualization of vitreous adhesion over the posterior border of a retinal dialysis and typical microcystic degeneration in the pediatric group. We also observed RPE hyperplasia with hyperreflective shadowing seen in a demarcation line in chronic RRD, differentiating it from scarring due to laser retinopexy. UWF-SS-OCT was performed longitudinally before and/or immediately after laser retinopexy (n=22) and cryopexy (n=4). These OCT changes were consistent with histological changes previously described in the literature. We observed microstructural changes immediately after treatment and we found that there is likely chorioretinal adhesion immediately after laser retinopexy compared to cryopexy where there is still retinal separation at Day4 and chorioretinal adhesion noted only by Day6. This has significant implications for the use of these procedures for retinal tears and RRD.

Conclusions
Single-capture ultra-widefield confocal scanning laser ophthalmoscope with integrated guided, navigated, swept-source OCT was useful in the diagnosis and management of common vitreoretinal conditions. Furthermore, it has enabled novel insights in vitreoretinal diseases and their management.

Financial Disclosure
None
Evaluation of the repeatability of macular vascular analysis with swept-source optical coherence tomography angiography (SS-OCTA) in young high myopic patients

Purpose
We aimed to evaluate SS-OCTA repeatability and its relationship to the value of refractive errors in high myopic patients.

Setting/Venue
The study was conducted on high myopic patients who came to the Eskisehir Osmangazi University hospital ophthalmology clinic for routine examination.

Methods
Refractive error values of minus 6 and below were considered as high myopia and between minus 6 and 12 were included in the study. In addition to a routine eye examination, macula superficial and deep vascular plexus (SVP and DVP) density parameters were measured twice in one hour with SS-OCTA. Repeated measurements were compared statistically. Intraclass correlation coefficient(s) (ICC) based on a 2-way random-effects model were used to evaluate the consistency of paired measurements. ICC values less than 0.5 were interpreted as an indicator of poor repeatability, values between 0.5 and 0.75 as moderate repeatability, values between 0.75 and 0.9 as good repeatability, and values greater than 0.90 as excellent repeatability.

Results
A total of 40 high myopic eyes were included in the study. Both SVP and DVP 1mm center density measurement repeatabilities are excellent (ICC values are 0.969 and 0.968 respectively). SVP inferior quadrant, DVP superior and nasal quadrant measurement repeatabilities are good (ICC values are 0.787, 0.81 and 0.779 respectively). SVP superior, temporal, nasal and DVP temporal, inferior quadrant measurement repeatabilities are moderate (ICC values are 0.612, 0.642, 0.651, 0.631 and 0.615 respectively). Poor repeatability was not seen on any quadrant measurement.

Conclusions
The repeatability rates in macular field measurements with SS-OCTA in highly myopic patients are adequate.

Financial Disclosure
No financial interest
### Purpose
To analyze the characteristics of the choriocapillaris and the choroid in patients with Alport syndrome (AS), in particular choriocapillaris flow deficits (FD) density and choroidal vascularity index (CVI), and to investigate their clinical and demographic associations.

### Setting/Venue
Multi-center, cross-sectional study held in the Department of Ophthalmology at Northwestern University (Chicago, Illinois) and the Department of Ophthalmology of the Medical University of Vienna (Vienna, Austria).

### Methods
Twenty-one patients with AS and 18 healthy controls consecutively enrolled. Demographics and past medical history data were collected for each participant. Each eye underwent a complete ophthalmic examination, 3x3 swept-source optical coherence tomography angiography (PLEX® Elite 9000 2.0, Carl Zeiss Meditec, Dublin, CA), and macular spectral-domain OCT (Spectralis HRA2; Heidelberg Engineering, Heidelberg, Germany). FD were segmented with the Phansalkar method using a radius of 4 pixels. The CVI was calculated as the ratio between the luminal choroidal area and the total choroidal area. Factors influencing FD density and CVI in AS patients were explored with multivariable linear mixed models.

### Results
Choriocapillaris FD were more numerous (p=0.02) and smaller in size (p=0.01) in patients with AS compared to controls. Patients with history of kidney transplant had larger FD mean area (p=0.04), larger total FD area (p=0.008) and higher FD density (p=0.005) than AS patients never transplanted. The CVI in AS eyes was similar to controls, irrespective of history of kidney transplant. The FD density was higher with older age (estimate= 0.41 for each year) and in patients with history of kidney transplant (estimate= 8.57 with positive history). The CVI was lower in eyes with dot maculopathy (estimate= -3.62 if present) and anterior lenticonus (estimate= -6.69 if present).

### Conclusions
The quantitative evaluation of the choriocapillaris may be used as a clinical biomarker of kidney involvement in Alport syndrome. Lower choroidal vascularity was found in concomitance of other ocular structural abnormalities.
Angiographic changes in early Type-2 DM correlated with FAZ parameters and visual acuity

**Purpose**
To quantify and correlate microvascular changes, FAZ parameters and visual acuity in patients with early type-2 DM using optical coherence tomography angiography compared to healthy age & gender- matched controls.

**Setting/Venue**
Department of Ophthalmology, Minia University, Minia, Egypt

**Methods**
Angiographic changes in patients with type-2 DM (No or early retinopathy) obtained by OCTA AngioVue (RTVue XR Avanti;Optvue Inc.) were correlated with FAZ parameters & LogMAR VA, and compared to age-matched healthy controls using Spearman correlation test. Comparison between VD, LogMAR VA and FAZ values in both groups computed by Mann-Whitney U test.

**Results**
A significantly worse best corrected visual acuity was found in diabetic eyes than controls (-0.43 ± 0.42, -0.008 ± 0.03, P < 0.001). By OCTA, diabetic eyes showed significantly reduced superficial retinal plexus VD layer of the whole image and para-foveal areas; (P = 0.003, P ≤ 0.001) respectively. CMT had a significant positive moderate correlation with the vessel density of SCP and DCP in the para-foveal area. Correlations were found between VD, FAZ parameters and LogMAR VA.

**Conclusions**
The early microvascular changes in diabetic patients (type-2) were detected in the FAZ area with micro-aneurysms found in both superficial and deep retinal layers in all patients with higher density in the deep retinal layer. FAZ parameters (Area, Perimetry and Circularity) were negatively correlated with LogMAR VA and positively correlated with vessel density in both para- & perifoveal areas. Correlating those changes together and serial measurements could help to identify biological biomarkers for early disease detection and status monitoring.

**Financial Disclosure**
NA
Monitoring and managing Candida chorioretinitis with secondary choroidal neovascular membrane (CNV) through multimodal imaging

**Purpose**
To show how multimodal imaging techniques allow us to detect complications secondary to chorioretinal infections and monitor the response to treatment.

**Setting/Venue**
Ophthalmology service, Hospital Universitario Miguel Servet. Zaragoza, Spain

**Methods**
Clinical case of a 22-year-old female patient with candida chorioretinitis with secondary CNV followed-up for three months with Spectral Domain OCT (SD-OCT), OCT Angiography (OCTA) and ultra-wide field retinography (UWF).

**Results**
Combined images from SD-OCT, OCTA and UWF allow us not only to clearly diagnose the pathological entity, but to monitor the associated complications. Thanks to these multimodal techniques we could see total regression of the CNV after treatment with aflibercept as well as the resolution of the infectious process with systemic and intravitreal treatment with voriconazole.

**Conclusions**
Multimodal imaging is key in the fast and accurate diagnosis of retinal pathology. It helps us to monitor an intensive treatment in cases in which visual acuity is seriously threatened.

**Financial Disclosure**
Authors declare no conflict of interest
**Title**
The effect of contact lens use on the macula and optic disc parameters during swept-source optical coherence tomography (SS-OCT) and OCT-Angiography (SS-OCTA) imaging in young high myopic patients

**Purpose**
To investigate whether the use of contact lenses during imaging with SS-OCT and SS-OCTA has any effect on the macular and optic disc parameters in young patients with high myopia.

**Setting/Venue**
The study was conducted at Eskisehir Osmangazi University hospital ophthalmology clinic on high myopic patients used to wearing contact lenses.

**Methods**
Refractive error values of minus 6 and below were considered as high myopia and between minus 6 and 12 were included in the study. All patients were between the ages of 18-35, and all had best-corrected visual acuities of 20/20. In addition to a routine eye examination, macular vascular density, macular thickness measurements and optic disk parameters were measured with SS-OCT and SS-OCTA before and after wearing contact lenses. All examination results were analyzed with paired samples t-test for statistical analysis. p < 0.05 values were accepted statistically significant.

**Results**
A total of 20 patients, 38 myopic eyes were included in the study. No statistically significant difference was observed in macular thickness and optic disk area measurements before and after contact lens fitting (p > 0.05). In macular vascular density analysis with SS-OCTA, after contact lens fitting, a decrease was observed in the superficial capillary plexus vessel density (SVP) in all quadrants, while the decrease in density in the upper and nasal quadrants in the right eye and the upper and temporal quadrants and central in the left eye were found to be statistically significant (p= 0.02, 0.004, 0.04, 0.001 respectively). In the deep capillary plexus vessel density (DVP), a decrease was observed superior quadrant and central area and an increase was observed at nasal, inferior and temporal quadrants bilateral. The decrease of the central field of both eyes and increase of the right inferior quadrant were found to be statistically significant (p= 0.02, 0.01, 0.001 respectively). In optic disc retinal nerve fiber layer analysis with SS-OCT, all quadrant values were increased while temporal and inferior quadrants in the right eye and the nasal quadrant in the left eye were found to be statistically significant (p= 0.02, 0.04, 0.002 respectively).

**Conclusions**
Since it may cause significant changes in test results, it would be appropriate for patients to remove their contact lenses during SS-OCT and SS-OCTA measurements to obtain more reliable results.

**Financial Disclosure**
No financial interest
Title
Retinal microvascular changes in rhegmatogenous retinal detachment after pars plana vitrectomy: An OCT-angiography study

Purpose
Rhegmatogenous retinal detachment (RRD) is a separation of the sensory retina from the retinal pigment epithelium (RPE). Pars Plana Vitrectomy (PPV) is the most common surgical approach. Nevertheless, even with successful anatomic repair, functional result shows a wide range of visual outcomes. The purpose of this study is to identify vascular factors associated with visual outcome after successful surgery in patients with RRD using OCT-Angiography.

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
Fifteen eyes of 15 patients that underwent a three-port 23-gauge PPV for RRD, involving the macula, were enrolled in this study. We used OCT-Angiography (Optovue RTVue XR Avanti, AngioVue) to assess the vessel density (VD) in the superficial capillary plexus (SCP) and deep capillary plexus (DCP) in all patients four months after PPV. We compared PPV eyes with fellow unaffected eyes. Furthermore, we studied the peripapillary Retinal Nerve Fiber Layer (pRNFL) in all subjects.

Results
Four months after surgery, no significant difference was reported in the SCP VD nor in the DCP VD of treated eyes compared to fellow unaffected eyes (all p > 0.05). The pRNFL thickness was significantly lower in PPV eyes compared with fellow eyes (p = 0.003). Final best-corrected visual acuity (BCVA) in eyes with macula-off RRD was not affected by VD in the SCP nor DCP (p = 0.11).

Conclusions
There is no significant retinal microvascular changes in OCT-Angiography after PPV for RRD. Visual outcome after PPV doesn’t seem to be related to the macular vessel density.

Financial Disclosure
NO
Evaluation of retinal microvascular changes in reproductive-aged women with low ferritin levels with or without anemia

**Purpose**
Iron deficiency anemia (IDA) affects a large proportion of the world's population, especially women in reproductive age. The estimated prevalence of IDA in this population is approximately 30.2%. Iron is essential for oxygen transport and also for normal myelinization, neurotransmitter synthesis, and neurometabolism. Central retinal vein occlusion, retinal hemorrhage, ischemic retinopathy, and papilledema are ocular manifestations reported in IDA patients, and it is considered that it might be associated with hypoxia. In the present study, we aimed to investigate the retinal microvascular changes in reproductive age women with iron deficiency with or without anemia using optical coherence tomography angiography (OCT-A). Also, we evaluated the differences between iron deficiency with and without anemia.

**Setting/Venue**
Sivas Cumhuriyet University Department of Ophthalmology.

**Methods**
This prospective observational study consisted of 200 eyes of 100 reproductive-age women. Iron deficiency was defined as a lower ferritin level than 40 ng/ml with higher hemoglobin levels than 12 g/dl, and iron deficiency anemia was defined as lower ferritin and hemoglobin levels than 20 ng/ml and 12 g/dl, respectively. All subjects were imaged with Solix Fullrange OCT (Optovue Inc, Freemont CA, USA), a new ultra-high-speed SD-OCTA device that operates at 120,000 A-scans per second with the split spectrum amplitude-decorrelation angiography (SSADA) algorithm. OCT-A scans were performed in a 6.4 × 6.4 mm area centered on the macula. The foveal avascular zone (FAZ) area, FAZ perimeter (PERIM), foveal, parafoveal, and perifoveal vessel densities (VDs) in both superficial capillary plexus (SCP) and deep capillary plexus (DCP) and central foveal thickness (CFT) were evaluated.

**Results**
The mean age of the study population was 29.1±9.07 years. Forty-three (43%) patients had normal serum ferritin levels. While 36 (36%) women had low serum ferritin levels without anemia, 21 (21%) women had IDA. The mean CFT was significantly lower in women with IDA compared to women with normal ferritin levels (240.5±13.2 µm vs. 251.9±20.7µm, p=0.002). The mean FAZ and PERIM were significantly higher in women with IDA compared to women with normal ferritin levels (0.309±0.07 mm2 vs. 0.253±0.11 mm2, p=0.009 and 2.16±0.24 mm vs. 1.92±047 mm, p=0.006). Although women with low ferritin without anemia had lower CFT and higher FAZ and PERIM than women with normal ferritin levels, the difference was not significant (p>0.05, for all). While the mean foveal VDs in SCP was significantly lower in women with low ferritin levels with or without anemia compared to women with normal ferritin levels (29.66±3.3% vs. 30.4±3.9% vs. 32.1±4.6%, p=0.005 and p=0.03), temporal and nasal regions of parafoveal VDs in DCP were significantly lower in women with IDA compared to women with normal ferritin levels (56.18±3.06%, p=0.03 and 56.4±2.5% vs. 57.2±3.13%, p=0.02, respectively).

**Conclusions**
Although retinal microvascular changes begin to occur with iron deficiency before anemia development, the main significant changes occur with the development of anemia. Therefore, it is crucial to identify and treat patients with low ferritin levels before developing anemia to prevent possible further ischemic changes.

**Financial Disclosure**
none
**Title**
Widefield imaging of the peripheral vitreoretinal interface in patients with horseshoe tear and rhegmatogenous retinal detachment

**Purpose**
Surgical treatment of rhegmatogenous retinal detachment (RRD) is aimed to relieve the main pathogenetic factor – vitreoretinal tractions (VRT). The development of modern diagnostic instruments provided the possibility to reveal areas of VRT and vitreoretinal adhesion (VRA) with widefield methods of retinal visualization. The study aimed to evaluate the peripheral vitreoretinal interface in patients with a horseshoe retinal tear and RRD with widefield methods of diagnostics.

**Setting/Venue**
S. Fyodorov Eye Microsurgery Federal State Institution, 59а, Beskoudnikovsky blvd, Moscow, 127486, Russian Federation.

**Methods**
The study included 88 patients (88 eyes) with a horseshoe retinal tear; 45 of them had isolated horseshoe tear and 43 patients had RRD developed due to the horseshoe tear. In addition to the standard ophthalmologic examinations, all patients underwent widefield diagnostics including optical coherent tomography (WF-OCT), multi-spectral laser scanning, and infrared video registration. All the diagnostic procedures were performed using “Spectralis HRA+OCT” (“Heidelberg Engineering Inc.”, Germany) with a 55º lens. Differentiation of horseshoe tears was performed by their shape with a method of hierarchical clustering. The horseshoe tear shape was determined as the length to width ratio of the tear (l/b). Further, a correlation between the shape of a retinal tear and the length of VRA was established using Spearman’s correlation analysis. Furthermore, the analysis of the RRD development probability was performed based on the shape of a retinal tear.

**Results**
The mean age of patients was 52.13 ± 8.94 years old. Ward’s dendrogram revealed 4 shapes of retinal tears. Each kind of shape corresponded with a certain localization of VRA. The Spearman’s correlation analysis have found that there was a strong negative correlation between the shape of a retinal tear and the length of VRA. The low l/b ratio was associated with a high probability of the RRD development.

**Conclusions**
Widefield diagnostic methods allow a morphometrical evaluation of the peripheral vitreoretinal interface and identification of the VRA localization. The revealed correlations can help an ophthalmologist to identify the localization of VRA based on the shape of the retinal tear, evaluate the risks of the RRD development, and choose the treatment tactics even in cases when the WF-OCT is not available.
OCT angiography findings in eyes with epiretinal macular membrane

Purpose
To assess pre- and postoperative retinal vascular changes in patients undergoing epiretinal macular membrane (ERM) surgery by using Optical Coherence Tomography Angiography (OCT-A).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
An observational study was conducted between December 2019 and September 2020. Eyes affected by ERM which underwent posterior vitrectomy associated with ERM peeling were included in the study. All subjects underwent baseline ophthalmic examination including medical and ocular history, measurement of best-corrected visual acuity (BCVA), slit-lamp examination, dilated fundus examination. Spectral domain OCT and 6 mm x 6 mm OCT-A were obtained before surgery, at 1 month and 3 months postoperatively.

Results
Ten eyes of 10 patients (6 female and 4 males) affected by ERM and which underwent surgery were enrolled in the study. A significant progressive improvement in visual acuity from baseline to the 3-month follow-up was noted. A statistically significant increase in vessel densities (VD) in both superficial and deep capillary plexus from the preoperative values to the 3-month follow-up (p=0.03). However, there was a statistically significant decrease in the perfusion density (PD) of the choriocapillaris (CC) from baseline to the first month and a significant increase in CC PD at the 3-month follow-up compared to the baseline value (p=0.021). The FAZ area after surgery significantly increased during follow-up (p < 0.001).

Conclusions
In our study, OCT-A detected vascular abnormalities due to the presence of the ERM. Macular VDs can be used as biomarkers to evaluate the long-term visual prognosis in patients with history of ERM surgery. However, further research with larger sample sizes is needed.

Financial Disclosure
The authors declare no conflict of interest.
The effect of increasing A-scan rate on OCTA images: A qualitative and quantitative analysis

**Purpose**
To evaluate the effect of A-scan rate increase on qualitative and quantitative parameters in optical coherence tomography angiography (OCTA) images as well as the quantitative data agreement.

**Setting/Venue**
Oftalvist Clinic, Valencia, Spain

**Methods**
Healthy individuals undergoing comprehensive ophthalmic examination were scheduled for OCTA imaging using a modified SPECTRALIS device allowing for 85,000 and 125,000 A-scans/second. Consecutive, registered, 20ºx20º OCTA images using both speeds were acquired using the follow-up tool. The quality values of each B-scan were extracted and analyzed. The image quality was also qualitatively and blindly graded in pairs of images with different speeds. It was assessed if they were equal, or one was better than the other or even meaningfully better so the other was not usable. Vascular densities were calculated and the agreement between OCTA pairs was also assessed.

**Results**
Fifty-four eyes of 54 patients (35 female, mean age 64.6 years) were included in the present study. A significant reduction in the acquisition time was achieved with no significant differences in the Q values of the OCTA scans or in the qualitative blind assessment and vascular density values.

**Conclusions**
The benefit of speed on OCTA imaging is well established. Higher scan rates improve workflow, but also reduce image sensitivity and image quality might be compromised. In the present study, 125,000 A-scan rate showed benefit with a significant reduction on the acquisition time with no significant clinical differences between scan pairs. Further studies with different devices are required to confirm these results.

**Financial Disclosure**
We have research support by Heidelberg Engineering provided to the clinic with the possibility to use the prototype described in the present abstract.
# Title
Ocular findings of Multisystem Inflammatory Syndrome in children with COVID-19

## Purpose
Severe acute respiratory syndrome coronavirus 2 continues to spread worldwide. Although children typically have a mild course of coronavirus disease 2019 (COVID-19) symptoms compared to adults, a multisystem inflammatory syndrome in children (MIS-C) with a more severe course has been shown to be associated with COVID-19. Gastrointestinal, cardiovascular, hematologic, mucocutaneous and respiratory symptoms are more common in patients with MIS-C. It has also been reported that MIS-C patients may develop conjunctivitis in their eyes. Apart from conjunctivitis, it is not known exactly which pathologies MIS-C can cause in the eye. In this study, the ocular findings of two cases diagnosed with MIS-C in the Pediatric Infectious Diseases Department were examined.

## Setting/Venue
Case Series

## Methods
Case 1, 8 years-old male patient presented with a complaint of floaters in the right eye. Fundus examination revealed a splinter retinal hemorrhage around the optic nerve in the right eye, and there was no pathology in the fundus of the left eye. Optical coherence tomography (OCT) imaging revealed several vitritis-like hyperreflective dots in the posterior vitreous the right eye. At the follow-up three weeks later, the splinter retinal hemorrhage around the optic nerve in the right eye regressed, and that there was regression in the vitritis-like hyperreflective dots detected by OCT. Case 2, 10 years-old female patient presented with the complaint of conjunctival hyperemia and periorbital rash in both eyes. Biomicroscopic examination revealed non-purulent conjunctivitis in both eyes. Fundus examination revealed dilatation and minimal tortuous increase in the retinal arteries and veins in both eyes. OCT imaging revealed several vitritis-like hyperreflective spots in the posterior vitreous in both eyes. It was found that conjunctivitis regressed spontaneously in the follow-up three days later. In the follow-up after 2 weeks, it was found that dilatation and tortuosity in the retinal arteries and veins decreased in both eyes, and that there was minimal regression in the vitritis-like hyperreflective dots detected by OCT.

## Results
While no pathology was observed in the anterior segment examination in Case 1, non-purulent conjunctivitis and resemble Kawasaki disease periorbital rash on the eyelids were detected in Case 2. Fundus examination revealed a splinter retinal hemorrhage around the optic nerve in only one eye in Case 1, and dilatation and minimal tortuous increase in the retinal arteries and veins in both eyes in Case 2. In the OCT imaging of both cases revealed vitritis-like hyperreflective dots in the posterior vitreous. In the short-term follow-up of the cases, it was found that the vitritis-like hyperreflective dots detected with OCT continued despite the decrease in only case 2, and other ocular findings regressed in both cases.

## Conclusions
Various eye findings affecting both the anterior and posterior segments of the eye may develop in patients with MIS-C. Although most ocular findings regress in a short time, their long-term effects are unknown. Future studies with larger sample sizes will be needed.

## Financial Disclosure
None
**Title**
The association between retinal neurodegeneration and plasma neurofilament light chain: A population-based study

**Purpose**
Both plasma neurofilament light chain (NfL) levels and retinal volume have emerged as sensitive biomarkers of central neurodegeneration, the former highlighting neuroaxonal damage, the latter as an extension of the brain susceptible to similar injuries; but to date, the extent to which the two biomarkers are associated is unknown. This would provide information on 1) their complementary value as biomarkers 2) how closely retinal volume reflects brain pathology

**Setting/Venue**
We used baseline data from the first 5000 participants of the Rhineland Study, a population-based prospective cohort study in people aged 30 years and above in Bonn (Germany), with complete spectral-domain optic coherence tomography (SD-OCT) and plasma NfL data available (N=4327, after outliers’ removal).

**Methods**
Firstly, we calculated correlation coefficients between individual retinal layers and plasma NfL; secondly, we applied multivariable regression analysis to investigate associations between different retinal layers volume and plasma NfL levels; lastly, we assessed effect modification by age, hypertension and presence of neurological diseases (N=111).

**Results**
NfL levels showed a mean 3.04% increase, while ganglion cell layer (GCL) volume a decrease of 0.29% with advancing age; both showed an exponential trend in ageing with an acceleration in the 60s. Plasma NfL and GCL showed a correlation of -0.287, but after adjusting for age, sex, GFR and spherical equivalent, retinal pigmented epithelium volume (RPE) was the only retinal layer significantly associated with plasma NfL levels (std. beta = 0.030, CI [0.010 – 0.050], p = 0.0037). A weak association between GCL and plasma NfL was noted in older age and in participants with hypertension (std. beta for interaction -0.055, 95% CI [-0.098 – -0.013], p=0.011) and a stronger association in individuals with a neurological disorder (std. beta -0.023, 95% CI [-0.041 – -0.006], p=0.011).

**Conclusions**
Our findings indicate that: 1) among retinal layers, RPE most closely reflects plasma NfL levels in the general population and 2) despite plasma NfL and GCL having similar trajectories with ageing and being highly correlated, they showed no association in the general population after covariates adjustment. Nevertheless, elderly, hypertension and the presence of neurological disorders could determine an association, indicating that retinal neurodegeneration is a valid metric of neuroaxonal degeneration in the brain.

**Financial Disclosure**
None
**Title**
Peripapillary and macular microvasculature in neovascular age-related macular degeneration in long-term versus recently started anti-vascular endothelial growth factor therapy and healthy controls

**Purpose**
To investigate alterations in the peripapillary and macular microvasculature in eyes with neovascular age-related macular degeneration (nAMD) in recently started versus long-term anti-vascular endothelial growth factor (VEGF) therapy compared to healthy controls using swept-source optical coherence tomography angiography–based (OCTA) microangiography (OMAGc).

**Setting/Venue**
Non-interventional prospective single-visit study.

**Methods**
All eyes were recruited at Vista Eye Clinic, Switzerland, between 2019 and 2021. Eyes with nAMD receiving intravitreal anti-VEGF injections using a treat-and-extend regimen (TER) were assigned to group 1 (less than 5 injections) or 2 (≥20 injections) whereas group 3 constituted the healthy age-matched controls. Blood flow signals were acquired using OMAGc algorithm of PLEX® Elite 9000 Swept-Source OCTA (Carl Zeiss Meditec, Inc., Dublin, USA) in 6x6mm scans centered on the fovea and the optic nerve head (ONH). Spectral-domain OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) scans were obtained of the macular and ONH region. Quality of the OCTA scans, intraocular pressure (IOP) following the intravitreal injection and hemodynamic parameters were assessed. Comparisons between subgroups were calculated using ANOVA analysis.

**Results**
A total of 80 eyes whereof 40 eyes in the control group were included. Macular superficial perfusion density in the central 3 and 6mm was significantly reduced in group 1 and 2 compared to controls (p=0.001; p=0.010) without a significant difference between groups 1 and 2. The presence of subretinal fluid was associated with a better superficial macular perfusion density in the central 6mm (p=0.036). Mean peripapillary flux index was significantly lower in group 2 than in controls (p=0.023) in the absence of a significant correlation with neither IOP elevation after the injection nor the number of anti-VEGF injections received. An increased pulse pressure was observed in group 2 in comparison to groups 1 and 3 (p=0.003; p=0.012).

**Conclusions**
Reduced perfusion density of the inner retina might be related to a local vasoconstrictor effect of anti-VEGF treatment. Increased pulse pressure in long-term treated subjects may be linked to systemic side-effects of the treatment. Neither repeated injections nor postoperative IOP elevations were correlated to an altered peripapillary microvasculature.

**Financial Disclosure**
No
# Intravenous ultra-wide field fundus fluorescein angiographic analysis following intravitreal bevacizumab for retinopathy of prematurity

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**Purpose**
To identify ultra wide field fluorescein angiographic (UWF – FFA) findings in preterm infants who received intravitreal bevacizumab (IVB) for the treatment of retinopathy of prematurity (ROP).

**Setting/Venue**
Karadeniz Technical University, Faculty of Medicine, Department of Ophthalmology

**Methods**
Between January 2020 and January 2021, preterm infants who underwent UWF – FFA imaging following IVB therapy were studied. After obtaining informed consent from parents, UWF – FFA analysis were performed with Optos® California device. Imaging sessions were performed under topical anesthesia. UWF – FFA was performed in the presence of either incomplete retinal vascularization or suspected disease persistence and/or recurrence signs following IVB treatment. Exclusion criteria included, rejection of the procedure by the parents, history of liver and/or renal insufficiency, cardiovascular and/or cerebrovascular disorder. Procedures were done under supervision of a pediatric anesthesiologist. Following monitorization, sodium fluorescein 10% was injected intravenously at a dose of 0.1 mg/kg body weight followed by an isotonic saline flush. Any complication during UWF – FFA procedure was noted.

**Results**
Ten infants underwent UWF – FFA analysis during the study. Mean gestational age, birth weight and postmenstrual treatment time were 27.1 weeks, 986 g and 35.4 weeks. Initial UWF – FFA analysis was performed at a mean of 42.3 postmenstrual weeks. UWF – FA images clearly demonstrated nonperfused retinal areas, fluorescein leakage, macular edema, retinal vascular abnormalities or status of peripheral vascular termini. Some infants received multiple UWF – FFA sessions.

**Conclusions**
UWF – FA may be an alternative option to assess retinal vascular changes following IVB treatment. Primary advantage of this procedure seems to be applicability with topical anaesthesia without need for general anesthesia in a preterm child. Furthermore, it has fast imaging speed with high resolution images capturing a 200° field of retina.

**Financial Disclosure**
Authors have no financial relation with any company.
Title
Parent’s satisfaction assessment for retinopathy of prematurity screening with screening methods

Purpose
Analysis of the parent’s satisfaction for retinopathy of prematurity screening using binocular indirect ophthalmoscopy versus wide field retinal imaging

Setting/Venue
This was an observational, questionnaire survey-based study. The study cohort comprised of consecutive Asian Indian premature infants enrolled for retinopathy of prematurity screening (for infants less than 2000 gms and/or 34-weeks gestational age) using binocular indirect ophthalmoscopy (BIO) with scleral depression and b) wide field retinal imaging using the 3Nethra Neo Camera (Forus Health, India). We evaluated the retina for the presence or absence of stages of ROP and plus disease.

Methods
The survey analysis used closed-ended (multiple-choice) and open-ended questions for assessing 1) parents’ experience/preference among the two screening modalities namely, BIO and wide field imaging used in the study, 2) knowledge prior to ROP screening, 3) knowledge gained post ROP screening, in the outpatient ophthalmologic care unit in our hospital.

Results
A total of 90 infants (180 eyes) were included in the study. Among the 90 parents who filled in the questionnaire, 62.3% were referred by their pediatrician, 23.3% came for self check-up and 14.4% incidentally came to the hospital for complaints like ocular discharge and were screened. 93.3% parents were satisfied with either ROP screening modality in our study, with 54.4% stated a preference for retinal imaging. In the study 20% of the parents felt that retinal imaging was painful for the infant and 31.1% felt that BIO was painful for the infant.

Conclusions
Wide Field imaging is increasingly becoming an effective tool and screening tool in ROP screening and helps in better understanding of the disease amongst parents.

Financial Disclosure
Nil
Title
Retinal vasculature and pituitary adenomas: Quantitative analysis using optical coherence tomography angiography

Purpose
To assess the vasculature changes in the peripapillary and macular areas associated with pituitary adenomas (PA) using Optical Coherence Tomography Angiography (OCT-A).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
Prospective study was carried out between August 2020 and February 2021, including 20 eyes of 10 PA patients and 20 eyes of 10 healthy subjects. PA patients were divided into PA with optic neuropathy (12 eyes) and PA without optic neuropathy (8 eyes). Spectral domain (SD) OCTA 6 × 6 mm scans of the superficial (SCP) and deep capillary plexus (DCP) were analyzed in all eyes. A 4.5 × 4.5 mm images for the Radial Peripapillary Capillaries (RPC) were obtained. Peri-papillary Retinal Nerve Fiber Layer thickness (RNFL), whole image (wi), inside disc (id), peripapillary (pp) and macular vessel densities were evaluated in all eyes.

Results
Compared to healthy eyes, the RNFL was significantly thinner in the PA group (105.42± 2.61 and 92.12 ± 3.89 respectively, p<0.001). Whole image, id and ppVD in PA eyes were significantly lower compared to healthy eyes (p = 0.024). Adjusted to the presence of optic neuropathy, this difference remained significant between PA patients with optic neuropathy and healthy subjects (p=0.011), whereas there was no significant difference between PA patients without optic neuropathy and healthy subjects (p=0.062). Macular VDs in both plexuses were also significantly reduced in PA eyes (p=0.003). Pearson’s correlation coefficient showed a correlation between RPC VDs and RNFL thickness (r=0.76, p=0.019).

Conclusions
Vessel densities in PA eyes are significantly lower than in healthy eyes. A diminished microvascular network is associated with RNFL thinning. Retinal VDs changes can be used as biomarkers to evaluate the vision prognosis in long-term follow-up in PA eyes.

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Financial Disclosure
The authors declare no conflict of interest
**Title**
The presence of intervortex vein anastomosis and associated OCT findings in central serous chorioretinopathy

**Purpose**
To evaluate the optical coherence tomography (OCT) findings of patients with central serous chorioretinopathy (CSC) according to the presence of intervortex vein anastomosis (IVA) on indocyanine green (ICG) angiography.

**Setting/Venue**
Clinical records and OCT, fundus fluorescein and ICG angiography images of patients diagnosed with CSC were reviewed retrospectively. Patients without history of treatment for CSC were included and categorized in 2 groups according to presence or absence of intervortex vein anastomosis at presentation: presence of IVA (Group A) or absence of IVA (Group B). If OCT and angiography findings were in accordance with CSC, both eyes of patients were included, otherwise fellow eye was excluded.

**Methods**
LogMAR visual acuity (VA), OCT findings including intraretinal cysts, serous retinal detachment (SRD), subfoveal choroidal thickness (SFCT), inner choroidal attenuation (ICA), classic or flat pigment epithelial detachment (PED), irregular lesions (deposits) on retina pigment epithelium (RPE), photoreceptor disruption (PD), intraretinal hyperreflective dots (IHD), choroidal excavation and angiographic findings including localization of IVA, leakage on IVA and smokestack configuration were evaluated. Photoreceptor disruption was classified into shaggy, atrophy or combined subtypes based on the appearance on OCT. Localization of IVA categorized in 3 areas according to ETDRS grid containing three concentric circles 1, 3, and 6 mm in diameter: inner 1mm circle (area 1), 1-3mm middle circle (area 2) and 3-6 mm outer circle (area 3). One sample t-test and Pearson Chi-Square test were applied to compare the numerical variables between 2 groups. Linear regression analyses were performed for the multivariable analyses of VA, OCT and angiography findings. P values less than 0.05 were considered significant.

**Results**
Fifty-two eyes of 39 patients (23 males, 16 females) were included. Thirty-one eyes were in group A, 21 eyes were in group B. The mean ages of the patients at presentation were 52.5 ± 11.3 years in group A, 47.2 ± 11 years in group B (p <0.001). The mean VA of the patients were 0.38 ± 0.38LogMAR in group A and 0.19 ± 0.21 LogMAR in group B (p <0.001). The mean SFCT of the patients were 436.3±134.3µ in group A and 480.2±136.6µ in group B (p <0.001). There were no significant difference in the other OCT findings between 2 groups (p >0.05). Leakage on IVA was detected in 93.6% of patients. 35.5% of eyes had IVA in area 1, 38.7% of eyes in area 2, 25.8% of eyes in area 3. Localization of IVA in area 1 was correlated with both ICA and leakage on IVA(r=0.412, p=0.011 and r=0.371, p=0.02). Localization of IVA in area 3 was correlated with irregular lesions on RPE(r=0.314, p=0.042). Smokestack configuration, intraretinal cysts, ICA were significantly correlated with worse initial VA (p <0.001, p=0.011 and r=0.042). Shaggy subtype of PD was significantly associated with better initial VA (r=0.380, p=0.003).

**Conclusions**
Intervortex vein anastomosis is recently defined entity in patients with CSC and/or pachychoroid spectrum disorders. IVA has also been reported in normal population. We detected older age, worse initial visual acuity and thinner SCFT in patients diagnosed with CSC and IVA. Long term follow-up of patients with and without IVA may exhibit the difference in treatment outcomes and development of neovasculopathy.
Quantitative optical coherence tomography angiography biomarkers for Alport syndrome

**Purpose**
To evaluate microvascular abnormalities of patients with AS using optical coherence tomography angiography (OCT-A) quantitative biomarkers.

**Setting/Venue**
Department of Ophthalmology, Centro Hospitalar Universitário São João, Porto, Portugal

**Methods**
Cross sectional, prospective evaluation of consecutive patients with AS and healthy subjects. AS diagnosis was performed by genetic test. All participants underwent a retinal vasculature evaluation by spectral domain optical coherence tomography (SD-OCT) and OCTA of the macula. Quantitative analysis included: whole vascular density (VD, %), foveal avascular zone area (FAZ, mm2), fractal dimension (FD) and lacunarity (LAC).

**Results**
Ninety-four eyes were included in this study, 45 eyes from patients with AS and 49 eyes from healthy subjects. The pathogenic mutation in the COL4A5 gene on the chromosome X was found in 14 patients the pathogenic autosomal recessive mutations in the COL4A3 gene were found in 9 patients. The age of the patients with AS ranged from 21 to 57 years. Quantitative evaluation demonstrated a significant difference between AS and healthy subjects on LAC of the SCP and DCP (p<0.001 and p<0.001, respectively) and on FD in the DCP (p<0.001).

**Conclusions**
The DCP Alport patients has a higher vessel nonuniformity than DCP of healthy subjects. We hypothesize that endothelial cells lesion in the setting of low resistance at the DCP circuit that could lead to long term structural disorganization.

**Financial Disclosure**
None
The impact of optic disc morphological characteristics on peripapillary retinal nerve fiber layer thickness in non-glaucomatous subjects with high myopia

**Purpose**
To analyze peripapillary retinal nerve fiber layer (pRNFL) thickness (pRNFLT) alterations in non-glaucomatous eyes with high myopia (HM), and to describe its relationship with some optic disc (OD) morphologic features.

**Setting/Venue**
University of Health Sciences, Ulucanlar Eye Research and Education Hospital.

**Methods**
A cross-sectional case control study includes 185 Caucasian subjects with HM and 122 healthy controls. Results of the pRNFLT analysis provided by optical coherence tomography were compared between the HM and control group, and the effects of some morphological features of OD, including tilt, OD radius, and peripapillary chorioretinal atrophy (pCRA) extension, on pRNFLT analysis were investigated.

**Results**
The mean pRNFL of the HM group was significantly thinner than the control group in the inferior (p <0.001), superior (p <0.001), and nasal (p =0.001) quadrants. In the HM group, the superior quadrant pRNFL was significantly thinner in the tilted OD subgroup compared to the non-tilted OD subgroup (p <0.001). The mean pRNFLT was negatively correlated with pCRA extension in the inferior (r =-0.209 and p =0.020), superior (r =-0.308 and p <0.001), and nasal (r =-0.235 and p =0.008) quadrants. In the no-pCRA subgroup, only superior quadrant pRNFL was significantly thinner than the control group (p <0.001) and the magnitude of alteration was calculated as 7μm. In the pCRA extension ≤1x OD radius subgroup inferior (p <0.001), superior (p <0.001), and nasal (p =0.009) quadrant pRNFL was significantly thinner than the control group and the magnitude of alteration was calculated as 21μm in the inferior quadrant, 23μm in the superior quadrant, and 5μm in the nasal quadrant. The inferior (p <0.001), superior (p <0.001), and nasal (p <0.001) quadrant pRNFL was also significantly thinner in pCRA extension >1x OD radius subgroup than the control group and the magnitude of alteration was 24μm in the inferior quadrant, 40μm in the superior quadrant, and 17μm in the nasal quadrant.

**Conclusions**
In non-glaucomatous Caucasian subjects with HM, pRNFL is thinner compared to controls in the inferior, superior, and nasal quadrants, and this thinning is negatively correlated with pCRA extension. Superior quadrant pRNFL is also thinner in tilted OD than non-tilted OD. The morphological characteristics of OD give some opportunities to a physician to interpret pRNFLT analysis without requiring other software or automatized device.

**Financial Disclosure**
none
# Title

Early retinal and choriocapillary vascular changes in multiple sclerosis: A longitudinal study

## Purpose

To investigate the vessel density (VD) in macular and papillary regions, by means of Optical Coherence Tomography Angiography (OCTA) over two-years after an initial demyelinating event (IDE) in multiple sclerosis (MS) patients to identify early biomarkers in diagnosis of this disease.

## Setting/Venue

University of Naples “Federico II”, Naples, Italy

## Methods

A total of thirty eyes from 15 IDE patients (7 females, 8 males, mean age 28.4 ± 9.6 years) was enrolled by Multiple Sclerosis Centre. They underwent a neurological evaluation and a subsequent complete ophthalmological assessment. The VD was analyzed, using OCTA, in superficial capillary plexus (SCP), deep capillary plexus (DCP), choriocapillaris (CC) and radial peripapillary capillary plexus (RPC) at baseline and after one and two years of follow up. We also evaluated structural OCT parameters (ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL)) changes.

## Results

GCC and RNFL thicknesses did not change over time. After one year, compared with baseline we did not identify changes in OCTA and OCT measures. After 2 years, a reduced VD was found in SCP, DCP and RPC respect to baseline (coeff. $\beta = -2.779$, p= 0.013; coeff. $\beta = -4.055$, p= 0.018 and coeff. $\beta = -2.687$, p =0.001; respectively). These changes were confirmed when comparing measures obtained after 2 years with those observed 1 year after. Conversely, VD of the CC did not show significant differences from baseline at any time point. VD reduction was not associated with EDSS change, relapses occurrence and magnetic resonance imaging activity.

## Conclusions

Our findings showed in IDE patients a progressively increasing blood flow rarefaction, that could reflect a cerebrovascular degenerative process during the follow up. Retinal vascular loss occurs in early stages of MS independently from clinical and radiological disease activity and it is not associated with retinal atrophy. OCTA could be considered as an early biomarker in IDE patients follow up, showing abnormalities before the appearance of subsequent neuroaxonal loss. OCTA could represent a novel and helpful early biomarker in order to better define the vascular involvement in MS pathogenesis and to monitor the MS progression.

## Financial Disclosure

None

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**Title**
Effectiveness, safety and choroidal changes of a fovea-sparing technique for the treatment of chronic central serous chorioretinopathy with yellow subthreshold laser

**Purpose**
To analyze the effectiveness and safety of 577 nm yellow subthreshold laser (STL) in the treatment of Chronic Central Serous Chorioretinopathy (CCSC) delivered in a fovea-sparing pattern as well as the changes in choroidal structure visible on Swept-Source Optical Coherence Tomography (SS-OCT).

**Setting/Venue**
The study was conducted at the Joan XXIII University Hospital in Tarragona from 2018 to the present time as a prospective, interventional, non-randomized, case series.

**Methods**
Diagnosis of CCSC was based on clinical examination, SS-OCT, Fundus Autofluorescence (AF) and Fluorescein Angiography (FA). Patients enrolled received treatment with 577nm subthreshold yellow laser titrated at 1/3 of minimum power to deliver minimally visible burn using 160µm spots at 5% duty cycle. Spots were delivered in a confluent pattern guided through OCT, AF or FA avoiding the fovea and 200µm area around it. Results were recorded at 6-12 weeks and from there on a basis determined by every individual’s evolution as well as the decision to administer further treatment. We registered Best Visual Acuity (BCVA, Snellen charts), SS-OCT and AF. Every case was analyzed for changes in BCVA, subretinal fluid (SRF) and Choroidal Thickness (CT) as well as visible laser changes on OCT or AF. Patients with a history of use of steroid treatment in the previous 6 months and other evolving ocular conditions were excluded. The same experienced surgeon performed STL treatment in all cases. The study was conducted in accordance with the Declaration of Helsinki. Statistical analysis was performed using StataCorp2020. Student’s t test was used to determine the significance of the differences in mean values. A P value of 0.05 or lower was considered statistically significant.

**Results**
The study included 37 eyes of 34 patients diagnosed with CSC. All patients received STL treatment as described. Mean age was 54.3 ± 10.7 years old (range 37-77). Patients were mostly men (76.6%). After STL, BCVA improved in 72.7% of patients and remained stable in 27.3%. BCVA did not decrease after STL in any patient. Mean CT before STL was 364.2 ± 82.6µm (range 271 to 406). At 12 weeks follow-up, it was 280 ± 114.5µm (range 199 to 361, p<0.05). During this same period, Choriocapillaris and Sattler layer (C-S) thickness changed from 57.7 ± 22.6µm (range 34 to 150) to 34 ± 1.4µm (range 17 to 122, p<0.05). While Haller layer thickness changed from 306.5 ± 68.7µm (range 214 to 340) to 246 ± 115.9µm (range 164 to 328, p<0.05). The ratio between Haller and C-S layer thickness was 5.7 before treatment. It increased to 7.3 (p<0.05) at week 12. Overall, there was a reduction of 23.1% in total CT (40.9% in C-S layer and 19.7% in Haller layer). There were no changes at the level of retina or RPE observed in fundus photography, SS-OCT or AF that could be accounted as laser-related complications.

**Conclusions**
STL has yielded positive results in terms of effectiveness and safety for the treatment of CCSC, which do not seem to be diminished by the use of a fovea sparing technique, this may be of interest for novice laser practitioners. The changes observed in CT after treatment have consisted in a significant thinning both at the level of Choriocapillaris and Sattler layer and Haller layer, being proportionally higher in the former. This thinning might be related to a laser-induced change in the choroidal circulation.

**Financial Disclosure**
We have no financial relations to declare.
Peripapillary retinal nerve fiber layer and macula segmented inner retinal layers analysis of eyes with age related choroidal atrophy

**Purpose**
Age Related Choroidal Atrophy (ARCA) was first described by Richard F. Spaide in 2009 as an acquired disease that affects older individuals and may mimic the typical findings of age related macular degeneration (AMD). Spaide emphasized in this study that the patients with ARCA had higher risk for glaucoma. (Spaide RF. Age related choroidal atrophy. Am. J Ophthalmol. 2009;147;801-810) This cross-sectional study compared the peripapillary retinal nerve fiber layer (pRNFL) and macula segmented inner retinal layers in patients with age related choroidal atrophy (ARCA) and age-matched healthy controls.

**Methods**
This cross-sectional and prospective study included 84 eyes of 84 patients: 40 eyes with ARCA (group 1) and 44 age and axial length matched healthy controls (group 2). Serial horizontal SD-OCT scans of the macula and optic disc were acquired from all participants. Peripapillary retina nerve fiber layer (pRNFL) thickness analysis and thicknesses for retinal nerve fiber layer (mRNFL), ganglion cell layer (mGCL), inner plexiform layer (mIPL) were obtained with 6 mm macular grid. Subfoveal cho-roidal thickness was measured from the outer portion of the hyperreflective line corresponding to the RPE to inner surface of the sclera using EDI mode of SD-OCT. The ARCA patients were defined as at least 1 eye had a choroidal thickness of less than 125 micron without significant macular and retinal pigment epithelium problems as described by Spaide. Fundus autofluorescence imaging demonstrated the intact retinal pigment epithelium. The patients with AMD, any retinovascular abnormalities, epiretinal membrane, glaucoma, myopia higher than 3 diopters, axial length higher than 25.00 mm, a history of vitreoretinal surgery, intravitreal injection, photodynamic therapy, and argon laser photoacoagulation were excluded from the study. The mean pRNFL, mRNFL, mGCL and mIPL were compared between the two groups.

**Results**
There were no intergroup differences with regard to age, sex, best corrected visual acuity, intraocular pressure, and axial length (p value is higher than 0.05 for all). The mean age was 78±5 years in ARCA group and 77±6 years in the control group. The mean pRNFL thickness was 93.21± 10.45 in group 1, 98.29±8.11 in group 2 (p= 0.01). The mean mGCL thickness was 36.72±6.23 in group 1, 41.22 ±3.70 in group 2 (p=0.001). The mean mIPL thickness was 31.32 ±3.59 in group 1 and 33.94 ±2.63 in group 2 (p=0.001). There were no difference in mean mRNFL values of both groups (p=0.2).

**Conclusions**
This study detected lower mean thicknesses of mGCL, mIPL and pRNFL of eyes with ARCA. The marked choroidal thinning in eyes with ARCA may be associated with the pathophysiology of glaucoma as the structural glaucoma indicators demonstrated thinner values than healthy controls which were age and axial length matched.

**Financial Disclosure**
none
Purpose
To evaluate the repeatability of the peripapillary and macular vascular parameters using optical coherence tomography angiography (OCT-A) in healthy children.

Setting/Venue
Ophthalmology Unit, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain

Methods
Cross-sectional study including 34 eyes of 34 healthy children. After a complete medical examination, two consecutive OCT-A exams were done using AngioPlex Cirrus 5000 (Carl Zeiss Meditec, Dublin, CA, USA) in the same session. The scan area used was 6x6 mm for the analysis of the superficial vascular plexus (SVP) in the macula, and 4.5x4.5 mm for the peripapillary plexus. To study the repeatability of the measurements, the intraclass correlation coefficient (ICC) and the coefficient of variation (CV) of each pair of exams were calculated.

Results
The mean age of the children included was 10.77±2.49 years (range 6 to 15 years). Good and excellent ICCs were obtained for all the parameters considered. Peripapillary vascular parameters showed greater reproducibility than macular ones (global peripapillary perfusion density (pPD): ICC=0.834 CV=0.89% vs. whole macular area PD (w-mPD): ICC=0.697 CV=3.49%; global peripapillary flux index (FI): ICC=0.858 CV=1.28%; whole macular area vascular density (VD): ICC=0.699 CV=3.30%). Amongst the macular parameters, the characteristics of the foveal avascular zone (FAZ) were the ones showing higher rates of repeatability (FAZ circularity: ICC=0.858 CV=8.83%).

Conclusions
OCT-A is a non-invasive, time-efficient technology that may be useful in the evaluation of the retinal and peripapillary vascular network in healthy children. The repeatability of the measures will allow the follow-up and evaluation of any change occurring in the macular or optic nerve perfusion.

Financial Disclosure
NOTHING TO DECLARE
Choroidal features in two types of flat irregular pigment epithelial detachment associated with chronic central serous chorioretinopathy: Avascular versus vascularized

Purpose
To investigate the differences in the choroidal biomarkers between two forms of flat irregular pigment epithelial detachment (FIPED): avascular (aFIPED) and vascularized (vFIPED) in eyes with chronic central serous chorioretinopathy (CSC).

Setting/Venue
This case-control study included treatment naïve patients with chronic CSC who had FIPED, referred to the Retina clinic of Farabi eye hospital, Tehran University of Medical Sciences, Tehran, Iran, between March 2019 and July 2020.

Methods
Enhanced depth imaging optical coherence tomography (EDI-OCT) was done in eyes with FIPED correlated to chronic CSC, fellow eyes and also in healthy normal eyes. Eyes with FIPED was classified into two subgroups based on optical coherence tomography angiography (OCTA) findings: vFIPED and aFIPED. Different choroidal biomarkers such as subfoveal choroidal thickness (SFCT), total choroidal area (TCA) and choroidal vascular index (CVI) were compared between the groups.

Results
Forty-four eyes from 44 patients with chronic CSC and FIPED along with 20 healthy gender- and age-matched subjects (40 eyes) were included. OCTA identified vascularization in 14 eyes in FIPED group (31.8%). Mean SFCT was higher in FIPED group compared to two other groups (p = 0.005). In comparison to patients with aFIPED, patients with vFIPED had lower SFCT (p=0.003) and higher CVI (p=0.020) based on multivariate analysis.

Conclusions
The significant differences between aFIPEDs and vFIPEDs in terms of choroidal features suggest that these biomarkers can predict the evolution of FIPED in patients with CSC.

Financial Disclosure
No financial relation with any company.
Systematic review and meta-analysis of diagnostic accuracy of detection of any level of diabetic retinopathy using digital retinal imaging

Visual impairment from diabetic retinopathy (DR) is a rising global public health concern, which can be prevented with screening and early treatment. Digital retinal imaging has become a preferred choice as it enables higher accuracy, acceptability, and coverage of screening. A DR screening (DRS) modality using digital retinal imaging which is suited to the health system and its context is a key factor in the success of a programme. However, often there are gaps in evidence base to choose a DRS strategy using digital retinal imaging that fits to a programme requirement. The available reviews and summary estimates provided diagnostic test accuracy (DTA) of detection of DR by combining both digital and non-digital modalities.

The aim of this review is to evaluate how different characteristics of the DRS using digital retinal imaging, such as number of fields, pupil status impacts on diagnostic test accuracy (DTA), and its relevance to a low-income setting. This will inform decision making for choosing strategy in those aspects of a DRS programme. This is an assessment of different imaging strategies for a systematic clinic-based screening rather than a population-based screening tool.

We conducted a search to identify studies on DRS using digital retinal imaging of diabetics at health-care facilities. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed in preparation of the protocol and reporting. We developed a comprehensive search strategy and searched MEDLINE (Ovid), Cochrane Database of Systematic reviews (CDSR) and CENTRAL from the date of inception to September 2016. We included studies that aimed to evaluate the accuracy of DRS using digital imaging as the index test. We used the Early Treatment Diabetic Retinopathy Study (ETDRS) 7-field image interpretation as the gold standard, and mydriatic bio-microscopy by an ophthalmologist as the clinical reference standard where the gold standard was not performed. We assessed the bias using the Quality Assessment of Diagnostic Accuracy (QUADAS-2) framework. The outcome examined was sensitivity and specificity of detection of ‘any level of DR’. Summary estimates of different sub-groups were calculated using DTA values weighted according to the sample size. The DTA of each screening method was derived after exclusion of ungradable images, considering eye as the unit of analysis. We examined the effect on detection from using different combinations of retinal fields, pupil status, index test graders and setting.

Both non-mydriatic and mydriatic strategies showed very high discriminative power in ruling out presence or absence of any level of DR with the diagnostic odds ratio (DOR) of non-mydriatic strategies being 68.03 (95% CI 35.5-130.0) and positive likelihood ratio of 11.79 (SE 3.04, 95% CI 7.1-19.5). Diagnostic test accuracy for the detection of any level of DR showed that DRS using 2 fields delivered at non-primary care settings is a feasible approach. Dilatation of pupils did not improve the detection of any level of DR for those with gradable images, but such a wide range of ungradable were presented in these studies that this aspect must be taken into account when setting up DRSP. There wasn’t adequate evidence in primary studies to comment on DTA of non-ophthalmological human resources on DRSP, so this aspect requires further research. Good quality digital imaging has the potential for real time interpretation of retinal images, which together with counselling for risk factors may improve the acceptability of DRS and uptake of referral for ophthalmic assessment if conducted in a culturally acceptable way.
Multimodal imaging of a choroidal subfoveal macrovessel

**Purpose**
To describe the clinical and multimodal imaging features in a case of choroidal macrovessel (CM).

**Setting/Venue**
Hospital General Universitario Reina Sofía de Murcia.

**Methods**
Multimodal imaging features, including fundus photography (FP), near infrared reflectance, autofluorescence (FAF), spectral domain optical coherence tomography (OCT) with enhanced depth imaging (EDI), angiography by optical coherence tomography (OCT-A), B-scan ultrasonography (US) and fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA).

**Results**
An 80-year-old man with hypertension and type II diabetes came to routine examination. His best corrected visual acuity was 1 in both eyes and the anterior pole was normal. The fundoscopy was normal in the right eye and showed a slightly raised macula with discrete pigmentary changes in the left eye. FAF showed mottled hyperautofluorescence in this area, US was normal, FFA showed the presence of a great vessel beneath the fovea, with focal increased hyperfluorescence in late times. OCT showed a round hyporreflective area in the fovea corresponding to the CM, with mild elevation of the retina, alteration of the outer retinal layers and a thickened choroid. No subretinal fluid was observed. OCT en face highlighted the inferior-temporal course of the CM from the fovea. OCT-A confirmed the existence of a subfoveal macrovessel at the choroidal level, with a great caliber, a hyporreflective center and a serpiginous aspect.

**Conclusions**
The etiology of choroidal macrovessels is still unknown. Although some patients may experience metamorphopsia, most of them remain asymptomatic. Appreciating the described signs in the imaging techniques may favour the diagnosis. In our case no further changes were observed after two years of following.

**Financial Disclosure**
None
Title
Alterations in choroidal vascular parameters following pan-retinal photocoagulation using enhanced-depth imaging optical coherence tomography

Purpose
To investigate the alteration of choroid in patients with very severe non-proliferative diabetic retinopathy (NPDR) or early proliferative diabetic retinopathy (PDR) following panretinal photocoagulation (PRP).

Setting/Venue
Patients with very severe NPDR and early PDR without center-involved macular edema referred to the retina clinic of Farabi eye hospital, Tehran university of medical sciences, were recruited in this study from February 2019 to November 2020.

Methods
Thirty-nine eyes of 21 patients with very severe non-proliferative diabetic retinopathy (NPDR) (19 eyes) and early proliferative diabetic retinopathy (PDR) (20 eyes) were recruited. Enhanced-depth imaging optical coherence tomography at baseline, 1, and 6 months after PRP was employed to measure choroidal parameters including total choroidal area (TCA) and choroidal vascular index (CVI).

Results
In eyes with very severe NPDR, TCA decreased non-significantly at month 1, which increased significantly at month 6 (539±131µm², 502±134µm², 598±168µm² at baseline and month 1 and 6, respectively; P=0.003). CVI increased at month 1, and then decreased at month 6 (68.25±3.05, 69.74±3.62, 67.84±1.77 at baseline, month 1 and 6, respectively; P<0.001). A reverse pattern occurred in eyes with early PDR; a non-significant increase in TCA at month 1 followed by a decrease at month 6 (497±95µm², 514±133µm², 425±95µm² at baseline, month 1 and 6, respectively; P=0.011). CVI decreased at month 1 and remained relatively stable at month 6 (69.34±3.11, 68.33±3.41, 68.50±5.04 at baseline, month 1 and 6, respectively; P=0.023). Alteration of choroidal thickness was not statistically significant in both groups.

Conclusions
Eyes with very severe NPDR and early PDR exhibit a reverse pattern regarding choroidal indices after PRP.

Financial Disclosure
No any financial relations
**Title**
Optimization of the scan pattern in OCTA images in healthy subjects

**Purpose**
The aim of the present study was to assess the optimal scan pattern on Spectralis HRA-OCT2 device measuring macular microvasculature perfusion in healthy subjects.

**Setting/Venue**
This was an observational, cross-sectional study involving healthy eyes and conducted at the Eye Clinic of the S. Maria Della Misericordia Hospital (Perugia, Italy).

**Methods**
Consecutive healthy subjects were imaged within the same visit using the SPECTRALIS OCT-A Module (Heidelberg Engineering, Heidelberg, Germany) using different scanning protocols (10°X10°- 512 ART 7[P1], 10°X10°-256 ART 5[P2], 10°X10°-512 ART 5[P3], 15°X10°-256 ART 5[P4]) centered in the macular area. Vessel perfusion density (VPD) and vessel length density (VLD) of the superficial capillary plexuses were computed using ImageJ software (National Institutes of Health) to evaluate potential differences between diverse scanning patterns. A qualitative grading of the foveal avascular zone and of image quality was performed by two retina specialists.

**Results**
Twenty eyes of 10 healthy subjects were included in the present study. Mean VPD values of P1, P2, P3 and P4 were 35.60, 31.67, 31.18 and 31.16 respectively. Mean VLD values of P1, P2, P3 and P4 were 7.54, 5.86, 6.74 and 4.40 respectively. A statistically significant difference was reported between P1 and P2, P3, P4 values both for VPD and VLD. No statistically significant differences were reported between P2, P3 and P4 values. In the qualitative assessment, P1 had the highest score and P4 had the lowest score from both graders in the foveal avascular zone and image quality assessment.

**Conclusions**
In the overall analysis of the qualitative assessment a statistically significant superiority was demonstrated for P1 compared to the other scanning patterns. In the quantitative assessment, P1 was shown an optimal scanning approach in detecting blood flow and seems less suffering from noise.

**Financial Disclosure**
No
**Title**

OCT retinal microstructure as a strong marker of vigabatrin related visual toxicity based on wide-field multifocal electrophysiology results

**Purpose**

To investigate if the examination of retinal microstructures and retinal nerve fibre layer (RNFL) thickness using the Optical coherence tomography (OCT) could reveal a structural cause behind the wide-field multifocal electrophysiology (WF-mfERG) results in patients exposed to vigabatrin.

**Setting/Venue**

Electrophysiology unit, Gartnavel General Hospital, Glasgow G12 0YN

**Methods**

This is a prospective study of 28 participants who have all been exposed to vigabatrin. The subjects were analysed based on their WF-mfERG results where they are grouped as 'delayed' (based on 2ms delay in peripheral field compared to central field), or non-delayed. All patients underwent OCT macula volume and OCT

**Results**

Analysis of the OCT microstructures based on volume reveal distinctive thickness difference in the inner retinal layers of those in the ‘delayed’ group (p<0.01). Further analysis of the retinal microstructures reveal persistent statistically significant difference across the outer nuclear layer (ONL) (p<0.01), ganglion cell layer (GCL) (p<0.01) and the inner plexiform (IPL) (p<0.01), but not the outer retinal layers.

**Conclusions**

The changes detected points towards damage in the ONL, GCL and IPL; which concurs with historical pathological reports in animal studies. Our observations are striking and could be helpful in leading the way for improved and more objective methods for monitoring of vigabatrin related visual toxicity.

**Financial Disclosure**

no financial disclosures.
### Title
Axial length cut-off values to objectively define pathologic myopia and severe pathologic myopia: Clinical characteristics and ATN grading system correlation

### Purpose
This study had three aims: 1) determine AL cut-off values to distinguish between pathologic myopia (PM) and severe PM; and 2) identify clinical differences between PM and severe PM according to ATN grading system.

### Setting/Venue
Puerta de Hierro-Majadahonda University Hospital.

### Methods
Cross-sectional, non-interventional study. A series of 656 eyes from 352 highly myopic patients were included. All patients underwent complete ophthalmologic examination, ATN grading and multimodal imaging.

### Results
The eyes were graded on the ATN system and classified as PM (≥A2) or severe PM (≥A3, ≥T3, and/or N2). Significant between-group (PM vs. severe PM) differences (p<0.05) were observed on the individual ATN components (atrophic [A], tractional [T] and neovascular [N]). Patients classified with severe PM were older, had longer AL, and worse BCVA (p<0.05). ROC curve analysis showed the optimal AL cut-off value to distinguish between PM and severe PM at 28 mm (AUC ROC curve: 0.813, specificity: 75%, sensitivity: 75%) and 29.50 mm (AUC ROC curve: 0.760, specificity: 75%, sensitivity: 70%), respectively.

### Conclusions
The optimal cut-off points for axial length to detect PM and severe PM are 28 mm and 29.5 mm, respectively. These AL cut-off values would help to establish myopic conditions numerically by relying on the clinical features defined previously; and should be taken into account for closer follow-up, ophthalmic management and treatment.

### Financial Disclosure
No financial disclosures to declare
## Title
Evaluation of peripapillary perfusion alterations after haemodialysis using OCT angiography

## Purpose
To assess the peripapillary microvasculature before and after haemodialysis (HD) in end-stage renal disease (ESRD) using Spectral Domain Optical Coherence Tomography Angiography (SD-OCTA).

## Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

## Methods
Fifteen eyes of 15 patients with ESRD undergoing HD were included. All subjects underwent comprehensive ocular examination and OCTA within 15 min before and after HD session. The systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight and ultrafiltration volume were measured within 5 min before and after HD. OCTA scans were performed using AngioVue software of the Optovue RTVue XR Avanti. A 4.5 × 4.5 mm images for the Radial Peripapillary Capillaries (RPC) were obtained. Retinal Nerve Fiber Layer (RNFL) thickness, whole image (wi), inside disc (id) and peripapillary (pp) were evaluated.

## Results
The mean age was 51.88 ± 7.03. The sex ratio was 1.15. There was a significant decrease in body weight and SBP after HD (before :61.4 ± 11.3 kg; after :58.6 ± 11.5 kg; p = 0.011) and SBP (before: 151.8 ± 32.5 mmHg ; after :141.7 ± 29.5 mm Hg ; p= 0.014). All peripapillary vascular densities (wi, id, pp) deceased significantly after HD (all p<0.05). Compared to baseline, there was a thickening of the RNFL after HD session (p=0.02). The reduction in RPC VDs correlated with the decrease in SBP (R=0.654, p=0.02).

## Conclusions
OCT-A is a non-invasive imaging modality that may be useful to identify peripapillary vascular network changes associated with systemic vascular diseases. However, further studies are warranted to confirm the mechanism underlying these findings.

## Financial Disclosure
The authors declare no conflict of interest.
**Title**
Peripapillary microvascular changes in long-term hydroxychloroquine users: Quantitative analysis using optical coherence tomography angiography

**Purpose**
To evaluate changes in the peripapillary vascular network using spectral-domain optical coherence tomography angiography (SD-OCTA) in hydroxychloroquine (HCQ) users.

**Setting/Venue**
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

**Methods**
Twenty-five eyes of 25 patients and 25 eyes of 25 age matched healthy controls were enrolled. All subjects underwent a history taken about HCQ use (duration, cumulative dose, diagnosis) and comprehensive ocular examinations, including measurement of best-corrected visual acuity (BCVA), biomicroscopy and examination of the fundus. OCTA scans were performed using Angiovue software of the RTVue XR Avanti. A 4.5 × 4.5 mm images for the Radial Peripapillary Capillaries (RPC) were obtained. Retinal Fiber Layer (RNFL) thickness, whole image (wi), inside disc (id) and peripapillary (pp) were evaluated in both groups.

**Results**
The mean age was 41.73 ± 1.27 years in HCQ users group and 38.00 ± 12 years in healthy controls group (p= 0.243). The mean duration of HCQ usage was 63.6 ± 38.4 months, and the cumulative dose of HCQ was 528.1 ± 3.44 g. Four patients developed HCQ retinopathy. Compared to the control group, there was no significant difference in peripapillary vascular densities (wi, id, pp) (all p>0.05). RNFL thicknesses of the HCQ users did not significantly decrease compared to those of the normal controls. No significant correlation was found between the RNFL thickness and the duration of use or cumulative dose.

**Conclusions**
The peripapillary microvasculature and RNFL thicknesses did not change in the HCQ users. RNFL thickness is not a useful biomarker for the early detection of HCQ retinal toxicity.

**Financial Disclosure**
The authors declare no conflict of interest.
Comparison of vitreomacular interface in patients with macular pseudohole and idiopathic epiretinal membrane foveaschisis

Purpose
To compare the vitreomacular interface by SD-OCT optical coherence tomography (OCT) in patients with macular pseudohole (MPH) and idiopathic epiretinal membrane foveaschisis (ERM-Fs).

Setting/Venue
Retrospective study at the Ophthalmology Department of the University of Health Science, Ankara Ulucanlar Eye Training and Research Hospital, Turkey.

Methods
Based on the classification made by the International Vitreomacular Study Group, two groups are included in the report Group 1 includes the cases with MPH diagnosed with OCT images and Group 2 includes the cases with ERM-Fs, whose terminology has not been agreed yet (macular pseudohole with stretched edges, tractional lamellar hole). Accordingly, the study evaluates the presence of epiretinal membrane (ERM), status of the posterior hyaloid [(i) attached on central fovea, detached on the macula; (ii) detached on fovea and macula; (iii) fovea and macula attached], central macular thickness (CMT), central foveal thickness (CFT) and fundus autofluorescence (FAF) pattern (subgrouped as patchy, uniform-oval shaped and mixed).

Results
Thirty-nine eyes of thirty-four patients were included in the study. The mean age was 71.7±9. There were macular pseudohole in 21 eyes (54%) and epiretinal foveaschisis in 18 eyes (46%). All 39 eyes had ERM. In MPH, 17.6% of eyes were attached to the fovea, detached in the macula; 5.9% of eyes were detached on fovea and macula; and 76.5% attached in the fovea and macula. In the ERM-Fs group, it is found that 10% of eyes were attached to the fovea, detached on the macula; 40% of eyes were detached on fovea; and 50% of eyes were attached on the fovea, detached on the macula. CMT was 446.6 ± 50.8 in the MPH group and 571.4±48.7 in the ERM-Fs group, where the difference was statistically significant (p <0.0001). The CFT in OCT was 192.2±13.6 in the MPH group and 198.7±21.9 in the ERM-Fs group. The difference between the two groups was not statistically significant. In FAF images, relatively uniform oval hyperfluorescence (90.5%) in 15 eyes and mixed features in 2 eyes (9.5%) were observed in the fovea in the MPH group, while irregular, patchy hyperfluorescence was observed in all eyes (100%) of the 2nd group (ERM-Fs).

Conclusions
In eyes with ERM-Fs, it was observed that the CMT increased and the posterior hyaloid was separated on the fovea and macula at a higher rate as compared to eyes with MPH. This suggests that separation of the posterior hyaloid may contribute to the formation of foveaschisis in addition to the known ERM contraction effect. Moreover, it can be argued that the patchy FOF pattern detected in all eyes with ERM-Fs correlates with foveaschisis determined in SD-OCT images.

Financial Disclosure
None
Evaluation of optic nerve head microvasculature by optical coherence tomography angiography in myopic patients

Meher Henchiri, Tunisia

Purpose
To assess the peripapillary microvascular changes in patients with low-to-moderate myopia using optical coherence tomography angiography (OCTA).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
We conducted a cross sectional study including 40 eyes of 20 patients having mild to moderate myopic refractive error and 42 emmetropic eyes of 21 healthy age and sex-matched control subjects. The enrolment has been run between September 2020 and February 2021. Refractive error/spherical equivalent was calculated. All included individuals underwent a complete ophthalmic examination including visual acuity, anterior and posterior segment examination and Spectral Domain OCTA. OCTA scans were performed using AngioVue software of the Optovue RTVue XR Avanti. 4.5 mm × 4.5 mm images for the Radial Peripapillary Capillaries (RPC) were obtained. Peripapillary Retinal Nerve Fiber Layer (RNFL) thickness, whole image (wi), inside disc (id) and peripapillary (pp) vessel densities were evaluated.

Results
The mean age was 35.7 ± 5.3 years. The study group included 11 females and 9 males. Mean axial length was 24.25 ±0.91 mm. Mean SE was -3.02 ±1.93 DS. Best-corrected visual acuity was 20/20. Mean of average RNFL thickness in myopic patients was 96.32 ±9.13 µm. Furthermore, there was no statistically significant difference in peripapillary vessel density between low-to-moderate myopic and emmetropic subjects (p= 0.057). Correlation analysis among all subjects showed that the RNFL thickness had positive correlation with spherical equivalent (R = 0.42, p = 0.046).

Conclusions
We didn’t find any significant peripapillary microvascular changes associated with moderate myopia. It can partly be explained by the absence of parapapillary atrophy in our patients. However, further studies are warranted to confirm the mechanism underlying these findings.

Financial Disclosure
The authors declare no conflict of interest.
Acute effect of pseudoephedrine on macular microcirculation in healthy subjects: An optical coherence tomography angiography study

Ibrahim Tuncer
Turkey

Purpose
To quantitatively evaluate the acute effects of pseudoephedrine on the macular microvasculature using optical coherence tomography angiography (OCTA).

Setting/Venue
Alfa Medical Center, West Eye Center

Methods
In this study, 60 right eyes of 60 healthy subjects were divided into 2 groups. The study group received 60 mg of pseudoephedrine and the control group received a placebo. All participants underwent OCTA at baseline and 1 hour after oral intake. Superficial macular flow area, foveal avascular zone (FAZ) area, superficial macular vessel density, central foveal thickness (CFT) and subfoveal choroidal thickness (SFCT) were analyzed.

Results
Baseline superficial macular flow area, FAZ area, superficial macular vessel density, CFT and SFCT measurements in the study and control groups showed no significant difference (p>0.05 for all). Oral pseudoephedrine intake caused a significant reduction in baseline superficial macular flow area, FAZ area, superficial macular vessel density and SFCT measurements when compared with baseline (p<0.05 for all). However, there was no significant difference in CFT after oral pseudoephedrine intake (p>0.05).

Conclusions
Oral pseudoephedrine intake causes a significant decrease in superficial macular blood flow and SFCT. Impairment of macular microcirculation can be detected noninvasively and quantitatively by OCTA.

Financial Disclosure
The authors declare that they have no conflict of interest. The authors did not receive any financial support from any public or private sources.
Optical coherence tomography angiography in pulmonary hypertension

Purpose
Pulmonary hypertension (PH) is a rare disease characterized by an elevation in pulmonary artery pressure, leading to right heart failure and subsequent increase in systemic venous pressure. Adverse functional and structural changes in multiple organs may occur, and ocular involvement has been described. The suggested underlying mechanism for ocular complications in acute settings is retinal and choroidal congestion as a result of elevated venous pressure in the superior vena cava and, consequently, ophthalmic and ocular veins. These are considered rare events and affect mainly the posterior segment. In fact, the available literature on ocular involvement in PH consists mainly of case reports. In this study, an analysis of the retinal and choroidal vasculature in patients with PH using optical coherence tomography angiography (OCT-A) is made and compared with that of healthy sex and age-matched control subjects.

Setting/Venue
Ophthalmology Department, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal.

Methods
A cross-sectional study was performed at a tertiary practice Ophthalmology department. Patients with PH from the Pulmonology outpatient clinic and healthy control subjects were recruited. All participants underwent a comprehensive ophthalmological examination and an en face OCT-A using 15°x15° macular scans (Spectralis, Heidelberg Engineering Inc.). OCT-A images were automatically segmented, and images from the superficial vascular plexus (SVP), intermediate capillary plexus (ICP), deep capillary plexus (DCP), choriocapillaris and choroid were retrieved. For a quantitative comparison of retinal and choroidal OCT-A imaging, vessel density, junction density and average vessel length were analyzed using AngioTool software (Center for Cancer Research, National Cancer Institute). A comparative case-control analysis was performed, and a correlation between disease duration and OCT-A quantitative parameters was made in the study group.

Results
A total of 16 PH patients and 16 control subjects were enrolled. All PH patients had an established diagnosis and were under systemic treatment at the time of the study. Namely, 13 patients were classified as World Health Organization PH Group 1 and 3 patients as Group 4. Eyes in the study group had a significantly lower vessel density in both SVP and ICP compared to the control group (44.0%, interquartile range [IQR] 42.6 – 46.1% in the study group, 46.2%, IQR 44.5 – 47.6% in the control group, p=0.015; and 46.0%, IQR 45.0 - 47.0% in the study group, 47.1%, IQR 46.2 - 47.9% in the control group, p=0.035; respectively). Junction density in SVP layer was also significantly lower in the study group (0.0012, IQR 0.0011 - 0.0015 in the study group, and 0.0014, IQR 0.0012 - 0.0016 in the control group, p=0.047). No other significant differences were found between both groups in the analyzed vascular layers. No correlation was found between disease duration and OCT-A quantitative parameters in the study group.

Conclusions
To our knowledge, this is the first study to analyze the retinal and choroidal vasculature with OCT-A in PH. Small but significant differences were found between the study and control groups. In PH patients vessel density was lower in SVP and ICP, and junction density was lower in SVP. Although mostly described in acute settings, our preliminary OCT-A research suggests that retinal microvasculature is affected in PH even in patients with chronic and stabilized disease.

Financial Disclosure
No financial disclosures.
Purpose
To evaluate peripapillary microvascular changes in patients with acute non-arteritic anterior ischaemic optic neuropathy (NAION), using optical coherence tomography angiography (OCT-A).

Methods
We conducted a cross sectional study including 12 eyes of 12 patients with acute NAION, within 7 days after onset of symptoms and 24 eyes of 24 healthy age and sex-matched control subjects. The enrolment has been run between September 2020 and February 2021. All included individuals underwent a complete ophthalmic examination including visual acuity, anterior and posterior segment examination and Spectral Domain OCTA. OCTA scans were performed using AngioVue software of the Optovue RTVue XR Avanti. 4.5 mm × 4.5 mm images for the Radial Peripapillary Capillaries (RPC) were obtained. Peripapillary Retinal Nerve Fiber Layer (RNFL) thickness, whole image (wi), inside disc (id) and peripapillary (pp) vessel densities were evaluated.

Results
The mean age of the NAION and normal subjects was 65 (61–79) and 66 (59–80) years (p=0.3). OCT-A showed a global decrease in all peripapillary vessel densities (VDs) in eyes with NAION (52.48±4.2%) compared with normal eyes (62.3±4.4%) (p<0.001). The RNFL thickness analysis revealed a thickening in eyes with NAION (120.7±7.8%) compared with controls (95±4.0%) (p<0.001). In patients (7 eyes) with resolution of optic disc oedema, a repeated OCT-A analysis at one month revealed an improvement of the peripapillary VDs by 7.1±3.7% with normalization of the RNFL thickness (p=0.035). There was a negative correlation between the RPC VDs and the final BCVA (R=-0.48 ;p=0.036).

Conclusions
Using OCT-A, we revealed a global reduction of peripapillary densities at the acute stage of NAION, followed by partial subsequent recovery. Further studies are needed to establish the value of OCT-A for assessing the NAION.

Financial Disclosure
The authors declare no conflict of interest.
**Title**
Benefit of high axial resolution optical coherence tomography in AMD

**Presenter**
Rosa Dolz-Marco – Spain

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**Setting/Venue**
Unit of Macula, Oftalvist Clinic, Valencia, Spain

**Purpose**
To evaluate the clinical benefit of high axial resolution optical coherence tomography (OCT) imaging in age-related macular degeneration using an OCT prototype (High-Res OCT) with 3 µm optical resolution.

**Methods**
Patients diagnosed with AMD undergoing comprehensive evaluation were scheduled for High-Res OCT imaging. The examination included regular optical coherence tomography (OCT) and OCT angiography, fundus autofluorescence, multispectral imaged and High-Res OCT images that were acquired using a prototype. Findings observed on the High-Res OCT images were compared and correlated with the conventional OCT and multimodal approach.

**Results**
A better delineation of every retina layer was achieved with the increase of axial resolution. A significant split between the retinal pigment epithelium (RPE) layer and Bruch’s membrane was observed in the majority of cases in the foveal area and also extending throughout the macula. The content of the RPE detachment both in neovascular and non-neovascular cases was better assessed as well as the status of the outer retinal bands was observed with an improved visualization of the external limiting membrane in cases of complete and incomplete RPE and outer retinal atrophy.

**Conclusions**
High-Res OCT images provided a detailed representation of structures in the retina not seen with conventional OCT axial resolution (about 7 µm). A better delimitation between layers was observed, and might be beneficial in the improvement of segmentation algorithms. The increase in axial resolution may offer additional confidence in the clinical evaluation of AMD cases. Furthermore, artificial intelligence analysis of fluid and other important biomarkers could benefit of these high-res images.

**Financial Disclosure**
The prototype OCT device was provided by Heidelberg Engineering.
# The relationship between myopic choroidal neovascularization activity and perforating scleral vessels in high myopia

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**Purpose**
To study perforating scleral vessels (PSV) in patients with high myopia with swept-source optical coherence tomography (SS-OCT) and to determine their relationship with myopic choroidal neovascularization (mCNV) and its activity.

**Setting/Venue**
Puerta de Hierro University Hospital, Majadahonda, Madrid (SPAIN)

**Methods**
Retrospective analysis of patients with high myopia (≥-6 D or ≥ 26 mm of axial length) using multimodal imaging. The presence of PSVs and mCNV was assessed using SS-OCT images (TRITON, Topcon Corporation, Japan).

**Results**
564 eyes from 297 highly myopic patients were studied. 155 eyes showed signs of mCNV (27.5%) while PSVs were found in 500 eyes (88.6%). PSVs were found in 93.5% (145/155) of eyes with mCNV and they were under or in contact with the mCNV in 80.6% (117/145). The mean number of intravitreal injections (IVI) received by mCNV patients was 4.06±4.17 along 66.9±4.1 months of follow-up. The number of injections per year was 1.32±1.56, the mean number of relapses was 1.11±1.83 and the mean number of relapses/year was 0.25±0.41.

**Conclusions**
PSVs are more common among highly myopic patients suffering from neovascular complications. Myopic CNV complexes that are coincident with PSVs on OCT show higher rates of activity, needing more injections to control them and being more prone to relapses in time.

**Financial Disclosure**
none
High resolution imaging of normal and pathological retinal pigment epithelium (RPE) using a transscleral illumination adaptive optics camera

**Purpose**

Retinal pigment epithelium (RPE) cell mosaic can be resolved in the living retina using an adaptive optics (AO) system with transscleral illumination (TSI), as recently shown by Laforet et al. The combination of autofluorescence imaging with adaptive optics scanning laser ophthalmoscopy (AF-AOSLO) has also led in the past to the precise imaging of the RPE mosaic, as reported by our group (K. Grieve et al). The present study evaluates the RPE cells mosaic in the normal retina and other clinical features such as pigment clumps in patients with age related macular degeneration (AMD) and Stargardt disease, using with a commercially available flood-illumination AO retinal camera modified by the addition of TSI, and compared with AF-AOSLO images.

**Setting/Venue**

Patients were recruited and examined at the clinical investigation center 1423 in the National Quinze-Vingts Ophthalmology Hospital, Paris in France. The procedures used in this study conformed to the tenets of the Declaration of Helsinki, and they were approved by our local ethics committee. A written informed consent was obtained from each subject.

**Methods**

An infrared LED projector was attached to an AO retinal camera (rtx1-e, Imagine Eyes, France) in order to illuminate the retina with an 850 nm beam focused at the pars plana. This system illumination is composed of two led arrays illuminating the retina through the sclera on both sides of the pupil. The system complied with ANSI regulations. The oblique trans illumination of the posterior retina leads to the generation of phase images that could show the boundaries of the RPE cells. These images were averaged using customized ImageJ software. Infrared AF AOSLO images were registered to TSI images. For AMD and Stargardt disease cases, conventional multi-imaging, including infrared scanning laser ophthalmoscopy (IR SLO), IRAF SLO, SD-OCT (Spectralis), AO-SLO (PSI, USA), AO fundus camera was performed.

**Results**

We have currently imaged 3 normal subjects, aged between 28 and 56 years, 3 AMD patients and a Stargardt disease patient. In three normal eyes, circular cell-like structures with dark centers surrounded by brighter rings were visible in almost all images. At eccentricities beyond 5 degrees, cell-like structures were visible in the entire field of images. Cell density ranged between 4.4x10^3 and 6.2x10^3 cell/mm^2 across subjects, which showed good correlation with AF AOSLO results and lie within the ranges reported in the literature. In AMD and Stargardt eyes, pigment clumps were visible in the pathological area with a high contrast.

**Conclusions**

The implementation of TSI on an AO camera allowed visualization and quantification of the RPE mosaic in healthy subjects. The RPE images taken by TSI and AF AO-SLO were similar in shape and density. In pathological eyes, pigment clumps are electively detected with a high contrast. TSI could thus be a valuable addition to a conventional trans-pupillary flood-illumination AO camera, not only for seeing the RPE cells, but also for detecting clinical features such as pigment clumps.

**Financial Disclosure**

Christophe RONDEAU is employee of Imagine eyes
**Title**
Extrafoveal Müller cells detection in vivo in the human retina: An optical coherence tomography study

**Purpose**
Müller cells (MC) play a fundamental role in the homeostasis regulation of the vertebrate retina, are the most represented glial cells within retinal structure and are found involved in several retinal diseases. In the recent years, optical coherence tomography (OCT) techniques offered powerful ways to perform non-invasive, in vivo, detailed histology-like analyses of the human retina. Further information can be achieved by using post-processing algorithms. Through these methodologies, it is possible to use the light properties of each retinal component to perform dedicated analyses. The main purpose of this study was to propose a new post-processing technique to detect and analyze MC in the human retina and to compare our imaging findings with histologic analyses.

**Setting/Venue**
Clinical setting; Department of Ophthalmology, IRCCS San Raffaele Scientific Institute, Vita-Salute University, via Olgettina 60, Milan (Italy).

**Methods**
The study was designed as a cross-sectional, observational case series. Consecutive healthy human subjects and patients affected by ocular neoplasia, not involving the macular region and requiring surgical enucleation, to obtain histologic samples. The imaging protocol included high resolution 3x3mm macular OCT angiography (OCTA) acquisitions (DRI Triton Topcon; Topcon Corporation; Tokyo, Japan) (wavelength 1050nm; 100.000 A-Scans per second; in-depth resolution digital 2.6µm and optical function 8µm). The MC detection started with the assumption that extrafoveal MC are vertically oriented elements, not interfering with light passage and absorption. From this point of view, the analyses focused on the isolation of the non-reflective vertical signal included between the internal limiting membrane and the external limiting membrane. The method consists in a set of algorithms composed of the following blocks: data intermediate format, registration, layer extraction, MC counter. Blood flow signal, detected by OCTA, was excluded to improve data accuracy. With respect to the histologic analyses of the enucleated eyes, after the OCTA acquisition and the surgical enucleation, a 3x3mm area of the macular region was examined by means of Vimentin and glial fibrillary acidic protein. Imaging based reconstructions and histologic samples were qualitatively evaluated to assess morphologic agreement.

**Results**
Overall, 18 healthy subjects (10 men, mean age 35±10 years) and 2 patients (1 man, mean age 51±9 years) affected by peripheral intraocular melanoma, not involving the macular region, without any other ocular or systemic disorder, and underwent surgical enucleation were included. Best corrected visual acuity was 0.0±0.0 LogMAR (20/20 Snellen equivalent) for all the eyes. Our approach allowed to analyze, from structural OCT images, the trans-retinal, vertical, linear, hyporeflective signal, included between the internal limiting membrane and the external limiting membrane. This signal was characterized by a continuous “single-line” morphology. Remarkably, the signal isolated by structural OCT images showed high qualitative matching with histologic samples. MC signal resulted more detectable in the extrafoveal region than in foveal one. Our quantitative analysis showed an overall MC number of 42232±3478 cells localized in the macular volume of 3x3mm (~42.000/9 mm2 cells).

**Conclusions**
Most of MC studies are based on histologic analyses performed in animal models. Our methodology represents the first effort to perform dedicated MC analyses in-vivo, in the human retina. The qualitative comparison with histologic reconstructions showed a very good matching with respect to the vertical trans-retinal orientation of the MC in the extrafoveal region. Our analyses showed an underestimation of MC signal detection in the fovea than in the extrafoveal regions. We may advance two hypotheses to explain this finding. The first one is related with resolution limitations, making current structural OCT images not sufficient to detect foveal MC in their entirety. Indeed, foveal MC are more numerous within the fovea than in the rest of the retina, thus making assumable MC sizes below the 8µm threshold of structural OCT sensitivity. Moreover, MC show a very peculiar anatomy at the level of the fovea, following a z-shape morphology, making possible the change of their optical properties and interfering with the proper detection through our approach. The quantitative analysis showed good agreement with previous reports (~42.000/9 mm2 vs ~15.000 cells/mm2 found by previous histologic studies). In conclusion, our study proposed a new method to analyze MC in-vivo, in the human retina.

**Financial Disclosure**
N/A
Retinal microvascular findings in β-thalassemia patients: An optical coherence tomography angiography study

**Purpose**
To assess retinal microvascular changes in β-thalassemia major patients as shown in Optical Coherence Tomography Angiography (OCT-A).

**Setting/Venue**
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

**Methods**
Ten patients with β-thalassemia major and 20 healthy individuals were enrolled in the study. All subjects underwent a history taken and a comprehensive ocular examination. OCT-A scans and metrics were performed using AngioVue software of the Optovue RTVue XR Avanti. Data included 6 mm × 6 mm sections with measurement of the foveal avascular zone (FAZ), non-flow area and vessel densities (VD) in both superficial (SCP) and deep (DCP) capillary plexus.

**Results**
The mean age was 12.8 ± 4.2 years (range: 6-19 years) in β-thalassemia major group and 13.5 ± 3.5 years (range: 7-20 years) in the control group. The mean foveal avascular zone value was 0.264 ± 0.11 mm² in the study group and 0.295 ± 0.13 mm² in the control group. The mean non-flow area value was 0.464 ± 0.12 mm² in the study group and 0.478 ± 0.13 mm² in the control group. The mean whole VD SCP was 52.65 %±2.10 in the study group and 52.70 % ±2.08 in the control group. The mean whole VD DCP was 54.42% ±5.70 in the study group and 55.44%±5.57 in the control group. There were no statistically significant differences between groups with regard to the FAZ and non-flow area (p=0.12 and p=0.45 respectively). No statistically significant difference was found between the two groups in terms of SCP densities (p=0.64). However, there was a statistically significant difference in DCP VDs between the two groups (p=0.04).

**Conclusions**
By using Optical Coherence Tomography Angiography, subclinical retinal anomalies can be detected. Further research with larger sample sizes is needed.

**Financial Disclosure**
The authors declare no conflict of interest.
Early changes in choriocapillaris flow voids as an efficacy biomarker of photodynamic therapy in central serous chorioretinopathy

**Purpose**
To assess the early changes produced in the choriocapillaris (CC) and choroidal (CH) vasculature using swept-source optical coherence tomography angiography (SS-OCTA) in patients with chronic central serous chorioretinopathy (CSCR) as predictors of the efficacy after photodynamic therapy (PDT).

**Methods**
Prospective observational study. A cohort of 52 eyes of 52 patients with chronic CSCR and persistent subretinal fluid (SRF) was included. SS-OCTA scans of the 6x6mm macular region were assessed before; and 2-3 days, one month and three months after half-fluence PDT. Best-corrected visual acuity (BCVA), height of SRF and vessel occlusion in the CC and CH was measured as flow signal voids (FSV). Main Outcome Measures were early increase in FSV in the CC and CH after PDT, and the recanalization after treatment.

**Results**
BCVA before PDT was 75.3 ±12.0 letters in the ETDRS scale, which improved to 81.3 ±11.0 after 3 months (p<0.001). A 3.67 ±4.12 and 2.76 ±3.63 fold increase in CC and CH FV, due to vessel occlusion, was observed at 2-3 days after PDT versus baseline. There was less SRF at 3 months in patients with an increase in FSV (≥1-fold) compared to those without this increase (<1-fold) after PDT (p=0.003). An association between the increase in CC and CH FSV at the early control (2-3 days) and the amount of SRF at 1 month was found (R=-0.405; p=0.002 and R=-0.356; p=0.008 respectively). In a multivariate model, the amount of SRF at one month was not associated with age, gender, axial length, baseline BCVA, baseline CC or CH FSV (p≥0.288). However, there was an association with the increase in CC and CH FSV after PDT (p=0.007). At 3 months, recanalization was achieved in the CH versus the baseline (p=0.619), but there was a persistent increase in the CC FSV (p=0.008).

**Conclusions**
Early vessel occlusion by OCTA after PDT in CSCR was associated with an excellent treatment response. Therefore, an increase in FSV immediately after PDT could be a robust biomarker to predict SRF resorption.

**Setting/Venue**
Hospital Clínico San Carlos, Madrid, Spain

**Financial Disclosure**
Not applicable
**Title**

Autofluorescence lifetime characteristics of optic nerve head drusen

**Purpose**

To investigate fluorescence lifetime characteristics of optic nerve head drusen (ONHD).

**Setting/Venue**

Imaging study in patients with optic nerve head drusen conducted at the University Hospital in Bern, Switzerland.

**Methods**

A fluorescence lifetime imaging ophthalmoscope (Heidelberg Engineering Germany) with 473nm excitation wavelength and two channels to detect emitted fluorescence (498-560nm and 560-720nm) was used. A cohort of 14 eyes with optic nerve head drusen was analyzed. Autofluorescence lifetimes of the ONHD, the optic nerve and the retina were investigated in both spectral channels.

**Results**

ONHD were clearly identifiable as hyperfluorescent deposits in fundus autofluorescence intensity imaging. They featured fluorescence lifetimes of 1200 to 1600 ps (long and short emission spectrum, respectively) compared to 700 and 900 ps in the area of optic disc without hyperfluorescent ONHD. The surrounding retina featured fluorescence lifetimes of 300 ps.

**Conclusions**

Optic nerve head drusen as acellular deposits of metabolic byproducts and components of degradation, feature clearly prolonged fluorescence lifetimes. Fluorescence lifetime analysis of hyperfluorescent deposits may be useful in order to identify its specific content and development over time. This might be helpful for further insight in the pathogenesis of deposits in the retina and the optic nerve head.

**Financial Disclosure**

none
Presenter
Anushree Chauhan India

Purpose
To enhance our understanding of structural changes in Welders' arc maculopathy by obtaining high resolution in vivo En face OCT images. Maculopathy associated to the use of welding devices is an infrequent entity, usually seen in under developed and developing countries. Retinal toxicity secondary to chronic exposure is more frequent. Acute toxicity caused by exposure to welding is very rare.

Setting/Venue
An observational study involving a case series of 6 patients (12 eyes) all males and welders by occupation who presented with blurring of vision after exposure to photo toxic radiations at Vitreoretina department at Shri Ganpati Netralaya, Jalna, Maharashtra, India.

Methods
A comprehensive ocular examination was done including BCVA (best corrected visual acuity), slit-lamp bio microscopy examination, dilated fundus examination by indirect ophthalmoscope and amsler's grid test. Image acquisition with Swept source OCT (b scans), OCT angiography (OCTA) & En face OCT (Topcon DRI Triton) and fundus photography was done.

Results
The age of the patients ranged from 21 to 44 years (mean age 31.17 years).The duration of exposure varied from 1 month to 60 months (mean 19.33 months). BCVA ranged from 6/7.5-6/12 with normal anterior segment. Fundus examination showed yellow spot at the fovea in 8/12 eyes. OCT b scans revealed defect in ellipsoid & interdigitation zone at fovea in all eyes. OCTA was within normal limits. En face OCT revealed hyper reflective area with central hypo reflectivity at the level of outer retina (ellipsoid zone) in all eyes corresponding to central scotoma on Amsler’s grid. The area of defect noted on En face OCT ranged from 124.10 μm² to 1187.57 μm² (mean 496.85 μm² ).The area of defect showed a positive correlation with the duration of exposure. Also an inverse relationship was found between area of defect and BCVA.

Conclusions
To the best of our knowledge no one has studied En face OCT changes in welders' maculopathy till now. It is one of the first series to describe these observations & can be an adjunct in understanding pathology and natural history in photic retinopathies. Corresponding reflectivity changes can be seen on En face OCT, especially in the outer retina. OCTA reveals no changes in vasculature. There is a need for educating people involved in this profession who are mainly in the young age group, regarding appropriate protective measures mainly in the developing countries where the prevalence is more.

Financial Disclosure
NO FINANCIAL DISCLOSURE
Contrast sensitivity in diabetics with and without retinopathy overtime

Purpose
To assess changes in Contrast Sensitivity (CS) in diabetics with no retinopathy (group 1), with retinopathy but no macular edema (group 2) and retinopathy with macular edema (group 3) over a period of one year.

Setting/Venue
Prospective, non-interventional study done in the out patient department of regional referral centre

Methods
30 eyes each of patients in group 1, 2, and 3 were studied over 1 year with follow up at 6 months and 12 months. All patients underwent a complete eye exam, dilated indirect ophthalmoscopy, SD-OCT of macula and Contrast sensitivity using Pelli-Robson chart at 1 metre. The main outcome measure was changes in CS overtime from baseline in all three groups.

Results
The Contrast sensitivity in-group 1: 1.49 +/- 0.19 at baseline, 1.47 +/- 0.21 at 6 months, and 1.46 +/- 0.21 at 12 months. Contrast sensitivity in-group 2: 1.46 +/- 0.15 at baseline, 1.47 +/- 0.15 at 6 months, and 1.37 +/- 0.15 at 12 months. Contrast sensitivity in-group 3: at baseline, 6 months, and 12 months was 1.21 +/- 0.23, 1.20 +/- 0.22, 1.19 +/- 0.22. On comparing groups 1 with 3 and 2 with 3, significance was noted at all 3 time zones.

Conclusions
There was no deterioration in CS over baseline during the 1-year follow-up in Group 1 and at 6 months in-group 2. However, deterioration in CS became significant in group 2 at 12 months. Interestingly, CS did not deteriorate significantly overtime within group 3 but was significantly lower when comparing group 3 with either 2 or 1.

Financial Disclosure
None
Comparison of conventional color fundus photography and multicolor fundus imaging in the detection of lesions in diabetic retinopathy and retinal vein occlusion

To evaluate the degree of agreement for detection of lesions in eyes with diabetic retinopathy (DR) and retinal vein occlusion (RVO) between conventional fundus photography (CFP) and multicolor fundus imaging (MFI).

A cross-sectional analysis of consecutive eyes with DR and RVO who underwent CFP (Topcon TRC-50DX® fundus camera) and MFI (Spectralis HRA+OCT Heidelberg Engineering® platform) between January and March 2021. Images were obtained in the same day, after proper pupil dilation. Images in which the details of the optic disc and vascular arcades were not defined were excluded. The following lesions were considered in DR: microaneurysms (MA), microhemorrhages (MH), soft exudates (SE), hard exudates (HE), neovascularization (NV) and laser treatment (LT). In RVO we considered hemorrhages (HR), venous engorgement (VE), venous sheathing (VS) and optociliary shunts (OS). Firstly, an independent and blind analysis of all images was carried out by two experienced medical retina doctors (Observer 1 [O1] and Observer 2 [O2]), and lesions were classified as "present" or "absent". Then, each observer performed a paired comparison in cases where lesions presented in both images of the same eye, to assess if lesions were similarly detected in CFP and MFI. The degree of agreement between observers and between exams was assessed with a Cohen's Kappa. Cohen's Kappa values between 0.41 and 0.60 indicate moderate agreement, between 0.61 and 0.80 indicate substantial agreement and from 0.81 to 1.00 indicate almost perfect agreement.

A total of 115 eyes with DR and 33 with RVO were analyzed. Regarding DR, the agreement between CFP and MFI for O1 was almost perfect for MA, MH and NV and substantial for SE, HE and LT. For O2 was almost perfect for MA, MH, NV and HE and substantial for SE and LT. SE were detected more frequently in MFI by both observers (O1: 17.4% vs 11.3%; O2: 17.4% vs 10.4%), as well as LT (O1: 54.8% vs 38.3%; O2: 52.2% vs 35.7%) and HE (O1: 44.3% vs 38.8%; O2: 45.2% vs 40.0%). Regarding RVO, for O1 the agreement was almost perfect for HR, NV, VE and OS and substantial for VS. For O2 was almost perfect for HR, NV, VE and VS and moderate for OS. VS was detected more frequently in MFI by O1 (12.1% vs 6.1%) and OS in CFP by O2 (24.2% vs 12.1%). On paired analysis O2 considered that in 75% of cases VS was easier to identify in MFI and O1 that in 71.4% of cases OS were better identified in CFP. Agreement between observers was substantial to almost perfect for all lesions in both exams except for OS in MFI (moderate).

The agreement of MFI and CFP to detect lesions in DR and RVO was substantial to almost perfect for most lesions. Despite this, MFI seems more appropriate to detect SE and LT in eyes with DR and VS in eyes with RVO and OS seem easier to detect in CFP. The use of both types of fundus imaging may increase the rate of detection of lesions that otherwise might not be noticed.

No financial disclosures regarding any of the authors.
Purpose
To measure the anatomical characteristics of the macula in fellow eyes of patients with unilateral idiopathic epiretinal membrane (ERM) and to compare them with normal control.

Setting/Venue
One medical center in Taiwan.

Methods
A total of 94 fellow eyes with unilateral idiopathic ERM were gathered as the study group, and their age and gender-matched subjects with no vitreomacular diseases were recruited as the control group. Macular structure parameters including foveal base width (FBW), central foveolar thickness (CFT), central subfield thickness (CST), area of foveal avascular zone (FAZ), and retinal artery trajectory (RAT) were measured using optical coherence tomography (OCT) and OCT angiography and were compared between two groups. Macular structure parameters were compared between the two groups. Regression analysis was performed to evaluate factors that affect FBW.

Results
For the study group, the FBW (418.9 ± 68.7 µm) and area of FAZ (0.38 ± 0.12 mm2) were significantly larger than those in the control group (323.2 ± 74.3 µm, 0.31 ± 0.17 mm2). Their CFT and CST were thinner, and their RAT was wider than those of the control group (p < 0.05 for all). In normal population, females had a wider FBW, a thinner CFT and CST and a wider RAT than males (p < 0.05 for all). Regression analysis showed that female, a thinner CST and a larger FAZ were all correlated with a larger FBW.

Conclusions
Fellow eyes of the unilateral ERM had a larger FBW, a larger FAZ, a thinner CST and a wider RAT than the normal population. This implicates that some centrifugal tractional force may exist on their macula, which eventually may result in the formation of idiopathic ERM. Females had a wider FBW, a thinner CST and a wider RAT than males, which may explain the higher prevalence of idiopathic ERM in females.

Financial Disclosure
No financial relations
Title
Age, gender and ethnic variations of foveal avascular zone parameters and correlation to central retinal thickness

Purpose
The main aim of the study was to assess age, gender and ethnic variation in foveal avascular zone morphology and explore whether such changes correlate with differences in retinal thickness.

Setting/Venue
Patients attending the medical retina clinics at Moorfields Eye Hospital City Road, London with at least one healthy eye who had optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) performed on the same day in between September 2016 to December 2018 were included in the study.

Methods
Retrospective observational study. Healthy eye of participants aged 20 years and above from White, Afro-Caribbean, or South Asian ethnic background were imaged using spectral domain optical coherence tomography (SD OCT) and Angioplex OCT angiogram. Macular angiometrics for superficial capillary plexus was compared between ethnic groups. Correlation between retinal thickness and OCTA parameters were assessed using Pearson's or Spearman's coefficient. Regression analysis was performed to assess the statistical significance of age, sex on macular thickness and OCTA parameters in each of the three ethnic groups. All statistical tests were two tailed (α=0.05) and a p-value less than 0.05 was considered statistically significant.

Results
Among 110 individuals included in the study 47 were Whites, 30 Afro-Caribbean and 33 Asians. The study sample consisted of 68 males and 42 females. The mean age ± Standard Deviation of the Whites were 62.36±12.21 years, 56.47±11.36 years in Afro-Caribbean and 56.39±13.82 years in Asian. The central SVD was significantly lesser in Afro-Caribbean (9.06±3.76 vs 11.26±3.82, p=0.02) and South-Asian (9.04±3.44 vs 11.26±3.82, p=0.009) compared to Whites. The FAZ circularity was similar in the 3 groups. Compared to the Whites, the FAZ area and FAZ perimeter were both significantly larger in Afro-Caribbean (area p=0.001, perimeter p=0.006) and Asian groups (area p<0.001, perimeter p<0.001). Macular thickness in the innermost 1mm ETDRS zone (CST) was significantly lesser in Afro-Caribbean (268.40±31.65 vs 283.44±28.42, p=0.03) and South-Asian (263.21±40.33 vs 283.44±28.42, p=0.01) compared to Whites. Although the FAZ area in females was slightly higher than in males. None of the imaging markers reached statistical significance. FAZ area and perimeter are negatively correlated with central subfield thickness (CST) for whole cohort and among individual ethnic groups. Positive correlation was observed between SVD centre and CST(p<0.01). In age adjusted analysis, CST, superficial central vessel density, FAZ area and perimeter maintained statistical significance like initial unadjusted analysis.

Conclusions
Our study show Caucasians have higher retinal thickness and superficial capillary vessel density with relatively smaller FAZ area and perimeter compared to the Afro-Caribbeans and Asians. However, these parameters were not significantly different when Afro-Caribbeans were compared with Asians. These observations hold true even after age adjustment, although not so when adjusted for sex. Our results also suggest CST is negatively correlated with FAZ area and perimeter while a positive correlation exist between retinal thickness and vessel density of individual sectors of ETDRS recommended 3mm inner ring.

Financial Disclosure
No financial interest
Title
Dark-field scanning laser ophthalmoscopy for prediction of central serous chorioretinopathy responsiveness to laser therapy

Purpose
To study the potential of dark-field scanning laser ophthalmoscopy (DF-SLO) for the prognostication of non-chronic central serous chorioretinopathy (CSC).

Setting/Venue
Prospective single-center cohort study.

Methods
Fifty-two eyes of 52 patients (44 males and 8 females, mean age of 45.4 ± 8.8 years) with acute CSC were included in this prospective cohort study. At baseline, all patients received multimodal imaging including DF-SLO and then were observed until resolution of subretinal fluid or, in non-resolving cases, treated with laser therapy. At the end of the follow-up, each case was categorized as either, self-resolving, resolving after laser treatment, or non-resolving after laser treatment. Presence of granular retinal pigment epithelium (RPE) pattern and the lucency of RPE/choroid complex at the leak on DF-SLO images were used by the masked grader to identify non-resolving after laser treatment CSC cases.

Results
Using baseline DF-SLO images, the masked grader correctly classified 45 of 52 (86.5%) CSC cases as being self-resolving (demonstrated no changes on DF-SLO), resolving after laser treatment (demonstrated only RPE granular pattern), or non-resolving after laser treatment (demonstrated RPE/choroid complex lucency). Among cases which resolved and those non-resolved after laser treatment, the grader correctly classified 33 of 36 (91.4%) of cases. The area under the ROC, sensitivity, and specificity of DF-SLO used by the masked grader to identify cases which are non-resolving after laser treatment were 0.92 (confidence interval (CI) 0.79 to 0.98), 86.7% (CI 59.5% to 98.3%), and 96.6% (CI 82.2% to 99.2%), respectively.

Conclusions
DF-SLO at baseline may be a useful technique in prediction of self-resolution and response to laser treatment in acute CSC. Self-resolving cases typically demonstrate no changes with DF-SLO, while cases requiring laser treatment usually show granular RPE changes with or without the lucency at the leak. The presence of the lucency and the large area of granular RPE changes may indicate a higher risk of laser treatment failure.

Financial Disclosure
The authors have no proprietary or financial interest in any aspect of this report.
Title
Macular changes in Mucopolysaccharidosis type I patients

Purpose
To describe retinal findings in two patients with mucopolysaccharidosis type I (MPS I).

Setting/Venue
Department of Ophthalmology, Centro Hospitalar Universitário São João, Porto, Portugal

Methods
A complete ophthalmologic examination, fundus photography, near infra-red imaging (NIR), spectral-domain optical coherence tomography (SD-OCT), and En face SD-OCT were performed.

Results
We describe a case of a 12-year-old female with a diagnosis of Hurler’s syndrome with a severe genotype (homozygous status for the mutation c.1293G>A; p.W402X, exon 9, in the IDUA gene) that underwent HSCT and ERT on the first year of life. The visual acuity was 5/10 in both eyes and bilateral grade 2 corneal haze. Spectral domain optical coherence tomography (SD-OCT) revealed thickening of the external limiting membrane (ELM) at the fovea. In the parafoveal and perifoveal regions, SD-OCT displayed a loss of the interdigitation, ellipsoid, and myoid zones and of the ELM accompanied by progressive thinning of the outer nuclear layer. Fundus infrared imaging revealed a hyperreflective ring centred on the fovea and hyporeflective areas in temporal parafoveal regions in both eyes. En face OCT imaging revealed two hyperreflective rings on the outer retinal level. The second case is a 5-year-old female with a diagnosis of Hurler- Scheie’s syndrome with a moderated genotype (homozygous status for the mutation c.1598C>G; p.P533R, exon 11, in the IDUA gene). She had bilateral grade 2 corneal haze. SD-OCT revealed thickening of the ELM at the fovea. In the parafoveal and perifoveal regions, SD-OCT displayed had no changes.

Conclusions
These patients developed macular changes with foveal deposition of hyperreflective material and parafoveal thinning, despite early systemic treatment. Systemic therapies can provide an increase in life expectancy and stabilize visual acuity and corneal clouding, although their effect on retinal degeneration is unknown.

Financial Disclosure
None
Incidence and predictors of radiation retinopathy after plaque brachytherapy with I25 for the treatment of uveal melanoma

Purpose
The Collaborative Ocular Melanoma Study (COMS) trial helped establish the efficacy of plaque brachytherapy for the treatment of medium choroidal melanomas, allowing preservation of the globe and, to some extent, of visual acuity. Although local control of the tumor after plaque brachytherapy has excellent success rates, the exposure to radiation inevitably damages the surrounding ocular structures, especially vascular endothelium. Radiation retinopathy (RR) is the most frequent cause of visual loss following plaque brachytherapy and while its incidence may vary according to different centers, it can affect up to 42% of eyes within 5 years of treatment. Our center started treating patients with plaque brachytherapy nearly 8 years ago and is the only center with such expertise in Portugal. We aim to report the incidence of RR, as well as determine the predictors for its development in a group of patients submitted to plaque brachytherapy for the treatment of uveal melanoma (UM).

Setting/Venue
Ocular Oncology Reference Centre, Department of Ophthalmology, Coimbra University Hospital Centre, Portugal

Methods
Retrospective case series of patients consecutively submitted to plaque brachytherapy with I125 for the treatment of UM between November 2013 and October 2020. Patients with a follow-up of less than 3 months were excluded. We reviewed electronic and paper medical records for collection of demographic and clinical variables, as well as tumor variables. Categorical variables were reported as percentages and numerical variables as mean ± standard deviation (SD) or median (interquartile range, IQR) when normally distributed or skewed, respectively. The primary outcome of the study was the development of radiation retinopathy, defined by the presence of microaneurysms, cotton-wool spots, hard exudates, cystoid macular edema, vitreous hemorrhage, and retinal or iris neovascularization. Incidence rates were calculated with 95% Confidence Intervals [95% CI]. We used Cox Proportional Hazards models to identify statistically significant predictors for the development of radiation retinopathy.

Results
We included 147 eyes of 147 patients. Mean age was 61.5 ± 13.4 years and 56.5% (n=83) were female. Median follow-up time was 24 (3-69) months. Choroidal melanomas comprised 89.8% (n=132) of the study sample, followed by the ciliary body melanomas (8.2%) and melanomas of both iris and ciliary body (2%). The incidence rate of radiation retinopathy was 27.7/100 person-years. The incidence rate of rubeosis iridis and neovascular glaucoma were 5.3 and 4.2/100 person-years, respectively. Local tumor control with plaque brachytherapy was achieved in 94.6% (n=137) of patients, while 5.4% (n=8) patients had to be submitted to secondary enucleation, 2 for therapy-resistant neovascular glaucoma and 6 for local tumor recurrence. On a stepwise multivariable model, higher initial tumor thickness (p<0.001) and peripapillary location (p=0.039) were positively associated with the outcome of radiation retinopathy, while higher patient age (p=0.039) and higher radiation dose to the lens (p<0.01) were inversely associated with it.

Conclusions
Concerning tumor control, our results display an excellent local tumor control rate after I125 plaque brachytherapy. Nevertheless, a considerable incidence rate of radiation retinopathy was apparent in our series. This study identified initial tumor thickness, peripapillary location, patient age and radiation dose to the lens as significant predictors for the development of RR.

Financial Disclosure
None
Molecular characterization of retinal hemangioblastomas

Purpose
Retinal hemangioblastomas (RH) are highly vascularized histologically benign neoplasms that can result in blindness due to detachment of the retina or massive exudation of the RH. Patients can either have sporadic mutations in the VHL gene or germline variants seen as part of autosomal dominant Von Hippel-Lindau disease. The VHL protein is part of the VCB-CR complex with ubiquitin ligase activity. This complex can target proteins for degradation by the proteasome. An unstable VCB-CR complex is prone for degradation and deleterious mutations in VHL result in an unstable complex. In the CNS, the cells of the vasculature are VHL+/− whilst the neoplastic haemangioblast precursor like cells are VHL−−. In contrast to retinal or central nervous system haemangioblastomas, malignant Clear Cell Renal Carcinoma’s (CCRC, VHL−−) are extensively characterized, these tumour cells have additional somatic driver mutations. So far, no RH specific (somatic) mutational or copy number variation signatures have been described in literature. It is not known whether RH are distinct entities with other somatic mutations and different from central nervous system hemangioblastomas. Future therapeutic strategies (eg gene therapy or small molecule inhibition) could depend on the presence or absence of additional changes.

Setting/Venue
This research presented here has been performed at the Erasmus MC Sophia Children's hospital in collaboration with the Rotterdam Eye Hospital

Methods
Using whole genome sequencing, we compare the DNA of RH to the patient’s germline DNA. Using publicly available bulk-RNA expression profile datasets we identify cell population markers to be used in single cell sequencing experiments. Next, we selected the gene expression profiles of the stromal cell, pericyte cell and endothelial cell populations from previously published single cell experiments. These signatures are subsequent used to compare the expression profiles of central nervous system and retinal hemangioblastoma transcriptome profiles. Using immunohistochemistry, we evaluate VHL expression and biomarkers for the identification of pericytes, endothelial cells and stromal cells in different tumours of patients of which we determined the somatic mutation signature.

Results
We have isolated sufficient quantity and quality DNA from 4 retinal hemangioblastomas and corresponding germline DNA. The somatic changes in these samples - including Single Nucleotide Variants, small Insertions & Deletions and structural variants - have been assessed. To better appreciate the relevance of the detected damaging alterations, we determined which genes are expressed in normal retina and retinal stromal cells, endothelial cells and pericytes specifically. For this purpose, we first evaluated publicly available bulk-RNA expression profile datasets of micro-vessels, endothelial cells, pericytes, mesenchymoangioblasts, mesenchymal stem cells, smooth muscle cells, retina and choroid too and identified cell population markers. Using these expression profiles, we selected the gene expression profiles of the stromal cell, pericyte cell and endothelial cell populations from previously published eye specific single cell experiments. We developed a core marker set that distinguishes these cells from pericytes, endothelial cells and stromal cells of other locations in the body. Additionally, we evaluated the gene expression signatures of these “retina micro-vessel genes” in central nervous system and retinal hemangioblastoma transcriptome profiles.

Conclusions
RH tumour material is very rare. We have characterized the mutational landscape of four RH and compared it to the other tumours present in four patients. Using a biomarker set we created from bulk-RNA transcriptome profiles of pericytes, endothelial cells and stromal cells, and we characterized retinal micro-vessel & RH transcriptome profiles. This biomarker set can be used in in-vitro induced pluripotent stem cell or direct transformation protocols. We evaluated the genomic landscape of RH using these expression profiles and are currently performing CRISPR/Cas9 gene editing experiments to confirm the results of our experiments.

Financial Disclosure
not applicable
Incidence of uveal melanoma is 1.3 - 8.6 per million in European populations (EUROCARE, 2007), with incidence increasing at higher geographical latitudes. The incidence in Ireland though is notably higher at 9.5 per million. The incidence of uveal melanoma in Northern Ireland (NI) which shares a land border with Ireland, has not been previously reported, but might be expected to be similar or greater than in Ireland given its higher latitude. Survival rates in uveal melanoma have remained stable despite advancements in detection and treatment, with around 30% mortality at 5 years. Within Europe, broad geographic variation was described, with published survival rates from the UK (England and Wales) being the highest. Ireland’s data are awaited. The purpose of this study was threefold: 1) to investigate the incidence of uveal melanoma in NI; 2) to investigate clinical outcomes including recurrence and metastatic rates of patients from NI treated at Sheffield Ocular Oncology Service and 3) to determine the survival rates from uveal melanoma of those patients.

A collaborative study between Sheffield Ocular Oncology Service, Royal Hallamshire Hospital, Sheffield, United Kingdom, and the Northern Ireland Cancer Registry (NICR), Belfast, UK.

To identify incidence data: Anonymised data from NICR were analysed alongside population data from NISRA (Northern Ireland Statistics and Research Agency) to identify the incidence of uveal melanoma in NI. To identify clinical outcomes: Patients with uveal melanoma from NI treated in Sheffield were identified from Sheffield Ocular Oncology Database and pertinent patient data collected from case notes review. Data collected included patient demographics at diagnosis, the site and laterality of the melanoma, basis of diagnosis, tumour dimensions, stage of the primary tumour, date and type of treatment, any tumour recurrence or metastases, and any further treatments. To identify survival data: Information including the date and cause of death, and information on systemic metastases of patients with uveal melanoma treated in Sheffield was collected from NICR in October 2020.

Based on the anonymised NICR data, the incidence of uveal melanoma in NI was 6.9 (95% confidence interval 6.1 – 7.8) over the period from 1999 – 2019. 182 patients from Northern Ireland were diagnosed with uveal melanoma in Sheffield, from 1998 to May 2020 (date of database interrogation), 80 fewer cases than was identified on reviewing the population-based database in the NICR. Data were available for all patients in the Sheffield cohort. All patients were diagnosed clinically, with only 50 patients having histological confirmation of diagnosis. No patients had evidence of metastatic disease at diagnosis. Of those patients treated, 74% received globe sparing treatment, while recurrence of the primary tumour occurred in 7.6%. The median follow-up duration of the cohort was 79.5 months, during which, 27 (14.8%) patients developed systemic metastases from their melanoma, detected a median of 23.0 months following initial treatment of melanoma in Sheffield. As of October 2020, 43 (23.6%) patients had died, 135 (74.2%) were alive and mortality status was unknown for 4 patients (2.2%). The all-cause 5-year survival across all Northern Irish patients treated in Sheffield was 83.9%.

With an incidence of 6.9 per million, the rate of uveal melanoma in NI is much lower than in Ireland, and more in keeping with those published from the rest of the UK and northern Europe. Given the ethnic similarities and that Ireland and NI share the same landmass, we had expected the incidence rate for uveal melanoma to be similar in these two countries. The discrepancy may be due to the Irish data only covering 5 years, in contrast with this study and others which span decades. Given the rarity of uveal melanoma, random variation may have accounted for the difference in incidence over a short period of time. Northern Irish patients treated in Sheffield had excellent clinical outcomes: three quarters of patients were treated with globe-sparing treatments, with low recurrence rates and an all-cause 5-year survival rate of over 80%. This study adds to the body of evidence regarding uveal melanoma on the island of Ireland, in the UK, and Europe as a whole, by presenting data that has not been published before. Given the rarity of uveal melanoma, population-based studies are necessary to complete the picture but further study from more centres is needed.
To suture or not to suture? Comparing clinical outcomes by globe immobilisation technique in Gamma Knife stereotactic radiosurgery for uveal melanoma

Stereotactic radiosurgery (SRS) is an effective treatment for uveal melanoma used widely in Europe, offering excellent local tumour control rates and eye preservation. Its efficacy relies upon accurate localisation of the radiation-dose to the tumour, which is challenging in a mobile eye. Various methods of globe immobilisation have been used; practice at the National Centre in the United Kingdom is local anaesthetic (LA) block with or without suturing of two extraocular muscles. Suturing is employed to limit posterior globe movement during inevitable anaesthetic reabsorption. Some studies have shown that the addition of muscle suturing to LA improves absolute globe immobilisation, as measured by comparing pre- and post-procedure radioimaging. However, controversy and debate exist regarding the clinical relevance of this observation, as no studies have published data comparing immobilisation technique with clinical outcomes. Ocular oncologists differ in their choice of immobilisation technique, even within our national centre. This work was designed to answer this debate.

Methods
We performed a retrospective review of all cases that underwent gamma knife stereotactic radiosurgery for uveal melanoma over a 10-year period (May 2008 to May 2018) at our national centre, with at least 24 months follow up. Data collected for each patient included demographic information, operating ophthalmic surgeon, the globe immobilisation technique used, and follow up duration. The outcomes assessed were primary treatment failure of SRS, local recurrence of melanoma, secondary enucleation and all-cause death rate. At the single National Centre, the three operating oncologists differed in their choice of immobilisation technique: surgeon X always employed retrobulbar LA plus muscle suturing; surgeon Y, prior to 2013, always used peribulbar LA plus muscle suturing, but changed his practice to peribulbar LA alone in all cases; surgeon Z only used peribulbar LA without sutures. The decision as to suture or not depended entirely on operating surgeon preference, the allocation of which was based on organisational convenience not patient-specific factors. Patients who received LA plus muscle suturing were grouped together (Group A) and compared to those who were given LA alone (Group B).

Results
290 eyes in 290 patients were treated during the inclusion period; 118 patients in group A (sutured) and 172 patients in group B (not sutured). The length of follow-up was significantly longer in group A than group B (92 months cf. 53 months, p<0.001). This was a result of the surgeons operating as per their preferences: surgeons who sutured were the longest-serving, and surgeon Y, who performed 233 of the 290 cases, stopped suturing in 2013. This skewed the follow-up duration between the groups. There were no cases of primary treatment failure in either group. With a minimum of 24 months follow-up, only 3 patients experienced tumour recurrence (1 in group A and 2 in group B). There was no significant difference between the two groups with regards to recurrence, enucleation and all-cause death rate, though there was a trend towards a higher secondary enucleation rate in group B. Secondary enucleation was only performed for complications of radiotherapy (e.g. painful blind eye due to rubeosis) and not local recurrence, which was treated by other means.

Conclusions
In this retrospective observational cohort study, no significant difference in clinical outcome was identified between those patients sutured (group A) and those not sutured (group B) during globe immobilisation. This suggests that although extraocular muscle suturing may enhance globe immobilisation in absolute terms, this does not translate to altered clinical outcomes. Limitations of this study include the patients not being randomised between groups: the decision to suture, or not, was made according to the operating ophthalmic surgeon's preference. This led to a significant difference in follow-up duration between the two groups, which must be considered when interpreting the results. It is possible that further recurrences, enucleations or deaths could be identified with longer follow-up, meaning that significant differences in clinical outcomes could occur. Indeed, there is a trend towards a higher secondary enucleation rate in group B, which also has the shorter follow-up. That being said, secondary enucleations are not related to eye movement leading to inaccurate targeting of the tumour, and therefore are unlikely to be due to globe immobilisation technique. Further study is needed examining clinical outcomes with longer follow-up to more clearly answer the debate.

Setting/Venue
The National Centre for Stereotactic Radiosurgery and the Sheffield Ocular Oncology Service, Royal Hallamshire Hospital, Sheffield, United Kingdom.

Financial Disclosure
The authors have no financial relations to disclose and no conflicts of interest.
**Title**
Presumed natural history of combined hamartoma of the retina and retinal pigment epithelium (CHRRPE)

**Purpose**
To correlate structural changes of combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) with patient age.

**Setting/Venue**
Retrospective study. There were 50 eyes of 49 patients (age range 1-74 years) with CHRRPE studied at nine tertiary vitreoretinal institutions.

**Methods**
We analyzed the clinical findings with respect to lesion topography and pigmentation as well as investigated the optical coherence tomography (OCT) findings regarding the thickness, vitreoretinal interface, outer plexiform layer distortion, ellipsoid zone disruption and retinal pigment epithelium/Bruch’s membrane complex involvement of CHRRPE. Main outcomes: Clinical and imaging findings of CHRRPE at different ages.

**Results**
Analysis of 50 CHRRPE revealed younger patients were more likely to have partial thickness involvement of the retina ($p = 0.009$) with predominantly inner retinal layer involvement ($p = 0.04$). The inverse was true for older patients with CHRRPE. In addition, older patients more commonly showed pigmentary changes. Eyes with CHRRPE were more likely to have an increase in central macular thickness independently of tumor location.

**Conclusions**
Based on these findings, we believe that CHRRPE typically begins in the inner retina and continues towards the outer retina over time, with increase in central macular thickness, despite the location of the tumor.

**Financial Disclosure**
K. Bailey Freund is a consultant to Regeneron, Allergan, Zeiss, Bayer, Heidelberg Engineering and Novartis. He receives research funding from Genentech/Roche. Jay Chhablani is a consultant for Allergan, Novartis and OD-OS. The remaining authors have no relevant disclosures.
# Transpupillary thermotherapy in children with retinoblastoma: 10-year experience

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## Purpose
To evaluate the efficacy of transpupillary thermotherapy for retinoblastoma.

## Setting/Venue
National Medical Research Center Academician S.N. Fyodorov Intersectoral Scientific and Technical Complex “Eye microsurgery”, Ministry of Health of Russia; 59a Beskudnikovsky Blvd., Moscow, 127486, Russia

## Methods
In a retrospective study, we reviewed case series of 177 children with retinoblastoma (1156 tumors in 224 eyes) treated with transpupillary thermotherapy at the S. Fyodorov Eye Microsurgery Federal State Institution in Moscow between October 2011 and December 2020. The median patient age at the time of treatment was 16.8 months. The mean tumor thickness was 1.1 mm (from 0.2 to 4.5), the mean basal diameter was 2.2 mm (from 0.3 to 13.4). Transpupillary thermotherapy was performed using a diode laser with the following parameters: wave length-810 nm, spot diameter-1200 microns, power from 200 to 800 mW (mean - 350 mW), exposure-from 3 to 15 s in the application mode, and continuous in the scanning mode.

## Results
Overall tumor control was achieved in 92.7% (1072 tumors). Tumor recurrence was observed in 7% (82 tumors) and these tumors were treated with other local methods. 209 eyes (93%) were preserved. 15 eyes (7%) were enucleated due to tumor progression, total retinal detachment, vitreous hemorrhage or subatrophy of the eyeball. Complications after transpupillary thermotherapy included local vitreous hemorrhage (2 eyes; 0.9%), pretumoral hemorrhage (3 eyes, 1.3%), local vitreous opacities (2 eyes; 0.9%), iris atrophy and anterior synechiae (1 eye, 0.45%). The median follow-up was 35.5 months.

## Conclusions
Transpupillary thermotherapy is an effective treatment for retinoblastoma with excellent local tumor control and few complications. It can be used for destruction of small primary tumors of both post-equatorial and pre-equatorial localization, residual tumors after inefficiency of other local methods, and is also effective in the treatment of cavitary tumors located in functionally significant areas of the fundus.

## Financial Disclosure
No
### Purpose

Choroidal melanoma is the most common primary intraocular malignancy in adults. ILs and small CMs represent early-stage disease and many of these are monitored closely before treatment. Current therapies focus on local control of tumor growth, most often with radiotherapy, which is associated with severe adverse effects including irreversible vision loss. VDCs are a new drug class, analogous to antibody drug conjugates (ADCs), consisting of a recombinant virus-like particle (VLP) that specifically targets malignant cancer cells and a cytotoxic payload that is conjugated to the surface of the VLP. AU-011 is a first in class VDC that binds selectively to malignant melanoma cells in the eye and upon light activation causes acute necrosis of the tumor cell. The pro-immunogenic mechanism of cell death may lead to long-term anti-tumor immunity. Safety and preliminary efficacy of AU-011, has previously been observed in a Phase 1b/2 trial which utilized the intravitreal route of administration. The current Phase 2 trial is designed to evaluate the safety and efficacy of AU-011 when administered via suprachoroidal (SC) injection. Trial design using SC administration and interim safety from the open-label dose escalation phase will be presented.

### Setting/Venue

Phase 2, multicenter trial with an open label dose escalation phase and a dose expansion phase to assess the maximum tolerated dose (MTD) and the initial safety and efficacy of AU-011, respectively. This ongoing trial is being conducted at 19 ocular oncology sites in the US.

### Methods

Dose escalation comprised of an open-label, ascending single and repeat dose phase of the trial designed to determine the highest tolerated dose using up to 3 dose levels with one or two laser applications per treatment and repeat dosing to determine the maximum therapeutic regimen of AU-011 via SC administration in subjects with primary IL/CM. Clinically diagnosed subjects with small IL/CM received SC administration of AU-011 at doses of 20µg or 40µg followed by application of near infrared light (689nm) with a laser at a fluence of 50 J/cm². Regimens consisting of 1, 2 or 3 weekly administrations of AU-011 each followed by 1 or 2 laser applications (one cycle) have been evaluated in 5 dose escalation cohorts with the last cohort to receive up to two cycles of treatment. The dose escalation phase will be followed by a randomized dose expansion phase to assess safety and efficacy of the highest tolerated treatment regimen.

### Results

Twelve (12) subjects have been treated in the dose escalation phase of the trial with single and repeat doses up to one cycle for Cohorts 1 through 5, with two cycles planned for Cohort 5. No serious adverse events, dose limiting toxicities or grade 3 or 4 (severe or very severe) adverse events have been reported to date. Key treatment-related adverse events included three reports of mild anterior chamber inflammation in Cohorts 2 & 5 and one report of moderate anterior scleritis in Cohort 3. These events were treated with topical steroid eyedrops, were transient and resolved without sequelae, indicating AU-011 was generally well-tolerated with this route of administration up to the maximum dose tested to date.

### Conclusions

Preliminary results of the trial indicate a positive safety and tolerability profile for AU-011 via suprachoroidal administration with all treatment regimens assessed to date. Due to the favorable safety and tolerability at the highest planned dose of 40 µg and 2 laser applications per treatment day with 1 cycle of therapy, the Sponsor is planning to assess one more dose escalation with an increase in the dose to 80 µg and 2 laser applications per treatment day. The randomized dose expansion phase of the trial is planned to begin later in 2021 in subjects with documented growth to evaluate the safety and efficacy of AU-011 with the highest tolerated and feasible regimen for the treatment of IL/CM.
Purpose
The aim of this study was to review and describe the clinical features, management and outcomes of twenty consecutive patients with circumscribed choroidal hemangioma (CCH).

Methods
The clinical records of twenty eyes of twenty patients with CCH diagnosed at our center from 2008 to 2020 were retrospectively reviewed. Data were collected from electronic medical records, angiographies, retinographies and optical coherence topographies (OCTs). Main outcome measures included: absence of exudative retinal detachment 12-months after photodynamic therapy (PDT), number of PDTs, combined treatment (PDT and anti-angiogenic intravitreal injections) and final visual acuity (VA). Twenty patients (20 eyes) aged from 37 to 79 years (mean 61.5) diagnosed of CCH were included in the study. Six patients were females, and fourteen patients were males. Mean age at presentation was 54.6 years with a follow up period between 1 and 12 years. Only one patient lost follow up after 6 months since he moved to another city. At first visit, diagnosis was done based on clinical features and fluorescein angiography and indocyanine green angiography were performed to confirm the diagnosis in some cases. OCT was done in all follow-up visits.

Results
5 patients (25%) were asymptomatic and didn’t have exudative retinal detachment. These five patients were observed with a follow up period ranging from 1 to 12 years and VA remained stable. Exudative retinal detachment was observed in 15 patients (75%), 8 of which also had cystoid macular edema in OCT. Blurred vision was the main symptom followed by metamorphopsia. Patients were treated if VA decreased due to the presence of subfoveal fluid and treatment was stopped when foveal exudation resolved completely. When subfoveal fluid was detected, 2 patients had VA of counting fingers due to macular atrophy and the rest had a mean VA of 20/50. Six patients (40%) were treated with PDT only; four of them required more than one session (mean of 3.5). The remaining patients (53.33%), were treated with both PDT and Anti-VEGF intravitreal injections 5 cases at treatment initiation, and the other three after lack of complete response to PDT. One patient developed subfoveal fluid during COVID-19 lockdown and was treated with one anti-VEGF intravitreal injection with complete and maintained resolution of fluid after 6 months. Final VA improved in 5 patients and stabilized in 6 patients with a follow-up of at least 12 months.

Conclusions
Circumscribed choroidal hemangiomas are rare, benign vascular intraocular tumors without systemic associations. They have a typical clinical appearance and symptoms vary considerably and range from an asymptomatic lesion found incidentally to cases of severe vision loss. Overlying subretinal fluid, serous retinal detachment and cystoid macular edema are common findings. Observation is recommended in asymptomatic cases. In our practice, we consider, as previously demonstrated by several studies, that photodynamic therapy is the treatment of choice for symptomatic hemangiomas, with high rates of subretinal fluid resorption and minimal complications. Recently new therapies such as anti-VEGF agents have been introduced. Our aim when using anti-VEGF agents prior to PDT is to reduce tumor thickness through resorption of subretinal fluid and thus try to maximize the effect of PDT. Although we obtained satisfying results when combining PDT and anti-VEGF, we believe that the role of antiangiogenic agents in the treatment of choroidal hemangioma is still uncertain and more multicenter and prospective studies are required.
Neuroretinal inflammatory biomarkers anticipating radiation-induced macular edema

**Purpose**
To evaluate, using spectral domain optical coherence tomography (SD-OCT), the presence of hyper-reflective retinal spots (HRS) as an early imaging biomarker anticipating the development of radiation induced macular edema (ME) in patients treated by Iodine-125 (I-125) brachytherapy because affected by posterior uveal melanoma (UM).

**Setting/Venue**
Institutional, observational, cross-sectional study with prospective enrollment.

**Methods**
Thirty eyes of 30 patients scheduled for I-125 brachytherapy for a primary uveal melanoma without posterior pole involvement by the tumor and/or macular involvement in the irradiation field were prospectively enrolled. Patients were followed every 3 months for 5 years from brachytherapy. All subjects underwent full ophthalmologic examination, including macular SD-OCT, even in en face modality. HRS were localized and measured both in the inner and outer retina by two independent masked graders. HRS were defined as discrete intraretinal reflectivity changes ≤30 μm, characterized by reflectivity similar to nerve fiber layer and absence of back shadowing.

**Results**
Seventeen patients developed ME at a mean time of 24.2 months (±15.1) (group 1). No evidence of ME was identified in 13 patients at 5-year follow-up (group 2). HRS significantly increased in number in group 1 patients between baseline and the last visit before the evidence of ME, both in the inner (p=0.005) and outer retina (p<0.05). HRS increased in number in group 2 patients between baseline and the last 5-year follow-up visit without reaching statistical significance (p>0.05). In group 1, the number of HRS spot at last follow-up before the evidence of ME was statistically related to the OCT central subfield thickness at ME appearance (P =0.05). The intergrader agreement was at least substantial for all HRS measurements (ICC=0.80).

**Conclusions**
SD-OCT documents early discrete intraretinal reflectivity changes (HRS) in eyes treated with eye irradiation. HRS significantly increase in number in patients developing ME, even 6 months before the evidence of ME. HRS could be considered as an early clinical biomarker of intraretinal inflammation in patients treated with eye irradiation, anticipating radiation-induced ME.

**Financial Disclosure**
no
### Title
Complex diagnostic technology for assessing the vascular network of choroidal melanoma

### Purpose
To study the diagnostic capabilities of various research methods in visualization of the neovascular network of small and medium-sized choroidal melanoma.

### Setting/Venue
S. Fyodorov Eye Microsurgery Federal State Institution, St. Petersburg Branch

### Methods
45 patients (45 eyes) with choroidal melanoma (19 men, 26 women), aged 22 to 84 (56.03 ±15.29) years, underwent complex diagnostics using various methods of studying the blood supply to the tumor: ultrasound in the color Doppler mode mapping, indocyanine green angiography and spectral optical coherence tomography-angiography.

### Results
The different diagnostic significance of instrumental methods for the identification of neovascular vasculature in small and medium choroidal melanomas was established: indocyanine green angiography – 89%, OCT angiography – 71%, ultrasound – 77%. In case of “small” choroidal melanomas, indocyanine green angiography (83%) and OCT angiography (79%) are highly diagnostic in detecting tumor blood supply, while the first type of angioarchitectonics of the neovascular bed was diagnosed with a significantly higher frequency. In case of medium melanoma of the choroid, the informative value of angiography with indocyanine green and ultrasound examination was highly significant and made it possible to diagnose the vascular network in all the cases studied. Choroidal melanomas of these sizes are characterized by the presence of predominantly the second type of angioarchitectonics (81%), in which the hypervascular nature of blood flow was significantly more often determined.

### Conclusions
The results of this study demonstrate that the use of an integrated diagnostic approach provides a high diagnostic value in the study of blood supply to choroidal melanoma, which determines the prospects for continuing this study with the aim of a detailed study of the angioarchitectonics of choroidal melanoma.

### Financial Disclosure
The study had no sponsorship.
Minimally invasive prognostication in uveal melanoma patients

Purpose
In uveal melanoma eye-sparing treatment options are being used increasingly. This poses a new challenge: without tissue, molecular analyses cannot be performed, and when therapeutic options arise early detection of metastases will be beneficial. To reduce prognostic uncertainty and detect metastases at an earlier stage, we aim to discover novel ways for prognostication without ocular biopsies. Minimally-invasive prognostication by capturing circulating tumor cells (CTCs) from peripheral blood of uveal melanoma patients. Especially in patients undergoing radiotherapy and for early detection of metastases.

Setting/Venue
The research presented was performed at the Erasmus MC, departments of Clinical Genetics, Ophthalmology and Radiotherapy Rotterdam The Netherlands in collaboration the Rotterdam Eye Hospital, Rotterdam, The Netherlands.

Methods
Nanobead-based immunocapturing of CTCs was performed using magnetic activated cell sorting (MACS). Multiple (uveal) melanoma bead-bound antibodies for capturing and markers for staining of CTCs were used. Blood was drawn at time of diagnosis and at different time points during stereotactic radiation treatment (SRT) and CTCs were isolated. Subsequently, plasma of patients with localized and metastatic disease was isolated and CTCs were retrieved. Slides were scanned and analyzed using Zeiss LSM700 microscope and software.

Results
Blood of patients undergoing stereotactic radiation treatment, metastatic patients and patients with localized disease was analyzed. We were able to quantify circulating tumor cells in 80% of irradiated patients and observed a difference in CTC yield for different days of irradiation. In patients with metastatic disease more CTCs were captured compared to those with localized disease.

Conclusions
CTCs can be captured in UM-patients and more CTCs are seen in patients receiving radiation treatment and when metastases arise. Thus, when no tumor tissue is available, CTC capturing could provide a novel way for minimally invasive prognostication.

Financial Disclosure
none
### Purpose
The aim of this study was to review and describe the clinical features, etiology, management and outcomes of 43 consecutive patients with vasoproliferative tumor of the retina (VPT).

### Setting/Venue
Ocular Oncology Services of the Retina Department in Vall d’Hebron Hospital and in Ocular Microsurgery Institute (IMO) Barcelona, Spain.

### Methods
Clinical records of 43 patients treated at the two centers from 1999 through 2018 were reviewed. Main outcome measures included: type of treatment, visual threatening complications, retreatments needed, tumor regression and final visual acuity. Forty-three patients (46 eyes) aged from 26 to 88 years (mean 55.7) with VPT were included in the study. 21 patients were females, and 22 patients were males. Mean age at presentation was 40.82 years with a follow up period between 1 and 16 years.

### Results
Primary VPT occurred in 58.69% (n = 27) and secondary VPT in 41.3% (n = 19) of patients. Pars planitis was the main pre-existing ocular disease in secondary VPT (42.1%). Patients consulted mainly for vision loss (43.47%) followed by myodesopsias (19.56%). Most frequent visual threatening complications included serous retinal detachment (n=17), vitreous hemorrhage (n= 11), epiretinal membrane (n = 10), posteriorly extending hard exudates (n =9) and macular edema (n=8). Treatment consisted in vitrectomy with endophotocoagulation (n =19), cryotherapy (n=7), slit lamp photocoagulation (n=13) and observation (n=7). Although 20.51% (n=8) of the treated VPT presented a recurrence after primary regression, final regression was observed in all treated cases. A total of 16 eyes (41.02 %) of all treated patients required at least 1 retreatment. When divided into primary and secondary VPT, Visual acuity (VA) of 67.85% of primary VTP eyes (n= 19) were found to be improved or unchanged at last follow-up with a median VA of 20/40 while only 55.55% of the secondary VTP eyes (n = 10) presented similar results with a median VA 20/50.

### Conclusions
Vasoproliferative tumors of the retina are benign, acquired vascular tumors. Most are primary tumors, but in some cases a preceding ocular disease is present. They have heterogeneous evolutions from being asymptomatic to complete visual loss. Therefore, needs to be tailored according to the VA and the visual threatening complications.
# Primary oculo-cerebral lymphoma: A diagnostic challenge

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**Purpose**
to report a case of panuveitis revealing oculo-cerebral lymphoma and demonstrate the supporting role of multimodal imaging in the diagnosis of primary vitreoretinal lymphoma.

**Setting/Venue**
Department of Ophthalmology, Habib Bourguiba University Hospital, Faculty of Medicine, University of Sfax, Tunisia

**Methods**
case report

**Results**
A 53-year-old man patient presented with complains of visual loss in both eyes for the past month. He had not previous medical history. Visual acuity was 2/10 in the right eye, light perceptions in the left eye. Biomicroscopy showed keratic precipitates with cells in the anterior chamber in both eyes. Fundus examination revealed vitritis in both eyes, papillary edema and creamy-yellow subretinal lesions in the right eye; retinal detachment in the left eye. Fluorescein angiography showed hyperfluorescent and hypofluorescent lesions in the right eye. On indocyanine green angiography, hypofluorescent lesions were seen. Optical coherence tomography scans through the lesions revealed subretinal hyperreflective material with pigment epithelium detachments in the right eye. The patient underwent extensive blood work, neurological examination and brain MRI that resulted all negative. He received corticosteroids. A slight improvement was noted after one week of treatment. One month later, the patient developed neurological symptoms. A brain MRI was repeated and an expansive lesion in the internal capsule extending to the midbrain suggestive of lymphoma was detected. Lumbar puncture showed atypical cells and IL10 levels was elevated. The patient deteriorated rapidly, dying a week later despite an attempt of treatment.

**Conclusions**
Primary oculo-cerebral lymphoma is rare (1% of brain tumors) affecting people over 50 years old. It is a serious disease with highly varied clinical presentations. Ocular signs precede neurological manifestations in 80% of cases. The disease typically masquerades as chronic intermediate and/or posterior uveitis in aged patients with no history of uveitis, and it is unresponsive to corticosteroid therapy. In many cases the initial positive response to corticosteroid therapy for presumed uveitis, delay accurate diagnosis. Some characteristics on multimodal imaging, should raise suspicious for primary vitreoretinal lymphoma and lead to a diagnostic vitrectomy and/or retinal biopsy. The prognosis is related to early diagnosis. This case report stresses two points: first, a lymphoma must be one of the diagnosis to evocate if multimodal imaging shows infiltrative signs, second: it emphasizes the value of vitreous analysis searching for lymphoma during chronic uveitis in aged patients.

**Financial Disclosure**
Financial disclosure: None
Long-term results of brachytherapy with 106 ruthenium and 90 strontium plaques for retinoblastoma

Elena Kotova, Russian Federation

Purpose
To evaluate the efficacy of 106Ru and 90Sr plaque brachytherapy in the management of retinoblastoma.

Setting/Venue
National Medical Research Center Academician S.N. Fyodorov Intersectoral Scientific and Technical Complex "Eye microsurgery", Ministry of Health of Russia; 59a Beskudnikovsky Blvd., Moscow, 127486, Russia

Methods
In a retrospective study, we reviewed case series of 120 children with retinoblastoma (194 tumors in 137 eyes) treated with 106Ru and 90 Sr plaques at the S. Fyodorov Eye Microsurgery Federal State Institution in Moscow between November 2007 and December 2020. Median follow-up length was 52.6 months. The median patient age was 26 months. Treated tumors had a mean height and diameter of 2.9 ± 1.2 mm and 6.5 ± 2.5 mm, 1.9 ± 0.5 mm and 4.8 ± 1.7 mm, respectively. Median prescribed doses of 106Ru and 90Sr plaques at reference depth and outer surface of the sclera were 89 Gy and 330 Gy, 174 Gy and 700 Gy, respectively.

Results
Overall tumor control was achieved in 93%. Tumor recurrence was observed in 7% (14 tumors). Eye retention was achieved in 89% of cases (122 of 137 eyes). Radiation complications included retinal detachment (7%), non-proliferative retinopathy (14%), proliferative retinopathy (3%), optic neuropathy (25%), and subcapsular cataract (8%).

Conclusions
Brachytherapy using 106Ru and 90Sr plaques is an effective treatment for retinoblastoma with excellent local tumor control and few secondary complications.

Financial Disclosure
No
**Title**
Multimodal imaging and differential diagnosis of astrocytic hamartoma of the optic nerve head

**Purpose**
To report left optic nerve head astrocytic hamartoma (AH) in a patient with retinitis pigmentosa and make a differential diagnosis of AH by multimodal imaging and ultrasound.

**Setting/Venue**
Morales Meseguer Hospital, Murcia, Spain.

**Methods**
We present an observational case of AH documented photographically. Clinical data were gathered retrospectively from several visits. The data included corrected visual acuity (BCVA), anterior segment features, fundus examination, ultrasound scan, optical coherence tomography (OCT), autofluorescence and fluorescence angiography (FA).

**Results**
Periodic revision of a 60-year-old female patient being followed up for retinitis pigmentosa, treatment with Tamoxifen for breast cancer. BCVA was 20/50 in both eyes. Five years later, the ocular examination was unchanged except for the appearance of the optic nerve head lesion in the left eye. Fundus examination revealed a non-pigmented nodular lesion with translucent appearance, visible retinal vessels and bone spicule pigmentary changes at the retinal mid periphery typical of retinitis pigmentosa. OCT revealed a hyperreflective intraretinal mass. Autofluorescence and FA confirmed the diagnosis of optic nerve head hamartoma. Finally, the lesion was diagnosed as a non-calcified endophytic AH. The appearance of a new mass in the optic nerve head made us to consider other differential diagnoses such as circumscribed choroidal haemangioma, amelanotic melanoma adjacent to the optic papilla, capillary haemangioblastoma excluded due to pinker colouring of vascular nature and breast cancer metastasis due to personal history, ruled out by absence of leopard skin, retinal folds and serous detachment.

**Conclusions**
AH of the optic nerve head and optic nerve is a rare tumor, which has been described in patients with retinitis pigmentosa, is very important to document any growth during the follow-up which is suggestive of AH. Multimodal imaging provides further insight and facilitates an early diagnosis. Differential diagnosis of a solitary mass in the optic nerve head is essential for the monitoring and treatment. Further investigations recommended to exclude tuberous sclerosis and neurofibromatosis if the lesion is bilateral.
Multimodal imaging of retinocytomas: A retrospective case series

Purpose
Retinocytoma is a retinal tumor regarded as the benign equivalent of retinoblastoma (RB) but with the same genetic implications. Gallie et al reported a characteristic clinical triad, which, along with an absence of progression, could diagnose a retinoma: translucent retinal mass (“fish flesh”), calcific nodules (“cottage cheese”) and retinal pigment epithelial (RPE) alterations. Presence of retinocytoma is definitive evidence of the presence of the RB1 gene. This is especially important in patients with unilateral RB, normal contralateral eye and no family history of retinoblastoma. Knowledge of retinocytoma is limited due to its rarity and based mainly on clinical findings. Few histopathologic studies, performed on eyes that have been enucleated on suspicions of malignancy, reported well-differentiated features. However, there are infrequent reports of malignant transformation, highlighting the importance of regular follow-up with photographic documentation of lack of tumor growth. Advent of imaging modalities like OCT has made ‘optical biopsy’ possible, with a resolution similar to histological sections. Furthermore, OCT Angiography (OCTA) enables non-invasive visualization of the chorioretinal microvasculature within the tumor. This study aims to assess the role of multimodal imaging (MMI) in the diagnosis and monitoring of retinocytomas while attempting to

Setting/Venue
This study includes patients diagnosed with retinocytoma at the Ocular Oncology Clinic of a tertiary ophthalmic institute in South India over a period of five years (2015-2020).

Methods
This was a retrospective case series including 12 retinocytomas in 11 eyes of 10 patients. The age of presentation, chief complaint, past and family history, previous misdiagnoses, laterality, best-corrected visual acuity (BCVA) were recorded. MMI including colour fundus photography (CFP), fundus autofluorescence (FAF), ultrasound B scan (USG), MRI brain and orbit, ultra-widefield (UWF) imaging, fundus fluorescence angiography (FFA), swept-source OCT (SS-OCT) and OCT Angiography (SS-OCTA) were performed. Children below 10 years of age were examined under general anesthesia and underwent Retcam imaging. The presence of the three classical features and additional features like chorioretinal atrophy (CRA), irregular blood vessels, vitreous deposits or cystic changes were documented. Size of each tumour was measured along its largest dimension in disc diameters (DD). Their location was categorized as: • Zone 1 – circle centered on foveola, including optic disc • Zone 2 – ring surrounding zone 1, extending up to posterior end of vortex veins (mid-periphery) • Zone 3 – area beyond zone 2 (far periphery) Qualitative analysis of retinal layers and choroid on SS-OCT and the superficial capillary plexus (SCP), deep capillary plexus (DCP), choriocapillaris (CC) on SS-OCTA was also performed. At each visit, the tumor was documented as stable, progressing or regressing.

Results
The median age was 11.5 years and 80% were males. A family history of retinoblastoma was present in 20%. The mean size of the retinocytomas was 6.45DD. 33.33% of tumours involved zone 1, 25% involved zone 2 and zone 3 each and 16.67% involved both zones 1 and 2. Macular involvement was present in 27.27%, optic disc in 18.18% while both were affected in 18.18%. Translucent mass was present in 66.67%, calcification in 50%, RPE disturbance in 75% and the entire triad in 50% of tumours. 66.67% had CRA. FAF revealed heterogenous pattern with iso- and hyper-autofluorescence centrally and hypo-autofluorescence peripherally. A superficial hyperreflective layer was found in 100% of eyes that underwent OCT, corresponding to the retinal nerve fibre layer (RNFL). In 50% of eyes, inner retinal layers (IRL) including ganglion cell layer (GCL), inner plexiform (IPL) and inner nuclear layer (INL) were further discernible. 66.67% had cystic spaces within the tumour, mainly in the INL. Choroidal thinning was universal. OCT angiography showed choriocapillaris loss with intact SCP and DCP. FFA showed diffuse faint hyperfluorescence with fuzzy margins and corkscREWing of overlying vessels. During a mean follow-up of 5 years, none of the tumours exhibited growth or malignant transformation.

Conclusions
This is the largest case series to date describing the MMI features of retinocytomas. On including CRA as a fourth finding, diagnostic yield increases from 50% to 66.67% for a combination of any 3 of the 4 features. Cysts have been previously suggested to be associated with increased malignant potential; in this study, cysts were seen in 66.67% of tumours but none exhibited malignant changes. Earlier studies have reported retinocytomas as featureless masses on OCT without any discernible layer. One case report identified a hyperreflective superficial layer. In this study, among tumours that underwent OCT, RNFL was identified in 100% and additional IRL in 50%. Preliminary neurosensory retinal differentiation in retinocytomas is a novel finding that has not been previously reported. It provides further evidence that retinocytomas arise de novo and are not spontaneously regressed RBs as previously believed. Retinoblastomas have full-thickness retinal replacement with disorganized tissue on OCT. Preserved retinal layers on OCT not only indicate a benign nature but can also be used to distinguish retinocytomas from RB. FFA and OCTA findings suggest intrinsic vascularity of retinocytomas. Thus MMI provides new insights into the pathology and natural history of retinocytomas and is an excellent tool for serial monitoring.
Involvement of heparin binding protein midkine in vitreous of patients with proliferative diabetic retinopathy

**Purpose**
This study aimed to evaluate whether midkine (MK) expression in the vitreous of proliferative diabetic retinopathy (PDR) patients and non-diabetic patients can play a role in pathogenesis.

**Setting/Venue**
Trakya University, School of Medicine, Edirne, Turkey

**Methods**
Patients who underwent surgery for epiretinal membrane and macular hole were considered as the first group (control group, n=20). Patients who were operated on for vitreous hemorrhage (VH) and tractional retinal detachment (TRD) secondary to PDR were considered as the second group (without aflibercept) (No preoperative anti-VEGF application: NPa-VEGF, n=15). The third group consisted, patients who were operated on for VH and TRD secondary to PDR, and who were injected with intravitreal aflibercept one week before the PPV surgery (with aflibercept) (Preoperative anti-VEGF application: Pa-VEGF, n=14). The concentration of MK, interleukin (IL) 6, and IL8 found in vitreous samples were determined by Enzyme-Linked Immunosorbent Assay (ELISA) using specific kits.

**Results**
The study included a total of 49 eyes of 49 patients undergoing PPV. The expression of IL-6 in vitreous samples of NPa-VEGF and Pa-VEGF was not significant (p> 0.05) compared to controls. Similar to IL-6, there was no difference in IL-8 concentrations between patient groups in vitreous samples (p> 0.05). The NPa-VEGF (p<0.007 vs control) and Pa-VEGF (p<0.046 vs control) groups had a significantly higher concentrations of MK in the vitreous fluid of the patients compared to the control group.

**Conclusions**
The findings of this study suggest that increased MK levels may play a role in PDR pathogenesis and may be used to prevent PDR or define new treatment strategies.

**Financial Disclosure**
No financial relationship with any of the commercial products or vendors in this presentation.
Barriers to adherence to neovascular age-related macular degeneration and diabetic macular edema management plans: A multi-national qualitative study

**Purpose**
Real world evidence has shown that patients with neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) treated with anti-vascular endothelial growth factor (anti-VEGF) therapies achieve lower vision improvements compared to patients in clinical trials. This has been partly attributed to treatment burden, which can impede a patient’s ability or willingness to follow their management plan (i.e. adherence). This study aimed to understand the current treatment experiences, satisfaction and barriers to adherence in nAMD and DME from patients’, caregivers’, and physicians’ perspectives in a multinational setting and to suggest how future therapies might improve treatment experience.

**Setting/Venue**
This multinational qualitative study was conducted in USA, Canada, France, Germany, Italy and Spain. One-time individual concept elicitation-style telephone interviews with patients, caregivers and retina specialists were conducted between June and October 2020 by trained and experienced interviewers.

**Methods**
Adult patients with nAMD/DME treated with anti-VEGF injections for ≥12 months, their caregivers, and experienced retina specialists participated in 1:1 individual concept elicitation-style phone interviews. Participants were recruited through recruiting databases, physician referrals, and social media for patients and caregivers, and through panels for retina specialists. Interviews were audio-recorded, transcribed verbatim, translated into English when needed, and de-identified to ensure participants’ confidentiality. Interview transcripts were analyzed qualitatively using thematic analysis methods based in the grounded theory tradition to identify concepts related to treatment experience and drivers of and barriers to following a management plan.

**Results**
Altogether, 62 retina specialists, 49 nAMD and 46 DME patients and 79 caregivers (of 47 nAMD, 33 DME patients) were interviewed. Seventy-nine percent of patients and caregivers reported disruptions in their routine on or the day after anti-VEGF injection. The non-adherence rate estimated by physicians was between 0-20%. The majority of nAMD patients (84%) and nearly 2/3rd of DME patients (63%) reported never missing an injection visit. Doctor-patient relationship (70% of patients, 16% of caregivers and 15% of retina specialists), education (36% of patients, 45% of retina specialists but zero caregivers), and overall treatment effectiveness (35% of patients, 24% of caregivers and 31% of retina specialists) were reported as key drivers for patients to follow management plan. Aspects of treatment leading to patient burden and/or non-adherence could be grouped into 3 main categories: tolerability, logistical parameters and human factors. Side effects were reported as barriers by 67% of patients and 66% of caregivers, but only 26% of physicians. All participant types reported fear or anxiety about injections and frequency of visits as barriers similarly, at 42-54% and 18-26%, respectively. Physicians mentioned travel logistics, comorbidities, and overall treatment effectiveness more frequently than patients and caregivers.

**Conclusions**
To conclude, this international qualitative study provides valuable insights into areas for improvement within the nAMD and DME treatment experience. New therapies offering improved or longer-acting effectiveness and better tolerability profiles, along with enhanced patient education may improve nAMD/DME patient compliance with their management plan and help in achieving better real-world vision outcomes. It is important to note that the patient sample may underrepresent non-adherent patients who may have been less likely to volunteer to participate in the study. In addition, adherence was derived from patient self-report, asking patients if they had ever missed an injection visit. Therefore, a complementary quantitative study using medical records should be conducted to provide a more accurate assessment of patient adherence. This quantitative study may also help describe the impact of the COVID-19 pandemic on treatment adherence, which might not have been fully captured both in the interview and the analysis.
Peripapillary pachychoroid syndrome (PPS) is a newly described entity from the pachychoroid disease spectrum (PDS). Distinctively, in PPS, the pachychoroid features are centered in the optic nerve, with peripapillary choroidal thickening, intraretinal and/or subretinal fluid and optic nerve head edema in some eyes. We report a case of an asymptomatic 60-year-old woman with PPS.

Methods
A 60 year’s old woman presented in a routine ophthalmology appointment for glaucoma screening due to positive family history. Complete ophthalmic examination was performed, which included assessment of best corrected visual acuity, biomicroscopy gonioscopy and fundoscopy. Optical coherence tomography (OCT) and Fluorescein Angiography (FA) images were obtained using the Spectralis®.

Results
Upon examination, best corrected visual acuity (BCVA) was 10/10 in the right eye (OD) and left eye (OS). Slit-lamp biomicroscopy gonioscopy, intraocular pressures were all normal, and fundoscopy revealed minor peripapillary atrophy with normal optic discs in both eyes. Optical coherence tomography (OCT) showed no changes in the macula with a decrease in RNFL thickness in the nasal sector that warranted follow-up. An OCT was repeated 8 months later revealing de novo intraretinal fluid extending from the temporal margin of the optic. Six months later, another OCT showed, in both eyes, intraretinal fluid in the nasal macular region extending from the temporal margin of the optic disc, multiple small serous pigment epithelial detachments, peripapillary choroidal thickening and pachyvessels. Fluorescein Angiography demonstrated peripapillary granular transmission hyperfluorescence without leakage. Indocyanine green angiography revealed multiple peripapillary punctate hyperfluorescence spot lesions in mid-to late phase.

Conclusions
Peripapillary pachychoroid syndrome has a relatively benign course, with visual acuity stability, decrease in subfoveal subretinal fluid and nasal macular intraretinal fluid over time. For this reason, watchful waiting is usually the option. When progression is detected, treatments such as PDT and anti-VEGF may be considered. We report a well-documented initial case of this newly described entity. This patient was followed from normal baseline exams to the development of bilateral peripapillary pachychoroid syndrome in one year. Despite its good prognosis, diagnosis and awareness of this entity are in the patients’ best interest.
Clinical characteristics and trauma associated factors with poor visual outcomes in post-surgical removal of posterior segment intraocular foreign bodies in a low-resource setting, Guatemala.

**Purpose**
To identify predictive factors for visual outcomes in post-surgical removal of posterior segment intraocular foreign bodies.

**Setting/Venue**
National Unit of Ophthalmology, Guatemala City, Guatemala

**Methods**
Retrospective chart review of 22 eyes were included. Patients underwent surgical removal of intraocular between January 2018 to April 2020 foreign body from at National Unit of Ophthalmology, Guatemala City. Patients with known history of previous ocular injury, optic disc anomalies, signs of any previous retinopathy were excluded. Clinical characteristics included visual acuity, age, sex, and time from trauma to treatment. In addition, trauma associated variables were size of intraocular foreign body (IOFB), entry site, lesions in anterior and posterior segments. We then retrospectively used the ocular trauma score (OTS) as a predictor of visual outcome. Poor visual outcome was defined as best corrected visual acuity less than 20/200 after surgical removal. Analyses were done using SPSS.

**Results**
Mean (SD) age at presentation was 31.7 (14.09) years old and most were male (95%). Mean time to surgery since trauma was 12.21 hours (8.56 SD) and mean follow-up was 21 (2.2) weeks after surgery. Nearly half of injuries (41%) occurred during unprotected work-related activities (metal was the most common IOFB). Most of eyes had a corneoscleral injure as entry site with formation of traumatic cataract and during the first evaluation, Light Perception visual acuity was documented in more than half (57%) the eyes studied. Larger size IOFB bodies were associated with poor prognosis as with low visual acuity on admission. Predictions of visual outcomes using the OTS correlate with statistical significance the visual outcome on post-surgical removed posterior segment IOFB. Larger size IOFB bodies were associated with poor prognosis as with low visual acuity on admission.

**Conclusions**
According to our findings, the OTS could be a useful tool to predict poor outcomes after IOFB trauma in a low-resource setting like Guatemala. Corneoscleral site of entry, large IOFB and retinal tears were all associated with poor outcomes. The OTS should be implemented upon admission of all eye trauma patients in order to predict poor outcomes.

**Financial Disclosure**
NONE
Retinal microvasculature density and morphology changes in COVID-19 patients

Purpose
To observe possible retinal capillary changes associated to COVID-19 infection and relate them to disease severity. It is well known that global pandemic SARS-CoV-2 causes a prothrombotic state and binds to ACE2 receptors.

Setting/Venue
A case-control study was designed and performed at Vall d’Hebron University Hospital (VHUH) in Barcelona, Spain

Methods
Participants between 18 and 55 years old with PCR-confirmed SARS-CoV-2 infection during the previous 3 months were randomly selected as cases (n=69) and stratified into groups (mild disease, moderate disease and severe disease). Last group included patients who developed acute respiratory distress syndrome with IL-6 values above 40 pg/mL. Control group was composed of 27 healthy subjects. All patients underwent a structured questionnaire, a retinography, a macula-centered OCT and a fovea-centered OCT-A. Statistical analyses were performed to detect vascular density differences in the superficial plexus of the retina.

Results
There were no differences in statistical analyses regarding age, gender, smoking habit, comorbidities or drug intake (ACEI or ARB). Groups of moderate and severe disease had a statistically higher proportion of patients with Latin American origin (p=0.001). No macroscopic abnormalities were observed in retinographies, OCT macular images or in the vascular architecture, but a tendency to a bigger foveal avascular zone area was noted. Vessel densities had a normal distribution in means for central superior and nasal areas. In an ANOVA analysis, after Bonferroni correction for multiple measurements, statistically significant higher central VDs in controls and mild disease groups were noted (control group vs group 2, p=0.009; control group vs group 3, p=0.026; group 1 vs group 2, p=0.006; group 1 vs group 3, p=0.017).

Conclusions
The main finding of the study is the decrease of vessel density in central retina related to severity of COVID-19 disease but absence of macroscopic retinal lesions. There may be several explanations for this fact, for example, indirect consequence of the infection such subnormal oxygenation levels and requirement of supplemental oxygen. For another side, SARS-CoV-2 has been demonstrated to target endothelial cells. This fact could be responsible for capillary closure and micro-thrombotic events, which we eventually could detect as decreased vessel density in the retina and other organs. As angiography OCT is an easy non-invasive study, vessel density in central retina could be a future biomarker for microvascular abnormalities after the infection of SARS-CoV-2.

Financial Disclosure
none
Purpose
To report a case of an acute macular edema with serous retinal detachment on the first day after uncomplicated phacoemulsification surgery with the use of a standard dose of intracameral cefuroxime at the end of the surgery.

Methods
Case report. Uneventful 2.4 mm phacoemulsification surgery with single piece acrylic monofocal intraocular lens implantation into the lens capsule was performed under topical anesthesia (lidocaine 2%) by an experienced surgeon in the right eye (RE). Standard dose of 1mg/0.1mL intracameral cefuroxime (Aprokam) was administered into anterior chamber for prophylaxis at the end of the surgery. Full ophthalmic examination (best corrected visual acuity (BCVA) and intraocular pressure (IOP) measurement, slit lamp (SLE) and fundus examination) was performed before and after surgery. Patient was dismissed with standard topical postoperative therapy: 1 mg/ml Diclofenac eye drops 4 times a day + 2mg/ml+5mg/ml Betamethasone+Chloramphenicol eye drops 4 times a day. On postoperative day 1 color fundus picture and swept source optical coherence tomography (SS-OCT) were acquired using Topcon DRI OCT Triton (Topcon Corporation, Tokyo, Japan). On postoperative day 3 spectral-domain OCT, OCT angiography and multicolor images were obtained with Spectralis HRA OCT (Heidelberg Engineering, Heidelberg, Germany).

Results
A 65-year-old lady underwent an uneventful RE phacoemulsification surgery using a standard dose of cefuroxime solution. She had no significant medical or drug history. Preoperative BCVA was 20/100 in the RE and 20/20 in the left eye (LE). SLE showed a corticonuclear cataract RE and mild nuclear sclerosis LE. IOP was 15 in the RE and 14 mmHg in the LE. Axial length was 24.13 mm in the RE and 24.17 mm in the LE. Fundus examination was unremarkable in both eyes. On the first postoperative day, the patient complained about painless visual acuity deterioration in the RE. BCVA was 20/200, IOP was 19 mmHg, anterior segment was clear with no signs of inflammation. Fundus examination showed diffuse macular edema in the absence of cotton wool spots or retinal hemorrhages. SS-OCT image revealed a serous macular detachment with extensive subretinal fluid and intraretinal cystoid macular edema (CME), especially in the outer nuclear layer. On postoperative day 3, BCVA recovered up to 20/20, IOP was 16 mmHg, anterior segment remained quiet. OCT showed fully reabsorption of the macular edema and subretinal fluid, with complete restoration of the physiological macular architecture. OCT angiography did not show any alteration.

Conclusions
Based on the findings, a diagnosis of cefuroxime toxic retinopathy was made. In the literature there are several reports of early serous macular detachment and CME following the use of intracameral injection of cefuroxime sodium in a high dose. Our case illustrates that, in the absence of vascular or inflammatory causes, a standard dose of cefuroxime may still be associated with sporadic cases of toxic retinopathy. The etiology is not fully understood and might be related to transient RPE Na⁺/K⁺ pump dysfunction and/or Müller cells impairment. Cefuroxime toxic retinopathy should be considered in cases of low visual acuity during the early postoperative period after uncomplicated phacoemulsification surgery. In clinical practice, many cases might go undetected since the poor vision on the first day follow-up can be attributed to other factors such as corneal edema and inflammation and the retinopathy usually improves by the 1-week follow-up. Standard topical anti-inflammatory treatment appears to be safe and effective in such cases and allows to achieve an excellent functional result.
# Endogenous Fungal Endophthalmitis Post COVID-19

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## Purpose
To report endogenous fungal endophthalmitis, post recovery from severe COVID-19 infection in otherwise immunocompetent individuals, treated with prolonged systemic steroids.

## Setting/Venue
Two tertiary care referral ophthalmic institutions in North India.

## Methods
Retrospective chart review of cases with endogenous fungal endophthalmitis post severe COVID-19 infection treated at two tertiary care referral eye institutes in North India.

## Results
Seven eyes of five cases of endogenous fungal endophthalmitis were studied. All cases had been hospitalized for severe COVID-19 pneumonia and had received systemic steroid therapy for an average duration of 42 +/- 25.1 days (Range 18 - 80 days). All the cases initially complained of floaters with blurred vision after an average of 6 days (range 1 to 14 days) following discharge from hospital. They had all been misdiagnosed as noninfectious uveitis by their primary ophthalmologists. All eyes underwent pars plana vitrectomy with intravitreal antifungal therapy. Five of the seven eyes grew fungus as the causative organism (Candida sp. in four eyes, Aspergillus sp. in one eye). Post-operatively, all eyes showed control of the infection with marked reduction in vitreous exudates and improvement in vision.

## Conclusions
Floaters and blurred vision developed in patients after they recovered from severe COVID-19 infection. They had received prolonged corticosteroid treatment for COVID as well as for suspected noninfectious uveitis. We diagnosed and treated them for endogenous fungal endophthalmitis. All eyes showed anatomical and functional improvement after pars plana vitrectomy with antifungal therapy. It is important for ophthalmologists and physicians to be aware of this as prompt treatment could control the infection and salvage vision.

## Financial Disclosure
NIL
Purpose
Myopic choroidal neovascularization (CNV) is the most common sight-threatening complication associated with high myopia. The present study evaluated the efficacy and safety of the intravitreal injection of ziv-aflibercept in patients with myopic choroidal neovascularisation.

Methods
This prospective interventional study was conducted on 20 eyes of 20 patients with active myopic CNV. Twelve patients were 40 years or older. This study was performed in the Ophthalmology Department of Tanta University Eye Hospital, Tanta University, Egypt. Optical coherence tomography (OCT) was performed for all patients at baseline and monthly after injection during the 6-month follow-up period. The main outcome measures were changes in BCVA and CMT. The exploratory outcome measures were CNV size, IOP, and the number of injections needed in each age group during the study period.

Results
Patients with myopic CNV younger than 40 years needed fewer injections (2.00 ± 0.76) than patients older than 40 years (2.50 ± 1.00), with no statistical significance detected between the two groups (p-value 0.246). CNV was smaller in the younger age group (p-value 0.209), best corrected visual acuity (BCVA) improved significantly in the younger and older age groups (p-values 0.001 and 0.028, respectively), and central macular thickness (CMT) decreased significantly after 6 months, from 242.88 ± 23.83 μm to 191.13 ± 13.83 μm in the younger age group and from 251.33 ± 26.60 μm to 197.08 ± 17.64 μm in the older age group (p = 0.001). No significant correlation was found between the final BCVA and either the spherical equivalent or central macular thickness after 6 months, with p-values of 0.135 and 0.145, respectively. No significant changes in IOP were detected in either group after the intravitreal injection.

Conclusions
Ziv-aflibercept is a highly effective and safe drug in cases of active myopic CNV; however, a larger number of patients and a longer follow-up period are needed to confirm our results. This study was retrospectively registered at clinicaltrials.gov (ID: NCT04290195) on 26-2-2021.
Title
Real-life implementation of smartphone-based home vision monitoring in a high volume intravitreal injection service for patients with neovascular Age-related Macular Degeneration and Retinal Vascular Disease

Purpose
A patient-centric approach to modern eye care involves not only bringing care to patients’ homes, but ideally to the palm of their hands. Smartphone-based apps have been developed that allow self-testing of visual function by patients at home. These technologies could contribute to de-centralisation of care for patients with medical retina disease by reducing the number of hospital visits. Potential applications of home vision monitoring include early detection of progression from intermediate to neovascular Age-related Macular Degeneration (nAMD), fellow eye conversion in patients with nAMD in the first eye as well as monitoring of patients receiving anti-vascular endothelial growth factor (anti-VEGF) treatment for nAMD, Diabetic Macular Oedema (DMO) or macular oedema secondary to Retinal Vein Occlusions (RVO). A significant consideration for real-life deployment of home vision monitoring technologies is assessing their uptake and usability by patients and addressing issues around digital exclusion, particularly in an elderly patient population such as patients with nAMD.

Setting/Venue
This service improvement project was conducted in the high volume intravitreal treatment service of Moorfields Eye Hospital, London, UK - a major tertiary care ophthalmology centre. Patients receiving anti-VEGF treatment for nAMD, DMO or RVOs were prescribed a smartphone-based app (Home Vision Monitor, HVM) linked with a web-based data store and associated portal for review of vision testing results by prescribing clinicians. The HVM app has received FDA 510k clearance (myVisionTrack, Vital Art and Science, Richardson, USA) and uses shape discrimination tasks to detect metamorphopsia in the central degrees of vision as a metric of visual function.

Methods
Consecutive patients attending Moorfields Eye Hospital for planned anti-VEGF treatment between May 2020 and February 2021 were offered the HVM smartphone app and advised to self-test their vision at least twice a week. A unique link is established between each patient and the prescribing clinician through a registration code. Vision test results (HVM scores) are reviewed by the prescribing clinician on the on-line portal. A change in visual function equivalent to 0.2 on the LogMAR scale triggers an alert and notification message to the clinical team. A patient survey was conducted for a sub-set of patients using the HVM app to assess patient experience and perceptions as well as capture patient characteristics that could influence uptake and engagement. Data from the HVM portal (frequency of use), the Electronic Health Record (demographic and clinical data) and the patient surveys were used to inform an analysis of parameters influencing uptake (defined as successful installation and use of the app at least on one occasion) and engagement/compliance (defined as any continuous period of 4 weeks with use of the app more than once per week) for participating patients. Analysis was performed as part of a registered Moorfields Eye Hospital service improvement audit.

Results
418 patients were included in analysis of factors influencing uptake and engagement for home-vision monitoring. Of those, 258 patients were active users and 160 non-active (uptake assessment). Of active patients with adequate length of follow-up to determine engagement, 166 patients fulfilled the definition of compliance and 92 did not. 114 active patients completed the patient survey. Uptake was significantly associated with age (every 5 years of older age reduced uptake by 5%, p=0.031), biological sex (female users 1.4 times higher uptake than male users, p=0.036) and positively associated with visual acuity in the better seeing eye (p=0.014) and number of intravitreal injections (p= 0.039). Engagement/compliance was significantly associated with diagnosis (nAMD patients were more compliant than patients with DMO or RVO, p=0.003) and was positively associated with white British ethnicity (p=0.025) and visual acuity in the better seeing eye (p=0.007). In the group that completed the patient experience survey, engagement was higher in patients who reported English as their first language (p=0.006) and had a borderline association with higher satisfaction with app use (p=0.06). After adjusting for age, biological sex and diagnosis, engagement was associated with patients’ level of comfort with digital technologies and visual acuity in the worse seeing eye.

Conclusions
Home vision monitoring with smartphone-based apps has potential meaningful applications for the care of patients with common medical retina disease. The expected benefits from their deployment in real-life clinical practice pertain to early disease detection, personalised re-treatment intervals, reduction of unnecessary hospital visits and patient empowerment for self-care. Before assessing the potential benefits of home vision monitoring, it is crucial to consider the feasibility of wide-spread real-life deployment of such digital tools for self-care. Uptake and usability of self-monitoring technologies are crucial determinants for their meaningful real-life deployment at scale. In this work, we examined the uptake and engagement with home vision monitoring of patients attending a busy injection clinic for treatment of common retinal conditions. This is the first report of real-life deployment of home-vision monitoring at scale in this patient population. A number of demographic, clinical, socioeconomic and patient perception-related factors were shown to affect uptake and compliance of patients with the use of the prescribed smartphone-based app. As healthcare systems increasingly adopt digital models of care, issues such as digital exclusion require careful consideration to ensure equitable access to high quality care for every patient.

Financial Disclosure
Roche provided funding for the service improvement initiative involving the introduction of home-vision monitoring for the care of patients receiving intravitreal injections at Moorfields Eye Hospital, City Road.
**Title**
Unescorted clinic visits: practical consequences of a stressor imposed by the COVID-19 pandemic

**Purpose**
One of the restrictive measures of COVID-19 (coronavirus disease 2019) pandemic control is the prohibition of escorted clinic visits. Ophthalmological patients’ specific features imply different degrees of dependency, directly affecting their response to such quarantine impositions. This study aims to assess the effects of unaccompanied medical appointments in outpatients’ stress level and absorption of medical advice.

**Setting/Venue**
OPHTHALMICA EYE INSTITUTE

**Methods**
A questionnaire-based survey was conducted during September 2020. Suitable subjects were requested to self-administer a 7-item questionnaire addressing subjective perception of stress and their ability to fully understand and recall doctor’s instructions, considering eye examination in the absence of an escort.

**Results**
Analysis was based on two hundred consecutive patients who completed the survey. Sixty-three patients (31.5%) reported unescorted clinic visits increasing stress, with a median value of 7.5 (mean 6.77±2.7) in a scale from 1 to 10. A large proportion of patients (30%) claimed difficulty recalling doctor’s comments or instructions and 24.6% anticipated not fully understanding them, should they attend the clinic unaccompanied. Patients living in smaller towns report the highest stress levels (p=0.002) when attending the clinic alone. A marked impact on women and the elderly above 70 years (up to threefold) was identified.

**Conclusions**
This is the first study specifically addressing practical repercussions of unescorted clinic visits during COVID-19 pandemic. A negative effect on patients’ emotional status and counseling effectiveness was demonstrated. Female gender and advanced age were found as determinants of the highest vulnerability.

**Financial Disclosure**
BAYER NOVARTIS ALLERGAN THEA SPONSORING OF TRAVELLING EXPENSES, SPONSORED LECTURES
**Title**

Optic disc and retinal nerve fiber morphology using optical coherence tomography angiography in systemic lupus erythematosus patients

**Purpose**

To evaluate the optic nerve head and peripapillary retinal nerve fiber layer parameters by optical coherence tomography angiography (OCTA) in patients with systemic lupus erythematosus (SLE) and to compare the findings with healthy eyes.

**Setting/Venue**

Health Sciences University, Antalya Training and Research Hospital, Department of Ophthalmology, Antalya/TURKEY

**Methods**

In this observational cross-sectional study, eyes of 21 SLE patients and 25 healthy subjects were evaluated by OCTA imaging. Only the right eye of each participant was included in the study. Bilateral OCTA images (4.5 × 4.5 mm2) centered at the optic nerve head were obtained using a commercial spectral domain OCTA system. Optic nerve head perfusion was quantified using the split-spectrum amplitude decorrelation angiography algorithm.

**Results**

Optic disc morphology measurements including rim area, horizontal and vertical cup / disc (C / D) ratio were significantly different between the study groups (p = 0.009, p = 0.031, p = 0.031, respectively). Disc area and cup volume were not significantly different between the study groups. Peripapillary and inferior thickness of the retinal nerve fiber layer (RNFL) were significantly lower in the patient group compared to controls (p = 0.034, p = 0.003, respectively). There was no statistically significant difference between the groups in terms of both superficial and whole-area peripapillary perfused capillary density (respectively; p = 0.839, p = 0.497).

**Conclusions**

The results show that C / D ratio is increased and RNFL thickness is decreased in SLE patients compared to control subjects. In the examination of SLE patients, regular evaluation of the optic disc and the clinician's alert for early changes seem important.

**Financial Disclosure**

I have no financial relations.
Quality of life and treatment satisfaction in patients under anti-VEGF intravitreal injections

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Portugal

Purpose
Anti-VEGF intravitreal (IV) injections are the main treatment for diabetic macular oedema (DME) and exudative age-related macular degeneration (AMD). Most studies focus on the clinical results of this therapy, with few evaluating the experience of the patient submitted to this procedure. Our main goal is to evaluate the experience of patients undergoing therapy with IV injections of anti-VEGF, and the impact of the disease and treatment on quality of life (QoL).

Setting/Venue
Department of Ophthalmology, Hospital Garcia de Orta E.P.E, Almada.

Methods
Cross-sectional study with the application of two questionnaires (Retinopathy Dependent Quality of Life and Retinopathy Treatment Satisfaction Questionnaire), adapted to assess satisfaction and QoL of patients undergoing anti-VEGF IV injections. Patients with diabetic macular oedema and exudative AMD were included. Data analysis was performed using SPSS and statistical significance defined by p <0.05.

Results
66 patients answered the survey, 35 (53%) with DME and 31 (47%) with exudative AMD. Mean age was higher in the patients with AMD (73 years vs 69 years). 45% of patients report having poor QoL. The factors with the greatest impact in QoL were the loss of independence, difficulty in pursuing hobbies and financial situation. Patients with DME report worse QoL compared to patients with exudative AMD (p <0.05). Regarding intravitreal injections, 27 patients (43%) refer feeling worried about the pain they may feel during the treatment, however 61% of them classified the treatment as not unpleasant. 65% of the surveyed patients are satisfied with anti-VEGF IV injections and 75% would encourage other patients with the same pathology to undergo it.

Conclusions
This was the first study in Portugal to evaluate the experience of patients undergoing therapy with IV injections of anti-VEGF. We can conclude that the patients surveyed are globally satisfied with the therapy instituted. Despite this, more studies should be carried out to improve therapy compliance.

Financial Disclosure
no financial relations
**Title**
Effect of treatment delay on the outcomes of patients receiving anti VEGF therapy during the first lockdown of COVID-19 pandemic

**Purpose**
Covid-19 pandemic called for a nationwide lockdown in United Kingdom on March 23, 2020 which impacted eye clinic services. Although patients receiving intravitreal treatments for sight threatening conditions like Neovascular Age related macular degeneration (nAMD), diabetic macular oedema (DMO) and retinal vein occlusions (RVO) with macular edema were advised to continue the treatment. Nonetheless, due to the fear of contracting the virus or due to issues like unavailability of transport, many patients were unable to attend their routine appointments which resulted in delay in intravitreal injections, termed as ‘Forced extension’ in the current study. In the current audit, we aim to study the effect of forced extension of treatment interval on the visual outcomes of patients with macular diseases, which include nAMD, RVO, and DMO.

**Setting/Venue**
Intravitreal services at Sunderland Eye Infirmary in United Kingdom

**Methods**
This is a retrospective consecutive case series. Case notes of patients who were already on intravitreal therapy for nAMD, BRVO, CRVO and DMO and had a forced extension in treatment interval during March- June 2020 were reviewed. The parameters recorded were age, visual acuity in letters, treatment interval before and after lockdown, OCT features including central macular thickness.

**Results**
231 eyes of 203 patients were included in the audit of which, 143 eyes had AMD, 47 had DMO and 41 eyes had RVO. The average age was 78 years. Mean VA loss was 5 letters. A spontaneous improvement in VA was noted in 28.6% cases. Stable VA was noted in 6.4% cases overall, where DMO group showed relatively higher percentage of cases (12.8%) maintain stable VA. Amongst cases showing loss of VA, AMD showed maximum cases with loss of vision (67.8%), while RVO group showed maximum cases with Severe loss of VA (7.3%). Cases with moderate and severe loss of vision had a greater number of cases with gain in central macular thickness more than 50 microns. The mean retreatment interval increased from 7 weeks pre-lockdown to 10 weeks post-lockdown. While most cases were being treated at 4-8 weeks at baseline, after lockdown, maximum eyes were being treated at 16 weeks.

**Conclusions**
Post lockdown, a greater number of cases were in 16-week group, suggesting more were observed. Gain and loss of VA are comparable across all disease groups however DMO group had no case of severe loss of vision and RVO had significantly more cases of severe loss of vision. Cases with preexisting intraretinal fluid may be at risk of developing severe or moderate visual loss. These results can be helpful for future patient education, triaging, and treatment decision making.

**Financial Disclosure**
none
Purpose
As cases of COVID-19 continue to fluctuate in “waves” across regions, ophthalmologists must adapt quickly to the changing epidemic pressure to ensure that patients with retinal disease are receiving appropriate treatment while minimizing the risk of COVID-19 transmission. Clear and efficient communication with patients, many of whom will be concerned about how the pandemic affects their access to sight-saving treatment, is more important than ever. This is particularly true for patients with speaking and hearing challenges who may not receive the individualized care they require at a time when healthcare systems are overwhelmed. Here, we discuss simple guidance that can be implemented during the pandemic to ensure optimal treatment, safety, and patient communication.

Setting/Venue
The Vision Academy comprises over 90 international retinal experts who collaborate to provide collective recommendations on clinical challenges in areas where there is a lack of conclusive evidence. The 14-member Vision Academy Steering Committee met in March 2020 to review existing guidance developed for general eyecare visits during the pandemic by ophthalmological societies including the American Academy of Ophthalmology, the French Society of Ophthalmology, the German Ophthalmological Society, and the Royal College of Ophthalmologists.

Methods
The Vision Academy was the first expert group to develop a set of recommendations specifically addressing the need for guidance regarding the management of patients with retinal diseases receiving intravitreal injections of anti-vascular endothelial growth factor (VEGF). As the pandemic progressed with significant local and regional variation in new COVID-19 cases, the guidance was reviewed by the Academy’s membership during its Annual Meeting in August 2020, and updated and graded according to three levels of epidemic pressure. In addition, guidance was developed on how to support patients with hearing and/or speaking challenges during the pandemic. Guidance was voted on by the Vision Academy Steering Committee for consensus.

Results
Management of patients with retinal disease should continue at as close to normal levels as possible during low epidemic pressure and include physical distancing and use of regulation face masks. During high and extreme epidemic pressure, simplification of intravitreal anti-VEGF treatment regimens is recommended to reduce the need for frequent monitoring and dose adjustment. In these situations, those with neovascular age-related macular degeneration (particularly those with ≤2 years of treatment), new patients with significant vision loss, neovascular glaucoma, and monocular/quasi-monocular patients (only one eye >20/40) should be prioritized. Safety measures to limit the spread of COVID-19 can be detrimental to communicating with patients, particularly those with hearing and/or speaking challenges. Face masks disguise facial expressions and prevent lip reading which aids understanding. Masks also alter the audibility of speech, making it more difficult to understand, while physical distancing further reduces the attenuated speech signal, making the conversation even more challenging. Simple steps to improve communication include choosing a quiet, well-lit location with good lighting to aid eye contact and facing the patient directly when speaking. Slow, clear speech with regular pauses, use of written information, hand gestures/body language, and rephrasing rather than repeating the same words can also enhance understanding.

Conclusions
Management of patients during the COVID-19 pandemic should be adapted according to the local epidemic pressure, with prioritization of treatment for those at greatest risk of irreversible vision loss when infection rates are high. Adjustment of anti-VEGF treatment regimens may be required to minimize the risk of patient exposure to COVID-19, but special care must be taken to ensure that patients continue to receive appropriate treatment to avoid long-term vision loss. Clear communication is essential to reassure patients during this challenging time, and small adjustments to how to approach patient conversations can enhance understanding and help ensure the delivery of best possible care.
**Title**
Assessment of the response to multiple photodynamic therapies in patients with chronic central serous chorioretinopathy

**Purpose**
Photodynamic therapy (PDT) is one of the main effective options for chronic central serous chorioretinopathy (cCSCR) treatment. When this therapy fails to achieve complete resorption of the subretinal fluid (SRF), no other rescue therapy has demonstrated to be highly effective. Therefore, the purpose of the present study is to assess the efficacy of an additional PDT in cCSCR patients who underwent two or more previous failed PDTs.

**Setting/Venue**
Hospital Clínico San Carlos, Madrid, Spain

**Methods**
Ten patients with cCSCR who have received two or more PDTs without complete resolution of the SRF or with early recurrence (before 3 months) were included. An additional half fluence PDT was performed at least three months after the previous PDT. Best-corrected visual acuity (BCVA), swept-source optical coherence tomography (OCT) and OCT angiography were performed before, 3 days, 1 month and 3 months after treatment. Age, gender, axial length (AL), subfoveal choroidal thickness (SFCT) and SRF height were collected. A 6 x 6 mm scan centered in the macula was performed to assess the vessel occlusion in the choriocapillaris (CC) and choroid (CH) measured as flow signal voids (FSV) (Plex Elite 9000, Zeiss, Germany). Wilcoxon test for paired samples was calculated.

**Results**
Median age was 55.5 years (range 42 to 62). The median number of previous PDTs was 3 (range 2 to 4). The median SFCT before the additional PDT was 418 µm (340 to 711) and after treatment was 379 µm (294 to 579) (p=0.008). The BCVA before and after treatment was 80 letters (50 to 95) and 82 letters (55 to 95) (p=0.109). Median SRF was 94 µm (50 to 306), being after PDT 0 µm (range 0 to 77) respectively (p= 0.005). After the additional PDT, 6 out of 10 patients (60%) had a complete response in SRF resorption. 3 of the 4 non-responders did not present CC occlusion 3 days after PDT. On the contrary, all patients who had a complete response (6/6) had an occlusion in the CC at 3 days after PDT.

**Conclusions**
Despite previous PDTs have failed in patients with cCSCR, good anatomical results could be achieved. Therefore, it seems to be a good option to perform a new attempt since there are no other superior effective treatment alternatives. Moreover, if an early vessel occlusion in the CC was observed it is more likely to achieve a complete response.
Purpose
Retinal manifestations have been described in COVID-19 patients, but it is unknown whether SARS-CoV-2, the causal agent in COVID-19, can directly infect posterior ocular tissues. Here we investigate SARS-CoV-2 host factor gene expression levels and their distribution across retinal and choroidal cell types.

Methods
Query of single-cell RNA sequencing data from human retina and choroid.

Results
We find no relevant expression of two key genes involved in SARS-CoV-2 entry, ACE2 and TMPRSS2, in retinal cell types. By contrast, scarce expression levels could be detected in choroidal vascular cells.

Conclusions
Given the current understanding of viral host cell entry, these findings suggest a low vulnerability of the posterior eye segment to SARS-CoV-2 with a potential weak spot in the vasculature, which could play a putative causative role in ocular lesions in COVID-19 patients. This might qualify the vasculature of the human posterior eye segment as an in vivo biomarker for life-threatening vascular occlusions in COVID-19 patients.
Efficiency of various dual blade vitrectomy systems

**Purpose**
With understandable limitations on the minimalistic size and designs of vitreous cutter, more recent interest has been in the development of dual blade / twin blade cutters that effectively double the cut rate; and at the same time, provide more stable and efficient vitreous fluidics. Furthermore, Dutch Ophthalmic Research Center (DORC) has recently introduced Two Dimensional Cutting (TDC) vitrectome with twin angled blades that promise cut rates up to 16,000 cuts per minute and vastly improved fluidics. Other similar novel twin blade cutter designs include Constant Flow Blade (CFB; Twedge Cutter Blade; Optikon 2000 Inc, Rome, Italy) offering up to 20,000 cuts per minute, Mach2 in megaTRON S4HSP (Geuder, Heidelberg, Germany) and Continuous Flow Cutter in OS4 (Oertli Instruments AG, Switzerland) offering 10,000 cuts per minute. Faster cut rates and small gauge vitrectors have also paved the way for higher infusion pressures. These infusion pressures range from 30mmHg for 20-gauge vitrectomy up to 50 mmHg for 25- and 27-gauge vitrectomy systems. This arrangement facilitates better flow rates through small-bore instruments. The primary objective of this experimental study is to evaluate the efficiency of various vitrectomy platforms as a function of cutter speeds and vacuum in varying in vitro environments.

**Setting/Venue**
In this in vitro experimental study, we used EVAI (Dutch Ophthalmic Research Center, Zuidland, The Netherlands), REVOLUTION! (Optikon 2000 Inc, Rome, Italy) and OS4! (Oertli Instruments AG, Switzerland) as vitrectomy platforms. EVAI vitrectomy system employs a peristatic pump whereas REVOLUTION! and OS4! house both peristatic and venturi pumps. We employed 23-gauge vitrectomy cutters for simplicity and comparison on standardized approach, although smaller gauge cutters were available. For all experiments, we used the dual blade proprietary cutters respective for the machines. this study was conducted in The Aga Khan University, Karachi in 2020.

**Methods**
We use goat eye vitreous, albumin (egg white) and distilled water as vitreous substitutes. All vitrectomy samples were collected using 23-gauge dual blade cutters of respective vitrectomy platforms. The samples included goat eye vitreous, egg white albumin and distilled water contained in 40ml beaker. The samples were obtained at room temperature of 25°C. The samples contained in beaker were placed on a standard precise (up to 0.01g) micro balance (Ohaus Corporation, Pine Brook, NJ, USA). Vitrectomy was initiated at 1000 cuts / minute at 100 mmHg vacuum pressure. The cut rate was incrementally increased by1000 cuts / minute till the maximum capacity. Similarly, all cut rate increments were measured against varying aspiration rates (increments of 100 mmHg) till the maximum aspiration rate. Vitrectomy cutter was switched on for 30 seconds and 3 separate readings (weight in grams) were taken for every single setting. Measurement of aspirated mass in grams was recorded before the start of vitrectomy and then remeasured after 30 seconds of vitrectomy.

**Results**
A direct association of aspirated mass and CPM ranging from 1000-10000 was observed at vacuum pressure varying from 100 to 700 mm Hg for all three machines for water. EVAI and REVOLUTION! aspirated almost similar mass whereas OS4! aspirated low water mass. For egg white, aspirated mass was higher at 4000 CPM both for EVAI and OS4! at 680 and 500 mm Hg of maximum pressure. For REVOLUTION!, maximum aspiration was achieved at 7000 CPM and 4000 CPM at 600 and 700 mm Hg pressure respectively. For goat vitreous aspiration, EVAI aspirated maximum at 4000, 6000 and 8000 CPM at 680 mm Hg, REVOLUTION! aspiration was maximum at 9000 CPM at maximum pressure of 700 mm Hg. OS4! performance was high at maximum CPM and vacuum pressure of 5000 and 500 respectively.

**Conclusions**
When comparing distilled water flow rate across three cutter platforms, we observed linearly increasing mass aspirated as the vacuum increased. Vitrectomy machine with highest vacuum generation ability (REVOLUTION!) has most aspirated at highest vacuum. There was no significant difference in mass aspirated as the cut rate increased; also, the mass aspirated at a certain midrange identical settings also did not differ significantly across three platforms for this Newtonian fluid. This finding is similar to the experiment conducted by Oravecz et al when comparing EVAI and megaTRON! S4 dual bladed cutters while using water as vitreous substitute. A similar experiment was conducted by Abulon et al where he compared Ultravit 23 and 25+ gauge cutters of Constellation Vision system (Alcon Laboratories, Inc., Forth Worth, TX,USA) in a model eye with water as vitreous substitute. He showed that with port biased open, the flow rate decreased with increasing cut rate for any given vacuum settings. This observation is different from ours as we used dual blade cutters in all our experiments whereas single blade cutter was used in Abilons experiment; thus showing superiority of dual blade cutters at maintain stable flow rate across various machine settings.
### Purpose
The pandemic caused by the novel Coronavirus (2019-nCoV) has promoted a global response and created several challenges for the care of ophthalmic disease. Telemedicine refers to the practice of remotely providing healthcare to a patient using telecommunications and has become one of the pioneering strategies in providing safe healthcare in the context of the COVID-19 pandemic. However, large setup costs and new infrastructure is often required to create a fully virtual healthcare platform. Conventionally, this has been avoided in the vitreoretinal service due to the risk of missing peripheral retinal breaks. During the pandemic we have launched a hybrid model of telemedicine. Patients attend clinic, or an offsite location, for a streamlined episode of data acquisition. Several modalities were available, including: widefield imaging, optical coherence tomography (OCT), visual acuity and intraocular pressure measurement and colour photos. A telephone consultation with a VR consultant was then arranged within one week. We have evaluated for traditional endpoints and also the patient experience during this process.

### Setting/Venue
The VR service in an NHS Foundation Trust in the United Kingdom

### Methods
A retrospective observational analysis of consecutive attendees in hybrid vitreoretinal clinics between April and August 2020. Electronic medical records (EMR; MedisoftTM) were then reviewed retrospectively. A random sample of this cohort was interviewed to assess patient satisfaction with the hybrid model of outpatient care.

### Results
Data was analysed for 250 patients. 183 (76%) were follow-ups and of these 13% were within three months of having had surgery. The most frequently encountered diagnoses were full thickness macular hole (26%), retinal detachment (25%) and epiretinal membrane (12%). The most frequent outcome was to be discharged from the VR service (87 patients, 36%). However, 10% of patients required an additional face to face appointment to complete the consultation. 17% of patients were listed for surgery, and 94% of these patients had no changes made to the operative plan during their procedure. 5% (11 patients) of the studied patients had an unplanned appointment within 6 months of attending their hybrid clinic. The unplanned attendances were all due to new symptoms and one patient was identified to have developed a retinal detachment. Satisfaction with this model of care was high with 100% of patients strongly agreeing that they were satisfied. Scoring was also high in areas of convenience, information delivery, safety and expectations. 60% of patients favoured a hybrid clinic appointment in comparison to a traditional face to face outpatient service.

### Conclusions
Initial conclusions from this new service suggest that a hybrid model of patient care offers a viable alternative to virtual or traditional approaches of VR service provision.
Title
The COVID-19 impact on retinal diseases requiring anti-VEGF treatment

Purpose
To investigate the impact of the coronavirus disease 2019 (COVID-19) pandemic in the management and compliance of newly diagnosed treatment-naïve with exudative macular disease (mainly neo-vascular age-related macular degeneration (nAMD), diabetic macular oedema (DME) and retinal vein occlusions (RVO)) or proliferative diabetic retinopathy (PDR), and secondarily its impact on the disease progression.

Setting/Venue
Medical Retina Unit, Ophthalmology Department – Central Lisbon Universitary Hospital Centre

Methods
125 consecutive patients with diagnosis of nAMD, DME, RVO and PDR requiring intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections for the first time, were consecutively enrolled between March 1, 2020, and October 31, 2020, (representing the COVID-19 group). 125 patients presenting between January 1, 2019 and August 31, 2019 (pre-COVID-19 group) meeting the same criteria, were also included for comparison. The number of injections, ophthalmology visits, intervals between them, absences and their reasons, and eventual loss of follow-up, within 6 months after the first injection were assessed for each patient. Best-corrected visual acuity (BCVA) and structural changes to the retina using ocular coherence tomography (OCT) were obtained before and 6 months after the first injection. The two groups were compared to establish if COVID-19 was connected to any treatment delay or loss of follow-up. The BVCA and OCT findings were analysed to assess whether the pandemic resulted in worse visual and structural outcomes.

Results
A total of 250 eyes from 250 patients was included in the study (COVID-19 group: 125 eyes; pre-COVID-19 group: 125 eyes). The first was slightly younger (70.34±13.36 vs. 73.51±11.27; p=0.043). Indications for anti-VEGF treatment were similar in both groups (chi=1.712; p=0.887) and the majority included DME (29.6% in the COVID-19 group and 32.8% in the pre-COVID-19 group) and nAMD (28.8% in both groups). Throughout the 6-month follow-up period, the mean number of injections were significantly reduced in the COVID-19 group (3.08±1.36 vs. 3.54±1.20; p=0.005). The rate of loss of follow-up (for any reason) was smaller in the COVID-19 group (p=0.020). The median number of missed clinical visits or treatment sessions (for any reason) was smaller in the COVID-19 group (p=0.001). There was no significant difference in the interval between injections (COVID-19: 49.89±34.61; pre-COVID-19: 54.56±27.42 days; p=0.258). Baseline BCVA was similar in both groups (COVID-19: 0.71±0.45; pre-COVID-19: 0.74±0.47 logMAR; p=0.577). Baseline central retinal thickness was similar in both groups (COVID-19: 475.98±233.39; pre-COVID-19: 444.74±193.74 micrometres; p=0.287). BCVA improvement (COVID-19: -0.14±0.31; pre-COVID-19: -0.20±0.32 logMAR; p=0.202) and central retinal thickness reduction (COVID-19: -149.00±251.32; pre-COVID-19: -131.54±177.28 micrometers; p=0.575) after treatment were similar in both groups.

Conclusions
Despite the diminished number of intravitreal procedures, the COVID-19 pandemic proved to have no impact in the interval between injections, and there were fewer absences and follow-up losses during the COVID-19 period. This was probably a result of the well-established protocol in our ophthalmology department that prioritized this group of patients, as well as the raised awareness among the Portuguese population for the importance of not neglecting their medical comorbidities despite the pandemic. There were also no significant differences in the BCVA and OCT findings at presentation, supporting the theory that referrals for diagnosis and treatment were not delayed. Furthermore, the COVID-19 restrictions were not associated with worse functional or structural outcomes in these patients.

Financial Disclosure
None
# Central serous retinopathy vs lupus choroidopathy in a patient with systemic lupus erythematosus debut.

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## Purpose
To present the case of a 44 year old male that referred blurred vision after the initiation of corticosteroid therapy for the treatment of systemic lupus erythematosus (SLE). We aim to describe the approach to the differential diagnosis between central serous chorioretinopathy (CSC) secondary to corticosteroid therapy or lupus choroidopathy.

## Setting/Venue
Ophthalmology clinic - La Paz University Hospital. Madrid.

## Methods
This study is conceived as a case presentation, consisting of the clinical and multimodal imaging data gathered by the same ophthalmologists in each visit, during and after the hospitalization of the patient due to severe SLE.

## Results
A 44 year old patient arrived to the Emergency room presenting with anasarca and hypoproteinemia. Due to the finding of positive ANA titles as well as a renal biopsy showing class V nephritis the diagnose of SLE was made and high doses corticosteroid treatment was started. After several days, the patient referred loss of visual acuity (VA). On the first ophthalmological evaluation, visual acuity was 0.25 for the right eye (OD) and 0.4 for the left eye (OS). Funduscopic exam showed a massive neurosensory retinal detachment. Optical coherence tomography imaging (OCT) showed subretinal fluid up to temporal retinal vasculature and papilla on both eyes as well as multiple retinal pigment epithelium (RPE) detachments. Treatment with acetazolamide was initiated. However, the subretinal fluid kept increasing, and worsening of VA was proven (Worse VA achieved: OD: 0.125 OI: Counting fingers at 3 m), while systemic symptoms kept on improving with steroid treatment. Multimodal imaging such as indocyanine green and fluorescein angiography would have been useful, although they could not be performed due to compromised renal function. Improvement of systemic symptoms drove to tapering of the steroids resulting in subretinal fluid regression, achieving a final VA of 1 on both eyes.

## Conclusions
Systemic lupus erythematosus is a heterogeneous rheumatic systemic disease with exceedingly varied clinical manifestations and a diverse pathogenesis. The presence of subretinal fluid during treatment of an outbreak makes it necessary to make the differential diagnosis between CSC and lupus choroidopathy. In our patient, the worsening of ocular findings with steroid treatment while systemics symptoms improved favored the diagnosis of CSC. It was also the more plausible diagnosis due to the reabsorption of the subretinal fluid and improvement of the visual symptoms secondary to tapering of steroids. Lupus choroidopathy is a rare clinical entity that has proven to be a risk factor for severe renal and central nervous system involvement, as well as an indicator of active disease. On reviewing the literature, lupus choroidopathy has shown to respond only to high corticosteroid doses in pulses, which not only improves the visual sympotms but also at the systemic manifestations. It is crucial to detect lupus choroidopathy on time not only to improve the visual acuity prognosis, but also the systemic one.

## Financial Disclosure
No financial interests.
Purpose
Electrical stimulation (ES) of the eye represents a therapeutic approach in various clinical applications ranging from retinal dystrophies, age-related macular degeneration, retinal artery occlusion and nonarteritic ischemic optic neuropathy. In clinical practice, ES of the eye is mainly performed with a transcorneal or transpalpebral approach. These procedures are non-invasive and well-tolerated by the patients, reporting only minimal and transient adverse events recorded while serious adverse effects were not observed. Despite the growing literature on animal models, only clinical parameters have been investigated in humans and few data are available about biochemical changes induced by ES of the eye. The purpose of this study is to investigate the possible mechanism that regulates the beneficial effects of ES on retinal cells function and survival in humans.

Methods
28 patients undergoing pars plana vitrectomy (PPV) for idiopathic epiretinal membrane (iERM) were randomly divided in two groups: 13 patients were treated with transpalpebral ES before surgery and 15 directly underwent surgery. Vitreous samples were collected for biochemical analysis during PPV. Concentration of IL-6, IL-8, IL-10 (as the main cytokines correlated with ES treatment) and VEGF was evaluated. In addition a lipidomic analysis focusing on the amount of ceramides and lysophosphatidylcholines as the relevant (sphingo)lipid classes potentially involved in inflammation was performed.

Results
ES treatment leads to a reduction in the vitreous expression of both pro-inflammatory cytokines, namely IL-6 and IL-8, and pro-inflammatory lipid mediators, such as lysophosphatidylcholine. Indeed, we observed a 70% decrease of lysophosphatidylcholine 18:0, which has been proven to exert the greatest pro-inflammatory activities among the lysophosphatidylcholine class. The content of triglycerides is also affected and significantly decreased following ES application.

Conclusions
The vitreous composition of patients undergoing PPV for iERM changes following ES treatment. Pro-inflammatory cytokines and bioactive lipid mediators’ expression decreases, suggesting an overall anti-inflammatory potential of ES. The investigation of the mechanism by which this treatment alters the retinal neurons leading to good outcomes is essential for supporting ES therapeutic application in various types of retinal diseases.

Financial Disclosure
I do not have any financial relation with any company
Combining Morphology and Function for a more comprehensive Understanding of Retinal Diseases - Exploring new Opportunities of Representing functional and structural Characteristics side-by-side

Purpose
Patients suffering from chronic retinal pathologies, require individually tailored, long-term monitoring and therapy. Usually patient management consists of frequent visits to the ophthalmologist and relatively cost-intensive diagnostic imaging. Both in view of the current pandemic and the availability of long-acting treatment the need for reliable home monitoring strategies are gaining importance. Besides the well-established optical coherence tomography (OCT) imaging, further methods are necessary to quantify visual function. Recently, two self-examination and self-monitoring apps to assess visual distortions that run on mobile devices have become available. The Alleye® mobile hyperacuity task (Oculocare medical Inc. Zurich, Switzerland) is the first application allowing to quantitatively measure and assess the location of visual impairment within the central retina. Using data from a previously published cohort, this study explored a new method of matching morphological features present on OCT scans, with corresponding functional impairment on a spatial level. When the collection time was near, OCT data were matched with corresponding functional data from Alleye®. By studying the interplay between morphological and functional features on the central retina, this study set out to provide new information on the underlying mechanistic relation, a topic that is a lively dynamic, especially on the part of the function, and that repeated measurements are necessary to better describe a patient’s disease state and progression. Overall, this study offers a first step for a system's approach to improve an individual patient’s outcome by integrating information about morphology and function.

Setting/Venue
Originally, patients attending the Medical Retina Service of the Eye Clinic of the Cantonal Hospital Lucerne between March and June 2016 were eligible to be included in the prospective implementation study of the Alleye® application. Primary criterion for the inclusion of patients in the present retrospective study, was the availability of high-quality data from self-examinations via self-monitoring Alleye® test, as well as OCT images acquired during clinical visits in the same time period. Finally, a total of 77 eyes of 53 patients were included and their data extracted from the clinical electronic medical records and imaging databases.

Methods
307 OCT scans of the 77 eyes were transmitted to the Moorfields Ophthalmic Reading Center. Consecutively, a deep learning algorithm was used for segmentation of four morphological features: intraretinal and subretinal fluid (IRF and SRF), drusen and pigment epithelial detachment (PED) and subretinal hyperreflective material (SRHM). From the segmented results 2D enface maps for each morphological feature were created. Using the Gullstrand’s reduced eye model the macular areas associated with the twelve Alleye® tasks (p1-p12) were projected onto the near infrared image acquired with the OCT scans. To create Alleye® heat maps the achieved score values (0-1) were interpolated using an inverse distance weighting function. Temporal matching of hyperacuity tests and OCT scans for every patients was conducted by applying the Hungarian algorithm. Only matching examinations with a maximum of 2 days between the two examination entities were considered. Correlation analysis with pairwise Spearman's and Pearson's tests between Alleye® score values (0-1) of the twelve tasks (p1-p12) and volumes of the four morphological features (SRHM, SRF, IRF and PED), as well as pixel-by-pixel comparison for the Alleye® heat maps and the enface images of the four morphological features were conducted.

Results
Overall, mean age of the 53 study participants was 75 years. The large majority (n=57, 74%) of eyes were diagnosed with age-related macular degeneration (AMD). A maximum time interval of two days between OCT acquisition and the Alleye® self-test date was found for 208 cases. Mean best-corrected visual acuity was 71 (ETDRS, number of letters), mean total Alleye® score (0-100) was 51 (range: 2-100). Considering the temporally first best matching observation per eye pairwise comparisons of Alleye® score values and volumes of the four morphological features showed a small negative correlation for SRHM (rs = -0.164, p <.001 for n=77) and very low, statistically insignificant, but still inverse correlations for PED, SRF and IRF, respectively. Juxtaposition of Alleye® heat maps and enface images of morphological features demonstrated varying patterns with main observations being: (1) When higher volumes of PED, SRF, IRF and above all SRHM were present, the Alleye® heat maps also showed more areas with low score values. (2) While the morphological volumes summarized in the enface images remained relatively stable in a certain case, the corresponding Alleye® heat maps showed changes in appearance, i.e. location change of areas with lowest score values.

Conclusions
In summary, a novel approach for the graphical juxtaposition of morphological and functional data on a two dimensional level is introduced, which allows for a side-by-side comparison of results acquired through these two different diagnostic entities. Due to the retrospective design of the study the preliminary findings require further investigation and confirmation in more controlled future settings. Nevertheless, the available data showed that often high volumes of morphological features PED, SRF, IRF and SRHM go in parallel to reduced hyperacuity function. At the same time, it is determined that there is a lively dynamic, especially on the part of the function, and that repeated measurements are necessary to better describe a patient’s disease state and progression. Overall, this study offers a first step for a system's approach to improve an individual patient’s outcome by integrating information about morphology and function. Hence, the importance of a complementary application of both imaging diagnostic tools and functional testing procedures for precise and earlier monitoring of disease onset and progression needs to be emphasized.

Financial Disclosure
None.
Infectious endophthalmitis: A 10-year retrospective study at a tertiary referral centre

**Purpose**
The aim of this study was to review the number and type of infectious endophthalmitis seen in the emergency ophthalmology service in a tertiary-referral hospital from January 2010 to March 2020. This study also evaluated the diagnostic yield of the different intraocular fluid (aqueous and vitreous samples), as well as blood culture yield when performed.

**Setting/Venue**
Retinal Department of a tertiary-referral hospital (Vall d’Hebron Hospital, Barcelona, Spain)

**Methods**
This was a retrospective study including 106 patients (110 eyes) with clinical diagnosis of infectious endophthalmitis from January 2010 until March 2020 in our hospital. Electronic medical records, as well as microbiology and pathology results were reviewed. All patients had signs and symptoms consistent with infectious endophthalmitis such as redness, pain, decreased vision, >2+ anterior chamber cells, hypopyon, fibrin and/or vitreous haze, as well as a surgical history or a local or systemic infectious focus. Eyes were divided in exogenous (Group 1) or endogenous endophthalmitis (Group 2). Subsequently, Group 1 was divided according to the etiology of exogenous endophthalmitis (postoperative, traumatic, filtering-bleb associated, after intravitreal injection, corneal ulcer associated or other causes). Among Group 1, the diagnostic yield of the cultures of aqueous and vitreous samples was reviewed. In Group 2, blood cultures were also analysed.

**Results**
The series included 106 patients. In 4 patients the disease was bilateral, so 110 eyes were diagnosed with infectious endophthalmitis. In Group 1, 90 eyes were included. Among this group, 32 endophthalmitis were secondary to cataract surgery, 15 happened after intravitreal injection, 14 occurred after pars plana vitrectomy, 11 were attributable to an extension of corneal infection, 7 were due to bleb infection 6 were caused by a penetrating trauma (with or without intraocular foreign body) and 5 were related to other causes. Group 2 included 20 eyes of 16 patients. 78 samples of aqueous humor cultures were performed before starting antibiotic therapy (71 in Group 1 and 7 in Group 2) with a positive result in 22 eyes (31%) and 1 eye (14.3%) respectively. Vitreous cultures were done in 17 patients of Group 1, with a positive result in 6 eyes (35.3%), and in 7 cases of Group 2, with a positive result in 3 eyes (42.8%). In all cases, the vitreous sample was performed by a vitreoretinal surgeon after starting antibiotic therapy. Blood culture tests were analysed in 16 patients of Group 2, getting a positive result in 8 cases.

**Conclusions**
Endophthalmitis is a severe eye infection that can lead to irreversible vision impairment and even loss of the eye. Exogenous endophthalmitis is the most common etiology representing 90 cases (84.9%) in our series, being cataract surgery (35.5%) and intravitreal injections (16.6%) the procedures that cause it most frequently, especially because they are performed with great assiduity in our clinical practice. Endogenous endophthalmitis was diagnosed in 17 patients (16.1%). It is a less common etiology and it is important to suspect it in cases of bilateral disease and when there is no surgical or traumatic history or if there is a distant infection. The diagnosis is clinical, but it is important to search for the causative agent for treatment. Aqueous humor culture is the most widely used test but it is the one with the lowest yield in our series, getting a positive result only in 23 of the samples performed (29.5%), which represents a poorer result compared to the 9 positive results (37.5%) among vitreous culture, even antibiotic treatment had already been established. When endogenous endophthalmitis is suspected, blood culture is a good diagnostic tool with a positive result in 50% of the cases.
**Title**
Impact of COVID-19 lockdown on visual acuities of patients with macular diseases.

**Purpose**
To describe visual outcome of patients who were undergoing intravitreal injection treatment for Age related macular degeneration (AMD), Diabetic macular edema (DME) and retinal vein occlusion (RVO) when COVID-19 pandemic hit UK.

**Setting/Venue**
Macula clinic of a large teaching hospital in UK.

**Methods**
A retrospective observational study was conducted on 500 randomly selected patients receiving intravitreal therapy for AMD, DMO or RVO at the macula clinic at the time of UK national lockdown (16th March 2020) for COVID-19. Patients commencing intravitreal treatment post lockdown, those not attending a face to face follow-up and patients who died post lockdown were excluded from the study. The last recorded visual acuity pre-lockdown was compared to the visual acuity recorded at first visit post lockdown. A significant reduction in vision was defined as a drop of 5 or more EDTRS letters. Where vision loss was recorded, patient’s visual acuity at last visit (at least 12 weeks) after further intravitreal injection treatment was recorded. Delayed treatment was defined as >2 weeks delay than planned interval. Patient demography, indication for injection and total number of injections were also collected from Electronic medical records (EMR).

**Results**
Data was collected from 500 randomly selected patients receiving intravitreal therapy at our dedicated macula service 180 patients were excluded: 141 new presentation post lockdown, 30 no face to face visit, 9 died. The remaining 320 (133 Male, 187 Female, mean age 76), consisted of 175 nAMD, 67 RVO, 68 DME and 10 other macular conditions. A total of 116 patients of 320 (36.25%) had loss of >5 letters at the last visit post lockdown. The highest proportion was AMD patients, 72 of 175 AMD (41.14%). While 26 of 67 (38.8%) RVO patients and 17 of 68 (25%) DME patients had lost >5 letters. AMD patients were less likely to regain visual acuity to pre lockdown level despite further treatment compared to RVO and DMO patients.

**Conclusions**
COVID-19 related lockdown caused disruption of clinical services, resultant delays in intravitreal treatment causes significant loss of vision in patients with macular diseases. The impact is highest for AMD (41%), followed by RVO (38%) and DME (25%). In patients with AMD, it is more difficult to regain vision with further treatment. It is important to recognise potential of irreversible loss of vision in macular patients due to disruption of services. Efforts should be made to continue intravitreal injection treatments in future lockdowns.

**Financial Disclosure**
NA
Purpose
To investigate the impact of Beck Anxiety Inventory Score (BAIS) on choroidal thickness (CT) profile and to determine the use of BAIS to predict CT.

Methods
Between December 2020 and March 2021, participants who underwent BAIS survey were included in the study. Demographic data along with blood pressure (BP) measurements, oxygen saturation and pulse measurements were noted. A comprehensive ophthalmic evaluation was done. Ocular biometry (LenStar LS 900, Haag Streit Diagnostics) was performed. Spectral domain optical coherence tomography (SD-OCT, Heidelberg, Germany) was used to analyse central macular thickness (CMT), retinal nerve fiber layer thickness (RNFLT) and ganglion cell layer thickness (GCLT). Enhanced depth imaging (EDI) OCT technique was used to evaluate CT with a manual caliper. The CT profile included central, nasal, temporal, superior and inferior CT with 1 mm and 2 mm distances away from central region. All measurements were performed at the same time period of the day (between 8.00 AM – 9.00 AM). Exclusion criteria were, any topical or systemic drug use, past ocular surgery and/or ocular trauma, any history of ocular and/or systemic disease and non-optimal OCT measurements.

Results
Totally 31 female and 17 male subjects with an average age of 39.6 ± 8.4 years were included in the study. Mean systolic and diastolic BPs were 104.3 ± 17.2 mmHg; 70.5±10.2 mmHg, respectively. Mean pulse oxymetry was 98.1 ± 1.5 and pulse rate was 84.5 ± 13.1 per minute. The mean AL was 23.6 ± 0.8 mm. The mean BAIS was 8.9 ± 8.8 in the study. Mean CT was 333.5 ± 82.6 µm, 307.2 ± 83.1 µm, 256.9 ± 82.0 µm, 318.5 ± 80.4 µm, 293.2 ± 68.6 µm, 332.6 ± 71.6 µm, 329.4 ± 66.5 µm, 315.9 ± 76.6 µm and 305.1 ± 66.3 µm, in central, nasal 1 mm, nasal 2 mm, temporal 1 mm, temporal 2 mm, superior 1 mm, superior 2 mm, inferior 1 mm, inferior 2 mm quadrants, respectively. No significant differences of CT were present between subjects with high BAIS and without high BAIS (p=0.35). There was no significant correlation between the BAIS score and CMT, GCLT and RNFLT. In a multivariate regression model, as subfoveal CT a dependent variable; age, gender, BMI, pulse rate, systolic and diastolic BPs, AL, BAIS were an independent variables, only AL had a significant association with subfoveal CT (p=0.007).

Conclusions
The BAIS may not be a significant predictor in CT evaluation.
### Title
Relationship between ocular and systemic manifestations of Transthyretin amyloidosis

### Purpose
Patients suffering from Transthyretin (TTR) amyloidosis have been described to show ocular alterations. The objective of this study is to present the relationship between these ocular manifestations and the systemic disorders associated with amyloidosis.

### Setting/Venue
Puerta de Hierro University Hospital, Majadahonda, Madrid (Spain).

### Methods
Cross-sectional, non-interventional study including 52 eyes from 26 patients with hATTR amyloidosis under follow-up by Cardiology and Ophthalmology Departments. A complete ophthalmological examination was performed including: Best-corrected visual acuity (BCVA), axial length measurement, slit-lamp anterior segment examination, pachymetry, endothelial count, funduscopy, fundus photography, optical coherence tomography (OCT), OCT angiography (OCTA), fundus autofluorescence (FAF), infrared reflectance (IR) and fluorescein angiography (FA) in the cases that showed alterations on OCTA. In addition, a retrospective review of clinical records to describe the systemic hATTR involvement was carried out.

### Results
18 out of 52 eyes (34.6%) showed signs of ocular affectation, been women more likely to have their eyes compromised (n=12/18; p<0.05). Most of the affected eyes showed signs of ocular amyloidosis at the posterior pole, been the most frequent ocular manifestation the vitreous deposits (34.61%, 18/52). Among other signs, highlight the presence of amyloid deposits in crystalline lens (n=4/18), vascular deposits (n= 3/18) and retinal parenchyma (n=10/18). The mean time from diagnosis to ophthalmological assessment was 29 months (Range 0-194). Regarding systemic hATTR involvement, 84.61% (22/26) patients showed neurological amyloid related manifestations, 84.61% (22/26) cardiac, 45.4% (10/22) digestive and only 3.84% (1/6) showed renal involvement. 100% of the patients with ocular amyloidosis presented neurological and cardiac involvement simultaneously. Patients under treatment had mild cardiac pathology in contrast to those without treatment (p<0.05); nevertheless, there were not statistically significant differences regarding ocular or cardiac involvement between treatments (p>0.05). Cardiac involvement was related not only with ocular involvement but also with worse visual acuity (p<0.05). Mutations found included: Vall30Met (30.8 %), Glu89Lys (26.9%), Vall22Ile (30.8%), Ser43Asn (11.5%). None of them presented statistical differences in relation with ophthalmological involvement (p>0.05).

### Conclusions
Patients suffering from familial TTR amyloidosis should be subject to a complete ophthalmological examination, specifically those with cardiac involvement, due to their willingness to suffer from ophthalmological complications that may compromise their visual acuity.

### Financial Disclosure
none
Title
Timely management of a Post Injection Cluster Endophthalmitis (PICE) in a low income setting, Guatemala

Purpose
To prove that prompt evaluation post intravitreal antibiotics (12 hours at the most) and not deferral of vitrectomy improves visual outcomes in PICE patients.

Setting/Venue
National Ophthalmology Unit, Guatemala City, Central America

Methods
Retrospective analysis of a Fulminant PICE that occurred in the first week of January 2020 after poor handled multi-dose bevacizumab bottle; At first visit, all patients were managed with intravitreal antibiotics (IVATB), topical and oral antibiotics, and topical corticosteroids. Second visits was scheduled 12 hours after, if their condition worsened, they were admitted for pars plana vitrectomy (PPV); contrary, if their condition remained stable or improved. Patients were then evaluated daily. UCVA and slit lamp examination were obtained in every follow up visit.

Results
Achrombacter xylosoxi was isolated in the bevacizumab bottle In total, 13 eyes of 10 patients were studied. Pre-event BCVA was a mean of 20/80 (ETDRS chart). Immediately after the infection was diagnosed, mean VA decreased to a mean of hand motion (HM). Posterior pars plana vitrectomy was performed in 9 patients (5 on the 2nd visit and 4 on the 3rd visit); the rest of patients were managed as described above. 1 week after treatment, BCVA was a mean of 20 400. Three months post infection BCVA was a mean of 20/80. Only one patient remained with a poor VA, as of her pre-event evaluation.

Conclusions
Prompt diagnosis and aggressive treatment of PICE (IVATB / prompt PPV) can result in excellent visual and anatomical outcomes as in the pre-event setting of patients.

Financial Disclosure
NONE
Photodynamic therapy–induced exudative maculopathy in central serous chorioretinopathy patients

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Purpose
To describe the incidence, clinical features, risk factors, and outcomes of photodynamic therapy (PDT)-induced acute exudative maculopathy (PAEM) in patients with chronic central serous chorioretinopathy (CSCR).

Methods
Prospective observational case series including 87 eyes that underwent PDT. Best-corrected visual acuity (BCVA), swept-source optical coherence tomography (OCT) and OCT angiography were performed before, 3 days, 1 month and 3 months after half-fluence PDT. Inclusion criteria were: CSCR with persistent subretinal fluid (SRF) at or near the fovea (<500 µm) for at least 3 months without any previous treatments in the last 6 months. Moreover, patients should be susceptible to undergo a standardized PDT with a spot laser size of 4000 ±500 µm. A 6 x 6 mm scan centered in the fovea was performed to assess the vessel occlusion in the choriocapillaris and choroid measured as flow signal voids (FSV) (Plex Elite 9000, Zeiss, Germany). Two groups were established depending on the presence or absence (group 1, N=26 and group 2 or control, N=61 respectively) of PAEM (considered as an increase ≥50 µm in the SRF height 3 days after PDT). The presence of a bacillary detachment characterized by a splitting between the myoid inner segment (IS) and the ellipsoid IS was also registered. Age, gender, axial length (AL), subfoveal choroidal thickness (SFCT) and the presence of choroidal neovascularization (CNV) were collected and compared between groups.

Results
The incidence rate of PAEM was 26/87 (29.9%). There was no difference in the mean age (p=0.394), gender (p=0.298), AL (p=0.094) or SFCT (p=0.205) between groups. There was no difference in the mean SRF at baseline (136.4 ±61.9 versus 133.5 ±69.9 µm; p=0.854). At 3 days after PDT mean SRF was larger in the group with PAEM than in the control group (330.9 ±160.3 versus 105.5 ±59.4 µm respectively; p<0.001). However, no differences persisted in the SRF at one and three months after PDT between groups (35.4 ±50.2 µm versus 42.0 ±55.7 µm, p=0.601; and 34.0 ±52.3 versus 38.6 ±56.1 µm, p=0.834 respectively). Patients with PAEM had worse baseline BCVA compared to controls (68.9 ±14.2 versus 77.8 ±11.8, p=0.004), but there was no difference in the mean BCVA gain at three months (4.5 ±4.5 versus 4.0 ±6.6 letters, p=0.825). At one month, 15/26 cases had complete resorption of SRF despite the development of PAEM. CNV at the baseline was present in 29.6% of the cases in the PAEM group and 14.3% in the control group (p<0.05). All cases with PAEM had a large early vessel occlusion (increase in FSV). A bacillary detachment was observed in 12 patients with PAEM.

Conclusions
Photodynamic therapy-induced acute exudative maculopathy was frequent in patients with chronic CSCR. However, a self-resolving evolution and favourable prognosis were observed in most cases, similar to patients that did not develop this side effect. The possibility of PAEM should be warned to CSCR patients undergoing PDT. There was no association between PAEM and age, gender, AL or SFCT. On the contrary, PAEM was associated with a large increase in FSV, CNV, and worse baseline BCVA.

Financial Disclosure
None
In case of: A novel scoring system for easier differential diagnosis between PNV and neovascular AMD in patients older than 50 years

**Purpose**

The purpose of our study was to develop a novel scoring system aiming at guiding the differential diagnosis between pachychoroid neovasculopathy (PNV) and neovascular age-related macular degeneration (AMD) in patients affected by macular neovascularization (MNV) aged 50 years and older.

**Setting/Venue**

Multicenter retrospective study performed at University Vita-Salute San Raffaele (Milan, Italy) and Creteil University Eye Clinic (Paris, France).

**Methods**

We included consecutive patients who were diagnosed with either treatment-naive PNV or nAMD, and who were 50 years of age and older. At the time of diagnosis, all patients underwent comprehensive ophthalmologic evaluation including best-corrected visual acuity (BCVA) assessment, slit-lamp biomicroscopy and fundus examination by an experienced retina specialist, infrared reflectance (IR), fundus autofluorescence (FAF), spectral-domain optical coherence tomography (SD-OCT), fluorescein angiography (FA), indocyanine green angiography (IA) and optical coherence tomography angiography (OCTA). Univariate comparison between PNV and neovascular AMD group was performed to identify the main clinical predictors for PNV. The selected predictors were taken into a binomial logistic regression and eventually served as the basis for the development of a scoring system, dubbed InCASEOf scoring system. Receiver operating characteristic (ROC) curves were used to study the model performance.

**Results**

Fifty-three eyes from 53 patients with MNV secondary to pachychoroid and 39 eyes from 39 patients with neovascular AMD were considered in this study. Age, sex, choroidal thickness, early pachyvessels, and evidence of MNV at OCTA were factors associated with an increased likelihood of exhibiting PNV. InCASEOf scoring system with a high score of 7 points was built based on these results and the cutoff value of 4.5 showed good accuracy in separating PNVs from neovascular AMDs.

**Conclusions**

This is the first study to develop and propose a straightforward clinical scoring system, accessible to comprehensive ophthalmologists, with the purpose of enabling easy distinction and expert-like diagnosis of PNV and neovascular AMD in patients aged 50 years or older.

**Financial Disclosure**

We do not have financial disclosure.
**Purpose**
To report on two cases of sclerochoroidal calcifications (SCC) in two patients with no relevant past medical history. Review of existing literature.

**Methods**
A 72 year-old female and a 81-year-old male were referred to our department due to bilateral fundus abnormalities discovered on routine ophthalmic evaluation. Both had no systemic or ocular complaints, no relevant previous medical history and no long-term medication. A comprehensive ophthalmic examination was done, including best corrected visual acuity (BCVA), intraocular pressure (IOP) measurement, ocular ultrasonography and retinal multimodal imaging with fluorescein angiography (FA), Autofluorescence (FAF) and optical coherence tomography (OCT). Laboratory investigations for calcium metabolism abnormalities have been undertaken.

**Results**
Both patients had unremarkable anterior segment examination. In both cases, posterior segment examination revealed two large elevated yellow white subretinal lesions seen along the superotemporal vascular arcade in both eyes, with a few smaller satellite lesions surrounding each one of the larger lesions. OCT showed scleral masses causing distortion of the overlying structures. There was no associated subretinal fluid or significant retinal pigment epithelium (REP) changes. B-scan ultrasonography confirmed elevated solid lesions with high internal reflectivity and posterior shadowing, consistent with calcium deposits. On FAF pictures the lesions showed hyperautofluorescence and fluorescein angiography disclosed early and late hyperfluorescence staining corresponding to the lesions. The patients were diagnosed with bilateral sclerochoroidal calcification and a systemic work-up is being conducted to exclude disturbances of calcium metabolism.

**Conclusions**
Sclerochoroidal calcification is a benign and uncommon condition, commonly related to calcium, potassium or magnesium metabolic abnormalities, in which calcium salts are deposited within the scleral and choroidal leading to minimally elevated mass that can mimic a tumor. Classically the lesions are found along the superotemporal area, between the equator and the retinal vascular arcades, although the reason for this is unclear. In hypercalcemia, in other organs calcium is typically deposited in the vasculature. Sclerochoroidal calcification is typically an incidental finding as it usually has no impact on visual acuity neither is associated with visual symptoms. It is important to recognise this diagnosis in order to avoid unnecessary and resource-consuming investigations for tumoral lesions, as well as to prompt investigation of underlying endocrinological disorders which may be associated with this condition and may require systemic therapy.

**Financial Disclosure**
No financial disclosure
Title
Improving digital competency of ophthalmic clinicians and allied health professionals.

Purpose
According to the Royal College of Ophthalmologists’ Workforce Census conducted in 2018, the UK has seen a large increase in demand for ophthalmic services in the last 10 years, owing to the ageing population and advent of novel therapies. With 9 million outpatient appointments annually and a forecasted rise of 40%, the current workforce is ill-equipped to meet the growing demand. The implications of this imbalance is highlighted by 22 patients facing severe visual loss every month waiting to access ophthalmic services. The NHS long term plan seeks to mitigate the disparity between demand and supply through digital transformation. Increasing utility of ophthalmic allied health professionals undertaking extended roles is also forming part of the response. To harmonise these strands, it is pivotal to improve the digital literacy of the NHS workforce. The aim of our study was to design and implement a comprehensive digital health education programme to improve telemedicine competency in clinicians and allied health professionals.

Setting/Venue
This study was conducted in the joint University College London (UCL) - Moorfields Education department based at the Institute of Ophthalmology and Moorfields Eye Hospital, London, United Kingdom.

Methods
We designed and created a comprehensive and bespoke modular program incorporating diagnostic imaging, telemedicine and digital health. We identified important curricula objectives using the clinical teaching cycle. Course tutors were recruited based on their expertise in the various specialist fields. Teaching content was initially produced on PowerPoint, which was subsequently transcribed to a cloud based learning platform. Using this application, we published SCORM- and Tin Can API compliant courses that play seamlessly in learning management systems of smartphones, tablets, laptops and desktops. We evaluated the utility of this education program by collecting feedback from the inaugural cohort of students using a questionnaire. An anonymous, online survey was sent to 14 students partaking in the course. The questionnaire was created using Google Forms, a secure online platform and distributed via email. Responses were uploaded automatically and anonymously. The 65-item questionnaire was designed using a combination of quantitative and qualitative closed, multiple-choice and open questions. Demographic data such as age, region of practice and years in practice were procured. The main body of questions focused on students perspectives’ on different aspects of telemedicine and their competency before and after undertaking the course. Opinion was primarily gauged using a combination of quantitative and qualitative closed, multiple-choice and

Conclusions
Based on the findings of our study, we conclude that there is an appetite for telemedicine based courses to improve digital competency. Areas of importance highlighted by the survey were setting up a diagnostic imaging service, virtual clinics, implementing home monitoring tools and artificial intelligence in ophthalmology. Prioritisation of certain competencies were highly dependent on the individuals as clinicians tended to rank diagnostic imaging and modules assisting decision making more highly in terms of importance; whereas, optometrists and ophthalmic technicians regarded image interpretation skills and 75% (n=6) aspired to facilitate digital transformation in healthcare. All participants (n=8) reported 4-5 out of 5 on importance of telemedicine for patient care delivery during and following the COVID-19 pandemic (on a likert scale where 5 is the most important). 75% of respondents felt that the course was relevant in addressing the challenges of socially-distanced patient care (4-5/5 on a Likert scale where 5 was the most relevant).

Results
The curriculum was divided into four modules: diagnostic imaging in retina (1), cornea and glaucoma (2), telemedicine (3) and digital health (4). The inaugural cohort consisted of 14 students, 8 of whom completed the feedback questionnaire. The level of competency ranged from ophthalmic photographer (n=1), retinal image grader (n=1), optometrist (n=1) to junior medical doctor (n=2) and ophthalmology consultant (n=1). Only 37.5% (n=3) of respondents practiced in the UK; whereas, 62.5% (n=5) practiced outside the UK. Most participants (75%, n=6) were predominantly operating in a primary care setting. Exploration of students’ motives for enrolling on the course identified the following pull factors/stimuli: 100% (n=8) reported a desire to hone their image interpretation skills and 75% (n=6) aspired to facilitate digital transformation in healthcare. All participants (n=8) reported 4-5 out of 5 on importance of telemedicine for patient care delivery during and following the COVID-19 pandemic (on a likert scale where 5 is the most important). 75% of respondents felt that the course was relevant in addressing the challenges of socially-distanced patient care (4-5/5 on a Likert scale where 5 was the most relevant).

Financial Disclosure
Nil
How did the COVID-19 pandemic impact the delivery of intra-vitreal injection therapies in a busy eye hospital?

Intra-vitreal therapies delivered through dedicated injection clinics in an outpatient setting are vital sight saving procedures for the treatment of conditions such as age related macular degeneration (AMD), diabetic maculopathy (DMO) and retinal vein occlusion. In pre-COVID 2019, with the aim to improve efficiencies in the injection clinics, we introduced a dedicated Failsafe officer, who joined a wider team, to help track patients. In 2020, the COVID 19 pandemic led to major reorganisation of the service to enable safe and continued care. Social distancing meant that intensive high volume clinics were replaced with high flow clinics. The twin injection room model, running 3-4 sessions per week, was switched to a single injection room model running 10 sessions per week. This actually increased the weekly clinic capacity from 120 to 150 injection slots. The additional workforce challenge was met by using allied healthcare professionals as assessors and dedicated nurse specialists as injectors, with overall supervision delivered by a senior Nurse and a Retina Consultant. In this study we have assessed, over a three year cycle, the impact of COVID 19 on our service.

Setting/Venue
Barts Health NHS Trust, Whipps Cross University Hospital, Eye treatment Centre

Methods
The data was extracted from Medisoft electronic patient records over a three year cycle between 2018-2020. Inclusion criteria: all patients attending the intra-vitreal injection clinics at Whipps Cross University Hospital in the month of September. There was no exclusion criteria. The primary outcome measures included the percentage of patients with delays in follow-up and treatment and an analysis of the level of clinical harm. Secondary outcome measures included causes of delays to treatment, mean changes in visual acuity & central macular thickness (CMT). Delay in follow-up/ treatment was defined as any appointment which exceeded 25% of the requested time interval. Clinical harm was defined as a loss of 15 or more ETDRS letters or 3 lines on the logMAR chart. The cause for delay to follow-up was categorized as patient initiated (ie: patient unwell or unwilling to attend), hospital initiated (rescheduled due to capacity issues, clinic cancellations, administrative errors) or ‘did not attend’ or DNA. For data gathered in 2020 we also identified delays and risks of harm specific to the COVID 19 pandemic. Data analysis was done with Microsoft excel.

Results
Total patients seen in September 2020 following the first COVID surge was 454 compared to 260 (2018) and 285 (2019). The average age group was higher in 2020: 80-89 years versus 70 -79 years (2018 & 2019). In 2018, delays in follow-up were 43% of total. Following the inception of a dedicated Failsafe officer numbers fell significantly in 2019 (9.4%) and remained low in 2020 (9.7%) despite the pandemic. In 2018 & 2019 the follow-up delays were mainly due to hospital rescheduling as a result of capacity issues. In 2020, COVID-19 was the leading cause follow-up delays with most due to patient-initiated rescheduling. Interestingly, the mean duration of delay leading to clinical harm was longer in 2020 (140 days compared with 44 days in 2018 and 28 days in 2019). The overall proportion of patients that suffered clinical harm was low (0.7%-1.0%) for all time points with an average of 19 ETDRS letters lost. Of these patients, the mean CMT increased for those with RVO (278 µm) and DMO (164.67µm). However, with AMD, CMT either increased or decreased. Only 2 persons in 2020 experienced harm due to follow-up delays because of COVID-19.

Conclusions
The inception of a dedicated Failsafe officer reduced hospital initiated delays but lack of capacity in the service remained a major cause of appointment delays. By reorganising our service in 2020 in response to the COVID 19 infection prevention control policies, we were able to increase capacity and maintain low levels of delays to care . The unit was able to maintain pre and post pandemic efficiency and safety levels as delays to follow-up and care remained below 10% and risk of harm below 1% in 2020.
Recurrent chronic endophthalmitis in pseudophakic patient after capsulotomy 6 years after cataract surgery

**Purpose**

Delayed-onset endophthalmitis after cataract surgery occurs when a microorganism with low virulence is trapped inside the capsular sac. It can on rare occasions be triggered by the release of the microorganism after laser capsulotomy. Patients with chronic endophthalmitis have progressive and chronic intraocular inflammation. In many cases, and despite repeated vitreous biopsies, it is difficult to identify the germ that caused the process. Even so, antibiotic therapies that show symptom improvement might have to be used for an extended period.

**Setting/Venue**

An 86-year-old male patient with only the left eye underwent cataract surgery 6 years ago without incident and underwent capsulotomy 1 year ago due to vision loss related to capsular fibrosis. Two months after the capsulotomy, the patient was admitted to consultation reporting that he had lost a significant amount of vision since then.

**Methods**

The examination revealed a visual acuity of less than 20/200, while biomicroscopy revealed thick retrokeratic precipitates, Tyndall grade 2+ with no hypopyon level, white precipitates in the anterior surface of the lens and fibrous cyclic retrolental membranes and moderate vitritis, which allowed for an eye fundus examination, showing no foci. The intraocular pressure was 2 mm Hg. We requested general laboratory tests, infectious serology and autoimmune markers. Based on the high suspicion of delayed-onset endophthalmitis, we obtained vitreous samples and administered treatment with an intravitreal injection of vancomycin and ceftazidime. In addition, we prescribed oral therapy with clarithromycin (500 mg every 12 h for 5 days) and dexamethasone eye drops (1 drop every 4 h) and cycloplegic eye drops (1 drop every 8 h). Fifteen days later, the patient was admitted with a vision of 20/100, with no membranes or deposits in the lens. Optical coherence tomography showed a thinned retina with abnormal retinal pigment epithelium but no acute condition. The oral treatment was maintained for the rest of the month.

**Results**

The patient was admitted 15 days after stopping the treatment, with the same precipitates in the lens as before the treatment and having once again lost vision. We once again treated with intravitreals and oral clarithromycin, and we once again took a 0.2-mL vitreous sample. Three days later and after reporting an initial improvement, the patient is admitted for total vision loss. In the examination, the patient presented rhegmatogenous retinal detachment with inferior bag. There was no inflammation or precipitates in the lens. The patient underwent pars plana vitrectomy, leaving SF6 gas as a buffer. A vitreous sample collected during the surgery was once again sent for tests, which came back negative. After the surgery, the patient recovered his vision to 20/100. Three months later, the patient returned with vision loss and the same precipitates as at symptom onset. The decision was made not to treat with intravitreals due to the traction that might have been generated in the last episode. The patient was given only oral clarithromycin, which he will take for 2 months. Surgery to extract the lens and capsular sac was ruled out due to the patient’s conditions (poor general condition, only eye, previous vitrectomy after retinal detachment ...).

**Conclusions**

Chronic recurrent endophthalmitis can represent a diagnostic and therapeutic challenge due to the difficulty in resolving the disease in a definitive manner. In our case, the patient showed recurrance of the infection, even after being vitrectomised. Although we usually recommend extracting the sac and lens in persistent cases, there are patients such as the one in question who are not good candidates and for whom other options include maintaining oral antibiotic therapy for months.

**Financial Disclosure**

NO FINANCIAL RELATIONS
A Rare Case of a Full Thickness Macular Hole after Air Puff Tonometry

Purpose
A variety of precipitating factors have been described for full-thickness macular holes. To the best of our knowledge, full-thickness macular holes after air puff tonometry have not previously been described in the literature. We present a rare case of full-thickness macular holes caused by air puff tonometry.

Methods
A 66-year-old male with bilateral pseudophakia presented to his optometrist with a visual acuity of 6/6 in both eyes. Following air puff tonometry, he immediately noticed reduced vision in his left eye. On immediate rechecking, his left eye visual acuity had reduced to 6/24. He was then seen in the emergency eye clinic. A fundal examination of his left eye showed a full-thickness macular hole. Based on optical coherence tomography, a stage 2 full-thickness macular hole was confirmed.

Results
After a period of observation of 5 weeks, the patient's vision had deteriorated to 6/60 in the left eye. He was treated successfully with vitrectomy, internal limiting membrane peel, with cryo-retinopexy and gas tamponade. The final visual acuity of the patient was 6/24.

Conclusions
This is the first case demonstrating the possible role of air puff tonometry in precipitating the formation of a full-thickness macular hole. It is imperative that machines using this method are regularly calibrated and serviced so that they use the lowest and safest air pressures necessary to determine intraocular pressure.
### Title
Effects of the COVID-19 pandemic on anti-vascular endothelial growth factor treatment in China

### Purpose
To evaluate the impact of the COVID-19 pandemic on anti-VEGF treatment in ophthalmology patients in a single hospital in northern China.

### Setting/Venue
Retrospective case series.

### Methods
We retrospectively reviewed the charts of all patients who received anti-VEGF treatment in The China Medical University First Hospital Department of Ophthalmology from January 21, 2020 (the day on which the outpatient services and operations were restricted because of the pandemic), to June 1, 2020. Clinical characteristics and visual acuity outcomes of these patients were evaluated.

### Results
A total of 93 anti-VEGF injections were administered to 85 eyes of 72 patients at The China Medical University First Hospital Department of Ophthalmology during the COVID-19 pandemic. Compared to the same period in 2019, the number of injections decreased by 70%. Fifty-nine eyes of 46 patients were receiving 3+PRN anti-VEGF treatment prior to the outbreak of the COVID-19 pandemic; all of these patients experienced treatment interruptions due to COVID-19-associated reasons. Anatomic and functional outcomes suggest that patients with anti-VEGF treatment interruptions are at risk for severe adverse visual sequelae. Moreover, deferred anti-VEGF treatment due to patient-related or department-related reasons during the COVID-19 pandemic may result in poor visual outcomes for new patients.

### Conclusions
Our results suggest that COVID-19 has had a significant negative effect on anti-VEGF treatment in ophthalmology patients. Detailed guidance from global experts in ophthalmology is highly sought after in these challenging circumstances.

### Financial Disclosure
None
Purpose
The novel coronavirus-2019 pandemic has provided a disruptive impetus for rapid evolution of the healthcare landscape, including the education sector. This has precipitated educators to expeditiously adapt teaching to mitigate disruption to ophthalmology training. In light of social distancing measures, digital education has come to the forefront of education delivery. The aim of our study was to assess the perspectives of ophthalmology trainees on the importance of digital education during the pandemic and explore its utility in the future.

Setting/Venue
This study was conducted on ophthalmology specialty trainees based in London, United Kingdom.

Methods
We assessed the perspectives of ophthalmology trainees by collecting feedback through an anonymous, online survey. The questionnaire was created using Google Forms, a secure online platform and distributed via email. Responses were uploaded automatically and anonymously. The 29-item questionnaire was designed using a combination of quantitative and qualitative closed, multiple-choice and open questions. Demographic data such as age, region of practice and years in practice were procured. The main body of questions focused on trainees’ experiences with disrupted education during the COVID-19 pandemic and subsequent redeployment to a non-ophthalmology specialty. It also enquired into trainees’ perspectives on digital education and its utility in the current and future medical education sphere. Opinion was primarily gauged using ordinal and Likert scale ratings.

Results
Feedback was received from 10 specialty trainees ranging from year 1 to 7 across London. During the COVID-19 associated lockdown, 60% of trainees (n=6) were redeployed to a non-ophthalmic specialty. The majority of respondents (70%, n=7) reported that COVID-19 adversely affected their surgical training. 70% of trainees indicated that digital education was important by scoring 4 - 5 out 5 (5 being the most important on a likert scale). A large proportion of trainees (60%, n=6) delineated increased utility of digital education during the pandemic. With regards to e-learning, half of the survey participants rated its usefulness as 2 out of 5 (5 being the most useful). Conversely, 60% (n=6) of trainees reported 4 out of 5 for the usefulness of 'EyeSi', a virtual reality simulator emulating surgery. There were mixed responses on the usefulness of telemedicine to deliver education: 30% (n=3) scored 1-2 out of 5, 40% (n=4) rated 3 out of 5 and 30% indicated 4 out of 5. 70% of trainees indicated that digital education will be important in meeting training following COVID-19 as they scored 4-5 out of 5 (where 5 is the most important).

Conclusions
In summary, our study findings were congruent with published literature that the COVID-19 pandemic disrupted medical education and surgical training. Our results shed light on the importance of digital education as a means of mitigating this disruption. In particular, augmented / virtual reality instruments such as the eye simulator were recognised to have the most utility. Tools including e-learning and telemedicine were found to be less useful in delivering education. Although current social distancing measures only allow for virtual teaching methods, we conclude that digital education tools will continue to be important in the future.

Financial Disclosure
Nil
Quantitative analysis of retinal and choroidal vasculature in patients with chorioretinal folds secondary to hyperopia

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Purpose
There is a lack of information on quantitative parameters of optical coherence tomography angiography (OCTA) in cases of chorioretinal folds (CRF). The aim of this study was to compare OCTA retinal and choriocapillaris (CC) vessel density (VD) between normal subjects and patients with CRF secondary to primary hyperopia.

Setting/Venue
We conducted an observational retrospective study in the Retina service at the Consorcio Hospital General Universitario of Valencia, Spain. A total of 16 eyes of 8 patients were recruited (8 eyes with CRF and 8 control eyes).

Methods
Data on best-corrected visual acuity (BCVA), refractive error, central macular thickness (CMT), central subfoveal thickness (CST), and OCTA findings (VD and foveal avascular zone (FAZ) area in superficial capillary plexus (SCP), middle capillary plexus (MCP), and deep capillary plexus (DCP), and VD in CC) were recorded in each eye.

Results
Compared with control group, CRF group showed decreased VD in the foveal region of SCP and MCP (p value 0,003 and 0,001), and increased VD in nasal region of SCP and MCP (p value 0,02 and 0,001), and in parafoveal area of MCP (p value 0,005). No differences were found in DCP and CC layers. Furthermore, we observed an enlargement of FAZ in CRF group at SCP and MCP slabs (p value <0,001 and 0,015). Respect to optical coherence tomography parameters, we demonstrated a thicker choroid in the CRF group (p value 0,002).

Conclusions
To the best of our knowledge, our study quantified VD of retinal capillary plexus and CC in a group of patients with a diagnosis of CRF secondary to primary hyperopia. We did not find a significant decrease of VD in DCP and CC, suggesting that there is no vascular involvement, but further studies with bigger population are needed to confirm this hypothesis.

Financial Disclosure
None
Inter-eye comparison of retinal vascularization and angiographic findings following unilateral bevacizumab therapy

**Purpose**
It is known that peripheral retinal vascularization is not fully completed, even if a significant portion of the eyes treated with anti-vascular endothelial growth factor (VEGF) treatment has a positive response to the treatment. It is not yet fully known whether the incomplete retinal vascularization in infants treated with anti-VEGF is due to the nature of the disease or is a condition secondary to anti-VEGF treatment. With the widespread use of fluorescein angiography (FA) in the follow-up of premature retinopathy (ROP), a few recent studies are reporting that incomplete vascular maturation, and angiographic findings are detected in spontaneously regressed ROP. The aim of this study is to compare retinal vascularization progression rate, final retinal vascularization, and fluorescein angiography findings in infants who received intravitreal bevacizumab (IVB) treatment in one eye and spontaneously regressed the other eye.

**Setting/Venue**
Health Sciences University, Istanbul Kanuni Sultan Suleyman Training and Research Hospital, Tertiary ROP Center.

**Methods**
Retrospective, comparative, case series. Between June 2018 and August 2019, 30 eyes of 15 infants who underwent IVB in one eye due to severe retinopathy, who had pre-treatment fundus photographs and FA, and who did not receive additional treatment until FA were included in the study. All images were taken with a 130-degree Panocam Pro device. Fundus photographs and FA images were analyzed quantitatively with the Image J program. Horizontal optic disc diameter (HODD), optic disc fovea distance (ODFD), and temporal retinal vascularization distance (TRVD) were measured three times by the same observer. The intraclass correlation coefficient of measurements was more than 0.90 in all parameters. Further analysis was continued by taking the average of three measurements. TRVD is the measurement of the length starting from the center of the optic disc, passing through the fovea, and extending to the temporal avascular border. The longest measurable temporal avascular retina distance (LMTARD) is the measurement of the longest avascular distance that can be measured in the line extending from the optic disc to the fovea and extending to the pars plana. Inter-eye comparison was made by paired sample t-test, Wilcoxon, and McNemar tests.

**Results**
All 15 eyes treated had plus disease, and 14 had stage 2-3 ROP. Of the 15 eyes that were not treated, 3 had preplus, and 14 had stage 2-3 ROP. The mean age of treatment and FA were 40.38 ± 3.35 and 68.72 ± 10.52 PMA weeks, respectively. The pre-treatment TRV / ODF ratio was 3.10 ± 0.40 in the treated group and 3.26 ± 0.43 in the untreated group (p = 0.053). The final TRV / ODF ratio was 4.23 ± 0.38 in the treated group and 4.33 ± 0.36 in the untreated group (p = 0.286). The TRV / ODF ratio increased by 39 ± 27% in the treated group and 35 ± 20% in the untreated group (p = 0.427). The LMTARD / HODD ratio was 2.34 ± 0.90 in the treated group and 2.23 ± 0.75 in the untreated group (p = 0.605). In the treated and non-treated groups, mild staining of the vessels in 8 and 9 eyes, hyperfluorescent focus in 11 and 8 eyes, irregular branching of vessels in 11 and 9 eyes were detected, respectively, (p = 1.000; p = 0.250; p = 0.625).

**Conclusions**
Vascular progression rate was similar between the treated eyes and the non-treated eyes of the same babies. Our study supports that anti-VEGF therapy does not cause cessation in outgrowth of retinal vascularization, the incompletion of retinal vascularization is due to the nature of the disease. Ascertainment of similar angiographic findings between fellow eyes suggests that the silent disease activity in the non-treated eye that can only be shown in FA may be associated with incomplete retinal vascularization.

**Financial Disclosure**
We declare that we have no financial relationship with companies.
Effect of oral citicoline therapy on retinal thickness and choroidal thickness in patients with primary open-angle glaucoma

This study aims to evaluate the effects of oral citicoline therapy on the retinal thickness and choroidal thickness in patients with primary open-angle glaucoma (POAG).

This prospective study was performed in the Department of Ophthalmology at Ordu University. The study was approved by the local Ethics Committee and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Methods
This study included 20 eyes of 20 patients with POAG glaucoma. In addition to a topical hypotensive, 250-mg oral citicoline (Cebrolux®NF) was administered to the patients. Retinal and choroidal images of the participants were obtained with spectral-domain optical coherence tomography at 1 day before treatment and 3 months after the initiation of treatment. The central fovea in the horizontal section image passing through the fovea were used as measurement point for subfoveal choroidal thickness. All data were analysed using the SPSS statistical software package, version 21.0 (SPSS Inc., Chicago, IL, USA). A normality check was performed using the Shapiro–Wilk W test. P < 0.05 was accepted as a statistically significant level. Wilcoxon test were used for statistical analysis.

Results
The mean age was 50.05 ± 7.67 years (range, 33–58 years). The intraocular pressure did not exceed 21 mmHg in any of the patients during follow-up. The average choroidal thickness measurements at the baseline and the third month of citicoline treatment were 303.65±70.47 µm and 298.80±73.09 µm, also central retinal thickness values (the central 1-mm diameter circle) were 245.01±17.01 µm and 244.50±14.94 µm, respectively. No statistically significant changes were observed in the retinal and choroidal thickness values at 3 months after the initiation of treatment (p = 0.850 and p = 0.349, respectively).

Conclusions
Despite the neuroprotective and neuromodulatory effects, oral citicoline therapy had no significant effect on the central retinal and subfoveal choroidal thickness.

Financial Disclosure
No person or organisation supported this work financially.
Purpose
To report the findings of a case of maculopathy associated with tacrolimus treatment, a rare complication of the treatment with tacrolimus.

Setting/Venue
Department of Ophthalmology of the San Cecilio University Hospital of Granada, Spain.

Methods
An observational case report. The description of a 41-year-old woman with a maculopathy associated with tacrolimus treatment. We portrait the findings in the retinography, OCT, OCT angiography, computerized campimetry and electroretinogram. We consulted the PubMed data base in search to similar cases.

Results
A 41-year-old woman with a history of kidney transplant consulted for acute wavy vision in the right eye. She had treatment with tacrolimus for 4 months. She had unstable tacrolimus plasmatic levels, and had headache and trembling attributed to tacrolimus. The best corrected visual acuity was 0.8 in the right eye and 1 in the left eye. On the slit lamp examination, the anterior segment did not show significant finding, but the fundoscopy revealed a yellow pigmented lesion in the central macular area in both eyes, the optic nerve did not show pallor or swelling. OCT scanning revealed central subretinal deposits and a small parafoveal pigmented epithelial detachment (PED), without signs of choroidal neovascularisation, more severe in the right eye. OCT-A findings revealed a small ischemic area in correlation with the PED. The filed test showed general loss of sensitivity, more pronounced in the macular area. The neurophysiology test showed as follow: Visual evoked potential demonstrated a mild P100 delay in both eyes, the multifocal ERG showed general suppression, more marked in the macular region. The ERG showed p50 wave amputation. During the follow up for 2 months the lesions were stable.

Conclusions
Tacrolimus ocular side effects are rare and can be serious. Among the ocular surface alterations that may develop during the treatment with tacrolimus, visual alteration may be associated with alteration in the visual cortex or ocular neuropathy. There is only one case reported of maculopathy, with similar findings to our patient in the ERG, VEP and visual field, but without any alteration on the OCT or the posterior segment observation. This case may support furthermore the association of tacrolimus and the possibility of an alteration in the RPE, cone cells or rod cells, resulting in a maculopathy similar found in treatments with cyclophosphamide. Although the mechanism is unknown, this shows the necessity to perform carefully complete ophthalmologic examinations in patients with this treatment and any visual disturbance.
### Title
Outcomes and risk of reactivation of myopic choroidal neovascularisation – A multi-centre study with long-term follow-up

### Purpose
Myopic choroidal neovascularisation (mCNV) is a common vision threatening complication of myopia, reported to affect 5-11% of individuals with pathologic myopia. Long-term outcomes and the risk of reactivation of mCNV are unclear and especially poorly described in a predominantly Caucasian population. The aim of this study is to describe long-term visual acuity (VA) outcomes in a large cohort of eyes treated with anti-vascular endothelial growth factor (VEGF) injections for mCNV; describe the number of treatments over time; and analyse reactivation episodes in a large cohort of eyes with mCNV, to understand the pattern of injections within and between each episode.

### Setting/Venue
Patients undergoing anti-VEGF treatment for mCNV in 27 National Health Service (NHS) secondary care healthcare providers in the UK between 2008 and 2018.

### Methods
The electronic health records (Medisoft EMR) of patients receiving anti-VEGF treatment for mCNV were analysed. The end of one mCNV reactivation episode was derived from the distribution of plotting the interval between the injection episodes and was found to be 90 days. As such, any successive injections would have to be less than 90 days between each other to be considered in one episode. Main outcome measures included visual acuity and number of injections.

### Results
Overall, 822 eyes of 732 patients were included in the study. Of all patients, 503 (68.7%) were female. In the first year of treatment, VA improved from around 0.50 logMAR to around 0.43 logMAR, but then steadily declined to around 0.78 logMAR at approximately nine years from baseline. It dropped below baseline after three years on average. The median time for 15 letter loss was 4.5 years. At 3.5 years, 62% of eyes gained 15 letters of vision. The number of injections across reactivation episodes decreased, starting at 2.9 average injections per episode for the first reactivation episode, decreasing to an average of 1.7 injections per episode by the fifth episode. The average number of injections per year also decreased over time, from a mean of 2.21 injections in the first year to 0.54 in year 5 and 0.01 in year 6.

### Conclusions
Our data shows a long-term decline in visual acuity in patients with mCNV. The mean number of episodes and the mean number of treatments decreased over the years, suggesting that neovascularisation may not be the main cause of visual loss over time in these patients. Further investigation of the determinants of long-term visual loss in this predominantly Caucasian cohort is warranted as to whether this is driven by progressive atrophy or suboptimal treatment.

### Financial Disclosure
No relevant financial relations
Title
Practice patterns of intravitreal injections during the first wave of the COVID-19 pandemic in Greece: A comparison between the public and private health sector

Purpose
To record and analyze the practice patterns of intravitreal injections during the lockdown phase of the pandemic in two health care settings in a metropolitan city

Setting/Venue
G Gennimatas Athens General Hospital NHS Trust, Athens, Greece, Athens Vision Eye Institute, Athens, Greece

Methods
Retrospective, observational, cross-sectional study.

Results
218 patients received a total of 249 injections over the 6-week period of the first lockdown, as compared to 292 patients and 369 injections over the same time frame the year prior (overall -32.8% in the number of injections). While the demographics of both cohorts remained stable, a significant increase in the “no show” events was observed (15.6% vs 7.4%, p <0.05) driven by the public venue (-19.2% vs -0.8%). In terms of per disease practice analysis, a similar drop of injections was recorded in the AMD cohort in both venues (-20% vs -19.3%) as well as the DR cohort, albeit more pronounced in the latter (-30.5% vs -48%). Most patients in the public venue initiated treatment, whereas most in the private venue continued treatment in predefined, fixed intervals. A similar drop was observed in the percentage of patients residing outside of the Attica prefecture (-10% in both venues).

Conclusions
The first lockdown resulted in a significant drop in the number of intravitreal injections in both the public and the private health sector, while the preset prioritization of injections resulted in a more pronounced decrease in the number of treatments for the complications of diabetic retinopathy. Interestingly, the number of “no show” events were significantly higher in the public venue, and further comparative analysis of the particulate measures targeting patient compliance is presented herein.

Financial Disclosure
none
Demographic risk factors of retinopathy of prematurity: A systematic review of population-based studies

Purpose
Current national retinopathy of prematurity (ROP) guidelines use gestational age (GA) and birth weight (BW) as the basis for screening. The epidemiology of infants with ROP is evolving, and an evaluation of risk factors is necessary to facilitate early diagnosis and treatment. This systematic review was conducted to analyze the association between demographic risk factors and the incidence of ROP in regional population-based studies to inform screening guidelines.

Setting/Venue
Systematic review of population-based studies.

Methods
The review was conducted according to PRISMA guidelines (PROSPERO CRD42020185343). Ovid MEDLINE, EMBASE, and Cochrane Library were searched from January 2010 through May 2020. Original studies investigating the incidence of ROP in a region and cohort demographic risk factors were included. Risk of bias was assessed using a validated tool for prevalence studies. Quality of evidence was assessed using the GRADE methodology. A weighted mean was used for pooling of continuous outcomes. ROP incidence was reported in proportions and compared based on cohort demographics and criteria for screening guidelines.

Results
From 4091 results, 18 studies (n=20,701,040) were included. The risk of bias across studies was low, and the certainty of evidence was moderate for most outcomes. The overall incidence of ROP across all studies was 0.15%. Overall, ROP stages ≥3 accounted for 20.5% of ROP cases. The mean GA and BW for infants with any ROP ranged from 26.5 to 28.5 weeks and 723 to 950 grams, respectively. The weighted incidence of any, severe, and treatment-requiring ROP was highest at 23 weeks GA (66.5%, 40.3%, and 39.4% respectively). For every week decrease in GA, there was a median adjusted odds ratio (aOR) of 1.4 times of developing ROP. For every 100 gram decrease in BW, the median aOR was 1.8 times. A higher incidence of ROP was also found for infants with neonatal sepsis (n=3 studies, median OR=2.02) and bronchopulmonary dysplasia (n=2, median OR=7.57). The review was limited by inter-study heterogeneity secondary to geographic location and methodology.

Conclusions
The overall incidence of ROP among live births was 0.15%. The incidence increased proportionally with lower GA and BW, with a diagnosis of ROP occurring in 2 of 3 infants born at GA 23 weeks and 1 of 3 infants born at BW ≤1000 grams. The strongest risk factors for ROP are GA, BW, neonatal sepsis and bronchopulmonary dysplasia. Based on demographic risk factors, national ROP screening guidelines should focus efforts on screening infants at risk and optimizing examination schedules. Future studies should continue to investigate risk factors for ROP and examine if current screening guidelines can be optimized based on the latest evidence.

Financial Disclosure
MMP: Financial support (to institution) – PSI Foundation. PJK: Advisory board – Novartis, Allergan, Bayer, Roche, Novelty Nobility; Financial support (to institution) – Allergan, Novartis, Bayer, Roche; Financial support – Novartis, Bayer, Zeiss; Equity owner – ArcticDx. RHM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis. KM: Advisory board – Santen Inc; Non-Financial Support – Bayer.
Title
Comparison of particle contamination and protein aggregation from syringes used for intravitreal injection

Purpose
The type of syringe used for the intravitreal injection of anti-VEGF agents can influence the quality, safety and efficacy of the drug injected. Previous investigations have shown that syringes can vary in the accuracy of drug volume measurement and proclivity for silicone oil contamination; however, few studies have investigated how syringes can influence protein aggregation.

Setting/Venue
Laboratory experiment.

Methods
Different polypropylene and glass syringes were tested for particle contamination by filling the syringes with particle-free water and then expelling the contents through a 0.4\(\mu\)m pore polycarbonate filter. Microscopy and elemental analysis of particles captured by the filter were performed using a scanning electron microscope at an independent ISO 17025 accredited laboratory. The syringes were then tested with aflibercept solution (Regeneron Pharmaceuticals Inc., Tarrytown, NY). Particles identified from these samples were analyzed with energy dispersive X-ray spectroscopy (EDS).

Results
In the test with particle-free water, all syringes produced samples with low but detectable levels of precipitated particles which measured within USP 789 guidelines (mean \(\geq 10\mu \text{m particle count} = 2.5\pm0.4/\text{ml})). In the analysis of the aflibercept samples, all syringes demonstrated particle level counts exceeding USP 789 standards. EDS analysis identified these particles as aggregated protein. Glass syringes demonstrated significantly higher levels of protein aggregation compared to polypropylene syringes across a range of particle sizes (Chi-square test, \(p<0.001\)).

Conclusions
Intravitreal injection syringes are associated with low levels of particle contamination. Significant protein aggregation can occur in any syringe, with glass syringes exhibiting higher levels of aggregated protein compared to polypropylene syringes. These findings may have important safety implications for patients.

Financial Disclosure
speaker and advisory board - Novartis pharmaceuticals Canada, Bayer Inc.
Self reported vision problems among diabetic individuals: a European population-based study

**Purpose**

There are few available data on vision impairment in European diabetic patients. The aim of this study was to evaluate the prevalence of diabetes in Europe and self-reported vision impairment in diabetic populations.

**Setting/Venue**

The European Health Interview Survey is a population-based cross-sectional survey including 28 European countries, even though Iceland and Norway do not belong to the European Union.

**Methods**

Data were collected through a standardized questionnaire reporting medical, demographic and socio-economic data on individuals aged 18 years old and older.

**Results**

The study population included 298,617 individuals (54.3% females). Among them, 7.11% declared to have diabetes (52.1% females) with the highest prevalence in France (10.27%) and the lowest in Norway (4.36%). Among self-reported diabetic patients, 28.53% [27.67 - 29.40] reported visual problems versus 17.71% [17.51 - 17.90] in individuals without self-reported diabetes. All in all, the odds of having a visual impairment are 1.63 times higher for diabetics.

**Conclusions**

This study showed sizable disparities in the prevalence of diabetes between different European countries and demonstrated that visual impairment is more frequent in self-reported diabetic patients.
# Presenter
Leire Juaristi Eizmendi
Spain

# Title
Retina virtual clinic during the COVID-19 pandemic: Results and patient satisfaction

# Purpose
To demonstrate that retina virtual clinic (RVC) is a useful and safe platform for monitoring selected retinal stable diseases during the COVID-19 pandemic decreasing COVID-19 virus expose and to assess patient satisfaction.

# Setting/Venue
Prospective observational study of patients with stable retinal diseases such as diabetic retinopathy (DR), dry age-related macular degeneration (AMD), retinal vein occlusion (RVO), chronic central serous chorioretinopathy (CSC), choroidal nevus, hydroxychloroquine (HCQ) retinopathy screening, epiretinal membrane (ERM), vitelliform lesions and others: toxoplasma scar, macular telangiectasia...in the Ophthalmology Service of Donostia University Hospital (Spain) during the COVID-19 pandemic between September 2020 and March 2021.

# Methods
All of the patients were attended in the RVC with measuring visual acuity (VA), intraocular pressure (IOP), optical coherence tomography (OCT) of the macula, wide field (WF) or ultra-wide-field (UWF) Clarus fundus retinography and visual field test (VF) in some cases. To evaluate the quality control of the RVC results, a double-blind-control was performed in some patients. Two different ophthalmologists reported the same case: on one hand the expert in RVC and on the other hand, the second ophthalmologist, in the face-to-face (F2F) clinic. It was compared if the outcome of RVC and the F2F clinic coincided. To assess patients satisfaction and their perceived quality of hospital care, it was utilized an adapted SERVQUAL model questionnaire.

# Results
Four hundred eighty one patients were included in the study, 261 women and 220 men. The mean age was 67 years, SD ± 14, with a range between 18 and 97 years. Regarding the retinal disease condition, 93 patients (19.3%) were referred to F2F consultation due to; disease progression (57 patients (61.3%)) or for other reasons (38.7%): not suitable patients, added symptoms, poor image quality, preferred F2F. Thirty-two patients (6.6%) were discharged because of stable disease and 356 (74%) were eligible to continue at the RVC platform. The most frequent disease reviewed was DR (146 patients (30.3%)), followed by dry AMD (105 patients (21.8%)). One hundred fourteen patients (23.7%) had a double control of the RVC in a F2F consultation. Hundred percent of patients, who were not stable and needed treatment in the F2F control, had been diagnosed in RVC to refer to F2F clinic. The ophthalmologist could report twice more cases in RVC than in F2F clinic. RVC took less time for patients than the F2F clinic, 15 versus 25 minutes. Global satisfaction of patients in RVC, measured in the adapted SERVQUAL questionnaire, was 9.83 points out of 10. Three hundred ninety-two patients (81.5%) preferred RVC than F2F clinic.

# Conclusions
The RVC is an additional platform that supports F2F clinic for the follow-up of patients with selected stable retinal diseases during times of pandemic. More than 70% of the patients could be seen in RVC safely. RVC decreases COVID-19 virus expose: the less time expended at the hospital, the less risk. Patients’ satisfaction is very good in RVC.

# Financial Disclosure
Authors do not have financial relations
Title
Cardiometabolic factors and risk of non-arteritic anterior ischemic optic neuropathy: A systematic review and meta-analysis

Purpose
The purpose of this systematic review and meta-analysis of the literature is to evaluate the association between cardiometabolic risk factors (hypertension, diabetes mellitus, hypercholesterolemia/dyslipidemia, HDL cholesterol, LDL cholesterol, lipoprotein(a) and triglycerides) and non-arteritic anterior ischemic optic neuropathy (NAION).

Setting/Venue
2nd Department of Ophthalmology, National and Kapodistrian University of Athens, Athens, Greece

Methods
Pertinent publications were identified through systematic search in PubMed and EMBASE databases, without language restrictions. The pooled odds ratios (OR) and standardized mean differences (SMD), with their 95% confidence intervals (95% CI) were estimated using random effects (DerSimonian Laird) models, as appropriate. A set of subgroup analyses and meta-regression analysis models were performed.

Results
21 studies (including 1560 patients with NAION and 2292 controls), examining the association between NAION and cardiometabolic risk factors were eligible for the systematic review and meta-analysis. Hypertension (pooled OR= 1.50; 95% CI: 1.16-1.94), diabetes mellitus (pooled OR= 1.71; 95% CI: 1.33-2.21), hypercholesterolemia/dyslipidemia (pooled OR=2.00; 95% CI: 1.53-2.62) were associated with NAION. Among the components of dyslipidemia, higher serum triglycerides were associated with NAION, with a medium effect size (SMD= +0.58, 95% CI: +0.12 to +1.04), whereas synthesis of four studies reporting on HDL and LDL cholesterol did not reveal any significant associations. A significant association between NAION and higher serum lipoprotein(a) levels (pooled OR=2.88; 95%CI: 1.01-8.21) was also noted.

Conclusions
This systematic review and meta-analysis found that NAION was associated with cardiometabolic factors, namely hypertension, diabetes mellitus, dyslipidemia and elevated lipoprotein (a), suggesting that vascular dysfunction may be implicated in the pathogenesis of the disease. Our findings may alert health care providers to pay attention to patients with cardiometabolic factors for visual symptoms indicative of NAION, as well as try to modify these risk factors for the prevention of NAION.

Financial Disclosure
No
Cancer-associated retinopathy in a patient with thyroid papillary carcinoma presenting unusual Vitreous Opacity

Purpose
Cancer associated retinopathy (CAR) is a rare cause of painless vision loss, associated with an underlying systemic malignancy. It usually damages photoreceptors and causes acute/subacute vision loss and visual field defects but seldom vitreous opacity. This report describes the case of a 71-year-old Chinese woman with binocular visual disturbance and vitreous opacity as the first symptom. She was subsequently diagnosed with thyroid papillary carcinoma.

Setting/Venue
Xi'an People's Hospital (Xi'an Fourth Hospital), Affiliated Guangren Hospital, School of Medicine, Xi'an Jiaotong University, Xi'an Ocular Fundus Disease Research Institute, Xi'an, 710004, China

Methods
The patient had painless, blurred vision for 1 year without redness. She denied any history of other diseases. Best-corrected visual acuity was 0.5 (10/20) OU. Anterior segment were within normal limits. Dilated fundus examination demonstrated bilateral vitreous opacity with gray cells. Both fundus were without bleeding or exudation; FA showed faint leakage of the small vessels; The aqueous humor IL-10, IL-6 were 0 pg/ml. Tuberculosis, syphilis, immunodeficiency were excluded; Her blood, HbAlc, Liver and renal functions, head MRI were normal. Chest CT showed multiple nodules in lungs, abdominal B-ultrasound scan showed liver cysts. Recoverin antibody and tumor-related antigens were negative. 3 months later, both eyes’ vision declined to 0.3 (6/20) OD and 0.25 (5/20) OS, and vitreous opacity aggravated. The patient’s symptom improved after using glucocorticoids on both eyes. But 2 months later, the symptoms worsened again, and she felt that the occlusion was obvious in the left eye. Scattered yellow-white spots besides blood vessels could be seen on the right fundus and the left fundus was blurred. OCT showed loss of IS/OS junction, subretinal hyper-reflective foci and ONL thin in peripheral macula. The ERG showed rod and cone responses severely decreased. Both eyes showed peripheral visual field defects.

Results
Advanced systemic examination performed and papillary thyroid carcinoma in the right lobe and isthmus was confirmed by pathological examination. The patient accepted PPV on the left eye because she could not tolerate the obvious occlusion. The vitreous biopsy showed no obvious atypical lymphocytes, and the postoperative visual acuity was improved to 0.6 (12/20). The patient had clinical features of CAR, such as progressive loss of vision, retinal vasculitis, photoreceptors damages, visual field defects, abnormal ERG, and subsequently diagnosed with thyroid papillary carcinoma. All of these support the diagnosis of CAR. this case is special with vitreous body turbidity obviously and transient perivascular scattered yellowish-white spot, sarcomatoid lesions in lung and liver which seems as paraneoplastic sarcoid-like reactions.

Conclusions
CAR is a rare disease caused by the distant effect of the primary malignant tumor. But CAR seldom appears with vitreous opacity. This case shows an unusual vitreous opacity with CAR complicated by papillary thyroid carcinoma.

Financial Disclosure
No
Ocular involvement in severe acute leukemia, a case report

Purpose
To report a case of bilateral serous retinal detachment with choroidal thickening in acute bilineal leukemia.

Setting/Venue
Department of Ophthalmology, Habib Bourguiba University Hospital, Faculty of medicine, University of Sfax, Tunisia

Methods
A 25-year-old man, presented with sudden vision loss of the left eye since 3 days. His personal medical history included bilineal acute leukemia treated initially with acute lymphoblastic leukemia chemotherapy protocol with persistence of predominant myeloblasts population at his presentation to our department. Complete ophthalmologic examination, fluorescein angiography and optical coherence tomography were performed.

Results
On examination, best corrected visual acuity was 8/10 in both eyes. No obvious inflammation in the anterior chamber or vitreous was found. Biomicroscopic fundus examination revealed bilateral serous retinal detachment (SRD) in the posterior pole. We noted the presence of an optic disc pit in the right eye. Fluorescein angiography showed in both eyes multiple and diffuse leakage points (pinpoint pattern) distributed mostly in the periphery of the subretinal fluid area and pooling of dye corresponding to SRD in the late phase. Spectral domain optical coherence tomography showed a multiple SRD, hyporeflective deposits above the pigmentary epithelium, retinal folds and overall thickening of the choroid with alterations of its layers while the architecture of the retinal layers was preserved in both eyes. B-scan ultrasonography revealed bilateral choroidal thickening. This choroidal thickness increase, associated with the SRD, was interpreted as a choroidal leukemic infiltration. Unfortunately, the patient passed away few days after his medical checkup in our department.

Conclusions
Bilineal leukemia is type of mixed phenotypal acute leukemia that comprises acute leukemias with admixed populations of myeloid and lymphoid blasts. Ocular involvement is common in acute leukemia; it has been reported to occur in up to 90% of patients with this disease. Intraretinal hemorrhages, cotton wool spots, Roth spots and optic nerve head infiltration are fairly common in the fundus of leukemic patients. On the opposite side, SRD, sign of choriocapillaris ischemia secondary to choroidal leukemic infiltration, is a less common ocular finding in leukemia. It has been described in acute lymphoblastic leukemia and less frequently in acute myeloblastic leukemia. This is the first case describing SRD as manifestation of bilineal leukemia. Our case emphasis also the importance of optical coherence tomography imaging which offers a detailed description of the choroidal features when choroidal infiltration is suspected in leukemic cases.

Financial Disclosure
no financial disclosure
Clinical manifestations and imaging characteristics of optic disc pit: A single center case series over 3 decades

Purpose
The purpose of this study was to evaluate the characteristic features, clinical course, and outcome of treatment if given for patients with optic disc pit (ODP).

Setting/Venue
Ulm University Medical School, Department of Ophthalmology

Methods
We retrospectively investigated a consecutive series of patients with a diagnosis of ODP treated between 1993 and 2020 at the Ophthalmology Department of Ulm University. The main outcome measures were age of onset, gender, eye, length of follow-up, location and depth of optic pit, location of subretinal/intraretinal fluid, treatment, visual acuity during presentation and last visit. Patients without optical coherence tomography (OCT) data were excluded.

Results
Twenty-one eyes of 19 patients were included. Mean age during onset was 35 years (2-76 years). Six patients (%31.6) were female while 13 patients (%68.4) were male. Only two patients had bilateral ODP while 17 patients had an unilateral involvement (right eye:5; left eye:12). Multiple ODPs were not observed. Mean depth of the ODP was 568µm (200-1000µm). The ODP extended over 45° in 7 eyes, 90° in 9 eyes, 135° in 2 eyes and 180° in 3 eyes. All eyes except one had a temporally located ODP while one eye had an inferior location. Optic pit maculopathy was associated in 13 eyes (%62). Four eyes with optic pit maculopathy underwent surgical intervention. Among these patients the visual acuity did not vary during follow-up.

Conclusions
In this study, eyes with ODP were observed over a period of up to three decades and almost all eyes demonstrated stable visual acuity. In eyes with surgical intervention the outcomes showed minor changes, and persistent subretinal fluid or retinoschisis was a common occurrence during long term follow-up.

Financial Disclosure
Novartis, Clinical Trial
Title
Photo-optical method and retinal photosensitivity analysis in the multimodal study of the vitreous opacities’ treatment effectiveness by YAG-laser vitreolysis

Purpose
To assess the dynamics of the retinal photosensitivity, the best corrected visual acuity (BCVA) and using photo-optical method the dimming intensity index before and after the YAG-laser vitreolysis.

Setting/Venue
S.N. Fedorov NMRC "MNTK "Eye Microsurgery", Volgograd Branch

Methods
A retinal photosensitivity study (MAIA – CenterVue, Italy) was conducted in 69 patients (69 eyes) aged 20 to 88 years before and after YAG-laser vitreolysis using the Ultra Q Reflex system (Ellex Medical, France). The average age is 58.7 ± 1.8 years, 24 men and 45 women.

Results
Both the BCVA (from 0.69 ± 0.04 to 0.75 ± 0.23) and the average photosensitivity of the macula (from 25.5 ± 0.6 to 26.34 ± 0.6 dB) increased 2 months after the last stage of the YAG-laser vitreolysis. The fixation stability didn’t change significantly. The average floaters area decreased from 3.22 ± 0.89 to 0.8 ± 0.25 mm² (p<0.05). The average value of the dimming intensity index significantly decreased from 59.75 ± 14.17 to 10.02 ± 2.76 (p<0.01).

Conclusions
YAG vitreolysis is a safe and effective treatment of vitreous opacities. The method for quantitative assessing vitreous opacification can be used in diagnosis, monitoring and evaluation of the effectiveness of YAG-laser vitreolysis. The use of the photo-optical method together with microperimetry data extends the possibilities of comprehensive assessment of the effectiveness of YAG-laser vitreolysis.

Financial Disclosure
none
The impact of the COVID-19 pandemic on ophthalmology care

Lucia Gonzalez-Buendia
Spain

Purpose
The disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), COVID-19, has caused a global pandemic with millions of infected people around the world. This unprecedented situation led to a lockdown in many countries, in which population’s movements were strongly restricted. In Spain, this quarantine lasted for more than three months, from March 15th to June 21st 2020 and affected remarkably how outpatient care was provided in health facilities. In this study, we wanted to evaluate the impact of the lockdown on number of visits, intravitreal injections and surgeries in the department of ophthalmology of a Hospital in Madrid, Spain. Deeper understanding of the effects of this situation will allow us to optimize resources and design new strategies to mitigate the negative effect of the pandemic and therefore improve clinical care.

Setting/Venue
Puerta de Hierro-Majadahonda University Hospital, Madrid

Methods
We performed a retrospective, cross-sectional study with data collected from hospital’s administrative services. We reviewed the data from the year 2020 and compared the variables before, during and after the lockdown in Spain, from March 15th 2020 to June 21st 2020. Primary outcome measures studied were number of outpatient (general ophthalmology and retina) and emergency room (ER) visits, number of intravitreal injections and number of surgeries per week. Data were assessed with one-way analysis of variance followed by Dunnett’s multiple comparisons test.

Results
Number of visits per week was 1050.5± 164.21 before, 489.2± 419 during and 811.1± 243.48 after the lockdown. This reduction was significant during the lockdown (p=0.0007). Retina visits per week were 428.33± 50.29 prior, 210.93± 165.1 during and 342.07± 98.89 after, being this difference significant in the lockdown period (p=0.0009). Similarly, ER weekly visits significantly decreased during the lockdown (p less than 0.0001); 174± 53.56 before, during 93.40± 51.05 and after 154.3± 18.61. There were no significant differences regarding number of general ophthalmology, retina nor ER visits before and after lockdown. Intravitreal injections per week were 89.17± 15.96 before, 72.00± 34.96 during and 99.67± 25.64 after. We found no significant differences during nor after the lockdown in this number. Moreover, no differences between the drugs used were seen. Weekly surgeries were 80.33± 15.49 before, 21.53± 30.47 during and 60.04± 33.39 after. Among these, retina surgeries were 9.33± 2.34 per week before, 5.4± 3.29 during and 6.04± 1.63 after. A significant decline in surgeries was observed during the lockdown (p=0.0005). However, a decrease in number of retina surgeries was observed during (p=0.0021) and after lockdown (p=0.0056).

Conclusions
A significant decrease in the number of visits and surgeries during the lockdown was observed. After the lockdown, although still reduced, no statistically significant differences were found regarding number of visits and surgeries between the pre-pandemic and post-lockdown periods. Number of weekly intravitreal injections was dramatically reduced during the first weeks of the quarantine, but interestingly, we saw no statistically significant decline in this variable and the number of injections remained unchanged throughout the lockdown. Further investigation regarding the effect of this pandemic in the clinical setting is mandatory to warrant optimal ophthalmology care.

Financial Disclosure
Jose M. Ruiz-Moreno: Grant of the Spanish Ministry of Health, Instituto deSaludCarlos III, Red Temática de Investigación Cooperativa en Salud: “Prevención, detección precoz, y tratamiento de la patología ocular prevalente, degenerativa y crónica” (RD16/0008/0021). Research support from Topcon, Co. Advisory board of Allergan, Bayer and Novartis. The rest of the authors have no financial relations to disclose.
Purpose
Idiopathic Macular Telangiectasia type 2 (MacTel) is an idiopathic bilateral symmetric macular disease characterized by a slow decrease in visual acuity due to exudation from telangiectatic vessels in the juxta-foveal zone, mainly temporally. Macular pigment (MP) comprises three carotenoids; lutein, zeaxanthin and meso-zeaxanthin. Helb et al first described the unique topographic pattern of abnormal central depletion of MP in MacTel. This was further categorised by Zeimer et al into three classes, corresponding with the severity of the disease. However quantitative analysis of the MP distribution in MacTel and its correlation with functional parameters and OCT morphologic features have not been studied. Moreover, significant differences in the distribution profile of MP have been reported among different ethnicities. This study assesses the quantitative and spatial distribution of macular pigment optical density (MPOD) in eyes with MacTel in comparison to healthy eyes of the Indian population using dual-wavelength autofluorescence. The quantitative MPOD values were correlated with the best-corrected visual acuity (BCVA), OCT features and clinical staging of MacTel.

Methods
The study population included patients with MacTel and healthy controls of South Indian origin. MacTel was classified according to the 5 stages described by Gass-Blodi and Yannuzzi et al. MPOD was measured with dual-wavelength (486, 518nm) autofluorescence on Spectralis HRA+OCT. 30°×30° fovea-centred raster scans were taken after dilation. OCT features noted were foveal pit blunting, inner and outer retinal cavities (IRC and ORC), ILM draping, intraretinal hyperreflective lesions, ELM disruptions, foveal thinning and subretinal neovascularization. Heidelberg Eye Explorer software (HEYE) was used to create MPOD density maps. The plateau (reference point for the absence of MP) was set at 6° eccentricity. Average MPOD at 1°, 2° radii and macular pigment optical volume (MPOV) corresponding to eccentricities of 1°, 2° and 6° radii were calculated. ImageJ software was used to calculate MPOD in 9 zones of the ETDRS grid and 30° radial sectors (15°, 45°, ... , 345°). MPOD in the desired central region and surrounding ring in MacTel patients were also measured with an ImageJ tool. MPOD values were expressed in density units (d.u.) and MPOV (sum of optical density values at all points) in d.u.degrees². SPSS Statistics 21 software was used for statistical analysis. P<0.05 was considered statistically significant.

Results
60 eyes of 31 controls and 41 eyes of 22 patients were enrolled. The mean age was 39.10 ± 12.74 years in controls and 58.09 ± 10.19 years in patients. There was a significant difference between patients and controls in the mean MPOD and MPOV at all radii eccentricities (1°, 2°, 6°) and mean MPOD in all radial sectors. At 1° eccentricity, mean MPOD was 0.38 ± 0.11 d.u. and -0.10 ± 0.14 d.u. while mean MPOV was 787.95 ± 225.13 d.u.degrees² and -211.63 ± 223.42 in controls and patients respectively. Highest MPOD was noted in central 1mm ring (0.29) in controls and peripheral 6mm ring (0.01) in patients, with significant differences in all ETDRS zones except 3 peripheral ones. Clinically, no patient was diagnosed with stage 1 MacTel; stages 2-3 were combined in one group and stages 4-5 in another. MPOD was significantly higher in the surrounding ring than the central region in stages 2-3 and 4-5. There was a positive and significant correlation of mean MPOD in the surrounding paracentral ring with BCVA. On correlating with OCT features, there was a significantly lower mean MPOD of the central area in eyes with inner retinal cavities and ELM disruption.

Conclusions
This study shows reduced MP across various spatial profiles in MacTel as compared to healthy subjects among the South Indian population. In all stages of MacTel, there was well-defined central depletion with high MP in the surrounding ring. The high paracentral MP could be due to abnormal binding or centrifugal displacement of central MP. There were no significant differences in the quantitative MPOD between the MacTel stages, implying that central MP loss is not an indicator of early disease. In addition to the measurement and distribution of MP being affected in MacTel, MP levels were associated with structural changes on OCT and functional changes like visual acuity. MP depletion was related to the presence of IRC and ELM disruption on OCT, both of which may be due to Muller cell loss or damage. These findings add to the evidence that Muller cell dysfunction plays an important role in the pathophysiology of MacTel including the redistribution of MP. The positive correlation between paracentral MPOD and BCVA suggests a potential for visual improvement with lutein or zeaxanthin supplementation. These findings may have implications for novel therapeutic strategies targeting Muller cells or involving dietary supplementation.
**Title**

Existence of SARS-CoV-2 RNA (genomic and subgenomic) in Retina and Optic Nerve of COVID-19 patients

**Purpose**

Evaluation of the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ribonucleic acid (RNA) in human retinal biopsies (RB) and optic nerve biopsies (ONB) in deceased patients with confirmed novel coronavirus disease 2019 (COVID-19).

**Setting/Venue**

Retrospective Study on 14 enucleated eyes of 14 deceased COVID-19 patients.

**Methods**

Retinal biopsies and ONB were taken during autopsy. Biopsies were assessed by molecular detection of viral RNA, virus cultivation and immunohistochemistry on SARS-CoV-2 spike protein. SARS-CoV-2 RNA loads of RB and ONB were compared to RNA loads of the respective throat-swabs, vitreous humor- and blood samples.

**Results**

Genomic SARS-CoV-2 RNA was detected in 50% of RB and in 76% of ONB and subgenomic RNA (sgRNA) in 40% of RB and 60% of ONB. Virus isolation failed and immunohistochemistry of SARS-CoV-2 spike protein was negative in all biopsies.

**Conclusions**

SARS-CoV-2 RNA exists in RB and ONB of COVID-19 patients. But, as virus isolation failed and immunohistochemistry of SARS-CoV-2 spike protein was negative in all biopsies an active infection of the retina and optic nerve seems unlikely.

**Financial Disclosure**

Competing interests: All authors declare that there is no actual or potential conflict of interest in relation to this article.

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**Title**

Evaluation of Choroidal Vascularity Index in Sarcoidosis Patients without Ocular Involvement

**Purpose**

To evaluate choroidal structural changes in sarcoidosis patients without ocular involvement using choroidal vascularity index (CVI) which was computed from image binarization tool on enhanced depth imaging-optical coherence tomography (EDI-OCT) scans.

**Setting/Venue**

HAYDARPASA NUMUNE TRAINING AND RESEARCH HOSPITAL, ISTANBUL.

**Methods**

Thirty-two eyes of 16 biopsy-proven sarcoidosis patients without ocular involvement and 20 age-, sex-, and spherical equivalent matched healthy controls were included in this study. None of the patients had cardiac involvement and a history of corticosteroid use for at least three months at the time of OCT shots. Total choroidal area was segmented into luminal (LA) and stromal interstitial area (SA) by the binarization technique using ImageJ software (Bethesda, MD). CVI was defined as the ratio of LA to the total choroidal area (TCA).

**Results**

The CVI was computed 70.63 ± 4.93 % in patients with sarcoidosis, which was significantly higher compared to healthy controls (67.6 ± 2.04, p < 0.001). The SA and LA were found significantly lower in patients with sarcoidosis than the controls (2.47 ± 1.22 vs. 3.60 ± 1.11, p < 0.001; 4.81 ± 0.02 vs. 6.42 ± 0.17, p < 0.001, respectively).

**Conclusions**

In the presented study, it was found that patients with sarcoidosis had higher CVI values when compared to normal subjects. It seems both luminal and stromal areas of choroid were affected in sarcoidosis patients without ocular involvement.

**Financial Disclosure**

The authors declared that this study received no financial support.
Title
To evaluate patient compliance for prone positioning after surgery using an innovative device.

Purpose
To investigate the use of an innovative device (post vitrectomy recovery system) that has a sensor embedded in the headrest (horse shoe shaped) with data-logging function in real time to measure compliance of patients to maintain face down positioning (FDP) after vitrectomy surgery.

Setting/Venue
All patients were enrolled after taking an informed consent for the Vitrectomy surgeries requiring face down positioning in the post operative period. All surgeries were performed by a single surgeon. Surgeries done included macular hole, retinal detachment with inferior retinal breaks and open globe injury with IOFB with retinal detachment.

Methods
Patients were asked to use the cushion to maintain face down positioning as soon as the patient reached home after surgery. The sensor relayed the data via an inbuilt SIM card to our server online which helped to track the data in real time regarding the duration for which the prone position was maintained. Within our pilot study, we investigated the use of a (patent pending) pressure sensor embedded in the headrest of a supportive furniture with data-logging function to measure the compliance of patients after vitrectomy surgery. The sensor was build to relay the data as soon as it is pressed and so the duration for which the sensor is pressed could be tracked. 13 patients were evaluated but 2 patients had to be excluded as they could not maintain FDP in the post op period due to chest pain and Breathlessness during FDP. 11 patients were evaluated in this pilot project, out of which 6 were male and 5 were females with the age group ranging from 28 - 71 years. The duration of prone position maintained, varied from 4 days to 12 days.

Results
The average duration of face down positioning was 5.5 hours in the first 24 hours. Compliance for FDP reduced over the next few days. The adherence was significantly better after MH surgery than after RRD surgery. Adherence was higher in female than in male patients. Out of 11 patients, 5 underwent macular hole surgeries which showed a successful closure of MH in all cases. Out of 5 patients of retinal detachment, 4 cases achieved anatomical success and one case required re surgery in the postoperative period. Patients were given a questionnaire which suggested the device did help them in improving compliance to maintain FDP in the post op period.

Conclusions
To summarize, we observed a good acceptance of our device to measure compliance of patients after vitrectomy surgery to maintain FDP. Further studies are needed to analyse how much time of FDP is sufficient to improve the surgical success in the indicated cases.

Financial Disclosure
YES i do have financial relation with the company that i have developed the device along with. company name is Vision cure private LTD. and i have an equity stake in this company that will providing this device in the future. my role has been of advisory, in the development of this innovative device.
**Title**
Retinal tomographic changes associated with hydroxychloroquine (HCQ) in patients with early functional retinal damage

**Presenters**
Raquel Maroto Cejudo, Spain

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**Purpose**
To evaluate retinal layer thickness using spectral-domain optical coherence tomography (SD-OCT) in patients under HCQ treatment, depending on the presence of multifocal electroretinogram (mFERG) alteration

**Setting/Venue**
Transversal study that included tomographic analysis of patients under treatment with HCQ for at least 5 years or with risk factors associated, that underwent mFERG study.

**Methods**
Tomographic images obtained with SD-OCT were automatically segmented. Visual field and autofluorescence were also performed. Eyes were divided according to the presence or absence of early alterations in the mFERG. p value <0.05 was considered statistically significant.

**Results**
78 eyes of 39 patients with a mean age of 54.8 ± 15.4 years were included. 40 eyes presented incipient retinal toxicity in the mFERG, with a mean duration of HCQ treatment of 8 ± 4.4 years. No difference in age between groups was observed. Any patient without damage in the mFERG secondary to HCQ showed alteration in the visual field, autofluorescence or the external retina, while in the mFERG affected group 11 patients had damage in the visual field, 6 in the autofluorescence and 2 in the external retina. Total retinal thickness was lower in patients with central mFERG and external ring damage. There were statistically significant differences in the following layers: Ganglion cells (external ring), internal plexiform (external ring), internal nuclear (lower), and external plexiform (lower and temporal). There were no differences in the outer nuclear layer neither the pigment epithelium of the retina.

**Conclusions**
Early damage in the multifocal electroretinogram caused by the administration of hydroxychloroquine is accompanied by a thinning of the internal retina from very early stages, even before being able to appreciate the tomographic changes described in the external retina.

**Financial Disclosure**
No financial relations
Half-dose photodynamic therapy versus 577 nm subthreshold pulse laser therapy in treatment-naive patients with central serous chorioretinopathy

**Purpose**
To compare real-life anatomical and functional outcomes of half-dose photodynamic therapy (HD-PDT) and 577 nm subthreshold pulse laser therapy (SPL) in treatment-naïve patients with central serous chorioretinopathy (CSC).

**Setting/Venue**
Retrospective

**Methods**
We retrospectively reviewed consecutive treatment-naive CSC patients with non-resolving subretinal fluid (SRF)>2 months, who received HD-PDT or SPL treatment. One repetition of the same treatment was allowed in patients with insufficient response. Functional and anatomical outcomes were assessed after first treatment and at final visit.

**Results**
We included 95 patients (HD-PDT, n=49; SPL, n=46). In the HD-PDT and the SPL group, 21 patients (42.9%) and 19 patients (41.3%, P=0.878) exhibited complete resolution of SRF after the first treatment, respectively. 22 patients (44.9%) and 20 patients (43.5%) received a second treatment due to persistent SRF, and the remainder opted for no second treatment despite persistent SRF. Following the second treatment, SRF resolution was observed in 61.2% (n=30) and 60.9% (n=28; P=0.972) of all patients, respectively. Mean BCVA improved significantly in both groups with a similar median change of BCVA of 0.10 logMAR.

**Conclusions**
High-density 577 nm SPL resulted in as good anatomical and functional treatment and may represent an alternative treatment for CSC.

**Financial Disclosure**
No Relation
Management of intraocular pressure elevation in patients with retinal diseases receiving intravitreal injections of anti-vascular endothelial growth factor

Studies have demonstrated that 66–100% of patients with retinal disease receiving treatment with intravitreal injections (IVI) of anti-vascular endothelial growth factor (VEGF) experience an immediate rise in intraocular pressure (IOP), while according to some authors, 4–15% of patients may develop long-term ocular hypertension. Consensus is required on the optimal management of IOP elevation for ophthalmologists treating patients with anti-VEGF IVI.

A team of retinal disease experts from the Vision Academy collaborated to develop recommendations on key principles for managing elevation in IOP that results from anti-VEGF IVI. The Vision Academy comprises over 90 international retinal experts who collaborate to provide collective recommendations on clinical challenges in areas where there is a lack of conclusive evidence. Vision Academy recommendations are subject to a validation process to ensure there is consensus and endorsement from the entire group.

Literature searches were performed using the MEDLINE/PubMed database; the cut-off date was November 2020 and searches were restricted to English-language publications. The results were used to inform the Vision Academy recommendations.

Risk factors for IOP elevation during anti-VEGF treatment include previous diagnosis/family history of glaucoma, history of retinal vein occlusion, frequent injections, and higher pre-treatment IOP. Topical anti-glaucoma monotherapy is often sufficient to reverse moderate IOP elevation; some patients may require 2–4 medications, laser trabeculoplasty, or filtering surgery. Patients with sustained IOP elevation require regular assessment by a glaucoma specialist to ensure optimized treatment/monitoring. Measurement of IOP and direct observation of the optic disc should be performed prior to each injection. Additional monitoring may include automated static perimetry and optical coherence tomography for retinal nerve fiber layer imaging at baseline and every 8–12 months. For patients with retinal vein occlusion or severe diabetic retinopathy, gonioscopy should be performed at baseline and every 4–6 months to exclude angle neovascularization. For patients with advanced glaucoma or reduced retinal nerve fiber layer thickness, IOP should be measured after each injection and prophylactic anti-IOP treatment prior to each IVI considered. Post-injection acetazolamide may be required where glaucomatous optic neuropathy is progressing despite IOP-lowering treatments. As higher IVI frequency has been linked to IOP elevation, switching to a treat-and-extend regimen may reduce the risk of visual function loss due to glaucoma.

Ophthalmologists should be aware of the risk factors for IOP elevation in patients receiving anti-VEGF IVI, and they should ensure appropriate monitoring and treatment with the involvement of a glaucoma specialist. The risk of decline in visual function due to glaucoma versus retinal disease must be balanced; if a critical stage of glaucoma is reached, discontinuation of anti-VEGF IVI may need to be considered.

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**Title**
Long Term Fluorescein Angiography Results of the Babies Who Underwent Intravitreal Bevacizumab Injection due to Retinopathy of Prematurity

**Presenter**
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**Purpose**
To evaluate the long-term Fluorescein Angiography (FA) results of the babies who underwent intravitreal Bevacizumab Injection due to retinopathy of prematurity (ROP) disease.

**Setting/Venue**
We retrospectively reviewed the angiograms of patients with ROP disease who underwent intravitreal Bevacizumab injections.

**Methods**
Gestational age at birth and birth weight, ROP zone, ROP stage, mean age at treatment, the recurrences and avascular zone findings in FA were recorded. FA was obtained at the gestational age of 60 weeks. Aggressive posterior ROP (APROP) and other ROP stages were evaluated individually.

**Results**
Nineteen eyes of 19 premature infants were included in the study. The mean gestational age at birth was 28.5 (range 25 to 32) weeks, mean birth weight was 1163 (range 700 to 2500) g, mean age at treatment was 33.5 (range 32 to 36) weeks, mean gestational age at the time of FA was 62.2 (range 60 to 65) weeks. The avascular area in the patients who were treated because of APROP disease and other ROP stages was 6.8 (range 5-8) and 2.4 (range 2-4) optic disc diameter respectively and it was statistically significant. All of the eyes in two groups underwent one Bevacizumab injection. No recurrence or leakage was observed in all groups.

**Conclusions**
The avascular retina areas were greater in APROP patients who were treated with intravitreal bevacizumab injection. No recurrence or leakage was identified by FA in the two groups. Laser photocoagulation treatment may be a safe treatment option for avascular retina areas.

**Financial Disclosure**
none
Infective endocarditis diagnosis after acute unilateral visual loss

**Purpose**
We present a case of visual loss as the first manifestation of an infective endocarditis, in order to describe the importance of a detailed systemic examination after ophthalmic signs.

**Setting/Venue**
Ophthalmic symptoms could reflect clinical manifestation of systemic diseases. Ophthalmologists need to be alerted to discover uncommon diseases which debut as visual loss or any sign in fundus examination.

**Methods**
A 67-year-old male was admitted in the ER complaining blurred vision in his left eye during 10 days, associated with 40°C fever and intense fatigue. He also referred spots and painful nodules on both hands and feet. We underwent a complete clinical examination. Visual acuity was 20/20 in the right eye and 20/40 in the left eye. Slit-lamp examination was unremarkable, as well as the intraocular pressure, which was 12 mmHg in both eyes. Fundoscopy and retinography were normal in the right eye; his left eye showed peripheral retinal microhemorrhages associated with vitreous opacities.

**Results**
The microhemorrhages observed in the fundoscopy matched with retinal Roth's spots. The association of fever, fatigue, skin lesions and Roth's spots suggested an infective endocarditis as a first diagnosis. The patient was admitted to internal medicine, where he had blood analytics and cultures performed, showing 18000 leukocytes with neutrophilia and positiveness to Staphylococcus aureus. An echocardiography confirmed the diagnosis of infective endocarditis.

**Conclusions**
Infective endocarditis is an infection of the inner heart's surface that can produce septic emboli, leading to severe complications such as retinal hemorrhages with vision loss, brain strokes and other fatal complications. It is crucial to suspect it when an acute unilateral vision loss is associated with systemic symptoms such as fever, fatigue and skin lesions. Although not being pathognomonic, Roth's spots are strongly associated with infective endocarditis. A rapid diagnosis may improve the patients' prognosis and avoid eventual fatal complications.

**Financial Disclosure**
None
**Title**
Vitreo-Retinal Cases dan Surgeries at Cipto Mangunkusumo National General Hospital in the Era of COVID-19

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**Purpose**
This study aimed to describe the clinical characteristics and demographics of patients with vitreoretinal disease visiting the outpatient clinic and undergoing surgery at Cipto Mangunkusumo National General Hospital during Indonesia’s large-scale social restriction due to COVID-19 pandemic.

**Setting/Venue**
Vitreoretina division, Department of Ophthalmology, Cipto Mangunkusumo National General Hospital, Faculty of Medicine, Universitas Indonesia, Jakarta

**Methods**
We conducted a retrospective descriptive study of patients visiting vitreoretinal division at Cipto Mangunkusumo National General Hospital from March 2020 to June 2020. Demographical data, comorbidities, BCVA, diagnosis, types of surgery, and anesthesia was obtained from patient’s medical records and presented as percentage.

**Results**
755 outpatient cases and 245 surgery cases were included in this study. Mean age for outpatient and surgery case was 51.6 years and 52 years, respectively. Five most common diagnosis in the clinic was post vitrectomy and endolaser (26.6%), proliferative diabetic retinopathy (18%), post vitrectomy (17.8%), rhegmatogenous retinal detachment (10.5%), and vitreous hemorrhage (6.6%). Meanwhile, for surgery cases, rhegmatogenous retinal ablation accounts for the highest diagnosis (48.2%), followed by silicon filled eye (16.3%), diabetic retinopathy (9%), retinal detachment (8.2%), vitreous hemorrhage (5.3%). Diabetes and hypertension are the two most common comorbidities found in outpatient clinic (58.5%) and in these cases were the result of readjustment made according to the recommendation of American Academy of Ophthalmology (AAO) for patient care during COVID-19 pandemic to reduce unnecessary visits and procedures in order to decrease COVID-19 transmissions.

**Conclusions**
The COVID-19 pandemic has required hospitals to adapt by making readjustments in order to reduce the transmission of the virus. In the vitreoretinal division, Cipto Mangunkusumo National General Hospital, protective measures have been implemented using screening and prioritization methods recommended by AAO. Since then, the number of outpatient and surgery cases have dropped, proving the effectiveness of the readjustments made.

**Financial Disclosure**
None
### Title
Parapapillary sparing in two cases of retinal dye-induced toxicity after macular pucker surgery: is a parallelism possible with Stargardt' disease?

### Purpose
The aim of this abstract is to describe the pattern of retinal damage in two patients that showed an adverse dye-related event after macular surgery for pucker. Since the day after an unusual retinal inflammation was noted in both patients and during the follow-ups the absence of recovery with progressive degeneration of stained tissues became evident. Vital dyes are commonly used in chromo-vitrectomy and macular surgery. Their toxicity is clearly reported in pre-clinical, clinical and real-life studies, with the report of a possible compromise of cell viability and their apoptosis. In our cases, in the hypothesis of a combined effect of dye- and light- mediated toxicity a similitude with the most common inherited macular dystrophy was made, the Stargardt' disease. This retinal dystrophy recognizes the formation of a peculiar lipofuscin, the A2E, in photoreceptors, that are progressively intoxicated by this compound. A biallelic mutation in ABCA4 gene is considered causative for this disease as for other retinal degenerations, that show the sparing of the parapapillary area (in up to 98% of patients) as common marker. In all of them the role of light as mediator of this damage has been hypothesized and partially demonstrated, but still under research.

### Setting/Venue
The setting of our findings was the ophthalmology complex operative unit of “spoke” hospital “Alto Vicentino” (VI)- (Garziere St. 42, 36014 Santorso VI) in the north of Italy. Both patients were followed for macular pucker in the surgical retina service of our unit since 2020. When ocular surgery became indicated, the procedure was scheduled and done; both during the same week of this year. Informed consensus from Italian Society of Ophthalmology was obtained and signed by each patient and all internal protocols were respected to ensure traceability and documentation for each visit and procedure.

### Methods
The method of investigation for this study is a case report with critical literature review in the effort of interpretation for our findings. A micro incisional vitreoretinal surgery (MIVS) with 3 standard 25 gauges sclerotomies was performed. Both patients’ retinas were stained for 30 seconds two times during the procedure with a vital dye, to highlight both epiretinal membrane and internal limiting membrane (ILM). A commercial sterile solution of Trypan Blue and Brilliant Blue G, solved in a physiologic phosphate buffer of sodium chloride, was used. Polyethylene glycol (PEG) was the support in this dye and lutein was present. A comprehensive ocular examination was obtained in the pre-op, Patient 1 underwent a ff-ERG; this exam showed no abnormal assessment for both of our patients. Optical Coherence Tomography (OCT), Optical Coherence Tomography Angiography (OCT-A), Fluoresceine Angiography (FA), Indocianine Green Angiography (ICGA), blue Auto-Fluorescence (AF) and Multi Color images (MC) were also obtained using the Spectralis (Heidelberg Engineering Inc. - Franklin, USA). A complete full-field electroretinogram (ff-ERG) was done post-op in one patient. Immediately, when the adverse event was firstly hypothesized, the hospital committee was alerted. A formal report to the Italian pharmaceutical agency was also made, to let them investigate if impurities or contaminations were present into the pharmaceutical lot.

### Results
Both patients were Caucasian, Patient 1 was a 70-year-old female, Patient 2 was an 83-year-old male. Pre-op best correct visual acuity (BCVA) was respectively 0.3 LogMAR in for patient 1 and 1.0 LogMAR for patient 2. Post-op follow-up immediately showed an inner retina inflammation (starting from the retinal nerve fiber layer), that progressively deepened in the external layers and progressively destroyed photoreceptors/retinal pigmented epithelium/choriocapillaris. When external retina damage appeared, the OCT showed a sort of “crumbling” with multiple hyper-reflective spots and accumulation of drusen-like lipofuscin material, extended from posterior pole to nasal retina. In this scenario we observed complete parapapillary sparing in a circular area of about 700 microns. Both FA and ICGA showed a “salt and pepper” appearance with complete parapapillary sparing from the damage, AF and MC also confirmed this finding. In all exams we observed again a complete parapapillary preservation. The OCT-A too showed a circular parapapillary area of choriocapillaris sparing. After completing the surgical recovery, post-op BCVA was 1.6 LogMAR in both patients with many uncertainty and research, linked to the reported presence of a central scotoma. Furthermore, 2 months post-op, Patient 1 underwent a ff-ERG; this exam showed no abnormal responses from photoreceptors.

### Conclusions
To investigate how the retina of our unfortunate patients was destroyed, we decided to perform many exams that all coherently showed sparing of the structure and function of parapapillary retina. This area, where the dye is mainly concentrated by gravity action during the procedure, appeared curiously preserved in both patients, in a really superimposable fashion. We don’t know if impurities or contaminations may have been present in our dyes, but in a pathogenic hypothesis the presence of a toxic light-activated compound in the external retina could have been present. The parapapillary sparing may represent an effect of a better choriocapillaris washout of toxic substances in this area, and the presence of a different vascular flow could be the reason. A similar mechanism may also be hypothesized in ABCA4-related diseases.

Literature has shown in many case-reports how colorants can cause damage, mainly if they come in contact with the external retina, as it may happen during full thickness macular hole surgery. Further investigations may be needed to better understand the pathophysiology of the reported damage. Nevertheless, a lesson from this unlucky story may come out for many other ophthalmologists and patients.
Assessment of Macular Parameters measured by OCT-A in patients with Graves’ Disease with and without Graves’ Orbitopathy

目的
Graves’ Orbitopathy (GO) 与视网膜变化相关，由于视神经组织的水肿和缺氧导致的缺血。我们的目标是评估Graves’ Disease (GD) 病人与GO病人的黄斑血管和形态参数。

方法
本研究包括了GD病人与GO病人，以及年龄和性别匹配的健康对照。受试者进行了全面的眼科检查，包括通过光学 coherence tomography angiography (OCT-A) 测量的黄斑血管和形态参数。

结果
24只正常眼睛被纳入对照组，平均年龄为41.00±13.65岁，34只被纳入GD组，18只GO病人和16只非GO病人，平均年龄分别为44.44±14.95岁和45.75±10.59岁。所有GO病人都有静息病(平均CAS: 1.33±0.69)。GO亚组的黄斑厚度测量最低，特别是在黄斑中央厚度(GO vs Controls: 251.38 ± 31.99 vs 258.42 ± 22.33µm，GO vs GD without GO: 251.38 ± 31.99 vs 255.31 ± 28.06µm，p<0.05)。形态学参数在GO病人和非GO病人之间没有差异(p>0.05)。

结论
我们的结果证实了GD对黄斑参数有负面影响。虽然黄斑结构变化与GO相关，但在GO病人中，黄斑密度和流速降低(p<0.05)。血管参数在GD病人之间没有差异，只有中央密度和流速(GO vs GD without GO: 7.84 ± 4.11 vs 9.09 ± 4.40mm⁻¹, p=0.04; 0.15 ± 0.09 vs 0.22 ± 0.02 mm⁻¹, p=0.01, respectively)。

财务披露
无。
The relationship between central serous chorioretinopathy and an increased risk of depression: A population-based cohort study

**Purpose**
To investigate the association between central serous chorioretinopathy (CSC) and the risk of developing depression. The risk factors associated with depression in CSC patients were also analyzed.

**Setting/Venue**
Population-based, retrospective cohort study.

**Methods**
Using the Taiwan National Health Insurance Research Database which was conducted from January 2001 to December 2013, a total of 25,939 subjects with CSC were enrolled in the CSC group and 103,756 subjects without CSC were enrolled in the control group. The two groups were matched on age, gender, and index year at a ratio of 1:4, and were followed until the end of 2013 to see whether they developed depression. Kaplan-Meier curves were generated to compare the cumulative hazard of subsequent depression between the two groups. A Cox regression analysis estimated the crude and adjusted hazard ratios (HRs) for depression. The confounders adjusted included age, gender, Charlson comorbidity index, insurance cost, urbanization level, hypertension, peptic ulcer, and smoking. Subsequently, we focused on the CSC group to investigate the risk factors leading to depression.

**Results**
The mean age of the cohort was 42.9 years. The CSC group had a significantly higher cumulative incidence of depression than the control group (6.0% vs. 4.6%, p value smaller than 0.0001). The Cox regression model indicated that the CSC group had a significantly higher risk for depression prior to and after adjustment of confounders (unadjusted HR= 1.32; adjusted HR = 1.29, both p value smaller than 0.0001). Within the CSC group, significant risk factors for depression included age, female gender, low income, first-onset CSC, peptic ulcer, and smoking. The recent use of steroids prior to CSC, by all routes of administration, also significantly increased the risk for depression. However, treatment of CSC reduced the risk of developing depression but did not reach a statistical significance.

**Conclusions**
Patients with CSC are at significantly greater risk of developing depression. Among CSC patients, age, female gender, low income, first-onset CSC, peptic ulcer, smoking, and recent use of steroids prior to CSC were significant risk factors for depression. Furthermore, treatment of CSC did not significantly reduce the risk for depression.

**Financial Disclosure**
The authors have no financial or other conflicts of interest to report.
Recurrent Choroidal Detachment in Peritoneal Dialysis Patient with Hypervolemia and Dilutional Hypoalbuminemia: A Case Report

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United Kingdom

Purpose
The following presents a case of recurrent choroidal detachments (CD) correlated with changes in serum albumin levels and the patient's fluid status.

Setting/Venue
Chulalongkorn University and King Chulalongkorn Memorial Hospital

Methods
A 71-year-old female patient presented with a four-day history of blurry vision in her left eye. Pertinent medical history included end-stage renal disease treated with continuous ambulatory peritoneal dialysis. Previously, the patient's left eye was treated for primary angle-closure glaucoma by trabeculectomy. While this resulted in a low baseline intraocular pressure (IOP) of 2–7 mmHg, the patient never developed any hypotony-related complications for the past six years. After examination, CD was diagnosed and treated with transscleral surgical drainage. The patient further developed two additional episodes of CD in the same eye. All episodes were also associated with bilateral pitting edema, weight gain, and hypoalbuminemia. Thus, the patient was recommended to take a protein supplement and limit her fluid intake. Additionally, the dialysis treatment regimen was altered to achieve greater daily fluid removal.

Results
After 12 weeks, there was no recurrent episode of CD, and the patient was clinically stable with a final visual acuity of 20/30 and an IOP of 3 mmHg. The serum albumin levels improved slightly, and there were no signs of hypervolemia.

Conclusions
In this case of recurrent CD, a possible association between the development of CD, hypoalbuminemia, and hypervolemia in patients with end-stage renal disease is demonstrated. Clinicians should be aware that these systemic factors can be tied with recurrent CDs, especially among patients with a low baseline IOP.

Financial Disclosure
No conflict of interest
Localised injection site inflammation following intravitreal anti-VEGF therapy

To report a case series of patients who developed localised ocular surface inflammation following intravitreal anti-VEGF injection. In addition, to characterise the clinical appearance of these reactions and how they can be appropriately managed.

The patients within this study attended the macular department at University Hospital Ayr for intravitreal anti-VEGF treatment of macular oedema.

A retrospective case review of patients presenting with similar injection site reactions following their intravitreal treatment. Patients within this study had received either Eylea (Aflibercept) or Lucentis (Ranibizumab). Assessment included slit lamp examination, clinical photographs and anterior segment OCT directly over inflamed area.

The patients developed symptoms within a week following injection, were highly symptomatic and had some clinical similarities to localised anterior scleritis. All patients were reported to have resolution of symptoms following the use of topical steroid. The observed reaction appears to be unrelated to previous injections, site of injection or drug type.

This is an uncommon side-effect observed in patients undergoing intravitreal anti-VEGF. Early identification of injection site inflammation, and prompt distinction from more serious adverse events such as endophthalmitis is essential to ensure appropriate management.

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Systematic review of myopic choroidal neovascularization management and long-term outcomes

**Purpose**
To summarize the current understanding of myopic choroidal neovascularization (mCNV) and to review the latest data regarding predictive factors of long-term morphological and visual outcomes in patients with mCNV treated with intravitreal anti-vascular endothelial growth factor (anti-VEGF) drugs.

**Setting/Venue**
Systematic review conducted by investigators from the Ophthalmology department of Centro Hospitalar Universitário S. João (Porto, Portugal), a tertiary university hospital.

**Methods**
We conducted a literature review in September 2020 of all English-language articles in PubMed resulting from searches of the following MESH terms: “choroidal neovascularization” AND “myopia” OR “Myopia, degenerative” OR “myopic macular degeneration” OR “myopic maculopathy” OR “myopic retinopathy” OR “pathological myopia” OR “pathologic myopia”. The titles and abstracts of the retrieved articles were independently scanned by 2 authors to gather information and determine whether they met inclusion criteria. After the preliminary search of the target database, we reached 431 articles. After reading the title and abstract, 62 articles were deemed as relevant for full publication review. After reading the full text, 18 articles were excluded (but we included an additional 29 studies after search of reference lists within the selected publications). To assess the risk of bias of each individual study we used the National Institutes of Health criteria. A questionnaire of four questions was applied according to the design of each study. If at least two of the four questions were positively answered, we concluded that the study was of adequate quality and included it in our review. The questionnaire was independently applied by 2 authors. This resulted in 73 articles being used to develop this review.

**Results**
Pathological myopia (PM) is one of the main causes of low vision worldwide. It is estimated around 3% of the world population suffers from PM. Of the affected individuals, 5-11% will develop mCNV. Furthermore, 35% of the patients with mCNV will develop bilateral disease in an 8-year period. Highly myopic patients experiencing a sudden loss of central vision should be referred for further examination. Once a diagnosis of myopic CNV has been confirmed, treatment initiation should be prompt and anti-VEGF agents should be considered as first-line therapy. Both intravitreal ranibizumab and intravitreal aflibercept have been approved for myopic CNV, but intravitreal bevacizumab has proven to be equally effective in non-randomized clinical trials and has been used off-label in clinical practice for a long time. Available long-term data for anti-VEGF agents are encouraging and significant gains in best corrected visual acuity (BCVA) have been observed at up to seven years of follow-up with anti-VEGF therapy for mCNV.

**Conclusions**
Available long-term data for anti-VEGF agents are encouraging and significant long-term gains in BCVA have been recently demonstrated. Notwithstanding, many patients experience stabilization or a decrease in their BCVA over time due to development or progression of perilesional chorioretinal atrophy (CRA). In fact, anti-VEGF treatment does not prevent development of new or enlarged areas of CRA around the regressed CNV lesion (perilesional CRA). Future studies are required to identify therapies that prevent perilesional CRA development/progression.

**Financial Disclosure**
No financial disclosures.
Intravitreal Brolucizumab in poor-responsive neovascular age-related macular degeneration

**Purpose**
To evaluate the long-term safety and efficacy of Brolucizumab in pretreated poor responsive nAMD patients.

**Setting/Venue**
Prospective study at the Department of Ophthalmology, Ulm University

**Methods**
Pretreated eyes with poor-responsive nAMD were switched to Brolucizumab and were consecutively evaluated during standardized Brolucizumab treatment. Functional and morphological parameters including best-corrected visual acuity (BCVA), central retinal thickness (CRT), presence of pigment epithelium detachment (PED), presence of retinal fluid compartments ((intraretinal fluid (IRF) and subretinal fluid (SRF)) as well as adverse events were assessed and evaluated over a follow-up period of 32 weeks.

**Results**
A total of 36 eyes from 32 consecutive patients (13 males and 19 females) with nAMD were included. The mean age at enrollment was 78.12 years. Although mean CRT improved from 312µm at baseline to 270µm at 16 weeks and 260µm at 32 weeks, BCVA remained unchanged during the follow up period (0.65 LogMAR at week 32). IRF and SRF were present in 21 and 28 eyes at baseline, in 9 and 11 at week 32, respectively. Five study eyes developed intraocular inflammation (IOI) after administration of Brolucizumab (1 retinal vasculitis with vitritis and 4 anterior or intermediate uveitis), none of the Patients developed a decrease of BCVA.

**Conclusions**
Brolucizumab seems to offer an alternative for poor responsive nAMD patients with longer injection intervals while preserving visual acuity and improving morphological parameters. Longterm evaluation of improved morphological parameters is mandatory. Monitoring for IOI seems indispensable.

**Financial Disclosure**
Armin Wolf receiving honoraria for advisory services from Novartis.
**Title**

In-vitro comparison of pharmacological substances for the prophylaxis of proliferative vitreoretinopathy.

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**Purpose**

The current treatment of proliferative vitreoretinopathy (PVR) is a surgical one and shows high recurrence rates accompanied by a reduced visual outcome. To our best knowledge, there is no clinically available pharmaceutical option to prevent or treat PVR. Yet, numerous drugs have been proposed in the literature to be useful for this purpose. This study is to systematically compare the substances described in order to determine the most promising candidates. Those could then be explored in further experiments and research.

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**Setting/Venue**

Cell- and molecular Biology Laboratory, Department of Ophthalmology, University Hospital, LMU Munich, Munich, Germany

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**Methods**

A structured literature review was conducted using the "PubMed" database to identify previously published agents proposed for the prevention of PVR. After a manual review, 117 substances emerged as possible candidates. Substances were included when being approved by the Food and Drug Administration and the European Medicines Agency for other purposes and without genotoxicity. 36 substances remained and were compared systematically regarding their toxicity and antiproliferative effect. Human primary retinal pigment epithelial cells (hRPE) served as a model for PVR, because they differentiate to a myofibroblastic phenotype after cultivation in cell culture medium with fetal calf serum. To ensure the cell phenotype, cell lines were tested for their epithelial origin by immunofluorescence staining. The cell viability on non-proliferating cells was determined with a colorimetric viability assay (XTT and WST-1). In the subsequent proliferation experiments, the cells were exposed to the non-toxic concentrations and the proliferation was also measured by WST-1.

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**Results**

Of the 36 substances and ingredients tested, 13 showed neither toxic nor antiproliferative effects. 6 substances had a significant (p \(\leq 0.05\)) toxic effect in higher concentrations. When excluding those, no antiproliferative effects could be detected. The remaining 17 substances showed significant antiproliferative effects (p<0.05). In some cases, concentrations that proved to be toxic were excluded in advance and replaced by lower concentrations. Five substances stood out in particular and appear to be the most promising for safe clinical use. These five - dasatinib, methotrexate, retinoic acid, tacrolimus and tranilast - at least showed a range of one power-of-ten between the significantly toxic and the antiproliferative concentration.

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**Conclusions**

Dasatinib, methotrexate, retinoic acid, tacrolimus and tranilast could inhibit the myofibroblastic hRPE growth without being toxic and thus may be potential candidates for further investigation.

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**Financial Disclosure**

Neither the presenting author nor any co-author has a financial interest in the subject matter or receives money from any mentioned company.
**Title**
Eupatilin attenuates TGF-β2-induced proliferation and epithelial-mesenchymal transition of retinal pigment epithelial cells

**Purpose**
Proliferative vitreoretinopathy (PVR) is a disease that commonly develops after retinal detachment surgery and causes an important threat to vision. The main characteristic of PVR is the migration, adhesion and epithelial-mesenchymal transition (EMT) of retinal pigment epithelial cells (RPE). There is currently no pharmacological agent effective in preventing the development of PVR or treating the disease. Eupatilin is a naturally occurring flavone that has the potential to inhibit cell proliferation and EMT of different cells. However, its efficacy on cell proliferation and migration caused by transforming growth factor-2 (TGF-β2) is unknown. In the present study, the potential impact of eupatilin on RPE cell proliferation and EMT was investigated.

**Setting/Venue**
Department of Ophthalmology, School of Medicine, Trakya University, Balkan Campus Edirne, Turkey Department of Medical Biology, School of Medicine, Trakya University, Balkan Campus, Edirne, Turkey

**Methods**
Serum starved human RPE cells (ARPE-19) were treated with 10 ng/ml TGF-β2 alone or co-treated with 25 μM eupatilin for 48 h. The mRNA and protein expression was evaluated by quantitative real-time PCR and Western blotting, respectively. Apoptosis and cell cycle progression were assessed by image-based cytometry. The effect of treatment on cell migration was evaluated by the wound healing assay.

**Results**
Eupatilin inhibited TGF-β2-induced RPE cell proliferation via regulating the cell cycle and inducing apoptosis. TGF-β2 upregulated mRNA expression of mesenchymal markers fibronectin and vimentin was significantly downregulated by eupatilin, while the epithelial markers E-cadherin and occludin expression was upregulated. Eupatilin administration significantly suppressed TGF-β2 encouraged cell migration through downregulating the expression of transcription factors Twist, Snail and ZEB1 induced by TGF-β2. Furthermore, eupatilin significantly inhibited the expression of MMP-1, -7 and -9, and suppressed NF-κB signaling.

**Conclusions**
These results suggest that eupatilin could inhibit the proliferation and transformation into fibroblast-like cells of RPE cells; thus eupatilin may be a potential therapeutic value in treating PVR.

**Financial Disclosure**
none
Combined Intravitreal Dexamethasone and Bevacizumab Injection for the Treatment of Persistent Diabetic Macular Edema (DexaBe Study): A Phase I Clinical Study

Purpose
Objective: To investigate the safety of intravitreal injection of dexamethasone aqueous-solution (IVD) in combination with bevacizumab (IVB) and, secondarily, its effect on best-corrected visual acuity (BCVA) and central subfield thickness (CSFT) in patients with refractory diabetic macular edema (DME).

Setting/Venue
Department of Ophthalmology, Ribeirão Preto Medical School, University of São Paulo, Brazil.

Methods
This prospective study included 10 patients (10 eyes) with DME refractory to laser and/or anti-vascular endothelial growth factor (anti-VEGF) therapy. The patients underwent a complete ophthalmological examination at baseline, during the first week of treatment, and monthly through week 24. Therapy consisted of monthly injections of combined IVD and IVB “pro re nata” (PRN) if CST higher than 300 µm. We investigated the impact of the injections on intraocular pressure (IOP), cataract development, Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) and CST measured by spectral-domain optical coherence tomography (OCT).

Results
Results: Eight patients (8 eyes, 80%) completed the 24 weeks of follow-up. Mean IOP was significantly (p<0.05 = p inferior to 0.05) increased at weeks 1, 16, 20 and 24, compared to baseline and five patients (5/10, 50%) showed sustained increased IOP (higher or equals to 20 mmHg) after week 16, compared to the baseline visit and required IOP-lowering eye drops. Although CSFT had reduced significantly at all follow-up visits compared to baseline (p<0.05 = p inferior to 0.05), mean BCVA was not significantly improved compared to baseline at any of the follow-up visits. One patient who experienced cataract progression which precluded OCT evaluation at week 20 was referred for phacoemulsification; another patient showed vitreoretinal traction with increased CSFT at week 24 and was referred for vitreoretinal surgery. No intraocular inflammation was observed.

Conclusions
Conclusion: Treatment of DME refractory to laser and/or anti-VEGF therapy with PRN combined IV dexamethasone aqueous-solution and bevacizumab was associated with adverse effects typically related to the use of corticosteroids, and was associated with significant improvement in CSFT, although improvement in BCVA was not observed.

Financial Disclosure
No financial interest
Single-Cell RNA-Seq Analysis Maps Early Retinal Development of Mouse and Human Retina

**Purpose**
Vision starts with image formation at the retina, which contains diverse neuronal cell types that extract, process, and relay visual information to higher order processing centers in the brain. Though there has been steady progress in defining retinal cell types, very little is known about early retinal development in mouse and human, which starts well before birth.

**Setting/Venue**
Single-cell RNA-sequencing of retinal cells from mice and humans

**Methods**
In this study, we performed transcriptomic profiling of developing mouse embryonic and early-born retinas, including embryonic (E) days 14.5, 17.5 and postnatal (P) day 3, which correspond to early, intermediate, and late stages of retinal neurogenesis, respectively. Using single-cell RNA-sequencing (scRNA-seq) and pseudotime analysis, the developmental trajectories of retinogenesis were reconstructed. Also we analyzed human fetal retinae of gestational weeks 8 and 9.

**Results**
Our analysis revealed transcriptional programs driving differentiation from retinal progenitor cells (RPCs), to fate-deciding RPCs and ciliary marginal zone cells, and then down to three different cell types, which suggested that fate-deciding RPCs might serve as embryonic progenitors in early retinal development. In addition, we also showed that transcriptional differences separated into distinct subtypes and used this information to reconstruct RPC developmental trajectories and cell fate. Our results supported a hierarchical program of differentiation governing cell-type diversity in the developing mouse and human retina.

**Conclusions**
In summary, our work details comprehensive molecular classification of retinal cells, reconstructs their relationships, and paves the way for future mechanistic studies on the impact of gene regulation upon human retinogenesis.

**Financial Disclosure**
Not applicable
Feasibility of FocalView App in nAMD and DME to Assess Self-Visual Acuity at Home and in Clinic

Purpose
Following the COVID-19 pandemic in March 2020, clinic visits were limited to reduce the risk of COVID-19 exposure. Reliable and reproducible home visual acuity (VA) monitoring via smart phone applications (apps) have the potential to reduce the number and reliance on face-to-face clinical practice or clinical trial visits for neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) patients. Such apps might facilitate data collection between visits potentially providing further insights on treatment efficacy and/or natural history of ocular diseases. The FocalView app is a mobile medical research platform that includes a VA self-assessment module. The app presents a series of Landolt C rings in various orientations and sizes on a mobile device screen. By tapping a button on the screen corresponding to the gap in each ring, the app analyzes and measures VA. The purpose of this study is to determine the feasibility of the FocalView app for self-VA assessment at home and in the clinic after first introducing the app to the participant. Strategies to optimize testing frequency and accuracy of the VA obtained from the app, compared with standardized VA charts, will be pursued if the app is judged feasible to use in this way.

Setting/Venue
The study is an open, non-randomized, multi-site feasibility study conducted in 90 participants with nAMD or DME at several clinical sites. This study was designed starting in November 2019 and received IRB approval initially from Johns Hopkins University in October 2020. All participants provided written informed consent prior to enrollment. The study consists of three visits (Screening, V1, Baseline, V2; and End of Study, V3) matching three consecutive standard-care clinic visits of the participants for the management of nAMD or DME. Duration of study participation has been up to 180 days.

Methods
Patients with nAMD and DME, aged ≥18 years, VA better than 20/200 and receipt of intravitreal anti-vascular endothelial growth factor therapy within 4 to 24 weeks prior to V2 in their study eye were eligible. At V1, participants were assessed for best-corrected near VA (BCNVA) and best-corrected distance VA (BCDVA) using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart or electronic-ETDRS, and instructed on how to use the app for monocular VA self-assessment with their near correction. Between V1 and V2 (screening period), participants were asked to use the app 3 times in a single day, at least weekly, in order to familiarize themselves with the app. Ability to use the app was assessed by an investigator’s direct observation at V1 and V2, and review of home usage data. Participants were excluded from further study participation if they were unable to perform the VA test with the app or follow the testing schedule. Participants who completed the screening period then continued using the app at different frequencies per session and days, according to pre-specified group allocations. For the preliminary analysis for this abstract, the feasibility to use the app during the screening period is reported using descriptive statistical analysis.

Results
From the preliminary results based on the initial 45 participants from the Johns Hopkins University clinical site, 38 (84%) had nAMD, mean (±SD) age was 73.3 (9.8) years and 25 (56%) were male. Forty-three participants (96%) could perform VA self-assessment in the clinic after the first introduction at V1 and 39 participants (87%) completed home VA self-assessment during the screening period consisting of at least one single day in which they performed three testing sessions. Among the 6 participants (13%) who did not successfully complete V1 or the screening period, 4 had nAMD, mean age (range) was 73.5 (45 to 88) years and 4 were male. Reasons for feasibility failure were as follows: 3 (7%) did not comply due to frequency of the testing schedule, 2 (4%) misunderstood the instructions, and 1 (2%) physically could not use the app.

Conclusions
To our knowledge, this is the first clinical study designed to identify the feasibility of successfully using a self-testing VA app at home and in the clinic in patients with nAMD or DME. Preliminary data showed the majority of participants could perform the VA self-assessment using the app without any physical or cognitive barrier, whether at home or in the clinic. Ability to adhere to the testing schedule may be challenging for some patients. Potential future analyses may include identification of optimal conditions in which to use the app and assess the agreement of the VA obtained from the app relative to in clinic VA measurements using standardized VA charts. Validating clinical use of this app relative to in clinic VA measurements among this population may facilitate home monitoring in these common diseases in the future.

Financial Disclosure
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Type: Free Paper
### Purpose
PU-91, an FDA-approved drug, is a pro-drug that when metabolized is a PPARα (peroxisome proliferator-activated receptor α) ligand and which was developed for the treatment of dyslipidemia. PU-91 upregulates PGC-1α (Peroxisome proliferator-activated receptor γ Coactivator-1α) which is a critical regulator of mitochondrial biogenesis, promotes mitochondrial-stabilization, cytoprotection of age-related macular degeneration (AMD) ARPE-19 trans-mitochondrial cybrid cells by preserving mitochondrial health, reducing apoptotic cell loss, and inducing upregulation of the MDP (mitochondrially-derived peptides)-coding MT-RNR2 (Mitochondrially Encoded 16S rRNA) gene. Based on this, we decided to evaluate the protective effects of PU-91 in different concentrations to analyze their protective effects on Human Retinal Pigment Epithelium (ARPE-19) cells in vitro stressed with amyloid beta (Aβ), which is neurotoxic and can mimic retinal diseases.

### Methods
Human ARPE-19 cells were cultured for 24 hours in 96 well plates. They were pre-treated with PU-91 (50 µM and 100 µM) for 6 hours and stressed with 5µM amyloid-beta (Aβ) plus PU-91 in different concentrations. After overnight incubation, cell metabolism/viability was measured (MTT assay) along with levels of reactive oxygen species (ROS/H2DCFDA assay) and mitochondrial membrane potential (JC-1 assay). The following conditions analyzed were: untreated, Aβ 42-1 (inactive), Aβ 1-42 (active) and PU-91 (50 µM and 100 µM) plus amyloid-beta. The experiments were repeated two times. P values <0.05 were considered significant. All the results were analyzed with unpaired t-test using the GraphPad Prism version 9.0. for Windows (GraphPad Software, San Diego, CA).

### Results
In our results, the untreated was normalized for 100% and compared with the Aβ 42-1 (inactive). The Aβ 42-1 (inactive) was also compared with the Aβ 1-42 (active) with a significant reduction on cell metabolic/viability with p= 0.0106 and no significant results on ROS levels (p=0.1325) and JC-1 assay (p=0.5246). ARPE-19 cells exposed to 5µM amyloid-beta and rescued with PU-91 had no effect on cell metabolism/viability in both groups: 50µM PU-91 (p=0.8719) and 100µM PU-91 (p=0.5209). The ROS levels after 5µM amyloid-beta treatment showed a protective result on ARPE-19 cells pre-treated with 50µM PU-91 (p=0.0159) and no significant result when pre-treated with 100µM PU-91 (p=0.3927). 5µM amyloid-beta-treated ARPE-19 cells incubated with 50µM PU-91 not altered the JC-1 assay (p=0.2595) while 100µM PU-91 increased mitochondrial membrane potential with p=0.0086.

### Conclusions
Prior studies demonstrated that PU-91 preserved AMD mitochondrial function and integrity beyond the protection of AMD RPE cybrids against oxidative stress-induced and mtDNA-induced apoptotic cell death. Amyloid-beta is a drusen component found in AMD and other neurodegenerative diseases as Alzheimer’s disease; it was used in our experiment as a stressor to mimic a retinal disease. Our results suggest that PU-91 was helpful to protect the cell against the oxidative stress caused by amyloid-beta decreasing the levels of reactive oxygen species on ARPE-19 cells. The mitochondrial membrane potential demonstrated a protective effect with an increased in amyloid-beta-treated ARPE-19 cells incubated with 100µM PU-91. However, the cell metabolism/viability had no significant effect in in amyloid-beta-stressed cells rescued with PU-91. Our approach may be helpful to identify novel drugs and pathways to protect against retinal diseases. Additional studies are needed to prove the efficacy of this drug in retinal diseases.

### Financial Disclosure
NA
Stimulation of c-Kit+ Retinal Progenitor Cells by Stem Cell Factor Confers Immunomodulatory Protection against Retinal Degeneration

**Title**

Xi Chen

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**Purpose**

Transplantation or endogenous activation of stem/precursor cells represents a promising therapeutic modality for treating retinal degeneration (RD). We previously identified a population of C-Kit+ retinal progenitor cells (RPCs) in retinas of both postnatal and adult mouse. However, whether endogenous C-Kit+ RPCs can exert protective effects during RD remains unclear.

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**Methods**

Three days after N-methyl-D-aspartate (NMDA) injury, C-Kit ligand stem cell factor (SCF), C-Kit antibody aC-Kit and selective glial cell inactivating agent α-aminoadipic acid (AAA) were injected respectively. Morphological changes of the inner retina were demonstrated by immunochemistry.

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**Results**

Stimulation of endogenous C-Kit+ RPCs by SCF conferred immunomodulatory protection against RD, via downregulating the pro-inflammatory effects of microglia and inhibiting gliosis. In retinas, the C-Kit ligand SCF was mainly expressed in Müller cells under physiological conditions, while significantly decreased upon NMDA challenge. Both electroretinogram and light/dark transition tests manifested that intravitreal injection of exogenous SCF effectively protected mice against NMDA-induced ganglion cell loss. By the parallel RNA sequencing and the Gene Ontology analysis, a number of differential expressed genes (DEGs) closely related to immune responses were found in the transcriptome of SCF-treated retinas. Consistently, we showed that the SCF treatment prevented the gliosis and the activation of microglia in the retinas of NMDA-challenged mice, therefore improving the degenerative microenvironment and inhibiting the apoptosis of ganglion cells.

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**Conclusions**

These results not only demonstrate that stimulation of endogenous C-Kit+ RPCs by SCF may have the potential to treat for retinal diseases, but also expand our understanding of the role of endogenous C-Kit+ RPCs in the neuronal regeneration and tissue repair during RD.

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**Financial Disclosure**

Not applicable
The role of RUNX1 in experimental choroidal neovascularization

Purpose
To evaluate the inhibition of Runt-related transcription factor 1 (RUNX1) as a novel therapeutic strategy for choroidal neovascularization (CNV). RUNX1 has been identified as a key mediator of retinal neovascularization by transcriptomic analysis of surgically removed fibrovascular membranes from patients with proliferative diabetic retinopathy. Additionally, RUNX1 inhibition with small-molecule inhibitor Ro5-3335 prevented the formation of retinal neovessels in experimental oxygen-induced retinopathy, a model of retinopathy of prematurity. Furthermore, Ro5-3335 topically administered has recently proved to reduce the severity of proliferative vitreoretinopathy in a rabbit model. CNV is a prevalent cause of blindness in different ocular diseases such as age-related macular degeneration and high myopia. Current treatment for CNV involves repeated intravitreal injections with drugs targeted against vascular endothelial growth factor (VEGF). Despite the initial improvement on visual acuity, several studies show visual decline in the long term, and incomplete response to anti-VEGF agents has been reported in almost half of the patients. Based on our data, we believe that RUNX1 has a critical role on pathologic ocular angiogenesis and that RUNX1 regulation could be a new therapeutic approach to control neovascularization.

Results
RUNX1 expression was found in the main cell types known to be involved in CNV complex: endothelial cells (CD31+), mononuclear phagocytes (i.e. macrophages/microglia) (CD11b+), retinal pigment epithelial cells (RPE65+), vascular smooth muscle cells/myofibroblasts (alpha-smooth muscle actin+) and Muller cells (glial fibrillary acidic protein+). Importantly, there was no RUNX1 expression in uninjured retina and RUNX1 positive cells were only seen at the lesion site. Fluorescence quantification of choroidal flatmounts at different time points revealed the peak of RUNX1 expression levels on day 3 after laser. mRNA levels quantified by PCR were also higher at day 3. Treatment with Ro5-3335 achieved a significant reduction in CNV area compared with vehicle, but these results were also found in aflibercept and Ro5-3335 + aflibercept groups, in which we saw significantly smaller lesions. Moreover, animals treated with Ro5-3335 and aflibercept exhibited a significant reduction on vascular leakage, but combination of both Ro5-3335 + aflibercept reduced vascular leakage area and severity more effectively than aflibercept or Ro5-3335 alone.

Conclusions
In this study, we demonstrate RUNX1 expression in the main cell types involved in a laser-induced model of CNV in mice. Additionally, we report the preclinical efficacy of Ro5-3335, a small-molecule inhibitor of RUNX1, in experimental CNV. Intravitreal injection of Ro5-3335 achieved a significant reduction of CNV area seven days after laser injury, and when combined with aflibercept reduced vascular leakage more effectively than aflibercept in monotherapy. These data suggest that RUNX1 inhibition alone or in combination with anti-VEGF drugs should be further investigated as a novel treatment for patients suffering from CNV.

Setting/Venue
Schepens Eye Research Institute of Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts, USA

Methods
Laser-induced CNV model was used in this study. To evaluate the efficacy of RUNX1 inhibition, a single intravitreal injection of either phosphate-buffered saline (vehicle), Ro5-3335 (75 µmol/L), aflibercept (10 µg) or combination of Ro5-3335 (75 µmol/L) + aflibercept (10 µg) was performed immediately after laser. Vascular permeability was assessed by fluorescein angiography (FA) performed at day 6 and eyes were enucleated on day 7. RUNX1 expression in CNV lesions was evaluated by immunofluorescence of cryosections and timecourse characterization of its expression was performed by polymerase chain reaction (PCR). All measurements were performed by two different observers in masked and randomized images. CNV lesion size was quantified from images acquired from choroidal flatmounts stained with isoclin B4 using Image-J with Versatile Wand tool plugin. Vascular permeability or leakage area was quantified by measuring the difference between the area of the lesion in the late phase and the early phase of the FA. Finally, leakage severity was assessed by FA image grading. Data were assessed with analysis of variance (one-way ANOVA) followed by Dunnett’s multiple comparisons test. Two-tailed unpaired T-test was used for comparison between two groups.

Financial Disclosure
Leo A. Kim and Joseph F. Arboleda-Velasquez: listed as inventors in a patent application for the use of RUNX1 inhibition in aberrant angiogenesis. Jose M. Ruiz-Moreno: Grant of the Spanish Ministry of Health, Instituto de Salud Carlos III, Red Temática de Investigación Cooperativa en Salud: “Prevención, detección precoz, y tratamiento de la patología ocular prevalente, degenerativa y crónica” (RD16/0008/0021). Research support from Topcon, Co. Advisory
A silicone oil-free syringe specifically developed for intravitreal injection of antibody-based biologics

Despite numerous reports of symptomatic deposition of silicone oil (SiO) droplets in the vitreous body, syringes lubricated with SiO are extensively used for intravitreal injections (IVIs) of antibody-based biologics. To address this adverse event, we aimed to develop a SiO-free syringe with no dead volume specifically designed for IVIs. The aim of this study was to investigate the properties of this syringe.

Compounding and storage of aflibercept, ranibizumab, and bevacizumab in the new syringe for up to 30 days did not compromise protein concentration, aggregation, or binding to VEGF. The new syringe also demonstrated a favourable safety profile regarding particle release compared to the other syringes, including PFS with aflibercept and ranibizumab.

We describe the properties of a new SiO-free syringe that allows for pharmaceutical compounding and storage of anti-VEGF antibody-based biologics for up to 30 days without compromising their functional binding properties. The novel syringe is an appealing alternative to SiO-lubricated syringes.
12-month effectiveness of the fluocinolone acetonide implant (ILUVIEN®) in retinal vein occlusions - two clinical cases

**Purpose**
Retinal vein occlusion is an important cause of vision loss, being the second most common cause of retinal vascular disease in the world. Despite the differences in frequency and natural history, branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) can both often complicate with macular edema. Corticosteroids represent one of the possible therapeutic approaches due to their anti-angiogenic and anti-inflammatory effect. Although widely studied in diabetic macular edema, little information is available on the effectiveness of intravitreal fluocinolone acetonide (FAc, 190 µg) implant ILUVIEN® (Alimera Sciences Inc., Georgia, USA) in macular edema after BRVO and CRVO. The purpose of this study was to evaluate the anatomical and functional response in patients with macular edema following BRVO and ischemic CRVO, 12 months after the placement of the FAc implant.

**Setting/Venue**
Department of Ophthalmology of Centro Hospitalar e Universitário São João, Portugal.

**Methods**
Prospective interventional review of two clinical cases (two eyes) of chronic persistent macular edema after BRVO and ischemic CRVO treated with ILUVIEN® implant. Description of demographic and clinical data in addition to anatomical (central retinal thickness [CRT]) and functional (best corrected visual acuity [BCVA] in ETDRS scale) outcomes during a 12-month period of follow-up after a single administration of the FAc implant. Both patients were female with 73 and 71 years. One patient had a diagnosis of BRVO of the superior temporal branch of the right eye after cataract surgery and the other developed an ischemic CRVO of the left eye (also pseudophakic). No systemic steroids were given at the time ILUVIEN® was administered or during the 12 months of follow-up.

**Results**
The patient with BRVO presented a baseline BCVA of counting fingers at two meters and a CRT of 616 µm. She was initially treated with 6 intravitreal injections of 1,25mg bevacizumab followed by 7 injections of 2 mg triamcinolone, with good anatomic response but minimal functional improvement (BCVA of 23 letters). Subsequently, a dexamethasone intravitreal implant (OZURDEX®) was administered, with better functional response (BCVA of 36 letters); however, not sustained beyond 3 months, requiring the use of 3 OZURDEX implants. After this an FAc implant was injected, resulting in a complete and sustained resolution of the macular edema at 12 months (CRT of 198 µm and BCVA of 38 letters). The patient with the ischemic CRVO presented a baseline BCVA of 29 letters and a CRT of 664 µm. In the absence of response to anti-VEGF (bevacizumab and aflibercept) and triamcinolone intravitreal injections, she was proposed to a dexamethasone implant (OZURDEX). She showed an anatomical improvement (CRT of 364 µm), although not sustained, despite a total of 5 implants. An FAc implant was then administered, with a significant and sustained functional (BCVA of 38 letters) and anatomical (CRT of 271 µm) improvement at 12 months.

**Conclusions**
Retinal vein occlusion is presumed to be a potentially chronic disease. The existence of several therapeutic modalities for macular edema highlights that there is no perfect solution. However, the most adequate approach will be the one that best fits the patient’s needs, given its side effects and the least interference with patient’s quality of life. ILUVIEN® was effective in treating the macular edema secondary to BRVO and CRVO with a favorable and sustained clinical and anatomical response throughout a 12-month period, reducing the burden of numerous intravitreal procedures and visits to the hospital.
Chronic and Exuberant Central Serous Choroidoretinopathy (cCSC) successfully treated with Aflibercept

**Purpose**
Chronic Central Serous Choroidoretinopathy (cCSC) may course with permanent visual impairment due to persistent subretinal fluid, prolonged RPE detachment and damage to photoreceptors. PDT with verteporfin, either full dose or half dose, although commonly used, may cause choriocapillaris hypoperfusion, transient upregulation of VEGF and inflammatory mediators and RPE damage. Anti-VEGF agents (mainly bevacizumab) have been used to reduce choroidal hyperpermeability in cCSC, with studies showing conflicting results regarding reduction in Central Macular Thickness (CMT) and Best Corrected Visual Acuity (BCVA) improvement. In this study we describe three cases of cCSC with bilateral, exuberant and persistent subretinal and intraretinal fluid, previously treated with eplerenone and Photodynamic Therapy (PDT) with verteporfin, without evidence of neovascularization on fluorescein angiography (FA), indocyanine green angiography (ICGA) and/or OCT. All patients had limited anatomical and functional response to a treat and extend regimen of bevacizumab and were switched to aflibercept with remarkable and sustained anatomical response though very dependent on monthly injections. These results support the notion that anti-VEGF agents and especially aflibercept may have an important role in cCSC unresponsive to conventional treatment, even in the absence of neovascularization.

**Setting/Venue**
Single-center retrospective cohort at Instituto de Oftalmologia Dr. Gama Pinto in Lisbon, Portugal.

**Methods**
Retrospective study of three cases referred to our Retina Department with previous diagnosis of cCSC unresponsive to PDT and eplerenone. All patients denied prior or current use of corticosteroids and had no relevant ophthalmic history. At presentation, BCVA for the right eye (RE) and left eye (LE) were, respectively: 10/100 and 10/40 for Patient 1, less than 5/200 and 5/80 for Patient 2 and less than 5/200 and 5/80 for Patient 3. Colour fundus images showed macular atrophy, pigment alterations and serous macular detachment. On OCT, all patients had extensive retinal pigment epithelial (RPE) atrophy, increased diameter of Haller layer vessels with decrease of Sattler layer thickness and exuberant subretinal and intraretinal fluid. In addition, in the RE of the Patient 3, OCT showed an extensive macular hyperreflective subretinal lesion with well defined borders associated outer retinal tubulation, consistent with disciform scarring. FA showed a diffuse mottled pattern of leakage from the macular area in the absence of focal leaking or enhancing structures. ICGA revealed increased diameter of the choroidal vessels, without choroidal neovascularization or polyps. In addition, patients underwent blood workup and imaging to exclude hypercortisolism.

**Results**
All patients were initiated on a treat and extend regimen with bevacizumab, and all three cases started with their best-seeing eye after considering visual prognosis with treatment. There was no significant improvement in vision and only partial decrease of subretinal and intraretinal fluid with bevacizumab. Patients were then switched to aflibercept with remarkable absorption of subretinal and intraretinal fluid and stabilization or modest increase in BCVA – for instance, there was an improvement from 5/80 to 5/63 of BCVA in Patient 2 after two years of treatment. Sustained response was highly dependent on monthly aflibercept injections, with exuberant recurrence of subretinal and intraretinal fluid with more than 4-6 weeks of injection interval.

**Conclusions**
The remarkable and sustained anatomic response in cCSC with monthly injections of anti-VEGF cannot be attributed to pachychoroid neovasculopathy or polypoidal vasculopathy in these cases, as these complications, as well as alternative diagnoses such as posterior uveitis with diffuse capillary leakage, were excluded with FA and ICGA. The significant anatomical and more modest functional responses in this case series, as well as their dependance on continued injections, support the hypothesis that choroidal vascular hyperpermeability is a major and persistent factor in CSC and that it can successfully be mitigated through inhibition of VEGF, which acts as a hyperpermeability factor through induction of vascular fenestration and microvascular permeability. The larger response obtained after switching to aflibercept further supports this notion, since aflibercept has a superior binding affinity to VEGF, and inhibits both VEGF-A and VEGF-B and PIGF, whereas bevacizumab only inhibits VEGF-A. Improvement in vision in this series was modest; however this can be attributed to subfoveal photoreceptor damage already caused by chronicity of subretinal and intraretinal fluid before treatment with anti-VEGF was initiated. Our findings suggest a role for a prolonged treat and extend regimen of anti-VEGF for cCSC unresponsive to conventional treatment, even in the absence of neovascularization.

**Financial Disclosure**
None

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Suprachoroidal Injection of Triamcinolone with 30 Gauge Needle using Novel Suprachoroidal Injection Device: Long term Evaluation

Purpose
Evaluate safety & efficacy of Suprachoroidal Injection of Triamcinolone Acetonide (SCITA) with novel Suprachoroidal Injection Device (SCID) in patients with macular edema due to diverse retinal pathology and in cases of uveitis and to evaluate the long-term efficacy after repeat injections

Setting/Venue
Non-randomised interventional case series in a tertiary care retina practice

Methods
SCITA 0.1ml/4mg was given in 76 eyes of 72 patients with 30G needle using novel SCID. Eight patients had repeat second injection and two had a third repeat injection. The angulation of the base plate to the scleral entry was a critical determinant of correct plane of injection. BCVA, IOP and central subfield thickness (CST/SDOCT) was measured on day (D) 1, 7, 30, 60 and 90

Results
SCITA was pain free, well tolerated and no eye developed retinal/choroidal injury. However in 6 eyes the injection became intravitreal four of them requiring antiglaucoma medications. Mean baseline CST (486µm) decreased to normal range (246 µm) at D7; was maintained at 232µm/ D30 & 309 µm/ D90. Edema resolution occurred in 66% at D30 & 57% eyes remained edema free at D90. BCVA improved 1 line in 59% & 3 lines in 35% at D30. No eye had increased IOP if there was no intravitreal injection of Triamcinolone (TA)

Conclusions
SCITA using the novel SCID is cheap, safe, effective, well tolerated and devoid of adverse ocular event. It does require a learning curve and the angulation of the baseplate to the sclera is critical. Repeated SCITA injections are effective and without apparent clinically evident complications. It may be used as an alternative to intravitreal injection of Ozurdex.
Partial recovery of visual function in a blind patient after optogenetic therapy for Non-Syndromic Retinitis Pigmentosa

**Purpose**
Retinitis pigmentosa (RP) is a neurodegenerative eye disease in which loss of photoreceptors can lead to complete blindness. RP is a progressive, inherited, monogenic or rarely digenic blinding disease caused by mutations in more than 71 different genes. It affects more than two million people worldwide. With the exception of a gene replacement therapy for one form of early-onset RP caused by mutation in the gene RPE65, there is no approved therapy for RP. Optogenetic vision restoration is a mutation-independent approach for restoring visual function at late stages of RP after vision is lost. The open-label phase I/IIa study named PIONEER (NCT03326336) was designed to evaluate the safety (primary objective) and efficacy (secondary objective) of an investigational treatment for patients with advanced non-syndromic RP that combines injection of an optogenetic vector (GS030-DP) with the wearing of a light-stimulating goggles (GS030-MD).

**Setting/Venue**
The optogenetic vector, a serotype 2.7m8 adeno-associated viral vector encoding the light-sensing channelrhodopsin protein ChrimsonR fused to the red fluorescent protein tdTomato, was administered by a single intravitreal injection into the worse-seeing eye to target mainly foveal retinal ganglion cells. The light-stimulating goggles capture images from the visual world using a neuromorphic camera that detects changes in intensity, pixel by pixel, as distinct events. The goggles then transform the events into monochromatic images and project them in real-time as local 595-nm light pulses onto the retina.

**Methods**
We describe the partial recovery of vision in one subject of the PIONEER study. This 58-year-old male, who was diagnosed with RP 40 years ago, had a visual acuity limited to light perception at the inclusion in the study. The worse-seeing eye was treated with 5.0E10 vector genomes of optogenetic vector. Both before and after injection, we performed ocular examinations and assessed the anatomy of the retina on several occasions over 15 visits spanning 84 weeks according to the protocol. We analyzed the visual improvement under 3 conditions with 3 psychophysical tests. The 3 conditions were: ‘natural binocular’ (both eyes open without the light-stimulating goggles); ‘natural monocular’ (non-treated eye covered, treated eye open without the goggles); and ‘stimulated monocular’ (non-treated eye covered, treated eye open and stimulated with the goggles). The first test consisted of perceiving, locating, and touching a single object placed on a white table. The second test included perceiving, counting, and locating more than one object. For the third test, the subject had to assess the presence or absence of a tumbler placed in front of him. The behavioral responses and brain activity were simultaneously recorded during the third visual test.

**Results**
We tested the light-stimulating goggles on the subject three times before vector injection. On none of these occasions did the subject report any change of vision nor any photophobia. The subject could not visually detect any objects before injection with or without the goggles, or after injection without the goggles. The subject perceived, located, counted, and touched different objects using the vector-treated eye alone whilst wearing the goggles. During visual perception, multi-channel electroencephalographic recordings revealed object-related activity above the visual cortex. There was no intraocular inflammation, no changes in the anatomy of the retina, and no ocular or systemic adverse events over the period of follow-up. The treated eye retained light perception over the 84 weeks of testing.

**Conclusions**
This is the first reported case of partial functional recovery after optogenetic therapy for a neurodegenerative disease. Taken together, the psychophysical and neurophysiological evidence suggest that the optogenetic stimulation of human retinal ganglion cells by a light-projection system linked to a camera is a promising way to partially restore vision in blind patients affected with advanced RP.

**Financial Disclosure**
Personal financial interests in GenSight Biologics, Pixium Vision, Sparing Vision, Prophesee, Tilak, VegaVect, NewSight and Chronolife
Low-Vision Multi-Parameter Test for Monitoring Visual Function of Patients with Advanced Retinal Diseases

Severe to near-total loss of vision in patients occurs due to a variety of ocular diseases including inherited retinal degenerations, age-related macular degeneration, and glaucoma. In the case of low vision patients, measurement of functional vision is challenging and requires multiparametric test methods to distinguish between patient sub-groups. Though there exists a number of devices to measure visual function in low-vision subjects, individually, these methods provide a measure of a single parameter. Further, it is unclear if these existing tests measure a clinically meaningful outcome, and therefore, are not widely accepted as a primary efficacy endpoint for low-vision studies. Low Vision Multi-Parameter Test (LVMPT) was developed to quantitatively measure the visual level of low vision patients in clinical use and evaluate the progression of vision recovery after treatment.

The LVMPT device was deployed in a clinical study to evaluate functional vision and therapeutic outcome of patients with Advanced Retinal Degeneration having poor vision (no better than PL and HM). The study was conducted after approval from the Drug Controller General of India (DCGI) registered Institutional Ethical Committee of a tertiary eye care center in eastern India.

The LVMPT device consists of two modalities: Two-dimensional (2D) LCD display to emulate real-world interaction with tablets and cell phones, and three-dimensional (3D) objects to emulate everyday interaction with objects. 2D display creates optical flow at different speeds and directions which tests the ability of subjects to recognize optical flow. Different shapes and sizes of objects are displayed on the 2D screen for the evaluation of low vision subjects. The 3D LVMPT device consists of a 3D enclosure with a top-lit LED panel, 3 possible object placement and is equipped with a slot containing sensors for object recognition. Subjects are evaluated based on correctly demonstrating the ability to recognize and pick up the directed object. The randomization of objects, light level control, recording of exact location and accuracy of the subject’s tap are automated by software.

The LVMPT device was deployed in a clinical study with advanced retinal degenerated subjects. The functional vision evaluated by the LVMPT device was well correlated to the patient-reported outcome (evaluated by NEI VFQ-25 Questionnaire). The LVMPT-measured accuracy in shape recognition and/or threshold intensity, size, and speed of optical flow was found to correlate with visual acuity and functional vision measured by behavioral performance (light guided navigation test) of low-vision subjects. LVMPT device was able to discern between various subgroups of low vision patients.

The LVMPT device allows ophthalmologists to quantitatively measure low vision function and has wide use for quantifying degradation of vision and evaluation of drugs and therapeutic interventions. Further validation of the LVMPT in low-vision subjects will provide a correlation of clinically meaningful outcomes with treatment in various clinical trials focused on the advanced retinal degenerated patient population.

Financial Disclosure
Nanocospe Instruments Inc-Employee and Equity (Michael Carlson, Sanghoon Kim, Samarendra Mohanty) Nanocospe Therapeutics Inc-Employee and Equity (Sai Chavala, Samarendra Mohanty, Subrata Batabyal)

**Purpose**
We describe an experience of a large-scale self-initiated recruitment of patients to a self-monitoring initiative for macular pathology over the COVID-19 pandemic.

**Setting/Venue**
A total of 2272 patients from the Singapore National Eye Centre (SNEC) whose visits were rescheduled over lockdown (13 April to 1 June 2020) were offered participation in a self-monitoring initiative administered by SNEC with the Alleye application as the testing instrument.

**Methods**
This was an observational study with retrospective analysis. Demographics and characteristics were compared between those that signed up and those that did not. Similar comparisons were made between compliant patients versus those that were not. Outcomes were tracked for 6 months starting from the commencement of lockdown. Main outcome measures were participation and compliance rates. Patient characteristics that were more likely to participate and remain compliant.

**Results**
A total 732 (32%) patients participated in this self-monitoring initiative. Those who participated were younger (62 vs. 68 years, p<0.001), men, and living with family. Patients not on treatment, and those with poorer vision in their worse-seeing eye were more likely to participate. When grouped according to diagnosis, the proportion who participated was highest for diabetic macular edema (52%), non-neovascular age related macular degeneration (nAMD) (42%), diabetic retinopathy (35%), retinal vein occlusions (18%), and nAMD (15%) (p<0.001). Testing compliance rate was 43% (315/732). Compliant patients were older, on treatment, and had poorer vision in the worse-seeing eye. Trigger events occurred in 33 patients with 5 patients having clinically verified disease progression (1.6%).

**Conclusions**
We provide real-world data on characteristics of patients with stable retinal diseases who were offered and participated in, and were compliant, with a self-monitoring program. The lower participation rate compared to standardized clinical studies reflects the difficulties in implementation for such initiatives in real-world settings. Despite this, self-monitoring continues to show promise in relieving clinic resources, suggesting the feasibility of scaling such programs beyond the COVID-19 pandemic.

**Financial Disclosure**
NA
Voretigene neparvovec: Real-world data from 11 patients with biallelic RPE65 mutations, treated at the University Eye Hospital Bonn

Purpose
Description of patient characteristics and analysis of outcomes of subretinal voretigene neparvovec (VN) as gene-augmentation therapy for RPE65-mediated inherited retinal disease.

Setting/Venue
Post-marketing analysis of patients treated with VN at a single center between February 2020 and March 2021.

Methods
Indication for VN therapy was based on the national guidelines (https://link.springer.com/article/10.1007/s00347-019-0906-2) and included conclusive phenotype, disease-causing biallelic mutations in RPE65 and sufficient viable retinal photoreceptor cells. Examinations included multimodal retinal imaging (SD-OCT, fundus-autofluorescence FAF, widefield colour fundus photography CFP) and functional testing (best corrected visual acuity VA, chromatic and white full field stimulus testing FST, kinetic visual fields VF) performed prior to treatment and at months 1, 4 and 10 post intervention. Treatment was as per application guidelines including perioperative immunomodulation with oral steroids, 3-port vitrectomy (23G), posterior vitreous detachment (with or without triamcinolone staining), subretinal injection of 300 µl VN through a teflon cannula entering at the superior temporal arcade, fluid air exchange and supine positioning for 24 hours postoperatively.

Results
A total of 18 eyes of 11 patients were treated until March 2021 with a mean age of 23 years (range 7-39; 8 male and 3 female). Mean postoperative review period was 4 months (range 1 – 13 months). Surgical protocol deviations included 3 eyes with peripheral laser- or cryoretinopexy due to presence of small retinal tears. There was a significant improvement of white FST with a mean change of -13.0 cd.s/m2 (SD ±11.0; n=17) at month 1 and -11.5 cd.s/m2 (SD ±11.8; n=11) at month 4, correlating with strong subjective improvement in the vast majority of patients in dim lighting conditions. Mean VA at baseline was 40 ETDRS letters (SD ±35; n=18) and stayed stable at month 1 with 36 letters (SD ±35; n=17) and month 4 with 38 letters (SD ±26; n=12). Mean change in total degrees of VF III4e did not change significantly with +51° (SD ± 202°; n=15) at month 1 and +60° (SD ±147°; n=8) at month 4. Minimal foveal thickness by OCT was 160 µm (SD ± 29; n=18) and did not change significantly at month 1 (148 µm; SD ± 28; n=18) and month 4 (143 µm; SD ±38; n=12).

Conclusions
In a real world setting, VN demonstrated similar postoperative safety short-term outcomes as previously reported also in the context of the pivotal trial. While subjective improvements, significant treatment effects in FST and stable VA and central retinal structure in OCT were as described in the literature, VF did not significantly change after treatment so far. Extended longitudinal observations appear mandatory to assess long-term efficacy and safety.

Financial Disclosure
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Prevalence of X-linked Retinitis Pigmentosa due to Mutations in the RPGR Gene Among Males in Europe and the United States

Divya Narayanan
United States

Purpose
X-linked retinitis pigmentosa (XLRP) is a rare, X-linked inherited retinal dystrophy that predominantly affects males. XLRP initially presents as night blindness in childhood and early adolescence, followed by reduction of the visual field. In advanced XLRP, profound central vision loss and legal blindness can occur. The phenotype of XLRP can vary, generally presenting as a more severe form of retinitis pigmentosa (RP). XLRP is associated with different genetic mutations, of which RPGR accounts for a majority of XLRP cases. Although several potential treatment strategies for XLRP are being investigated, there are currently no approved disease-modifying therapies. The objective of this study was to determine the prevalence specifically for RPGR-mutated XLRP among males in Europe and the United States (US).

Setting/Venue
A comprehensive literature review was conducted on the basis of a broad search of PubMed and EMBASE databases.

Methods
Published literature related to RP prevalence, XLRP prevalence, classification of inheritance types, misdiagnosis, and RPGR mutation occurrence was reviewed. English-language studies from Europe and the US were screened for inclusion. For studies of prevalence and proportions of inheritance types, only studies of male populations were included. To estimate the prevalence of RPGR-mutated XLRP among males, four components were estimated: (1) the prevalence of nonsyndromic RP in males; (2) the proportion of RP in males that is X-linked; (3) the proportion of male RP cases for whom the presumed pattern of inheritance is reclassified as X-linked after genotyping; and (4) the proportion of XLRP that is RPGR-mutated XLRP. Individual estimates of these components were extracted from the studies identified in the literature review and, for each component, a sample size–weighted average of the individual study-level estimates was calculated. The prevalence of RPGR-mutated XLRP among males was estimated by multiplying components 1 and 2, factoring in misclassification using component 3, and then multiplying by component 4. In a parallel analysis of studies that provided a direct estimate of XLRP prevalence among males, a weighted average was corrected per reclassification analysis of X-linked cases (component 3) and multiplied by component 4.

Results
Two studies assessed the prevalence of XLRP directly among males, one from Denmark (3.8/100,000 males) and one from the US (2.3/100,000 males); median prevalence was 3.1/100,000 males and weighted average was 3.5/100,000 males. To indirectly measure the prevalence of XLRP, studies estimating the prevalence of RP among males and studies estimating the proportion of XLRP inheritance among RP cases were examined. Seven studies reported the prevalence of nonsyndromic RP among males in the US and Europe (range: 12.2-28.0/100,000 males; median: 21.5/100,000 males; weighted average: 19.6/100,000 males). Seven studies from the US and Europe reported on the proportion of RP cases classified as X-linked among males (range: 4.0%-21.2%; median: 10.4%; weighted average: 14.0%). Together, these estimates indirectly provided a prevalence estimate of approximately 2.7/100,000 males. The proportion of RP cases reclassified as X-linked from other inheritance types (simplex or autosomal dominant) was estimated, resulting in a corrected prevalence of XLRP of 4.0/100,000 males for the indirect estimate and 5.2/100,000 males for the direct estimate. Lastly, the proportion of RPGR-mutated XLRP was assessed from the literature (range: 74.7%-91.9%; median: 85.7%; weighted average: 84.1%). Applying this proportion to the prevalence of XLRP yielded an overall prevalence of 3.4-4.4/100,000 males with RPGR-mutated XLRP.

Conclusions
The prevalence of RPGR-mutated XLRP is estimated to be 3.4-4.4/100,000 males in Europe and the US. This number was adjusted for misclassification of RP cases as X-linked from autosomal dominant or simplex inheritance. Among XLRP cases, the majority were due to mutations in the RPGR gene. These findings address an important gap in the understanding of RPGR-mutated XLRP by providing additional clarity around the prevalence of this rare condition. This information may help medical institutions, physicians, and other stakeholders in the health care system support people living with this inherited retinal disease.

Financial Disclosure
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Title
Sector retinitis pigmentosa: one in a kind. Report of a new mutation and an atypical case among a family with a typical presentation

Purpose
Retinitis pigmentosa (RP) is one of the most common hereditary retinal dystrophies. Although genetically and phenotypically heterogeneous, it is typically characterized by a diffuse progressive bilateral dysfunction of predominantly rod photoreceptors with subsequent degeneration of cone photoreceptors and the retinal pigment epithelium. Therefore, this condition evolves into a centripetal, asymmetrical but diffuse pattern. Sector RP is an atypical form of RP that is present in circumscribed areas, usually with bone spicules distribution in the inferior quadrants of the retina. The present study intended to describe clinical, structural and genetic features of a three-generation family composed of three elements with typical RP and one member with sector RP.

Setting/Venue
Description of a familial case series from a single tertiary referral center in Portugal (Department of Ophthalmology of Centro Hospitalar e Universitário São João).

Methods
Four members of a three-generation family underwent ophthalmological examination including best corrected visual acuity (BCVA) and multimodal imaging of structural features with fundus photography, fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (SD - OCT). Functional evaluation included visual field and electrophotographic testing. All patients underwent genetic testing to identify the molecular etiology of their disease.

Results
All four patients were molecularly confirmed, with identification of a new variant of the RHO gene - c.545G>A[p.(Gly182Asp)], representing a replacement of one amino acid of glycine for an aspartic acid. All members were heterozygous for this autosomal dominant mutation. Among the three patients (from three different generations) with the typical form of RP, it was observed that the oldest family member presented worse BCVA (51 letters oculus dexter (OD) and 48 letters oculus sinister (OS) in the ETDRS score) and more diffuse anatomical, visual field and electrophotographic impairment, with foveal involvement, in comparison to the second (BCVA of 73 letters OD and 83 letters OS and structural and functional involvement into the macular periphery, preserving the fovea) and the third (BCVA of 85 letters OD and OS, no macular involvement) generation members. The patient with sector RP, corresponding to the first member of the second generation, presented a BCVA of 82 letters OD and 72 letters OS, normal electrophotographic findings and visual field and impairment and anatomical findings limited to the inferior and nasal peripheral retina.

Conclusions
To date, this is the first case of a single member with sector RP among a three-generation family with autosomal dominant RP with the same new mutation. This finding supports the well documented clinical heterogeneity for mutations of the same nature. There is a clear gradient of severity according to age and throughout generation, with worse functional and structural outcome in the older member among family members with typical RP. The patient with sector RP presented relatively good outcomes. This three-generation case series reflects the progressive behaviour of RP, with diffuse RP presenting worse outcomes than sectoral RP, an atypical form with slower rate of progression. Although there is no current treatment, it is important to detect these patients in order to elucidate patients’ expectations and prognosis, provide genetic counseling and inform them of potential participation in the increasing numbers of trials of novel therapeutics and possible access to future treatments.

Financial Disclosure
NONE
**Title**
Dose-dependent visual-field preserving effect of transcorneal electrical stimulation in retinitis pigmentosa

**Purpose**
After the onset of retinitis pigmentosa (RP), progressive visual field loss follows an exponentially decreasing course, leading to legal blindness in most cases. Any therapy, which is given or started at any stage of the disease, should stop, or at least significantly slow down the further decrease. So far, a dose-response relationship for the therapeutic effect of transcorneal electrical stimulation (TcES) on annual decline rate of the visual field is missing. To test whether TcES has a current-dependent effect on progressive visual field loss, we conducted an a posteriori analysis of raw data and a reappraisal of the outcome of a closed clinical trial.

**Setting/Venue**
We analysed raw data from 52 adult patients with RP who participated in an interventional, randomized, single-masked study at the University Eye Hospital Tübingen (EST2 trial, clinicaltrials.gov: NCT01837901). At that time, patients were randomly assigned to TcES with 0 mA (sham stimulation), 150% or 200% of their individual threshold current for phosphene perception. Over the period of 52 weeks, TcES was applied monocularly once per week for 30 min with biphasic current pulses (OkuStim, 5 ms each phase, 20 Hz). The visual field areas (VFA) were repeatedly assessed in both eyes (Octopus 900).

**Methods**
In contrast to the group-based statistics of the VFA of the stimulated eyes in the previous analysis (Schatz et al., IOVS, 2017, 58:1), we now determined the individual percentage reductions of the VFA in the stimulated (R1) and non-stimulated fellow eyes (R0) and analyzed the dependency of the reductions and the differences D = R1 - R0 on the individual current strengths. Mean current strength over 52 weeks stimulation was analyzed as a continuous variable (linear regression). We focused on the data obtained with Goldman target V4e.

**Results**
In the sham group (n=20), the mean percentage reduction of VFA was 7% in both eyes, as expected for the natural course of RP. A different picture emerged in the stimulated patients. The mean reduction R1 and R0 in the stimulated and non-stimulated fellow eyes (both n=32) was 4.5% ± 15.4%, and 8.1%±16.6% (mean ± SD), respectively. The two distributions were statistically significant different (p = 0,031, Wilcoxon signed rank test). As a result, TcES with current amplitudes from 0.2 to 1.0 mA led to an overall deceleration D/R0 of 44% in annual VFA decline compared with non-stimulated eyes. There was a significant linear relationship (p = 0.049, F test) between the difference D and the current strength. As the current strength increased, the VFA decreased more slowly. The effect was particularly pronounced in the subgroup of patients stimulated with the highest current amplitude from 0.8 mA to 1.0 mA (n=9). While in this subgroup R0 was 8.6% ± 9.0%, R1 was reduced to 0.8% ± 7.1% (difference between both eyes: p = 0.098). Thus, TcES with high current amplitudes resulted in a mean deceleration of annual VFA decline by 90%.

**Conclusions**
For the first time, a dose-response relationship for the effect of TcES on the progression of the visual field area has been created from the data from a clinical trial with RP patients. Depending on the current strength, TcES slowed down the annual decline rate of the VFA to less than 1%. The results provide clinical evidence that TES significantly has a therapeutic effect and is an efficient method to delay or stop the disease progression in RP.

**Financial Disclosure**
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Title
Safety and efficacy of sepofarsen in the second treated eye in the Phase 1b/2 extension trial in Leber congenital amaurosis due to mutations in the CEP290 gene (Insight Trial)

Purpose
Leber congenital amaurosis type 10 (LCA10) is a severe, degenerative inherited retinal disease due to mutations in the CEP290 gene resulting in childhood blindness for which there is no treatment. Sepofarsen is an intravitreal RNA therapy that showed clinically meaningful improvements following unilateral injection in a Phase 1b/2 trial for LCA10 due to the c.2991+1655A>G mutation in the CEP290 gene.

Setting/Venue
An extension trial (Insight; NCT03913130) examined safety and efficacy of treatment with sepofarsen dosed in the second eye of patients who completed the Phase 1b/2 trial, and long-term follow up of treatment in the first eye.

Methods
Patients who completed the Phase 1b/2, multicenter, open-label, multiple dose-escalation sepofarsen trial were given the opportunity to enroll into the extension trial for continued dosing in their first treated eye as well as initiation of treatment in their second eye with either a 160 or 80 µg loading dose followed by 80 µg maintenance doses of intravitreal sepofarsen, using a 6-monthly dosing interval. Nine out of 11 patients from the Phase 1b/2 trial enrolled in the extension trial. As main efficacy parameters, change in best-corrected visual acuity (BCVA) and full-field stimulus test (FST) were assessed.

Results
At data cut-off in July 2020, 4 patients aged 15–45 years had received 1 intravitreal injection of sepofarsen in their second eye and had completed a 3- or 6-month visit. The safety profile of sepofarsen dosed in the second eye of participants was consistent with that observed in the Phase 1b/2 trial. At the 3-month (or equivalent) visit, clinically meaningful (change from baseline) BCVA improvements were reported in 2 of 4 second treated eyes (~2.50, ~0.80, ~0.06 and 0.00 logMAR compared to baseline), similar to the improvements observed in their first treated eyes (~2.66, ~1.28, ~0.19 and 0.00 logMAR, respectively). All 4 patients showed red and blue FST improvements (delta reported were ~1.10 and ~1.60; ~0.74 and ~0.77; ~0.87 and ~0.96; ~0.81 and ~2.35 log cd/m², respectively compared to baseline), generally similar to the red and blue FST improvements observed in their first treated eye at comparable follow-up visits (~0.51 and ~1.15; ~0.18 and ~0.46; ~0.92 and ~0.72; ~1.81 and ~1.85 log cd/m², respectively).

Conclusions
This data analysis strongly corroborates the clinically meaningful vision improvements and safety profile previously observed in the Phase 1b/2 trial. Second-eye responses to sepofarsen parallel the first-eye treated responses both in visual acuity and retinal sensitivity (FST) improvements. Further analyses on this ongoing extension trial, the Phase 2/3 trial (Illuminate; NCT03913143) and a pediatric trial (Brighten, EudraCT 2020-000535-45) are expected.

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### Title
The efficacy of subtenon triamcinolone acetonide injection on choroidal structure by perfusion of retinal plexus and choriocapillaris in patients with retinitis pigmentosa who had cystoid macular edema refractory to carbonic anhydrase inhibitors

### Purpose
To evaluate the efficacy of subtenon triamcinolone acetonide injection (TA) on the choroidal structure by perfusion of the retinal plexus and choriocapillaris in patients with retinitis pigmentosa (RP) who had cystoid macular edema (CME) refractory to carbonic anhydrase inhibitors (topical and systemic CAIs)

### Setting/Venue
Subtenon TA is safe and effective in these patients. There is no publication in the literature regarding the evaluation of the choroidal and retinal structure.

### Methods
In this prospective study, 26 eyes of 26 patients with CME secondary to RP were analyzed. Enhanced in-depth imaging optical coherence tomography (EDI-OCT) and optical coherence tomography angiography (OCTA) images were recorded 1 day before and 1 month, 3 months and 6 months after performing subtenon TA. Total choroidal area (TCA), luminal area (LA), and stromal area (SA) were calculated under Image J software.

### Results
The mean baseline best corrected visual acuity (BCVA) increased from 1.05±0.49 to 0.53±0.30 logarithmic minimum angle of resolution (log MAR) (p = 0.001) at 6 months after subtenon TA. TCA decreased to 2.13±0.51 mm² from 2.08±0.45 mm² (p<0.001); LA decreased to 1.51±0.23 mm² from 1.45±0.19 mm² (p<0.001); and SA decreased to 0.56±0.37 mm² from 0.49±0.28 mm² (p<0.001). The choriocapillaris vascular density detected by OCTA decreased from 38.82±11.92 at baseline to 32.97±10.87 at month 6 (p = 0.031). The density of deep capillary plexus vessel detected as 33.45±11.49 at baseline increased to 28.46±9.78 at month 6 (p = 0.020). The average IOP increased from 13.51±2.71 mmHg to 14.81±2.69 mmHg (p = 0.052). All parameters increased in the 1st month and decreased during the following periods (p<0.05). Multiple injections (4 injections) in 1 eye, 2 injections in 3 eyes, and 1 injection in rest of the other eyes were implemented at 3-months intervals. Complications such as glaucoma and cataract were not detected in any eyes during and following injections.

### Conclusions
OCTA demonstrated a significant increase in deep capillary plexus, choriocapillaries perfusion and TCA, LA, SA at 1 month after performing subtenon TA. The increase in all parameters at month 1 can be considered as increment of choroidal blood flow following subtenon TA.

### Financial Disclosure
None.
**Title**
Case series of TRPM1-associated complete congenital stationary night blindness: phenotypic characteristics and novel variants.

**Purpose**
To describe phenotypic features and novel genotypes in a series of ten patients diagnosed with autosomal recessive complete congenital stationary night blindness (CSNB) with molecularly confirmed pathogenic variants in the gene TRPM1.

**Setting/Venue**
Our series of ten probands were assessed in the Genetics Service of Moorfields Eye Hospital, London, between 2001 and 2021.

**Methods**
Ten patients with a confirmed molecular diagnosis of autosomal recessive congenital stationary night blindness (CSNB) secondary to pathogenic variants in TRPM1 were found by retrospective search of the electronic patient record. The following clinical features were noted where available: reported nyctalopia; type of refractive error; visual acuity at first available visit; findings on multimodal retinal imaging and electrophysiology. Particular note was made of the ratio of b-wave to a-wave amplitude (b:a ratio) in the standard scotopic bright flash (DA10) and the standard photopic flash (LA3) in those patients who had undergone international standard electroretinogram recording. A search using the PubMed database and the ClinVar resource was conducted to establish which missense variants had been previously reported.

**Results**
Of the 10 probands, six (60%) were male. Ages ranged from 9 months to 48 years, with a mean (SD) of 14.0 (14.0) years. Mean (SD) best corrected logMAR visual acuity was 0.58 (0.19). Nine patients had myopic refractive error and fundus features compatible with myopia. One patient was reported to have hypermetropic refractive error and fundus features compatible with myopia. One patient was reported to have hypermetropic refractive error. Congenital nyctalopia was reported in 9 patients (90%). ERG results were available for 8 patients: in 3 patients, a non-standard protocol was employed due to their young age; in the remaining 5 patients, standard testing was performed. All showed ERG features typical of complete CSNB. For the 5 patients undergoing standard testing, mean (SD) b:a ratio was 0.48 (0.04) for the DA10 stimulus, with a median of 0.47 (range 0.42 to 0.54); for the LA3 stimulus, mean (SD) b:a ratio was 2.6 (0.9), with a median of 2.6 (range 1.5 to 4.0). Two missense variants (found in two patients) were not found in previously reports: p.(Cys932Tyr) was found in heterozygosity in one patient; a second patient was homozygous for p.(Leu682Pro). These variants were absent from the gnomAD database.

**Conclusions**
We report phenotypic characteristics in a series of 10 patients with complete CSNB associated TRPM1 (each patient having with 2 molecularly confirmed variants). Two rare missense variants are reported that were not found in the published literature. All patients had typical ERG findings. Whilst the DA10 b:a ratio was very similar across patients, the LA3 b:a ratio varied, but was always well above 1. As pathogenic variants in TRPM1 affect ON bipolar cell responses, the latter finding is consistent with OFF bipolar cells contributing significantly to the b-wave in the LA3 flash response.

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Outer retinal tubulations in maternally inherited diabetes & deafness – associated macular dystrophy: case report

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**Co-Author 7**

**Purpose**

The presence of outer retinal tubulations (ORTs) is a tomographic sign described as round to oval structures with hyper-reflective borders surrounding a relatively hyporeflective cavity and are mainly detected at the outer nuclear layer of the retina. This finding is attributed to the disarrangement of the photoreceptors – mostly cones – that takes place in various degenerating conditions of the retina associating choroidal neovascularization or subretinal fibrosis. Maternally inherited diabetes and deafness (MIDD) comprises a rare form of diabetes and is associated with the m.3243 A > G point mutation in mitochondrial DNA. The accurate recognition should meet one or more of the following criteria; 1) impaired fasting glucose and normal BMI, 2) matrilineal transmission, 3) sensorineural hearing loss, 4) maculopathy and 5) genetic analysis compatible with mutations of mitochondrial genes linked to MIDD. Our aim is to describe the presence of ORTs in a case of a patient with typical MIDD presentation and enrich the currently available data about the formation of these structures in a progressively degenerative entity such as MIDD.

**Setting/Venue**

This is a case of a 57-year-old diabetic patient referred to our clinic complaining of mild, bilateral vision loss and difficulty in reading few years prior to her visit.

**Methods**

The patient underwent clinical examination including best-corrected visual acuity (BCVA), anterior segment evaluation, fundoscopy, optical coherence tomography (OCT) as well as audiological evaluation.

**Results**

BCVA was 8/10 (Snellen) for the right and 9/10 for the left eye. Fundus examination demonstrated diffuse areas of chorioretinal atrophy located in the posterior pole bilaterally in a symmetrical pattern. These areas surrounded the fovea, preserving a central island of normal retina and were accompanied with smaller areas of pigment clumping. OCT demonstrated disruption and loss of photoreceptors and RPE that corresponded with the atrophic areas as well as the presence of a number of ORTs seen as ovoid structures with hyperreflective borders and hyporeflective interior located in the outer nuclear layer of the retina. Follow-up seven months after her initial visit showed no alterations in the clinical and imaging status of the patient. Audiological evaluation revealed severe sensorineural hearing loss affecting high frequencies bilaterally. In the context of family screening, the patient’s sister was also assessed and subsequently diagnosed with pre-diabetes. Her BCVA was 8/10 bilaterally, while fundoscopic examination revealed mild non-proliferative diabetic retinopathy bilaterally and mild RPE changes in the posterior pole. OCT did not show any significant pathology in either eye. Audiological examination revealed a moderate sensorineural hearing loss bilaterally.

**Conclusions**

MIDD is a rare entity, frequently under- or misdiagnosed by physicians. History of diabetes along with hearing impairment and typical findings in fundoscopic examination should prompt the further investigation for MIDD. Due to its mitochondrial inheritance pattern, a strong family history with the transmission of the mutated mitochondrial DNA from the mother to all the descendants may also contribute to the accurate diagnosis. ORTs are a non-specific finding that can be found in MIDD and other retinal dystrophies, including neovascular age-related macular degeneration and retinitis pigmentosa. To date, a limited number of publications presented the detection of ORTs in MIDD patients. Taking under consideration the extremely low percentage of this entity in the diabetic population and also the possible misdiagnosis in daily clinical practice, the detection of ORTs in a patient with diabetes should raise the possibility of a MIDD diagnosis. Finally, the presence of ORTs in the context of MIDD can set the ground for further population-based studies and investigation of the molecular mechanisms involved in pathophysiology and disease progression.

**Financial Disclosure**

The authors received no financial support for the research, authorship and/or publication of this work.
Title

'Target Sign' - A novel near infrared feature and multimodal imaging in a pluri-ethnic cohort with RDH5-related fundus albipunctatus

Purpose

Retinol dehydrogenase (RDH)5 related fundus albipunctatus (FAP) can present with phenotypic variability. Our purpose was to investigate new clinical characteristics and multimodal imaging findings in patients from different ethnic origins, carrying different mutations.

Setting/Venue

This international multicenter retrospective case series included five centers (Tel Aviv Medical Center, Israel; Shamir Medical Center, Israel; Sheba Medical Center, Israel; Schneider Children’s Medical Center, Israel; University of Campania Luigi Vanvitelli, Naples, Italy). Patient records from January 1, 2016 to August 1, 2020 were reviewed for consecutive cases of FAP which had a genetically confirmed diagnosis and OCT imaging.

Methods

Eighteen patients who were diagnosed with FAP and had pathogenic bi-allelic RDH5 mutations (GeneBank Accession Number NM_001199771) were studied. Patients’ files were reviewed for fundus images, visual acuity, macular optical coherence tomography (OCT) scans, near-infrared images, fundus autofluorescence (FAF), electroretinogram (ERG), and genetic mutations. Main Outcome Measures: Imaging and ERG findings.

Results

All eyes (n=36, 100%) showed small circular findings seen on near infrared images, termed as the “target sign”, correlating to the yellowish dots seen clinically and to the distinct hyperreflective linear lesions on OCT at the level between ELM and RPE. Perifoveal atrophy with foveal sparing was seen in 4 eyes of 2 patients (both RDH5 - c.160C>T, p.R54X mutation). FAF revealed small hyperautofluorescent dots (n=16, 44.4%). Scotopic ERGs were significantly reduced in all cases with an electronegative pattern, 66.7% displayed cone dysfunction.

Conclusions

Our results show distinct imaging findings present in all FAP patients independent of ethnicity or genetic mutation. Using the imaging features described here, we can accurately target the genetic testing for RDH5 mutations. This finding may also guide the genetic counselling given in the scenario of a patient with night blindness towards a stationary nature of the disease rather than a deteriorating one, thereby alleviating the anxiety and stress of the patients and their family.

Financial Disclosure

Bayer, Allergan, Novartis, Roche - Consultant. No financial disclosures related to this study
### Title
The prognostic value of optical coherence tomography (OCT) biomarkers in Stargardt Disease

### Purpose
To describe longitudinal structural OCT and visual acuity changes in patients with Stargardt disease and evaluate OCT changes as a predictive biomarker for Stargardt disease.

### Setting/Venue
Electronic patient records (EPR) and digital images of patients diagnosed with Stargardt disease at a specialist medical retina/genetics eye clinic in large teaching hospital in UK.

### Methods
Patients of any age with a diagnosis of Stargardt disease of any subtype were identified using hospital EPR Medisoft (Leeds, United Kingdom) and their digital retinal images and OCT scans were sourced from the image database. Baseline and follow up OCT (Spectralis OCT, Heidelberg Engineering, Heidelberg Germany) scans and documented visual acuity (VA) necessary for inclusion. Eyes with coexisting macular pathology were excluded. Data was systematically harvested and analyzed independently by two ophthalmologists. At each eligible visit, visual acuity, central retinal thickness (CRT), retinal pigment epithelium (RPE) and inner segment/outer segment (IS/OS) junction disruption sizes at the geographic centre of the macula were recorded. All discrepancies exceeding 100 microns were resolved by joint review or a third assessor if still remaining. A mean of these values was calculated and used for the data analysis.

### Results
53 patients with Stargardt disease were identified from the EPR, of which 59 eyes of 31 patients (average age 46 years, 15-81, 48% male) were eligible for inclusion. Exclusions: 13 missing OCT images, 6 missing data and 3 coexisting macular pathology. 29% (n=9) of patients had one clinic visit, 35% (n=11) had two visits, 13% (n=4) had three visits, 10% (n=3) had four visits and 10% (n=3) had six visits. The mean time interval between the baseline and sixth visit was 63.4 +/- 6.4 months. Average VA deteriorated from 0.94 LogMAR to 1.33 over the course of the patients visits. Correspondingly, a deterioration was reported in all OCT biomarkers (average CRT deteriorated from 110 to 84 microns, mean RPE defect from 4007 to 5039 microns and IS/OS junction defect from 4361 to 5820 microns). The VA at baseline ranged from 6/6 to Hand Movements. At individual eye level, longitudinal OCT scan showed progressive increase in RPE defect size as well as IS/OS junction disruptions with progressive loss of vision. In eyes with good baseline VA, progressive loss—especially of central island of IS/OS junction was associated with significant loss of vision.

### Conclusions
OCT can pick up photoreceptor and RPE disruption in Stargardt patients at baseline although visual acuity can be highly variable. A progressive increase in mean RPE defect size and IS/OS junction disruption size on the OCT scans at each follow up is associated with a decline in visual acuity. Central macular IS/OS and RPE defects on OCT images correlate with visual acuity. OCT scan using retinal photoreceptor- RPE complex appears to be a useful prognostic biomarker for vision. Further studies are needed to confirm this useful, non-invasive biomarker for Stargardt disease. Future studies with machine learning of these OCT biomarkers and structural OCT analysis can help with predicting course of the disease as well as outcome of treatments. None of the Authors have a financial interest in the subject matter or receives money from any mentioned company.

### Financial Disclosure
None
### Title
Molecular and Multimodal Retinal Imaging Findings in a Portuguese Cohort of Stargardt Disease

### Purpose
Stargardt disease (STGD) is the most frequent juvenile macular dystrophy, with an estimated prevalence of 1: 8,000 to 10,000 people. It is caused by biallelic mutations in ABCA4 gene, following an autosomal recessive inheritance pattern, and generally resulting in central vision loss at school age or early teenage years. Classical findings include macular atrophy associated with yellowish-white flecks at the posterior pole. However, high phenotypic variability has been described, including cases of late onset disease and a wide severity spectrum regarding symptoms and morphological changes.

Genotype-phenotype correlations have been established, with genetic variants’ functional consequences presumably associated with phenotype severity. This study aimed to characterize the molecular and multimodal retinal imaging findings in a cohort of Portuguese patients with a clinical diagnosis of STGD.

### Setting/Venue
Ophthalmology Department, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; Genetics Department, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; Clinical Academic Center of Coimbra (CACC), Coimbra, Portugal; University Clinic of Ophthalmology, Faculty of Medicine, University of Coimbra (FMUC), Coimbra, Portugal; University Clinic of Genetics, Faculty of Medicine, University of Coimbra (FMUC), Coimbra, Portugal

### Methods
Cross sectional study conducted at an Inherited Retinal Dystrophies (IRD) reference centre in Portugal. Consecutive patients with a clinical diagnosis of STGD were identified using the IRD-PT registry. The study followed the tenets of the Declaration of Helsinki for biomedical research and was approved by the local Ethics Committee. Informed consent was obtained for every included subject. Clinical and demographic data were collected from each individual patient file. All patients underwent a complete ophthalmological examination complemented by multimodal imaging, comprising colour fundus photography (CFP), fundus autofluorescence (FAF), optical coherence tomography (SD-OCT) and OCT-Angiography (OCT-A). CFP and FAF aspects were classified according to the presence/absence of typical findings and their extension, whereas for SD-OCT and OCT-A, a quantitative analysis was performed. For probands with available genetic testing results, genetic variants were classified according to the American College of Medical Genetics and Genomics. The diagnostic yield was calculated from the number of families whose variants were classified as pathogenic or likely pathogenic, and these probands were divided into the following genotype groups: Group A included patients harbouring two predictive truncating variants; Group B consisted of patients presenting one truncating variant and one missense/in-frame variant; and Group C included predictive truncating variant and one missense/in-frame variant; and Group D included heterozygous missense variants.

### Results
Sixty eyes from 30 patients (mean age 43.30±16.69 years; 46.67% female), 26 of which unrelated, were included. A diagnostic yield of 70.59%(12/17) was obtained for the 17 families with available genetic results. Group C genotype was the most frequent (7/12); only 1 patient was included in Group A. Presentation before 18 years was reported by 19 patients. Only 4 had late-onset symptoms (after 30 years). Age of onset did not differ across genotype groups. The most frequent CFP pattern was central atrophy with macular and/or peripheral flecks (29/60 eyes), followed by multiple extensive atrophic changes (n=22). On FAF, 10 eyes showed a homogeneous background associated to localized central hypoAF (pattern 1), with the remaining 50 eyes distributing equally through patterns 2 (heterogeneous background of hypo/hyperAF foci associated to localized central hypoAF) and 3 (multiple areas of hypoAF in a heterogeneous background). Disease duration superior to 20 years (51.67%) was associated to more severe CFP (p=0.001) and FAF patterns (p<0.001). Worse visual acuity significantly correlated with advanced CFP (p=0.003) and FAF (p=0.001) patterns, reduced central macular thickness (p=0.001), larger foveal avascular zone (p<0.001), reduced density of the superficial and deep capillary plexuses (both p=0.001), and increased area of choriocapillaris atrophy (p=0.013).

### Conclusions
This study describes the phenotypic and genotypic spectrum of STGD in a Portuguese cohort, revealing a high detection rate of disease-causing genotypes using clinically-oriented genetic testing. Deep phenotyping using multimodal retinal imaging (CFP, FAF, OCT and OCT-A) was shown to be of clinical utility in the evaluation of these patients. Imaging biomarkers evaluated here presented a strong correlation with visual acuity and disease progression. These qualitative and quantitative imaging features may represent important outcome measures in the efficacy evaluation of new therapeutic targets. Due to the small sample size, our study was not powerful enough to establish genotype-phenotype correlations. Longitudinal, multicenter studies engaging larger samples are warranted to assess genotype-phenotype correlations and predict disease progression, based not only on molecular aspects but also on deep phenotyping by means of multimodal retinal imaging.

### Financial Disclosure
No financial relations to declare related to this work.

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### Purpose

Retinitis Pigmentosa (RP) is a clinically and genetically heterogeneous group of inherited retinal dystrophies (IRD) characterized by diffuse progressive dysfunction of predominantly rod photoreceptors with subsequent degeneration of cone photoreceptors and the retinal pigment epithelium. It has a global prevalence of 1:4000, making it the most common IRD and an important cause of visual disability and blindness across the world. Although usually presenting as non-syndromic (nsRP), in 20-30% of cases the disease may take part of a syndrome such as Usher or Bardet-Biedl Syndromes. The genetic profile of RP varies among regions and ethnic groups, thus emphasizing the importance of obtaining reference population-based data. The purpose of this study was to characterize for the first time the genomic landscape of Portuguese patients with syndromic RP.

### Setting/Venue

Ophthalmology Unit, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; Genetics Unit, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; Clinical Academic Center of Coimbra (CAC), Coimbra, Portugal; University Clinic of Ophthalmology, Faculty of Medicine, University of Coimbra (FMUC), Coimbra, Portugal; University Clinic of Genetics, Faculty of Medicine, University of Coimbra (FMUC), Coimbra, Portugal

### Methods

Cross-sectional study conducted at an IRD reference centre in Portugal. The IRD-PT registry was used to identify patients with syndromic RP and available genetic testing results. The study followed the tenets of the Declaration of Helsinki for biomedical research and was approved by the local Ethics Committee. Informed consent was obtained for every included subject. Clinical and demographic data were recorded from each individual patient file. A comprehensive ophthalmologic examination, complemented by multimodal imaging, comprising colour fundus photography (CFP), fundus autofluorescence (FAF), optical coherence tomography (SD-OCT) and OCT-Angiography (OCT-A) and functional testing was performed in all subjects. Genetic testing was clinically-oriented in all probands and included Sanger sequencing, multiplex ligation-dependent probe amplification (MLPA) or next generation sequencing (NGS). For probands with available testing results, genetic variants were classified according to the American College of Medical Genetics and Genomics. Whenever possible, segregation analysis was conducted in family members. Genetic counseling was provided to all families. The diagnostic yield was calculated from the number of variants classified as class IV (likely pathogenic) or V (pathogenic).

### Results

Seventy consecutive patients (61 families) were included. Consanguinity was present in 24 families (39.3%), while family history of RP was noted in 40.9%. Overall the diagnostic yield was 81.9% (50/61). Usher Syndrome was the most frequent diagnosis (40/61), followed by Bardet-Biedl (10/61), Hallervorden-Spatz (5/61), Senior-Loken (4/61), Jalili (1/61) and Shwachman-Diamond (1/61) syndromes. All the unsolved cases had clinical diagnosis of Usher Syndrome. Variants of uncertain significance (VUS) were identified in 36.4% (4/11), while in the remaining families no clinically significant variants were found. The diagnostic yield of Usher Syndrome was 68.3% (28/41) and 100% for all other types of syndromic RP. Forty-three pathogenic and likely pathogenic (24 and 19, respectively) variants were found across 16 different genes. Variants in 5 genes (USH2A, MYO7A, BBS10, BBS1 and PANK2) responded for 75.5% of solved cases. USH2A was the most frequently implicated gene, explaining 24% of the disease-causing genotypes (12/50). The remaining solved cases were explained by mutations in USH1G, CDH23, ADGRV1, WDR19, NPHP1, TTC8, PCDH15, DNAJC21, SDCCAG8, ARSG or CNNM4.

### Conclusions

Achieving strong population-based data is the first step towards better genetic and prognostic counselling as well as guidance for future therapeutic interventions. This study obtained a satisfactory detection rate of disease-causing genotypes using clinically-oriented genetic testing. Our results demonstrate the genomic landscape of syndromic RP in Portugal, providing evidence that USH2A-associated Usher Syndrome is a major cause of syndromic RP in our country.
Title
Genetic Diagnosis: A standard-of-care for inherited retinal diseases on the horizon of precision medicine

Purpose
Inherited retinal diseases (IRDs) represent a heterogeneous group of rare visually debilitating diseases that are caused by mutations in over 300 critical genes for retinal function. Overall, the clinical diagnosis of IRDs is challenging due to several levels of complexity, including locus and allelic heterogeneity with variable expression. Therefore, reporting the precise phenotype with optimum genetic testing selection is critical to confirm clinical diagnosis and build up a genotype-phenotype correlation.

Setting/Venue
An ophthalmological clinical setting optimized to precisely diagnose IRD cases.

Methods
Molecular diagnosis is needed to provide a complete and comprehensive clinical diagnosis of IRDs; this requires a multidisciplinary team including an IRD specialist and a molecular geneticist, bioinformatician, clinical scientist, and genetic counselor. This has resulted in an impressive database of families with phenotypic information under the umbrella of IRDs in which state-of-the-art recent molecular techniques are applied to deliver a precise diagnosis. A detailed ophthalmological examination, including best-corrected visual acuity, refraction, slit-lamp examination, fundus imaging, optical coherence tomography, and assessment of electrophysiological functions of the entire retina by full-field electroretinography is mandatory to obtain a clear phenotype. Clinical examinations should be followed by selecting the best genetic testing strategy and genetic sequencing tool for a given patient by opting for one of the advanced molecular techniques including clinically-oriented gene panels, whole-exome sequencing (WES), or whole-genome sequencing (WGS). An understanding of the capabilities and limitations of each modality is necessary, with harmonization between the multidisciplinary team to resolve cases with inconclusive data, such as variants of uncertain significance, missing inheritability, or novel findings.

Results
The clinical diagnosis of IRDs alone is considered to be incomplete according to American Association of Ophthalmology (AAO) guidelines. This fact relies on the principle that the ophthalmological examination is largely unremarkable; this leads to a dilemma of frequent referral by a non-expert in IRDs. To date, the AAO has listed genetic testing as an integral component for diagnosing IRD cases; this creates a paradigm shift in diagnostic rates. Success relies on the application of clinically-oriented gene panels, WES, and WGS leading to the identification of disease-causing mutations in known and novel genes. Nowadays, most genetic laboratories are applying a uniform classification system of 5 classes to rank the pathogenicity of identified variants based on American College of Medical Genetics guidelines: (1: pathogenic, 2: likely pathogenic, 3: unknown significance, 4: likely benign, and 5: benign). Variants ranked as 1 or 2 can be reported with genotype-phenotype correlation.

Conclusions
Given the advantage of the eye with its anatomically and immunologically preserved structure, approximately 30 ongoing gene therapy-based clinical trials are being conducted worldwide applying different molecular techniques aimed at target IRD genes and variants. Establishing the correlation between genotype and phenotype is mandatory in the diagnosis of IRDs. The resulting diagnostic yields from genetic testing approaches and resolution of cases with inconclusive data, such as variants of unknown significance (VUS) are applied to serve the goal of precision medicine and will help to translate these findings into proof-of-concept clinical trials and enhance the enrolment of all targeted patients in ongoing worldwide therapeutic interventions.

Financial Disclosure
Dr. Basamat Almoallem has nothing to disclose; Dr. Manar Aoun is an employee of Novartis Pharmaceuticals, Italy.
Title
Cross-border treatment and management experience of voretigene neparvovec (ocular gene therapy) in the European Union

Purpose
Voretigene neparvovec (VN) is the first ocular gene therapy approved for the treatment of patients with visual impairment due to confirmed biallelic RPE65 mutation-associated inherited retinal dystrophy (IRD) and who have sufficient viable retinal cells. Due to the novelty of the treatment and the limited number of patients, VN is administered in treatment centers that fulfill specified European Union (EU)-mandated risk mitigation criteria. This also ensures that safety and efficacy are kept a top priority. EU regulation and directive furthermore govern planned cross-border interventions, under which a patient may travel to another EU country to receive treatment, and have the cost reimbursed by their own health insurance scheme. Herein, we present the experience of, and coordination between, a VN treatment center in Croatia and a patient management center in Slovakia.

Setting/Venue
Cross-border ocular gene therapy treatment and management between the University Eye Department, University Hospital “Sveti Duh”, Zagreb (UEDUHSDZ), Croatia and the National Institute of Children’s Diseases (NICHD), Faculty of Medicine, Comenius University, Bratislava, Slovakia, following S2 form authorization. The S2 (formerly E 112) form is issued by the health insurance authority in the patient’s home country to permit planned healthcare treatment in another EU country. The form is then submitted to the health insurance authority in the treating country.

Methods
The IRD registry at the NICHD, Slovakia was retrospectively evaluated to identify patients diagnosed with IRD owing to RPE65 mutations, as confirmed by genetic analysis and segregation analysis of first degree relatives. Five pediatric patients were identified, with two patients subsequently recommended as suitable for VN treatment following examination of visual acuity (VA), fundoscopy, wide-field fundus photography (WFFP), autofluorescence, perimetry, optical coherence tomography (OCT), color vision (CV), contrast sensitivity (CS), visually evoked potentials (VEP), electroretinography (ERG), tonometry, biometry, refraction and a visual function questionnaire. Three certified VN treatment centers in the EU were contacted to participate in the cross-border care of the two NICHD patients. UEDUHSDZ, Croatia accepted NICHD’s treatment application and a cross-border treatment agreement was established. As VN treatment is covered by health insurance in Slovakia, prior reimbursement authorization was requested and a S2 form was issued. Patients were referred to the multidisciplinary team in UEDUHSDZ, which comprises a pediatric ophthalmologist, an IRD specialist, three retinal surgeons with experience in subretinal application and a geneticist. Surgery was scheduled in Croatia in December 2020, with patients enrolled in PERCEIVE (a post-authorization, multicenter, multinational, type IIa, observational, prospective, non-interventional study) with the aim of improving quality of life. No adverse events were observed. The patients will be further followed by NICHD at month 3, month 6 and 1 year.

Results
Following a negative COVID-19 PCR test, both patients were admitted to UEDUHSDZ four days prior to their scheduled surgical procedure. Patients were examined by the multidisciplinary team in UEDUHSDZ, with WFFP, autofluorescence, biometry, tonometry and OCT performed to confirm eligibility for VN treatment. An immunomodulatory regimen was subsequently initiated in accordance with the recommended VN product information pre-operative schedule. On day four, patients received 300 μl of VN in the first (more severely affected) eye, followed by treatment of the contralateral eye, one week later. Post-surgery, information on the procedure was immediately communicated to NICHD to update the PERCEIVE registry. Patients were discharged from UEDUHSDZ four days after their second surgery and presented to NICHD 30 days post-operatively for follow-up clinical examinations. Follow-up assessment revealed a significant improvement in central visual acuity in one of the two patients, with both patients reporting an improvement in quality of life. No adverse events were observed. The patients will be further followed by NICHD at month 3, month 6 and 1 year.

Conclusions
A willingness to collaborate, straightforward funding arrangements and positive relations between the Croatian and Slovakian teams contributed to the successful cross-border treatment and management of patients. In this case example, patients were diagnosed with biallelic RPE65 mutation-associated IRDs by the multidisciplinary team at the NICHD, Bratislava and referred to UEDUHSDZ, Croatia for VN surgical treatment. Following successful gene therapy administration in UEDUHSDZ, patients were discharged and returned to Bratislava for post-operative follow-up at the NICHD. Communication and collaboration between UEDUHSDZ and NICHD was seamless and efficient, with a positive cross-border experience reported by the patients, families and both multidisciplinary teams. Due to treatment and management center cooperation and positive collaboration, a further three patients from the NICHD IRD registry will be evaluated for cross-border VN treatment.

Financial Disclosure
Mirjana Bjelod: Voretigene neparvovec post-authorisation safety study (PASS) principle investigator; Beata Busanyova: Voretigene neparvovec post-authorisation safety study (PASS) principle investigator; Natalia Filimonova: Employee of Novartis; Gabriella Germán: Employee of Novartis
Purpose
Achromatopsia (ACHM) is a rare inherited retinal disease, characterized by serious cone dysfunction, affecting approximately one in every 30,000 live births worldwide. Over 150 mutations in CNGA3 and CNGB3 genes have been identified as pathologic, accounting for approximately 70–80% of all cases of ACHM. The diagnosis is based upon clinical findings as reduced central visual acuity on early childhood, pathologic myopia, pendular nystagmus, photophobia, eccentric fixation with central scotomas and reduced or complete lack of colour vision (CV), suggested by signs of central macular atrophy on funduscopic examination, disruption of external segments of foveal photoreceptors on Optical Coherence Tomography (OCT), abnormal Colour Vision Testing (CVT), abnormal Visual Fields (VF) and abolished cone function on Electrorretinography (ERG) and confirmed by genetic testing. The nature and early onset of sight impairment can be severely disabling, with significant impact on activities of daily living. We propose to describe 4 families with ACHM from our database, in order to raise awareness about this entity among Ophthalmologists.

Methods
Research of ACHM cases from our Ocular Genetics database brought out 4 cases of different families that we decided to include in this report: Case 1: 29 years old female Case 2: 46 years old male Case 3: 9 years old male Case 4: 15 years old male

Results
Case 1: Complaints of myopia, photophobia, nystagmus and colour vision deficiency (CVD) since childhood. Her parents shared consanguinity. Best Corrected Visual Acuity (BCVA) was 20 / 160 on both eyes (OU). Funduscopy showed orange-stained macula. VF revealed central escotomata and ERG photopic cone response was extinct. Genetic testing disclosed homozygous mutation in CNGB3. Case 2: Complaints of myopia, photophobia, nystagmus and CVD since 2. BCVA was 20 / 160 Right Eye (RE) and 20/200 Left Eye (LE). Funduscopy showed altered bilateral foveal reflex. VF revealed tunnel vision and ERG showed abolished photopic cone responses and diminished scotopic response. Genetic testing disclosed compound heterozygous mutation in CNGA3. Case 3: Complaints of myopia, photophobia, congenital nystagmus and severe CVD since 2. BCVA was 20 / 160 Right Eye (RE) and 20/200 Left Eye (LE). Funduscopy showed altered bilateral foveal reflex. Genetic testing disclosed compound heterozygous mutation in CNGA3. Case 4: Pakistanis, with myopia, photophobia, nystagmus and color blindness since birth. His parents are first cousins and his brother has similar vision problems. BCVA was 20 /160 RE and 20/200 LE. Funduscopy showed orange-stained macula and ERG showed abolished photopic cone responses and diminished scotopic response. Genetic testing disclosed homozygous mutation in CNGB3.

Conclusions
ACHM is a rare disease that progressively leads to serious loss of cones and consequently vision deficiency. It is inherited as an autosomnic recessive pattern. A complete vision checkup is mandatory, including complementary exams as OCT, ERG, FAF, VF and CVT. Genetic counselling is recommended after genotyping. Novel mutations and pathologic variants are being constantly discovered, giving place for scientists and geneticists to develop innovative therapeutic genetic strategies.
Title
High-resolution adaptive optics retinal imaging analysis of patients with autosomal dominant retinitis pigmentosa caused by HK1 mutation

Purpose
The hexokinase 1 (HK1) gene encodes one of the four human hexokinases that play essential roles in glucose metabolism. Recently, several cases of E847K mutation in the HK1 gene were reported to cause inherited retinal dystrophy. The purpose of this study was to identify the phenotypical characteristics of patients with a recurrent E847K mutation in the HK1 gene.

Setting/Venue
All subjects were recruited and examined at a university hospital, the Nippon Medical School Chiba Hokusoh hospital in Japan. The procedures used in this study conformed to the tenets of the Declaration of Helsinki, and they were approved by the Institutional Review Board of the Nippon Medical School. A signed written informed consent was obtained from the patient and family members after the nature and possible consequences of the study were explained.

Methods
Three generations of one family with autosomal dominant retinitis pigmentosa were examined. Whole exome sequencing was performed on the DNA. The ophthalmological examinations included measurements of the best-corrected visual acuity (BCVA), slit-lamp bio-microscopy, ophthalmoscopy, Goldman kinetic perimetry, fundus photography, fundus auto-fluorescence imaging (FAF) with short-wavelength excitation, spectral domain optical coherence tomography (SD-OCT), full-field electroretinography (ERG), and multifocal ERGs (mERGs). The ERGs were recorded using the extended testing protocol conforming to the International Society for Clinical Electrophysiology of Vision protocol (ISCEV). Fundus imaging by an adaptive optics fundus camera was used to obtain high-resolution photoreceptor images, and cone densities of the families were compared to that of normal eyes of healthy subjects.

Results
Fundus examination of the proband showed degeneration of the mid-peripheral retina, and SD-OCT images showed an absence of the ellipsoid zone (EZ) and interdigitation zone (IZ) in the parafovea and more peripherally. SD-OCT images of the mother of the proband showed an absence of the EZ and IZ, and fundus autofluorescence images showed hypo-autofluorescence surrounding the macular region. One daughter of the proband had only mild night blindness, however, the density of the cone photo-receptors was reduced in the parafoveal region. Whole exome sequencing identified a heterozygous variant, E847K, in the HK1 gene. This variant was found to co-segregate with the disease in three family members.

Conclusions
Fundus, FAF, and OCT imaging revealed that the areas of photoreceptor degeneration were mainly in the parafovea to mid-peripheral region. High-resolution retinal imaging by AO revealed that the cone photoreceptor densities were significantly reduced in the parafoveal area at the age of 20 years, though fundus examinations showed only slight abnormalities without functional visual defects at this age. High-resolution retinal imaging analysis, such as that by AO and FAF analysis would be helpful in identifying patients with HK1-retinopathy caused by an E847K mutation. AO examination in between the different generations might be helpful to understand the prognosis and progression of the diseases.

Financial Disclosure
Kiyoko GOCHO (spouse) : imagine eyes
External limiting membrane and outer retinal modifications in Choroideremia: three differentially impaired retinal regions.

Choroideremia (CHM) is a X-linked inherited retinal dystrophy characterized by a progressive centripetal chorioretinal degeneration. Although the main alterations can be detected at the level of the outer retina and the retinal pigment epithelium (RPE), an intriguing pathogenic hypothesis suggested Müller cells might also provide a primary site of pathogenesis. Müller cells represent a transretinal cytotype included between the internal limiting membrane (ILM) and the external limiting membrane (ELM), which are direct extensions of the Müller cell’s structure. ILM can be poorly visualized on structural optical coherence tomography (OCT), whereas ELM is easily detected. The main goal of the present study is to quantitatively investigate ELM and outer retinal features in order to assess if ELM could be considered a useful biomarker to monitor the evolution of CHM.

Setting/Venue
Clinical setting; Department of Ophthalmology, IRCCS San Raffaele Scientific Institute, Vita-Salute University, via Olgettina 60, Milan (Italy).

Methods
The study was designed as prospective, observational, case series, with at least two years of follow-up. Patients affected by CHM, confirmed by the genetic assessment of CHM gene mutation, were recruited. For the quantitative comparisons, we included also a cohort of healthy age- and refractive-matched male subjects. All the eyes underwent complete ophthalmologic examinations including best-corrected visual acuity (BCVA) measurement and multimodal imaging assessment. The main outcome of the study was the measurement of thickness and reflectivity of ELM changes over the follow-up. Secondary outcome included the relationship with atrophy progression as assessed on enface OCT and fundus autofluorescence (FAF). Additional investigations regarded the relationship between ELM features and OCT angiography (OCTA) findings. We separately considered the modifications detected in the following three regions: 1) partially preserved islet (PPI); 2) region of the partially preserved islet evolving to atrophy over the last follow-up; 3) region surrounding the borders of the partially preserved islet. The statistical analysis was performed comparing baseline vs last follow-up data.

Results
We included 16 CHM eyes (mean age 39±14 years; LogMAR BCVA 0.0±0.0) and 20 controls (mean age 40±10 years; LogMAR BCVA 0.0±0.0). The mean follow-up was of 3.5±1.4 years. ELM thickness always resulted lower than controls (p<0.01), whereas ELM reflectivity was not statistically different compared to controls (p>0.05). Interestingly, ELM thickness and ELM reflectivity of the borders evolving towards atrophy resulted significantly worse than PPI (p<0.01). OCTA showed preserved superficial capillary plexus and significantly impaired deep capillary plexus in CHM. Regarding the choriocapillaris (CC), we found three different regions. The first region corresponded to the PPI, with CC vessel density (VD) resulting preserved (p>0.05). The second region corresponded to the CC surrounding and extending beyond the borders of the PPI, showing significantly lower VD at baseline (p<0.01) but resulting stable at the last follow-up (p>0.05). The third region was represented by the CC of the PPI undergoing atrophic changes at the last follow-up. This region showed significantly reduced CC VD at baseline, compared to the rest of the PPI (p<0.01) and did not show significant changes over the follow-up (p>0.05). The correlation analyses showed a significant negative association between retinal atrophy progression and both ELM reflectivity and ELM thickness (p<0.01).

Conclusions
The ELM is formed by the apical processes of Müller cells attached to the inner segments of the photoreceptor cells. Both Müller cells and photoreceptors have been implicated in the complex pathogenesis of CHM. In the present study, we showed ELM as a useful quantitative biomarker of CHM evolution. Our results reported significant ELM thinning and reflectivity reduction in CHM eyes compared to healthy controls. ELM changes were more pronounced in those retinal regions undergoing atrophic expansion, and well correlated with the progression of atrophy. Furthermore, the detailed quantitative evaluation of outer retinal changes allowed to detect three significantly different CC regions. Although limited by the relatively low number of eyes, our findings might have useful implications both for disease monitoring and for the optimization of gene therapy administration.
Clinical/demographic, functional testing and multimodal imaging differences between genetically solved and unsolved retinitis pigmentosa

Purpose
Retinitis pigmentosa (RP) is the most common inherited retinal dystrophy. The changes are usually bilateral with a high degree of inter-eye symmetry. However, the disease exhibits an immense phenotypic variability and several atypical RP phenotypes have been described, including unilateral or asymmetric cases. One contributing factor is the genetic heterogeneity that characterizes RP. Additionally, a substantial number (30-50%) of RP cases remain genetically unsolved despite state-of-the-art genetic testing. Possible explanations include undetected/unknown genotypes (e.g., inappropriate genetic test selection; hypomorphic variants; deep intronic mutations; variants within non-coding regions or variants in genes that have not yet been associated with RP) or an incorrect clinical diagnosis (i.e., disease entities that mimic RP such as paraneoplastic retinopathy, inflammation, infection or autoimmune disease). Clinical/demographic and multimodal imaging patient characteristics may also impact clinical pre-selection for efficient genetic testing and patient counselling. With the development of new therapeutic options and a growing number of gene therapy clinical trials, the importance of deep phenotyping and genetic testing cannot be overemphasized. The purpose was to compare clinical/demographic, functional testing and multimodal imaging differences exist between genetically solved and unsolved nsRP cases. We found that significant clinical/demographic, functional, and multimodal imaging features should be considered when diagnosing and counselling patients with RP. The purpose was to compare clinical/demographic, functional testing and multimodal imaging differences between genetically solved and unsolved nsRP cases.

Setting/Venue
Department of Ophthalmology, Centro Hospitalar e Universitário de Coimbra (CHUC); Clinical Academic Center of Coimbra (CACC); University Clinic of Ophthalmology, Faculty of Medicine, University of Coimbra (FMUC); Department of Ophthalmology, Centro Hospitalar e Universitário do Porto (CHUP); Instituto Ciências Biomédicas Abel Salazar (ICBAS); Department of Medical Genetics, Centro Hospitalar e Universitário de Coimbra (CHUC); University Clinic of Medical Genetics, Faculty of Medicine, University of Coimbra (FMUC); University Clinic of Pediatrics, Faculty of Medicine, University of Coimbra (FMUC)

Methods
Cross-sectional study conducted at the Retinal Dystrophies Clinic and Medical Genetics Unit of Centro Hospitalar e Universitário de Coimbra (CHUC), an IRD reference center and only Portuguese healthcare provider represented in the ERN-EYE. The IRD-PT registry was used to identify consecutive patients with non-syndromic RP and available genetic testing results. All patients with clinically suspected and/or genetically confirmed syndromic RP were excluded. Clinical/demographic, functional and anatomical features were compared between genetically unsolved (Group 1) and genetically solved (Group 2) patients. Genetic testing was clinically-oriented in all probands and coordinated by a medical geneticist from the Medical Genetics Unit of CHUC. Variants were classified in accordance with the American College of Medical Genetics and Genomics (ACMG). All variants classified as pathogenic (class V) or likely pathogenic (class IV) were further confirmed by Sanger sequencing. The diagnostic yield was calculated from the number of variants classified as pathogenic or likely pathogenic. Genetic counselling provided by a medical geneticist was granted to all subjects.

Results
The study included 175 patients (350 eyes) of 146 families: 68 patients (59 families; 136 eyes) in group 1 and 107 patients (87 families; 214 eyes) in group 2. The average age at diagnosis was significantly higher in group 1 (p<0.001). Age of first symptoms <25 years (p<0.001), consanguinity (p=0.019), evidence for a particular inheritance pattern (p=0.044) and absence of indicators for phenocopies (p=0.007) were significantly more prevalent in group 2. The onset of symptoms in childhood (OR=1.650; 95% CI=1.021-2.665), history of consanguinity in family (OR=1.821; 95% CI=1.040-3.191) and absence of potential phenocopies (OR=2.689; 95% CI=1.215-5.951) were predictors of a solved case in our nsRP cohort (x2(1)=16.101;p=0.001, R2Negekerke=0.064). No significant differences were observed on best-corrected visual acuity (p=0.099). The visual field index (VFI) was significantly higher (p=0.020) in group 1 than in group 2. VFI (AUC=0.688, p=0.037, 95% CI=0.518-0.857) was able to identify solved and unsolved cases with <53.50% as the optimal cut-off (75% sensitivity and 63% specificity). The frequency of atypical features on multimodal imaging did not differ between groups. On optical coherence tomography, the mean retinal layer thickness was higher (p=0.032) in group 1 than in group 2.

Conclusions
We found that significant clinical/demographic, functional, and multimodal imaging differences exist between genetically solved and unsolved nsRP cases. Overall, our study provides evidence that an older age of symptom onset, absence of consanguinity, absence for a particular inheritance pattern, presence of indicators for phenocopies, larger fields, a VFI>53.5% and a higher RLT negatively impact the diagnostic yield in patients with nsRP. Careful medical history taking and deep phenotyping have shown to impact the genetic diagnostic yield and prognosis in nsRP. Individual clinical/demographic, functional testing and multimodal imaging features should be considered when counselling patients about the probability of identifying disease-causing variants. Given the genotypic and phenotypic heterogeneity that characterizes nsRP, it is critical to obtain predictive models for different populations in order to increase the efficiency of genetic testing and provide accurate genetic counselling.

Financial Disclosure
None.
### Purpose
The market approval process for gene therapies faces unique regulatory challenges due to the novelty, as well as the unidentified risks associated with such therapies. Therefore, regulatory agencies may request that the applicant implement post authorization measures, documented in a risk management plan (RMP) specific to the drug. In line with EMA guidelines, Novartis prepared and submitted a risk-management plan (RMP) on applying for EMA marketing authorization, in order to document the risk management system for voretigene neparvovec treatment. Here, we describe the Committee for Medicinal Products for Human Use (CHMP) risk minimization requirements for voretigene neparvovec, and outline the approved RMP that was developed and submitted to the European Medicines Agency (EMA) in compliance with requisite CHMP procedures.

### Setting/Venue
The implementation of a RMP for ocular gene therapy by Novartis Pharma AG, Switzerland in accordance with EMA guidelines for gene therapy products, including the incorporation of virtual educational sessions and a novel educational virtual reality modality designed as a practical alternative to surgical wet labs.

### Methods
Risk minimization safety measures for voretigene neparvovec were considered and examined under three categories: i) the drug ii) target population and iii) disease/condition. A pharmacovigilance plan was formulated, identifying both routine and additional pharmacovigilance activities to ensure the acquisition of additional safety and efficacy data following market approval. Furthermore, additional risk minimization measures were developed for ocular gene therapy treatment facilities, which included the rollout of medical and pharmacy standardized educational sessions, to ensure the correct use of the treatment and minimize the risks associated with administration and/or the surgical administration procedure. The procedures include: (1) the presence of a specialist ophthalmologist with expertise in care and treatment of patients with inherited retinal diseases; (2) the presence of, or affiliation with, a retinal surgeon experienced in sub-retinal surgery and capable of administering a gene therapy; (3) the presence of a clinical pharmacy capable of handling and preparing AAV vector-based gene therapy products. Prior to product distribution to a treatment facility, surgeons and pharmacists must also complete mandatory surgical and pharmacy medical educational programs on the preparation and administration of the product, as stipulated in the RMP.

### Results
More than 30 surgical and 50 pharmacy medical educational programs have been completed to date (excluding the United States [US]). In response to the COVID-19 pandemic, educational sessions are now held virtually, ensuring continued treatment facility onboarding. This has included virtual theoretical sessions, alongside practical surgical sessions using a novel virtual reality surgical simulation tool (SIRIUS VR tool), to simulate administration of voretigene neparvovec as an alternative to physical surgical wet lab attendance. To ensure site readiness, dry run sessions are completed prior to the first surgery. Another additional post-marketing risk minimization condition includes providing patients and caregivers with an information pack. The pack includes the Patient Information Leaflet, also available in alternative formats including large print and audio, and a patient card highlighting the importance of attending follow-up visits and reporting side effects. The patient card also serves as information for other healthcare professionals that may treat the patient. Alongside routine pharmacovigilance activities, additional post-authorization pharmacovigilance activities outlined in the RMP include a non-interventional safety registry study (PERCEIVE) in Europe (and other countries, excluding the US), and a post-intervention 15 year Long-Term Follow-Up Study in subjects enrolled in the US pivotal trials.

### Conclusions
The EMA granted regulatory approval for voretigene neparvovec following the preparation and submission of a marketing authorization application and accompanying RMP. In line with the RMP for voretigene neparvovec, the drug is only distributed through treatment centers that fulfill the specified RMP criteria and where qualified and experienced staff (i.e. vitreoretinal surgeons and pharmacists) have completed the mandatory educational program/training in relation to the administration of the gene therapy. Further additional risk minimization measures, as outlined in the approved RMP, include providing patients with auxiliary supports to access the information provided to them. The RMP for voretigene neparvovec further details the ongoing routine and additional pharmacovigilance activities required due to the novelty of the treatment and the limited number of patients treated in pivotal trials.
**Title**
Genomic landscape and natural history of sector retinitis pigmentosa

**Purpose**
Sector retinitis pigmentosa (sRP) is a rare, atypical, and milder variant of rod-cone degeneration, in which only one or two quadrants of the retina are involved. Despite being historically associated with the RHO gene, the mutational spectrum of sRP is evolving with other causative genes recently implicated. This study aimed to characterize the genotypes, phenotypes, and natural history of a Portuguese cohort with sRP.

**Setting/Venue**
Ophthalmology Unit, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal.

**Methods**
Retrospective, observational study. Patients with a clinical diagnosis of sRP and available genetic testing results were identified using the IRD-PT registry. Genetic testing was clinically oriented in all probands. Variants were classified according to the American College of Medical Genetics and Genomics standards and guidelines. Only class IV (Likely Pathogenic) or V (Pathogenic) variants were considered to be disease causing. The clinical diagnosis was established based on functional testing [best corrected visual acuity (BCVA) and visual field testing] and multimodal imaging [color fundus photography, fundus autofluorescence (FAF) and optical coherence tomography (OCT)]. Clinical progression was evaluated throughout follow-up.

**Results**
Fourteen patients from twelve families were included. Mutations in syndromic and non-syndromic RP-related genes were identified in 8 families, for a diagnostic yield of 66.7%. EYS was the most frequently implicated gene (4 families), followed by RHO (2 families), and finally MYO7A and NPHP1 (1 family each). In most unsolved cases, no clinically significant variants were found. However, for one unsolved case, a variant of uncertain significance (class III) was identified in the RHO gene. All cases were bilateral and symmetrical except for two, which were unilateral (1 unsolved and 1 solved, in association with NPHP1 variants). Inferior and/or nasal involvement of the retina on FAF was noted in all cases, with a crescent shaped hyper-autofluorescent band separating the atrophic area from the unaffected, iso-autofluorescent retina. Visual field testing revealed superior visual field defects of varying extents, always in close association with the observed FAF findings. Over a median follow-up period of 32.5 months, BCVA remained stable and ≥20/32 OU in 9/14 patients. Multimodal imaging revealed no progression over the follow-up period.

**Conclusions**
This study highlights the genotypic heterogeneity of sRP in a Portuguese cohort. Inferior and nasal predilection was common across the different genotypes, and a high proportion of patients maintained good central vision. The longitudinal data provided herein will help to provide patients with accurate prognoses and counseling.

**Financial Disclosure**
None
X-linked retinoschisis: Long-term follow-up and genetic spectrum of 340 patients

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A detailed knowledge on the clinical and genetic characteristics of X-linked retinoschisis (XLRS) is necessary to provide patients with a more accurate prognosis, but also to identify clinical endpoints and optimal patient selection for (gene) therapy. This study aims to improve clinical counseling and acquire crucial information for the development process of treatment by evaluating the largest cohort of XLRS patients to this date.

Multicenter retrospective study.

This international multicenter retrospective study reviewed medical records for medical history, symptoms, best-corrected visual acuity (BCVA), ophthalmoscopy, full-field electroretinography and retinal imaging (fundus photography, spectral-domain optical coherence tomography (SD-OCT), fundus autofluorescence).

In total, 340 patients, from presumably 178 different families, were included with a mean age of 28.6±19.3 years at last visit. The median BCVA of the better-seeing eye at last examination was 0.52 logarithm of the minimum angle of resolution (logMAR) (Interquartile range, Q1: 0.30, Q3: 0.70 logMAR). Severe visual impairment below 1.0 logMAR was predominantly present in patients above 40 years old, with a prevalence of 13.5% in that age group. Linear mixed models revealed a slow annual decline of 0.39% in BCVA (P < 0.001), with a relatively stable visual acuity until the age of 20 years. The integrity of the ellipsoid zone (EZ) as well as the photoreceptor outer segment (PROS) length on SD-OCT were significantly correlated with visual acuity (Spearman’s r = -0.604, P < 0.001; r = -0.759, P < 0.001; respectively). Fifty-three different RS1 gene mutations were found. The most common variants were two founder mutations: c.214G>A (p.Glu72Lys; 102 subjects, 38.2%) and a deletion of exon 3 (38 subjects, 14.6%). There was no significant difference in decline of BCVA between mutations that were predicted to be severe and mild (p=0.852).

In general, XLRS showed a slowly progressive decline, starting around the age of 20, suggesting an optimal window of opportunity for treatment within the first three decades of life. However, there are notable exceptions that include severe early-onset vision loss, often due to vitreoretinal complications such as retinal detachment. The integrity of EZ as well as the PROS length on SD-OCT may be important potential clinical endpoints in future therapeutic studies. No clear genotype-phenotype correlations were found.

None to report.
Portable S-cone electroretinography recordings in healthy participants and in a patient with NR2E3-associated retinopathy

**Purpose**
To explore use of an S-cone specific setting on a portable hand-held electroretinogram (ERG) device to detect differences in ERG waveform between healthy participants and a patient with NR2E3-associated Enhanced S-cone Syndrome.

**Setting/Venue**
Recordings were obtained from a patient with NR2E3-associated Enhanced S-cone Syndrome whilst in the retinal genetics clinic, and from healthy control participants in clinic or office settings.

**Methods**
ERG waveforms were recorded using the portable RETeval device (LKC technologies, Gaithersburg, MD, USA) together with skin electrodes following pharmacological mydriasis. The stimulus was a blue flash (0.25 photopic m-2 s then 1.0 photopic cd m-2 s) delivered at 4.2 Hz in the presence of a red background (560 cd m-2). Averaged traces from up to 500 stimulus presentations were obtained. The patient was a 35 year old female who was homozygous for the c.119-2A>C variant in NR2E3. Healthy control participants of similar age with no known ocular disorders were recruited and underwent the same testing. All study participants gave informed consent and the study had ethics committee approval.

**Results**
Recordings from 5 healthy participants (including 3 females and 2 males) were analysed. Mean (SD) age was 32 (6.8) years (median 30; range 24 to 42 years). ERG waveforms from these participants were similar, with a-wave amplitudes of less than 5 microvolts and less than 8 microvolts for the 0.25 and 1.0 cd m-2 s flashes respectively, and a-wave peak times of 15-18 ms. B-waves were larger than a-waves, and usually showed 2 or more peaks. Responses from the patient showed a much larger a-wave (>10 microvolts and >15 microvolts for the two stimuli respectively) with a simplified waveform. The patient’s ERG b-waves were of similar size to the a-waves, and the b-waves peaked at a markedly later time point (>50 ms after the flash) in comparison with the control traces.

**Conclusions**
Using a hand-held portable ERG device and S-cone specific setting, we were able to detect characteristic waveform features of Enhanced S-cone Syndrome in a patient with variants in NR2E3. This ERG waveform was clearly distinguishable from healthy control participants. The recording procedure was well-tolerated, simple to conduct and completed in 5 minutes or less per eye. Large S-cone ERGs are quite specific for disease associated with bi-allelic pathogenic variants in NR2E3 (or more rarely bi-allelic variants in NRL). This technique can be of value in guiding genetic screening. Where genetic testing has already been performed, these recordings can help establish the likely pathogenicity of variants of uncertain significance in these genes.

**Financial Disclosure**
No financial disclosures
Gene therapy rescues cone and rod function in a pre-clinical model of CDHR1-associated retinal degeneration through restoration of photoreceptor outer segments

**Purpose**
To evaluate the efficacy and safety of retinal gene therapy in a pre-clinical model of CDHR1-associated retinal degeneration – an as yet untreatable, blinding disorder characterised by shortened photoreceptor outer segments and progressive cone and rod photoreceptor degeneration. Biallelic hypomorphic variants in CDHR1 result in late-onset macular dystrophy which may be clinically misclassified as dry age-related macular degeneration.

**Setting/Venue**
Nuffield Department of Clinical Neurosciences, University of Oxford

**Methods**
Cdh1 +/- (n=28) and C57BL6J control mice (n=23) underwent paired sub-retinal injections of AAV8.GRK1.CDHR1 (1.5x10⁸) and PBS vehicle control in the fellow eye at 4 weeks of age. Dark- and light-adapted electroretinography (ERG) was undertaken at 2, 4, 6, 8, 10 and 12-months post-injection. Photoreceptor layer thickness measurements were compared using optical coherence tomography (OCT) imaging at 1, 6- and 12-months post-injection.

**Results**
In Cdhr1-/- mice, AAV8.GRK1.CDHR1 rescued A-wave amplitudes (p<0.0001 at all time points) and B-wave amplitudes (p<0.0001 from 6 months) on dark-adapted ERG when compared with PBS-injected control eyes. Light-adapted and flicker ERG amplitudes were greater in AAV-treated eyes at all time-points (p<0.0001 from 8 months post-injection). The photoreceptor layer was preserved versus PBS-injected control eyes to 12-months post-injection (mean 70.2µm versus 29.3µm; p<0.0001). OCT changes consistent with the regeneration of photoreceptor outer segments were only identified in AAV-treated eyes, with therapeutic effect seen as early as 1-month post-injection (p<0.0001 versus PBS-injected eyes). The extent of outer segment regeneration in AAV-treated superior retinas increased significantly between 1- and 6-months (p<0.0001) and was sustained to 12-months post-injection. In C57BL6J mice, there was no difference in ERG responses at 12-months (A-wave, p=0.052; B-wave, p=0.56; Cone responses, p=0.99) or photoreceptor thickness measurements on OCT imaging at 12 months between AAV and PBS-injected eyes (p=0.58).

**Conclusions**
These data provide proof-of-principle of the efficacy and safety of CDHR1 gene therapy in a pre-clinical model of CDHR1-associated retinal degeneration. Rod and cone rescue occur through prevention of photoreceptor cell death and regeneration of photoreceptor outer segments. A follow-on clinical trial in patients with CDHR1-associated retinal degeneration is anticipated.

**Financial Disclosure**
A patent has been filed on behalf of the University of Oxford for the vectors described in this abstract in which the authors are listed as inventors.
**Title**
Treatment with antiVEGF in Slovene family with Sorsby fundus dystrophy

**Purpose**
To report the result of anti-VEGF treatment in a patient with CNV secondary to AD Sorsby fundus dystrophy with confirmed heterozygous likely pathogenic variant in TIMP3 gene (NM_000362.5(TIMP3):c.509C>G (p.Ser170Cys)), and to describe phenotype in her sister and niece.

**Setting/Venue**
Eye Hospital, University Medical Centre Ljubljana, Slovenia

**Methods**
Three patients from the same family (57 years old lady, her 61 years old sister and 30 years old niece) with Sorsby retinal dystrophy with confirmed TIMP3 mutation underwent ophthalmological examination including visual acuity measurement (VA) and multimodal imaging (autofluorescence, fluorescein angiography, ICG and OCT) and electrophysiology testing (ISCEV standards).

**Results**
The 57 yrs old patient with PEX syndrome manifested 20 years ago with symptoms of night blindness. Ishihara and visual acuity was normal, visual fields showed paracentral scotoma, dystrophic changes with drusae and atrophic changes were seen on the fundus. Electrophysiology showed normal PERG 50, borderline N95 response and abnormal photopic and scotopic ERG. She experienced sudden worsening of vision in her left eye at the age of 56 years. CNV secondary to Sorsby dystrophy was confirmed with fluorescein angiography and ICG, first in the left, later also on the right eye. OCT showed fibrovascular PED with serosis, and thickened Bruch's membrane. Blockage of fluorescence was seen on ICG in late phases. After 4 injections of antiVEGF (Ranibizumab) in her right eye and 14 injections in her left eye VA improved (ETDRS RE: 47 to 53, LE: 57 to 70), due to regression of CNV. Her sister had dystrophic retinal changes with good vision in right eye and poor VA in the left eye due to amblyopia. Electrophysiology showed abnormal PERG 50 and N95 responses and abnormal photopic and scotopic ERG. The niece had good vision with early signs of bilateral retinal dystrophy.

**Conclusions**
Sorsby retinal dystrophy manifests first with symptoms of night blindness and paracentral scotoma in the visual field. Sudden visual loss later on may be due to secondary CNV. In our patient it responded well to treatment with antiVEGF. It is important to regularly follow other family members with retinal changes, as CNV may develop in the future; with timely treatment permanent vision drop can be postponed.

**Financial Disclosure**
none
**Title**

AAV5-RPGR Gene Therapy for RPGR-Associated X-Linked Retinitis Pigmentosa Reverses Natural Disease Progression

**Presenter**

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**Purpose**

To evaluate how intervention with a gene therapy for X-linked retinitis pigmentosa (LRX) associated with disease-causing sequence variants in Retinitis Pigmentosa GTPase Regulator (RPGR) affects the natural progression of the disease. RPGR-associated LRX is among the most severe forms of retinitis pigmentosa, which is the most prevalent inherited retinal dystrophy.

**Setting/Venue**

MGT011 (NCT03349242) is a prospective longitudinal natural history study of individuals with retinal dystrophy associated with variants in RPGR. A subset of participants from MGT011 were enrolled into MGT009, a multi-centre open-label Phase 1/2 trial of an AAV5-RPGR gene therapy (NCT03252847) conducted at 5 sites across the United States and United Kingdom.

**Methods**

Participants in MGT011 were assessed at baseline, every 6 months for 2 years, and then annually for up to 5 years. Retinal assessments included Octopus 900 full-field static perimetry and mesopic fundus-guided microperimetry, with analyses including mean retinal sensitivity (MS), visual field modeling and analysis (VFMA), and point-by-point comparisons. Ten adult males aged 18-30 years with RPGR-associated LRX from MGT011 were identified as suitable for gene therapy intervention and were enrolled in MGT009. In the dose-escalation phase of MGT009, up to 1 mL of 1 of 3 doses (low, intermediate, and high) of AAV5-RPGR was administered to the participant’s poorer-seeing eye. The untreated contralateral eye served as a control. AAV5-RPGR was delivered by subretinal injection. The central retina was targeted, including foveal detachment, with multiple retinotomies permitted to enable coverage of all viable retina. Retinal function was assessed at baseline through 12 months post-treatment. Changes in MS and central 30-degree hill of vision (V30) were examined up to 48 months pre- (MGT011) and 12 months post-intervention (MGT009).

**Results**

AAV5-RPGR was generally well-tolerated as previously reported. Twelve months following treatment in the low (n=3) and intermediate (n=4) dose cohorts, 6 participants demonstrated improvement or stability in treated-eye retinal sensitivity. For all patients who received the intermediate dose, based on a linear regression model that began in MGT011 ≥36 months prior to enrollment of these patients in MGT009 and continued through 12 months post-intervention, treated eye MS at 12 months post-intervention improved back to levels observed at least 24 months prior to the intervention. Similarly, treated eye VFMA-derived improvement in V30 at 12 months post-intervention reflected levels observed at least 24 months pre-intervention. For the intermediate dose cohort, the natural history MS and V30 data collected ≥36 months pre-intervention were trending downward for both eyes in nearly all participants. For all intermediate dose recipients, the downward trend in MS and V30 results continued for the untreated eye through 12 months post-intervention, indicating continued natural disease progression. Significant differences (P<0.05) were observed between treated and untreated eyes at 12 months for the intermediate dose cohort in MS (1.05 dB [90% CI: 0.81, 1.29]) and V30 (1.26 dB-sr [90% CI: 0.65, 1.86]).

**Conclusions**

At 12 months post-intervention, treatment with the low and intermediate doses of AAV5-RPGR resulted in clinically meaningful improvements in retinal sensitivity across multiple metrics and modalities. For the intermediate dose cohort, intervention with AAV5-RPGR therapy in the poorer-seeing eye altered the course of natural disease progression. At 12 months post-intervention, MS and V30 in the treated eye were similar to levels observed 24 months pre-intervention, while the untreated eye showed a continued downward trajectory. Given the robust safety and efficacy signals observed at the low and intermediate doses, these two doses are being further explored in a randomized controlled Phase 3 clinical trial (NCT04671433).

**Financial Disclosure**

Dr. Michaelides is a consultant and holds equity in MeiraGTx, and serves on advisory committees for MeiraGTx and Janssen; he also serves as a consultant for Acucela, 2CTech, Roche, and Stargazer. Dr. Besirli is a consultant for MeiraGTx and Janssen, and receives clinical trial support from the University of Michigan. Dr. Sahel receives grants from LabEx LIFESENSE (ANR-10-LABX-65), IHU FOReSIGHT (ANR-18-IAHU-01), and personal fees from GenSight Biologics.
A systematic review and meta-analyses of interventional clinical trial studies for gene therapies for the Inherited Retinal Degenerations (IRDs)

Purpose

IRDs are one of the leading causes of visual loss in children and young adults. Mutations in over 271 genes lead to retinal dysfunction, degeneration and sight loss. Though no cure exists, gene augmentation therapy has brought the field hope. This systematic review sought to assess the effectiveness of available gene therapy treatments for IRDs. Databases and public resources were searched for randomised controlled trials (RCTs) and non-randomised studies of interventions (NRSIs). Standard methodological procedures were used, including a risk-of-bias assessment. One RCT and five NRSIs were assessed, all for adeno-associated virus (AAV)-mediated treatment of RPE-specific 65kDa (RPE65)-associated LCA. Five outcomes were reported for meta-analyses. Modest improvements in visual acuity, ambulatory navigation/mobility testing or central retinal thickness was observed. There was significant improvement in red and blue light full-field stimulus testing (FST) (red light risk ratio of 1.89, treated v control, p=0.04; and blue light risk ratio of 2.01, treated v control, p=0.001). Study design assessment using a ROBIN-I tool showed risk-of-bias judgement to be "low/moderate", whilst there were "some concerns" for the RCT using a RoB-2 tool (Cochrane Library). FST improvements demonstrate a proof-of-principle for treating IRDs with gene therapy and there remains scope.

Setting/Venue

IRDs include Retinitis pigmentosa (RP) which comprise a group of disorders causing the deterioration of rod and cone photoreceptor cells in the retina leading to visual impairment or blindness. There is currently no cure for RP. Leber Congenital Amaurosis (LCA), a juvenile form of RP, shows an early infant-onset form of the disease characterised by severe retinal dystrophy, vision loss, nystagmus and an almost non-recordable ERG. Gene therapy is a potential treatment for LCA with previously published trials aimed at addressing several clinical outcomes, including visual acuity, mobility, visual field testing and retinal thickness, amongst others.

Methods

Search methods Ovid databases for MEDLINE (from Jan. 1946 to Jun. 2020) and EMBASE (Jan. 1980 to Jun. 2020) were searched for IRDs, methodology, gene therapy and outcomes, including other terms. Additional public resources were searched in the FDA, the EMA, ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and international patient organisations. Selection criteria Randomised controlled trials (RCTs) and non-randomised studies of the effects of interventions (NRSIs) with any gene therapy treatment for any human patients diagnosed with any syndromic or non-syndromic RP. Data collection and analysis Standard methodological procedures of the Cochrane Collaboration for screening, data abstraction, and study assessment. A structured PICOS search strategy used screened records and abstracted data following with a review and assessment of risk-of-bias tools with included studies (with two independent authors). 115 records were found, 7 articles were duplicated and removed, 108 publications were screened, 87 were excluded and 21 articles were accessed for eligibility; of these, 15 articles were excluded: one (1) was not applicable (choroideremia), five (5) were follow-up studies and nine (9) articles included duplicate data. A final six (6) primary articles were conducted for review and meta-analyses, summarised in a PRISMA flowchart.

Results

Six (6) clinical trial studies reported one (1) RCT and five (5) NRSIs, including a sample of n=84 LCA2 (RPE65) patients across three countries (UK, France and the USA). A gene therapy augmentation treatment for recombinant AAV-RPE65 was sub-retinally transfected for a range of subjects spanning ages from 4-44 years. Twelve meta-analyses were reported but only one (1) assay, visual acuity (VA), was common to all six (6) papers. ETDRS logMAR results found a summary weighted mean difference (MD) of -0.06 logMAR improvement over treated vs. untreated eyes (95% CI -0.14, 0.02), p=0.16, including six (6) studies with a I2 heterogeneity of 65%. An ambulatory navigation / mobility test across a light-intensity level of 4 lux showed an RR (risk ratio) improvement of 1.03, over treated vs. untreated eyes (95% CI 0.75, 1.42), p=0.84, including four studies with a I2 heterogeneity of 0%. A summary weighted mean difference (MD) of FST (full-field stimulus testing) (red) showed an RR (risk ratio) improvement of 1.69 log10(cd.s/m2) over treated vs. untreated eyes (95% CI 1.21, 2.16), p=0.00001. Modest improvements in visual acuity, ambulatory navigation/mobility testing or central retinal thickness was observed. There was significant improvement in red and blue light full-field stimulus testing (FST) (red light risk ratio of 1.89, treated v control, p=0.04; and blue light risk ratio of 2.01, treated v control, p=0.001). Study design assessment using a ROBIN-I tool showed risk-of-bias judgement to be "low/moderate", whilst there were "some concerns" for the RCT using a RoB-2 tool (Cochrane Library). FST improvements demonstrate a proof-of-principle for treating IRDs with gene therapy and there remains scope.

Conclusions

Results of this overall systematic review and meta-analyses showed no clinically meaningful benefit and no statistical significance with the six (6) trials combined. One RCT found a clinically meaningful benefit for an assessment for a primary endpoint for mobility, a MD of 1.6 (95% CI 0.72-2.41), p=0.0013. All other studies however, showed variable and modest benefits. A significant loss of outcome data showed a considerable amount of under-reporting across all of the trials. While gene therapy is an extremely positive field capable to deliver an enormous new medical opportunity, there are clear weaknesses to be addressed to ensure that patients can be benefitted at the earliest opportunity.

Financial Disclosure

No conflicts.
Current management of patients with RPE65 mutation-associated inherited retinal degenerations (IRDs) in Europe. Results of a multinational survey by the European Vision Institute Clinical Research Network, EVICR.net

Purpose
US FDA in 2017 and EMA Europe in 2018 have approved the first ocular gene augmentation therapy, voretigene neparvovec VN, for clinical use. Since then, many more countries worldwide have followed. Among the EVICR.net clinical centers, we conducted the first multinational survey to understand distribution, diagnostic work-up, and management of inherited retinal degenerations (IRD) cases in Europe with a special focus on RPE65 mutation-associated IRDs.

Setting/Venue
All 101 EVICR.net clinical centers during May and June 2019.

Methods
An electronic survey questionnaire including 35 questions specifically addressing RPE65 mutation-associated IRDs was sent to the responsible person of the Clinical Center and to its representative for the EVICR.net Retinal Dystrophies Scientific Section of the 101 EVICR.net clinical centers. Only one reply per Clinical Center was considered for analysis. A reminder was sent to the non-repliers after 2 weeks, the deadline was extended by 2 weeks and new reminders were sent on week 3 and 4. The questionnaire comprised five sections: Section 1: IRD demographics, Section 2: Local setting, Section 3: IRD Genetic testing and counselling, Section 4: Involvement in Clinical Trials and Section 5: RPE65 mutation-associated IRDs. The results from Sections 1 to 4 were reported separately. We conducted a descriptive analysis to all variables. Continuous variables were summarized using the following statistics: number (n), mean, standard deviation (SD), median (P50), first and third quartiles (P25 and P75), minimum (Min) and maximum (Max). The frequency and percentages of observed levels were reported for all categorical measures. For statistical analyses, we used Excel version 15.0.4433.1508 (Microsoft Office Home and Business 2013) and R version 3.6.0 (2019-04-26).

Results
The overall response rate was 49%. Forty-two centers see IRD patients, and 22/42 follow patients with confirmed biallelic RPE65 mutations. Fifteen of the 22 centers (68%) and 3/22 (14%) follow 1-5 and 6-10 patients with homozygous RPE65 mutations, respectively. Additionally, 15/22 (68%) and 3/22 (14%) follow 1-5 and >20 patients with compound heterozygous RPE65 mutations, respectively. Fifty-nine percent of mutations were American College of Medical Genetics (ACMG) Class 4 and 5 (at least one allele), 82.8% had been reported previously and 17.2% were novel. Referral diagnoses (mean per center) were Leber Congenital Amaurosis (38.2%), Early-onset severe retinal degeneration (16.8%), Rod-Cone-Dystrophy/Retinitis pigmentosa (RP) (28.1%), and unclassified visual impairment (17.0%). Twenty-five percent of the centers changed the referral diagnosis in 48% of cases; 32% follow a specific referral process for RPE65 mutation-associated IRD patients. Annual follow-up visits are done in 55% of the centers, and biannual visits in 23%. In 32%, other centers also follow the patients. Kinetic perimetry is done in 82%, static perimetry in 45%, microperimetry in 18% of the centers, chromatic Full-field Stimulus Test (FST) to quantify rod and cone function is used in 6/22 centers (27%). A mobility course is available in one center (5%).

Conclusions
This first multinational survey on management of patients with RPE65 mutation-associated IRDs in Europe shows that about half of the responding EVICR.net centers have such patients under care. There is heterogeneity in diagnoses and management practices. At the start of clinical practice experience with voretigene neparvovec, these data provide a useful baseline and highlight the need for consensus/guidelines to inform standard of care in this new era of gene therapy.

Financial Disclosure
Novartis Pharma AG through a Scientific Collaboration Agreement between Novartis and AIBILI, the Coordinating Center of EVICR.net funded this study. Novartis provided non-binding comment/input to the IRD Survey Expert Committee into all elements of the scientific collaboration agreement. Dr. Birgit Lorenz: paid talks or consultant for: Novartis GmbH (RPE65) and Janssen Global Services, LLC (XLRP). Dr. Hendrik Scholl is supported by the Swiss National Science Foundation (Grant 31003A_184652).
**Title**
OCT-angiography of retinal blood flow in pregnant women with diabetes mellitus

**Purpose**
To investigate retinal blood flow in pregnant women with diabetes mellitus using OCT angiography.

**Setting/Venue**
The work was performed in the S.N. Fyodorov NMRC «MNTK «Eye Microsurgery», Khabarovsk, Russia

**Methods**
The study involved 60 pregnant women: 24 with type 1 diabetes and 36 healthy women with a physiological course of pregnancy (control group). The average age of pregnant women with diabetes was 29.1±4.7 years, the average duration of diabetes was 11.1±8.4 years. The average HbA1c value was 6.3±1.5%. In 10 patients no diabetic retinopathy (DR) was detected during pregnancy. 14 pregnant women (58%) were diagnosed with DR. In 5 patients DR was detected during the pregestational period. In 9 patients DR manifested itself during pregnancy. By the third trimester of pregnancy, 6 patients had proliferative DR (PDR), 5 patients had severe nonproliferative DR (NPDR), and 3 had NPDR. All patients with PDR and severe NPDR underwent retinal laser coagulation prior to examination. In the group of healthy pregnant women the average age of the patients was 30±4.2 years. OCT angiography with HD Angio Retina 6.0 mm scanning protocol was performed. Vessel density Whole Image (VDWI), Foveal Vessel density (VDF), area of foveal avascular zone (FAZ) in the superficial retinal plexus were investigated. One random eye was included in the analysis. Pregnant women with diabetes were examined in all three trimesters, healthy pregnant women - in the third trimester.

**Results**
In pregnant women with diabetes in the third trimester, the mean VDWI values were 50.47±4.45%, VDF - 27.15±8.08%, FAZ - 0.36±0.15 mm², in the control group - VDWI – 51.93±3.16%, VDF – 34.52±6.32%, FAZ – 0.27±0.1 mm², respectively. In the third trimester, VDF in pregnant women with diabetes was significantly less than in the control group, in the absence of differences in VDWI and FAZ. This decrease in VDF was not associated with an expansion of FAZ, which may indicate the presence of vascular dysregulation due to chronic impairment of glycemic status, a decrease in perfusion, and the development of an ischemic process - microangiopathy in the fovea zone, even in patients showing no clinical signs of DR. In pregnant women with diabetes without DR in the third trimester, the mean VDWI values were 52.26 ± 3.22%, VDF – 24.37±8.47%, FAZ – 0.30±0.07 mm², in pregnant women with DR – VDWI – 48.68±4.89%, VDF – 29.93±6.93%, FAZ – 0.43±0.18 mm², respectively. VDWI was significantly lower, and FAZ was significantly higher in pregnant women with DR than in pregnant women with diabetes mellitus without DR, which is consistent with literature data and characterizes the defeat of the retinal microvasculature. In 11 pregnant women with DR (6 women with PDR, 5 – with severe NPDR), retinal nonperfusion zones were visualized in the posterior pole, the area of which in 6 patients during pregnancy from the 1st trimester to the 3rd trimester tended to expand, which indicated the

**Conclusions**
1. Pregnant women with diabetes mellitus showed a statistically significant decrease in Foveal Vessel density in the superficial retinal plexus in the third trimester, compared with healthy women with physiological pregnancy, in the absence of significant differences in Vessel density Whole Image and the area of the foveal avascular zone. The data obtained are of practical importance for the diagnosis of the manifestation of diabetic retinopathy during pregnancy. 2. In pregnant women with diabetic retinopathy in the third trimester of pregnancy, a statistically significant expansion of the foveal avascular zone with a decrease in the total vascular density in the superficial plexus was revealed, in comparison with pregnant women with diabetes mellitus without retinopathy. 3. There were no statistically significant differences in the indices of retinal blood flow in the superficial vascular plexus in different trimesters of pregnancy in women with diabetes mellitus. 4. OCT-angiography is a valuable diagnostic method that allows non-invasive diagnostics of the presence of areas of retinal nonperfusion in the absence of ophthalmoscopic signs of diabetic retinopathy in pregnant women with diabetes mellitus, as well as to assess the state of areas of retinal nonperfusion during pregnancy in patients with diabetic retinopathy.
**Phase 1b/2 interim results of QR-421a RNA therapy in retinitis pigmentosa due to mutations in the USH2A gene (Stellar trial)**

**Purpose**
Retinitis Pigmentosa (RP) is a group of inherited retinal diseases causing progressive blindness. USH2A mutations are the most common cause of autosomal recessive RP (aRP). Exon 13 mutations in USH2A are present in non-syndromic (nRP) and syndromic forms of RP called Usher syndrome type 2, the leading cause of deaf-blindness; neither has an approved treatment. The Stellar trial evaluates the safety and tolerability of QR 421a, an RNA antisense oligonucleotide, in subjects with biallelic mutations in exon 13 of USH2A.

**Setting/Venue**
The Stellar trial (NCT03780257) is a 24-month, multicenter Phase 1b/2 dose-escalation single-dose study in aRP patients aged ≥18 years that are homozygous or compound heterozygous for exon 13 mutations in USH2A. The study enrolled subjects at 7 sites (USA, Canada, and Europe).

**Methods**
The population varied in disease characteristics (Usher syndrome or nRP), genetic background (homozygous or compound heterozygous USH2A exon 13 mutations), and disease stage (advanced stage defined as participants with baseline best-corrected visual acuity [BCVA] of less than 70 letters on the Early Treatment Diabetic Retinopathy Study [ETDRS] chart, or early moderate stage with a baseline BCVA of ≥70 ETDRS letters). Three cohorts were assessed where participants received a single intravitreal QR-421a injection at dose levels of 50, 100, or 200 μg administered unilaterally. The first subjects in dose cohort 1 and 2 were treated with active treatment; further recruitment to at least 6 subjects per dose cohort was double-masked using a 2:1 ratio of randomization (QR-421a : Sham). Dose cohort 2 was expanded to recruit 3 additional participants in an open-label fashion. Dose cohort 3, also open label, included 3 subjects. The maximum follow-up duration was 24 months. Primary endpoints were frequency and severity of ocular adverse events (AEs) and non-ocular AEs. Secondary endpoints included change in functional (BCVA; static perimetry) and structural (ellipsoid zone [EZ] area by optical coherence tomography) outcome measures in QR-421a-treated eyes (TE), untreated eyes (UE), and sham-treated eyes (SE), and serum pharmacokinetics.

**Results**
20 subjects were enrolled, 14 participants received QR-421a (50-μg dose: 4, 100-μg dose: 7, 200-μg dose: 3) and 6 received sham. No serious AE or inflammation was observed. One participant had worsening of pre-existing cataracts (deemed not treatment-related by treating physician). One participant had progression of pre-existing cystoid macular edema, being managed with standard care. BCVA stabilization (no decline compared with baseline) was observed in QR-421a-TE, versus a decline in UE, in keeping with the natural history of the disease. At week 48, mean BCVA benefit was 6.0 letters and 9.3 letters in all QR-421a-treated and advanced participants (n=6) respectively. No BCVA benefit was observed in SE (2.2 letters difference between both eyes). Mean change from baseline of the EZ-area was +15.0% in QR-421a-TE, –26.4% in UE, and –12.5% in SE at week 24. For static perimetry, mean change from baseline of number of locations (loci) that improved by ≥7 dB in QR-421a-TE versus UE was up to 9.2 loci versus 6.1 loci in all QR-421a-treated participants and up to 12.9 loci versus 6.9 loci in early moderate-stage participants (n=8; week 12). SE responded similarly to QR-421a-UE. Response to QR-421a was similar in all cohorts.

**Conclusions**
QR-421a was observed to be well tolerated at all doses in participants with exon 13 mutations in USH2A. QR-421a demonstrated encouraging evidence of disease stabilization in visual acuity and clinically significant improvements in retinal sensitivity, supported by objective retinal structural imaging data, after a single dose compared with UE and SE. An open-label extension trial is planned to follow up the Stellar trial participants, and 2 Phase 2/3 trials are planned.

**Financial Disclosure**
DGB reports grant funding from ProQR Therapeutics during the course of the study.
Usher Syndrome is the association between Retinitis Pigmentosa (RP) with sensorineural hearing loss. Showing autosomal recessive inheritance, there are at least 16 genetic loci identified as associated with Usher Syndrome. With a prevalence of about 3-4 cases per 100,000 persons, there are 4 types of Usher Syndrome. The purpose of this work is to present a family with different genotypes and phenotypes, with the mother having homozygosity to a mutation in USH2A (gene associated with Usher Syndrome), and her son and daughters being compound heterozygotes.

Case reports of 4 patients, from the same family (mother, son and daughters), in which the mother (born from a consanguineous marriage), shows the association between RP and sensorineural hearing loss since her 50 years (Usher Syndrome), and her children only exhibit RP until now. Case 1: Female, 62 years Case 2: Female, 41 years Case 3: Male, 36 years Case 4: Female, 29 years

Results
The following is a summary of the last appointment of the 4 cases: Case 1: The patient refers Nyctalopia, Photophobia, Photopsies, and visual field (VF) loss; Best Corrected Visual Acuity by the Snellen Chart (BCVA 6/10 Right eye (R); 5/10 Left eye (L)); Fundoscopy shows thin vessels and scarce pigmentation in a bone-spicule configuration at the periphery. Scotopic and photopic Electretinogram (ERG) extint; VF (Goldmann) with Tunnel Vision. Case 2: Patient refers Nyctalopia, Photophobia and Photopsies; BCVA (10/10 R; 10/10 L); Fundoscopy shows mid peripheral Choriorretinal atrophy without pigmentation; VF (Goldmann) shows peripheral constriction. Case 3: The patient refers Photophobia; BCVA (10/10 R; 10/10 L); Fundoscopy shows thin vessels and pigment in a bone-spicule configuration at the periphery. VF (Goldmann) shows peripheral constriction. Case 4: The patient refers Photophobia, VF loss, Nyctalopia and Photopsies; BCVA (10/10 R; 10/10 L); Fundoscopy shows thin vessels and scarce pigmentation in a bone-spicule configuration at the periphery. The son and daughters all had OCTs exhibiting atrophy of the external retinal layers, except at foveal zone.

Conclusions
In a family with an apparent autosomal dominant vertical transmission for RP, sensorineural hearing loss, and consanguinity in the first generation, the result of a genetic test denotes that a compound heterozygosity can explain the vertical transmission in this family. Therefore, the genetic testing can be of vital importance in the identification and prediction of vision loss in some families that show some form of retinal hereditary disease.
## Title
LIGHT - Observational study on the use of voretigene neparvovec in patients with inherited retinal dystrophy at CHNO des Quinze-Vingts: A 1-year follow-up of a 12-case series

## Purpose
RPE65-related IRD is a rare condition caused by biallelic mutations in RPE65. Loss of RPE65 function causes photoreceptor dysfunction and degeneration, leading to blindness. The launch of voretigene neparvovec, a gene therapy product indicated for treatment of patients with sufficient viable retinal cells and confirmed biallelic RPE65 mutations constitute a first gene therapy success for IRD. The CHNO was the first European center to use voretigene neparvovec and has so far one of the largest and longest follow-up in an European cohort of treated patients. It has significant experience with treatment administration and follow-up in real-life conditions. In the development program of voretigene neparvovec, efficacy was measured by the Multi-Luminance Mobility Test, specifically-developed for IRD-patients. This test requires patients to follow a maze and avoid obstacles, under different light levels. As it is difficult to implement, it is not usually used in routine follow-up and centers rely on usual assessments. The CHNO has access to a similar maze platform called Streetlab® which can test functional vision through mobility testing, and is able to use it in routine follow-up. The study’s purpose was to report one-year effectiveness and safety outcomes of voretigene neparvovec treatment including functional vision with the

## Setting/Venue
This is a descriptive, non-interventional study with secondary use of data of patients with inherited retinal dystrophy associated with biallelic mutations in RPE65, treated with voretigene neparvovec subretinal gene therapy at CHNO des Quinze-Vingts between December 2018 and November 2019 and with at least a 1-year follow-up period who did not object to the secondary use of their data. Data were collected from patients’ medical records.

## Methods
Voretigene neparvovec is a one-time treatment, administered at a dose of 1.5 x 1011 vector genomes to each eye, delivered in a total subretinal volume of 0.3 ml. The individual administration procedure to each eye was performed on separate days, no fewer than 6 days apart. Baseline visit was defined as the last visit before the surgery. Patient’s follow-up visits in routine practice usually take place at 1, 3, 6 and 12 months after the surgery of the second eye. The data collected aimed to evaluate efficacy, safety and to describe the surgical procedure. Efficacy was assessed by both visual function and functional vision assessments. Visual function was assessed using visual acuity of each eye, full-field stimulus threshold (FST) of each eye and monocular and binocular kinetic visual field. Functional vision was assessed using the Streetlab® system. It was designed to evaluate the evolution of mobility following treatment. The courses were set up to represent a daily life street and included elements of varying contrast and volume. Patients were instructed to follow the path under four lighting conditions (2, 7.5, 50 and 500 lux), while avoiding touching obstacles and walls.

## Results
Due to the recent implementation of the LIGHT study, a full and complete analysis of the data, while pending, is not yet available at this time. Nevertheless, our preliminary results were promising as all 12 patients reported having improved vision in dimly lit environment. Analysis are being finalized and will be shared during at the congress.

## Conclusions
This study is the first study to generate real-world data using such a large cohort of patients with a one-year period follow-up. The addition by the CHNO of a mobility test to assess the evolution of functional vision in their routine follow-up protocol in addition to the FST allows this study to give further insights on the efficacy of voretigene neparvovec treatment during the first year post-surgery.

## Financial Disclosure
RESEARCH COLLABORATION FUNDED BY NOVARTIS
**Title**

Longitudinal Phenotypic Study of Late-Onset Retinal Degeneration due to a Founder Variant c.562C>A p.(Pro188Thr) in the C1QTNF5 Gene

**Purpose**

Longitudinal, detailed phenotypic analysis in a 7-generation Belgian family with autosomal dominant late-onset retinal degeneration (L-ORD) due to the c.562C>A p.(Pro188Thr) variant in the C1QTNF5 gene, using a mixed cross-sectional and longitudinal approach.

**Setting/Venue**

Twenty-six patients (21 - 81 years) with a mean follow-up time of 8 years (range 1-37 years).

**Methods**

Extensive ophthalmic work-up including psychophysical, electrophysiological testing and multimodal imaging.

**Results**

Sequencing of the C1QTNF5 gene detected c.562C>A p.(Pro188Thr). SNP-based haplotyping revealed a common haplotype of 9.7 – 11.4 Mb, and genealogical investigation identified a common ancestor, rendering c.562C>A p.(Pro188Thr) a Belgian founder variant. Best-corrected visual acuity (BCVA) and visual fields were maintained up to 50 to 55 years (n=8), with a gradual decline but conservation of functional central vision between 55 to 65 years (n=9). Classic anterior segment findings in L-ORD of abnormally long, anteriorly-inserted lens zonules were absent in most patients (n=24/26). In contrast, findings of iris transillumination and sphincter pupillae atrophy with poor dilation were novel. Patients presented with three completely different initial fundus phenotypes: adjoining pavingstone-like atrophic patches (type 1) (n=6/20); tiny yellow-white subretinal dots (type 2) (n=8/20); or larger yellow, thick, round sub-RPE drusenoid deposits (type 3) (n=4/20). Two patients had a mixed phenotype (type 1 and 2). Although different in presentation phenotype, patients eventually all progressed to a common panretinal atrophy with diffuse intraretinal pigment migration beyond the age of 65. Progression pace, and thus visual prognosis, differed depending on presentation phenotype. Specifically, type 2 appears to have the more benign course.

**Conclusions**

Phenotypic analysis showed 3 distinct presenting phenotypes with a considerable intrafamilial variability both in age of onset of clinical signs, as well as in disease progress, with a fair visual potential (> 20/40) until the seventh decade. This study provides novel insights into clinical signs and symptoms, as well as visual prognosis, emphasizing the phenotypic heterogeneity of L-ORD.

**Financial Disclosure**

Member of Advisory Boards for Novartis, Bayer, Abbvie
Title
Epidemiology of mutations in the 65 kDa retinal pigment epithelium (RPE65) gene-mediated inherited retinal dystrophy: A systematic literature review

Purpose
Inherited retinal dystrophies (IRDs) comprise a wide range of phenotypically and genetically heterogeneous group of rare genetic diseases that are generally characterised by progressive loss of vision. Mutations in more than 270 different genes have been identified as the cause of IRDs. Among these, biallelic mutations in the RPE65 gene i.e. retinal pigment epithelium (RPE)-specific protein 65 kiloDalton (kDa) affects the visual cycle in the retinal epithelium, resulting in a progressive rod (primarily) and cone degeneration. Biallelic mutations in the RPE65 gene are often associated with Leber’s congenital amaurosis 2 (LCA2) and retinitis pigmentosa 20 (RP20). The current evidence base for the epidemiology of RPE65 gene-mediated IRDs is limited. Such epidemiological evidence will be important for evaluating impact of the disease in the population in terms of disease burden and unmet needs. Thus, this study aims to understand the epidemiology landscape of RPE65 gene-mediated IRD through a systematic review of the literature.

Setting/Venue
not a relevant section for this abstract

Methods
A review of the global medical literature was conducted by following the systematic principles of the Cochrane handbook for systematic reviews and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The electronic databases (Embase, Medline, and Cochrane Library) were searched from inception until the 12 January 2021 to retrieve studies reporting prevalence and incidence of LCA and RP and the proportion of biallelic RPE65 mutations in these IRDs. The Orphanet rare diseases platform and the bibliography of relevant literature reviews was also screened for including potential studies. The databases were searched for terms related to RPE65, RPE65-IRD, RPE65-RP, RPE65-LCA, incidence, prevalence and/or epidemiology. The search results were limited to English language. Publications were included in the full-text review if they reported on the epidemiology of IRDs caused by RPE65 gene mutations or prevalence/ incidence of RP or LCA (irrespective of any mutation) or proportion of RPE65 gene mutation in RP or LCA.

Results
The literature search yielded 3744 citations from which 69 studies were identified with relevant epidemiology data for inclusion. The prevalence of LCA was estimated to be 1.24 to 2.37 per 100,000 based on three studies conducted in Denmark, Norway and the US and the prevalence of RP ranged between 11.09 to 26.43 per 100,000. For Israel, the prevalence of RP was reported to be high (47.62 per 100,000) probably because of a high level of consanguinity and a high number of siblings within certain ethnic groups. The worldwide proportion of RPE65 mutations in LCA was estimated at 6.10% and varied between 1.0% to 22.2%. The proportion of RPE65 mutations in LCA and RP ranged between 1.79% to 16% and 0.23% to 7.41% for the European region, respectively. For the US, the proportion of RPE65 mutation ranged between 3.0% to 15.55% for LCA and 0.81% to 1.85% for RP patients. A recent Mexican study had reported that RPE65 in RP occurred in 3.28% of clinically diagnosed RP and LCA patients.

Conclusions
Patients with RPE65 gene-mediated IRD are reported from across the world including Europe, North America, South America, Middle-East, and Asian countries. Robust epidemiology data for RPE65-mediated IRDs is limited and therefore accurate assessments of prevalence and incidence are challenging. Insufficient data on prevalence have contributed to the insufficient funding and resources available to conduct genetic testing for IRDs, and to provide genetic counselling for IRD patients and families. There is also a high heterogeneity in reporting of the data and the lack of sufficient high-quality studies highlights the need to conduct higher quality studies on rare genetic diseases. Therefore, further research is needed to generate strong evidence with high quality studies to get a better understanding of the disease. This can help in early identification of the affected patients and their early treatment can prevent progression to severe visual impairment or complete blindness.

Financial Disclosure
• Juliana MF Sallum has nothing to disclose
• Judit Banhazi, Claudio Spera, and Daniel Viriato are employees of Novartis Pharma AG
• Vinay Preet Kaur and Javed Shaikh are employees of Novartis Healthcare Pvt. Ltd.
• Professor Fischer reports consulting fees from Advent France Biotechnology, Alphasights, Atheneum, Axiom Healthcare Strategies, Biogen, Decision Resources, Dialectica, Frontera Therapeutics, Janssen Research &
# Title

**Pediatric patients with degenerative retinal diseases: 6 month follow-up results after stem cell implantation**

## Purpose

This study aimed to investigate the safety and efficacy of suprachoroidal mesenchymal stem cell (MSC) implantation in 11 pediatric patients with degenerative retinal diseases.

## Setting/Venue

Prospective clinical study

## Methods

Eleven eyes of 11 patients were operated by Limoli Retinal Restoration Technique and received 5 million suprachoroidal MSC implantation. Patients were evaluated on the first day, first month, third and sixth month postoperatively. BCVA, anterior segment and fundus examination, color photography, optical coherence tomography (OCT), visual field examination were carried out at each visit. Fundus fluorescein angiography (FFA) and multifocal electroretinography (mf ERG) recordings were performed at baseline and at the end of the sixth month.

## Results

Nine of the patients had retinitis pigmentosa and two had Stargardt’s macular disease as a diagnosis. Age of the patients ranged between 5 and 18 years. Preoperative visual acuity ranged between 0.05 and 0.60 Snellen lines. All 11 patients completed the sixth month follow-up period. None of them had any systemic or ocular complications. BCVA improved in 9 eyes and remained unchanged in 2 eyes. The eyes with visual acuity improvement also showed improvement in visual field and mf ERG recordings. We found no ocular pathologies on OCT and FFA of the patients.

## Conclusions

Stem cell treatment with suprachoroidal implantation of MSC seems to be safe and effective in the treatment of degenerative retinal diseases in pediatric patients.

## Financial Disclosure

No financial interest
**Title**

Inflammatory choroidal neovascular membranes: Clinical profile, treatment effectiveness and visual prognosis

**Purpose**

To characterise a sample of patients with Inflammatory Choroidal Neovascularization (I-CNV), including clinical profile, underlying aetiology of I-CNV and its course, treatments performed and associated clinical and structural response, and visual prognosis.

**Setting/Venue**

This is a retrospective study conducted in Centro Hospitalar Universitário de São João, in Porto, Portugal.

**Methods**

Retrospective analysis of patients with a diagnosis of I-CNV followed in the Ophthalmology Department of Centro Hospitalar Universitário de São João (CHUSJ). Clinical characterisation and visual outcome classification according to the difference in best corrected visual acuity (BCVA) after treatment. Eyes with a variation in BCVA higher or equal to 5 letters were considered improved, between -4 and 4 letters were counted as stable, and an outcome equal or lower than -5 letters was classified as worsened.

**Results**

Twenty eyes from 17 patients were analysed (11 female patients and 6 male patients, mean age 41.90 ± 16.457 years at CNV diagnosis). Punctate Inner Choroidopathy/Multifocal Choroiditis was the predominant inflammatory aetiology (10 patients, 58.82%). Intravitreal anti-VEGF agents were used in all patients, with a median number of 7.00 injections (IQR, 4.25 to 29.00) per eye. Median total anti-VEGF injections was superior in eyes belonging to patients with cardiovascular risk factors (35.00 versus 7.00; P=0.035), eyes belonging to dislipidemic patients (36.50 versus 6.50; P=0.010) or eyes that developed cataract (35.00 versus 7.00; P=0.031), when compared with patients without these conditions. BCVA among 20 eyes had a mean gain of 15.10 ± 12.998 ETDRS letters after anti-VEGF treatment. During follow-up, 16 had an improved outcome (80,00%), 3 had a stable outcome (15.00%) and 1 patient had a worsened visual outcome (5.00%). In addition, 13 eyes (65.00%) had a final BCVA equal or superior to 65 letters.

**Conclusions**

A combined approach with anti-VEGF agents and anti-inflammatory therapy was effective in I-CNV treatment and an overall good visual prognosis was attainable. Intensive follow-up was fundamental in the management of both the primary inflammatory and secondary neovascular conditions. The number of anti-VEGF injections needed to manage neovascularization was significantly associated with the presence of dyslipidaemia, the presence of general cardiovascular risk factors or the development of cataract.

**Financial Disclosure**

None
**Title**

Post covid – 19 bilateral anterior uveitis : A report of 2 cases

**Purpose**

We present two cases of bilateral anterior uveitis following covid-19 infection with one of them presenting with raised intracranial pressure and papilloedema as well. There was no previous history of uveitis in either patient and no previous medical history. Extensive investigations in both cases came back negative. Both patients recovered well, with good vision and no other sequelae.

**Setting/Venue**

Ophthalmology Department, Konstantopouleio General Hospital, Nea Ionia, Athens, Attica, Greece

**Methods**

Case 1 : a 16 years old male patient was admitted in the internal medicine department of our hospital with fever (39°C) and rash. One month earlier his mother was tested positive for Covid-19 and although he experienced mild symptoms at that time, no PCR test was done at that time. On presentation PCR test for COVID-19 was negative and U/S of abdomen showed enlargement of liver and spleen and mild lymphocytopenia and thrombopenia. His CRP was 7.2mg/dl. During his admission the rash regressed but he developed photophobia and red eyes. Case 2 : a 29 years old male patient presented to our A&E department with a history of left painful red eye for one day. He was tested COVID-19 positive by PCR a month before.

**Results**

Case 1: On ophthalmic examination his vision was 10/10 in both eyes with conjunctival injection in both eyes and cells +1 in both anterior chambers. Intraocular pressures were normal. On dilated examination optic discs appeared with blurred margins but no evidence of inflammation in the vitreous, retina or choroid. An OCT of discs and macula, a visual field test and an OCT angio were done. His Covid-19 antibodies were positive. After 2 lumbar punctures his intracranial pressure dropped and his condition improved. All investigations including neurological, infectious diseases and autoimmune screening were negative. At the last eye examination, patient was asymptomatic and his vision was 10/10 in both eyes. Case 2: On examination his vision was 9/10 in both eyes. Slit lamp examination showed +- cells in the right eye, +3 cells in the left eye with small non granulomatous KP’s and normal intraocular pressures. Dilated examination was unremarkable. A diagnosis of bilateral anterior uveitis was made and he was put on dexamethasone 0.1% drops and cycloplegia. His mantoux test was positive (15mm) and quantiferon negative. All other tests came back negative. After two months of treatment his right iritis resolved but he was still on drops for the left eye.

**Conclusions**

There have been several reports regarding ocular manifestations during the active stage of Covid-19 infection and few reports post infection. The commonest one is bilateral conjunctivitis but there are also reports regarding episcleritis, unilateral anterior uveitis, retinal changes, oculomotor nerve palsies, isolated intracranial hypertension, optic neuritis and unilateral panuveitis. Unilateral papillophlebitis and vitreous cells have been reported in patients recovering from Covid-19. Our cases have few things in common: Uveitis occurred following Covid-19 infection, no obvious cause was found despite extensive investigations and they both recovered well. Although Covid-19 was not related directly to their signs and symptoms, we could not rule out that this was a post-covid-19 inflammatory reaction either, given the negative results of the investigations and the lack of past medical history in our patients.

**Financial Disclosure**

NO FINANCIAL RELATIONS
**Title**
Bilateral posterior uveitis after IOL scleral fixation: post-surgical inflammation or something else?

**Purpose**
The aim of this case report is to evaluate whether the clinical features developed in this patient clinical case were due to a simple posterior ocular inflammation after surgery or if they were related to a posterior uveitis of uncertain origin. The ultimate aim is to underline the importance of a correct diagnostic pathway in bilateral posterior uveitis and the value of multidisciplinary collaboration.

**Setting/Venue**
Medical Retina Service, Ophthalmology Unit, ASST Sette Laghi - University of Insubria, Varese, Italy

**Methods**
We collected the clinical history of a patient undergoing a bilateral IOL scleral fixation in 2019 and 2020. After the surgery on each eye, he referred a visual acuity decrease, with a diagnosis of macular edema persisting for several months he had stopped follow-ups and treatments due to COVID19 restrictions. On January 2021, coming back for a check, we decided to perform a diagnostic pathway to evaluate the aetiology of ocular inflammation. We performed fluorescein (FA), green indocianine angiography (ICGA) and SD-OCT examination. The exams showed a petaloid macular edema associated to hyperfluorescent spots diffused on the whole retina on FA, and hypofluorescent spots on ICGA which could be related to a suspected tuberculosis or sarcoidosis. A local therapy with indomethacin eye drops twice/day and dexamethasone eye drops five/day was started, and in the meantime a complete serological and radiological examination for uveitis was performed. As the Mantoux and QuantiFERON TB Gold tests resulted positive, with a negative chest CT, in agreement with the infectious specialist, we decided to start a therapy based on a prophylactic treatment with isoniazid 5mg/kg/day for six months and oral prednisone starting with 1mg/kg/day to control retinal inflammation.

**Results**
After the application for 30 days of a topical therapy with indomethacin and dexamethasone, the patient showed an increase in visual acuity in both eyes (RE from 0.5 to 0.7 Snellen, LE from 0.025 to 0.05) and a decrease of central retinal thickness CRT (RE from 566 to 382 micron; LE from 517 to 340 micron). We also appreciated an improvement of inflammatory retinal signs on fluorescein angiography. Considering the persistence of macular edema, we added oral steroids and isoniazid. After 1 month of systemic therapy, we appreciated a complete visual recovery in RE (0.9 Snellen) and a slight improvement in LE (0.1 Snellen). Macular edema was completely resolved in both eyes with a CRT of 317 micron in RE and 267 in LE. Fluorescein angiography performed at the same time showed an almost complete resolution of retinal inflammation in RE, while in LE we appreciated a persistence of inferior-temporal hyperfluorescent retinal spots. The patient is now visited monthly to evaluate the presence of recurrences.

**Conclusions**
Because of the persistence and the severity of macular edema and retinal inflammation, we performed a wide screening with instrumental and serological examinations. Indeed, the evidence of a severe macular edema associated to hyperfluorescent spots in the retinal periphery in both eyes did not confirm the diagnosis of post-surgical macula edema. For this reason, the positivity of serological tests and the presence of retino-choroidal signs on ICGA addressed for a hidden role of TBC in the pathology. It's reported that TBC could cause an immuno-mediated reaction without a direct involvement of the bacteria, presenting angiographic features referable to our patient. However, a systemic isoniazid therapy was added to avoid the development of a clinical TBC, when oral steroids had started to resolve inflammation. Finally, the efficacy of the applied therapy supported our clinical hypothesis of multiple aetiology: surgical intervention and a concomitant immuno-based reaction which caused a posterior uveitis with a severe and persistent macular edema in this patient.

**Financial Disclosure**
None
# Multimodal imaging in Acute Zonal Occult Outer Retinopathy (AZOOR)

**Presenter:** Joana Roque

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## Purpose
Acute Zonal Occult Outer Retinopathy (AZOOR) is a rare retinal disease characterized by one or more areas of outer retinal dysfunction. Typical presentation includes acute visual field loss accompanied by photopsia, and minimally evident fundus changes. We describe the multimodal imaging tests of a case of late-stage AZOOR.

## Setting/Venue
Hospital Prof. Doutor Fernando Fonseca, Amadora, Lisbon, Portugal.

## Methods
Retrospective medical chart review of multimodal imaging investigations, including fundus photography, optical coherence tomography (OCT), fluorescein angiography (FA), indocyanine green angiography (ICG), fundus autofluorescence (FAF), electroretinography (ERG) and automated perimetry.

## Results
A 45-year-old woman with no known diseases reported a subacute vision loss in her left eye (OS). At the time, she was observed at a different hospital, yet obtaining no diagnosis. Two years later, she was examined at our hospital, with stabilized visual complaints (BCVA OD 20/20, OS 20/200). Fundus examination showed discrete peripapillary discoloration in both eyes (OU) and a slightly abnormal macular reflex in OS. OCT revealed a slight attenuation of the ellipsoid zone in OD but a profound thinning of the outer retina in OS. FAF images showed a trizonal pattern of autofluorescence abnormalities suggesting of AZOOR: speckled hyperautofluorescence within the AZOOR lesions, hypoautofluorescence corresponding to the areas of chorioretinal atrophy (both peripapillary regions and macular area in OD), along with normal FAF in the areas outside the delineating line. ICG was unremarkable but FA showed hyperfluorescence areas compatible with this pattern of chorioretinal atrophy OU. Multifocal ERG presented slightly reduced amplitudes in OD and a markedly reduced outer retinal function in OS. Automated perimetry in OD showed a blind spot enlargement whereas a cecocentral scotoma with generalized loss of retinal sensitivity was found in OS.

## Conclusions
This patient’s abnormal electroretinograms and visual field loss correlated with the areas of retinal structural changes in both eyes. A multimodal imaging approach is crucial to demonstrate the photoreceptor dysfunction responsible for vision loss in AZOOR. This disease should be considered as a differential diagnosis in patients with complaints of photopsia or decreased vision accompanied by normal fundus examination.

## Financial Disclosure
No financial interests
### Title
Retinal vasculitis is the most frequent finding in uveitis associated with multiple sclerosis

### Purpose
To describe the clinical findings and outcomes in patients who presented with uveitis associated with multiple sclerosis (MS)

### Setting/Venue
King Abdulaziz University Hospital, College of Medicine, King Saud University Medical City, Riyadh, Saudi Arabia

### Methods
Retrospective review of 20 patients (38 eyes)

### Results
The most frequent ocular finding was multifocal elongated retinal perivenous "sheathing" with focal vascular leakage on fundus fluorescein angiography (FFA) in 29 eyes followed by vitreous snowballs and debris in 26 eyes, anterior chamber inflammation in 15 eyes, mutton-fat keratic precipitates in 14 eyes, posterior synechiae in 13 eyes, cystoid macular edema (CME) in 9 eyes, iris nodules in 4 eyes, optic neuritis in 3 eyes. Patients with CME were treated successfully with systemic corticosteroids combined with mycophenolate mofetil. Ocular complications were cataract in 6 eyes, glaucoma in 2 eyes and vitreous hemorrhage in one eye.

### Conclusions
Multifocal elongated retinal perivenous "sheathing" with focal vascular leakage on FFA is the most frequent finding in uveitis associated with MS.

### Financial Disclosure
Non to declare.
Late Onset Blau Syndrome Masquerading as Sympathetic Ophthalmia

Purpose
To report a case of late onset Blau Syndrome that presented as sympathetic ophthalmia.

Setting/Venue
Tertiary care ophthalmology center in Middle East

Methods
A retrospective chart review of a 10 years old boy who presented with a rhegmatogenous retinal detachment following congenital cataract surgery and later developed persistent panuveitis.

Results
The patient presented 3 weeks after retinal repair with bilateral granulomatous panuveitis. The impression was sympathetic ophthalmia and he was treated with systemic steroids and oral methotrexate. On subsequent follow-up, he developed an aggressive recurrence of multifocal choroiditis associated with skin lesions and joint pain. Genetic testing revealed a heterozygous intronic c.2798+158C>T mutation in NOD2/CARD15 gene. After the addition of systemic adalimumab, a better control of panuveitis was achieved.

Conclusions
The c.2798+158C>T mutation in NOD2/CARD15 is associated with a late-onset Blau syndrome which has masqueraded sympathetic ophthalmia in our patient. Differentiation between the two entities has important prognostic and management considerations.

Financial Disclosure
none
Purpose: Intravitreal injections are commonly used intraocular medication in the management of retinal diseases. The application has been described as causing sterile endophthalmitis and with the presence of impurities through the plastic syringe use and silicone bubbles. The presence of silicone oil drops associated with intravitreal injections has been reported in up to 1.73% of patients, causing floaters. Sterile endophthalmitis is an infrequent complication of intravitreal injections.

Methods: We present two patients. One patient presented with floaters days after the intravitreal injection. The exploration showed silicone bubbles with a big central one. The symptomatology improved over time. The other patient complained of loss of vision in the left eye days after receiving the intravitreal injection. The exploration showed conjunctival hyperemia, cellularity, a granulomatous reaction in the anterior segment with keratic precipitates, silicone bubbles, and vitreous inflammation. Medical treatment with topical steroids and cycloplegics did not improve symptomatology or exploration.

Results: One patient improved the symptomatology and is under observation. The other patient did not improve with medical treatment and required a vitrectomy with vitreous sample analysis. The vitreous sample did not show any microorganisms, only the presence of silicone bubbles and histiocytes with silicone in their cytoplasm. The patient improved the symptomatology and exploration. The visual acuity improved to the previous situation. The patient is under treatment with intravitreal injections.

Conclusions: Small droplets have been reported after intravitreal injections of different medications attributed to silicone oil bubbles. It has been related to the presence of polydimethylsiloxane, a lubricant in the syringe barrel that reduces the friction of the plunger within the barrel going to the vitreous cavity. The cause of the droplets remains unclear, and the manufacturing companies of both the syringes and the drugs used in the injections should investigate this phenomenon. Oil droplets are not always symptomatic, and when symptoms arise, they have been transient in the patients we have been able to monitor over time. Patients report floaters with spots of light usually (68%), which can improve with time, only 12% of patients continuing to report the floaters. The oil droplets may migrate out of the visual axis, or the patients adjusted to their presence over time.

Financial Disclosure: no
**Title**
0.19 mg Fluocinolone acetonide intravitreal implant (ILUVIEN®) effectiveness and safety outcomes on the treatment and prevention of relapse in recurrent idiopathic posterior uveitis: a bilateral case report.

**Purpose**
Evaluation of the 16-month outcomes from two eyes from the same patient treated with 0.19 mg fluocinolone acetonide intravitreal implant (ILUVIEN®) for the treatment and prevention of relapse in recurrent bilateral idiopathic posterior uveitis with macular edema.

**Setting/Venue**
Bilateral case report from Hospital da Luz Setúbal, Portugal.

**Methods**
Review of a bilateral idiopathic posterior uveitis case treated with 0.19 mg fluocinolone acetonide intravitreal implant. Outcome measures included: best corrected visual acuity (BCVA; decimal scale), central retinal thickness (CRT; µm), intraocular pressure (IOP; mmHg) and vitritis presence or absence.

**Results**
57-year-old woman diagnosed in 2006 with a bilateral idiopathic posterior uveitis with macular edema. The patient was treated with repeated triamcinolone intravitreal injections (2006-2016), oral prednisolone 5-60 mg/day (2006-2019) and topical prednisolone 10 mg/ml (2018-2019). In 2014 the patient underwent bilateral cataract extraction. In October 2019, since the oral steroid therapy was not sustainable for this patient due to side effects and menopause, both oral and topical prednisolone were tapered and after 2 months, ILUVIEN® was injected in both eyes. Immediately before ILUVIEN administration the baseline values were recorded: BCVA of 0.3 OD/OS, CRT of 487/550µm OD/OS, IOP of 14 mmHg and vitritis in both eyes (VH 3+) - without any IOP-lowering medication-. Three days and 3 weeks post-ILUVIEN® injection, the anatomical and functional outcomes revealed significant improvement (3 days: 324 µm OD and 422 µm OS; 3 weeks: 0.5 BCVA in both eyes, 242 µm OD and 292 µm OD). 16 months post-ILUVIEN® the patient showed greater BCVA improvement (0.8 OD and 0.6+2 OS) and remained without macular edema (CRT 229 µm OD and 255 µm OD) and vitritis (VH 0). During the all follow-up period the IOP remain below 15 mmHg, without the need of IOP-lowering medication or surgery.

**Conclusions**
This bilateral case report reinforces the advantage of ILUVIEN® in the treatment and prevention of relapse in recurrent idiopathic posterior uveitis with macular edema. Since the 0.19 mg fluocinolone acetonide intravitreal implant is a long-acting implant that delivers 0.2µg/day of the active substance allowing the control of the inflammatory signals (i.e. in this case report, vitritis and macular edema) without systemic adverse events. Locally, ILUVIEN® was well tolerated without the need of IOP-lowering medication or IOP-lowering surgery. Considering that ILUVIEN® requires fewer injections than other alternative treatments, it gives added benefits to the patient with reduced risk of reinjection-associated adverse events, lower treatment burden, improved treatment adherence, and improved disease control.

**Financial Disclosure**
None
Purpose
To report a case showing a very rare association of bilateral retinal vasculitis (RV) and systemic sclerosis sine scleroderma (ssSSc).

Setting/Venue
Department of Ophthalmology of the San Cecilio University Hospital of Granada, Spain.

Methods
Observational case report. The description of a 40-year-old woman with a bilateral retinal vasculitis in association with systemic sclerosis sine scleroderma. We portray the findings of the visual acuity, fundus examination, OCT and angiography. We also used the PubMed database to find other prospective or retrospective studies.

Results
A 40-year-old woman presented at our Hospital for blurry vision with her left eye (OS). Her best-corrected visual acuity was 20/20 in both eyes. Funduscopy examination showed bilateral occlusive vasculitis with proliferative retinopathy and vitreous hemorrhages. Retinography showed temporary sheathed and some occluded veins, surrounded by large number of retinal hemorrhages in both eyes. In fluorescein angiography were found areas of not perfused retina, also with telangiectasia and staining of retinal vessel's walls. We found isolated microaneurysms in these ischemic areas. The ophthalmological treatment was confluent photocoagulation of the ischemic retina of both eyes, and vitrectomy of the right eye to treat his vitreous hemorrhage. The systemic treatment was corticosteroids and Adalimumab during two years; afterwards the stability was achieved. There was a lack of response to cyclosporine and azathioprine. The diagnosis comes after presenting: anticentromere antibodies, scleroderma pattern on capillaroscopy and esophageal manometry showing esophageal dysmotility with absent contractility.

Conclusions
- RV can precede the development of ssSSc by several years. - Systemic sclerosis sine scleroderma can occur with retinal vasculitis, and that may be underdiagnosed. - Positivity for anticentromere antibodies can alert us to look for possible systematic and organic involvement of the disease.

Financial Disclosure
NO FINANCIAL DISCLOSURE
The role of small-gauge vitrectomy in uveitis: surgical indications and results

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Esther Ciancas

Purpose
To describe epidemiological characteristics of patients with uveitis requiring small-gauge vitreoretinal surgery, the reasons for vitreoretinal surgery, and the outcome of these patients.

Setting/Venue
Single, tertiary-care, university-affiliated hospital in Madrid, Spain.

Methods
A retrospective, non-comparative cohort study was performed. All patients undergoing small-gauge vitrectomy between October 2018 and October 2020, including those in which vitrectomy was combined with other procedures like phacoemulsification, with a previous diagnosis of infectious or noninfectious uveitis were included. Only one eye per patient was included in the study. In those patients who had vitrectomy in both eyes during the study period, only the first eye was included in the analysis. Epidemiological, clinical and surgical data were retrieved from the electronic clinical records by 2 of the authors.

Results
Thirteen patients with uveitis required vitrectomy during the 2 year period. This represents 2% of the patients with uveitis who attended our uveitis clinic within that period. Median age was 55 years (range 22 to 86). Six were women (46.1%). Nine patients had a diagnosis of infectious uveitis (4 acute retinal necrosis secondary to VZV, 2 endogenous ocular candidiasis, 2 CMV-related uveitis and 1 ocular toxoplasmosis). Four cases were non-infectious uveitis (2 multiple sclerosis-related intermediate uveitis, 1 intermediate uveitis in B27+ psoriatic arthropathy and 1 idiopathic anterior uveitis). Reasons for vitrectomy were floaterectomy for vitreous debris in 7 patients (53.8%), regmatogenous retinal detachment secondary to acute retinal necrosis in 2 (15.4%), endophotocoagulation in acute retinal necrosis in 2 (15.4%), malignant glaucoma in 1 (7.7%), ERM peel in 1 (7.7%). Combined phacoemulsification and vitrectomy surgery was performed in 5 cases (38.5%). Median best corrected visual acuity (BCVA) changed from 1.0 LogMAR preop (range 0.3 to 2.7) to 0.5 LogMAR at discharge (range 0.0 to 2.7; Wilcoxon p=0.018). BCVA improved after surgery in 7 cases (53.8%), and remained stable in 6 (46.2%). Uveitis recurred in 4 patients. Median time to recurrence was 442 days (range 314 to 867 days).

Conclusions
One in fifty patients with uveitis may require vitreoretinal surgery. Infectious uveitis, specially viral retinitis and ocular candidiasis are more likely to require vitreoretinal surgery. BCVA improved in after surgery in approximately half of the cases. Vitrectomy did not appear to increase the risk of flare-up during the early postoperative period.

Financial Disclosure
The authors declare no potential conflicts of interests relevant to this abstract.
**Title**
Clinical case report of unusual presentation of probable Vogt-Kayanagi-Harada syndrome in multiple sclerosis

**Purpose**
To describe an unusual association of Probable Vogt-Kayanagi-Harada syndrome in a patient of Multiple Sclerosis. VKH spectrum is a multisystemic disorder autoimmune in nature, targeting melanocytes by a Th1 lymphocyte mediated action. It involves all pigmented structures like eye, inner ear, skin, meninges and hair. Bilaterality and absence of any history of trauma or intraocular surgery are diagnostic. Multiple Sclerosis is a chronic, inflammatory disorder involving the CNS, also autoimmune in pathogenesis, targeting myelin in axonal nerve sheaths. Association of uveitis with MS is commonly seen, with intermediate uveitis being the most common, followed by anterior uveitis, retinal vasculitis and panuveitis.

**Setting/Venue**
Clinical case report at a tertiary eye care centre in South India. A 38 year old female with demyelinating disease was referred to us for an uveitis opinion from a higher neuromedicine centre. She complained of progressive blurring of vision in both eyes since three months, with pain, redness, photophobia in both eyes since ten days. Since three years, she had numbness and tingling along with recurrent headaches with past history of panuveitis one year back. Neuroimaging showed bilateral frontoparietal white matter changes s/o demyelination. VEP and CSF studies were normal. She had been administered three loading doses of IVMP.

**Methods**
CBC, CRP, urinanalysis, ACE, serum Creatinine and CXR were normal. Erythrocyte sedimentation rate was raised (42 mm/hr). Anti- HIV 1 and 2, TPHA, Mantoux test were negative. Serum prolactin, thyroid profile were normal. Repeat MRI scan showed multiple T2/FLAIR hyperintense lesions in white matter and SC lesions.VPT showed bilateral generalized depression with centrocaecal scotoma.Repeat VEP showed prolonged P100 latency(Right Eye:115.70 ms,Left Eye:140.40ms). Serum ANA, ANCA, RA, NMO-MOG antibodies were negative. Repeat CSF analysis showed Oligoclonal bands.CSF ACE,NMO-MOG antibodies were absent. The diagnosis was established as MS as per revised McDonald Criteria. At presentation,BCVA was 6/18 OD and CFat1metre OS, shallow irregular AC, posterior synechiae, granulomatous KPs, cells and flare, hyperemic and edematous discs in both eyes. IOP was 12mm and 26mm of Hg in OD and OS.UBM showed malrotation of the inflamed and boggy ciliary body, with shallow AC on AS-OCT. USG B- scan showed choroidal thickening with disc edema.OCT showed vitreous cells, disc edema, multiple areas of shallow exudative retinal detachment over the posterior pole, choroidal folds, RPE undulations, Intraretinal fluid and hyperreflective dots in both eyes. The complete picture was suggestive of a Probable VKH presentation. FFA was not an option owing to the non-dilating pupil and...

**Results**
She was administered 4 loading doses of IV Methyl Prednisolone 1gm following which the vision in left eye dramatically improved to 6/24 along with resolution of inflammation with decrease in pain, photophobia and congestion in both eyes.Topical antiglaucoma medications (Brinzotim) was started. Repeat UBM scans showed resolution of malrotation of the ciliary body, along with opening up of the angles and reduction in IOP. Affordability being a factor, she was started on azathioprine 50 mg twice daily after discussion with the treating neurologist. Systemic corticosteroids were also started (40 mg per day). Over 3 weeks of immunosuppression coupled with oral steroids, the exudative detachments had resolved and choroidal folds had largely reduced in both eyes. The patient is doing very well with a visual acuity of 6/9 and 6/9P in right and left eye respectively at one month review. We plan to keep her on prolonged immunosuppression with very slow tapering of oral steroids.

**Conclusions**
This presentation of a probable VKH with MS is quite atypical and has only been documented twice in literature. MS commonly presents as intermediate uveitis, anterior uveitis or retinal vasculitis. In 2007, Montero et al. documented a similar case in a 34year female with MS who resented with complete VKH and was treated effectively with Interferon b1A and systemic corticosteroids. Alberto et al. in 2020 published about a 35year female who presented with VKH and was later diagnosed as MS. she was treated with IVMP, Azathioprine with meticulous tapering. Options of treatment include biologicals, rituximab or azathioprine. the cost being as important factor in our case, azathioprine was chosen. HLA typing can also be considered in such cases. Careful choice of immunosuppressants and long term follow up are of important value in such cases.
Cytomegalovirus retinitis treated with intravitreous injection of ganciclovir.

Purpose
To report a case of cytomegalovirus retinitis treated with intravitreous injection of ganciclovir in a patient followed for hodgkin's disease treated with chemotherapy.

Setting/Venue
Department of Ophthalmology, Habib Bourguiba University Hospital, Faculty of Medicine, University of Sfax, Tunisia.

Methods
Case report

Results
A 49-year-old man presented with complains of progressive visual loss in both eyes. Her personal medical history included hodgkin's disease treated with chemotherapy. Visual acuity was 6/10 in both eyes. Anterior segment was normal in both eyes. A fundus examination showed whitish inter papillo-macular bulge with hemorrhages in both eyes. Fluorescein angiography revealed hypofluorescence in early phase with late hyperfluorescence in area of active disease and vasculitis. Optical coherence tomography demonstrated retinal edema with serous retinal detachment in the right eye, nasal retinal thickening in the left eye. Serology for cytomegalovirus was positive. Diagnosis of cytomegalovirus retinitis was made. The patient was treated with an induction regimen of intravenous foscarnet for 14 days. At the end of induction, patient had stabilized and continued foscarnet in a maintenance regimen. Retinitis progressed after 4 weeks of maintenance therapy. Visual acuity was limited to counting fingers in both eyes. The patient received 4 intravitreal injections of ganciclovir once weekly in each eye. An improvement was noted after two months of treatment. Ocular examination showed visual acuity at 3/10 in both eyes and the retinitis completely resolved, leaving area of chorioretinal atrophy. One year following treatment the patient's vision remained stable without any recurrence.

Conclusions
CMV retinitis is a potentially blinding disease that occurs immunocompromised patients, including those with acquired immune deficiency syndrome and those on systemic immunosuppression or chemotherapy. Clinically, there are several recognized ophthalmoscopic patterns of CMV retinitis: wedge-shaped areas of whitening with associated hemorrhage, variable small dot-like lesions, or rarely, retinal vasculitis with perivascular sheathing. CMV retinitis typically begins in the peripheral retina and progresses centrifugally toward the posterior pole. CMV retinitis is a clinical diagnosis, based on the classic appearance of lesions in susceptible individuals. In cases where the diagnosis is unclear, CMV polymerase chain reaction may be performed on aqueous samples. Multimodal imaging may have utility for screening and monitoring CMV retinitis. Currently available therapies for CMV retinitis include intravenous and intravitreal ganciclovir and foscarnet, intravenous cidofovir, and oral valgancyclovir. Intravitreal ganciclovir injection delivers a high concentration of drug to the eye with minimal systemic toxicity. There are no randomized controlled trials on the rate of intravitreal ganciclovir injection for CMV retinitis. Our patient received 4 intravitreal injections of ganciclovir once weekly in each eye without maintenance treatment with good improvement. Further studies are required to optimize the dose and rate of injection for best

Financial Disclosure
Final disclosure: no
**Title**
Initial-Onset Acute Uveitis Associated with Vogt-Koyanagi-Harada Disease Presenting with Unilateral Exudative Retinal Detachment Despite Bilateral Choroidal involvement

**Presenter**
Abdulrahman AlBloushi
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**Co-Author 1**
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**Purpose**
To investigate the frequency of initial-onset acute uveitis associated with Vogt-Koyanagi-Harada (VKH) disease presenting with unilateral exudative retinal detachment.

**Setting/Venue**
A retrospective case series.

**Methods**
All patients with initial-onset acute uveitis associated with VKH disease seen at the Uveitis Clinic of King Abdulaziz University Hospital, Riyadh, Saudi Arabia, between January 1998 and November 2020 were retrospectively reviewed. A specific notation was made to the patients with VKH disease presenting with apparent unilateral involvement due to exudative retinal detachment in only one eye.

**Results**
During the period between January 1998 and December 2020, we identified 135 patients with initial-onset acute uveitis associated with VKH disease. Among them, 5 (3.7%) patients were referred to have unilateral uveitis due to the presence of exudative retinal detachment in only one eye. Optical coherence tomography confirmed the presence of unilateral exudative retinal detachment, however, indocyanine green angiography (ICGA) revealed characteristic findings of bilateral granulomatous choroidal inflammation typical for initial-onset acute uveitis associated with VKH disease.

**Conclusions**
Patients with initial-onset acute uveitis associated with VKH disease can present with unilateral exudative retinal detachment. ICGA assessment of the choroid revealed the presence of subclinical involvement of the fellow eyes.
A case of endophthalmitis associated with gonococcal sepsis

**Purpose**
To present a rare case of endophthalmitis secondary to gonococcal sepsis, and to highlight its clinical features.

**Setting/Venue**
Patient's history was significant for acute suppurative gonococcal prostatitis (with acute retention of urine, and severe sepsis with liver abscess, and suppurative tonsillitis), for which he had been treated as an in-patient at the Department of Urology of the city hospital. In addition, he had suppurative blepharitis of the left eye. A week after he was discharged from the Department of Urology, he was hospitalized to the Department of Ocular Trauma of the Filatov institute with the diagnosis of endophthalmitis in the left eye.

**Methods**
Visual acuity assessment, comprehensive eye examination, and microbiological examination. The left eye looked inflamed with mixed conjunctival injection. Other objective examination findings in the left eye included a clear cornea; moderately shallow and clear anterior chamber; abnormal iris color; circular posterior synechia; rigid pupil; lens haze; anterior lens capsule vascularity; and dim reflex. The right eye was quiescent. Other objective examination findings in the right eye included a clear and bright cornea; moderately shallow and clear anterior chamber; clear lens; pink reflex; pale pink optic disc with clear margins; and attached retina. Patient's visual acuity was 0 OS and 1.0 OD. In addition, intraocular pressure (IOP) measured by pneumotometry was 14.0 mmHg (with dorzotymol plus Brimonal 0.2% twice daily) OS, and IOP measured by palpation was normal OD. Ocular ultrasound findings included severe preretinal vitreous fibrosis, chorioretinal edema (suspected ciliary body and choroidal detachment), optic disc cupping and attached retina in the left eye. The patient received conservative treatment, including Azithromycin, 500 mg daily; Levofloxacin, 500 mg daily; Melbek, 15 mg i/m; Dexamglin, 25 mg i/m; Dorzotymol ophthalmic solution; Brimonal ophthalmic solution 0.2%; Vigamox ophthalmic solution 0.5%; Oftaquix ophthalmic solution 0.5%; Uniclophen ophthalmic solution 0.1%; and

**Results**
The patient poorly responded to treatment, and clinical manifestations of endophthalmitis were becoming more and more severe. He underwent evisceration of the left eye. The patient's postoperative period was unremarkable. A week after surgery, in the left eye, the conjunctival cavity was clear, and conjunctival sutures were clear, there was no edema, and the stump was movable in all directions. An ocular prosthesis was fitted in the orbit (Fig. 2). There was no bacterial growth in conjunctival samples.

**Conclusions**
We presented a rare case of disseminated gonococcal infection complicated by severe sepsis with liver abscess, suppurative tonsillitis, and suppurative blepharitis of the left eye leading to endophthalmitis, with subsequent evisceration. Gonococcal ocular lesions are associated with late presentation to the ophthalmologist, fast endophthalmitis development, and asymmetric involvement, but no corneal involvement. Consultations of allied health professionals and multiprofessional management of gonorrhea patients are required to prevent complications in various organs and systems should gonococcal sepsis develop.

**Financial Disclosure**
Presenting author and co-authors have not a financial interest in the subject matter and don't receive money from any mentioned company.
Subclinical Alterations in Retinal Layers and Microvascular Structures with OCTA in ANCA-Associated Vasculitides

**Purpose**
To evaluate the retinal layers and capillary network with OCTA in granulomatosis with ANCA associated vascul (AAV) patients who did not manifest apparent ocular involvement and to compare with healthy population.

**Setting/Venue**
Prospective/Izmir Katip Celebi University Ataturk Training and Research Hospital Eye and Ophthalmology Department

**Methods**
In this prospective, observational, and comparative study, total 22 AAV patients and 35 healthy control participants were included. Central foveal thickness (CFT), mean macular thickness (MMT), retinal nerve fibre layer (RNFL) and the Ganglion cell inner plexiform layer (GC-IPL), vessel density (VD), perfusion density (PD), and foveal avascular zone (FAZ) parameters were noted. Patients’ Birmingham vasculitis activity score (BVAS), five factor score (2009) (FFS), and vasculitis damage index (VDI) scores were recorded.

**Results**
Mean macular thickness and RNFL and GC-IPL thicknesses in most regions were significantly lower in the AAV group than in the control group. Positive correlations were observed between mean macular thickness and superotemporal, inferotemporal, and average GC-IPL. While the vascular indices were lower in the AAV group, except for the center 1 mm region, the FAZ parameters were similar between the two groups. There were significant correlations between CFT, MMT, and GC-IPL thicknesses and vascular indices. No significant correlation was observed between ANCA positivity and retinal vascular indices. There was an inverse correlation between BVAS and RNFL quadrants. There were also correlations between BVAS and FFS and vascular indices.

**Conclusions**
In AAV patients, subclinical changes in the retinal layers and superficial vascular plexus have been shown, and these changes have been associated with disease activity scores.

**Financial Disclosure**
NO, WE DON’T HAVE ANY FINANCIAL RELATIONS.
### Title
The risk of psoriasis in patients with uveitis: a nationwide population-based cohort study

### Purpose
To evaluate whether the risk of subsequent psoriasis and psoriatic arthritis development is increased in patients with uveitis.

### Setting/Venue
Population-based, retrospective cohort study.

### Methods
In Taiwan's national health insurance research database, we identified 195,125 patients with new-onset uveitis between 2001 and 2013. We randomly selected 390,250 individuals without uveitis who were matched 2:1 to uveitis cases based on age, sex and year of enrolment. The characteristics of the two groups were compared. Using multivariate Cox regression, hazard ratios (HRs) for psoriasis or psoriatic arthritis corresponding to uveitis were computed after adjustment for age, sex, insurance cost and comorbidities. In subgroup analyses, separate HRs for mild psoriasis, severe psoriasis and psoriatic arthritis were calculated.

### Results
The mean age of the study cohort was 50.2 ± 17.2 years. Hypertension, diabetes, hyperlipidaemia and obesity were more prevalent in the uveitis group (all p < 0.0001). The hazard of psoriasis or psoriatic arthritis development was significantly greater in the uveitis group than in the non-uveitis group (p < 0.0001); this increased risk persisted after adjustment for confounders (adjusted HR = 1.41; 95% confidence interval (CI), 1.33–1.48). Adjusted HRs showed an increasing trend from mild psoriasis (1.35; 95% CI, 1.28–1.44) to severe psoriasis (1.59; 95% CI, 1.30–1.94) and psoriatic arthritis (1.97; 95% CI, 1.60–2.42).

### Conclusions
This nationwide population-based cohort study revealed that patients with uveitis have an increased risk of subsequent psoriasis or psoriatic arthritis development.

### Financial Disclosure
Nil
**Title**
Macular microvascular changes in uveitic patients; OCTA quantitative observational study

**Presenter**
Mohamed Ahmed Egypt

**Co-Author 1**
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**Co-Author 2**
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**Co-Author 3**
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**Co-Author 4**
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**Co-Author 5**
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**Co-Author 6**
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**Purpose**
To quantitatively assess micro-vascular changes in retinal plexuses and choriocapillaries in patients with uveitis using optical coherence tomography angiography (OCTA).

**Setting/Venue**
Department of Ophthalmology, Minia University, Minia, Egypt

**Methods**
Patients with confirmed diagnosis of heterogenous subtypes of uveitis and age-matched healthy controls were imaged by a commercial 70-kHz spectral domain OCT system (RTVue-XR, Optovue). Macular 3x3 & 6x6 mm2 scans with accepted quality were exported for customized processing that included projection artifact removal, semi-auto segmentation of retinal layers, bulk motion subtraction and shadow artifact. Vessel densities were computed on superficial vascular complex (SVC), intermediate capillary plexus (ICP), deep capillary plexus (DCP), and choriocapillaries compared between both groups using Mann–Whitney U test.

**Results**
Thirty-seven eyes from 37 uveitic patients and 30 eyes from 30 age and gender-matched controls (43.90 ± 11.10, 52.28 ± 12.76 years) were studied. Parafoveal and perifoveal vessel density values were significantly lower in patients compared to controls (P = 0.03 & 0.01) respectively. The peripapillary inner retinal vessel density was significantly lower in patients (80.21 ± 3.59) compared to controls (84.45 ± 4.33), (P = 0.009); also, vessel and capillary densities were significantly reduced in patients compared to controls in all segmented retinal slabs; choriocapillaries capillary density reduction was not statistically significant.

**Conclusions**
OCTA proved to be a promising non-invasive diagnostic tool for disease status confirmation and monitoring in uveitic patients. Patients with uveitis have reduced macular and choriocapillaris vessel density compared to normal controls.

**Financial Disclosure**
NA
Long-term Outcomes of Uveitis Associated with Vogt-Koyanagi-Harada Disease in the Pediatric Age Group

Purpose
To investigate the outcomes of uveitis associated with Vogt-Koyanagi-Harada (VKH) disease in pediatric age group (aged 16 years and under).

Setting/Venue
A retrospective review of patients with VKH disease.

Methods
All patients with uveitis associated with VKH disease who were seen at the Uveitis Clinic of King Abdulaziz University Hospital, Riyadh, Saudi Arabia, between January 1998 and December 2020 were retrospectively reviewed. Children with a history of ocular trauma or intra-ocular surgeries were excluded.

Results
Among the 244 patients identified, 38 (76 eyes) were children. Among them, 5 had insulin-dependent diabetes mellitus. At presentation, 21 presented with initial-onset acute disease and 17 with chronic recurrent disease. The mean follow-up period was 59.1 months. At presentation, chronic recurrent disease was associated with more severe inflammation as indicated by presence of mutton-fat keratic precipitates (p<0.001), iris nodules (p=0.005) and posterior synechiae (p < 0.001). During follow-up, rate of complications was more in children with chronic recurrent disease compared with initial-onset acute disease (p<0.001). 92.4% of the eyes with initial-onset acute disease achieved final visual acuity of ≥20/40 compared with 70.6% of the eyes with chronic recurrent disease (p=0.013).

Conclusions
Chronic recurrent VKH disease in children is associated with worse outcomes.

Financial Disclosure
I have no financial interest to disclose.
### Purpose
Ocular Tuberculosis is a presumptive and clinical diagnosis when in presence of suggestive clinical and laboratorial findings, while excluding other causes of ocular inflammation. It can be caused by direct invasion by the tuberculosis bacilli or as a result of immunogenic reaction due to the extraocular infective foci. Its incidence is highly variable, ranging from 1.4% to 18% in endemic areas, having a relatively low incidence rate in Portugal (19.2 cases/100000 inhabitants). It is still a challenging diagnosis, presenting mainly as posterior uveitis and having no pathognomonic findings. This paper aims to analyse a clinical case where retinal vasculitis coexists with macular edema in a patient with possible ocular tuberculosis.

### Setting/Venue
The authors present a case of a 70 year old patient that came to our general ophthalmology appointment for progressive decreased visual acuity of the right eye for the past month. He presented a best corrected visual acuity of 1.30 logMAR, normal anterior segment and several exudates throughout the posterior pole and peripheral retina, with vascular sheathing and no evidence of vitritis.

### Methods
A retinography, an optical coherence tomography (OCT) and fluorescein angiography (FA) were promptly requested, as well as a full laboratory evaluation, chest x-ray and Interferon Gamma Release Assay (IGRA) test.

### Results
OCT revealed, in the right eye an extensive macular cystic edema with several hyperreflective spots surrounding it and a central macular thickness of 449 micras. FA showed marked leakage temporal to fovea, confirming also the vascular sheathing and showing a peripheral temporal and inferior area of chorioretinal scarring. Chest-X ray revealed normal, as well as the extensive laboratory work-up, but the IGRA test came back positive. The patient latter confirmed having a positive exposure to a tuberculosis (TB) infected friend when he was 18 years of age. Ocular TB was assumed and anti-TB therapy was promptly iniciated. He also initiated a three intra-vitreal injections regimen with aflibercept. Four months after initial diagnosis, continuing his course of anti-TB treatment, intraretinal liquid was fully reabsorbed with maintenance of hard exsudates around the fovea, a central macular thickness of 335 micras and visual acuity of 1.0 logMAR.

### Conclusions
This case represents a difficult setting of retinal vasculitis where an IGRA test and negative laboratory findings for other infectious diseases shove us in the direction of an Ocular TB. Treatment was initiated as soon as possible with anti-vascular endothelial growth factor (anti-VEGF) therapy and a multidisciplinary approach was taken to also treat the patient with anti-bacillary combined therapy. The treatment showed complete reabsorption of subretinal fluid with maintenance of the hard exsudates near the foveal region.

### Financial Disclosure
The authors have no financial disclosures.
Panuveitis Vogt-Koyanagi-Harada and intracranial meningioma: Is there a genetic correlation?

Both the Vogt-Koyanagi-Harada (VKH) syndrome and the intracranial meningioma are two possibly disastrous diseases, each with potential risk of irreversible visual loss, not to mention when combined. The purpose of this paper is to present a case with ocular Harada disease and meningioma and point out the possible genetic correlation of the two diseases, since HLA-DR4 gene association has been found in both entities.

A case report of a Caucasian 58-year-old woman, free of systemic symptoms, who presented in the eye emergency department complaining of bilateral progressing visual deterioration for the last 15 days. The patient was urgently admitted for further investigation to the State Ophthalmology Clinic, Gennimatas General Hospital, Athens, Greece.

The clinical ophthalmological examination (anterior segment examination, fundoscopy, fluorescein angiography, fundus photography, macular Optical Coherence Tomography, B-scan Ultrasound) revealed a bilateral anterior and posterior inflammation including exudative retinal detachments. The diagnosis of VKH chorioretinopathy was set; thus the patient was started on a treatment with topical steroids and cycloplegia as well as on a 3-day course of intravenous methylprednisolone immediately. Further systemic investigation with brain Magnetic Resonance Imaging (MRI) detected an 8-millimetre frontal lobe meningioma. Moreover, histocompatibility antigens testing, identified positive HLA DRw53, but also the HLA-DR4, which could suggest a strong causative association with VKH and meningioma.

The panuveitis of the patient rapidly improved and reached complete remission of the inflammation. Subsequently, she continued with a tapering dose of oral prednisolone and topical therapy for 3 months. Following review of the patient by the neurosurgical team, mycophenolat mophetil was safely added to the treatment regime.

According to our knowledge, this is the third case report in which the VKH is associated with a meningioma, and the only one which the patient complained of no neurological symptoms at the time of presentation and setting of the diagnosis. We should be more careful with the way we approach and treat these patients, especially when using immunosuppressive agents, which can aggravate the progression of the tumor. Further studies of histocompatibility antigens in meningioma cases are warranted, in order to establish a solid correlation between those two entities. Perhaps a neurosurgical assessment and brain MRI could be added to the routine emergency work up of VKH.
<table>
<thead>
<tr>
<th>Title</th>
<th>Ocular side effects secondary to COVID-19 vaccination</th>
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<tr>
<td>Purpose</td>
<td>To present a case series of ocular side effects secondary to COVID-19 inactive vaccine (Sinopharm’s China National Biotec Group)</td>
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<tr>
<td>Setting/Venue</td>
<td>Retrospective consecutive case series of patients presenting at the Retina and Uveitis Service of Cleveland Clinic Abu Dhabi from September 2020 to January 2021.</td>
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<tr>
<td>Methods</td>
<td>Main inclusion criteria were the report of ocular side effects that presented within 15 days from the first dose of Sinopharm COVID-19 vaccine. Each patient underwent Snellen best corrected visual acuity (BCVA) that was then converted to logarithm of the minimal angle of resolution (LogMAR) values, applanation tonometry, biomicroscopic examination with indirect ophthalmoscopy. Color fundus photography was obtained with a conventional 9-field fundus photography (Carl Zeiss Meditec, Dublin, CA) camera or with a wide-field fundus photography system (Optos Panoramic 200MA; Optos PLC, Dunfermline, Scotland, United Kingdom). Optical coherence tomography was obtained with a spectral domain machine (Spectralis HRA OCT; Heidelberg Engineering, Heidelberg, Germany) and swept source PLEX Elite 9000 (Carl Zeiss Meditec, Inc, Dublin, CA) was used for OCTA images.</td>
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<td>Results</td>
<td>Ten eyes of 8 patients (3 males) presenting with ocular complaints following COVID-19 vaccine were included in the study. Mean age was 41.4 +/- 9.3 years (range: 30-55); mean BCVA was 0.23 logMAR (range: 0-1). The mean time of ocular side effects manifestations was 5.2 days (range: 1-10). Three patients were diagnosed with episcleritis (Case #1) or anterior scleritis (Case #2 and Case #5) that responded to a tapering dose of topical steroid. Two eyes in our series (Case #3 and Case #4) presented with acute vision loss associated with SD-OCT hyperreflectivity of the outer plexiform/nuclear layer and 1 eye (Case #7) in the inner nuclear layer, compatible respectively with acute macular neoretinitis and paracentral acute middle maculopathy. One eye developed transient subretinal fluid (Case #6). One eye presented with multifocal choroiditis (Case #8) 5 days after receiving the first dose of the vaccine, that responded to oral steroidal treatment.</td>
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<tr>
<td>Conclusions</td>
<td>There is an urgent demand for a vaccine for control and prevention of the COVID-19 pandemic. This case series present some ocular inflammatory side effects in otherwise healthy patients that received COVID-19 inactive vaccine. The timing of complications 5.2 days following vaccination, point towards an association between COVID-19 vaccination and the ocular findings in our patients. As the urge for a vaccine against COVID-19 continues, we expect to see an increasing number of ocular side effects from the various candidates similar to those hereby presented that need to be detailed reported.</td>
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<td>Financial Disclosure</td>
<td>None</td>
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Multimodal Imaging of an Atypical Onset Acute Vogt Kayanagi Harada Disease: A Case Report

Ahmet Kaderli
Turkey

Sema Tamer Kaderli

Aylin Karalezli

Purpose
To present a case with an atypical onset of Vogt Kayanagi Harada Disease.

Setting/Venue
Muğla Sıtkı Koçman University Hospital.

Methods
A 54 years old female was referred to our hospital with reduced visual acuity in her left eye and severe headache. In her detailed ophthalmologic examination best corrected visual acuity was 20/20 in her right eye and 20/200 in the left eye. Nongranulomatous keratic precipitates, +2 cells in anterior chamber, posterior synechia were detected in the left eye in the anterior segment. Fundus examination in the left eye showed vitritis, disc edema and serous retinal detachment. Biomicroscopic view, wide-field fundus image, fundus fluorescein angiography (FFA) and Enhanced deep imaging optic coherence tomography (EDI-OCT) images are given in Figure 1. In her unaffected right eye, she had pigmented scars which were similar a scar of Toxoplasma retinochoroiditis. A widespread uveitis screening was performed. Toxoplasma gondii Ig M and Ig G were positive. Oral trimethoprim-sulfamethoxazole and clarithromycin treatment was performed and two days after antibiotics, oral prednisolone (1mg/kg) treatment was added with topical prednisolon asetat and tropicamid.

Results
1 week later she had reduced visual acuity in her right eye. In fundus examination, Optic disc edema and serous retinal detachment in the papillomacular bundle were detected. Fundus image, EDI-OCT, retinal nerve fiber layer (RNFL) thickness and indocyanine green angiography (ICG) of both eyes at first week of treatment were given in Figure 2. Sensoryneural deafness in audiometric test and increased lymphocytes in lumber puncture were determined. Toxoplasma Ig avidity test was resulted with low affinity. She was diagnosed with Acute Vogt Kayanagi Harada disease. Intravenous methylprednisolon asetate 1gr per day was performed for 7 days. Subretinal serous detachment and retina pigment epithelium ondulations was regressed and the thickness in choroidea was decreased in EDI-OCT. Intravenous corticosteroid therapy was switched to oral prednisolone (1mg/kg) with oral cyclosporine (50mg/day) after that. In the first month of treatment her visual acuity was 20/20 ou and serous detachment was regressed in both eyes. (Figure 3)

Conclusions
Clinical examination is often more important than laboratory tests. It is crucial to initiate early intravenous corticosteroid treatment in acute VKH to prevent the transition to the chronic stage. Immunosuppressant therapy should be added in addition to maintenance oral corticosteroid treatment.

Financial Disclosure
None.
The effectiveness of the 0.19 mg fluocinolone acetonide implant in treating non-infectious posterior uveitis in the Middle East clinical practices

Igor Kozak, United Arab Emirates

Avinash Gurbaxani

Maya Pandova

The 0.19 mg fluocinolone acetonide (FAc) implant (ILUVIEN; Alimera Sciences Inc., Georgia, USA) is approved for the treatment of non-infectious uveitis affecting the posterior segment of the eye. The purpose is to present the results from a prospective interventional case review of patients treated according to the licensed indication in the Middle East retinal practices with a focus on outcomes after 12 months of therapy.

Setting/Venue
Retina and uveitis clinics of the Moorfields Eye Hospital UAE in Abu Dhabi and Dubai, United Arab Emirates and retina clinic of Ahmadi Hospital in Kuwait City, Kuwait.

Methods
The case review involved a total of 16 eyes from patients with posterior non-infectious uveitis (which included retinal vasculitis/vitritis, pseudophakic cystoid macular edema/panuveitis, multifocal choroiditis, tuberculous uveitis, chronic uveitis) and treated with the FAc implant between December 2018 and February 2021. The median follow-up period was 12 months (range, 3 to 24 months) for all eyes. Patients were included for further analysis if they had completed 12 months of follow-up.

Results
Sixteen eyes from nine patients were included. Mean age was 55.0±17.5 years (SD; range, 38 to 84). The majority (9 eyes) had a pseudophakic lens and 3 eyes had a prior vitrectomy performed. Prior treatments included intravitreal injections (predominantly injections of dexamethasone in 7 eyes) and systemic therapy had been given and stopped in one patient. Twelve months after the FAc implant had been given, central retinal thickness decreased by 101.6±45.3 µm (P=0.0352, t-test; 95% CI -195.5 to -7.7) from a baseline of 424.2±126.5 µm and BCVA increased by 17.1±7.5 ETDRS letters (P=0.0333; 95% CI 1.5 to 32.7) from a baseline of 53.8±18.6 ETDRS letters. AC cells and vitritis scores also significantly improved with the proportion of eyes with an AC cell score ≥1 decreasing from 7 eyes at baseline to 0 eyes by Month 12 (P=0.0046, Fisher Exact test) and eyes with a vitritis score ≥1 decreasing from 7 eyes at baseline to 1 eye by Month 12 (P=0.0075, Fisher Exact test). Mean IOP remained relatively stable throughout (+1.3±2.3 mmHg (P=0.5865; 95% CI 3.7 to 6.3) from a baseline of 14.2±15.5 mmHg).

Conclusions
Results gained from real-world practice in the Middle East demonstrate the effectiveness of the FAc implant in the treatment of non-infectious posterior uveitis affecting the posterior segment of the eye.

Financial Disclosure
Novartis, Bayer - consultant
# Multiple sclerosis and Vogt-Koyanagi-Harada syndrome: Can they coexist?

**Presenter**

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## Purpose

Multiple Sclerosis (MS) is an immune-mediated chronic demyelinating disease of the central nervous system (CNS). Ophthalmic manifestations of MS are retrobulbar optic neuritis (ON) and papillitis, intermediate uveitis or peripheral vasculitis. Vogt Koyanagi Harada (VKH) Syndrome is a chronic disorder characterized by granulomatous inflammation of the uvea, meninges, auditory and integumentary systems. The association between VKH syndrome and MS has been established only a few times in the literature, suggesting that both conditions may have a common immunopathogenesis. The aim of this article is to report a case of VKH syndrome misdiagnosed as an acute episode of an atypical ON in a patient with MS.

## Setting/Venue

Hospital Professor Doutor Fernando Fonseca, Amadora, Lisbon, Portugal

## Methods

Description of a clinical case.

## Results

A 47-year-old female patient presented with sudden and painless loss of vision in the left eye (LE) and an inferior scotoma in the right eye (RE), preceded by intense headaches, photophobia and tinnitus. The patient had the diagnosis of relapsing-remitting MS, since an attack of dorsal myelitis, with multiple hyperintense lesions on brain and spine magnetic resonance imaging (MRI), 12 years earlier. At presentation, best corrected visual acuity (BCVA) was 20/200 in the RE and 20/800 in the LE. Pupils, despite reactive, constricted poorly to bright light, and fundoscopy showed discreet bilateral peripapillary retinal folds. A 5-day intravenous pulse steroid therapy was initiated for atypical ON, with good response. After treatment suspension, the patient complained of progressive decrease in vision. Ophthalmic evaluation found bilateral BCVA of hand movement, anterior chamber reaction, with mutton fat keratic precipitates and extensive exudative retinal detachments. Optical Coherence Tomography (OCT) revealed neurosensory retinal detachments surrounding the optic disc and reaching the macula. Ultrasonography showed diffuse choroidal thickening. VKH syndrome was considered and the patient was treated with systemic and topical corticosteroids, associated with rituximab. Visual acuity slowly returned to 20/20 and the subretinal fluid disappeared, replaced by retinal pigment epithelial patchy atrophy.

## Conclusions

We describe an unusual case of VKH syndrome associated with MS. The aetiology of MS and VKH is not completely understood. Both entities are associated with autoimmune T-lymphocyte response and simultaneous presentation suggests a common pathogenesis. Meticulous history, complete physical examination and multidisciplinary collaboration are of paramount importance to achieve the correct diagnosis and to implement the right treatment. Since the treatment and prognosis of both conditions are different, patients who have concomitant diseases are challenging to manage.

## Financial Disclosure

none
Atypical mycobacterial retinitis in a young patient of retroviral disease

Purpose
To describe a presentation of retinitis due to atypical mycobacterium subspecies Mycobacterium abscessus in a patient with Retroviral disease. Atypical mycobacteria are Mycobacteria other than Mycobacterium tuberculosis. They are opportunistic free living pathogens. Group IV, the rapid growers (according to Runyon’s Classification) - Mycobacterium abscessus, M. chelonae and M. fortuitum have been reported to be responsible for majority of the ocular infections caused by atypical mycobacteria. Risk factors include trauma, previous corneal infection or surgery, corticosteroid use and systemic immunosuppression. Laboratory detection, clinical diagnosis and management of ocular infections caused by atypical mycobacteria are quite challenging. Our purpose is to highlight the importance of cytology and culture in the diagnosis of these cases especially in immunocompromised patients who are more likely to develop intraocular atypical mycobacterial infections, which are associated with a greater risk of loss of vision.

Methods
At the time of presentation, his CD4 count was 280. BCVA was 6/18P in OD and 6/9 in OS. Anterior segment examination OU revealed medium sized keratic precipitates, grade 2+ AC cells and posterior subcapsular cataract. Fundus examination showed vitritis of grade 2+ and multiple confluent, creamy yellowish white lesions in the periphery suggesting retinitis. IOP was 14mm of Hg in OU. He was investigated to rule out syphilis, toxoplasmosis, viral and endogenous endophthalmitis. Antibodies to Toxoplasma in blood and CSF, HCV, HBsAg and VDRL were negative. CBNAAT for TB was negative. CSF culture was positive for Cryptococcus but vision and retinitis worsened with anti fungal treatment. Antibodies to Mycobacterium tuberculosis were positive. CSF culture revealed AFB and culture detected Mycobacterium abscessus. Patient received multiple intravitreal Amikacin injections and IV Meropenem which caused a reduction in biomicroscopic picture with fewer AFB suggestive of tubercular etiology. Mycobacterium abscessus was isolated on culture, which was sensitive to Imipenem, Azithromycin, Clarithromycin, Amikacin, Tobramycin and Gatifloxacin. He was started on Tab Azithromycin 500mg per day. OU received Intravitreal Amikacin injection(125mcg/0.1ml) following which retinitis showed signs of gradual resolution and consolidation. He received further injections of intravitreal Amikacin (total of five in each eye). Intravenous Meropenem 1g injections thrice a day was given for 6 weeks based on sensitivity profile. He was followed up over four months and is doing well with BCVA of 6/9 in OU. We plan to continue periodic follow ups with meticulous examination.

Results
Intravitreal injection of Vancomycin and Ceftazidime was given to OS. AC tap sample was sent for Gram’s stain, KOH stain, PCR to rule out bacterial (including mycobacteria) and viral pathology, which was inconclusive. 2 days following the injection, vision dropped to CFCF with worsening of vitreous haze. He underwent pars plana vitrectomy in OS with intravitreal injections of Vancomycin, Amikacin and Voriconazole. Vitreous aspirate was sent for cytology, PCR (eubacterial, panfungal, viral & mycobacterial species) and Culture (Bacterial, fungal & Mycobacterial). On Postoperative day 1, vision was 6/24 with resolution of hypopyon. Cytology revealed granulomatous picture with few AFB suggestive of tubercular etiology. Mycobacterium abscessus was isolated on culture, which was sensitive to Imipenem, Azithromycin, Clarithromycin, Amikacin, Tobramycin and Gatifloxacin. He was started on Tab Azithromycin 500mg per day. OU received Intravitreal Amikacin injection(125mcg/0.1ml) following which retinitis showed signs of gradual resolution and consolidation. He received further injections of intravitreal Amikacin (total of five in each eye). Intravenous Meropenem 1g injections thrice a day was given for 6 weeks based on sensitivity profile. He was followed up over four months and is doing well with BCVA of 6/9 in OU. We plan to continue periodic follow ups with meticulous examination.

Conclusions
Atypical mycobacterial infections are rare but can lead to serious vision-threatening complications. Management is challenging as the retinitis is usually attributed to other causes such as viral or fungal infection. In this case, presentation of granulomatous KP’s with retinitis was unusual in an immunocompromised patient with decent CD4 counts. CSF culture was positive for Cryptococcus but vision and retinitis worsened with anti fungal treatment. Multiple PCR did not reveal the causative agent. Vitreous aspirate revealed AFB and culture detected Mycobacterium abscessus. Patient received multiple intravitreal Amikacin injections and IV Meropenem which caused a dramatic improvement in vision and resolution of retinitis. In 2015, Kheir et al. reported that more than half of endogenous endophthalmitis cases were associated with immunodeficiency status. Pintpuwadol, Warinyupa et al in 2020 reported that M. abscessus was associated with poor visual outcome with majority of cases ending up with visual impairment, evisceration or phthisis. High index of suspicion is necessary. Repeated vitreous and aqueous cultures are required to identify causative organism. Treatment includes combination of local and systemic antibiotics based on drug sensitivity. Anti tuberculosis drugs are commonly prescribed. Amikacin, clarithromycin and azithromycin are considered to be the best antibiotics for these infections. It is crucial to identify the causal agent early as this helps in planning definitive therapy.
Title
Superficial and deep capillary plexus vessel density measurements in intermediate uveitis patients

Purpose
Our aim in this study is to analyse the alterations in superficial and deep capillary plexus vessel density measurements in patients with intermediate uveitis at the time of diagnosis.

Setting/Venue
Retrospective case series.

Methods
Medical records of 17 patients with the diagnosis of intermediate uveitis were reviewed (Group 1). Gender, age, initial and final best corrected visual acuity (BCVA) on Snellen chart, superficial (SCPVD) and deep capillary plexus (DCPVD) vessel density on optical coherence tomography angiography (OCTA) measurements were compared with age and gender matched control group of 17 patients (Group 2).

Results
Of 17 patients 9 were female and 8 were male. Mean age was 28.64±12.46 years, initial BCVA was 0.85±0.25 and final BCVA was 0.94±0.17 in Group 1. SCPVD was 47.59±3.66% and DCPVD was 47.15±5.44% in group 1. Same measurements were 50.90±2.35% and 50.20±5.20% in group 2 respectively. SCPVD and DCPVD measurements were statistically significantly lower in Group 1 than Group 2 (p<0.001, p<0.001).

Conclusions
In our study intermediate uveitis patients revealed decreased SCPVD and DCPVD measurements. Further prospective studies with larger patient numbers are required to analyse the anatomic changes in OCTA in this patient group.

Financial Disclosure
None
**Title**  
Candida albicans endogenous endophthalmitis in a coronavirus disease 2019 positive patient

**Purpose**  
To report a case of Candida albicans endogenous endophthalmitis in a COVID-19 positive patient.

**Setting/Venue**  
Mugla Sitki Kocman University, research and training hospital

**Methods**  
A 61-year-old woman presented to our clinic with progressively decreasing vision, pain, and redness in her left eye. The visual acuity was counting fingers at 3 meters in the left eye. A slit-lamp biomicroscopy exhibited a marked diffuse conjunctival injection and 1+ cells in the anterior chamber. Fundoscopy showed vitreous cells, 1+ haze and yellowish-white dots in the vitreous. There was a history that the patient was diagnosed with COVID-19 a month ago and hospitalized in intensive care unit for 20 days and used oral corticosteroids.

**Results**  
The vitreous sample was tested positive for culture-proven C. albicans. The patient's nasopharyngeal swabs tested positive for COVID-19 in a reverse transcription polymerase chain reaction (RT-PCR) assay. After culture positivity, the intravitreal Amphotericin B was administered and intravenous form of the drug was added to treatment as 3 mg/kg/day. She also received routine topical uveitis treatment (prednisolone acetate 0.1% and cyclopentolate hydrochloride 1.0%) for her left eye. The visual acuity improved to 20/40 and there were no signs of vitreous infiltrates after 2 week of treatment and the chorioretinitis lesion has regressed.

**Conclusions**  
The endogenous fungal endophthalmitis should be kept in mind in patients who present with panuveitis and hospitalized for COVID-19.

**Financial Disclosure**  
no financial disclosure
**Purpose**

In Europe, ILUVIEN® (0.19mg fluocinolone acetonide intravitreal implant [FAc]) is indicated for prevention of relapse in recurrent non-infectious uveitis affecting the posterior segment of the eye. The purpose of this analysis is, then, to report the outcomes of two cases of chronic non-infectious uveitis with macular edema (ME) treated with a single FAc intravitreal implant.

**Methods**

Retrospective descriptive study of 2 case of chronic non-infectious uveitis with macular edema, treated with FAc, based on information from clinical records, patient observation and analysis of complimentary diagnostic tests. Outcome measures included best-corrected visual acuity (BCVA; ETDRS letters score), central macular thickness (CMT; µm), macular volume (MV; mm3) and intraocular pressure (IOP; mmHg).

**Results**

Case 1: 62-year-old woman presented with bilateral panuveitis. Examination revealed the presence of “mutton fat” keratic precipitates and absence of cells or flare in the anterior chamber. Fundoscopy revealed vitreous opacities, disc oedema and Dalen-Fuchs nodules with no activity. Systemic workup made sarcoidosis diagnosis. Patient was treated with systemic corticosteroids. After systemic steroid tapering, patient presented flare and cystoid ME. Prior FAc, the patient received 1 sub-tenon triamcinolone and 3 dexamethasone intravitreal implant (DEX) injections with good morphologic and functional response but ME recurred around 5 months post-injection. During this period, patient underwent cataract surgery and vitrectomy. Post-FAc (3.5-years), she continued with controlled ME (CMT/MV of 463µm/10.46mm3 from a baseline of 614µm/11.6mm3) and improved BCVA +15letters from baseline (60 to 75letters).

Case 2: 63-year-old woman presented with flare in the anterior chamber. Fundoscopy revealed anterior vitreous organization, inferotemporal vasculitis and cystoid ME (suspicious of sarcoidosis diagnosis). Prior FAc, patient was treated with systemic corticosteroids, immunosuppressors, and 7 DEX injections – good anatomic and functional response but with recurrence. Patient underwent cataract surgery and vitrectomy. Post-FAc (1.75-years), she continued with controlled ME (CMT/MV of 386µm/8.10mm3 from a baseline of 482µm/10.17mm3) and improved BCVA +10letters from baseline (70 to 80letters).

**Conclusions**

The current cases reported here supports the benefit of ILUVIEN® in the treatment and prevention of relapse in recurrent non-infectious uveitis with macular edema.

**Financial Disclosure**

No financial conflicts of interest.
Increased Neutrophile to Lymphocyte Ratio and C-Reactive Protein to Albumin Ratio in Patients with Idiopathic Acute Anterior Uveitis

Purpose
Uveitis is defined as a common intraocular inflammation which is usually associated with multiple systemic diseases. Acute anterior uveitis (AAU) is the most common sub-type of uveitis. Approximately %50 of AAU cases the etiology is not identifiable and these cases are called idiopathic AAU. Neutrophile to lymphocyte ratio (NLR), C-reactive protein (CRP) and CRP to albumin ratio (CAR) are the inflammatory parameters which have been used usually in monitoring the severity of systemic inflammatory diseases. Since the idiopathic AAU is not related to systemic disease, increased NLR and CAR is not expected. Studies have reported increased NLR in uveitis but the literature is limited in terms of evaluating CAR in uveitis patients. Although the only study evaluating CAR in uveitis have reported increased CAR in uveitis patients; anterior, posterior and panuveitis were evaluated together and idiopathic uveitis and the others related to systemic diseases were not subgrouped. In this study we aimed to investigate the NLR and CAR in idiopathic AAU patients and to compare the results with the healthy controls. We studied also the correlation between these two parameters.

Setting/Venue
This study is conducted in Diskapı Yıldırım Beyazıd Research and Education Hospital Ophthalmology Department Uvea unit in Ankara.

Methods
This study was conducted in accordance with the declaration of Helsinki. Ethical approval was obtained from Diskapı Yıldırım Beyazıd Research and Education Hospital Human Research Ethics Committee. Retrospectively we reviewed the records of 103 patients diagnosed with uveitis who admitted to our clinic between January 2016 and January 2021. According to their conclusive diagnosis 37 idiopathic AAU patients and 35 age matched healthy controls were enrolled in study. All patients had routine ophthalmological assessment and we reviewed the results of complete blood count (CBC), CRP, renal and liver function tests which were performed during their acute anterior uveitis attack. NLR and CAR were calculated in uveitis and control groups.

Results
The mean age in the idiopathic AAU group was 35.08+/-8.56 while 33.51+/-6.80 in healthy subjects (p > 0.05). Neutrophile and lymphocyte counts were 4.78+/-1.25 (1000/μL) and 1.73+/-0.65 (1000/μL) in the AAU group and 4.03+/-1.01 (1000/μL) and 2.37+/-0.62 (1000/μL) in the control group respectively (p>0.0001). NLR was 3.05+1.20 in the AAU group and 1.77+/-0.54 in the control group (p<0.0001). CRP was 5.31+/-2.35 in the AAU group while 3.12+/-0.86 in the control group (p<0.0001). CAR was 1.23+/-0.55 in the AAU group and 0.69+/-0.18 in the control group (p<0.0001). Correlation analyse showed no correlation between NLR and CAR (r=-0.17 p=0.316).

Conclusions
Increased NLR is detected not only in many systemic inflammatory diseases but also in certain ocular diseases such as keratoconus, retinal veno-occlusions, age related macular degeneration. Although in uveitis patients without systemic disease the immune response is too localized to be detected in the peripheral blood, studies from uvea clinics are recently indicating increased NLR in idiopathic uveitis. In one study the authors concluded Behcet patients with AAU attacks had significantly increased NLR compared with Behcet without AAU. CAR is used as a marker of inflammation and mortality risk indicator in cardio-vascular disease and septic shock. The only uveitis study in the literature indicated that increased CAR levels are correlated with the severity of uveitis regardless of localization of uveitis. In our study we detected significant increase in NLR and CAR in idiopathic AAU patients. Depending on our study results NLR and CAR can be used to monitor patients with idiopathic AAU.
## Title
Acute retinal necrosis: How can we manage it?

## Purpose
To report a case showing an acute retinal necrosis (ARN) and to emphasize special aspects of the management. Factors that have to be taken into account.

## Setting/Venue
Department of Ophthalmology of the San Cecilio University Hospital of Granada, Spain.

## Methods
We present an 83-year-old woman examined for acute vision loss in her left eye (LE), Background: diabetes, pseudophakic in her LE; intraocular lens (IOL) subluxated and advanced pseudoxfoliative glaucoma in her right eye (RE). The visual acuity (VA) was hand movements' in both eyes. Funduscopic examination revealed vitritis, temporal area of retinal necrosis with peripapillary choroiditis' spots and macular haemorrhages in her LE and OCT showed a cystic macular edema.

## Results
A 53-year-old woman who goes to the emergency for acute painless vision loss of about 3 hours of evolution in her right eye (OD). Visual acuity in her left eye was (OS)=1 and hand movement in the right eye (OD). Marcus-Gunn sign in OD. Fundoscopy examination revealed a yellow embolus lodged at the level of papillary area that extends into the inferior temporal artery provoking perifoveolar retinal edema with "cherry red spot". Laser YAG was applied for photo-fragmentation of the embolus. We use YAG laser at 0.5 mJ, applying a total of 15 shots, then continuing with eye massage every 30 minutes for 2 hours. After that, we observed the appearance of laminar flow and repermeabilization of the artery. The visual acuity was AV(OD)= 1/30=0,33 24h later. The pupil was hyporeactive, the embolus and the retinal edema had disappeared.

## Conclusions
The YAG laser seems to be a hopeful technique in visual recovery and early vascular repermeabilization in CRAO with visible embolism performed in the first 6 hours post-occlusion, although it is not exempt from adverse effects such as vitreous hemorrhage. In our case, the early fragmentation of the embolus with YAG laser has allowed the repermeabilization of the vessel and a modest improvement in visual acuity. The patient must be made aware of the poor visual prognosis and know the origin of the thrombus to avoid recurrences.

## Financial Disclosure
No financial disclosure
**Title**
Dexamethasone implant in post fever retinitis (PFR) in Pregnancy: A rare case report

**Purpose**
Post fever retinitis is retinal manifestations seen after a systemic febrile illness caused by either bacteria, viruses, or protozoa. These manifestations may be the result of a direct invasion by the pathogen or by indirect invasion mediated through immune-modulated mechanisms. Retinitis and vasculitis manifested between 2 - 4 weeks after the fever irrespective of etiology. A case of post fever retinitis in a 23 year pregnant female managed successfully.

**Setting/Venue**
A 23 yr old female presented with sudden diminution of vision in left eye since 4 days while 28 weeks pregnant, in Vitreo- Retina department of SHRI GANAPATI NETRALAYA, JALNA, MAHARASHTRA (INDIA).

**Methods**
A 23 yr old female presented with sudden diminution of vision in left eye since 4 days while 28 weeks pregnant. She had a fever with chills a month ago (treated adequately). The Patient was investigated extensively to rule out any infectious etiology but none found (viz. enteric fever, HIV, Dengue, Cat-scratch disease, Chikanguniya, malaria, Syphilis, Lyme disease and Covid-19). At presentation, her BCVA in right eye was, 20/20, N6 & left eye 1/20, N36. Left eye fundus showed mild vitritis, a patch of vasculitis and retinitis along superior and inferotemporal arcade with gross macular edema, hard exudates on macula & hyperaemic disc. Her right eye was within normal limit. FFA deferred in view of pregnancy. Left eye OCT at presentation revealed increased hyperreflectivity with thickening of inner retinal layers, hyperreflective dots intraretinally with subretinal fluid in perifoveal area. Her right eye OCT was unremarkable. Systemic steroids are the mainstay of treatment in this condition. However, Patient and her treating Obstetrician denied for any systemic medication hence after obtaining informed consent from patient, she was treated with intravitreal dexamethasone implant (OZURDEX®).

**Results**
She did well post procedure- Inflammation resolved with anatomical and functional success with left eye visual acuity improved to 20/20, N6 at 6 weeks and maintained same throughout her visits (last follow up 3 months post delivery). No other adverse events occurred for the mother or baby neither during pregnancy nor after delivery.

**Conclusions**
This was a very challenging scenario and to the best of our knowledge, this is the first report of post fever retinitis treated with intravitreal dexamethasone implant in pregnancy. Many cases of post fever retinitis do not have etiological diagnosis & good response to steroids suggestive of possible immunological etiology. This may represent a suitable therapeutic option when other approaches are contraindicated.

**Financial Disclosure**
NO FINANCIAL DISCLOSURES
Purpose
To describe the clinical presentation, diagnosis, treatment modalities, and prognosis of Rickettsia rickettsii retinitis.

Setting/Venue
Department of Ophthalmology, Habib Bourguiba University Hospital, Faculty of medicine, University of Sfax, Tunisia.

Methods
A 60-year-old woman, living in a rural area, complaining of acute visual loss, floaters and ocular pain over a 5-day period. History was notable for skin rash and fever 3 weeks before clinical presentation. The patient underwent a comprehensive ocular examination, fluorescein angiography, swept-source optical coherence tomography (OCT).

Results
Ophthalmic examination revealed a best corrected visual acuity (BCVA) reduced to counting fingers, ciliary flush, granulomatous anterior uveitis and moderate vitritis. Intraocular pressure was normal. Fundoscopy showed large areas of multiple white spots at the level of the inner retina associated with vascular sheathing and hyperemic disc with slightly indistinct borders within both eyes. Fluorescein angiography showed early hypofluorescence and late staining of large retinal foci, while OCT revealed a serous retinal detachment. Serological analysis was positive for Rickettsia rickettsii. The patient was treated with a 2-week course of oral doxycycline 200 mg/day. One month later, almost all retinal lesions disappeared and visual acuity improved.

Conclusions
Rickettsia rickettsii is one of the many possible infectious agents that can cause retinitis. Mild vitritis, retinal vasculitis, optic disc staining, white retinal lesions, retinal hemorrhages, and multiple hypofluorescent choroidal dots are the most common manifestations of posterior segment manifestations of Rickettsia conorii infection. Highly suspicion based on history can guide testing, particularly in patients in endemic areas. Doxycycline is effective in treating the condition.

Financial Disclosure
Department of Ophthalmology, Habib Bourguiba University Hospital, Faculty of medicine, University of Sfax, Tunisia.
Purpose
to report two cases of posterior nodular scleritis

Setting/Venue
Department of ophthalmology, Habib Bourguiba University Hospital, University of Sfax, Tunisia

Methods
two case reports with multimodal imaging

Results
Case 1: A 21-year-old female presented with painful decreased vision in the left eye for three weeks. Fundus examination revealed a whitish lesion in the posterior pole of the left eye. Fluorescein angiography showed hypofluorescents dots. Swept Source Optical coherence tomography (SS-OCT) revealed elevated choroid associated with subretinal fluid. B-scan ultrasonography showed a hyperreflective nodular lesion with retrobulbar hyporeflectivity (T sign). The lesion was hyperintense on MRI T1 sections.

Case 2: a 56-year-old female with a past history of rheumatoid arthritis presented with a painful blurred vision left eye. Fundus examination showed a whitish mass in the posterior pole of the left eye with pinpoint hyperfluorescence on fluorescein angiography. SS-OCT revealed a thickened choroid with subretinal fluid. In both cases, clinical features and multimodal imaging were consistent with the diagnosis of posterior nodular scleritis. Both cases were treated with systemic non-steroidal anti-inflammatory drugs. A complete functional and anatomical recovery was noted in all cases.

Conclusions
Posterior nodular scleritis is an uncommon form of scleritis. It is often misdiagnosed as amelanotic melanoma. The distinction between these two affections is capital as the treatment, the workup, and the prognosis are different. Clinical features and multimodal imaging can help to identify the two of them.
# Optical Coherence Tomography Angiography Findings in Neuroretinitis – Case Report

## Purpose
The aim of this study is to examine a clinical case of neuroretinitis. Neuroretinitis is an inflammatory disorder of the eye presenting with optic disc edema and the delayed development of a macular star secondary to optic nerve swelling toward the macular structures. It can be either infectious (including neuroretinitis associated with cat-scratch disease) or non-infectious (including idiopathic). Optical coherence tomography angiography (OCTA) is a new non-invasive imaging tool to assess microvascular retino-choroidal changes. It can also play an important role in the diagnosis and management of optic nerve-related diseases.

## Setting/Venue
Department of Ophthalmology, Centro Hospitalar Vila Nova de Gaia/Espinho, Portugal

## Methods
Multimodal imaging in a case of Bartonella Neuroretinitis, including OCTA findings, at presentation and 3-month follow-up.

## Results
A healthy 32-year-old female presented with painless visual loss and central scotoma in her left eye (OS) for 3 days. She reported associated headaches and nausea. Best corrected visual acuity was 10/10 in the right eye (OD) and 1/10 in the OS. A left relative afferent visual defect and dyschromatopsia were noticed. Dilated fundus examination revealed right optic disc with blurred nasal edge and diffuse optic disc swelling with peripapillary haemorrhage in OS. Maculae appear normal in both eyes. Brain MRI, lumbar puncture and analytical study were uneventful. Two weeks following the initial symptoms stellate macular exudates developed. Optical coherence tomography (OCT) revealed hyperreflective lesions predominantly in the outer plexiform layer nasally and subfoveal fluid accumulation and OCT angiography showed peripapillary telangiectatic vessels with superficial and deep macular plexus without circulation impairment. When questioned, the patient referred previous contact with a litter of sick cats. Neuroretinitis was concluded, and Cat Scratch Disease (CSD) etiology was confirmed with serologies.

## Conclusions
Neuroretinitis is primarily a clinical diagnosis with characteristic findings of unilateral disc edema and a macular star. Given the delayed development of the maculopathy the diagnosis of neuroretinitis may be initially. Multimodal imaging is useful in characterizing and analysing optic disc involvement and associated choriretinal changes in both typical and atypical clinical presentations. Positive serology for Bartonella henselae is mandatory to establish the definitive diagnosis. OCTA displays finer vascular details of the optic nerve head and superficial and deeper retinal plexus by imaging the dynamic movements of red blood cells. It presents an interesting opportunity to diagnose and to track how the retinal vasculature is affected in patients with CSD neuroretinitis. More data are needed to establish specific patterns of vascular abnormalities and the extent to which OCTA may aid in the diagnosis and follow-up of neuroretinitis.

## Financial Disclosure
No
**Title**
A Rare Case of Bilateral Non-Simultaneous Herpes Simplex Virus 2 (HSV2) Panophthalmitis In An Immunocompetent Young Patient

**Purpose**
To describe the clinical presentation and management of bilateral non-simultaneous severe herpes simplex virus 2 (HSV-2) panophthalmitis causing severe vision loss in a young immunocompetent patient.

**Setting/Venue**
Manchester Royal Eye Hospital, United Kingdom.

**Methods**
A case report of a 22-year-old immunocompetent male with a history of previous right eye severe HSV2-panophthalmitis. He presented with a two-week history of left painful eye, periorbital swelling and vision loss. The right eye had presented with panophthalmitis, including total retinal necrosis, retinal detachment, marked scleritis five years previously and had become blind and phthisical. He was lost to follow-up. The left eye was normal at last the follow-up. The patient had a history of substance abuse and learning difficulties. We also present imaging findings, including intra-operative images, ultrasound images and computerised tomography (CT) findings.

**Results**
On examination, he had left severe periocular oedema, complete ophthalmoplegia, proptosis, chemosis, intraocular pressure of 35mmHg and no perception of light vision in both eyes. There were granulomatous keratic precipitates, fibrin and 3+ cells in the left anterior chamber. There was no fundal view, and ultrasound demonstrated vitritis, extensive serous detachments and scleral thickening. A CT orbit showed diffuse fat-stranding and scleral thickening but no collection. The vitreous tap was HSV2 polymerase chain reaction (PCR) positive. He received intravitreal Foscarnet (2.4mg/0.1ml) and was commenced on high-dose intravenous aciclovir and subsequently high-dose systemic corticosteroid. VA improved to perception of light following treatment; however, the eye became hypotonous without a fundal view. He underwent pars plana vitrectomy with silicone oil tamponade. Dense vitreous debris with 360° retinal necrosis, extensive occlusive vasculitis involving the posterior pole and pale optic nerve were observed. The panophthalmitis settled with final visual acuity of 6/48 at 1 meter at 2 months.

**Conclusions**
Panophthalmitis is a rare and extremely severe presentation of HSV intraocular infection, which can initially go unrecognised, leading to late diagnosis and poor outcome. To our knowledge, this is the first reported case of bilateral non-simultaneous HSV2-associated panophthalmitis. Prompt diagnosis with PCR vitreous tap and treatment with high dose systemic aciclovir and corticosteroid followed by vitrectomy led to improved orbital and ocular inflammation. Investigations for immunodeficiency, including specific susceptibility to HSV infection (HLA DQ7 and TLR-4), are recommended. HLA DQ7 was negative in our patient. Patients with a history of HSV retinal necrosis are at risk of second eye involvement, months or years after the first eye presentation. A high index of suspicion of an infectious agent as etiology with a low threshold for vitreous sampling is warranted in severe cases of panophthalmitis.

**Financial Disclosure**
No financial interest
Tuberculosis-related serpiginous choroiditis: aggressive therapy with dual concomitant multiple anti-tubercular and immunosuppressive agents is needed to halt the progression of the disease

Purpose
Serpiginous-like choroiditis is a rare sub-entity of tubercular uveitis with a usually deleterious outcome. Treatment is still controversial. The purpose in this case series is to indicate that only aggressive treatment comprising multiple anti-tubercular and multiple immunosuppressive agents seems to be able to halt the disease progression.

Setting/Venue
Centre for Ophthalmic Specialised Care (COS), Lausanne, Switzerland

Methods
This retrospective case series included patients diagnosed with IGRA-positive serpiginous choroiditis, seen at the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland, treated with combined multiple antitubercular and immunosuppressive agents at presentation and having a sufficient follow-up. Disease history before referral, appraisal of disease, treatment modalities and follow-up were analysed. Inclusion criteria were positive IGRA patients with serpiginous choroiditis with complete SD-OCT and angiography images.

Results
From 2001 to 2020, 24 of 1525 new patients (0.26%) were diagnosed as serpiginous choroiditis. 10/24 were related to tuberculosis (positive IGRA and/or hyper-positive Mantoux test), 8/24 were IGRA negative and in 6 there was no information available. 4/10 tuberculosis related serpiginous patients fulfilled the inclusion criteria. Mean age was 38.77 ± 5.77 years. Snellen best corrected vision acuity (BCVA) at presentation was 0.9 ± 0.59. Flare at presentation was 7.3 ± 2.1 ph/ms. In 3/4 patients, treatment with multiple tuberculostatic therapy combined with multiple immunosuppressive agents, started at presentation, was shown to stop the progression of the disease, with a retained visual acuity (BCVA 1.20 ± 0.3, p= 0.9315) and a mean flare of 8.3 ± 4.74 ph/ms, not statistically changed (p=0.5857). One patient with macular involvement and a bilateral visual acuity of 0.1 presented a visual field improvement and stability after 14 years of follow up with combined multiple anti-Tb treatment and immunosuppressors (Octopus® MD OD 15.5/OG 15.3 in 2006, MD OD 19.7/OG 19.6 in 2020).

Conclusions
IGRA-positive serpiginous choroiditis (serpiginous-like choroiditis) could be halted by combined multiple tuberculostatic and multiple immunosuppressive agents, as seen in our study where 3/4 patients had conserved central function, when treatment was introduced early enough, and substantial visual field stability in the late treated patient.
**Title**
Mapping choroidal thickness in patients with type 2 diabetes and healthy controls

**Purpose**
To examine and compare choroidal thickness (CT) profiles between patients with type 2 diabetes (T2D) and healthy controls based on swept source-optical coherence tomography (SS-OCT).

**Setting/Venue**
This prospective observational cross-sectional study was conducted at the Department of Ophthalmology, Habib-Bourguiba University Hospital, Sfax, Tunisia. The study included 258 eyes of 151 patients followed between March 3, 2020, and September 28, 2020.

**Methods**
188 eyes of 112 T2D patients (101 with no diabetic retinopathy [NDR], 87 with different stages of diabetic retinopathy [DR]), and 70 eyes of 39 control subjects were enrolled. A macular 7 * 7 mm cube, with 256 horizontal B-scans, was scanned with SS-OCT. Segmentation of choroid was performed automatically using the segmentation algorithm of the OCT device. Three-dimensional maps were created to represent the choroid. The scanned area was divided into 9 different zones. CT of equivalent zones were compared between groups.

**Results**
258 CT maps were analyzed. Mean age (standard deviation) was 54.17 (±9.12). All groups were similar regarding the prevalence of coexisting hypertension and dyslipidemia (P = 0.860 and 0.248 respectively) and regarding the sex ratio (P = 0.818). The CT pattern was similar in all the groups. The peri-foveal choroid was significantly thinner than the para-foveal choroid. The external nasal choroid was thinner than the others subfields. NDR and DR groups presented a lower CT than control eyes in all ETDRS subfields (mean CT was 232.17 ± 49.24 µm in healthy controls, 203.56 ± 58.98 µm in NDR patients and 192.65 ± 59.84 in DR patients ; p=0.000). When comparing the severe NPDR to PDR group and the mild to moderate DR group, CT was reduced in the nine ETDRS sectors. Considering the presence of DME within the DR group, we detected no differences (p>0.05) in the CT between DME and non-DME patients for the nine ETDRS sectors. After adjusting for age, gender, spherical equivalent and inter-eye dependence on a multivariate analysis; central, para-foveal and peri-foveal CTS in the NDR and DR groups maintained a statistically significant difference from the control group.

**Conclusions**
The choroidal maps showed an overall decrease of CT in diabetic eyes even in the absence of biomicroscopic evidence of DR. CT thinning was independent of the severity of the DR and the presence of DME. The findings indicate that in diabetic eyes, choroidopathy is disease rather than retinal vasculopathy dependent. Additional investigation into the effect of diabetes on the choroid is recommended.

**Financial Disclosure**
-
**Title**

VITrectomized vs non-vitrectomized eyes in DEX Implant treatment for DME - Is there any difference? The VITDEX study.

**Purpose**

We aimed to compare visual and anatomical outcome in vitrectomized and non-vitrectomized eyes treated with Dexamethasone (DEX) implant due to diabetic macular edema (DME). Design: Multicenter, retrospective, interventional study. Participants: 236 eyes from 234 patients with DME with or without previous vitrectomy performed with a follow up of 12 months.

**Setting/Venue**

Multicenter, retrospective, interventional study. Participants: 236 eyes from 234 patients with DME with or without previous vitrectomy performed with a follow up of at least 12 months involving multiple sites.

**Methods**

Methods: Main outcome measures: Change from baseline best corrected visual acuity (BCVA) and central subfoveal thickness (CST) over follow-up period. Secondary outcomes: cataract rate formation, intraocular pressure increase, number of implants needed.

**Results**

The non-vitrectomized group included 130 eyes (55.1%), the vitrectomized group included 106 eyes (44.9%). The groups were well balanced for age and gender (p=0.540, and p=0.053, respectively). Both groups showed statistically significant improvement in BCVA and CST (for all groups: p<0.001). There was no significant difference between the groups in terms of change in vision (p=0.89) and anatomy (p=0.65). The mean number of DEX implants given during follow-up was 3.5 in both groups, and there was no significant difference between the groups (p=0.81).

**Conclusions**

In patients with DME, we demonstrated similar anatomical and functional efficacy of DEX implant in non-vitrectomized and vitrectomized eyes. Its efficacy was not decreased by the consequences of full vitrectomy for Diabetic retinopathy complications. Safety profile was very well balanced between the groups.

**Financial Disclosure**

Allergan – Consultant  -Bayer -  Consultant  -Novartis- Consultant  -  Regeneron- PI  -Genentech-PI  -TSK Laboratory Europe B.V. consultant
Ranibizumab for refractory macular edema secondary to retinal vein occlusion: real-world outcomes

**Purpose**
Visual impairment in central (CRVO) or branch retinal vein occlusion (BRVO) is mostly caused by macular edema (ME). Numerous studies showed that intravitreal (IV) vascular endothelial-derived growth factor inhibitors (anti-VEGF) markedly improve anatomical and functional outcomes in the setting of retinal vein occlusions (RVO). When an insufficient response is observed after adequate therapy, switching to another anti-VEGF agent may be considered. This study aims to investigate the real world anatomical and functional outcomes after the anti-VEGF agent switch, from bevacizumab to ranibizumab, in patients with persistent ME secondary to CRVO or BRVO.

**Setting/Venue**
Department of Ophthalmology of Centro Hospitalar Vila Nova de Gaia/Espinho

**Methods**
Retrospective analysis of eyes with refractory ME secondary to CRVO or BRVO in which a therapeutic anti-VEGF switch from bevacizumab to ranibizumab was performed. Inclusion criteria were: a) diagnosis of RVO with treatment resistance, b) a minimum of three consecutive IV injections of bevacizumab before the switch and c) three IV injections of ranibizumab after the switch. Treatment resistance was defined as central foveal thickness (CFT) reductions <100µm and/or CFT> 350µm after treatment and/or absence of anatomical improvement after initial treatment with bevacizumab. Primary outcomes were best corrected visual acuity (BCVA) and CFT after 3 ranibizumab injections.

**Results**
Twenty-one eyes of 21 patients were included in the study: 13 BRVO and 8 CRVO. The median age was 74 (15) years. On average, the switch was performed 34.43 ± 3.47 months after diagnosis and after 9.57 ± 1.17 bevacizumab intravitreal injections. Before the switch, the mean BCVA was 0.65 ± 0.81 logMAR and the mean CFT was 507.10 ± 30.51µm. After three ranibizumab intravitreal injections, the mean BCVA improved 0.07 ± 0.05 logMAR (p = 0.171) and the mean CFT decreased 110.67 ± 29.83 µm (p = 0.001) compared to “pre-switch”. Subgroup analysis showed a significant decrease of mean CFT in both BRVO and CRVO (p=0.036 and p=0.015, respectively) after three injections of ranibizumab but no significant improvement was achieved in BCVA (p=0.082 and p=0.805, respectively). After 9.38 ± 1.15 injections of ranibizumab, the mean BCVA was 0.69 ± 0.13 logMAR (p = 0.324) and CFT was 353.48 ± 38.00 µm (p = 0.001). The duration of disease and the number of injections before the switch were not related to the BCVA or CFT after switch.

**Conclusions**
Our retrospective study showed that the switch to ranibizumab after suboptimal response to bevacizumab might lead to a significant anatomical improvement in eyes with macular edema due to RVO. However, visual function improvement was limited. Larger studies with early switch may validate and enhance our findings.

**Financial Disclosure**
none
COVID-19 associated central retinal vein occlusion: A case report

Abstract

Purpose: To report a case of impending central retinal vein occlusion (iCRVO) in a COVID-19 patient. Case report: A 48 years old male with COVID-19 related pneumonia presented to the emergency department with scotoma and decreased vision complaints. The fundoscopic examination and multimodal imaging revealed retinal hemorrhages, retinal whitening, and fern-like hypo-autofluorescent appearance typical to iCRVO in the left eye. He had no previous history of systemic risk factors other than a transient hypercoagulability status likely related to the ongoing infection. Conclusions: Retinal circulation should be considered as a potential site for thromboembolic complications of COVID-19. The patient was diagnosed as RVO secondary to COVID 19 and underwent intravitreal ranibizumab injections (0.5 mg/0.05 mL) twice. Elevated coagulation parameters should be carefully evaluated in COVID-19 patients to avoid microvascular complications even in those with no previous risk factors. Keywords: Covid-19; central vein occlusion; retina; thrombosis

Methods

A 48 years old male presented to the emergency department with visual symptoms that initiated in the last 72 hours. Besides, the patient suffered fatigue, muscle pain, headache, and relapsing fever complaints in the last 10 days. His COVID-19 nasopharyngeal swab PCR test was detected positive 6 days ago. His temperature was 37.3°C, blood pressure was 135/85 mmHg, pulse was 88 bpm, respiratory rate was 14 breaths per minute, and oxygen saturation was 98%. Complete blood count (CBC), coagulation, and inflammatory markers were evaluated and chest x-ray imaging was performed. In the biochemical blood analysis; C-reactive protein (CRP) was 33.4 mg/L (normal value <10.0 mg/L), erythrocyte sedimentation rate was 87 mm/h (normal value <40 mm/h), lactate dehydrogenase was 272 U/L (normal range 125–220 U/L), creatinine was 0.85 mg/ (normal range 1.70–4.00 g/l) and D-dimer was 414 µg/L fibrinogen equivalent units. Other ratio 1.26, (normal range 0.85–1.2), fibrinogen was 6.93 g/l (normal range <30), lactate dehydrogenase was 272 U/L, and D-dimer was 414 µg/L fibrinogen equivalent units. Other blood parameters including CBC, creatinine, bilirubin, glucose, electrolytes, and creatine kinase were within normal limits. Chest x-ray imaging demonstrated bilateral diffuse thickening of the interstitial structure and multiple opacities with ground-glass appearance. The patient was diagnosed with mild COVID-19-related pneumonia. The patient was immediately hospitalized Patients with Covid-19 — Preliminary Report. N Engl J Med. 2020 1720. https://doi.org/10.1056/nejmoa2002032 5. (2020) Dexamethasone in Coronavirus Disease 2019 in China Marinho et al.  N Engl J Med 382:1708–1720. https://doi.org/10.1056/nejmoa2002032 5. (2020) Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report. N Engl J Med. https://doi.org/10.1056/nejmoa20021436 6. Tang N, Li D, Wang X, Sun Z (2020) Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 18:844–847. https://doi.org/10.1111/jth.14768 7. Lalitha P, Rathinam S, Banushree K, et al (2007) Ocular Involvement Associated With an Epidemic Outbreak of Chikungunya Virus Infection. Am J Ophthalmol 144:552–556. https://doi.org/10.1016/j.ajo.2007.06.002

Results

COVID-19 is an enveloped, non-segmented positive-sense RNA virus from the newly identified Coronaviridae family. [4] Today, it is mostly associated with atypical pneumonia and acute respiratory failure, and the most common complication among ocular complications is conjunctivitis.[5] However, Marinho et al. identified retinal vascular abnormalities associated with COVID-19;[4] Virchow’s triad (hypercoagulation, endothelial damage, and stasis), which occurs in systemic thrombotic events, may also take part in microvascular thrombosis. [3] Therefore, the presence of any of these three conditions may increase the risk for retinal vessel occlusions. Our case report describes a young patient with CRVO without any comorbid diseases or systemic disorders such as diabetes, hypertension, and tuberculosis. In differential diagnosis, vasculitis should be excluded and this patient had no sign of vasculitis in the retinal examination. Therefore, we considered a hypothetical diagnosis as vasculitic-CRVO secondary to COVID-19.[6] Two separate hypotheses were proposed to explain the vascular damage due to COVID-19: the first is the pseudo-vasculitic condition caused by viral infiltration of vascular endothelial cells, and the latter is hypercoagulation, similar to disseminated intravascular coagulation. (DIC).[6] In this case, the high coagulation parameters of the patient point to the DIC-like situation rather than a pseudo-vasculitic situation caused by COVID-19. Besides we did not

Conclusions


Financial Disclosure

None of the authors have competing interest related to the paper
Title
Diagnostic Test Accuracy of Diabetic Retinopathy Screening by Physician Graders Using a Hand-held Non-Mydriatic Retinal Camera at a Tertiary Level Medical Clinic

Purpose
Diabetic retinopathy (DR) is a common complication of diabetes mellitus (DM), leading to sight loss if not detected and treated in time. Different models of DR screening (DRS) have been implemented in many parts of the world. In resource poor low and middle-income countries (LMICs) development of a DRS model is complex, due to lack of resources and skilled human resource. Therefore task-shifting and using locally adaptable technology is useful to initiate DRS. The evidence on diagnostic test accuracy (DTA) of DRS utilising retinal photographic studies by non-ophthalmologist personnell in LMIC settings is scarce. This study aims to demonstrate the functional and technical feasibility of using a hand-held non-mydriatic digital camera in a LMIC non-ophthalmic setting. We assessed the DTA of DR detection by general physicians using this method compared to the local clinical reference standard of mydriatic indirect ophthalmoscopy and bio-microscopic examination by a retinologist. This study was a component of a doctoral research project and Ethics approval was obtained from both Ethics Review Committees of the London School of Hygiene & Tropical Medicine-United Kingdom and the National Eye Hospital-Sri Lanka.

Setting/Venue
Nine general physicians from a tertiary level institution in Sri Lanka underwent a competency-based training programme following written informed consent, delivered by two retinologists. The training included the following: capturing retinal fields using a hand-held non-mydriatic fundus camera (Zeiss-Visuscout100®-Germany), identification of signs of DR using images and DR grading according to an adopted classification system based on the United Kingdom - National Screening System. The screening intervention validation study was conducted in a public sector tertiary level out-patient medical clinic in Sri Lanka.

Methods
A sample size of n=506 participants was chosen, in order to estimate the sensitivity within a margin of error 10% (based on 95% confidence intervals [CI]), with an expected sensitivity of 70% and prevalence of moderate non-proliferative DR among people with DM (PwDM) of 20%. This included an additional 25% to take account of ungradable images (i.e., <50% of the retina visible). Interim analysis was undertaken to ascertain the level of ungradable images and the sample size was increased to 700 PwDM. We selected 700 people with diabetes (PwDM) > 18 years of age, not previously screened or treated for DR, presenting at the medical clinic. Two-field retinal imaging was used to capture fundus images before and after pupil dilatation, using a hand-held non-mydriatic digital camera. The images were captured and graded by two trained, masked independent physician graders. The training included the following: capturing retinal photographic studies by non-ophthalmologist personnel in LMIC settings is scarce. This study aims to demonstrate the functional and technical feasibility of using a hand-held non-mydriatic digital camera in a LMIC non-ophthalmic setting, train the graders and assess the DTA of DR detection using non-mydriatic imaging compared to the local clinical reference standard of mydriatic indirect ophthalmoscopy and bio-microscopic examination by a retinologist. This study was a component of a doctoral research project and Ethics approval was obtained from both Ethics Review Committees of the London School of Hygiene & Tropical Medicine-United Kingdom and the National Eye Hospital-Sri Lanka.

Results
Eligible PwDM identified from medical clinical records and response rate was 84.7% (700/826). Mean age of the participants was 60.8 years (SD ±10.08). Ungradable image proportion in non-mydriatic imaging was 43.4% and decreased to 12.8% following pupil dilatation. Sensitivity of detection of any level of DR using non-mydriatic imaging (ungradable accounted as screen positive) was 82.7% (95% CI 78.4-86.5%) in grader-1 and 78.3% (95% CI 73.7-82.5%) in grader-2 and specificity values dropped to 70.4% (95% CI 67.6-73.1%) in grader-1 and 76.2% (95% CI 73.6-78.7%) in grader-2 in non-mydriatic imaging. As a pragmatic approach for a resource poor non-ophthalmic setting, we reported the DTA of DRS using non-mydriatic imaging and dilatation of the pupils of only those who have ungradable images (two-step process). In this sub-analysis, the eye which was ungradable even following mydriasis were considered as screen positives. We derived a sensitivity of referable level of DR 81.1% (95% CI 72.9-87.9%) for grader-1 and 82.1% (95% CI 74.0-88.6%) for grader-2. The specificity values were 95.4% (95% CI 94.2-96.5%) for grader-1 and 97.1% (95% CI 96.1-97.9%) for grader-2 in this approach. We observed an improved level of PPV (59.7-70.2%) and NPV (98.4-98.5%) in this strategy.

Conclusions
In this study we demonstrated that the diagnostic test accuracy of the physician graders was closer to the standard practice of national level screening programs in other settings. We conclude that 2-field retinal imaging using a hand-held digital camera at a medical clinic, by physician graders, with dilatation of pupil of those who have ungradable images, provides a valid modality to identify referable level of diabetic retinopathy. This strategy is an accurate screening method of detection of a referable level in a health care facility-based people with diabetes who are at risk of developing sight threatening diabetic retinopathy.

Financial Disclosure
None to disclose
PEDF receptors and VEGFR-1 are involved in the protection of retinal neurons

**Purpose**
The purpose of this study was to determine regulation of PEDF receptors (PEDFR and Laminin R) and VEGFR-1, by retinal ganglion cells (RGC) under hypoxia, which is a relevant pathological condition in retinal neurodegenerative diseases such as glaucoma or ischemic retinopathies. Changes in the expression of some neuron protective factors, such as PEDF and VEGF, when reducing the expression of PEDF receptors and VEGFR-1. In addition, we have explored the impact of all the receptors on the viability of retinal neuronal cells.

**Setting/Venue**
Department of Ophthalmology and Eye Hospital, Leipzig University, Germany

**Methods**
Using RGC isolated from mice eyeballs and the immortalized retinal cell line R28 as the main research objects. Immunocytochemical Staining, RNA Interference, qPCR, and western blot techniques, were used to detect the expression levels of PEDF-R, Laminin-R and VEGFR-1 under different stimulations. After knocking out PEDF-R, Laminin R and VEGFR-1 genes with interfering RNA, the expression level of neuroprotective factors and anti-apoptotic Bcl-2 family-related factors were detected.

**Results**
The PEDF receptors and VEGFR-1 are co-expressed in RGC and R28 Cells. Complex secretions from Müller cells enhance expression of PEDF receptors and VEGFR-1 in R28 Cells under Hypoxia. The mRNA expression levels of PEDF-R, Laminin R and VEGFR-1 in RGC and R28 cells are significantly increased after exposure to PEDF, VEGF and hypoxia. Expression of pro-survival factors and neuronal survival are under control of PEDF-R, LR and VEGFR-1.

**Conclusions**
Upregulation of PEDF-R, Laminin R and VEGFR-1 under hypoxia sensitizes retinal neurons to interaction with PEDF, which leads to increased cell viability through induction of anti-apoptotic Bcl-2 family members, expression of secretable pro-survival factors, and suppression of apoptosis. Elucidating PEDF-R, Laminin R and VEGFR-1 function and signaling pathways regulating receptor-promoted RGC survival may be helpful in developing more efficient treatment options for retinal neurodegenerative diseases.

**Financial Disclosure**
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# Title
En Face OCT analysis of Paracentral Acute Middle Maculopathy (PAMM)

## Purpose
To describe the pathological findings in the optical coherence tomography (OCT) images using high segmentation technology such as the En Face mode or the OCT – Angiography (OCT – A).

## Setting/Venue
Complejo Asistencial Universitario de León.

## Methods
Case report.

## Results
A 47-year-old caucasian woman presented with acute central scotoma in her left eye (OS) of 7 hours of evolution without other symptoms. Her best corrected visual acuity (BCVA) was 20/20 in the right eye (OD) and 20/70 in the OS. The OCT showed an hyper-reflective lesion in the inner nuclear layer (INL) and the outer plexiform layer (OPL). An identical shaped area was found in the OCT En Face analysis: an hyper-reflective zone in the middle retinal layers and hypo-reflective in the ellipsoid segmentation. In the OCT – A we found the hypo-reflective perifoveal area at the DCP level. Two and a half months later her BVCA was 20/20 with complete subjective resolution of the clinical process. The improvement was remarkable in the complementary tests with resolution of the ischemic area in the funduscopy, the disappearance of the hyperreflective area in the structural OCT (although a slight thinning of the internal layers was observed), and the resolution of the abnormalities in the En Face segmentation. A visual field test was performed to detect possible residual scotoma, however apparently the recovery was complete.

## Conclusions
The En Face OCT technology, although it was initially described in 2006, has experienced a growth in its clinical use in recent times. Instead of employing high-resolution cross-sectional scans, En Face analysis allows the physician to enjoy c-scan images in the coronal plane thanks to the cubic image obtained by a dense raster scan. The advantages of this technology include the ability to locate lesions with great precision in the different layers of the retina using the axial distribution of cross sections and tracking systems that use retinal vessels and other reference points. The role that En face OCT has played in the study of PAMM has made it possible to differentiate 3 types of lesions based on the pathogenetic mechanism of microvascular ischemia of the retina. Our patient presented a fern-like pattern in the context of a PAMM with associated venous occlusion, so it is assumed that an increase of the intraluminal hydrostatic pressure was transmitted from the obstruction to the venous drainage area, which clinically translated into a wide zone of parafoveal retinal whitening and an acute onset paracentral scotoma. The visual prognosis of PAMM is usually good. To date, the majority of bibliographic publications report patients with partial recovery of the scotoma in the visual field, as well as stable retinal changes during the months following the acute phase. These changes are atrophy with attenuation of INL and OPL. On the other hand,
Intravitreal aflibercept in routine clinical practice: 12-month results from the French cohort of treatment-naive patients with macular edema secondary to retinal vein occlusion in the AURIGA study

Abstract

Purpose

The aim of the 24-month AURIGA study is to evaluate the clinical outcomes of intravitreal aflibercept (IVT-AFL) in patients with macular edema secondary to retinal vein occlusion (RVO) or diabetic macular edema (DME) in routine clinical practice. Patients were enrolled from 11 countries, including France. The results of the 12-month analysis in treatment-naive patients with macular edema secondary to RVO who were enrolled in France are presented here.

Setting/Venue

AURIGA (NCT03161912) is an ongoing, prospective, multicenter, observational study evaluating IVT-AFL in patients with macular edema secondary to RVO or DME. This analysis summarizes the outcomes for the treatment-naive cohort of patients with RVO in France.

Methods

Treatment-naive patients (aged ≥18 years) with macular edema secondary to RVO (central RVO [CRVO] and branch RVO [BRVO; also including patients with hemicentral RVO]) were enrolled from April 2018 to January 2019. Decisions regarding IVT-AFL treatment were made at the discretion of the prescribing physician, according to their medical practice. The primary endpoint was the change in best-corrected visual acuity (BCVA; Early Treatment Diabetic Retinopathy Study [ETDRS] letters) from baseline to Month (M)12. Secondary endpoints included the proportion of study eyes with BCVA gains and losses (≥5, ≥10, and ≥15 letters), change in central retinal thickness (CRT) from baseline, number of IVT-AFL injections, mean duration of treatment intervals, and proportion of patients with macular edema on optical coherence tomography. Safety was also evaluated throughout the study. Patients who received at least one IVT-AFL injection and had at least one post-initial observation available were included in the full analysis set.

Results

Of 138 treatment-naive patients (mean age: 67.7 years; female: 50%; CRVO: n=62; BRVO: n=76), 76% (105/138 patients) completed 1 year of treatment. Overall median duration from diagnosis to IVT-AFL treatment was 0.3 months (range 0–53.5). By M12, mean improvements in BCVA (95% CI) were +13.6 (7.8, 19.3) and +14.6 (11.5, 17.6) letters in CRVO and BRVO patients, respectively (baseline±SD: 41.1±24.1 and 60.6±14.5); 98% of all patients had BCVA decreases <15 letters and 46% had BCVA improvements ≥15 letters. At M12, mean CRT decreased by -324.6 (-388.5, -260.8) μm (CRVO; baseline: 672.9±199.7), and -232.7 (-271.3, -194.1) μm (BRVO; baseline: 522.8±157.9). The proportion of RVO patients with macular edema decreased from 90% at baseline to 33% at M12. The mean number of IVT-AFL injections was 4.4±1.2 by M6 and 6.6±2.6 by M12 (53% received ≥5 injections by M6; 52% received ≥7 injections by M12). By M12, the last completed treatment interval (for patients who received ≥2 IVT-AFL injections) was ≥10 weeks in 31% (CRVO) and 65% (BRVO) of patients and ≥12 weeks in 21% (CRVO) and 50% (BRVO). Adverse events were consistent with the known safety profile of IVT-AFL. No cases of intracocular inflammation, retinal vasculitis, or endophthalmitis were reported.

Conclusions

In treatment-naive patients with macular edema secondary to RVO in the AURIGA study, 12-month treatment with IVT-AFL was associated with functional and anatomic improvements in routine clinical practice in France. The magnitude of BCVA gain and CRT improvement at 12 months was comparable to that achieved in interventional studies. No new safety findings were identified. The AURIGA study builds on the wealth of real-world evidence supporting the effectiveness and safety of IVT-AFL as evaluated in 22 published Bayer-sponsored studies in routine clinical practice treating more than 18,000 patients across 24 countries in multiple indications.

Financial Disclosure

Audrey Giocanti-Aurégan: Clinical investigator; Bayer Sylvia Nghiem Buffet: Clinical investigator; Bayer Maté Streho: Consultant: Alcon, Bayer, Novartis, and Quantel Medical Laurent Velasque: Consultant: Alcon, Bayer, and Novartis; Clinical investigator: Bayer Agnès Glacet-Bernard: Clinical investigator; Bayer Helmut Allmeier: Employee: Bayer Consumer Care AG, Basel, Switzerland Tobias Machewitz: Employee: Bayer AG, Berlin, Germany Kay D. Rittenhouse: l

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Intravitreal fluocinolone acetonide implant 0.19 mg (ILUVIEN®) for Diabetic Macular Edema: long term data of efficacy and safety from Hospital Pedro Hispano, Portugal

Purpose
Diabetic Macular Edema (DME) is the main cause of vision impairment among diabetic patients. The fluocinolone acetonide (FAc, 0.19 mg, ILUVIEN®) intravitreal implant is a therapy option for persistent and recurrent DME, releasing a sustained microdose of FAc for up to 3 years. The aim of the present study is to evaluate the visual and anatomical outcomes and also to draw a long-term safety profile of intravitreal FAc implant for the treatment of DME.

Methods
Retrospective study of 109 eyes from 76 patients with persistent DME treated with FAc intravitreal implant 0.19 mg. Demographic data of the patients, best corrected visual acuity (BCVA), central retinal thickness (CRT), duration of DME, number of previous intravitreal anti-VEGF or short-acting steroid injections and intraocular pressure (IOP) prior to FAc implant placement were recorded at baseline. BCVA, CRT and IOP were evaluated at month 1, 3 and then quarterly, and a comparison of these parameters was established over 3 years. The percentage of patients that improved or stabilized BCVA was ascertained. Adjuvant intravitreal therapies and IOP-lowering drugs needed throughout study were also recorded. Percentage of patients that performed FAc implant reinjection 36 months after the first one was recorded.

Results
The average follow-up period was 26.5 ± 10.8 months. At baseline, the mean age was 68.5 ± 8.8 years. Thirty-eight patients were men. At baseline, 30.5% of the eyes were phakic. The mean duration of DME was 4.6 ± 1.9 years. All eyes received intravitreal injections of anti-VEGF and/or short-acting steroids prior to the FAc implant, with an average number of 6.9 ± 4.8 anti-VEGF injections and 2.1 ± 1.5 short-acting steroids injections. The mean baseline BCVA was 49.3 ± 12.3 early treatment diabetic retinopathy study (ETDRS) letters, with an average increase of +9.2 ETDRS letters observed in the last observation, which was statistically significant (p<0.001). Eighty-seven percent of the patients maintained or improved BCVA compared to baseline. The mean CRT significantly decreased by 156.4 μm from the baseline 502.0 ± 176.1 μm (p<0.001). Throughout the study, 34.1% of the eyes required adjuvant intravitreal injections. Thirty-four percent of the eyes registered an IOP increase related to FAc implant requiring IOP-lowering medication and 14% of the eyes underwent selected laser trabeculoplasty (SLT). Eighty-one percent of the baseline phakic eyes underwent phacoemulsification surgery during the follow-up period. After 36 months post-FAc implant, 35.6% of the eyes underwent FAc reinjection.

Conclusions
This study demonstrates that FAc intravitreal implant is a valid treatment option in chronic and recurrent DME, with positive anatomical and functional responses maintained for a long-term period. The majority of patients who reached 36 months of follow-up after FAc implant did not need retreatment after this period. IOP monitoring remains essential in these patients, as well as cataract progression vigilance. Safety parameters and lateral effects were known, well managed and controlled during the follow-up period.

Financial Disclosure
No financial relations.
Evaluation of Peripapillary Perfusion alterations in Diabetic Retinopathy using OCT Angiography

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Purpose
To evaluate peripapillary region perfusion changes during different stages of diabetic retinopathy (DR) using Optical coherence tomography angiography (OCTA).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
Thirty-six eyes from 36 diabetic patients and 36 age-matched healthy controls were included in the study. After a complete medical examination, Spectral Domain OCT and OCT-A exams were performed using Optovue RTVue XR Avanti, AngioVue. The scan area used was 4.5 × 4.5 mm centered on the optic nerve head for measurement of Radial Peripapillary Capillaries (RPC) vessel densities including: whole image (wi), inside disc (id) and peripapillary (pp). Peripapillary Retinal Nerve Fiber Layer (RNFL) thickness was also evaluated in all subjects.

Results
The study population was divided into three groups: Group 1 of 13 eyes without DR, Group 2 of 11 eyes with minimal to moderate non-proliferative DR, Group 3 of 12 eyes with severe non-proliferative DR and proliferative DR and 36 age-matched healthy subjects (control group). The mean age was 51.88 ± 7.03 in control group, 48.78 ± 11.79 in group 1, 50.79 ± 9.02 in group 2, 52.00 ± 9.33 in group 3. The sex ratio was 1.15 in each group. A statistically significant decrease in all peripapillary vascular densities with increasing of DR severity was noted (From group 1 to group 3) (P <0.001). No significant difference in RNFL thickness was found between the 4 groups (p=0.34). There was a significant negative correlation between DR severity and peripapillary vascular densities (r=-0.54, p <0.001). However, no statistically significant association was found with RNFL thickness (r=0.008, p = 0.4). There was a significantly positive correlation between RPC vascular density and RNFL thickness only in group 2 (r = 0.72, P <0.001) (Spearman rank correlation analysis).

Conclusions
OCT-A is a non-invasive imaging modality that may be useful to evaluate peripapillary vascular network damages due to DR. Correlation between DR and peripapillary vascular alterations can be potentially of great help monitoring DR progression.

Financial Disclosure
The authors declare no conflict of interest.
Title
Pathophysiological mechanisms of the influence of oxidative stress on the pathogenesis of the proliferative stage of diabetic retinopathy. Preys N, Savitsky I.

Purpose
To investigate the links of the pathogenesis of the proliferative stage of diabetic retinopathy and, based on this, to optimize metabolic correction in type II sugar.

Setting/Venue
Modeling type II diabetes mellitus and its complications -diabetic retinopathy in laboratory Wistar rats

Methods
Modeling type II diabetes mellitus and its complications -diabetic retinopathy in laboratory Wistar rats by intraperitoneal injection of streptozotocin (Sigma, USA) at a dose of 70 mg/kg. A single administration of 3.5 μg of recombinant human VEGF 165, which allows to obtain a stable pronounced for 7 days.

Results
In the course of the study, key points were highlighted. Study of the roles for the lipid peroxidation system in experimental diabetic retinopathy in the proliferative stage. Determination of the balance of pro- antioxidant system’s during hipoxia, neoangiogenesis and the development of metabolic changes in diabetic retinopathy. Advancement of the dynamics of markers of hipoxia endothelial dysfunction in the pathogenesis of proliferative diabetic retinopathy. Determination of the informatrice value of the shifts of the nitric oxide cycle and its derivatives in the proliferative stage. Study of the development of endogenous intoxication and its relationship with pathological changes in proliferative diabetic retinopathy. Determination of the dynamic of pro-and anti-inflammatory cytokines in the pathogenesis of proliferative diabetic retinopathy. Determination of the participation of oxidative stress in the regulation of apoptosis and proliferation.

Conclusions
Modeling experimental diabetic retinopathy and analysis of these biochemical markers is an important component both of understanding the pathogenesis links of diabetic retinopathy and for further substantiated testing of corrective agents

Financial Disclosure
no companies
Are there any differences in treatment outcomes of anti-vascular endothelial growth factor monotherapy compared to diode laser therapy in eyes with aggressive posterior retinopathy of prematurity?

**Purpose**

Comparison of anti-vascular endothelial growth factor (VEGF) monotherapy with anti-VEGF plus diode laser therapy in eyes with aggressive posterior retinopathy of prematurity (AP-ROP).

**Setting/Venue**

Retrospective cross-sectional study / Health Sciences University, Antalya Training and Research Hospital, Ophthalmology Clinic.

**Methods**

Four hundred forty-five patients who were followed up and treated for retinopathy of prematurity (ROP) in our clinic between 2014 and 2020 were retrospectively investigated. Seventy-four eyes of 37 patients diagnosed with AP ROP and treated were included in the study. 49 eyes treated with anti-VEGF agent injections monotherapy in AP ROP treatment were included in the first group. In the second group, 18 eyes that received injection therapy and diode laser treatment were included. The clinical findings of the two groups were investigated and the treatment results of the two groups were compared.

**Results**

ROP findings didn’t recur in the second group (26.86%). In the first group, 30 eyes (44.77%) recovered with a single injection. Recurrence was observed in 19 eyes in the first group. Recurrence in 6 eyes (8.95%) in the first group improved with the second injection. In the first group, when the ROP finding has recurred in 11 eyes, fibrotic activity was observed and laser therapy was added to the second injection treatment. In addition, 8 eyes (11.94%) with recurrence in the first group improved when the laser was applied with the second injection. In the first group, a second recurrence occurred in 5 eyes despite the injection and laser treatment. While 2 of these 5 eyes were treated with reinjection and laser therapy, pars plana vitrectomy was performed in 3 eyes (4.47%) due to complications related to AP ROP. In the first group, there was a sequela in 3 eyes (4.47%) because the patients couldn’t be followed up due to other health problems. Despite this, the macula of these eyes wasn’t detached and their visual axes were open in their last examination. In the comparison of treatment results of both groups, no difference was found between the two groups (P=0.181)

**Conclusions**

It was observed that most of the eyes with AP ROP improved with the anti-VEGF agent injection monotherapy. However, the appearance of fibrotic activity in eyes with AP ROP may indicate the necessity of diode laser therapy.
### Title
Effectiveness and safety of intravitreal injection of Ranibizumab in Indian patients with visual impairment due to diabetic macular edema: A multi-center, open-label, observational study

### Purpose
Diabetic macular edema (DME) is one of the most common retinal vascular disease, which is caused by diabetic retinopathy. The visual impairment in diabetic retinopathy is mainly due to macular edema, which arises from increased permeability of the inner blood-retina barrier resulting in the accumulation of fluid in the retina, leading to deterioration in detailed vision. Vascular endothelial growth factor (VEGF) plays an important role in the development of DME. Ranibizumab, a humanized anti-VEGF monoclonal antibody fragment, has exhibited halting the growth of choroidal neovascularization lesions, reduce vascular leakage, and effectively controlling the macular edema in patients with DME. Clinical trials till date have affirmed the efficacy of ranibizumab in patients with DME, due to which it is already authorized in India since 17 July 2014. Hence, current study was done as part of the regulatory requirement to collect real-world effectiveness, safety, and tolerability data of ranibizumab in the management of DME.

### Setting/Venue
This was a non-interventional, prospective, observational, open-label study conducted across 10 centres in India for a period of 48 weeks. Participants included in the study were adult outpatients (men/women ≥18 years old) with decreased vision due to macular edema secondary to type 1/type 2 diabetes mellitus (DM); vision impairment due to DME; unsatisfactory outcomes from the prior DME treatment (Snellen Equivalent scores ranging from presence of perception of light [PL+] to 6/9 for the affected eye), and who were prescribed ranibizumab by their treating ophthalmologist in adherence with the local summary of product characteristics and prescribing information.

### Methods
Overall 125 patients were treated with intravitreal injection of ranibizumab (Accentrix®) 0.5 mg (0.05 mL volume) at baseline and then after every 4 weeks, for a duration based on clinical judgement of the treating ophthalmologist substantiated by the changes seen in visual acuity and optical coherence tomography (OCT). Injection was repeated as per the visual stability criteria for the prior DME treatment (Snellen Equivalent scores ranging from presence of perception of light [PL+] to 6/9 for the affected eye), and who were prescribed ranibizumab by their treating ophthalmologist in adherence with the local summary of product characteristics and prescribing information. Primary effectiveness endpoint was mean change from baseline in early treatment diabetic retinopathy study (ETDRS) letters in best-corrected visual acuity (BCVA) at 48 weeks. Secondary effectiveness endpoints included visit wise changes in the ETDRS letters in BCVA from the baseline; number (%) of patients gaining ≥15 ETDRS letters (or 3 ETDRS rows) at weeks 12, 24, and 48; change from baseline in the central retinal thickness (CRT) on OCT; progression of the avascular area since baseline assessed from the foveal avascular zone (FAZ) using fluorescein angiography; and change from baseline in the number (%) of patients with retinal hemorrhage determined by fundus photography. Safety was assessed through the adverse events (AEs), serious AEs (SAEs), and treatment-emergent AEs (TEAEs) reported during the study period.

### Results
Of the 125 patients, 68 (54.0%) patients completed the study. Mean (±standard deviation [SD]) age of the population was 59.6±8.28 years and ~65% were men. Each patient on an average received 3.5 intravitreal injections over 48 weeks. For primary effectiveness analysis, there was statistically significant improvement in ETDRS letters post 48-week treatment (change from baseline: 6.8±17.38, p=0.0019). A significant improvement (p<0.0001) was seen in this parameter across all study visits. Number (%) of patients gaining ≥15 ETDRS letters (or 3 ETDRS rows) at weeks 12, 24, and 48 were 26 (28.6%), 16 (22.5%), and 19 (27.5%), respectively. A significant (p<0.0001) and consistent decrease in mean CRT was observed from baseline (433.1±146.66 µm) till week 48 (307.2±122.65 µm). No statistically significant change was observed in the progression of avascular area over the treatment period (p>0.05). Number (%) of patients with retinal hemorrhage decreased from 80 (64.0%) at baseline to 24 (34.8%) at 48 weeks. Majority of patients (110 [88%]) did not experience any AEs. Five patients (4.0%) reported six SAEs with no suspected relation to ranibizumab/ocular injection. Most frequent TEAEs were vitreous hemorrhage (2.4%) and conjunctivitis (1.6%).

### Conclusions
This was the first real-world study conducted in the Indian population with DME. The ranibizumab 0.5 mg intravitreal injection was found to be effective in improving the visual acuity and the treatment was found to be well tolerated among the Indian patients with visual impairment due to DME. The overall findings were corresponding to the efficacy findings from the clinical trials and were consistent with the prescription details as well as the AEs reported in the summary of product characteristics of ranibizumab.
SAVE II A: Extension of the grading protocol for clinically significant diabetic macular edema using optical coherence tomography angiography

**Purpose**
The purpose of the study was to extend the well-established SAVE II protocol for clinically significant diabetic macular edema (CSME) using swept-source optical coherence tomography angiography imaging (SS-OCTA). OCTA metrics were evaluated for each SAVE II edema type respectively.

**Setting/Venue**
Patients with the diagnosis of diabetic macular edema (DME), who presented between 2018 and 2021 to the outpatient clinic at the Department of Ophthalmology, Kepler University Clinic Linz (Linz, Austria) were included in the prospective analysis, regardless of prior treatment.

**Methods**
Visual acuity testing was performed according to the Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol. Optical coherence tomography (OCT), fluorescence angiography (FA) and SS-OCTA imaging (Plex Elite 9000, Zeiss Meditec) were performed. SS-OCTA imaging was performed with a 6 mm x 6 mm, 3 mm x 3 mm and 15 mm x 9 mm field of view. OCT and FA imaging were evaluated according to the established SAVE II protocol by Bolz et al. FAZ size, vessel and perfusion density of the superficial and deep capillary plexus based on OCTA imaging were calculated for each SAVE II edema type respectively. Further the SAVE II grading was performed using solely OCT and SS-OCTA imaging by two blinded investigators (D.P., M.C.). Results were compared between the standard SAVE II protocol (OCT and FA imaging) and the SAVE II A protocol (OCT and OCTA imaging).

**Results**
45 eyes of 45 patients were included in the study. We included 8 patients with SAVE II edema type one, 13 patients with edema type two, 14 patients with edema type three and 10 with edema type 4 using the SAVE II grading protocol. Using the SAVE II A protocol, based on OCTA imaging, the patients were graded the same as by the standard SAVE II protocol. There were no statistically significant differences for calculated OCTA metrics between the SAVE II edema types. Detailed results of the OCTA metrics for each SAVE II group will be presented at the conference.

**Conclusions**
The SAVE II A grading protocol of CSME was extended using the image technology of OCTA. The novel imaging technique of OCTA is a valid tool for the grading protocol of SAVE II and may supersede the image technology of fluorescein angiography in the future, due to it's non invasive technology and high resolution.

**Financial Disclosure**
There was no financial support to conduct this study. None of the authors has a conflict of interest to declare.
Comparison between early and late switch to fluocinolone acetonide implant in DME based on prognostic biomarkers assessed by OCT

**Purpose**
Diabetic Macular Edema (DME) can result in permanent vision loss. Early intervention leads to greater preservation of visual function, as it reduces the development of chronic retinal damage. ILUVIEN® intravitreal implant (fluocinolone acetonide, FAc 0.2 μg/day) is indicated for the treatment of persistent and recurrent DME. Optical coherence tomography (OCT) offers cross-sectional imaging of the retina and it facilitates measuring specific morphologic features of this structure, offering both quantitative and qualitative information in a non-invasive and repeatable way. The purpose of this study is to analyze the effects of early and late switching to ILUVIEN® implant in patients with DME unresponsive to previous treatments, in relation to the inflammatory OCT retinal features.

**Setting/Venue**
Retrospective, non-randomized analysis of persistent DME eyes, evaluating the response to an early or late switch to ILUVIEN® at Centro Hospitalar Universitário do Porto, Portugal.

**Methods**
Retrospective observational analysis of 45 eyes/ 35 patients, with 3-year follow-up after ILUVIEN® implantation. The eyes were divided into 2 groups based on the number of previous intravitreous treatments: group A included 21 eyes that received less than 6 previous injections (i.e., early switch); and group B included 24 eyes that received ≥ 6 injections (i.e., late switch). The demographic data of the patients as well as duration of DME and number of prior intravitreal (IV) injections were recorded at baseline. Best Corrected Visual Acuity (BCVA) and central subfoveal thickness (CST) were recorded at baseline and then evaluated at month 6, 12, 24 and 36. All patients underwent OCT scanning before and after implantation of FAc, in all time-points, with 7 parameters being taken into account: (1) quantitative measurement of the CST; (2) the size of the intraretinal cysts (IRC); (3) the visibility of the external limiting membrane (ELM) and the ellipsoid zone (EZ) at the fovea; (4) the presence of disorganization of retinal inner layers (DRIL); (5) the presence of subretinal fluid (SF); (6) the presence and the number of hyperreflective foci (HF); and (7) the vitreoretinal relationship.

**Results**
At baseline, mean age was 70.7 ± 5.9 and 70.0 ± 9.0 years (A and B, respectively, p=0.6903) and average DME duration was 3.9 ± 0.9 and 4.6 ± 1.5 years (p= 0.0416). Before ILUVIEN®, all eyes received IV injections (anti-VEGF: 2.5 ± 1.6 (A) and 7.0 ± 5.0 (B), p=0.001; shorter-action steroids: 2.5 ± 1.9 (A) and 3.0 ± 12.9 (B), p=0.0337). There was an average increase of +19.2 and +8.8 ETDRS letters observed 3 years after ILUVIEN®, in group A and B, respectively (p=0.005). The mean CST decreased by 234.1 μm (A) and 132.0 μm (B) from the baseline to 36 months (p=0.005). After ILUVIEN®, presence of SF significantly decreased by month 6 (↓75% [A] and ↓49.5% [B]) and stabilized until end of follow-up. Same pattern was seen with EZ/ELM disruption decrease (↓17.7% [A] and ↓16.7% [B]) and IRC decrease (↓38.1% [A] and ↓29.0% [B]). Similar trends, without statistical significance, were observed in presence of HF and DRIL, in both groups. Staging of diabetic maculopathy, according to ESASO classification went from 24% at baseline to 95 % of eyes with early DME at 36 months in group A and from 28% to 80% in group B.

**Conclusions**
This analysis suggests that ILUVIEN® implant is effective in the improvement of various OCT parameters, such as decrease in CST, decrease in cysts, improvement in EZ / ELM disruption and decrease in the presence of SF with higher improvements in eyes that performed earlier switch to ILUVIEN®. It is also important to mention that in eyes that made earlier switch, there was a greater recovery of the anatomy and function of the retina to an earlier stage of the disease. There was observed notorious differences in terms of anatomical gains and statistical differences in functional gains between both groups, which may suggest that eyes that performed late switch could already have irreversible retinal damage. These results may suggest that earlier treatment with FAc implant may benefit patients with recurrent and persistent edema.

**Financial Disclosure**
The authors have nothing to declare.
Prevalence of vitreoretinal interface abnormalities in macular edema associated with retinal vein occlusion

**Purpose**
To describe vitreoretinal interface abnormalities detected by SD-OCT in eyes with macular edema associated with retinal vein occlusion (RVO).

**Setting/Venue**
Hedi Raies Institute, Ophthalmology Department B.

**Methods**
A total of 42 eyes (40 patients) with macular edema associated with RVO and treated with intravitreal bevacizumab injection were retrospectively analyzed on spectral-domain optical coherence tomography (SD-OCT) initially and at 24 months.

**Results**
The mean age of patients was 56 years and the mean number of injections was 7.49 at 24 months. Using SD-OCT, vitreoretinal interface abnormalities were detected in 31 eyes (73.8%) and were significantly more frequent in central vein occlusion ($P<0.001$). There was vitreomacular adhesion without traction in 3 eyes (7.1%) and with traction in 1 eye (2.4%). Epiretinal membranes were present in 25 eyes (59.5%) and were globally adherent in 19 eyes (70.4%) and focally adherent in 4 eyes (14.8%). A lamellar macular hole was present in 3 eyes and a full-thickness macular hole in one eye.

**Conclusions**
Vitreoretinal interface abnormalities seem to be frequent in macular edema associated with RVO and treated with intravitreal bevacizumab.

**Financial Disclosure**
None
Optical Coherence Tomography Characteristics of Responses to Intravitreal Bevacizumab in Diabetic Macular Edema

Purpose

To investigate factors associated with responses to intravitreal bevacizumab (IVB) in diabetic macular edema (DME) by spectral domain optical coherence tomography (SD-OCT).

Setting/Venue

Ankara Yildirim Beyazit University, Department of Ophthalmology, Ankara, Turkey
Ankara City Hospital, Ophthalmology Clinic, Turkey

Methods

In this retrospective study, patients with DME receiving intravitreal anti-VEGF therapy with PRN protocol after three months of loading therapy (1.25 mg bevacizumab/0.05 mL) were evaluated. Best corrected visual acuity (BCVA, Logmar), SD-OCT images were assessed before injection and at 3 months after injection. Central macular thickness (CMT), type of edema, number of hyper-reflective retinal spots (HRS, 0-20: mild, 20-40: moderate, above 40: advanced), extent of disorganization of inner retinal layers (DRIL), subretinal fluid (SRF), external limiting membrane irregularity, ellipsoid zone irregularity and vitreomacular interface were evaluated. Persistence of macular edema after three loading doses was evaluated as non-response to treatment. Patients who responded to the treatment were classified as group 1, and those who did not respond as group 2.

Results

A total of 37 eyes of 37 patients (22 eyes in group 1 and 15 eyes in group 2) were evaluated. The mean age of the patients was 60.7 ± 8 (49-78), the female-to-male ratio was 16/21 (43% / 57%). There was no significant difference between two groups in terms of age and gender. (p> 0.05). The mean follow-up period was 10.6 ± 5 (6-24) months. The mean baseline CMT and BCVA values were not different between the Group 1 and 2 (p>0.05). The mean BCVA was 0.31, 0.35, 0.34 in Group 1 and 0.25, 0.27, 0.24 in Group 2 at baseline, 1st month and 3rd month, respectively (p> 0.05 for all values). The mean CMT at baseline was 497 µm (320-782) in Group 1 and 524 µm (370-675) in Group 2. The mean CMT at 3 months were 352 (241-575), 432 (262-627) µm, in Group 1 and Group 2 respectively (p = 0.044). Diffuse macular edema and SRF were observed more in Group 1 than Group 2, which was not statistically significant (p> 0.05). In both groups, the SRF and HRN were tend to be lower after treatment but statistically insignificant (p> 0.05).

Conclusions

IVB treatment was associated with resolution of DME. Baseline OCT images can help us to determine prognosis in obtaining response to IVB. Nevertheless, we can get a better response to IVB in the presence of diffuse edema and subretinal fluid in diabetic macular edema.

Financial Disclosure

None of the authors have reported funding/support.
Acute macular neuroretinopathy following SARS-CoV-2 infection

**Purpose**
The ongoing pandemic of COVID-19 disease has been associated with variable ocular manifestations. An inflammatory and pro-coagulant state has been associated to COVID-19 disease, however its effect over the retinal vascular system has not been completely elucidated. There are some cases of retinal venous occlusion and retinal artery occlusion described in this context. This case report aims to describe an atypical case of acute macular neuroretinopathy (AMN) following SARS-CoV-2 infection.

**Methods**
Case report of a patient seen in the emergency department, with sudden onset of central scotomas and recent SARS-CoV-2 infection, who underwent a complete ophthalmological evaluation, which included multimodal evaluation of the posterior pole with retinography, spectral domain optical coherence tomography, angiography fluorescein, visual field and electrophysiological study.

**Results**
A 66-year-old woman presented to the emergency department with complaints of vision loss and sudden onset of central scotomas in her left eye (LE) for the past 24 hours. Her BCVA was “counting fingers” in the LE. Fundus examination of the LE revealed hypopigmented lesions involving the superior macula. SD-OCT imaging of the LE demonstrated hyperreflective band lesions at the level of the INL and OPL corresponding to the hypopigmented lesions observed. The ORL and RPE appeared completely normal. The patient had an innocent medical history with the exception of having a recent history of SARS-CoV2 infection one month ago. The diagnosis of AMN was suspected and the patient was followed without treatment. A larger study of potential causes was conducted, without abnormalities. The patient reported a progressive improvement in visual acuity about 48 hours after the acute episode. At one-month follow up, she stated a complete recovery of visual acuity and absence of scotomas. Her BCVA was 10/10 bilaterally and fundus examination demonstrated regression of the hypopigmented lesions. At this time, the SD-OCT showed INL thinning in areas where the hyper-reflective bands were previously seen. No recurrence was detected in subsequent follow-up examinations.

**Conclusions**
Thought the mechanism of AMN has been reported to be primarily due to ischemia of the capillary plexus, there is still much to be understood. The suspect of AMN raises a wide differential diagnosis that requires a systemic and pertinent workup to exclude potential infectious, inflammatory, vascular, toxic, and iatrogenic causes. A history of recent viral infection has also been associated with AMN. In this case report, we present a possible association between a SARS-CoV2 infection and AMN in a woman without any risk factors. Further studies should be achieved to better understand this association.
**Title**

Brolucizumab for the treatment of visual impairment due to diabetic macular edema: 52-week results from the KESTREL and KITE Phase III studies

**Purpose**

To present the 52-week results from KESTREL and KITE, two prospective Phase III studies evaluating the efficacy and safety of brolucizumab versus aflibercept for the treatment of patients with visual impairment due to diabetic macular edema (DME).

**Setting/Venue**

Patients were enrolled from 36 countries, across 197 sites.

**Methods**

KESTREL (NCT03481634) and KITE (NCT03481660) are two, 2-year, ongoing, double-masked, randomized, active-controlled, multicenter studies. Adults (≥18 years of age) with type 1 or type 2 diabetes mellitus, visual impairment due to DME with a best-corrected visual acuity (BCVA) score between 78 to 23 ETDRS letters, and DME involving the center of the macula with a central subfield thickness (CSFT) ≥320 μm on SD-OCT in the study eye at screening were included. In KESTREL, patients were randomized 1:1:1 to brolucizumab 3 mg, brolucizumab 6 mg or aflibercept 2 mg; in KITE, patients were randomized 1:1 to brolucizumab 6 mg or aflibercept 2 mg. The brolucizumab groups received 5 loading doses every 6 weeks (q6w) followed by q12w dosing in the first year, with an option to adjust to q8w if disease activity is identified at those pre-specified visits. The aflibercept group received 5 loading doses monthly followed by a fixed q8w dosing. The primary endpoint was the change from baseline in BCVA at Week 52; secondary endpoints included the proportion of brolucizumab patients maintained at q12w dosing up to Week 52 and the change from baseline in CSFT.

**Results**

In both studies, the primary objective was met with brolucizumab 6mg achieving non-inferiority (margin of 4 letters) to aflibercept in change of BCVA from baseline at Week 52 (KESTREL, letters: brolucizumab 6mg +9.2 vs aflibercept +10.5, mean difference -1.3 [95% CI, -2.9, 0.3], p<0.001; KITE, letters: brolucizumab 6mg +10.6 vs aflibercept +9.4, mean difference +1.2 [95% CI, -0.6, 3.1], p<0.001). Brolucizumab 3mg did not demonstrate non-inferiority in BCVA versus aflibercept in KESTREL. More than 50% of brolucizumab 6mg patients were maintained on a q12w dosing interval through Week 52, immediately after the loading phase. For the change of CSFT from baseline over the period Week 40 through Week 52, significant improvements were achieved with brolucizumab 6mg in both studies; in KITE, brolucizumab 6mg showed superior improvements in change of CSFT over the period Week 40 through Week 52 versus aflibercept (p=0.001). At Week 52, more patients treated with brolucizumab 6mg achieved a CSFT <280μm than with aflibercept (KESTREL: 54.0% versus 40.1%; KITE: 57.5% versus 41.4%). Fewer brolucizumab 6mg patients had SRF and/or IRF versus aflibercept at Week 52 (KESTREL: 60.3% versus 73.3%; KITE: 54.2% versus 72.9%). Brolucizumab demonstrated an overall well-tolerated safety profile.

**Conclusions**

Results from the KESTREL and KITE studies show that brolucizumab 6 mg achieved robust vision gains and improved anatomical outcomes with more than 50% of DME patients maintained on a q12w treatment interval after loading through Week 52, and demonstrated an overall well-tolerated safety profile.

**Financial Disclosure**

Advisor: Alcon, Allergan, Bayer, Genentech, Novartis, Oculis, Roche, Thea, Zeiss
How Covid 19 impacts the patients with diabetic macular edema during the lockdown in Morocco

**Purpose**
In this study, we aim to assess the impact of the duration of the lockdown on patients with diabetic macular edema and how it affects the visual acuity and macular thickness.

**Setting/Venue**
The World is experiencing a viral onslaught of COVID-19 caused by SARS-CoV-2. In an attempt to stem the spread of the virus a lockdown was decided in Morocco from the start of the pandemic. These restrictions led to cessation of intravitreal injection administration from March 2020 to June 2020.

**Methods**
This retrospective study included patients with diabetic macular edema planned for intravitreal injections before the lockdown (Before 19th of March 2020). Data included demographics, corrected distance visual acuity (CDVA), and central macular thickness on Optical Coherence Tomography (OCT) before the lockdown and three months later.

86 patients were studied, 50 (58.1%) patients were males, and the mean age was 61.3 (± 11.7) years. There were 135 eyes, 98 (56.9%) were bilateral eyes from 49 patients. Mean duration of delay in the planned injection was 91.8 (± 32.4) days. The last anti-VEGF agent used prior to the lockdown visit was: bevacuzimab (Avastin®) (96.2%), ranibizumab (Luncentis®) (2.2%), and dexamethasone (Ozurdex®) (1.4%). The average BCVA at the pre-lockdown was 3/10. Three months later, the average BCVA was 2/10. The mean macular thickness before the lockdown was 360 microns. It increased to 391 micros after the 3 months delay. 6 patients had an incidence of vitreous hemorrhage, and 3 patients had neovascularization of the iris.

**Conclusions**
The duration of lockdown is directly proportional to the worsening of diabetic macular edema. Such increase in these complications will put additional load on overburdened healthcare system.

**Financial Disclosure**
no financial interest
Title
Real-world evaluation of the effectiveness and safety of Ranibizumab intravitreal injection in Indian patients with visual impairment due to diabetic macular edema: Sub-group analysis

Purpose
Recent Indian survey reported a 16.9% prevalence of diabetic retinopathy among the individuals with diabetes mellitus (DM). Diabetic macular edema (DME) is evidently the most common cause of moderate vision loss in patients with diabetic retinopathy. Vascular endothelial growth factor (VEGF) plays an important role in the pathogenesis of DME, therefore anti-VEGF therapy is considered as current standard of care. Based on clinical trial outcomes, an anti-VEGF monocolonal antibody fragment, ranibizumab, has already been authorized in India since 17 July 2014 for the management of DME. Moreover, as part of the Indian regulatory requirement, a 48-week real-world study was conducted to evaluate effectiveness, safety, and tolerability of ranibizumab in patients with DME. Corresponding with the clinical trial findings, the real-world study demonstrated improved visual acuity with ranibizumab 0.5 mg intravitreal injection, which also was generally well tolerated in these patients. Evidence suggests that several factors—age of the patients, their HbA1c levels, smoking status to list a few—can influence the anti-VEGF treatment outcomes. Thus, the above-stated real-world study further analysed the treatment outcomes of ranibizumab in various subgroups of the study population. The present abstract focuses on the trends observed in various subgroups.

Setting/Venue
This 48-week, non-interventional, prospective, observational, open-label study was conducted at 10 centres across India between 29 July 2015 and 31 December 2017. Adult outpatients (≥18 years old) of either gender were included if they fulfilled the following criteria: decreased vision due to macular edema secondary to type 1/2 type 2 DM, vision impairment due to DME, unsatisfactory outcomes from prior DME treatment (Snellen Equivalent scores ranging from perception of light [PL] to 6/9 for the affected eye), and who were prescribed ranibizumab by their treating ophthalmologist in adherence with the local summary of product characteristics and prescribing information.

Methods
Overall, 125 patients were treated with intravitreal injection of ranibizumab (Accentrix®) 0.5 mg (0.05 mL volume) at baseline + every 4 weeks, for a duration as per clinical judgement of the treating ophthalmologist substantiated by the changes seen in visual acuity and optical coherence tomography (OCT). The study evaluated treatment effectiveness based on change from baseline in the following outcomes: early treatment diabetic retinopathy study (ETDRS) letters in best-corrected visual acuity (BCVA) at 48 weeks, visit-wise changes in this parameter, patients gaining ≥15 ETDRS letters/3 ETDRS rows with treatment; central retinal thickness (CRT) determined by OCT; progression of avascular area since baseline; and number of patients with retinal hemorrhage. The sub-group analysis was restricted to observing any trends for the mean change from baseline in the ETDRS letters in BCVA as well as in the CRT determined by OCT at 48 weeks. Pre-defined subgroups were patients’ age (18–64/65–74/75–84/>85 years), gender (men/women), smoking status (smokers/non-smokers), history of DM (type/duration), treatment of DM (oral hypoglycaemic agents [OHAs]/insulin/both), control of DM (based on HbA1c levels or blood sugar [BS] levels such as fasting [FBS]/post-prandial [PPBS]/random [RBS]/general random [GRBS]), and previous treatment for DME (not treated/laser

Results
Overall 68 (54.0%) patients completed the study. Mean ±standard error [SE] age of population was 59.6±0.74 years, majority were men (64.8%). Each patient on average received 3.5 intravitreal injections over 48 weeks. In overall population, there was statistically significant improvement in ETDRS letters in BCVA (change from baseline: 6.8±2.09, p=0.0019) post 48-week treatment. In the subgroup analysis for the given outcome, there was significant mean±SE change from baseline in ETDRS in BCVA observed in men (8.5±2.84, p=0.00445), non-smokers (7.2±2.17, p=0.0015), patients aged 18–64 years (6.6±2.31, p=0.0065), with type 2 DM (6.6±2.12, p=0.0026), and who did not receive any previous treatment for DME (7.4±2.62, p=0.0071). Based on OCT assessment in overall population, there was significant decrease in mean±SE CRT over 48 weeks (change from baseline: -89.7±19.02 µm, p=0.0002). For the subgroup analysis, change in CRT from baseline was significant in men (-89.7±28.92 µm, p=0.0040) and women (-89.7±22.2 µm, p=0.0005) aged 18–64 years (-105±19.69 µm, p=0.0001), non-smokers (-92.8±19.56 µm, p=0.0001), patients with type 2 DM (-87.4±19.22 µm, p=0.0001), which was controlled by FBS (-81.7±32.83 µm, p=0.0235) or PPBS (-111±33.54 µm, p=0.0050), patients using OHAs (-209±72.41 µm, p=0.0449), and those who did not receive any treatment for DME (-92.6±24.66 µm, p=0.0006).

Conclusions
The subgroup analysis of this real-world study concluded that with the ranibizumab 0.5 mg intravitreal injection, there was a significant improvement in visual acuity among patients aged 18–64 years, men, non-smokers, patients with type 2 DM, and who did not receive any prior treatment for DME compared with other subgroups.

Financial Disclosure
The prospective, open-label study was sponsored by Novartis Healthcare Private Limited (Mumbai, India).
Title
Evaluation of the incidence of unilateral treatment requiring ROP: Two centered two years follow up results

Purpose
It was aimed to evaluate the incidence of unilateral treatment requiring ROP in the study.

Setting/Venue
The study was set as two centered and retrospective design between January 2019 – March 2021 in Erzincan Binali Yildirim University Faculty of Medicine Department of Ophthalmology, Turkey and Diyarbakir Gazi Yasargil Training and Research Hospital Department of Ophthalmology, Turkey.

Methods
Data of 6214 eyes of 3107 infants were evaluated and recorded. Examination findings were recorded according to the Classification of Retinopathy of Prematurity guideline. The following informations were recorded: gestational age, birth weight, type of delivery, duration of staying in neonatal intensive care unit (NICU) and oxygen therapy, age at the time of diagnosis and treatment (weeks), the location, laterality and type of ROP, the severity of ROP, vascular characteristics of ROP, treatment status, postmenstrual age, treatment modality, and retinal vascular development.

Results
Seven hundred sixty nine (24.8%) of 3107 babies were diagnosed with ROP. Two hundred four eyes of 107 (3.4%) infants were treated for ROP [intravitreal anti VEGF (IVA), laser photocoagulation (LPC) or surgical (pars plana vitrectomy) treatment]. Fifty eyes had aggressive posterior ROP (AP-ROP), 154 eyes had type 1 ROP and 1324 eyes had type 2 ROP at first visit in the study. At first visit, 22 infants had asymmetric ROP. Ten eyes (4.9%) of 10 babies had unilateral treatment requiring ROP. One hundred ninety four eyes (95.1%) of 97 babies have bilateral treatment requiring ROP. There was no significant difference in gestational age, birth weight, type of delivery, duration of staying in NICU and oxygen therapy between two groups.

Conclusions
ROP was highly symmetric between the eyes of infants undergoing ROP screening. When AP-ROP or type 1 ROP develops in one eye and type 2 ROP in the fellow eye, the risk of progression to treatment requiring ROP in the fellow eye are higher in infants with AP-ROP.

Financial Disclosure
No financial relations consist in the study.
Suprachoroidal injection of triamcinolone acetonide using a custom-made needle to treat diabetic macular oedema post pars plana vitrectomy.

**Purpose**
To evaluate the safety and efficacy of suprachoroidal injection of Triamcinolone using a custom-made needle to manage diabetic macular oedema post pars plana vitrectomy.

**Setting/Venue**
Single-center at Marashi Eye Clinic Aleppo Syria Retrospective case report series

**Methods**
This was an interventional single-centre retrospective case report series which evaluated the efficacy and safety of injecting 0.1ml/4mg triamcinolone in the suprachoroidal space using a custom-made needle for eight weeks to treat diabetic macular oedema post pars plana vitrectomy (PPV). Follow up changes were evaluated in terms of central macular thickness (CMT) using spectral-domain optical coherence tomography (SD-OCT) and best-corrected visual acuity (BCVA) at baseline, one week, 4, and 8 weeks along with intraocular pressure (IOP), cataract progression, and ocular safety.

**Results**
A total of 11 eyes in 10 patients received 11 suprachoroidal injections. The improvement of vision was noted from 0.75 logMAR at baseline to 0.40 logMAR after treatment. Central macular thickness (CMT) reduced significantly from 456.45±113.42 μm at baseline to 247.63±53.40 μm at eight weeks of follow-up. No rise in intraocular pressure rise was noted, or cataract development was observed in the treated phakic eye in eight weeks follow up.

**Conclusions**
Suprachoroidal injection of Triamcinolone using a custom-made needle to treat DME post PPV shows promising results with acceptable safety outcomes in low resource countries. However, larger clinical trials with longer follow-up are needed to evaluate this treatment modality's safety and efficacy.
Comparison of changes in number of hyperreflective dots after intravitreal Ranibizumab or Dexamethasone implant in patients with branch retinal vein occlusion

Purpose
To compare the effect of intravitreal ranibizumab (IVR) or intravitreal dexamethasone implants (IVD) on regression of hyperreflective dots (HRDs) in branch retinal vein occlusion (BRVO).

Methods
37 eyes of 37 patients with cystoid macular edema who received IVR or IVD for at least 12 months were included in this study. The patients were divided into three groups according to intravitreal treatment. Group 1 consisted 12 eyes who received only IVD, group 2 consisted 10 eyes who received only IVR and group 3 consisted 15 eyes who received both IVD and IVR. IVD implant was administered at baseline, month 3, and month 6 in group 1 and group 3. OCT parameters (CMT, number of HRDs) and best-corrected visual acuity (BCVA) were compared between the groups and over the follow-up time. HRDs were categorized as HRD in inner retinal layers (from the internal limiting membrane to the inner nuclear layer) or HRD in outer retinal layers (from the outer plexiform layer to the outer border of the photoreceptor layer).

Results
There was no significant difference between groups in terms of BCVA, CMT, HRDs in the inner retinal layers and the outer retinal layers at baseline. (For all p>0.05) Compared to the baseline values in all groups, a significant decrease was observed in CMT in the first year. (For group 1; p=0.013, group 2; p=0.010; group 3, p<0.001) The BCVA was significantly increased after 1 year in group 1 and group 3. (p=0.001, p<0.001) The mean number of HRDs in inner and outer retinal layers were significantly decreased in group 1 and group 3. (p=0.001, p=0.008) Compared to the baseline values in all groups, a significant decrease was observed in CMT in the first year. (For group 1; p=0.013, group 2; p=0.010; group 3, p<0.001) The BCVA was significantly increased after 1 year in group 1 and group 3. (p=0.001, p<0.001) The mean number of HRDs in inner and outer retinal layers were significantly decreased in group 1 and group 3. (p=0.001, p=0.008) However, there was no significant change in terms of the mean number of HRDs in inner and outer retinal layers group 2. (p=0.496, p=0.06) At the first year, the CMT and number of HRDs in inner and outer retinal layers was significantly lower in group 1 and group 3 than in group 2. (p<0.001) The BCVA was higher in group 1 and group 3 than in group 2. (p<0.001) There was no significant difference in terms of post treatment CMT and the number of HRDs between group 1 and group 3 in posthoc tests(p=0.621, p=0.571, and p=0.831).

Conclusions
The reduction in HRDs at 12 months and better BCVA after IVD intimates that the HRDs should be considered as inflammatory markers in the follow-up of CME in BRVO. Thus, IVD injection could be more appropriate for patients with higher HRDs after BRVO.

Financial Disclosure
no financial disclosure
**Title**
OCT-A in the monitoring and evaluating the effectiveness of combined treatment of macular edema due to BRVO

**Purpose**
In retinal diseases with chronic vascular obstructions, it is difficult to predict the development of ischemia and the functional outcome. OCT-A may give additional insight into the vascular changes of retinal ischemia. The superficial and deep retinal vascular plexus can be observed separately using the en face visualization technique. Recent studies have revealed that the retinal vessels are associated with visual function in eyes with BRVO. The purpose of our study is to evaluate the effectiveness of anti-VEGF therapy in combination with OCT-A navigational laser in the treatment of macular edema secondary to BRVO by OCT-A quantitative indicators and to assess their informativity.

**Setting/Venue**
The S. Fyodorov Eye Microsurgery Federal State Institution

**Methods**
30 patients aged 45 to 76 years (on average 61±8.3 years) with macular edema secondary to BRVO were analyzed. The symptoms duration of the disease was 1-3 months. The 1st stage of the treatment was the intravitreal injection of Ranibizumab. After one or few injections the central retinal thickness (CRT) decreased to the level of 350 µm and less we carry out the OCT-A navigated laser. In the zone of retinal ischemia and macular edema non-involving the fovea, laser treatment was carried out in a continuous mode, in fovea – in microimpulse mode. Before the first injection and 12 months after, we studied the dynamics of best corrected visual acuity (BCVA), central retinal sensitivity (CRS) and quantitative indicators obtained during OCT-A –vascular density in the deep and superficial capillary plexus, peripapillary density and retinal-nerve fiber layer (RNFL) thickness.

**Results**
At the 1st stage of the treatment in order to reduce the CRT level to 350 µm and less on average of 3.87±1.02 injections of Ranibizumab were required and we carry out the OCT-A navigated laser. As a result of combined treatment the following results were achieved. BCVA increased from 0.34 ± 0.16 to 0.81 ± 0.07. CRS increased from 21.4±1.4 dB to 23.1±1.3 dB. The vascular density in the superficial capillary plexus decreased from 49.1±5.02 to 42.7±4.89, the vascular density in the deep capillary plexus decreased from 47.6±5.81 to 45.3±6.14. The vascular density in the peripapillary plexus decreased from 47.1±0.07 to 46.8±0.09, the thickness of RNFL decreased from 64.2±1.14 µm to 60.5±1.18 µm. We didn’t find a relationship between the BCVA with other studied indicators, but we were found a relationship between the vascular density in the deep vascular plexus and central retinal sensitivity before the treatment.

**Conclusions**
Quantitative parameters obtained by OCT-A (vascular density in the deep and superficial capillary plexus, peripapillary density and RNFL thickness) can be useful in assessing the efficacy and safety of combined treatment for macular edema due to BRVO. Indicators of vascular density in the deep capillary plexus and central retinal sensitivity before the treatment can determine the further functional outcome of the disease.

**Financial Disclosure**
no financial disclosure
Outcomes following cataract surgery combined with slow-release intravitreal steroid implants in patients with Diabetic Macular Oedema.

Purpose
Patients affected by diabetes mellitus have a 5-fold increased risk of developing visually significant cataract compared to the normal population of the same age. In addition, the increase of pre-existing macular oedema can be one of the post-operative complications of cataract surgery in diabetic patients. We aimed to evaluate real-world visual and optical coherence tomography (OCT) outcomes of combined cataract surgery and slow-release intravitreal steroid implant in patients with cataract and concomitant clinically significant diabetic macular oedema (DMO).

Setting/Venue
Tertiary referral centre; Newcastle Eye Centre, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, United Kingdom.

Methods
Retrospective data review of patients affected by DMO and cataract that underwent combined phacoemulsification with intraocular lens implant surgery and slow-release intravitreal steroid implant on the same sitting (from August 2017 to October 2020). Fifteen eyes of 12 patients with at least 6 months of follow-up were included in the analysis, of which 5 eyes of 4 patients receiving Fluocinolone Acetonide 0.19 mg implant (FA group) and 10 eyes of 8 patients receiving Dexamethasone 700 μg implant (DEX group). Data collected includes demographic findings, best corrected visual acuity (BCVA) in LogMAR and central retinal thickness (CRT) on OCT at baseline (preoperatively) and at 1, 3 and 6 months after surgery. Also noted was the occurrence and management of any intra/post-operative complications. Measures are presented as mean ± SD. Differences in the measures were assessed by t-test (significant p-value less than 0.05). The study adhered to the tenets of the Declaration of Helsinki.

Results
Mean age was 67.8 ±8.35 and 68.2 ±4.54 years in the FA and DEX group respectively (p=0.45). All patients had previously received intravitreal anti-vascular endothelial grow factor injection on average 15.4 ±13.2 weeks prior to the combined surgery. In FA group, baseline mean BCVA was 0.68 ±0.22 logMAR improving to 0.33 ±0.22 logMAR at month 6 (p=0.03). The CRT at baseline was 476.4 ±104.11μm and 339.8 ±87.49μm at month 6 (p =0.03). The DEX group had a baseline mean BCVA of 0.48 ± 0.39 logMAR improving to 0.33 ±0.22 logMAR at month 6 (p=0.13). The OCT showed a baseline CRT of 476.4 ±104.11μm decreasing over the follow up period to 436.4 ±147.72μm (p=0.44). When comparing the two groups, the FA showed improvement peaks of mean BCVA at months 3 and 6 (-0.42 ±0.43 and -0.42 ±0.41logMAR respectively) and of mean CRT at month 6 (-136.6 ±161.5μm). In the DEX group improvement peaks of mean BCVA (-0.17 ±0.22logMAR) and of mean CRT (-61.9 ±55.25μm) were detected at month 1 instead. Other than one eye in the DEX group that developed raised intraocular pressure (at month 1), which was successfully treated with topical drops, no other complications were observed.

Conclusions
Slow-release intravitreal steroids were safe and effective adjuvants to stabilize DMO in patients undergoing cataract surgery. The DEX group had quicker visual and anatomical gains, but the FA group showed better functional and anatomical outcomes over the study period.

Financial Disclosure
Sandro Di Simplicio is a KOL for Alcon. The other Authors have no financial interests to disclose.
### Title
Antioxidant effect of CoQ10 on ischemic retinopathy in animal models of diabetes mellitus

### Purpose
The effect of Coenzyme Q10 (CoQ10) on the development of ischemic retinopathy is not fully known. One hypothesis is that the higher reactive oxygen species (ROS) levels play an important role in the pathogenesis of it while the other is inflammation. This study investigated the antioxidant and antiinflammation effects of CoQ10 in our diabet-induced animal models.

### Setting/Venue
Afyonkarahisar Health Sciences University Department of Ophthalmology

### Methods
Twenty male wistar rats were included. Group 1 (n=5, diabet), group 2 (n=5 diabet+CoQ10), group 3 (n=5 healthy+CoQ10) and group 4 (n=5 control) animals divided into four groups. Control (group 4) and groups to be given CoQ10 alone received 0.01 M sodium citrate buffer intraperitoneally other rats 50 mg/kg i.p. in 0.01 M sodium citrate buffer at once. Group 1 and 2 were diabetic by giving streptozotocin. After 2 weeks, rats with a fasting blood glucose above 250 mg/dl were accepted as diabetes and the group 2 and group 3 were dissolved 0.35 mg of CoQ10 in 50 µl of pure olive oil daily and administered by gavage for two months. After 2 months, after the intraperitoneal injection of 100 mg/kg ketamine, the rats were sacrificed, after opening the ribcage and taking blood from the apex of the heart, biochemical evaluation was done. And than the eyes were enucleated and placed in 10% neutral formalin. After tissue follow-up, sections were taken from the tissues embedded in paraffin, and immunohistochemistry staining protocol was applied with TNF-α, NFKB, Bax, VEGF and VEGFR. H scoring was done by counting TNF-α, NFKB, Bax, VEGF and VEGFR positive stained cells in microscopic evaluation. Retinal thicknesses were measured.

### Results
In the groups had higher levels of GSH (P=0.009) group 3 and 4, NFKB had higher level in group 1 to group 3 (P=0.012), TOS had higher level group 2 to group 1 (P=0.012), in the one month respectively. TOS had higher level group 3 to 1 (P=0.007), VEGFR had higher level group 1 to 3 (P=0.014), TNF had higher level group 1 to 3 (P=0.023), Bax had higher level group 2 to 1 (P=0.017), NFKB had higher level group 1 to 3 (P=0.041) in 2nd month. Retinal thickness was higher group 1 to 4 in 2nd month (P=0.032) respectively.

### Conclusions
CoQ10 therapy causes a decrease in GSH, and NFKB and and increase in TOS levels indicating increased oxidative stress in the 1st month and second month.
Shall we change our attitude in screening for retinopathy of prematurity during the COVID-19 pandemic?

Purpose
The purpose of this study is to evaluate the incidence of conjunctival and faringeal swab sample positivity of SARS-CoV-2 virus in asymptomatic premature and newborns. Transmission from asymptomatic individuals is also a serious issue in controlling the spread of disease, therefore we aimed to detect the asymptomatic carrier potential in infants. By determining the incidence of asymptomatic carriers in infancy, it could be possible to decide whether patients and healthcare workers are likely to encounter the virus during the retinopathy of prematurity (ROP) screening and whether additional measures should be taken to prevent transmission during the examination.

Methods
Patients who were screened for ROP in our clinic between January and March 2021 were recruited in the study. Study group consisted of premature and term infants who had risk factors for ROP. The study was conducted according to the tenets of the Declaration of Helsinki and ethical approval was obtained from the institutional ethics committee. Previous history of possible exposure or contact with SARS-CoV-2 virus was questioned for each patient and only subjects with no previous history of COVID-19 infection or contact to COVID-19 were included. None of the patients had any signs of COVID-19 infection at the time of sample collection. Prior to ophthalmic examination pharyngeal and conjunctival swab samples were collected. Nucleic acid isolation from samples with automated system (SEEPREP32 ™, Seegene, Germany) was carried out. The presence of SARS-CoV-2 RNA in the extracted samples was screened with a commercial real time PCR kit (Allplex ™, Seegene, Germany) targeting the E, RdRP and N genes. Inc., USA) platform. SARS-CoV-2 RNA positive samples were reevaluated for variant virus. Allele-specific RT-PCR method using a commercial kit was used for identification of signature variant mutations (69-70 del, ORF1a del, 242 del, E484K mutation) which are defined by Word Health Organization.

Results
Fifty-nine patients with a median age of 40 (IQR 5) weeks postmenstrual age (PMA) at the time of sample collection were enrolled in the study. Mean gestational age (GA) of patients was 33.7±3.45 (range 23-45) weeks with a mean birth weight of 2193.44±735.23 (range 515-3880) grams. 56 patients had a positive history of newborn intensive care unit (NICU). Median NICU length of stay was 21 (IQR 5) days. Five patients (10.1%) out of 59 received intravitreal anti-vascular endothelial factor (anti-VEGF) treatment for ROP. SARS-CoV-2 RNA was found to be positive in 2 (3.38%) pharyngeal swab samples out of 59 infants included in the study. Also, conjunctival swab sample was positive in one of these two patients (No mutation was found in the variant sample). The patient positive for SARS-CoV2 RNA only in the conjunctiva and pharynx samples was a term infant with a history of NICU for 6 days. The patient positive for SARS-CoV2 RNA only in the pharynx was born at 34th week GA and stayed in the NICU for 9 days. No transmission of SARS-CoV-2 between patients and ophthalmology staff was observed.

Conclusions
The main transmission routes of SARS-CoV2 are droplet and direct contact transmission. Without the presence of ocular symptoms SARS-CoV2 positivity could be encountered in patients with COVID-19. During the examination for ROP screening aerosols created by the crying baby or conjunctival secretions may be the source of virus transmission. The rate of ocular surface positivity for SARS-CoV2 RT PCR among COVID-19 patients was found to be 0% to 28.57%. The ocular surface may, therefore, play a role in transmission of the virus. The incidence of asymptomatic infection in children was reported to be between 15.8% in a previous study, the median age of children was 6.7 years in this study. A meta-analysis reported that 29 (50%) patients out of 58 neonatal COVID-19 patients were symptomatic unlike the lower rate of clinically symptomatic older children. The rate of asymptomatic carriers was found to be 3.38% in our study group which consists of infants. Given the fact that almost 10% of our patients required treatment for ROP, we cannot postpone screening for ROP. But caution should be taken to prevent any spread of disease because asymptomatic carriers of the virus without any previous contact history could be encountered in infants.
Title
Treatment switch from aflibercept to ranibizumab in Canadian DME patients in a real-world setting: The PRECISE study

Purpose
Studies have shown that switching anti-vascular endothelial growth factors (anti-VEGFs) can help improve outcomes in diabetic macular edema (DME) patients with inadequate response to ongoing anti-VEGF therapy. However, real-world data are limited on switching from aflibercept (AFL) to ranibizumab (RBZ) and no study thus far has been reported on treatment switch to RBZ prefilled syringe (RBZ-PFS). PRECISE is the first study to evaluate treatment outcomes in DME patients with an inadequate response to ongoing AFL treatment who were switched to RBZ-PFS in a routine clinical setting. Here, we present the final results of DME patients in Canada who were switched from AFL to RBZ-PFS in real-world practice.

Setting/Venue
PRECISE is a prospective, observational, multicenter, real-world switch study of previously AFL-treated Canadian DME patients to RBZ-PFS.

Methods
Eligible consenting patients, aged ≥18 years, who received ≥3 AFL intravitreal injections for DME, switched to RBZ-PFS based on clinician’s discretion, and treated as per the product label, were enrolled into the study. Primary endpoint was mean change from baseline to day 90 in central retinal thickness (CRT). Secondary endpoints included change in best-corrected visual acuity (BCVA), reasons for treatment switch, functional outcomes, treatment injection interval, and safety. The study enrolled 48 eyes with DME from 15 clinical centers across Canada.

Results
Patients presented with a mean (SD) age of 67.4 (10.6) years, 47.8% were Caucasian, and 30.4% female; 6.5%/93.5% had Type1/Type 2 diabetes, 100% were medication-controlled, and 82.6% had hypertension. At baseline, mean (SD) CRT was 353.7 (84.4) µm and mean (SD) baseline visual acuity was 65.1 (12.5) ETDRS letters; 84.8% had presence of macular fluid (94.9% intraretinal fluid [IRF]; 5.1% IRF and subretinal fluid) with no pigment epithelial detachments. Median time since diagnosis to first RBZ-PFS was 1.9 years. Prior to study entry, patients received median of 12 injections of any anti-VEGF, with median of 8.5 AFL injections. Median time from last AFL to first RBZ-PFS was 1.3 months. Key reasons for treatment switch were due to a lack of response to AFL treatment (82.6% persistent fluid, 2.2% loss of vision, 2.2% unsatisfactory vision gains), unable to extend dosing (6.5%), ocular safety concerns (2.2%), and other (2.2%). Results demonstrated significant CRT reduction of -23.3 (57.5) µm (p=0.0063), 69.4% with continued presence of macular fluid, and significant improvement of visual acuity (+2.7 letters; p=0.0209) at Day-90 post-switch, with average treatment interval of 4.7 weeks during the study and average next planned interval of 5.2 weeks. There were no new safety signals.

Conclusions
Real-world evidence from the PRECISE study provides useful information on the baseline characteristics of DME patients who required the treatment switch from AFL to RBZ-PFS. Results demonstrated a significant reduction in CRT and improvement of visual acuity, and maintenance of safety. The key real-world reason for treatment switch from AFL to RBZ-PFS was lack of response to AFL treatment, primarily due to presence of fluid in the macula. These results will further our current understanding and enhance routine clinical care of DME patients.

Financial Disclosure
Advisory Board: Abbott, Alcon, Novartis; Research Grants: Allergan, Bayer AG, Chengdu Kanghong Biotechnology, F. Hoffmann-La Roche, Novartis; Speaker: Abbott, Alcon, Bausch & Lomb, Bayer AG, Novartis
**Title**

**Purpose**
Proliferative diabetic retinopathy (PDR) is a sight-threatening diabetic complication involving neovascular and fibrotic growth at the vitreoretinal interface and retinal surface. As the number of diabetics rises, and current treatment options are often ineffective, the search for novel targets for treatment and prevention of PDR progression is crucial. The purpose of our study is to determine gene expression patterns in the fibrovascular tissues excised from eyes of PDR patients in order to better understand the molecular mechanisms of the disease and identify potential target molecules and pathways.

**Setting/Venue**
In this prospective clinicopathologic single-center study, diabetic patients were enrolled in the tertiary-care ophthalmology clinic, unit of vitreoretinal diseases at Helsinki University Hospital (HUH) Eye Clinic between 2010-2019. The study was conducted according to the Declaration of Helsinki and approved by the Institutional Review Board and Ethical committee of HUH. Signed informed consent was obtained from each patient.

**Methods**
We sequenced RNA isolated from excised fibrovascular membranes of eleven PDR patients, and from avascular fibrous tissues of two non-diabetic patients with long-term rhegmatogenous retinal detachment and proliferative vitreoretinopathy and compared their transcriptomes. We determined differentially expressed genes between the two groups, identified processes and pathways overrepresented in PDR with pathway and gene ontology term enrichment analyses, and used immunohistochemistry on similar tissue samples to validate our findings.

**Results**
Multiple pro-angiogenic processes, including both VEGFA-dependent and -independent pathways, were overrepresented in PDR. Also overrepresented in PDR were processes related to lymphatic development, epithelial to mesenchymal transition (EMT), wound healing, inflammation, fibrosis, and extracellular matrix composition (ECM), demonstrating the complexity of PDR fibrovascular tissue formation.

**Conclusions**
We identified many genes, processes and pathways of interest in the PDR cohort, some of which are potentially useful for development of novel treatment options. Overrepresentation of angiogenic and anti-angiogenic processes may help to explain the transient nature of the benefits that many patients receive from current intravitreal anti-angiogenic therapies, and it highlights the importance of combinatorial treatments. Enrichment of genes and pathways related to lymphatic development indicates that targeting lymphatic involvement in PDR progression could have therapeutic relevance.

**Financial Disclosure**
none
Effect of Prophylactic Topical Tetrahydrozoline Administration in the Reduction of Subconjunctival Hemorrhage Incidence after Dexamethasone Intravitreal Implant

Purpose
Subconjunctival hemorrhage (SCH) is an essential minor complication of dexamethasone intravitreal implant (DEX implant), affecting satisfaction, quality of life, and treatment compliance of patients. Tetrahydrozoline is an imidazole derivative sympathomimetic agent, activating alpha-adrenergic receptors, resulting in vasoconstriction. We aimed to compare ocular bulbar redness, SCH incidence, and pain score responses after topical tetrahydrozoline in patients undergoing DEX implant.

Setting/Venue
This is a prospective, randomized, double-blinded, single-center study.

Methods
Ninety-five patients with diabetic macular edema or retinal vein occlusion who underwent DEX implant were evaluated. The patients were randomly assigned to receive either 0.5 mg/ml topical tetrahydrozoline (47 eyes) or control (48 eyes) 30 minutes before the DEX implant. Anterior segment images of all patients were taken immediately after injection and at the 24-hour follow-up. SCH incidence and area were assessed by slit-lamp 24 hours after the injections. Ocular bulbar redness and pain were immediately evaluated after the injections. SCH area and ocular bulbar redness were measured by ImageJ software. The percentage of the proportion of mean red-channel intensity to total color-channel intensity was expressed as an ocular bulbar redness. The pain was assessed by the numerical rating scale (NRS-11, 0 = no pain, 10 = highest level of pain).

Results
A total of 95 eyes from 95 participants (50 female and 45 male) with a mean age of 68.5 ± 9.6 years were included in the study. There were a history of diabetes mellitus and hypertension in 81% and 42% of patients, respectively. The patients’ indications for DEX implant were diabetic macular edema (72.6%), central retinal vein occlusion (16.9%), and branch retinal vein occlusion (10.5%). There were no significant differences between the two groups in terms of gender, age, systemic diseases, indication causes (for all, \( p \) less than 0.05). Ocular bulbar redness was 35.86 ± 0.70 in the tetrahydrozoline group and 41.23 ± 1.27 in the control group \(( p = 0.000)\). SCH occurred as a result of the DEX implant in 38.3% (18 eyes) of the tetrahydrozoline group and 60.4% (29 eyes) of the control group \(( p = 0.031)\). The mean size of SCH was 46.4 ± 17.2 mm² in the tetrahydrozoline group versus 60.6 ± 19.6 mm² in the control group \(( p = 0.01)\). The prevalence of local pain sensation in the overall study population was 77.9%. The mean pain score was 2.22 ± 1.62 in the tetrahydrozoline group and 2.06 ± 1.52 in the control group \(( p = 0.854)\).

Conclusions
The administration of topical tetrahydrozoline significantly decreased ocular bulbar redness. This intervention 30 minutes before the DEX implant is a harmless and effective method that reduces the incidence and size of SCH. It may be considered in patients undergoing DEX implant to improve treatment satisfaction and promote compliance and quality of life.
**Title**
Evaluation of Intravitreal Bevacizumab Upload and Followed by Dexamethasone Implant Monotherapy for Macular Edema due to Retinal Vein Occlusions

**Purpose**
To investigate the functional and anatomical outcomes of intravitreal bevacizumab (IVB) upload followed by intravitreal dexamethasone implant (IVD) monotherapy treatment for macular edema due to central/branch retinal vein occlusion (CRVO/BRVO).

**Setting/Venue**
Retrospective/Izmir Katip Celebi University Ataturk Training and Research Hospital Eye Department

**Methods**
Sixty eyes of 60 treatment-naive patients with centre-involving macular edema secondary to RVO were retrospectively included the study. All patients were treated with three upload doses of 1.25 mg IVB monthly which followed by the two 700 µg IVD doses given at 3-month intervals. Monthly follow-up was conducted for 9 months after the first injection and were followed for at least 12 months. Main outcome measures were changes in best-corrected visual acuity (BCVA) and central foveal thickness (CFT).

**Results**
The data of 60 patients were analyzed. There was 33 CRVO and 27 BRVO cases. Best-corrected visual acuity changes from the baseline to nine month follow-up were significantly higher in BRVO group (P = 0.03). In addition, nonsignificant differences were observed in central macular thickness in BRVO group throughout the study period (P = 0.298).

**Conclusions**
For macular edema secondary to RVO, IVB administered monthly and IVD administered PRN at 3-month intervals, yielded functionally and anatomically preferable outcomes at 12 months.

**Financial Disclosure**
We don't have any financial relations.
Comparison between early vs late switch to Fluocinolone acetonide (Fac 0.19mg, Iluvien®) implant in eyes with recurrent diabetic macular edema

Renato Correia Barbosa
Portugal

Diabetic Macular Edema (DME) is a major cause in visual loss in developed countries. Chronic inflammation due to DME results in irreversible retinal damage, with serious impact in visual function. Therefore, early intervention is generally related to a better visual prognosis. Fluocinolone acetonide implant (Fac 0.2 μg/day, ILUVIEN®) is indicated for the treatment of chronic DME with sub-optimal response to previous therapeutic strategies. In this study, we compared the anatomical changes and functional response between eyes with recurrent DME treated with intravitreal Fac implant after early switch (≤ 6 previous intravitreal injections) and late switch (> 6 previous intravitreal injections).

Methods
A retrospective, non-randomized analysis of 109 eyes of 76 patients with recurrent DME was conducted. The eyes were divided into 2 groups, based on the number of previous intravitreal injections: the early switch group (group A), was composed by 34 eyes with ≤ 6 previous intravitreal injections, and the late switch group (group B) was composed by 75 eyes with >6 previous intravitreal injections. At baseline, the following outcomes were evaluated: 1) best corrected visual acuity (BCVA), measured with Early Treatment Diabetic Retinopathy Study (ETDRS) table; 2) number of previous intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections and short-acting corticosteroid injections; 3) duration of macular edema; 4) use of ocular hypotensive medication; 5) intraocular pressure (IOP); 6) central foveal thickness (CFT). Results were obtained based on the mean changes in BCVA, CFT and IOP recorded in the first month after the treatment and quarterly thereafter.

Results
At baseline, mean age was 70.0 ± 10.0 and 67.7 ± 8.2 years (p=0.3256) and mean DME duration was 4.3 ± 2.2 and 4.8 ± 1.8 years (p=0.4165), in group A and B, respectively. The average follow-up period was 27.4 ± 10.6 (A) and 26.0 ± 10.9 months (B) (p=0.545). All eyes received intravitreal injections prior to Fac implant (anti-VEGF 2.3 ± 1.5 [A] and 8.3 ± 3.4 [B] (p<0.001); short-acting steroids: 1.8 ± 1.3 [A] and 2.1 ± 1.7 [B] (p=0.3421)). Group A had a baseline BCVA of 51.2 ± 18.2 letters ETDRS, which increased by 10.7 letters at the last observation. Group B had a baseline BCVA of 48.5 ± 15.7 ETDRS letters, which increased 6.1 letters at the last observation (p=0.0018 between groups). Mean decrease in CFT was 171 μm (group A) and 149.9 μm (group B) (p=0.0823 between groups). IOP was stable during the follow-up period (Δ +1.9mmHg [A] and +0.6mmHg [B]), having been controlled with topical hypotensive drops, needed in 32% and 36% patients, respectively. Three years after the initial implant, 3.3% (group A) and 34.1% (group B) patients underwent Fac re-implantations (p=0.016).

Conclusions
Results showed a significant difference in functional outcome between early and late switch groups. Early switchers had superior visual results, which is probably related to chronic retinal dysfunction due to prolonged inflammation in late switchers. Anatomical outcomes, objectified by variation in CFT, showed a similar tendency favouring the early switch group, without reaching statistical significance. Early treatment with Fac implant may be linked with better visual outcomes in patients with DME.

There are no financial relations with any company.
Title
How COVID-19 impacts the patients with diabetic macular edema during the lockdown in Morocco

Purpose
Description of a unilateral case of non-arteritic ischaemic optic neuropathy (NAION) with atypical features in a patient with long-term amiodarone treatment. Amiodarone-associated optic neuropathy (AAON) is a controversial entity at the present, as it shares many similarities with NAION, the most common optic nerve disorder that leads to sudden onset of vision loss in elderly patients. It usually occurs within the first year of treatment. The classic characteristics include: insidious onset, bilateral involvement and slow resolution of the papillary swelling. In addition to these elements, there is a more complex clinical assessment of the following features: mild degree of optic nerve dysfunction (preserved or mild decrease in visual acuity and low probability of relative afferent pupillary defect [RAPD]), structure of uninvolved disc in unilateral cases, and systemic toxic effects, when present.

Setting/Venue
Clinic of Ophthalmology, Cluj Napoca County Emergency Hospital, Romania

Methods
Retrospective description of clinical case based on international scientific data evidence. Data collected structured according to: age; laterality of disc swelling; onset of decrease in visual acuity (VA); amiodarone dosage per day, respectively cumulative dosage per week; VA involved eye, at the moment of the visit, and when possible, at the 3-month follow-up; visual field (VF) of involved eye; presence of RAPD; Cup/disc ratio (CDR) of uninvolved eye; presence of potential toxic systemic effects and time to resolution of papillary edema, if documented.

Results
Female patient, 69 years old, at her first ophthalmological visit, presents with insidious unilateral onset of decrease in VA of the left eye (LE). Patient remains hospitalized. Documentation of amiodarone intake of 200 mg/day (1400 g/week) for the past several years with antihypertensive and anticoagulant co-medication. Best corrected visual acuity (BCVA) for right eye (RE) 5/10 and in the involved eye (LE) 4/10, no RAPD. Anterior segment findings: Vortex Keratopathy and nuclear sclerotic cataract in both eyes (OU), the nuclear opacities being denser in RE. Fundoscopy reveals in RE slight disc pallor, whereas in LE mild papillary swelling, hyperemic disc with one hemorrhage inferiorly. CDR in uninvolved eye is 0,1. VF RE shows generalized decrease in retinal sensitivity; VF LE with generalized decrease in retinal sensitivity with superior altitudinal defect. Inflammatory and cardiovascular work-up is normal. Magnetic resonance imaging (MRI) identifies cerebral microangiopathy. Systemic intravenous steroids are administered during hospitalization with slow tapering of dosage. At discharge, BCVA slightly improved in LE (6/10), with no resolution of papillary swelling. Unfortunately, patient is lost at follow-up.

Conclusions
Patients undergoing amiodarone treatment should be considered for regular ophthalmological follow-up, in close collaboration with cardiologists, especially in the case of the high cardiovascular risk patients. Separation of the two entities NAION and AAON is difficult. There is a need for a guided monitoring protocol, that should primarily include VA, VF, fundoscopy and follow-up for reevaluation of resolution in the papillary edema and potential sequential disc swelling of the fellow eye when confronted with unilateral cases. Because of its various clinical presentation, one could hardly tell if it is a drug related condition with need for regular interdisciplinary collaboration, or whether it is a variant of NAION in patients at high risk for cardiovascular disease.

Financial Disclosure
NONE
Title
Differences between aggressive posterior retinopathy of prematurity (AP-ROP) and type-1 retinopathy of prematurity (ROP): Incidence, risk factors and treatment options

Purpose
To compare aggressive posterior retinopathy of prematurity (AP-ROP) with type-1 retinopathy of prematurity (ROP) with regarding risk factors, complications and treatment outcomes.

Setting/Venue
The study was conducted as two centered and retrospective design between July 2018-February 2021 in Diyarbakir Gazi Yasargil Training and Research Hospital Department of Ophthalmology, Turkey and Erzincan Binali Yildirim University Faculty of Medicine Department of Ophthalmology, Turkey.

Methods
Data of 6916 eyes of 3458 infants were evaluated and recorded. Examination findings were recorded according to the Classification of Retinopathy of Prematurity guideline. The following informations were recorded: gestational age, birth weight, type of delivery, duration of staying in neonatal intensive care unit (NICU) and oxygen therapy, age at the time of diagnosis and treatment (weeks), the location and type of ROP, the severity of ROP, vascular characteristics of ROP, treatment status, postmenstrual age, treatment modality, and retinal vascular development.

Results
Eight hundred eighty nine (25.7%) of 3458 babies were diagnosed with ROP. Two hundred forty eyes of 127 (3.7%) infants were treated for ROP (intravitreal anti VEGF (IVA) or laser photocoagulation (LPC) treatment). Sixty six eyes were AP-ROP and 174 eyes were type-1 ROP in the study. There was no significant difference in gestational age, birth weight, type of delivery, duration of staying in NICU and oxygen therapy between two groups. Sixty six eyes were treated with IVA therapy in AP-ROP group. In infants with type-1 ROP, 96 eyes were treated with IVA and 78 eyes were treated with LPC. ROP recurrence occurred in 18 eyes which 8 were treated with IVA and 7 were treated with LPC and 3 were treated with LPC + surgical intervention (pars plana vitrectomy) in AP-ROP group, while 2 eyes which were treated with LPC in type-1 ROP group.

Conclusions
Recurrence and retreatment (IVA, LPC and surgical intervention) are more frequent in AP-ROP than type-1 ROP even when treated with IVA and LPC.

Financial Disclosure
The authors declare no financial disclosure and conflicts of interest in the study.
Changes in macular capillary network measured with optical coherence tomography-angiography (OCT-A) in patients with systemic lupus erythematosus

Purpose
Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogeneous organ manifestations. SLE-related eye involvement occurs in approximately one-third of patients and is sometimes related to disease activity. Its early diagnosis and treatment are mandatory to prevent structural eye damage and visual acuity worsening.

Setting/Venue
To describe the parameters obtained by optical coherence tomography (OCT), both structural and foveal microvascularization in SLE patients and to relate them with the duration of SLE and the activity of disease.

Methods
A cross-sectional, single-center study was carried out in 78 patients with SLE treated at the Departments of Autoimmune Diseases and Ophthalmology of the Hospital Clinic, Barcelona. 80 sex and age matched individuals were also analyzed as a control group. Clinical, immunological data, activity and damage scores, and parameters of structural OCT (CIRRUS ™ HD-OCT model 5000, Carl Zeiss Meditec, Inc., USA) and OCT angiography (OCT-A) have been collected.

Results
Perifoveal vessel density in SLE patients was reduced compared to the control group (median 10.3 mm [range 9.6-11.4] versus median 12.5 mm [range 11.7-13.7]) (p=0.001) as well as vascular perfusion proportion compared to controls (0.35 [0.34-0.37] versus 0.38 [0.37-0.39]) (p=0.001). Likewise, SLE patients with >10 years of disease showed lower figures of vessel density (19.1 [18.2-20.2] versus 20.2 [19.7-20.9]) (p=0.04) and perfusion (0.34 [0.32-0.37] versus 0.36 [0.35-0.37]) (p=0.0017) compared to those with < 10 years of disease, respectively. Patients with SLE damage index score >0 had worse values in area (median 0.18 mm [range 0.15-0.21] versus 0.27 mm [range 0.23-0.31]) (p=0.002) and perimeter foveal avascular zone (FAZ) (median 1.84 mm [range 1.70-2.12] versus 2.19 mm [range 2.07-2.37]) (p=0.003). Likewise, patients with a clinical SLE disease activity index >4 showed a decrease in vessel density (14.6 mm [11.7-18.3] versus 17.6 mm [17.1-18.1]) (p=0.02) and vascular perfusion (0.33 mm [0.23-0.44] versus 0.43 mm [0.42-0.45]) (p=0.012).

Conclusions
The macular capillary network of SLE patients shows lower vessel density and perfusion proportion than healthy controls. In addition, retinal vascular findings in SLE patients could be associated with the duration of disease, SLE activity, and damage index. Retinal vascular imaging explorations based on OCT-A could be of great interest in future studies in SLE in order to further clarify systemic implications of such characteristics.
Risk of Renal damage Associated with Intravitreal Anti-VEGF Therapy for Diabetic Macular Edema in Routine Clinical Practice

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Purpose
Vascular endothelial growth factor inhibitors (anti-VEGF) have been shown to be effective in the treatment of diabetic macular edema. However, there is little information about the systemic effects of intraocular administration of anti-VEGF drugs. This may be particularly important in patients with coexistent diabetic maculopathy and nephropathy because it can produce adverse renal effects, such as decreased glomerular filtration rate (eGFR), proteinuria, hypertension or thrombotic microangiopathy.

Setting/Venue
Hospital Universitario Infanta Leonor. Av. Gran Via del Este, 80, 28031 Madrid, Spain.

Methods
This retrospective cohort study analyzed the effect of intravitreal anti-VEGF drugs (bevacizumab, ranibizumab or aflibercept) on eGFR and microalbuminuria (MicA) in patients with diabetic macular edema and non-proliferative retinopathy without chronic kidney disease (CKD).

Results
66 patients were included, 54.5% male and 45.5% female, with a mean age of 66.70 +/-11.6 years. 80.3% were hypertensive and with 15.05+/-7.79 years of diabetes evolution. The mean follow-up of patients with antiangiogenic treatment was 42.5+/-28.07 months. The mean number of injections was 10.91+/-5.44; 57.6% received bevacizumab; 9.1% aflibercept, and 33.3% a combination (bevacizumab and ranibizumab or aflibercept). In 12.1% of the cases there was a worsening of the glomerular filtration rate (eGFR) and a 19.7% worsening of the microalbuminuria (MicA). The number of injections was not related to the worsening of the eGFR (p = 0.74) or the MicA (p = 0.239). No relationship was found between the type of drug and the deterioration of the GFR (p = 0.689) or the MicA (p = 0.53).

Conclusions
Based on the results there is a small proportion of patients with increase in MicA and the decrease in eGFR after anti-VEGF therapy. There was no association between the number of injection or the drug type in worsening of eGFR or MicA, although bevacizumab was the main anti-VEGF drugs administered. Ophthalmologists should be aware of this effect, particularly for those patients with diabetic CKD in order to do a close monitoring of renal function and proteinuria after intravitreal administration of anti-VEGF and to be able to establish an early diagnosis of possible complications.

Financial Disclosure
None
Title
Real-life Outcomes of Patients Non-responsive to Anti-VEGF Intravitreal Injections Treated with Fluocinolone Acetonide Implant for Diabetic Macular Oedema

Purpose
To assess patients' structural and functional outcomes of diabetic macular oedema non-responsive to anti-VEGF intravitreal injections treated with intravitreal fluocinolone acetonide (Iluvien).

Setting/Venue
This is a retrospective analysis of clinical data collected at Moorfields Eye Hospital, London, UK.

Methods
We identified 23 eyes non-responsive to intravitreal anti-VEGF injections treated for DMO who had intravitreal Iluvien implant between 2014 and 2019. Among the eyes included, we stratified those who had had and hadn’t had intravitreal dexamethasone implant (Ozurdex) prior to the treatment with intravitreal Iluvien. We calculated visual acuity and anatomical outcomes for both subgroups and analysed the difference in overall results 12 months post-Iluvien implantation. The baseline for both subgroups was initiation with intravitreal anti-VEGF injections. Seventeen eyes met the criteria for this statistical analysis. We used ANOVA One-way analysis to calculate the p-value to compare the outcomes in each subgroup.

Results
The mean number of anti-VEGF injections received in all included patients was 8.2. Twelve eyes were switched from anti-VEGF to Iluvien implant (anti-VEGF/Iluvien subgroup) whilst 5 eyes were treated with Ozurdex prior to receiving an Iluvien implant (anti-VEGF/Ozurdex/Iluvien subgroup). The average number of Ozurdex implants was 1.75 (1-3). In anti-VEGF/Iluvien subgroup, the mean VA (SD) at baseline was 52.27 ± 15.6 ETDRS letters whilst the mean VA (SD) 12 months post-Iluvien was 59.33 ± 15.2 ETDRS letters (p-value greater than 0.05). The CFT(SD) at baseline was 540 ± 197 µm whilst the mean CFT 12 months post-Iluvien was 368 ± 114 µm (p = .033). In anti-VEGF/Ozurdex/Iluvien subgroup, the mean VA (SD) at baseline was 45.2 ± 15.6 ETDRS letters whilst the mean VA(SD) 12 months post-Iluvien was 52.4 ± 16.7 ETDRS letters (p-value greater than 0.05). The CFT(SD) at baseline was 641 ± 161 µm whilst the mean CFT 12 months post-Iluvien was 329 ± 51 µm (p = .02).

Conclusions
Our real-life results may indicate that Ozurdex implant brings additional benefit in CFT reduction in patients with chronic, anti-VEGF non-responsive diabetic macular oedema prior treatment with long-lasting Iluvien implant, whilst there was no statistically significant improvement in visual acuity gain.

Financial Disclosure
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Transcriptional determinants of proliferative diabetic retinopathy progression

**Purpose**
The retina is a complex tissue composed of functionally distinct cell types, organized into layers. Proliferative diabetic retinopathy (PDR) is characterized by ischemia- and inflammation-associated neovascularization and fibrosis at the vitreo-retinal interface. To date, the involved cell types have been characterized by immunological detection of selected markers. However, the details on the different cell types, their differentiation states and peculiar gene expression remain unknown. The aim of this study is to unravel the entire cell repertoire of the PDR fibrovascular tissues, the importance of blood and lymphatic vascular mechanisms, as well as the contribution of vascular and extra-vascular cell types in PDR pathophysiology and progression.

**Setting/Venue**
In this prospective clinicopathologic single-center study, diabetic patients were enrolled in the tertiary-care ophthalmology clinic, unit of vitreoretinal diseases at Helsinki University Hospital (HUH) Eye Clinic between 2018-2020. The study was conducted according to the Declaration of Helsinki and approved by the Institutional Review Board and Ethical committee of HUH. Signed informed consent was obtained from each patient.

**Methods**
We utilized omics and bioinformatics approaches to explore the cellular composition of patient-derived PDR fibrovascular tissues, unbiasedly classify cell types and study their differentiation signatures.

**Results**
The PDR fibrovascular tissues comprise a wider cell repertoire than has been previously described. A plethora of cell types was identified, including endothelial and smooth muscle cells, tissue stem cells, macrophages, as well as natural killer, T- and B- cell populations. The endothelial cell compartment showed a lymphatic differentiation signature.

**Conclusions**
Despite recent advances in PDR surgery, the most advanced PDR form remains a sight-threatening condition in many cases. Better understanding of the nature of complex PDR heterogeneity at a single-cell level will provide insights into the molecular level mechanisms and phenotypic output of PDR-initiating transcriptional pathways in support of DR progression as well as help identify functionally relevant biomarkers and potential novel therapeutic targets.

**Financial Disclosure**
None
Optical coherence tomography angiography in central retinal artery occlusion

Catarina Guedes Mota, Portugal

Purpose
To analyze Optical Coherence Tomography Angiography (OCTA) qualitative and quantitative data from patients with chronic central retinal artery occlusion (CRAO).

Setting/Venue
Medical Retina Unit, Ophthalmology Department – Central Lisbon University Hospital Centre, Portugal

Methods
Retrospective case-control study conducted with patients with CRAO. Patients and controls underwent spectral domain macular OCTA examination, performed at least one month after the acute event in the experimental group. En face OCTA vascular images of the superficial (SCP) and deep retinal capillary plexus (DCP) as well as of combined SCP and DCP (SCP+DCP), projecting from internal limiting membrane (ILM) to outer plexiform layer (OPL), were obtained. Images were further analyzed qualitatively and quantitatively. Vascular density (VD), junctions density (JD) and mean lacunarity (ML) were evaluated using a semi-automated vessel analyzing software (AngioTool 64. Version 0.6a). Peripheral retinal ischemia was also assessed by fluorescein angiography (AF) in the experimental group.

Results
The experimental group included 10 eyes from 10 patients with CRAO and the control group comprised of 10 healthy eyes from 10 patients. Mean age was 63.7 and 72.4 years-old and mean visual acuity was 1.9 and 0.0 logMAR in experimental and control group, respectively. Mean time between CRAO episode and OCTA examination was 4.4 ± 3.7 months among the study group. Macular ischemia was evident and the DCP was not clearly detectable on OCTA imaging in the majority of patients. Automated segmentation of SCP and DCP was considered unreliable and therefore a combined analysis (SCP+DCP) was performed. The experimental group demonstrated a significant reduction in VD and JD and an increased ML (p<0.05), comparatively with the control group. Three patients (30%) presented with peripheral ischemia on AF.

Conclusions
Although repermeabilization of the occluded artery occurred in the majority of the patients, the macular capillary blood flow was reduced, DCP being more affected than SCP. Segmentation errors induced by the atrophic inner retina limits the quantitative analysis of individual plexus. We suggest that combined retinal vasculature analysis would be preferable than separate SCP and DCP assessment.

Financial Disclosure
none.
Progression and response predictive factors of diabetic macular edema in patients treated with intravitreal therapy

**Purpose**
To study the safety and efficacy of PRN (pro re nata) pattern of ranibizumab in patients with naive diabetic macular edema (DME) in clinical practice and to study the relationship between diabetes’s systemic management, OCT biomarkers and patient’s evolution, in order to establish factors that may predict the response to treatment.

**Setting/Venue**
This study was performed in the retina section of the Ophthalmology department of the HCUV (Hospital Clínico Universitario de Valladolid).

**Methods**
Retrospective transversal study from patient records from patients under treatment with ranibizumab and PRN pattern in 2017 and their OCT images. Data were studied using descriptive and inferential analysis systems.

**Results**
After treatment, all patients were stable or achieved better anatomical and functional outcomes. The mean number of letters gained of best corrected visual acuity (BCVA) was 5.77 ± 6.41 letters. The average number of injections was 4.53 ± 2.06 (under 7 recommended injections on the first year of treatment). There was a CMT decrease of 110.77 ± 93.95 μm. Macular volume had a beneficial evolution too: Basal macular volume was 9.71 ± 1.65 mm³ and final macular volume was 8.43 ± 1.17 mm³. There was no relationship between systemic factors and DME evolution. No safety issues were found. Higher values of initial CMT and DME volume were related to better anatomical evolution after treatment (p<0.05).

**Conclusions**
Ranibizumab treatment with PRN pattern is effective for maintenance and improvement of visual function in DME. Patients with higher initial macular volume and higher CMT had better anatomical evolution after treatment. Alternatives for treatment and follow-up should be considered as injections and visits are below recommended values.

**Financial Disclosure**
None
Purpose
To evaluate the alterations in retinal oxygen saturation and retinal and choroidal blood flow in patients diagnosed with lipemia retinalis.

Setting/Venue
The study included five patients (10 eyes) with lipemia retinalis, and ten healthy controls were used for comparisons. Retinal arteriolar and venular oxygen saturation were measured using the non-invasive spectrophotometric retinal oximeter (Oxymap T1). The mean blur rate (MBR) of the optic nerve and choroidal blood flow was also analyzed by laser speckle flowgraphy (LSFG). Swept-source optical coherence tomography (OCT) angiography was evaluated.

Methods
This was a cross-sectional study. Patients with a confirmed history of lipemia retinalis were examined by two retina specialists before conducting LSFG and Oxymap T1. According to results of the recent fundus examination, patients were grouped into; 1) Untreated lipemia retinalis group (if the latest fundus examination was abnormal) or 2) Treated lipemia retinalis group (if the latest fundus examination was normal).

Results
Patients with untreated lipemia retinalis had a significantly higher retinal arteriolar and venular oxygen saturation (p=0.004 and 0.008, respectively). Furthermore, patients with untreated lipemia retinalis had significantly small retinal arteriolar and venular diameters when compared to the control group (p=0.001). On LSFG, untreated lipemia retinalis eyes exhibited a high overall MBR, vessel MBR, and tissue MBR of the optic nerve when compared to the control group (p=0.002, 0.008, and 0.040 respectively). Blow-out score was significantly elevated, while the resistivity index was significantly low in eyes with treated and untreated lipemia retinalis. OCT-angiography was unremarkable in all eyes with lipemia retinalis.

Conclusions
The increase in retinal blood flow and oxygen saturation may explain the preservation of visual acuity and function despite the severe morphological changes seen in patients with lipemia retinalis.
Foveal and extrafoveal effects of half-dose photodynamic therapy in chronic central serous chorioretinopathy: A cohort study

Purpose
During the last decade, verteporfin half-dose photodynamic therapy (HD-PDT) has been demonstrated to maintain efficacy when treating acute or chronic Central Serous Chorioretinopathy (cCSC) while reducing the risk of sight-threatening complications. In general, reduced-setting PDT can be broadly applied to treat subfoveal, juxtafoveal and extrafoveal leakage points, whereas a safety distance to the fovea has been traditionally imposed for conventional laser and high-density subthreshold micropulse laser to avoid central vision damage. This study aims to compare the efficacy and safety of foveal and extrafoveal HD-PDT for cCSC.

Setting/Venue
Department of Ophthalmology, Hospital de Braga, Braga, Portugal.

Methods
This retrospective, cohort study included cCSC eyes submitted to HD-PDT on foveal (F) or extrafoveal (E) areas. Patients were evaluated at baseline and 12 weeks after treatment for best corrected visual acuity (BCVA) and the following spectral-domain optical coherence tomography (SD-OCT) subfoveal parameters: central macular thickness (CMT), outer nuclear layer, external limiting membrane, ellipsoid zone, interdigitation zone, choroidal thickness and subretinal fluid (SRF).

Results
F group comprised 33 eyes (47.1%) and E group comprised 37 eyes (52.9%). Both groups showed an improvement of BCVA after HD-PDT with no significant differences in final BCVA (p=0.41). CMT and SRF showed a significant improvement after HD-PDT in both groups, but the rate of disruption of the external retinal layers remained stable. During follow-up, SD-OCT parameters and the rate of anatomical success showed no significant differences regarding the treatment location. No major sequelae were noticed.

Conclusions
Foveal and extrafoveal applications of HD-PDT for cCSC showed comparable efficacy and safety.

Financial Disclosure
This research received no financial support. The authors declare no financial, institutional nor commercial interests related to the research.
Title
Characteristics of retinal Neovascularization in proliferative diabetic retinopathy

Purpose
To analyze diabetic NV and their corresponding branching routes in PDR imaged by optical coherence tomography angiography (OCTA) for a better comprehension of the pathophysiology of neoangiogenesis during PDR and to highlight the role of PVD status.

Setting/Venue
Patients from the Department of Ophthalmology, Ulm University (Germany).

Methods
Eyes with PDR were consecutively evaluated by OCTA imaging and fluorescein angiography (FA). Neovascularization of the disc (NVD) and neovascularization elsewhere (NVE) were analyzed with 6x6 mm and 8x8 mm OCTA flow images and B-scans with flow registration. The automated segmentations of vitreoretinal interface (VRI) and superficial retina were obtained for analysis.

Results
61 eyes of 42 patients with PDR were analyzed. A total of 115 NV with their corresponding proliferation routes were visualized and characterized, marking 89 NV (77%) proliferating along posterior hyaloid membranes (PHM), 19 NV (17%) proliferating along epiretinal membranes and 7 NV (6%) along fibrovascular membranes. In 55 of 61 eyes (90%) the posterior vitreous was partially detached, in 1 eye the posterior vitreous was completely detached and in 1 eye adherent. In 4 eyes the PVD status was not assessable.

Conclusions
PVD and status of VRI seem to be involved in the progression of PDR. We identified PHM as the main proliferating route of diabetic NV. Thus, although complete PVD occurs less frequently than partial PVD in diabetic patients, complete PVD may protect against the formation of florid NV and progression to aggressive PDR. Therefore, assessment of the PVD status in patients with diabetic retinopathy is recommended.

Financial Disclosure
none
**Title**
Investigation of retinal microcirculation in diabetic patients using state of art imaging techniques

**Purpose**
To assess retinal microcirculation in patients with different stages of diabetic retinopathy and controls in an analytical observational study.

**Setting/Venue**
The current research includes seventy-four eyes from seventy-four subjects consulted in the Retina Clinic, Bucharest, in 2019 and 2020.

**Methods**
Adaptive optics ophthalmoscopy was used to measure the parameters of temporal retinal arterioles. Optical coherence ophthalmoscopy angiography was employed to assess foveal avascular zones and vessel densities of the superficial capillary plexuses.

**Results**
Diabetic patients with or without diabetic retinopathy presented retinal arterioles structural changes, depicted mainly by altered values of wall to lumen ratio and of vascular density in the retinal superficial capillary plexus.

**Conclusions**
Both adaptive optics ophthalmoscopy and optical coherence tomography angiography are providing useful information about the retinal microvasculature in diabetic patients, having a high potential to bring important information on the prognostic and pathophysiology of the disease in the future.

**Financial Disclosure**
no financial interest
An association between the intestinal permeability biomarker zonulin and the development of diabetic retinopathy in type II diabetes mellitus

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Ordu University Training and Research Hospital

This study was conducted with a total of 89 T2DM patients including 33 non-DR, 28 non-proliferative DR (NPDR), 28 proliferative DR (PDR), and 32 healthy controls. Zonulin levels were determined with the ELISA kit by taking a blood sample.

Zonulin levels were significantly higher in the PDR group compared to the other three groups (P=0.001). Also, it was significantly higher in the non-DR and NPDR groups compared to the control group. After multivariate logistic regression analysis, zonulin was found to be an independent predictor of DR (Odds Ratio: 1.781 95% CI: 1.122-2.829 P= 0.014).

The current results in this study showed that participants with T2DM had high levels of serum zonulin. Moreover, serum zonulin levels are much higher in participants with PDR than in participants with NPDR and non-DR. Zonulin is an important indicator of IP and GMD. Accordingly, IP regulation and GM restructuring may be one of the main targets in DR treatment. More studies are needed to determine whether there is a direct association of a eubiotic GM and IP with DR.

Euretina 2021 Virtual Abstracts

Title
An association between the intestinal permeability biomarker zonulin and the development of diabetic retinopathy in type II diabetes mellitus

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Purpose
Increased intestinal permeability (IP) and gut microbiota dysbiosis has been held responsible for low-grade chronic inflammation (LGCI). LGCI is an important underlying cause of diabetic retinopathy (DR) pathogenesis. This study aims to demonstrate the relationship between the IP biomarker zonulin and DR in patients with type 2 diabetes mellitus (T2DM).

Setting/Venue
Ordu University Training and Research Hospital

Methods

Conclusions
The current results in this study showed that participants with T2DM had high levels of serum zonulin. Moreover, serum zonulin levels are much higher in participants with PDR than in participants with NPDR and non-DR. Zonulin is an important indicator of IP and GMD. Accordingly, IP regulation and GM restructuring may be one of the main targets in DR treatment. More studies are needed to determine whether there is a direct association of a eubiotic GM and IP with DR.

Financial Disclosure
Financial Disclosure Authors have no financial or proprietary interest in any product mentioned in the article. Declaration of Interest No author has any possible conflict of interest. The authors alone are responsible for the content and preparation of the paper. Funding No funding was received for this research.
Assessment of clinical implications of peripheral diabetic retinopathy lesions using ultra-wide-field imaging with Clarus fundus camera in patients with type II Diabetes Mellitus

To assess the prevalence of Diabetic Retinopathy (DR) lesions in the retinal periphery using an ultra-wide-field (UWF) imaging device, and to evaluate the association between exclusively peripheral lesions (EPL) and predominantly peripheral lesions (PPL) and the presence of ischemia and macular morphologic and vascular changes in patients with type II Diabetes Mellitus (DM).

Setting/Venue
Ophthalmology Department of Garcia de Orta Hospital, Almada, Portugal.

Methods
This retrospective study included a cohort of patients who underwent DR screening by a single montage image from two UWF images obtained by using a non-contact and non-mydriatic high definition UWF imaging system with true color (Zeiss Clarus700). Patients records were reviewed for DM duration, glycemic profile, best corrected visual acuity and DR grading and location. UWF fluorescein angiography (FA) and optical coherence tomography angiography, obtained by using Zeiss Clarus700 and Zeiss Cirrus HD-5000 with Angioplex 6x6mm, were also assessed.

Results
This study included 102 eyes of 102 patients, with a mean age of 68.49±14.38 years. Forty-two eyes (41.18%) had DR, of which 23.81% had EPLs and 21.43% had PPLs. These patients had a longer duration of DM (EPLs vs PPLs vs non peripheral lesions (NPL): 25.80±7.13 vs 23.43±5.76 vs 17±6.66 years; EPLs vs NPLs p=0.01, PPLs vs NPLs p=0.02) and higher mean HbA1c (EPLs vs PPLs vs NPLs: 7.94±0.56 vs 8.40±0.22 vs 6.48±1.02%; EPLs vs NPLs p=0.06, PPLs vs NPLs p=0.03). Most subjects had mild non-proliferative DR (EPLs vs PPLs vs NPLs: 96.40±3.21 vs 92.62±1.76 vs 91.77±4.90%). Macular vascular density was reduced in EPLs and PPLs (central: EPLs vs PPLs vs NPLs: 27.32±2.11 vs 25.64±3.46% vs 29.24±3.04%; EPLs vs NPLs p=0.06, PPLs vs NPLs p=0.04). No differences were found in foveal avascular zone of patients with peripheral lesions compared to NPLs. No signs of peripheral ischemia were found on UWF FA of patients with EPLs and PPLs.

Conclusions
Our results suggest that EPLs and PPLs tend to occur in DM of greater duration and severity compared to patients with lesions predominantly located in the posterior pole. Although EPLs and PPLs were not associated with increased peripheral or macular ischemia or with worsening of most of the parameters evaluated, superficial vascular density seems to be reduced. These findings alert to the relevance of DR screening with true color UWF imaging even in patients with type II DM.

Financial Disclosure
None
Intravitreal aflibercept in routine clinical practice: 12-month results from the Russian cohort of treatment-naïve patients with diabetic macular edema in the AURIGA study

**Purpose**
The aim of the 24-month AURIGA study is to evaluate the clinical outcomes of intravitreal aflibercept (IVT-AFL) in patients with diabetic macular edema (DME) or macular edema secondary to retinal vein occlusion (RVO) in routine clinical practice. Patients were enrolled from 11 countries, including Russia. The results of the 12-month analysis in treatment-naïve patients with DME who were enrolled in Russia are presented here.

**Setting/Venue**
AURIGA (NCT03161912) is an ongoing prospective, multicenter, observational study evaluating IVT-AFL in patients with DME or macular edema secondary to RVO. The data below summarize the outcomes for the treatment-naïve cohort of patients with DME in Russia.

**Methods**
Treatment-naïve patients (aged ≥18 years) with DME were enrolled from April 2018 to August 2020. Decisions regarding IVT-AFL treatment were made at the discretion of the prescribing physician, according to their medical practice. The primary efficacy endpoint was the change in best-corrected visual acuity (BCVA; Early Treatment Diabetic Retinopathy Study [ETDRS] letters) from baseline to Month [M] 12. Secondary endpoints included the change in BCVA from baseline to M6, and, at both M6 and M12, the percentage of study eyes with BCVA gains and losses (≥5, ≥10, and ≥15 letters), change in central retinal thickness (CRT) from baseline, and number of IVT-AFL injections. Safety was also evaluated throughout the study. Patients who received at least 1 IVT-AFL injection and had at least 1 post-initial observation available were included in the full analysis set.

**Results**
Of 280 treatment-naïve patients (mean age: 61.2 years; female: 73%) enrolled with DME, 66% completed 1 year of treatment. Median duration from DME diagnosis to IVL-AFL treatment was 3.4 months (range: 0.0–148; interquartile range: 0.9–11.2). At M6 and M12, the mean±SD BCVA had improved by +8.6±13.1 and +7.1±13.5 letters, respectively (baseline: 53.6±19.1 letters). The mean number of IVT-AFL injections was 4.4±1.5 by M6 and 5.7±2.6 by M12; 62% (173/280) of patients received ≥5 injections by M6 and 40% (112/280) of patients received ≥7 injections by M12. At M12, 94.1% (254/270) of patients had maintained vision (≤15-letter loss), 38.9% (105/270) of patients had gained ≥10 letters, and 28.1% (76/270) of patients had gained ≥15 letters. By M12, the mean CRT had improved by −118.0±143.9 µm (baseline: 441.0±129.6 µm). Ocular treatment-emergent adverse events in the study eye occurred in 2.5% (7/280) of patients; conjunctival hemorrhage was the most common (1.1% [3/280]). There were no reported cases of endophthalmitis or retinal vasculitis; one case of intraocular inflammation was reported.

**Conclusions**
Treatment-naïve patients with DME who received IVT-AFL treatment in routine clinical practice in Russia achieved clinically relevant improvements in functional and anatomic outcomes that were maintained across the 12-month study period. The mean gain in BCVA at 12 months was +7.1 letters, similar to other observational studies. The majority of patients in this analysis received ≥5 injections in the first 6 months of treatment, and the BCVA gains achieved during this timeframe highlight the importance of intensive treatment to optimize functional outcomes. The safety profile of IVT-AFL was consistent with previous studies. The AURIGA study builds on the wealth of real-world evidence supporting the effectiveness and safety of IVT-AFL as evaluated in 22 published Bayer-sponsored studies in routine clinical practice treating more than 18,000 patients across 24 countries in multiple indications.

**Financial Disclosure**
Anzhella Fursova: None. Helmut Allmeier: Employee of Bayer Consumer Care AG, Basel, Switzerland. Tobias Machewitz: Employee of Bayer AG, Berlin, Germany. Daniel Molina: Employee of Bayer Consumer Care AG, Basel, Switzerland. Funding: The AURIGA study was funded by Bayer AG, Germany. Medical writing support was provided by ApotheCom, and funded by Bayer Consumer Care AG, Pharmaceuticals, Switzerland.
Purpose
To evaluate the distribution of capillary non-perfusion (CNP) in superficial and deep capillary plexuses (SCP and DCP) in eyes with diabetic retinopathy (DR).

Setting/Venue
Rassoul Akram Hospital, Tehran, Iran

Methods
In this retrospective case series, macular optical coherence tomography angiography (OCTA) images were obtained from eyes with DR without diabetic macular edema. The area of CNP in SCP and DCP was delineated using an automated approach after excluding the foveal avascular zone and major retinal vessels. The distribution and spatial correlation of the CNP in each layer was analyzed.

Results
Forty-three eyes of 27 patients with diabetic retinopathy with a mean age of 59.10± 9.05 years were included. The mean CNP area in SCP was statistically significantly higher than DCP (0.722± 0.437 mm2 vs 0.184± 0.145 mm2, respectively, P<0.001). There was a statistically significant association between mean BCVA (0.28±0.21 logMAR) and CNP area in DCP (P=0.01). After automated subtraction of CNP areas in DCP from SCP, 25.43±15.05 % of CNP areas in the DCP had co-localized CNP areas in SCP. The CNP percentage was statistically significantly different between the concentric rings on foveal center, both in SCP and DCP (both P<0.001) showing a decreasing trend from the outer ring toward the center.

Conclusions
In DR, SCP is more ischemic than DCP. This is in contrast to the previously described oxygenation dependent ischemic cascade following acute retinal vascular occlusions. This study provides further insight into the retinal ischemia in DR.

Financial Disclosure
I have no financial interest to report.
Title
Retinal and Choroidal Vascularization in Internal Carotid Artery Stenotic Disease

Purpose
To study retinal and choroidal vascularization in internal carotid artery (ICA) stenotic disease patients.

Setting/Venue
Central Lisbon University Hospital Centre

Methods
A case–control study including severe ICA stenotic disease patients and healthy controls was conducted. Choroidal binarization was performed using the Image J software, and total subfoveal choroidal area, luminal area and vascular choroidal index of the subfoveal 1500um, were obtained. Vessel density, junctions’ density and lacunarity of the superficial capillary plexus (SCP), and deep capillary plexus (DCP) from OCTA scans were calculated with AngioTool software. Foveal avascular area (FAZ) of the SCP and DCP was measured manually using the Heidelberg software. Subgroup analysis regarding the presence of ocular ischemic syndrome (OIS) was performed.

Results
Twenty eyes of 16 patients and 17 eyes of 17 sex and age matched healthy controls were included. Seven eyes of five patients had OIS. Patients’ group showed significantly lower values in SCP vascular density (p=0.019), SCP junctions’ density (p=0.034), and DCP vascular density (p=0.015) comparative to healthy controls. SCP lacunarity was higher in patients comparative to healthy controls (p=0.009). The OIS patients’ subgroup had lower values in DCP vascular density (p=0.026), and higher values in DCP lacunarity (p=0.019), comparative to stenotic patients without OIS. FAZ areas and choroidal parameters did not differ between groups or subgroups (p>0.05).

Conclusions
Retinal vascularization is impaired in severe carotid artery stenotic disease patients. DCP is even more affected in eyes with OIS.

Financial Disclosure
None
A comparative study on the choroidal vascularity index and the determination of cut-off values in optical coherence tomography patterns of diabetic macular oedema

Purpose
To compare the choroidal thickness (CT) and choroidal vascularity index (CVI) in different optical coherence tomography (OCT) patterns of diabetic macular oedema (DMO).

Setting/Venue
A retrospective comparative study at a single tertiary clinic.

Methods
A total of 301 eyes of 301 patients who had enhanced depth imaging-optical coherence tomography (EDI-OCT, Heidelberg Engineering, Heidelberg, Germany) imaging to assess the subfoveal CT and submacular CVI between 2017-2021 and diagnosed with DMO by OCT were included in the present study. EDI-OCT imaging of the patients before anti-VEGF treatment and one eye of each patient that meets the criteria were analyzed. OCT images of the patients were retrospectively examined and OCT features were classified into three patterns: diffuse retinal thickening (DRT); cystoid macular oedema (CMO), and serous retinal detachment (SRD). Of these 79 (26.3%) had DRT, 153 (50.8%) had CMO, and 69 (22.9%) had SRD. The choroidal areas were measured with ImageJ (National Institutes of Health, Bethesda) software. The CVI, the proportion of the luminal area to the total choroidal area, was assessed. CT and CVI analysis was performed from the foveal region.

Results
The mean ages of the DMO groups were similar (61.06 for the DRT, 61.82 for the CMO, and 60.27 for the SRD, all P>0.05). The mean values of subfoveal CT were determined as 272.86 µm for the DRT, 271.18 µm for the CMO, and 251.05 µm for the SRD. No significant difference was found between different DMO subtypes in terms of subfoveal CT (all P>0.05). The mean values of subfoveal CVI were determined as 60.80% for the DRT, 61.23% for the CMO, and 60.72% for the SRD. Similarly, there was no significant difference between different DMO subtypes in terms of subfoveal CVI (all P>0.05).

Conclusions
This study showed that similar diabetic choroidopathy patterns accompany different DMO subtypes. These findings may provide insights into the pathogenesis of different patterns of DMO, which may be primarily related to structural and vascular differences among the retinal layers.
Wyburn Mason Syndrome (WMS) is a congenital non-hereditary condition characterized by multiple arteriovenous malformations (AVMs) with less than a hundred cases reported in the literature. WMS has varied phenotypical expressions predominantly affecting the brain, orbit and face and is thought to result from embryonic maldevelopment. The aim of our work is to present a multimodal assessment of a WMS case and to highlight its main manifestations which can first be diagnosed by the ophthalmologist.

Methods
We describe the case of a 24-year-old male referred to our clinic to investigate abnormal conjunctival vascular changes. He had already been submitted to seven surgical procedures due to multiple facial and oral mucosal AVMs. His past medical history was otherwise unremarkable. On examination his best corrected visual acuity was 20/20 in both eyes. On slit-lamp observation an extensive conjunctival vascular malformation of the left eye (LE) was present. The LE fundus revealed multiple markedly dilated and tortuous arterioles and veins with several arteriovenous communications with a racemose distribution from the optic disc over all four quadrants to the retinal periphery. The right eye fundus was unremarkable. Multimodal imaging including fluorescein angiography (FA), optical coherence tomography (OCT) and standard automated perimetry (SAP) was performed. In order to understand if these vascular malformations were associated with similar lesions in the orbit and/or brain magnetic resonance imaging (MRI) was requested.

Results
The FA showed that there was no leakage from the enlarged medusa-like vessels nor signs of retinal ischemia. The OCT revealed enlarged choroidal vessels in the LE with normal retinal thickness and no macular edema. In the SAP of the LE there was a slightly diminished sensitivity in the superior quadrants with little significance. Head and neck MRI revealed AVMs in several territories including midbrain, left cerebellar hemisphere, orbit (with both intraconal and extraconal components), left buccal space (also pterygopalatine fossa) and superior lip. The case was then discussed in a multidisciplinary team meeting with neuroradiologists, neurologists and dermatologists to establish an optimal follow-up and treatment strategy.

Conclusions
In patients presenting with hemifacial vascular malformations phakomatoses should be considered and a thorough ophthalmologic evaluation must be performed. Due to phenotypic variance orbital and central nervous system involvement should be ruled out. As illustrated by this case, a multidisciplinary approach with multimodal imaging is of paramount importance.
Purpose
Retinal vein occlusion (RVO) is the second-leading cause of retinal vascular disease-related vision loss. The most common cause of visual loss in RVO patients is macular edema (ME). Recently, anti-vascular endothelial growth factor (anti-VEGF) therapy has been the standard treatment for RVO-related ME. The VIBRANT Study investigated the effect of anti-VEGF therapy on ME with branch retinal vein occlusion (BRVO), and the GALILEO Study investigated the effect of anti-VEGF therapy on ME with central retinal vein occlusion (CRVO). The findings in these large-scale, prospective, randomized clinical trial studies revealed the effectiveness of anti-VEGF treatment, however, the visual acuity (VA) of the patients before treatment in the studies was 20/40 or less. Thus, the purpose of this prospective observational study is to investigate the effects of intravitreal aflibercept (IVA) injections for BRVO and CRVO patients with a VA of better than 20/40.

Setting/Venue
Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan.

Methods
In this prospective observational study, untreated BRVO and CRVO patients with ME and a 20/40 or better VA were enrolled. We excluded the following patients: those with a history of laser therapy, other ocular surgery, topical steroid treatment or other anti-VEGF therapy; those with uncontrolled glaucoma; those with uncontrolled hypertension; and/or those with pathology of other retinal disorders that affect visual acuity. After obtaining written informed consent, the patients received IVA injections with a 'treat-and-extend' regimen. The primary endpoints were retinal sensitivity (RS) at central 4 degrees measured with microperimetry (MP-1) and best-collected visual acuity (BCVA) at 12-months post treatment. The secondary endpoints were central retinal thickness (CRT) measured by optical coherence tomography (OCT) and the mean deviation (MD) value of Humphrey 30-2 visual field analyzer (HFA) findings at 12-months post treatment.

Results
Thirty-seven eyes of 37 BRVO patients and 15 eyes of 15 CRVO patients were enrolled. Of those, 35 BRVO patients and 14 CRVO patients completed the study. In the BRVO group and CRVO group, from pre-treatment to at 12-months post therapy, mean RS significantly improved from 8.75±3.32 dB to 11.6±3.08 dB and from 6.30±3.49 dB to 10.59±4.68 dB, respectively (P<0.05), mean BCVA (logMAR) significantly improved from 0.19±0.12 to 0.06±0.16 µm (P<0.005) and from 0.15±0.13 to 0.07±0.16 (P=0.0805), respectively, thus showing no significant improvement in the CRVO patients, CRT significantly decreased from 402±116 µm to 245±51.1 µm (P<0.0001) and from 397±135 µm to 237±70.0 µm (P<0.005), respectively, and the MD values HFA changed from -4.5±3.4 dB to -4.5±4.4 dB (P=0.8619) and from -2.9±2.1 dB to -3.2±3.1 dB (P=0.8777), respectively, thus illustrating no significant change in both groups. In the BRVO and CRVO groups, the mean number of IVA injections was 5.9±1.6 and 5.4±1.1, respectively. Two BRVO patients and 1 CRVO patient were dropped out of the study. In the BRVO group, 1 patient developed endophthalmitis and treatment in 1 patient was interrupted. In the CRVO group, branch retinal artery occlusion developed in 1 patient.

Conclusions
Anti-VEGF therapy was found effective for treating RVO-related ME patients with a VA of 20/40 or better.
Title
Choroidal thickness alteration after photodynamic therapy for chronic central serous chorioretinopathy

Purpose
To analyze the influence of PDT on functional and morphological parameters of eyes with chronic CCS (cCCS).

Setting/Venue
Choroidal vascular hyperpermeability plays an important role in the pathophysiology of central serous chorioretinopathy (CCS). Increases choroidal thickness (pachychoroid) is associated with CCS and can be quantified by optical coherence tomography (OCT). Photodynamic therapy (PDT) is an effective treatment option for central serous chorioretinopathy.

Methods
We retrospectively analyzed all patients with fovea-involved cCCS treated with half-dose Verteporfin-PDT within the last five years at our center. Controls were age- and sex-matched. Best corrected visual acuity (BCVA, converted in LogMAR and backwards), clinical and the following OCT parameters (Spectralis, Heidelberg Engineering, Germany) were explored: the macular volume (mm³) and the presence of subfoveal fluid (SFF). The choroidal thickness (µm) was manually measured at the foveolar center. Prism 9 (version 9.1.0, GraphPadSoftware) was used for statistical analysis.

Results
16 eyes of 13 male patients and 1 female patient (mean age 53±11 (SD) years (ys)) with a duration of visual symptoms of 49.5±35 months and a follow-up of 68±29 days after PDT and 16 controls (15 male and 1 female control, age 53±12 ys) were included into the study. BCVA tended to improve from 0.26±0.34 to 0.47±0.36 after PDT. Macular volume and choroidal thickness tended to decrease from 8.6±1.1 to 8.1±0.6 (controls: 8.6±0.4) respective from 425±86 to 373±87 (controls 282±70). Pre- and post-PDT choroidal thickness were correlated (r=0.6951, 95% CI 0.3-0.88, p=0.0026). In all 9 eyes with resorbed SFF after PDT, pre-PDT choroidal thickness was lower (370±42, p=0.014) compared to eyes with persistent SFF (474±85). Macular volume or the duration visual symptoms were not associated with the resolution of SFF after PDT.

Conclusions
Higher level of pachychoroid in cCCS seems to be respond already shortly after PDT regarding resorption of SFF and decrease of choroidal thickness.

Financial Disclosure
none
**Title**  
Secondary macroaneurysm due to aberrant retinal macrovessel

**Purpose**  
Retinal arterial macroaneurysms are pathological round or fusiform dilations of retinal arterial branches. Although frequently related to chronic hypertension and lipid abnormalities, their exact pathogenesis remains undetermined. Retinal macrovessels consist of dilated vessels with end branches extending beyond the horizontal raphe. Arteriovenous transition of these abnormal vessels usually occurs via the capillary plexus, thus contributing to local blood flow turbulence and retinal vessel frailty. The aim of this report is to describe a clinical case where these entities overlap and their respective management, highlighting the importance of an appropriate follow-up.

**Setting/Venue**  
Egas Moniz Hospital, Western Lisbon Hospital Center. Lisbon, Portugal.

**Methods**  
A 54-year-old woman presented in the Ophthalmology Emergency Department complaining of floaters and photopsia in the left eye (LE). Ophthalmologic examination disclosed a LE best corrected visual acuity (BCVA) of 5/10, with unremarkable anterior segment observation. LE dilated fundus examination revealed an arteriolar dilation close to an aberrant retinal macrovessel, temporal to the macula and with surrounding exudates. The retinal macrovessel originated in the optic disk and coursed through the fovea and the horizontal raphe. The right eye had a BCVA of 10/10 and presented no abnormalities. Past ophthalmological history included LE pars plana vitrectomy 1 year before, due to a pre-macular haemorrhage secondary to Valsalva retinopathy. No vascular lesions suggestive of macroaneurysm were observed then. Remaining medical history reported smoking habits and previously treated breast neoplasm, with the absence of systemic hypertension and dyslipidaemia.

**Results**  
Pursuit of macular involvement required further characterization. Optical Coherence Tomography (OCT) demonstrated a round cavity with a hyperreflective wall in the inner retinal layers suggestive of a macroaneurysm, with associated lipid deposits and intraretinal fluid. Central Foveal Thickness (CFT) was 395 µm. OCT-Angiography presented retinal blood flow abnormalities and no signs of choroidal neovascularization. The patient was proposed for LASER treatment of the macroaneurysm to prevent further macular edema. Focal argon LASER photocoagulation was performed in two sessions using a direct LASER technique, to accomplish macroaneurysm sclerosis. 2 months follow-up OCT scans showed a CFT of 307 µm, vessel closure and subsequent resolution of macular edema. Last BCVA was 7/10.

**Conclusions**  
Retinal arterial macroaneurysms have an overall benign prognosis, however symptomatic and active lesions such as macular edema and exudates dictate treatment. LASER treatment choice remains controversial. This clinical case reported how retinal vascular abnormalities can severely affect visual function and may elucidate other pathological mechanisms for the development of vessel damage. Furthermore, it is important to emphasize the need to have a case-to-case follow-up plan to ensure early detection of complications associated with aberrant vessels and prompt LASER treatment.

**Financial Disclosure**  
no financial relations
### Purpose
Ranibizumab has been detected in the breast milk of lactating women following intravitreal injection but there is no study looking at the impact on the child of a nursing mother receiving ranibizumab therapy. The purpose of this study is to analyze the levels of ranibizumab and vascular endothelial growth factor (VEGF)-A in the breast milk of a nursing mother and in the bloodstream of her infant after intravitreal ranibizumab injections followed by a 3-day ‘pump and dump’ strategy.

### Setting/Venue
Single-center, prospective clinical study performed at Mount Sinai Hospital, Toronto, Canada.

### Methods
This study included both a 34-year-old nursing patient who required bilateral ranibizumab injections post-partum and her newborn child. The mother received an injection of ranibizumab 0.5mg in each eye with 1-week interval between eyes. The infant was regularly breastfed, except for 3 days following each injection, when a ‘pump and dump’ strategy was adopted, where the mother regularly pumped and discarded the breast milk while the infant was fed exclusively with formula. Breast milk samples were obtained at baseline and then daily for 14 days after the first injection. The infant’s blood samples were obtained daily for 11 days starting on the day before breastfeeding was resumed. Plasma and serum samples were obtained for VEGF-A and ranibizumab analysis, respectively. In addition, blood samples of 3 control infants of similar gestational age as the index infant were obtained and analyzed for plasma VEGF-A levels.

### Results
Ranibizumab levels remained below the lower limit of quantitation (LLOQ) of the assay at all time points in the mother’s breast milk and in the infant’s serum. VEGF-A levels in the breast milk gradually reduced from 5266pg/ml at baseline to 1537pg/ml at day 11, and then increased to 3438pg/ml at day 14. Plasma VEGF-A levels in the infant remained below the LLOQ at all time points, except for days 9 (20.45pg/ml) and 11 (13.19pg/ml). Plasma VEGF-A levels in the control patients were also below the LLOQ.

### Conclusions
Ranibizumab was not detected in the infant of a nursing mother who received intravitreal ranibizumab injection followed by a 3-day ‘pump and dump’ strategy and systemic VEGF-A levels did not seem to be affected. This suggests that a 3-day ‘pump and dump’ strategy could possibly be a safe option for nursing mothers who require intravitreal ranibizumab therapy but want to continue breastfeeding.
Title
OCT-A signs of preclinical diabetic retinopathy progression

Purpose
To analyse visual functions and dynamic OCT-A features in patients with type 1 diabetes mellitus (T1DM) with no clinical signs of diabetic retinopathy (DR)

Setting/Venue
A two-centric prospective study was conducted at the Department of Ophthalmology of Faculty of Medicine of Moscow State University and Department of Ophthalmology of Endocrinology Research Center, Moscow.

Methods
106 eyes of 58 T1DM patients with no apparent DR and 55 eyes of 31 healthy volunteers were included in the study. The mean duration of DM was 10.8 ± 6.9 years. All participants underwent BCVA, contrast sensitivity and LLVA assessment, as well as 3×3 mm optical coherence tomography angiography (DRI OCT Triton, Topcon (Japan) and Copernicus REVO, Optopol (Poland)). For OCT-A scans we evaluated the presence of non-perfusion areas (NPA), foveal avascular zone (FAZ) area (mm2), acircularity index, vessel density (VD) and skeletonized density in superficial vascular plexus (SVP), intermediate capillary plexus (ICP) and deep capillary plexus (DCP), choriocapillaris flow deficits (FD).

Results
There was no difference in FAZ area between the groups, however, acircularity index was higher in T1DM patients than in normal subjects (1.479 ± 0.245 and 1.333 ± 0.169). In the T1DM group vessel density and skeletonized density were reduced in the SVP and DCP. FD density was higher in the T1DM group than in normal subjects (12.10 ±1.82 and 10.53 ± 3.09). A 1-year observation revealed a decline in vessel density in SVP in T1DM patients (29.36 ± 2.56 and 27.11 ± 3.07)

Conclusions
We discovered an increase in FAZ acircularity and reduction of vessel density and skeletonized density in SVP and DCP, as well as changes in CC flow at the preclinical stage of DR. A 1-year decline in vessel density in SVP can be an early sign of DR progression in T1DM patients without apparent DR.

Financial Disclosure
No
Subthreshold laser therapy via non-damaging retinal therapy (NRT) in patients with non-center involved diabetic macular edema

Purpose
The aim of this study was to evaluate the efficacy of subthreshold laser therapy via Non-damaging Retinal Therapy (NRT) in patients with non-center involved diabetic macular edema (non-CI DME).

Setting/Venue
This prospective, controlled study comprised of patients with newly diagnosed non-CI DME who admitted to Ankara Numune Training and Research Hospital Eye Clinic between March 2017 and April 2019. As of April 2019, due to the hospital transfer, the examinations of the patients after this date until October 2019 were carried out at Ankara City Hospital. This study was approved by the local Ethics Committee of our institution. Informed consent was obtained from each patient.

Methods
The study included cases above the age of 18 who had naive non-CI DM. The best corrected visual acuity (BCVA) with log-MAR, slit-lamp and fundus examination findings, central macular thickness (CMT) and peripheral edema values from spectral domain OCT analysis were investigated at 3-monthly intervals. While NRT was performed to one group, the other group was followed at 3-monthly intervals as control without treatment sequentially. NRT was done with end-point management software of Pattern Scanning Laser (Pascal). Barely visible test spots with 200 µm and 0.015 s was set as the threshold at a non-edematous area inside the vascular arcade. The endpoint management was set to 30% and irradiation was performed to edematous area using a macular grid pattern. At each control visit, NRT was performed to the edematous parafoveal quadrant in the treatment group. If center involved DME developed in either group, intravitreal anti vascular endotelial growth factor (IV anti-VEGF) was performed and the eye was excluded from the study subsequently. Primary outcome measure was the change of retinal thickness over time and between groups. Secondary outcome measures were change in best corrected BCVA, difference in the rate of anti-VEGF requirement, and laser treatment effect on FAF imaging.

Results
A total of 75 eyes were evaluated, 36 in the treatment group and 39 in the control group. Mean follow-up period was 440.61±346,333 days and 400.56±305,567 days (P=0,75). There was no significant difference between the groups in age (P=0,271) and in terms of diabetic retinopathy severity (P=0,14). Ratio of female/male was 24/12 in the treatment group and 14/25 in the control group (P=0,008). The change in parafoveal superior, nasal and temporal quadrants over time and between groups assessed by removing the effect of gender was found significant (P<0,05). This difference seemed to be evident after the 21st month with more thinning in the treatment group. It was observed that parafoveal inferior quadrant thinned more in the treatment group compared to the control group and the difference between the groups was significant (P=0,03). The difference was evident at the 24th month, but the change between groups over time was not significant (P>0,05). CMT and BCVA changes over time and between groups were not significant (P>0,05). Rates of center-involved DME development requiring IV anti-VEGF treatment at the end of the first and second years between the groups were not different (P>0,05). No laser scar was detected in any eye in FAF imaging.

Conclusions
In conclusion, we applied NRT to some patients in eyes with non-CI DME and followed up some patients without treatment. At the end of the first and second year, we observed that BCVA was preserved in both groups. Parafoveal anatomical changes were significantly better in the treatment group. NRT alone is effective and safe in the treatment of non-CI DME at 30 months follow-up. With this method, it may be foreseen that visual acuity will be better preserved in the long term by avoiding the possible side effects of conventional laser treatment. The results of our study suggest that it would be appropriate to conduct large-scale studies examining whether the combination of IV agents and NRT treatment reduces the need for IV injection in DME involving the foveal center.

Financial Disclosure
I have no financial relationship with any company
Clinical Factors associated with Rate of Progressive Inner and Outer Retinal Thinning in Patients with Diabetic Macular Edema

Purpose
The occurrence of retinal thinning after diabetic macular edema (DME) resolution may significantly impact on visual outcomes of patients with diabetic retinopathy. The aim of this study was to assess the relationship of clinical characteristics to the rate of retinal thinning in eyes with DME treated with anti-vascular endothelial growth factor (VEGF) therapy.

Setting/Venue
Retrospective study at San Raffaele Scientific Institute, Milan, Italy.

Methods
In this IRB-approved retrospective analysis, we collected data from subjects with a long-term follow-up (≥3 years) and evidence of resolved DME in at least one visit after the initiation of anti-VEGF therapy (baseline visit). In order to measure the long-term rate of retinal thinning during treatment, a second visit (first visit with evidence of resolved DME after 3 years) was also considered. To assess macular structural changes over time, a longitudinal quantitative topographical assessment of the inner and outer retinal thicknesses was provided. Clinical characteristics were associated with rate of retinal thinning during the follow-up.

Results
We included 57 eyes (51 patients) in the analysis. Mean changes over the study period in inner and outer retinal thicknesses were -8.8±15.2 μm and -5.5±10.5 μm, -10.5±20.0 μm and -3.7±14.6 μm, -4.1±19.9 μm -2.0±14.1 μm in the perifoveal, parafoveal and foveal regions. In multivariate regression analysis, a thinning in perifoveal outer retina (p=0.021), parafoveal and foveal regions. In multivariate regression analysis, a thinning in perifoveal outer retina (p=0.021), parafoveal outer retina (p=0.003), foveal inner retina (p=0.002), and foveal outer retina (p=0.004) were associated with frequency of central macular thickness reaching a value superior to 350 μm within the study period. Similarly, a thinning in foveal outer retina (p=0.004) was associated with frequency of neuroretinal detachment within the study period.

Conclusions
Eyes with DME undergoing anti-VEGF therapy are characterized by a progressive inner and outer retinal thinning over a follow-up of 3 years. Frequency of neuroretinal detachment and central macular thickness reaching a value superior to 350 μm have a significant impact on macular thinning.

Financial Disclosure
None
**Title**
Risk factors for acute central serous chorioretinopathy in a tertiary urban hospital in Morocco

**Purpose**
To determine systemic risk factors associated with the development of central serous chorioretinopathy (CSC).

**Setting/Venue**
Central serous chorioretinopathy is a disorder characterized by serous retinal detachment and/or retinal pigment epithelial (RPE) detachment, and associated with leakage of fluid through the RPE into the subretinal space. Central serous chorioretinopathy is one of the most common retinal causes of vision loss. CSC can occur in an acute or chronic form. The majority of acute CSC cases resolve spontaneously within 2-3 months. Prognosis is highly dependent on presenting visual acuity.

**Methods**
It is a descriptive case series. We retrospectively reviewed medical records of 61 patients with CSC from January 2019 to January 2021. All participants underwent complete ophthalmological examination and information regarding their sociodemographic, clinical, medical and ophthalmological history were recorded, so as to assess potential risk factors for CSR.

**Results**
The mean age of study population was 33.62 ± 7.32 years with 54 (88.52%) male patients. 81.96% had unilateral disease, 18.04% had bilateral disease. 62.29% patients had emotional stress/psychiatric disorder, 44.26% had a Type A personality, 32.78% were chronic smokers, 19.67% had a chronic steroid use and 8.19% had hypertension. Obstructive sleep apnea, alcohol consumption, coronary heart disease, autoimmune disorders, H. pylori infection and pregnancy were also associated with CSR.

**Conclusions**
Male middle-aged patients with emotional stress or psychiatric disorder were significantly more likely to develop CSR. Other risk factors include smoking, chronic steroid use and hypertension. Most of these factors are modifiable. Acting on these factors would reduce the morbidity related to CSR.

**Financial Disclosure**
no financial interest
**Title**
Retinal morphologic changes in internal carotid artery stenosis: a case-control study

**Purpose**
To evaluate the effect of severe internal carotid artery (ICA) stenosis on retinal morphology as seen in spectral domain optical coherence tomography (SD-OCT).

**Setting/Venue**
Medical Retina Unit, Ophthalmology Department – Central Lisbon University Hospital Centre, Portugal

**Methods**
Retrospective case-control study comparing ICA stenotic disease patients and controls. All underwent full systemic and ophthalmic evaluation. SD-OCT was performed to study retinal morphology. The mean thickness was measured in all nine Early Treatment Diabetic Retinopathy Study (ETDRS) areas for seven separate layers and total retina. The superior, inferior, temporal and nasal sectors of the 3- and 6-mm circles were respectively designated as S3, I3, T3 and N3 and S6, I6, T6 and N6. Central choroid thickness (CT) was also measured.

**Results**
This study involved 20 eyes from 16 patients with ICA stenosis (study group) and 17 healthy eyes from 17 patients (control group). Mean age in study group was 71.2 years-old and in control group 74.8 years-old. Eleven patients (55.0%) had bilateral disease and mean ICA stenosis was 84.0% among the study group. There were no overall differences in the retinal layers thickness and CT between patients and controls. Regarding stenotic disease patients, a significant difference was found between patients with and without ocular ischemic syndrome (OIS). The sectorial thickness of the TR (central and I3 sectors), inner nuclear layer (INL) (S3 and S6 sectors) and retinal pigment epithelium (EPR) (S3) was greater in OIS patients (p<0.05).

**Conclusions**
The assessment of the intra-retinal layers thickness showed no overall significant changes between patients and controls. Among patients with ICA stenotic disease, patients with OIS revealed a sectorial increase in some retinal layers, particularly in INL and ONL. These findings may result from chronic hypoxia-induced metabolic stress.

**Financial Disclosure**
None
Is there a place for ophthalmological screening of internal carotid artery stenotic disease patients?

**Purpose**
The purpose of this study is to understand if ICA stenotic disease patients with proven indication to carotid endarterectomy or stenting procedures, but otherwise without ophthalmological symptoms, should or not be screened in order to detect ocular chronic hypoperfusion signs in an early stage.

**Setting/Venue**
Central Lisbon University Hospital Centre

**Methods**
Cross-sectional study of patients with ICA stenotic disease, who met the criteria to perform carotid endarterectomy or stenting procedures, were recruited from the Vascular Surgery Department of the same tertiary hospital. Patients with ophthalmological symptoms or submitted to retinal laser or surgery were excluded from the study. After clinical and systemic vascular data were collected, patients were submitted to a full ophthalmic evaluation, which included best corrected visual acuity (VA), biomicroscopy, gonioscopy and mydriatic fundoscopy. Complementary examination was done using spectral domain optic coherence tomography (SD-OCT) and fluorescein angiography (AF).

**Results**
A total of 20 patients, were included in this study, 7 females and 13 males, with a mean age of 73.3 (SD=8.3) years old. Nine had bilateral disease. Regarding cardiovascular risk factors, 20 patients had dyslipidaemia, 19 hypertension, 10 smoking habits, and 9 type 2 diabetes. Ten presented with previous history of arterial peripheral occlusive disease, 8 (40%) had suffered a stroke and 8 a myocardial infarct. Median VA was 0 (min=0, max=0.49) logMAR. Twelve (60%) patients presented signs of low ocular perfusion, 4 (20%) of them were critical and needed treatment. The best criteria to detect the presence of low perfusion signs was the degree of internal carotid stenosis (AUC 0.88; 95%CI: 0.76-0.99). A cut-off value of 80% has a sensitivity of 82.4% and a specificity of 73.9%. Regarding the presence of ocular ischemic syndrome (OIS), from the eight eyes of patients with bilateral disease with contralateral stenosis ≥70%, five of them (62.5%) had OIS while from the 32 eyes without this condition, only one (3.1%) had OIS (p<0.001).

**Conclusions**
Ophthalmological screening of selected ICA stenotic disease patients may play an important role in the early diagnosis of chronic ocular hypoperfusion signs and so may prevent vision loss. The detection of signs of ocular ischemia may change the priority for vascular surgery.
Transcriptomics of human choroidal endothelial cells after treatment with corticosteroids as a model for central serous chorioretinopathy

**Purpose**
Corticosteroids are a strong risk factor for central serous chorioretinopathy (CSC). However, the underlying pathophysiological mechanisms are unclear. CSC has been proposed to result from choroidal hyperpermeability. Therefore, choroidal endothelial cells (CECs), which are important for barrier function, are of particular interest. This study describes the effect of cortisol on human CECs, in order to identify potential target genes involved in CEC hyperpermeability as seen in CSC patients.

**Methods**
Human choroidal endothelial cells were treated with either cortisol (10-6 M) or vehicle (0.1% ethanol) medium, and subsequently whole transcriptome analysis was performed on a Novaseq Illumina platform.

**Results**
Bioinformatic analysis showed upregulation of 153 genes and downregulation of 169 genes. Classical corticosteroid target genes were upregulated in human CECs and included FKBP5 (log2 fold change 6.8) and TSC22D3 (log2 fold change 4.5). The strongest induced gene by cortisol was ZBTB16 (log2 fold change 7.0).

**Conclusions**
In summary, this study describes 322 genes regulated by cortisol in primary human CECs. This includes classical corticosteroid target genes, but also a subset of these genes that has been previously linked to endothelial cell dysfunction. Functional assays based on genes of interest found in this study may help to expand the understanding of mechanisms behind the induction of CEC hyperpermeability by corticosteroids, as observed in CSC patients.

**Financial Disclosure**
Nothing to disclose.
Evaluation of retrobulbar blood flow in patients affected by macular edema secondary to retinal vein occlusion treated with anti VEGF.

**Purpose**
Primary Outcome: to evaluate changes in retrobulbar blood flow by using colour Doppler ultrasonography (CDUS) in naïve patients affected by retinal vein occlusion (RVO). Secondary outcome: to study the behaviour of retrobulbar vascular flow after intravitreal injection of antiVEGF (IV antiVEGF) to treat macular edema (ME) as complication of RVO and to correlate functional and morphological retinal data to flow parameters.

**Setting/Venue**
Ophthalmology and Radiology Unit, Department of Medicine and Surgery, University of Insubria – ASST Sette laghi Varese, Italy

**Methods**
Prospective, cross-sectional interventional study to evaluate changes in retrobulbar vascular flow in patients affected by RVO and treated with IV antiVEGF for ME. Naïve patients diagnosed for ME secondary to central and branch RVO examined in our Medical Retina Service, Ophthalmology Unit, ASST Sette-Laghi in Varese, Italy were enrolled. Each patient underwent a complete ophthalmological examination completed by instrumental evaluation at baseline (fluorescein angiography, OCT-angiography and SD OCT for central retinal thickness-CRT) and after treatment at week 1, at month 1 and 4 (OCT-angiography and SD-OCT). Treatment was performed by a loading phase of IV antiVEGF every month for three months and then a PRN regimen. CDUS was performed to study vascular flow of retrobulbar vessel by means of Epiq, Philips, 12-3 MHz linear probe. In particular, central retinal artery (CRA) and vein (CRV), ophthalmic artery (OA), superior ophthalmic vein (SOV) and posterior ciliary artery (PSA) have been evaluated. The same operator M.V. measured for arteries Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Resistance Index (RI); for veins: Maximum (MV) and minimum Velocity (mV). Clinical and instrumental evaluations were performed in both eyes. All data were collected in a dedicated database for quantitative and inferential statistical analysis.

**Results**
In this preliminary study, we enrolled 14 patients affected by RVO, four CRVO and ten BRVO. Mean age was 67,43±23,31yrs. Eight patients completed the loading phase with three IV antiVEGF. Mean baseline VA in the affected eye was 0,283±0,135Snellen and mean CRT 647,86±231,54micron; 0,283±0,043Snellen and 291,15±71,35micron (p<0.01) at month 1 and 0,62±0,231 and 219,15±87,34 (p<0.01) at month 4, respectively. CDUS parameters revealed interesting results comparing baseline till month 1. CRA showed a progressive increase of mean PSV values from 11,26 to 13,86cm/s; EDV and RI remained almost stable. OA showed a decrease in mean PSV (from 51,72 to 39,92cm/s) as well as mean EDV (from 14,74 to 7,86cm/s); mean RI remained stable. PCA showed an increase in mean PSV (from 11,10 to 16,75cm/s) as well as mean EDV (from 3,35 to 4,63cm/s); mean RI was almost unchanged. CRV showed a stability of MV and mV from 6,09 to 5,62cm/s and from 4,06 to 3,96cm/s respectively. SOV showed a stability of mean MV from 7,47 to 7,37cm/s; mean mV was unchanged. All measurements were performed with a standardized methodology, by the same experienced operator M.V. No adverse events have been reported, due to diagnostic or treatment procedures.

**Conclusions**
The study confirmed, as known from literature, the efficacy of IV antiVEGF as the gold standard therapy to treat ME as a complication of RVO, and to improve visual acuity, in particular in naïve patients. However, the behaviour of retrobulbar vessels flow after occlusive venous pathology is nowadays limited, particularly before and after antiVEGF treatment. The possibility to apply this diagnostic method supported by an expert operator could give to ophthalmologists interesting and useful information that could be correlated to the retinal pathology and visual acuity impairment. The results reported in this preliminary study showed that after treatment, arterial and venous flow changes in the studied vessels specially, in central retinal and ophthalmic arteries. Again, venous flow did not show an increase in velocity probably due to the inner vascular obstruction. Actually, the role of antiVEGF drugs on retrobulbar vascular dynamics to improve retinal clinical features in RVO are not well known. In our study, we provided useful data to increase the basis of the knowledge of this mechanism, and to better understand the clinical significance of these changes in retrobulbar vascular flow.
**Title**
Long-term follow-up of exudative perifoveal vascular anomalous complex treated with subthreshold focal laser photocoagulation.

**Purpose**
To describe the long-term follow-up of a patient with exudative perifoveal vascular anomalous complex (ePVAC) successfully treated with subthreshold focal laser photocoagulation.

**Setting/Venue**
Multizone Unit of Ophthalmology of the Autonomous Province of Trento, Trento, Italy.

**Methods**
Case report. Full ophthalmic examination (best corrected visual acuity (BCVA) and intraocular pressure (IOP) measurement, slit lamp (SLE) and fundus examination) and multimodal imaging were performed at baseline and over a 29-month follow-up period. Spectral-domain optical coherence tomography (SD-OCT), fluorescein angiography (FA), near infrared (NIR) and blue autofluorescence (BAF) images were obtained with Spectralis HRA OCT (Heidelberg Engineering, Heidelberg, Germany). Nine spots of subthreshold focal laser photocoagulation (90 mW, 50 μm, 200 ms, using lens with no amplification factor) were performed in one laser session 10 months after diagnosis.

**Results**
A 79 year-old woman was referred to our Retina Service for evaluation of macular hemorrhages in the right eye (RE). The patient was in good general health with no significant medical or ophthalmological history. BCVA was 20/50 in the RE and 20/40 in the left eye (LE). SLE showed a corticonuclear cataract in both eyes (OU). IOP was 14 mmHg OU. Fundus examination showed an isolated perifoveal aneurysmal lesion accompanied by small hemorrhages in the RE and a small drusen in the LE. SD-OCT revealed cystoid macular edema secondary to a round hyperreflective lesion with hyporeflective lumen in the RE. FA demonstrated a well-defined hyperfluorescent lesion with late pooling of the dye in the intraretinal cystoid spaces in the RE. As the patient was asymptomatic, the lesion was initially followed. Cataract surgery was performed and BCVA improved to 20/32. However, fluid progressively increased and therefore subthreshold focal laser was performed 10 months after diagnosis. One month after focal laser, the intraretinal fluid almost completely reabsorbed. 8 months after focal laser the edema completely disappeared, PVAC lesion shrank and was no more visible on FA. 19 months after focal laser, BCVA remained stable at 20/32 with no recurrence of intraretinal fluid.

**Conclusions**
First reported in 2011 by Querques et al., perifoveal exudative vascular anomalous complex (PEVAC) has been described as isolated large perifoveal aneurysm, in the absence of retinal vascular or inflammatory diseases. Sacconi et al. recently described the pre-exudative stage of PEVAC and proposed to change the original acronym for the exudative lesion from PEVAC to ePVAC. The pathogenesis of this disease remains unclear, and ePVAC lesions appear to be unresponsive to intravitreal anti-VEGF and corticosteroid treatment. Focal thermal laser photocoagulation, which is an effective treatment for macular edema associated with microaneurysms in other contexts, was also effective for the larger PVAC aneurysmal lesion in our case. Our goal was to heat and coagulate the content and the wall of the aneurysmal lesion and induce a post thermal injury remodelling, with occlusion of the aneurysm, extended control of the exudation and as minimal perilesional injury as possible. After a single session of subthreshold laser, the core of the perifoveal aneurysm lesion shrank, with BCVA stabilization and sustained (>19 months) resolution of the intraretinal exudation. However, further studies are needed to better understand the nature of this clinical entity and to confirm the use of this laser technique as first therapeutic option.

**Financial Disclosure**
Authors have no financial conflicts of interest to disclose.
Title
Interobserver agreement for the detection of optical coherence tomography features of diabetic macular edema in clinical practice using the European School for Advanced Studies in Ophthalmology classification

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Purpose
To study the interobserver agreement for the detection of optical coherence tomography (OCT) features of diabetic macular edema (EDM) in clinical practice naïve patients.

Setting/Venue

Methods
A consecutive retrospective analysis of all naïve patients who came to our service presenting DME for 1 year was performed. Optical coherence tomography (OCT), were independently analyzed by two retinal specialist evaluators, determining the OCT tomography features of DME using the European School for Advanced Studies in Ophthalmology (ESASO) classification. An interobserver agreement analysis was performed.

Results
116 eyes of 76 patients were evaluated, being 65.8% male and 34.2% female, with a mean age of 66.3 +/- 13 years old. The Kappa analysis of intra-observer concordance in the evaluation of the different ESASO classification OCT features were: Cyst (C) (.45); Ellipsoid zone/External limitant membrane € (.4); Drill (D) (-.03); Hyperreflective foci (H) (.47); Subretinal fluid (F) (.84); and Vitreoretinal relationship (V) (.63)

Conclusions
The agreement between observers was strong for F, moderate for V and week for the rest of OCT ESASO classification features.

Financial Disclosure
No
Effectiveness of fluocinolone acetonide (FAC; 0.2 µg/day, ILUVIEN®) implant in diabetic macular edema based on prognostic biomarkers assessed by OCT

**Purpose**
At present, spectral domain optical coherence tomography (SD-OCT) represents the main technique for assessment and follow-up of diabetic maculopathy (DM), once it offers both quantitative and qualitative information in a non-invasive and repeatable way. ESASO group proposed an SD-OCT-based classification of DM, centered on standard figures, which considers specific morphologic features and quantitative indices of the entire spectrum of macular involvement in diabetic retinopathy. ILUVIEN® intravitreal implant (fluocinolone acetonide, FAC 0.2 µg/day) is indicated for the treatment of persistent and recurrent Diabetic macular edema (DME) and it is known to release a sustained microdose of FAC 0.2 µg/day for up to 3 years. The aim of this study was to evaluate the long-term effectiveness of FAC implant as a treatment of recurrent and persistent DME based on OCT biomarkers assessment.

**Setting/Venue**
This is a retrospective analysis in which efficacy parameters as well as OCT biomarkers assessments of patients with persistent and recurrent DME treated with a single ILUVIEN® implant were analyzed, performed at Centro Hospitalar Universitário do Porto, Portugal.

**Methods**
Retrospective observational analysis, with 36 months follow-up after FAC implantation. The demographic data of the patients as well as duration of DME and number of prior intravitreal injections were recorded at baseline. Best Corrected Visual Acuity (BCVA) and central subfoveal thickness (CST) were recorded at baseline and then evaluated at month 6, 12, 24 and 36. All patients underwent OCT scanning before and after implantation of FAC, in all time-points. The characteristics of DME were analyzed in all OCTs, according to the classification for diabetic maculopathy proposed by ESASO, taking into account 7 parameters: (1) quantitative measurement of the CST; (2) the size of the intraretinal cysts (IRC); (3) the visibility of the external limiting membrane (ELM) and the ellipsoid zone (EZ) at the fovea; (4) the presence of disorganization of retinal inner layers (DRII); (5) the presence of subretinal fluid (SF); (6) the presence and the number of hyperreflective foci (HF); and (7) the vitreoretinal relationship.

**Results**
Forty-five eyes from 35 patients with a mean age of 70.4 ± 7.6 years were evaluated. Sixteen patients (46%) were men. At baseline, 22% of the eyes were phakic. DME duration was 4.3 ± 1.3 years. All eyes received intravitreal injections of anti-VEGF and/or short-action corticosteroids prior to the FAC implant (6.9 ± 5.3). The mean BCVA at baseline was 42.1 ± 18.4 ETDRS letters, with an average increase of +14.1 ETDRS letters observed 3 years after FAC implant (p <0.001). The mean CST decreased by 182.9 µm from the baseline to 36 months (p <0.001). After the FAC implant, presence of SF (from 18.6% to 6.7%), EZ/ELM disruption (from 72.1% to 53.3%) and presence of IRC (from 97.7% to 64.4%) significantly decreased by month 6 (p<0.05) and stabilized until end of follow-up. Similar trends, without statistical significance, were observed in presence of HF and DRII. No variation was observed in vitreomacular interface, with no abnormalities since baseline. According to ESASO classification, staging of diabetic maculopathy went from 76% eyes with advanced DME to 14% at 36 months and from 24% of eyes with early DME at baseline to 86 % with early DME at 36 months.

**Conclusions**
This analysis suggests that intravitreal FAC implant is effective in the improvement of several OCT parameters, namely decrease in CST, decrease in cysts, improvement in EZ / ELM disruption and decrease in the presence of FS, thus showing that FAC implant allows an improvement in both the parameters associated with inflammation / edema and those associated with structural changes in the retina. The treatment of persistent and recurrent DME with FAC implant also proves to be effective, and this study has shown that there are anatomical and functional gains, maintained over 3 years.
OCT Angiography Biomarkers for Predicting Visual Outcomes after Aflibercept Treatment for Diabetic Macular Edema

Purpose
To correlate OCT angiography (OCTA) parameters with clinical features and to predict the visual outcomes after Aflibercept treatment for diabetic macular edema (DME).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

Methods
Forty eyes of 40 patients with DME and 40 eyes of 40 age-matched healthy controls were enrolled in the study. All subjects underwent a comprehensive ocular examination, including measurement of best-corrected visual acuity (BCVA) and a slit-lamp exam of the anterior segment and fundus. Spectral Domain OCT and OCT-A scans were performed using AngioVue software of the Optovue RTVue XR Avanti. A 6 mm×6 macular scans with measurement of the foveal avascular zone (FAZ) and vessel densities (VD) in both superficial (SCP) and deep (DCP) capillary plexus were analyzed in both groups. The OCT-A scans were obtained at baseline and after 3 monthly injections of Aflibercept in the study group.

Results
The mean age was 62.7 ± 10.6 years in the study group and 61.9 ± 13.5 years in the control group (P = 0.80). Twenty four of 40 patients in the study group were women, and 22 of 40 subjects in the control group were women (P = 0.45). The FAZ in the study group at baseline was larger compared to the control group (P < 0.001). As for VDs, the values of both SCP and DCP in the study group at baseline all were lower than those in the control group (P < 0.001 for all). After treatment with Aflibercept, the FAZ area significantly decreased (P = 0.032). Furthermore, the VDs also increased significantly (P < 0.05 for all). However, the values still did not return to the normal levels when compared with those of the control group. Among all biomarkers, higher SCP VDs at baseline correlated most significantly with visual gain after treatment (R=0.62, P < 0.001). No baseline OCTA biomarkers showed any significant correlation specifically with anatomic improvement.

Conclusions
Our findings suggest that for eyes with DME, VD SCP at baseline was an independent predictor for visual improvement after the loading Aflibercept treatment. However, further studies are warranted to confirm our results.

Financial Disclosure
The authors declare no conflict of interest.
### Title
Clinical efficacy of subthreshold navigated laser treatment of focal diabetic macular edema (short-term results)

### Purpose
Diabetic macular edema (DME) is the most common cause of vision loss in people with diabetic retinopathy. The modern and highly informative method of OCT-A diagnostics opens up new possibilities in the layer-by-layer study of the microcirculatory bed at the level of the superficial vascular plexus and deep vascular complex, as well as retinal pathological changes associated with DME. All of the above determines the relevance of topographically oriented methods of laser treatment of focal DME, based on the OCT-A data on the layer-by-layer state of the microvasculature. Micropulse laser treatment in subthreshold mode is the most selective in treating DME. The aim of our study was to evaluate the clinical efficacy of subthreshold navigated laser treatment for focal DME with individual selection of parameters of continuous and micropulse laser radiation based on multimodal imaging.

### Setting/Venue
The S. Fyodorov Eye Microsurgery Federal State Institution

### Methods
We observed 16 patients (16 eyes) with DME at the age from 25 to 71 years (on average 44±1.6 years). The initial best corrected visual acuity (BCVA) was 0.7 ±0.06. The maximum thickness of the retina in the area of edema was less than 350 μm. In 11 patients, the fovea was not involved in the edema zone. After the stage of diagnostic search for morphological changes in the retina and individual testing of the energy parameters of micropulse and continuous modes, the results of which were evaluated by the method of short-wave autofluorescence. The treatment was carried out in the zones of retinal ischemia and microaneurysms in a continuous mode excluding the foveal avascular zone (FAZ), and in a micropulse mode in the zones of edema and microaneurysms including the FAZ, in cases of fovea involvement. The study evaluated the retinal thickness in the foveal avascular zone and outside it, the area of retinal ischemia, microaneurysms and edema zones at the level of the superficial vascular plexus and deep vascular complex. Follow-up periods were 1, 3 and 6 months.

### Results
One month after laser treatment, all patients had positive dynamics, expressed in a decrease of edema height (the mean CRT for the group was: in the fovea – 294±5.38 μm, outside the fovea – 318.5±6.44 μm). BCVA increased on average to 0.8±0.06; mean central retinal sensitivity – up to 24.65±0.47 dB. After 3 months, a further decrease in the height of the edema was observed (CRT in the fovea was 252.5±2.19 μm, outside the fovea was 280.5 ± 3.75 μm). BCVA increased on average for the group to 0.85±0.06, mean central retinal sensitivity – 25.5±0.3 dB. According to OCT-A data, there were single cysts, decreased number of microaneurysms, decreased ischemic area. After 6 months, the average CRT for the group was: in the fovea – 246.5±1.81 microns, outside the fovea – 273.5 ± 4.56 microns. Stable increase of BCVA values – 0.85±0.06 and central retinal sensitivity- 26.65±0.16 dB was achieved. According to OCT-A data, isolated small cysts were persisted.

### Conclusions
Our preliminary results may reflect the efficacy of subthreshold navigated laser treatment of DME based on multimodal imaging data, which makes it possible to plan and conduct targeted topographically oriented laser exposure, including in the preclinical stages of DME development.

### Financial Disclosure
Financial Disclosure: no author has a financial or property interest in any material or method mentioned. There is no conflict of interests.
**Title**
Micropulse in treatment of vascular genesis focal macular edema

**Purpose**
To assess the effectiveness of subthreshold micropulse laser (SML) in the treatment of focal macular edema with a height up to 500 μm against the background of diabetic retinopathy (DR) or branch retinal vein occlusion (BRVO).

**Setting/Venue**
S.N. FEDOROV NMRC "MNTK "EYE MICRO轩URGERY", Volgograd Branch

**Methods**
102 patients (102 eyes) with focal macular edema (ME) up to 500 μm were examined. 72 cases were against the background of DR, 30 cases – BRVO. Patients underwent SML treatment in the area of ME using randomly either 532 or 577 nm laser, if necessary, in combination with panretinal laser coagulation or threshold laser coagulation in ischemic zones extramacularly. Evaluation of the treatment effectiveness was carried out according to the dynamics of the retinal neuroepithelium using optical coherence tomography, the dynamics of the best corrected visual acuity and the change in the focal photosensitivity in the area of neuroepithelial edema.

**Results**
As a result of treatment, it was possible to achieve a statistically significant increase in the focal photosensitivity of the retina up to 26% (p<0.05) and a decrease in edema of the retinal neuroepithelium (NE) up to -15.9% (p<0.05) in both clinical groups (SML 532 and 577 nm).

**Conclusions**
The SML treatment of ME up to 500 μm against the background of DR or BRVO is effective and safe, it allows to significantly reduce the NE thickness in the area of edema and improve clinical and functional parameters, reliably increase the focal light sensitivity of the retina. Lasers with a wavelength of 532 and 577 nm have shown equal efficacy in the SML mode.

**Financial Disclosure**
none
Comparison of long-term effectiveness and safety outcomes between fluocinolone acetonide intravitreal implant 0.19 mg (ILUVIEN®) monotherapy and combination with adjuvant therapy in patients with Diabetic Macular Edema

Purpose
Available therapeutic options for Diabetic Macular Edema (DME) include laser photoacogulation, intravitreal corticosteroids and intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents. However, single treatments are often not sufficiently effective to control DME during the course of the disease. The purpose of this study was to evaluate and compare the effectiveness and safety of fluocinolone acetonide (FAc, 0.19 mg, ILUVIEN®) intravitreal implant for the treatment of recurrent and persistent DME in monotherapy or combined with adjuvant therapy.

Setting/Venue
This study evaluates the long-term response to FAc intravitreal implant in monotherapy or combined with adjuvant therapies in patients with DME, at the ophthalmology department of Hospital Pedro Hispano, Portugal.

Methods
Retrospective study of 89 eyes from 63 patients, divided into 2 groups: A (n=67) receiving FAc monotherapy; and B (n=22) receiving FAc combined with adjuvant therapy. Demographic data of the patients as well as best corrected visual acuity (BCVA), central retinal thickness (CRT), duration of DME, number of intravitreal anti-VEGF or short-term steroid injections before FAc implant and intraocular pressure (IOP) were recorded at baseline. BCVA, CRT and IOP were evaluated after 1 month, 3 months and then quarterly, comparing these parameters over the follow-up period.

Results
From the overall population, 22 of the total 89 eyes needed additional therapy after FAc intravitreal implant. The mean age of patients in group A was slightly higher than group B (69.1 ± 9.2 vs. 65.5 ± 7.1 years, respectively, p=0.179) as it was the mean DME duration (4.7 ± 2.1 vs. 4.3 ± 1.3 years, respectively, p=0.588). The average follow-up period for groups A and B was 19.8 ± 13.0 months and 25.1 ± 9.1 months, respectively (p=0.081). All eyes received intravitreal injections (anti-VEGF: 5.8 ± 3.8 (A) and 6.7 ± 4.9 (B) injections, p=0.384; shorter-action steroids: 2.1 ± 1.7 (A) and 1.7 ± 1.0 (B) injections, p=0.567) before FAc implant. Mean change in BCVA from baseline to the last observation was +8.9 ± 11.1 early treatment diabetic retinopathy study (ETDRS) letters (p<0.001) in group A and +8.7 ± 16.8 ETDRS letters (p<0.001) in group B, without significant differences between the two groups (p=0.494). Mean CRT significantly decreased by 164.0 μm (p<0.001) in group A and 246.0 μm (p<0.001) in group B, from the baseline to the last observation, without statistically significant differences between groups (p=0.095). IOP remained stable over time in both groups (p=0.961).

Conclusions
This analysis suggests that intravitreal FAc implant monotherapy is an effective treatment option for the management of recurrent and persistent DME, insufficiently responsive to previous therapies. In a minority of patients, it may be required the use of additional therapies as part of an individualized management strategy for their DME, with similar effectiveness and safety profile. The multifactorial nature of this disease may explain why some patients require a combined treatment strategy, mainly in more complex DME cases where additional therapies are needed.

Financial Disclosure
No financial relations.
Purpose
To describe the clinical features of a case of Spontaneous Expulsive Suprachoroidal Haemorrhage, to discuss the risk factors and management for this rare condition.

Methods
A single case study of a 72 year old male patient who attended the Emergency Department following an atraumatic, acute, initially painful total loss of vision. At presentation visual acuity was no perception of light in the left eye and 0.9 in the right eye. On examination a expulsive suprachoroidal haemorrhage was diagnosed with almost complete loss of corneal tissue. This patient’s past ophthalmic history includes poorly controlled primary open angle glaucoma, previous bacterial keratitis and he is pseudophakic. Due to the destructive nature of this condition visual recovery was suggested to be unlikely; evisceration was suggested to be the appropriate management.

Results
Suggested mechanism for suprachoroidal haemorrhage from literature is decompression of the eye most commonly during surgery with or without choroidal effusion resulting in rupture of choroidal or ciliary vessels. It is likely that chronic raised intra-ocular pressure resulted in a large drop in IOP following a corneal rupture most likely caused by an undiagnosed bacterial keratitis. This loss of tamponade resulted in expulsion of intra-ocular contents. The patient was eviscerated and a good surgical outcome was achieved.

Conclusions
There are very few case reports of this rare condition. Those that are reported are seen on the back of poorly controlled glaucoma, steroid use or significant corneal disease.

Financial Disclosure
None.
### Title
Aflibercept for Diabetic Macular edema In real-life practice in GREEce: Two-year outcomes of the ADMIRE study

### Purpose
To evaluate the efficacy and safety of intravitreal aflibercept injections for diabetic macular edema (DME) treatment in a tertiary referral center in Greece.

### Setting/Venue
2nd Department of Ophthalmology, National and Kapodistrian University of Athens, Athens, Greece

### Methods
ADMIRE was a prospective, observational cohort study of patients with DME. Efficacy was assessed by change in best-corrected visual acuity (BCVA) and central retinal thickness (CRT) from baseline to month 24 after treatment with intravitreal aflibercept in treatment-naïve patients and previously treated patients. Safety was evaluated by recording any patients-reported events.

### Results
Results: Participants in the study were 94 patients with DME, 70 treatment-naïve and 24 previously treated with ranibizumab. At month 24 of the follow-up period, the mean change (SD) in BCVA was +9.6 (5.2) ETDRS letters in treatment-naïve patients and +6.4 (3.1) letters in previously treated patients, which differed significantly compared to baseline in both groups (p<0.05 in both groups). Accordingly, the mean change in CRT at month 24 was -134.7 μm at treatment naïve patients and -82.9 μm in previously treatment patients, which was significantly decreased in both groups compared to baseline (p<0.05 in both groups). Safety analysis showed that ocular treatment-related adverse events occurred in 18 out of 96 patients (18.8%) during the whole follow-up period of 24 months. All adverse events were mild and did not need urgent treatment.

### Conclusions
Intravitreal aflibercept was found to be safe and effective in real-life clinical practice in both treatment-naïve and previously treated patients with DME in a tertiary referral center in Greece.

### Financial Disclosure
None
Long-term analysis of OCT measurements of macular thickness and volume after the treatment with 0.19mg fluocinolone acetonide intravitreal implant (ILUVIEN®) for Diabetic Macular Edema – a single center real-word study

Purpose
Spectral domain optical coherence tomography (SD-OCT) technology led to an advanced knowledge of the structural alterations that happen in macular diseases, while offering a method of assessing quantitatively the outcomes of treatments on retinal thickness and volume. In this regard, the aim of this study was 1) to evaluate the anatomic effectiveness and safety outcomes after treatment with 0.19mg fluocinolone acetonide intravitreal implant (FAc; ILUVIEN®) in patients diagnosed with persistent and/or recurrent diabetic macular edema; and 2) to compare outcomes between vitrectomized eyes at baseline versus non-vitrectomized.

Setting/Venue
Non-interventional, retrospective, and single center real-world analysis conducted at the Ophthalmology Department, Centro Hospitalar de Leiria - Hospital Santo André, Leiria, Portugal.

Methods
A total of 56 eyes of 43 patients were treated with 0.19 mg FAc intravitreal implant for persistent/recurrent DME following an insufficient response to previous treatments (persistent/recurrent macular edema). The mean follow-up period was 15±8 months (mean±standard deviation) (range, 1 to 31 months) for the full population, and for vitrectomized (group 1, n=20) and non-vitrectomized eyes (group 2, n=36) was 16±3 months (range, 3 to 31 months) and 14±7 months (range, 1 to 27 months), respectively (p=0.27 between group 1 and 2). Standard measures included: central macular thickness (CMT; µm), macular volume (MV; mm3), best-corrected visual acuity (BCVA; ETDRS letters score), intraocular pressure (IOP; mmHg), IOP related events and presence of prior treatments. All parameters were assessed at baseline, and months 1 and 3, and then quarterly afterwards; all results are also reported at last observation. T-test, non-parametric and Fisher’s exact Chi-squared tests were performed using SPSS (version 25.0); statistical significance was taken as p-value<0.05.

Results
At baseline, the mean duration of DME was 5±2 years for the full population and 36% had prior vitrectomy. After FAc injection, the mean reduction of CMT/MV was -162µm/2mm3 for the full population (CMT/MV p<0.001/p<0.001 vs baseline), and for group 1 and 2 the median reduction was -198µm/2mm3 and -177µm/2mm3 (group 1 vs 2 CMT/MV p=0.76/p=0.37), respectively. All of the groups (full data and comparative data) showed a CMT reduction >20% and a stabilized or improved BCVA at last observation. Safety outcomes revealed a mean increase in IOP at last observation of +2mmHg for full population (p=0.01 vs baseline); at baseline 3 eyes were prior diagnosed of glaucoma, 36% of the remaining eyes were stabilized with IOP-lowering medication. Regarding vitrectomized versus non-vitrectomized groups, showed similar numerical trend for the percentage of eyes with IOP-lowering drops at last observation (40% group 1 vs 33% group 2, p=0.41) and similar trend for IOP rise (+0.2mmHg group 1 vs +0.8mmHg group 2, p=0.66).

Conclusions
This clinical practice study determines the anatomic benefit, for both full population and comparison analysis - vitrectomized versus non-vitrectomized eyes -, with the treatment with FAc implant after an insufficient response to previous treatments. Moreover, this analysis reinforces ILUVIEN® effectiveness and safety profile and is comparable with others ILUVIEN® real-world data. Still, monitoring stays essential in patients treated with the FAc intravitreal implant, mainly if is injected considering risk/benefit (patients with prior diagnosed with intraocular hypertension and glaucoma).

Financial Disclosure
No financial conflicts of interest.
Real life experience using the intravitreal fluocinolone acetonide implant (Iluvien) for refractory diabetic macular oedema

Purpose
To describe the changes in best corrected visual acuity (BCVA) and optical coherence tomography (OCT)-measured central foveal thickness (CFT) in patients receiving an intravitreal fluocinolone acetonide implant (Iluvien) for refractory diabetic macular oedema (DMO).

Setting/Venue
Single, tertiary-care, university-affiliated hospital in Madrid, Spain.

Methods
A retrospective, observational case series including all patients having at least one eye treated with Iluvien for refractory DMO and a minimum follow-up time of 3 months. Only one eye per patient was included in the analysis. For patients who had both eyes treated, only the first eye was included in the analysis. All included eyes had previous treatment with antiVEGF and/or dexamethasone implant, and their response to first line treatment was considered to be incomplete. Patient records were reviewed by 2 of the authors, and data was recovered about their demographic characteristics (age, sex), time since the onset of the macular oedema, previous treatments (laser, antiVEGF, Ozurdex), BCVA in each visit, OCT-measured CFT in each visit, and adverse events.

Results
Fourteen eyes from 14 patients were included in the study. Median age was 68.5 years (range 58 to 91). Seven patients were women (50%). Median baseline BCVA was 0.7 LogMAR (range 0.3 to 1.9), median baseline HbA1c was 7.55% (range 6.3 to 11.4), and median baseline central foveal thickness was 538 µm (range 190 to 780). Median follow-up time was 9 months (range 3 to 18 months). Median BCVA change was 0.0 logMAR at 1 month (range -1 to 0.4; p=0.149), 0.0 logMAR at 3 months (range -1 to 0.4; p=0.201), 0.0 logMAR at 6 months (range -1 to 0.4; p=0.197), 0.0 logMAR at 9 months (range -1 to 0.4; p=0.465), and 0.0 logMAR at 12 months (range -1.1 to 0.0; p=0.180). BCVA had improved at least three Snellen lines in 4 eyes (28.6%) at the last visit. Median OCT-measured CFT change was -85 µm at 1 month (range -393 to 0; p<0.003), -68 µm at 3 months (range -407 to 0; p=0.003), -55.5 µm at 6 months (range -419 to 3; p=0.021), -145 µm at 9 months (range -353 to -36; p=0.028), and -37 µm at 12 months (range -236 to 31; p=0.144). One of 2 phakic eyes required cataract surgery. No cases of ocular hypertension were observed.

Conclusions
Intravitreal injection of the fluocinolone acetonide implant (Iluvien) provided sustained anatomic improvement of refractory DMO during the first year after injection. BCVA remained stable in most patients, and improved at least 3 Snellen lines in 28.6% of the eyes, which is similar to the proportion reported in the FAME trial. Cataract development was the only observed adverse event.

Financial Disclosure
Esther CIANCAS has received honoraria from Brill Pharma. Julio J GONZALEZ-LOPEZ has received study grants from Allergan, Brill Pharma, Novartis and Théa.
Presever

Title
The use of advanced oxidation protein products to monitor oxidative stress levels in patients with hypertensive retinopathy

Purpose
The aim of the current study was to investigate whether advanced oxidation protein products (AOPPs), recognized as novel markers of oxidative lesions, determined in serum and tear samples, may be used as a single parameter to monitor oxidative stress in patients with hypertensive retinopathy (HR) and to determine whether there is a correlation between their level and the advancement of the disease.

Setting/Venue
In the research, were enrolled 90 hypertensive patients who came for a consult at the Ovisus Medical Center, Chisinau, Republic of Moldova, in the period 2018-2019 and who, for the first time, were diagnosed with HR, confirmed after a detailed specific ophthalmological investigation.

Methods
The subjects were divided into three groups, using the Keith-Wagner-Barker grading system of HR: GI–36 patients; GII–35 patients; GIII–19 patients. AOPPs were assessed in tear and serum samples and the received results were analysed in SPSS Statistics using non-parametric Kruskal-Wallis and Mann-Whitney tests. Correlation analysis was performed using Spearman correlation test with \( p \leq 0.05 \) statistically significant.

Results
In the serum samples of the patients with HR was determined a tendency to enhance of AOPPs values as HR advanced in grade, (GI vs GIII, +124%, \( p=0.07 \)). However, AOPPs tear level presented a tendency of reduction (GI vs GIII, -7%, \( p=0.655 \)). Only, serum AOPPs levels correlate significantly with low power with HR grade (\( r_s=0.243^* \), \( p=0.021 \)), meanwhile serum and tear AOPPs levels do not correlate significantly with each other (\( r_s=-0.037 \), \( p=0.731 \)).

Conclusions
Our findings suggest that serum AOPPs can serve as an extra biomarker for monitoring oxidative stress levels in HR patients and it is a potent indicator of the disease severity, while the changes of tear AOPPs level being unsignificant, imply that by themselves they cannot be used as a reliable indicator of an excessive OS. Acknowledgements. The authors declare no conflict of interest or any financial interest to disclosure. Research funding: Doctoral grant offered by Ministry of Education, Culture and Research of Republic of Moldova.

Financial Disclosure
The authors declare no conflict of interest or any financial interest to disclosure. Research funding: Doctoral grant offered by Ministry of Education, Culture and Research of Republic of Moldova.
Impact of pregnancy on diabetic retinopathy and maculopathy: a screening based study

**Purpose**
The aim of this retrospective study was to evaluate the screening frequency and progression of diabetic retinopathy in pregnant women with pre-gestational diabetes attending a single Screening Programme in England.

**Setting/Venue**
Wakefield Diabetic Retinopathy Screening Services

**Methods**
The diabetic retinopathy screening services record of all the pregnant women who had screening photographs, between 2013-2016, were retrieved. The information recorded included age, type of diabetes mellitus (type 1 or 2 DM), gravida, blood pressure (BP), glycosylated haemoglobin (HbA1c), the number of screening visits, any referral to the eye clinic and any investigation or treatment carried out, within one year post-partum. The National Standard was to screen pregnant women once in each trimester followed by one post-natal visit. For this study, adequate frequency of screening was defined as at least two or more retinal evaluations in separate trimesters. The diabetic retinopathy (DR) definitions used in screening programme were background (BDR), pre-proliferative (PPDR) and proliferative retinopathy (PDR). A one-step progression was defined as at least one stage of deterioration of DR and/or development of diabetic maculopathy in at least one eye. A two-step progression was defined as development of PDR in an eye with BDR or development of PPDR in an eye with no DR at baseline. Binary logistic regression was utilised to assess the association of multiple covariates (systolic BP, diastolic BP, HbA1c and gravida) with the progression of DR.

**Results**
Of the 200 pregnant women identified, 33 had to be excluded for various reasons (19 had gestational diabetes, 13 suffered a miscarriage before 24 weeks of gestation and 1 moved out of the area). Of the 167 women, the mean age was 31.2±4.7 years, mean gravida was 2 (range 1-8), and 71 women had Type DM. The mean systolic and diastolic BP recorded were 126±15.5 mm Hg (range 98-178) and 78.7±10.3 mm Hg (range 56-99) respectively. The mean HbA1c was 55.2±15.4 mmol/mol (range 30-110). No DR was seen in 54.1%, BDR in 35%, PPDR in 7.7%, PDR in 1.1% and 2.3% of eyes had panretinal photocoagulation (PRP) at baseline. Baseline maculopathy was seen in 3.6% of eyes. Three-quarters of these women had two or more screening photography visit. New DR developed in 3.5% of eyes with one-step and two-step worsening seen in 11.9% and 0.5% of eyes respectively. New maculopathy developed in 5.9% of eyes. Logistic regression analysis revealed that HbA1c more than 50 mmol/mol was associated with new maculopathy development (P=0.01), while other variables had no effect on DR progression. Of the 49 patients referred from diabetic screening to the eye clinic, 2 underwent macular laser and 5 needed PRP.

**Conclusions**
Nearly a quarter of pregnant women did not have the three mandated diabetic screening visits as per the standard set by the National Programme. The development of new retinopathy or progression of retinopathy was low as compared to previously published studies. Raised blood sugar at booking (Hba1c) was associated with new maculopathy development.

**Financial Disclosure**
received study, research and travel grant from Novartis and Bayer None for this study
Retinal sensitivity and structural changes after focal photocoagulation for diabetic macular edema – a multisectorial analysis.

Purpose
Focal photocoagulation in the macular area is an effective management option in diabetic macular edema (DME) and, in some countries, it remains the first-line treatment. Conflicting results have been published regarding its consequences in retinal sensitivity. Therefore, our purpose was to evaluate macular functional and structural changes after focal macular photocoagulation for DME.

Setting/Venue
Ophthalmology Department, Centro Hospitalar Universitário do Porto, Porto, Portugal.

Methods
Cross-sectional cohort study that included mild diabetic retinopathy eyes, submitted to focal macular photocoagulation as monotherapy for focal DME. Patients were included after the necessary number of treatment sessions for complete resolution of DME. No control group of healthy subjects was necessary for this analysis. In each macular sector (superior, temporal and inferior 1-3mm parafoveal ring), photocoagulation spots were enumerated in an infrared confocal scanning laser fundus imaging, individual retinal layers were automatically measured in a high-resolution spectral-domain optical coherence tomography scan (Heidelberg Spectralis, Germany), and retinal sensitivity was accessed with microperimetry (MP-3, Nidek, Japan). In a multisectorial analysis, eyes were compared in each sector according to the presence or absence of LASER spots. This means that one eye could be in the control group in one sector, but it could be in the study group in another sector. Relative sensitivity was calculated as sectorial sensitivity divided by general sensitivity. Non-parametric tests were used.

Results
Sixty-four eyes were included. General sensitivity was 24.8±2.6 dB and was associated with both BCVA and age. In sectors submitted to focal photocoagulation, we observed an inferior absolute (-1.0 dB, p=0.049, inferior sector) and relative sensitivity (-2.1 %, p=0.024, superior sector) together with a decrease in the outer nuclear layer thickness (-8 μm, p=0.015, inferior sector). In sectors with LASER spots, the outer nuclear layer thickness correlated with sensitivity (β=160 μm/%, r=0.544, p=0.006 for relative sensitivity and β=2.2 μm/dB, r=0.412, p=0.045 for absolute sensitivity for the superior sector). The time since the last treatment was not associated with the outcomes (p≥0.287).

Conclusions
In conclusion, multisectorial evaluation is a suitable and powerful tool in cases where the study factor spreads in different macular regions. We found a small reduction in retinal sensitivity in macular sectors that underwent photocoagulation for DME. These changes are followed by a reduction in the outer nuclear layer thickness. Outer nuclear layer thickness may be a biomarker of retinal sensitivity after photocoagulation.
Treatment of fibrovascular form of proliferative diabetic retinopathy using primary vitreoretinal surgery and delayed one-stage laser pattern scattered photocoagulation of the retina

Purpose
In 2005 the technology of pattern scattered photocoagulation of the retina was introduced into clinical practice and also for the treatment of PDR (pattern-PRLK). The technology has allowed to increase the volume of laser treatment, reduce the risk of complications after laser photocoagulation such as exudative choroid detachment and the progression of macular edema. However, in a number of cases during the initial treatment patients with severe forms of PDR when the time for PRLK is missed or laser treatment is technically unfeasible.

However, the issue of reducing the stages of laser and surgical treatments and determining the timing of PRLK after vitreoretinal surgery to achieve stabilization of the pathological process remains relevant. Purpose is to evaluate the safety and effectiveness of one-stage laser pattern scattered photocoagulation of the retina after primary subtotal vitrectomy in patients with fibrovascular form of proliferative diabetic retinopathy.

Methods
Diagnostic examination and treatment were carried out to 28 patients (28 eyes) with type 1 diabetes (4 patients) and type 2 (24 patients, of which in 18 cases insulin-required form) who first came to an ophthalmological clinic. A fibrovascular form of PDR complicated by hemophthalmos with local traction retinal detachment (1-2 stage of gliosis of the retina according to F.A. L'Esperance) was diagnosed in all cases. The average age of the patients was 53 ± 9.3 (from 37 to 75 years). The duration of the disease was 13 ± 6.6 years (from 5 to 21 years). In all cases, diabetes was sub- or decompensated, the level of glycated hemoglobin (HbA1c) in the observed group of patients varied from 9 to 11.5%. The best corrected visual acuity (BCVA) at admission ranged from pr.l.certae to 0.4. All patients were diagnosed with partial or subtotal hemophthalmus, which did not allow for PRLK. In 16 cases, according to B-scan data, areas of local traction retinal detachment, moorings and membranes fixed in the posterior pole of the eye were identified.

Results
All patients underwent 2 or 3 stage treatment: subtotal vitrectomy, followed by a one-stage laser pattern scattered photocoagulation of the retina followed by removal of silicone oil in cases where silicone oil was used during the primary vitrectomy. Depending on the intraoperative hemostasis and the state of the retina, the operation was completed with tamponade of the vitreous cavity with Oxane 5700 silicone oil (Bausch + Lomb, USA) (24 patients) or air tamponade (4 patients). After vitrectomy at 1-1.5 months a standard ophthalmological examination and SOCT in the posterior pole of the eye and in the middle periphery were performed. In cases of ischemic form of PDR (26 eyes), the second stage was carried out with one-stage laser pattern scattered photocoagulation on an Integre Pro Scan laser ophthalmocoagulator (Ellex, Australia). Power parameters were selected individually in a single pulse mode until 2-3 degrees coagulat according to L’Esperance was obtained. The average number of coagulates per session was 1750 ± 485. At the third stage in 1-2 months after laser treatment the silicone oil was removed and the vitreous cavity was filled in with a balanced solution. The stages of surgical and laser treatment were uneventful in 2.5-4.5 months period.

Conclusions
The proposed variant of staged treatment of fibrovascular form of proliferative diabetic retinopathy using primary vitreous surgery and delayed one-stage laser pattern scattered photocoagulation of the retina allows to stabilize the pathological process in a short time period reduce the volume of surgical intervention and reduce the number of patient visits.
Antiphospholipid syndrome complicated by central retinal artery occlusion

Purpose
We report the case of an occlusion of the central retinal artery in a 58-year-old patient revealing an anti phospholipid antibody syndrome.

Setting/Venue
Occlusion of the central retinal artery is a serious accident that represents one of the rare ophthalmologic emergencies where the delay in treatment is a crucial element. But it also represents an alarm signal that should lead to a search for an underlying systemic pathology that could threaten the vital prognosis. The assessment must be oriented according to the terrain, the interrogation, the ophthalmologic and general examination, because the etiologies are multiple and varied.

Methods
This is the case of a 58-year-old patient, with no particular pathological history, who had a brutal and painless unilateral decrease in visual acuity.

Results
Examination revealed a collapsed visual acuity limited to light perception with areflective mydriasis and at the fundus an ischemic white retinal edema and cherry red macula associated with a diffuse narrowing of the arterial caliber. The examination of the contralateral eye was unremarkable. Fluorescein angiography showed a delay in arterial perfusion followed by a prolongation of the retinal arteriovenous filling time. An emergency sedimentation rate was 80 mm and CRP was 20 mg/L. The patient received 3 boluses of corticoids in emergency. The workup was completed by a blood glucose level of 0.9g/l, a normal lipid profile, a blood count (leukocytes 7000/ul, platelets 375000/ul, hemoglobin 12g/ml), a normal hemostasis workup (PT, APTT, protein C, protein S, antithrombin III), Auscultation for carotid murmur was negative, Doppler of the neck vessels normal, ECG and cardiac ultrasound normal, temporal artery biopsy negative, ANCA and antinuclear antibody negative. In addition, the patient had a high blood pressure of 200/100 mm Hg and high anti phospholipid antibodies, which justified a hypotensive treatment and aspirin at a dose of 160 mg/day to avoid a possible recurrence.

Conclusions
Occlusions of the central retinal artery are often the translation of a suffering of the vascular system as a whole. They should constitute an “alarm signal” which should lead to the search for vascular risk factors.

Financial Disclosure
none
Optical Coherence Tomography Changes in Patients with Sickle Cell Disease

**Purpose**
The purpose of free paper is to compare the optical coherence tomography (OCT) changes of the control group and patients with sickle cell disease.

**Setting/Venue**
This study was conducted between December 2020 and March 2021 in Department of Ophthalmology, Faculty of Medicine, Mersin University, Mersin, Turkey.

**Methods**
The OCT examinations performed on 48 eyes of 24 patients with sickle cell diseases who applied to the Department of Ophthalmology, Faculty of Medicine, Mersin University between December 2020 and March 2021 were retrospectively screened. The changes seen were analyzed with a scale divided into 9 sectors according to the ETDRS protocol and compared with a control group (40 eyes of 20 patients) of completely healthy individuals with similar age and gender distribution.

**Results**
Of the 24 patients, 7 (29.2%) were male and 17 (70.8%) were female. The average age was 38.7 ± 10.129 years (min - max: 23 - 58 years). Four (20%) of the 20 patients in the control group were male and 16 (% 80) were female. The average age was 37.51 ± 8.45 years (min - max: 25 - 60 years). The OCT measurements for both groups were evaluated using a grid divided into 9 sectors (nasal inner, nasal outer, temporal inner, temporal outer, superior inner, superior outer, inferior inner, inferior outer and fovea) according to the ETDRS protocol. Full thickness measurements of the patients: nasal inner 334,25 ± 24,30 µm, nasal outer 313,5 ± 19,01 µm, temporal inner 304,75 ± 28,85 µm, temporal outer 275,66 ± 16,51 µm, superior inner 327,58 ± 27,53 µm, superior outer 268,25 ± 11,85 µm, inferior inner 322,41 ± 19,65 µm, inferior outer 288,6 ± 17,67 µm and fovea was 274,08 ± 41,27 µm. Macular volume was 8,32 ± 0,542 mm³. Changes in temporal inner, superior outer and macular volume were found to be significantly lower in the control group. (p = 0.01, p = 0.002, p = 0.01, respectively)

**Conclusions**
Consequently, sickle cell disease can cause blindness that may be accompanied by retinopathy. Those with this disease need careful examination of the retina and use of imaging methods. The importance of our study is to draw attention to the need for periodic ophthalmologic monitoring in patients with anemia since childhood, aiming at prevention, diagnosis and early treatment of the disease.

**Financial Disclosure**
We have no financial interest to disclose.
## Title
Factors Associated with the Response to Fluocinolone Acetonide 0.19 mg in Diabetic Macular Edema evaluated as the Area-Under-The-Curve

### Purpose
To investigate the impact of different baseline demographic, clinical, and optical coherence tomography (OCT) factors on the functional and morphologic response to fluocinolone acetonide (FAc) 0.19 mg implant in patients with diabetic macular edema (DME), evaluated as the area-under-the-curve (AUC).

### Setting/Venue
Single-center longitudinal retrospective study

### Methods
Pseudophakic eyes with DME who received FAc implant were recruited. The AUC of the best-corrected visual acuity (BCVA expressed as LogMAR) and the central macular thickness (CMT) changes up to 36 months were calculated with the trapezoidal rule. The AUC values were divided by the amount of available follow-up (expressed in months) of each eye, to correct for the heterogeneous follow-up. Demographic and clinical data and OCT features at the time of FAc administration were collected, and their predictive effect on BCVA and CMT was investigated with linear mixed models.

### Results
Eighty-one eyes of 63 patients with a minimum 12-month follow-up were enrolled; the median available follow-up was 26 months. All eyes had previously undergone a variable combination of intravitreal treatments with anti-VEGF, dexamethasone (DEX), and macular laser. BCVA improved following FAc implant (p=0.01). The mean AUCBCVA was 0.24±0.17 LogMAR/month. Lower AUCBCVA (better vision during follow-up) was associated with higher baseline BCVA (p<0.001), lower AUCCMT after FAc administration (p<0.001), type 2 diabetes (p=0.04), intact subfoveal ELM/EZ layer (p=0.01). CMT significantly decreased after FAc (p<0.001). The mean AUCCMT was 179.6±54.3 μm/month. Lower AUCCMT (thinner macula during the follow-up) was associated history of anti-VEGF injections administered before FAc (p<0.001). Eyes with higher CMT at baseline (p<0.001) and those with tractional DME (p=0.01) had higher AUCCMT during the follow-up. The need for additional treatments after FAc was also associated with higher AUCCMT for 36 months (p=0.001)

### Conclusions
Baseline visual acuity, retinal thickness, and photoreceptors’ integrity were associated with better functional response to FAc implant over time; severe macular edema, undertreated edema, and tractional DME had a worse response to intravitreal sustained-release corticosteroids. In our cohort of eyes with long-standing DME, the duration of the disease did not help to predict the treatment outcomes. These findings might guide clinicians in a more informed decisional algorithm in treating DME.

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Title
Conservative management outcomes of Non-ischemic Anterior Ischemic Optic Neuropathy (NAION) in Diabetic patients at Tertiary health care center of Anand, Gujarat, India

Purpose
The purpose of this study is to evaluate the outcomes of use of intravenous Methyl Prednisolone in Treatment of Non Arteritic anterior ischemic optic neuropathy in Diabetic Patients Presenting to a Tertiary Care Hospital at Anand, Gujarat, India.

Setting/Venue
Ophthalmology outpatient department of shree Krishna hospital, Anand, Gujarat, India.

Methods
Diabetic Patients who presented to our out-patient department with complain of sudden painless loss of vision were serially evaluated for their vision using Snellen’s chart for distance vision and romans chart for near vision, color vision with ishihara chart, contrast sensitivity with pelli Robson, visual field by confrontation test and dilated fundus examination with indirect ophthalmoscope. After having diagnosed them as non Arteritic anterior ischemic optic neuropathy, their blood pressure and blood sugars were checked. In patients whose random blood sugars or blood pressure were not within normal limits were given corticosteroids under supervision of physician. Patients were conservatively managed with intravenous 1-gram methyl prednisolone injections daily for up to 3 consecutive days. The outcomes were evaluated daily mainly on basis of visual acuity improvement along with color vision, contrast sensitivity improvements and reduction in disc edema compared to their day of presentation at outpatient department.

Results
8 Diabetic patients were selected for this study out which 4 were male and 4 were female with their mean age as 56.5 years. After giving them Intravenous Methyl prednisolone (1 gram) we saw that 5 out of 8 i.e. 62.5% patients showed improvement in vision on Day 1, 4 out of 8 i.e. 50% patients showed improvement of vision on day 2, and 6 out of 8 i.e. 75% patients vision improved on day 3. 4 patients’ i.e. 50% showed Contrast Sensitivity improvement, 4 patients’ i.e. 50% showed color vision improvement, 7 patients’ 87.5%patients confrontation test improved along with considerable disc edema reduction in all by day 3 as compared to their day of presentation.

Conclusions
NAION is a common risk factor in diabetic patients with an unclear pathology. Hence if a diagnosis of NAION is made then as per our study, intravenous high dose corticosteroids provide a faster resolution of the compartment syndrome for the treatment of NAION by possibly decreasing capillary permeability and thereby reduces the compression of capillaries in the optic nerve head and improves blood flow, which restores visual function prove to be a good option with no significant major adverse effects seen. Thus, we can conclude that use of high dose corticosteroid has been beneficial for treatment of NAION in diabetic patients who approach timely before the stage of optic disc atrophy sets in.

Financial Disclosure
NO FINANCIAL INTERESTS
Efficacy and safety of intravitreal aflibercept compared with laser photoagulation for patients with retinopathy of prematurity: The FIREFLEYE study

Purpose
Retinopathy of prematurity (ROP) is a proliferative vascular disease caused by abnormal vascularization of the retina in premature infants. Laser photoagulation is currently one of the standards of care for patients with ROP requiring treatment; however, it is associated with potential risks, such as loss of visual field and the development of high myopia, and usually requires longer sedation and breathing assistance. Currently available clinical data indicate potential advantages of anti-vascular endothelial growth factor (VEGF) agents, including intravitreal aflibercept (IVT-AFL), over laser photoagulation. Because there is a considerable unmet need for an effective, safe, less invasive, and tolerable treatment for preterm infants with vision-threatening ROP, prospective and longer-term data on the use of IVT-AFL for the treatment of ROP are required. The aim of the FIREFLEYE study was to compare the efficacy and safety of IVT-AFL injections with laser photoagulation for patients with ROP.

Setting/Venue
FIREFLEYE (NCT04004208) was a 24-week, randomized, controlled, open-label, multicenter, non-inferiority, Phase 3 study to assess the efficacy and safety of IVT-AFL versus laser photoagulation in patients with ROP. The study population comprised infants born at a gestational age of ≤32 weeks or birth weight of ≤1500 g, who weighed ≥800 g at baseline and who had ROP in at least one eye classified as Zone I Stage 1+, 2+, 3, 3+; Zone II Stage 2+, 3+; or aggressive posterior (AP)-ROP.

Results
The full analysis set comprised 113 patients (IVT-AFL: n=75; laser: n=38) with a mean±SD gestational age of 26 weeks and 2 days ±1.9 weeks and mean±SD birth weight of 862.1±282.9 g. ROP classification at baseline was 33.6% Zone 1 (including Zone I AP-ROP), 66.4% Zone II (including Zone II AP-ROP), and 16.8% AP-ROP. Bilateral treatment was performed in 71 (94.7%) IVT-AFL-group patients and 34 (89.5%) laser-group patients. The estimated success rate was 85.5% in patients treated with IVT-AFL and 82.1% in laser-treated patients. The 90% CI for treatment difference was −8.0% to +16.2%; therefore, non-inferiority could not be concluded. In the IVT-AFL group, 17.8% of eyes received one re-treatment. In the laser group, 6.9% of eyes received one re-treatment after ≤1 week, and 2.8% received two re-treatments. In the IVT-AFL group, 4.8% of eyes received rescue treatment. In the laser group, 11.1% received rescue treatment. Ocular and systemic SAEs were reported in 13.3% and 24.0% of patients in the IVT-AFL group, and 7.9% and 36.8% of patients in the laser group, respectively. No cases of endophthalmitis were reported. Three deaths were reported (2.7%), all in the IVT-AFL group, occurring 4–9 weeks after treatment and considered unrelated to the study drug.

Conclusions
FIREFLEYE is the first prospective, randomized, controlled, multicenter study to evaluate the efficacy and safety of IVT-AFL compared with laser treatment for patients with severe ROP. During this 6-month study, treatment success was numerically higher with IVT-AFL (85.5%) than with laser photoagulation (82.1%). Non-inferiority of IVT-AFL versus laser treatment could not be formally shown, because the observed laser success rate was higher than expected based on previously published data. Most infants in the IVT-AFL group required one single injection per eye. Ocular safety of IVT-AFL in infants was consistent with the established safety profile known from adults, and no ROP population-specific safety concerns were identified. The three deaths in the IVT-AFL group occurred between 4 and 9 weeks after treatment and were considered related to complications from prematurity, not study treatment. Overall, treatment with IVT-AFL showed a favorable benefit-risk profile, indicating clinical benefit of IVT-AFL in the treatment of premature infants with severe unilateral or bilateral ROP. Patients are being followed up for ocular, neurodevelopmental, and overall clinical outcomes until 5 years of age as part of the FIREFLEYE NEXT extension study (NCT04015180).

Financial Disclosure
Changes in choroidal thickness after anti-vascular endothelial growth factor treatment of diabetic macular edema, Real-life data, 2-year results

Purpose
To evaluate the long-term effect of intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection on central choroidal thickness (CCT), central macular thickness (CMT) and best corrected visual acuity (BCVA) in diabetic macular edema (DME).

Setting/Venue
The records of patients diagnosed with DME (Central MT more than 250 µm) and treated with anti-VEGF (aflibercept or ranibizumab) in the retina clinic between March 2017 and April 2019 were reviewed retrospectively. All patients diagnosed with DME were treated with a 3-month loading dose of ranibizumab or aflibercept followed by pro re nata (PRN) for up to 24 months.

Methods
Retrospective, cohort analysis of 90 eyes of 90 patients receiving anti-VEGF therapy for DME. In patients’ records, measurements of CCT, CMT, and BCVA before treatment and at 2 years after treatment were recorded. Using enhanced-depth imaging optical coherence tomography (EDI-OCT) images, choroidal thickness and macular thickness measurements were recorded in the subfoveal area and 1 mm nasal to 1 mm temporal to the central foveal area. The baseline and final CMT and CCT values measured from all three quadrants were analyzed statistically.

Results
The mean age of the patients was 59.60 ± 9.78 (range, 40-77) years, 43 (%47.8) female and 47 (%52.2) male. The mean HbA1c level of patients was 8.22±2.11, mean anti-VEGF number 6.00±2.49 (range, 3.0-14.0) (aflibercept 6.40±2.78, ranibizumab 6.11±2.18). Mean baseline measurements nasal-CT 226.4±52.5µm, central-CT 243.2 ± 51.1 µm and temporal-CT 224.6±47.9 µm. Mean final measurements nasal-CT 220.0 ± 50.2µm, central-CT 235.3± 53.6 µm, temporal-CT 220.5 ± 48.1 µm. Analysis of the data showed no statistically significant decrease in baseline and last follow-up choroidal thickness measurements in all three quadrants (P =0.122, p=0.056, p=0.184, respectively ). Mean baseline measurements nasal- MT 385.3 ±67.7, central-MT 345.5 ± 119.7 µm and temporal-MT 365.0±64.9 µm. Mean final measurements nasal- MT 359.6±59.2µm, central-MT 306.2 ± 98.4 µm and temporal-MT 353.4±63.3 µm. When macular thickness was evaluated, a statistically significant decrease was observed in the baseline and final measurements in the central and nasal quadrants, while the decrease was not significant in the temporal quadrant (P =0.001, p=0.002, p=0.234, respectively). The BCVA improved from 0.52±0.44 logMAR at baseline to 0.38±0.33 at final (P = 0.002).

Conclusions
Studies to evaluate the choroidal microvasculature or choroidal perfusion may prove valuable in delineating the role of the choroid in the pathophysiology of DME. We also hope that future studies and real-life data evaluating the relationship between diabetic macular edema and choroidal thickness may lead to different approaches in the treatment of DME.
**Title**  
Assessing microvascular changes in eyes of diabetic patients without clinical diabetic retinopathy: An Optical Coherence Tomography Angiography study

**Purpose**  
To evaluate the relevance of optical coherence tomography angiography (OCT-A) in assessing early microvascular changes in eyes of diabetic individuals without clinical retinopathy.

**Setting/Venue**  
A monocentric observational prospective study conducted in the Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

**Methods**  
We conducted a monocentric observational prospective study including 48 eyes of 29 patients with type 2 diabetes mellitus and 52 control eyes of 26 age-matched healthy subjects. All included individuals underwent a complete ophthalmic examination and OCT-A scans 6x6 mm (Optovue RTVue-XR Avanti, AngioVue) between September 2020 and February 2021. Eyes with existing retinal, vitreoretinal interface, optic nerve diseases or/and with poor-quality images were excluded. We assessed the size and the regularity of the foveal avascular zone (FAZ) as well as vessel beading, capillary non-perfusion, microaneurysms and vessel density (VD) in the superficial and the deep layers.

**Results**  
Foveal avascular zone size measured 0.321 mm² (0.124–0.593) in eyes of diabetic patients and 0.291 mm² (0.117–0.489) in control eyes (p = 0.03). Foveal avascular zone irregularity was seen more often in diabetic than control eyes (35.4% and 7.7%, respectively; p = 0.008). Capillary non-perfusion was noted in 27.1% of diabetic patients’ eyes and 3.8% of control eyes (p = 0.02). Microaneurysms and venous beading were noted in less than 8% of both diabetic and control eyes. On univariate analysis, whole and parafoveal vessel densities in the superficial capillary plexus (SCP) and the deep capillary plexus (DCP) were found to be associated with diabetes (Whole SCP density p = 0.031, Parafoveal SCP density p = 0.024, Whole DCP density p = 0.019, Parafoveal DCP density p = 0.006). We did not need to perform multivariate analysis in view of the comparability between diabetic patients and control subjects.

**Conclusions**  
Optical Coherence Tomography Angiography showed a noteworthy relevance in assessing foveal microvascular changes undetected by fundus examination in diabetic patients. Foveal avascular zone abnormalities, capillary non-perfusion and decrease in parafoveal vessel density especially in the deep layers may be considered as early retinal changes in diabetic patients. Although OCT-Angiography is a valuable non-invasive imaging tool, various artifacts caused by OCT image acquisition, intrinsic eye characteristics, motion, processing, and display strategies are to be considered. Therefore, special attention is required for interpretation of images, as artifacts may interfere with the diagnosis, classification, or measurement of lesions in OCT-A images.

**Financial Disclosure**  
The authors declare no conflict of interest.
Evaluation of Peripapillary Perfusion changes after panretinal photocoagulation using OCT Angiography in proliferative diabetic retinopathy

**Purpose**
To evaluate the effect of pan retinal photocoagulation (PRP) on Optic nerve head blood flow with OCT angiography in patients with proliferative diabetic retinopathy (PDR).

**Setting/Venue**
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia.

**Methods**
A prospective interventional study conducted over a period of five months (from February 2020 to June 2020) including 50 eyes of 25 patients with PDR. All subjects underwent comprehensive ocular examinations and OCTA. OCTA scans were performed using Angiovue software of the RTVue XR Avanti. A 4.5 × 4.5 mm images for the Radial Peripapillary Capillaries (RPC) were obtained. Retinal Fiber Layer (RNFL) thickness, whole image (wi), inside disc (id) and peripapillary (pp) were evaluated at baseline and one month after the last PRP session.

**Results**
The mean age was 51.88 ± 7.03 years. The sex ratio was 1.15. The mean session number was 6 ± 2. The mean laser shots per session was 1350 ± 400. All peripapillary vascular densities (wi, id, pp) deceased significantly after PRP (all p>0.05). Compared to baseline, there was significant thickening of the RNFL (p=0.04). A significant negative correlation was found between VDs and the total PRP shots (R=-0.45, p=0.02). Compared to baseline, there was significant increase of the central macular thickness (CMT) (p<0.05). However, BCVA was worse after PRP session with a negative correlation with the CMT (R=-0.42, p=0.048).

**Conclusions**
OCT angiography revealed there is significantly reduced optic nerve head blood flow in PRP treated eyes compared to baseline. Further investigations are needed to evaluate the clinical implications of these findings.

**Financial Disclosure**
The authors declare no conflict of interest.
Machine Learning Model to Predict the Development of Clinically Significant Macular Edema in Patients With Mild Non-proliferative Diabetic Retinopathy

Purpose
Use of artificial intelligence–based models to predict the risk of patients with non-proliferative diabetic retinopathy (NPDR) to develop clinically significant macular edema (CSME) could inform personalised monitoring and patient follow-up. Our objective was to develop and evaluate machine learning models employing systemic and/or retinal imaging features for predicting whether patients with mild NPDR will develop CSME within 2 years from baseline.

Setting/Venue
Analysis of data from a prospective observational cohort study (NCT00763802) in patients with type 2 diabetes and mild NPDR (Diabetic Retinopathy Severity Scale [DRSS] 20–35).

Methods
Systemic and retinal imaging features from 348 patients (129 female; mean age, 60.9 years), without CSME at baseline, enrolled in the study were pooled. Systemic measurements included glycated haemoglobin; systolic and diastolic blood pressure; total, high-density lipoprotein and low-density lipoprotein cholesterol; and triglycerides. Retinal imaging features, acquired using optical coherence tomography (Stratus) and stereoscopic 7-field colour fundus photographs, included central subfield thickness; inner ring temporal, superior, inferior and nasal thickness; number of microaneurysms; and 6-month microaneurysm turnover. Data were collected at 6 and 24 months from baseline. Linear regression models were evaluated for predicting these events using systemic data only, imaging features only and both combined. Area under the receiver operating characteristic (AUROC) curve was employed as a performance metric. Mean values and 95% CIs were computed over all the iterations of 10 repeats of a 5-fold cross-validation setup.

Results
Of 348 patients without CSME at baseline, 12 developed CSME in the study eye by month 6, and 34 patients by month 24. When using data obtained at baseline, CSME at month 24 was predicted with an AUROC = 0.550 (95% CI, 0.521, 0.580) with systemic data, 0.727 (95% CI, 0.700, 0.753) with imaging features and 0.734 (95% CI, 0.708, 0.760) with both combined. When using data from month 6, the 6 patients who developed CSME by month 6 were excluded. CSME at month 24 for the remaining patients was predicted with an AUROC = 0.536 (95% CI, 0.500, 0.573) with systemic data, 0.734 (95% CI, 0.702, 0.766) with imaging data and 0.713 (95% CI, 0.677, 0.748) with both combined. When using data combined from both month 6 and baseline, CSME at month 24 was predicted with an AUROC = 0.508 (95% CI, 0.471, 0.545) with systemic data, 0.749 (95% CI, 0.719, 0.778) with imaging features and 0.738 (95% CI, 0.707, 0.770) with both combined.

Conclusions
Our results indicate that development of CSME in patients with mild NPDR can be more accurately predicted with retinal imaging features than with systemic data alone. When predicting the development of CSME by month 24 using data obtained at month 6 only, the performance was not significantly different compared with using both baseline and month 6. Extending the evaluation to larger datasets is planned to enable more confident conclusions regarding the performance and predictive potential of the different types of data. Such predictive models of CSME in patients with NPDR could help inform personalised monitoring and follow-up, in both clinical development and clinical practice settings.
Exudative Retinal Detachment (ERD) is a vision threatening retinal disorder, whose aetiology is multi-factorial. The most frequent causes involve mechanisms of external (retinal pigment epithelium and choriocapillaris) and internal (vascular endothelium) blood-retinal barrier disruption. Therefore, vascular, inflammatory and tumoral pathologies should be considered in the differential diagnosis of ERD. The aim is to illustrate the clinical features of a patient with bilateral ERD associated with pigment epithelial detachment (PED) and to clarify the association between ophthalmologic findings and systemic aspects of renal disease and dialysis.

A 70-year-old male presented to the emergency department with decreased vision in both eyes, more severe in the left (LE), with 3 weeks of evolution. When questioned, the patient referred unquantified weight loss in the past month. There were no other systemic and ocular symptoms. As clinical history, he presented a hypertensive end stage renal disease (ESRD) under haemodialysis and ischemic heart disease with acute myocardial infarction. Clinical observation and multimodal imaging revealed: visual acuity of 4/10 in the right eye (RE) and 1/10 in the LE; pseudophakia in both eyes, without other anterior segment changes; normal intraocular pressure; posterior segment with multiple sub-retinal white deposits; PED over the posterior pole in both eyes, with a macular giant tear of the retinal pigment epithelium (EPR) in the LE; overlying temporal peripheral ERD in the RE and temporal inferior ERD in the LE, involving the macular area. The patient was admitted for systemic evaluation and for optimization of haemodialysis parameters. Systemic inflammatory, infectious and malignant diseases were excluded. Subsequent ophthalmologic evaluation showed progressive reduction of subretinal and sub-RPE fluid with visual acuity improvement.

According to literature, patients with ESRD on dialysis demonstrate an increased risk of ERD, with an incidence of 0.03%. The exact pathophysiology of ERD associated with dialysis is still not well established. Some authors suggest that the focal increase in choriocapillaris permeability in the uremic state plays a more important role. In opposition, others suggest that dialysis, for causing a variation in osmolality and intermittent hemodynamic alterations, induces fluid shifts between chorioretinal layers. The aetiology of PED is also unknown. Any condition that can destabilize the complex attachment of the basement membrane of the RPE and Bruch membrane can lead to PED. The most accepted theories, associated with renal disease, are: 1) deposition of antibodies on the basement membranes and 2) secondary dysfunction of EPR due to choroidal vasculature compromise. RPE tears may complicate disorders associated with PED and cause an acute decrease in visual acuity. Multidisciplinary collaboration between ophthalmologists and nephrologists is essential for timely diagnosis and treatment. In these cases, therapy of the ERD and PED consists primarily of treating underlying systemic alterations, with correction of renal function. In some cases, laser photocoagulation was performed.
### Title
Medically uncontrolled glaucoma after Fluocinolone Acetonide implant - a fair cost for an excellent control of Diabetic Macular Edema?

### Purpose
To describe a case of unilateral Fluocinolone Acetonide (FAc) implant for recurrent Diabetic Macular Edema (DME) which was complicated by medically uncontrolled severe glaucoma. We analysed the five-year outcomes of this long-acting corticosteroid implant compared with the repeated anti-VEGF injections in the contralateral "case-control" eye.

### Setting/Venue
Hospital Prof. Doutor Fernando Fonseca, Amadora, Lisbon, Portugal

### Methods
Retrospective medical chart review including clinical and imaging investigations.

### Results
We present the case of a poorly controlled type 2 diabetic male with mild ocular hypertension, which was treated with repeated anti-VEGF and triamcinolone injections for recurrent bilateral DME for three years. At the age 59 years old, OD was injected with a FAc intravitreal implant (baseline BCVA OD 20/50, OS 20/25). DME rapidly subsided to the FAc implant but approximately one year after the injection this eye showed significantly raised IOP refractory to maximum medical therapy and laser trabeculoplasty. OD was subsequently subject to trabeculectomy, allowing IOP control without the need for topical medication. This eye has exhibited sustained visual acuity (BCVA OD 20/25) and stable retinal thickness for 60 months without any additional interventions. Despite preservation of central vision, glaucomatous damage was severe, conditioning a significant inferior visual field defect. During the same follow-up period, the fellow eye has been managed with repeated anti-VEGF injections (n=22). Recurrent DME OS has been accompanied by macular structural changes and progressively worsening visual results (BCVA OS ≤ 20/100). Surprisingly, the patient reports having better vision in his left eye.

### Conclusions
FAc intravitreal implant is an effective treatment for recurrent DME but may be complicated by challenging cases of steroid-induced glaucoma. In this case, the FAc implant has provided excellent and longstanding outcomes in terms of macular edema. Nonetheless, the steroid-induced glaucomatous damage was equally pronounced in this patient. The dilemma still persists if this was a fair cost for the outstanding preservation of central vision, without the burden of repeated intravitreal injections. The authors recommend a careful selection of DME patients for FAc intravitreal implant, as well as an attentive approach towards IOP adverse events.

### Financial Disclosure
No financial interests
Identifying clinical predictors of proliferative sickle cell retinopathy

**Purpose**

Virtually all orbital and ocular structures can be affected by microvascular occlusions in patients with sickle cell disease (SCD) but the major cause of vision loss in these patients is proliferative sickle cell retinopathy (PSR). Clinical presentation is often unremarkable until late stages where vitreous hemorrhage or retinal detachment lead to a reduction in visual acuity. The purpose of this study was to identify systemic and/or ophthalmologic predictors of PSR in the population studied in order to better stratify patients and define a screening strategy that privileges patients at higher risk of developing ophthalmological complications.

**Setting/Venue**

Ophthalmology Department, Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal.

**Methods**

Cross-sectional study in which 45 patients with SCD were included. Patients received a complete ophthalmologic evaluation including Optical Coherence Tomography (OCT), OCT-Angiography (OCTA) and Fluorescein Angiography (FA). Using en-face OCT images and an image binarization software (ImageJ ®), total choroidal area (TCA) and luminal area (LA) were obtained, and choroidal vascular index (CVI) was calculated as the proportion of LA to TCA. Additionally, OCTA en-face images of the superficial and deep capillaryplexuses were evaluated and number of vessels, vascular density and lacunarity were calculated using Angiotool ® software.

**Results**

Forty-five eyes from 45 patients (21 male, 24 female) with electrophoretic confirmation of SCD were included in the study. Patients' mean age was 38.2 ± 12.2 years. Sickle cell genotypes included 36 patients with SS (80%), 5 patients with SC (11.1%) and 3 patients with S-Thal (6.7%). The majority of patients (n=38, 84.4%) had best corrected visual acuity of 1.0 at presentation. Based on FA imaging and according to Goldberg’s retinopathy classification, 86.7% of patients were diagnosed with sickle cell retinopathy, 69.2% (n=27) with non-proliferative retinopathy (NPSR) and 30.8% (n=12) with PSR. Mean corpuscular volume (MCV), lactate dehydrogenase (LDH) and percentage of fetal hemoglobin (HbF) were inferior in the subgroup of patients with PSR when compared with patients with non-PSR (p<0.001; p= 0.04; p= 0.007, respectively). The best predictor of PSR was MCV (ROC curve = 0.842; p=0.001). With a cut-off of 79.75 fL, sensitivity and specificity for the presence of PSR were 86.7% and 83.3%, respectively. The authors did not identify statistically significant differences between patients with PSR and non-PSR in any other systemic or ophthalmologic parameters studied, including in the quantitative analysis of the retinal vascularization using OCTA and choroidal vascularization using OCT (p>0.05).

**Conclusions**

Sickle cell retinopathy is a very common complication of SCD. According to our results, the incidence of SCR can be as high as 86.7% when assessed by fundoscopy and FA imaging. A significant number of patients with high-risk disease were asymptomatic at presentation and only identified in the setting of a mass screening program. Mean corpuscular volume was the best predictor of proliferative sickle retinopathy with a sensitivity and specificity of 86.7% and 83.3%, respectively, when a cut-off of 79.75 fL was used.

**Financial Disclosure**

None.
Evaluation of Proteoforms of the Transmembrane Chemokines CXCL16 and CX3CL1, their Receptors and their Processing Metalloproteinases ADAM10 and ADAM17 in Proliferative Diabetic Retinopathy

Purpose:
The transmembrane chemokine pathways CXCL16/CXCR6 and CX3CL1/CX3CR1 are strongly implicated in inflammation and angiogenesis. We investigated the involvement of these chemokine pathways and their processing metalloproteinases ADAM10 and ADAM17 in the pathophysiology of proliferative diabetic retinopathy (PDR).

Setting/Venue:
King Abdulaziz University Hospital, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Methods:
Vitreous samples from 32 PDR and 24 non-diabetic patients, epiretinal membranes from 18 patients with PDR, rat retinas, human retinal Müller glial cells and human retinal microvascular endothelial cells (HRMECs) were studied by enzyme-linked immunosorbent assay, immunohistochemistry and Western blot analysis. In vitro angiogenesis assays were performed and the adherence of leukocytes to CXCL16-stimulated HRMECs was assessed.

Results:
CXCL16, CX3CL1, ADAM10, ADAM17 and vascular endothelial growth factor (VEGF) levels were significantly increased in vitreous samples from PDR patients. The levels of CXCL16 were 417-fold higher than those of CX3CL1 in PDR vitreous samples. Significant positive correlations were found between the levels of VEGF and the levels of CXCL16, CX3CL1, ADAM10 and ADAM17. Significant positive correlations were detected between the numbers of blood vessels expressing CD31, reflecting the angiogenic activity of PDR epiretinal membranes, and the numbers of blood vessels and stromal cells expressing CXCL16, CXCR6, ADAM10 and ADAM17. CXCL16 induced upregulation of phospho-ERK1/2, p65 subunit of NF-κB and VEGF in cultured Müller cells and tumor necrosis factor-α induced upregulation of soluble CXCL16 and ADAM17 in Müller cells. Treatment of HRMECs with CXCL16 resulted in increased expression of intercellular adhesion molecule-1 (ICAM-1) and increased leukocyte adhesion to HRMECs. CXCL16 induced HRMEC proliferation and phosphorylation of ERK1/2. Intravitreal administration of CXCL16 in normal rats induced significant upregulation of p65 subunit of NF-κB, VEGF and ICAM-1 in the retina.

Conclusions:
The chemokine axis CXCL16/CXCR6 and the processing metalloproteinases ADAM10 and ADAM17 might serve a role in the initiation and progression of PDR
Title
Treatment of peripheral traction retinal detachment associated with proliferative diabetic retinopathy using modern laser technologies (case report)

Purpose
To present a clinical case and treatment results in peripheral traction retinal detachment associated with proliferative diabetic retinopathy using modern laser technologies without vitrectomy.

Setting/Venue
IRTC Eye Microsurgery Ekaterinburg Center, Ekaterinburg, Russia

Methods
A 26-year old female patient complained for floaters and a "curtain" in the upper-temporal quadrant of the right eye for one week. She had type I diabetes for 12 years. Clinical examination revealed proliferative diabetic retinopathy of both eyes, partial hemophthalmus, peripheral traction retinal detachment of the right eye. First, laser dissection of vitreoretinal traction which caused peripheral retinal detachment was performed using Tango Reflex YAG laser (Ellex). Then immediately barrier laser coagulation at the border of peripheral retinal detachment was performed. The third step included three sessions of panretinal laser coagulation (9 days, 1 month and 3 months after the start of treatment). Barrier and panretinal laser coagulation were performed using Navilas 577 S laser unit (OD OS, Germany).

Results
Immediately after vitreoretinal traction dissection the height of retinal detachment decreased. In 9 days ophthalmoscopy showed attached retina, but ultrasound B-scan revealed flat retinal detachment. In 1 month complete attachment of the retina was marked which allowed panretinal laser coagulation in this area.

Conclusions
Modern laser equipment, such as Tango Reflex YAG laser, gives a possibility to dissect peripheral vitreoretinal adhesions at early stage (without rough fibrous tissue and neovascularization). This procedure with subsequent barrier and panretinal laser coagulation provides attaching of peripheral traction retinal detachment without vitreoretinal surgery.

Financial Disclosure
None
**Title**
Foveal eversion: a biomarker of the outcome of fluocinolone acetonide intravitreal implant in patients with diabetic macular edema?

**Purpose**
Foveal eversion (FE), as diagnosed and defined by structural OCT, has recently been considered a potential marker of severity in diabetic macular edema (DME). Previous studies hypothesized that DME with this foveal phenotype might have a different pathogenic mechanism, with similarities to Irvine Gass syndrome or uveitic macular edema. Considering this hypothesis, the aim of this study is to assess the impact of the FE phenotype on the outcomes of 0.19 mg fluocinolone acetonide intravitreal implant (FAc; ILUVIEN®) in the treatment of diabetic macular edema.

**Setting/Venue**
Non-interventional, retrospective, and single center analysis performed at the Ophthalmology Department, Hospital Beatriz Ângelo, Loures, Portugal.

**Methods**
The authors performed a retrospective study in a clinical setting, including 22 eyes (16 patients) treated with a single FAc intravitreal implant for recurrent or persistent DME. Patient demographics and ocular baseline characteristics were collected. Outcome measures included best-corrected visual acuity (BCVA; ETDRS letters score), central macular thickness (CMT; µm), and intraocular pressure (IOP; mmHg). Prior treatments were noted. Patients were separated in two groups, based on the presence or absence of FE before treatment, and assessed at baseline, months 1 and 3, and then quarterly thereafter. Outcomes were analyzed at baseline and 1-year post-FAc injection for all parameters. Statistical analysis was performed using T-test, non-parametric test and Kruskal Wallis test of SPSS (version 25.0); statistical significance was taken as p-value lower than 0.05.

**Results**
Nine patients (56%) were male and, at baseline, the mean(±SD) age was 71±5.98 years. Distribution by lens status was 55%/45% phakic/pseudophakic, respectively. All eyes showed chronic DME, with median duration of 3.00±1.44 years, and sixteen of them (73%) presented foveal eversion. Comparing the two groups (FE versus absence of FE), the median(±SD) BCVA, CMT and IOP at 1-year indicated greater functional and anatomic improvement in eyes with foveal eversion (+7 ETDRS letters [p= 0.6], -165µm [p= 0.002]) and a slight IOP increase of +3mmHg (p=0.4) in this group. Our data also showed that eyes with FE required more intravitreal adjuvant therapy with anti-VEGF agents (69% vs 33% of eyes [p=0.2]).

**Conclusions**
This retrospective real-world analysis showed a higher prevalence of foveal eversion than described in the literature. Our study also revealed that the presence of foveal eversion is associated with higher retreatment percentages (p=0.2), which is supported by previous studies [Arrigo et al 2021]. However, eyes with foveal eversion showed greater functional and anatomic improvements, with the latter showing statistical significance. Considering the limitations of this study, higher patient numbers are needed to confirm the current findings.

**Financial Disclosure**
The authors acknowledge the support from Alimera Sciences in performing the statistical analysis of the data.
Systemic predictive factors of response to fluocinolone acetonide intravitreal implant in eyes with diabetic macular edema – a real-world analysis

Margarida Brizido, Portugal

**Purpose**
Diabetic macular edema (DME) is a major cause of visual impairment in diabetic patients. Current treatments include both anti-VEGF agents and corticosteroid intravitreal injections, as well as thermal laser photocoagulation. The fluocinolone acetonide intravitreal implant (FAc; ILUVIEN®) represents an alternative therapeutic approach, approved for persistent or recurrent DME, with a lower frequency of injections. The aim of this study is to investigate the correlation between systemic factors (metabolic control and comorbidities) and the functional and structural outcomes of the FAc implant injection, based on best corrected visual acuities (BCVA) and central macular thickness (CMT), as measured by optical coherence tomography (OCT).

**Setting/Venue**
Non-interventional, retrospective, and single-centre analysis performed at the Ophthalmology Department, Hospital Beatriz Ângelo, Loures, Portugal.

**Methods**
Real-world retrospective study including 22 eyes of 16 patients who received a single FAc implant for refractory or recurrent DME. Patient demographics and ocular baseline characteristics (BCVA [ETDRS letters], CMT [µm], intra-ocular pressure [IOP; mmHg] and previous treatments prior to FAc intravitreal injection) were collected. The authors analysed the following outcomes: baseline and 1-year measurements of BCVA, CMT and IOP and cataract-related events. A correlation analysis was performed, relating effectiveness outcomes and systemic factors, namely glycosylated hemoglobin [HbA1c ≤ 7.5% (good metabolic control), HbA1c higher than 7.5% (poor metabolic control)], arterial hypertension, dyslipidemia, chronic kidney disease, and anemia. Statistical analysis was performed using T-test and non-parametric test of SPSS (version 25.0). The cut-off point for statistical significance was set at p-value lower than 0.05.

**Results**
Data was collected from 22 eyes of 16 patients (9 males), with a mean age of 71 years (range 64 to 81). Regarding lens status, 12 were phakic (55%). The analyzed population revealed a median±SD DME duration of 3.00±1.44 years, with 3 eyes (14%) having proliferative diabetic retinopathy. Before the intervention, 5 eyes (23%) were under IOP-lowering medication. At baseline, median±SD HbA1c was 7,65±1,35, with 50% of patients having HbA1c ≤7.5%; 86% were diagnosed with arterial hypertension, 82% with dyslipidemia, 9% with chronic kidney disease and 46% with anemia. The median±SD BCVA, CMT and IOP before treatment was 50.00±21.72 ETDRS letters, 491.00±163.81µm and 14.00±4.75mmHg. In the 12 months that followed FAc intravitreal injection, 5 eyes underwent cataract surgery (42% of phakic eyes) and 3 additional eyes received IOP-lowering medication, with final IOP 15.00±6.32mmHg (p=0,2). Functional and structural outcomes globally improved to BCVA 53.00±20.45 ETDRS letters (p=0,2) and CMT 332.00±112.82µm (p=0,0001). Regarding the impact of the systemic factors, at 1-year post-FAc injection, eyes with good metabolic control, without arterial hypertension, dyslipidemia, chronic kidney disease or anemia revealed better functional-structural correlation outcomes: +10 letters (p=0.19)/-323µm (p=0.003); +15 letters (p=0.1)/-54µm (p=0.1); +16 letters (p=0.07)/-82.5µm (p=0.07); +7.5 letters (p=0.08)/-217µm (p=0.0002) and +6.5 letters

**Conclusions**
Regarding the structural outcomes after treatment, a good metabolic control and the absence of chronic kidney disease or anemia were significantly associated with an improvement in CMT values. Functional outcomes were also better in patients with well-controlled diabetes and without comorbidities, but the difference was not statistically significant between both groups. Overall, the current analysis shows that the efficiency of the FAc intravitreal implant might be influenced by systemic factors, but additional studies with larger sample size are needed to confirm these findings and investigate other demographic and metabolic biomarkers that may help to predict the response to treatment.

**Financial Disclosure**
The authors acknowledge the support from Alimera Sciences in performing the statistical analysis of the data.
**Title**
Real world data to evaluate the efficacy and safety of intravitreal aflibercept injections for the treatment of macular oedema secondary to Retinal Vein Occlusions (RVO).

**Purpose**
Real world data to evaluate the efficacy and safety of intravitreal aflibercept injections for the treatment of macular oedema secondary to Retinal Vein Occlusions (RVO).

**Setting/Venue**
Retrospective interventional non-randomized clinical study done at Yeovil District Hospital & NHS Foundation Trust between June 2016 to February 2021.

**Methods**
160 eyes of 160 treatment naïve patients with macular oedema secondary to retinal vein occlusion (73 eyes Branch retinal vein occlusion (BRVO), 80 eyes Central Retinal Vein Occlusion (CRVO) and 7 eyes Hemi Retinal Vein Occlusion (HRVO) treated with intravitreal 2.0 mg Aflibercept injections between June 2016 to February 2021 were included in the study. All the patients received 2 loading dose injections, after which Treat & Extend (T&E) regimen was followed. The primary efficacy end points were, improvement in best-corrected visual acuity (BCVA) from baseline and reduction in Central Retinal Thickness(CRT).

**Results**
We had a slight female preponderance (51.25 %) with a median age of 76 years. Patients received a median of 8 injections in BRVO eyes, (range 4 to 26) 9 injections (range 3 to 32) in CRVO eyes and 5 (range 2 to 8) injections in HRVO eyes. Median BCVA improved in all patients from baseline to T&E : 35 to 65 letters, 60 to 75 letters and 47.5 to 75 letters in CRVO, BRVO & HRVO eyes respectively and maintained subsequently. 43.13% (69 eyes) gained 15 or more ETDRS letters. Median CRT reduced significantly : CRVO (596 um vs 287.5 um), BRVO (457 um vs 292 um) and HRVO (449 um vs 289 um). 9.37% (15 eyes) had recurrence of disease activity while on T&E regimen and needed long term treatment to maintain the improvement.

**Conclusions**
Treatment with intravitreal aflibercept provided significant functional and anatomic benefits for all types of retinal vein occlusions. It was well tolerated and none of the patients on treatment developed neovascular complications. Some eyes needed long term treatment to maintain the visual gains.

**Financial Disclosure**
NONE
Macular retinal layers’ structure in diabetic patients with and without diabetic retinopathy

Catarina Castro

Purpose

To analyze macular retinal layers’ structure in diabetic eyes and to compare eyes with and without diabetic retinopathy (DR). Secondarily, we intend to assess the impact of laser treatment on macular structure.

Setting/Venue

Department of Ophthalmology, Centro Hospitalar Universitário do Porto, Porto, Portugal

Methods

Cross-sectional observational study that included diabetic patients with stable ocular disease and age-matched controls. Exclusion criteria were the presence of macular edema or epiretinal membrane and previous intravitreal treatment. Spectral-domain optical coherence tomography (SD-OCT) imaging was performed with Heidelberg Spectralis (Heidelberg Engineering®). The following layers were automatically segmented and its thickness was measured in the central 6 mm circle: Nerve Fibers Layer (RNFL), Ganglion Cell Layer (GCL), Inner Plexiform Layer (IPL), Inner Nuclear Layer (INL), Outer Plexiform Layer (OPL), Outer Nuclear Layer (ONL) and Retinal Pigment Epithelium (RPE). Thickness of Outer Retinal Layers (ORL, from external limiting membrane to Bruch’s membrane) and overall Retinal Thickness (RT) were also recorded. Best corrected visual acuity (BCVA) was recorded in the logMAR scale.

Results

A total of 289 eyes of 204 patients, with a mean age 69.1±11.2, 60.3% female, were included. That comprised 134 (46.4%) non-diabetic eyes, 63 (21.8%) diabetic eyes without DR, 45 (15.5%) eyes with untreated DR and 47 (16.3%) eyes with treated DR. There were no age differences between the groups compared (p>0.074). There was a significant decrease in RPE (p=0.040) and ORL thickness (p=0.025) in diabetic eyes without DR, when compared to non-diabetic eyes. There was an increase in INL thickness (p=0.015) of diabetic eyes with untreated DR compared to diabetic eyes without DR. There was an increase in OPL thickness (p=0.007) of diabetic eyes with treated DR when compared to diabetic eyes with untreated DR. In diabetic eyes, BCVA correlates with GCL (r=-0.278, p<0.001), IPL (r=-0.250, p=0.002), RPE (r=-0.162, p=0.043) and ORL (r=-0.198, p=0.013).

Conclusions

The earliest changes in retinal structure of diabetic eyes without DR may be localized in the ORL. Further changes may be localized in the INL, when DR is clinically first noticed and in the OPL when DR is submitted to laser treatment.

Financial Disclosure

The authors have no financial disclosures.
Purpose
This study aimed to evaluate the safety and the long, short-term effects of intravitreal anti-vascular endothelial growth factor (VEGF) injections on corneal features, anterior segment dynamics, and intraocular pressure (IOP).

Setting/Venue
Prospective, nonrandomized clinical trial

Methods
A total of 60 eyes from 60 patients who received intravitreal anti-VEGF injections (bevacizumab, ranibizumab, or aflibercept) of 0.05 ml volume were included in the study. Specular microscopy was performed to evaluate endothelial cell count (ECD); optical biometry was performed to evaluate central corneal thickness (CCT) and anterior chamber depth (ACD) and pneumatic tonometer was performed to measure intraocular pressure (IOP). Each patient received only 1 injection during the whole observation period. Comparative analysis was performed between measurements taken before the injection and 1 month, 3 months after the injection.

Results
Mean IOP 1 hour after the injection were found to be statistically significantly higher than the measurements before the injection (15.8 ± 3.7 mm Hg vs. 21.1 ± 9.6 mm Hg, P < 0.001). However, there was no significant difference in mean IOP between before injection and 1 month (15.0 ± 2.8 mm Hg, P = 0.061), 3 months (16.1 ± 2.7 mm Hg, P = 0.560) after injection. There were no significant differences in the mean ECD, mean CCT, and mean ACD value before injection and 1 hour after the injection (P = 0.688, P = 0.731, and P = 0.553, respectively). Comparison of the measurements of preinjection with 1 month (ECD, P = 0.48; CCT, P = 0.457; ACD, P = 0.825) and 3 months (ECD, P = 0.822; CCT, P = 0.325; ACD, P = 0.556) after the injection showed that there was no significant difference in all features.

Conclusions
Although intravitreal anti-VEGF injection causes a temporary increase in IOP in the short term, it does not affect the structural features of the cornea, anterior segment dynamics and IOP in the long term.

Financial Disclosure
I have no financial disclosure
Optical intensity increase of the inner retinal layers as biomarker for acute central retinal artery occlusion

**Purpose**
Typical signs of ischemia and acute central retinal artery occlusion (CRAO) are an increase in retinal thickness and optical intensity in the inner part of the retina. Previously, we could show within the first hours after symptom onset a very close correlation between time and relative retinal thickness increase in comparison to the fellow eye. Using the relative retinal thickness increase, patients within the first 4.5 hours after symptom onset could be differentiated from other CRAO-patients with a sensitivity of 100% and a specificity of 94.3%. Now we analysed the optical intensity in the inner part of the retina as another potential biomarker to monitor ischemic changes in the retina within the first 48 hours after CRAO onset.

**Methods**
The optical intensity of the inner part of the retina in OCT scans of 56 acute CRAO-patients (≤48 hours after symptom onset) was analysed in both eyes. Segmentation of the inner retinal layers was performed automatically. ImageJ was used to measure optical intensity. Both eyes had to be healthy prior to CRAO onset.

**Results**
In CRAO-patients optical intensity increased significantly (CRAO-eye: 176.53 ± 19.36 vs. healthy fellow eye 123.56 ± 4.36; p < 0.001). Most interestingly, no correlation between time since symptom onset and optical intensity increase existed.

**Conclusions**
The optical intensity increase in CRAO-patients in the inner part of the retina exists nearly instantly after symptom onset. Consequently, the optical intensity increase might be rather used as diagnostic tool in very acute CRAO-patients than to evaluate the ischemic damage.
Purpose
Diabetic macular ischemia (DMI) is a common complication of diabetic retinopathy (DR) that can lead to irreversible vision loss. Currently, there is no approved treatment for DMI. HORNBILL (NCT04424290) is an ongoing Phase I/IIa study investigating the safety, tolerability and early biological response of the intravitreal ischemia modulator agent BI-X in patients with DMI, in stable treated eyes with proliferative diabetic retinopathy (PDR).

Setting/Venue
In the non-randomised, open-label, single rising dose (SRD) phase of the study, 9 patients have been enrolled, with 3 more to be recruited. In the randomised, sham-controlled multiple dosing (MD) phase of the study, a further 30 patients will be enrolled and followed for 22 weeks.

Methods
Patients with PDR previously treated with pan-retinal photocoagulation (PRP) and evidence of DMI are eligible for study inclusion. In the SRD part, DMI is defined (using optical coherence tomography angiography [OCTA]) as the presence of any degree of disruption in retinal vascularity within the superficial and/or deep retinal plexus. In the MD part, DMI is defined (using OCTA) as a foveal avascular zone of ≥0.5 mm². To date, 9 patients have enrolled in three SRD cohorts in the SRD part of the study (0.5, 1.0 and 2.5 mg of BI-X; 3 per cohort), with 3 further patients planned in the 2.5 mg cohort. Each patient received one intravitreal dose of BI-X. The primary endpoint is the number of dose-limiting events. Secondary endpoints include the numbers of drug-related and ocular adverse events (AEs).

Results
The mean age of patients in the SRD part was 60.9 (standard deviation ±9.1) years, and most were Caucasian (66.7%). Mean % baseline HbA1c was similar between groups (0.5 mg: 8.1; 1.0 mg: 8.0; 2.5 mg: 9.3). Mean baseline best-corrected visual acuity (BCVA) varied between cohorts and was lowest in the 0.5 mg cohort (0.5 mg: 8.3; 1.0 mg: 52.7; 2.5 mg: 40.7). No dose-limiting events or drug-related AEs were reported. Overall, 6 AEs were reported, none of which were severe. Two ocular AEs were reported in the 0.5 mg cohort (conjunctival haemorrhage and ocular hyperaemia). Three procedure-related AEs were reported. One patient (0.5 mg) had a conjunctival haemorrhage that resolved without sequelae. A second patient (0.5 mg) with glaucoma experienced a temporary increase in intraocular pressure (IOP) but reported no pain or discomfort and was treated with topical anti-glaucoma therapies, after which IOP reduced. The third patient (2.5 mg) experienced mild post-procedural pain. To date, the 0.5 and 1.0 mg cohorts have completed 57 days' follow-up, with a reported increase in mean BCVA (0.5 mg: 8.3 to 9.0; 1.0 mg: 52.7 to 54.3).

Conclusions
In the SRD part of the HORNBILL study, single rising doses of BI-X were well tolerated by patients with DMI, with no dose-limiting events, severe AEs or drug-related AEs reported to date. There was also an increase in mean BCVA at 57-day follow-up. The effect of 2.5 mg BI-X on BCVA and foveal avascular zone size in patients with DMI will be further examined in the second part of this study through a sham-controlled, single-masked, randomised, MD cohort.
Purpose
To assess the choroidal alterations in diabetic patients with/without retinopathy and to evaluate the relationship of these alterations with the duration of disease and HbA1c level.

Setting/Venue
An observational comparative study

Methods
This study included 30 eyes of 30 patients with diabetic retinopathy (DR) (group 1), 30 eyes of 30 diabetic patients without DR (group 2), and 30 eyes of 30 healthy subjects (group 3). Patients were also grouped according to the duration of diabetes: long-term group (≥15 years, n=32) and short-term group (<15 years, n=28). The choroidal thickness was measured at three points; subfoveal, 1500 μm nasal, and 1500 μm temporal to the fovea. The choroidal area, stromal area, luminal area (LA), and choroidal vascularity index (CVI) were measured with the binarization method.

Results
The mean subfoveal, nasal, and temporal choroidal thicknesses were decreased in group 1 in comparison to controls (p<0.001, p=0.035, and p=0.005, respectively). The mean LA in group 1 and group 2 were both significantly lower compared to group 3 (group 1 vs group 3, p=0.004; group 2 vs group 3, p=0.020). CVI was significantly lower in group 1 and group 2 than in controls (group 1 vs group 3, p=0.019; group 2 vs group 3, p=0.025). CVI was significantly lower in the long-duration group than in the short-duration group (p<0.001). A moderate negative correlation was found between the duration of diabetes and CVI (r=-0.467, p<0.001). Additionally, a moderate negative correlation was found between HbA1c level and CVI (r=-0.425, p<0.000). Partial correlation analysis revealed a significant negative correlation between HbA1c and CVI (r=-0.312, p=0.016) when the effect of duration of diabetes was controlled. Also, there was still a significant negative correlation between the duration of diabetes and CVI (r=-0.352, p=0.006) when the effect of HbA1c was controlled.

Conclusions
Choroidal structure and CVI may alter even in the absence of clinically confirmed retinopathy and these alterations are related to the duration of diabetes and HbA1c level.
**Title**
Comparison of the effectiveness of conbercept and ranibizumab treatment for retinopathy of prematurity

**Purpose**
To compare the effectiveness of intravitreal conbercept and ranibizumab treatment for retinopathy of prematurity (ROP).

**Setting/Venue**
All infants analysed in the retrospective study were diagnosed as aggressive posterior ROP (APROP) or type 1 ROP were treated with anti-VEGF agents (conbercept or ranibizumab) between July 2012 and March 2018 at the Eye Center in Peking University People's Hospital and had at least 12 months of follow-up.

**Methods**
This was a single-centre retrospective study comparing intravitreal conbercept (IVC) and intravitreal ranibizumab (IVR) for the treatment of ROP. In this retrospective study, the date of patients with ROP treated with intravitreal conbercept or ranibizumab from July 2012 to March 2018 with at least 12 months of follow-up at the Eye Center in People's Hospital of Peking University were analysed. Regression, progression or recurrence and peripheral retina vascularization were evaluated. This study was approved by the Ethics Committee and Institutional Review Board of Peking University People's Hospital (Beijing, China). Before treatment, we told the parents of all infants enrolled that using IVR or IVC was off-label, which was an alternative according to the international guidelines for the treatment of ROP. The data were analysed using SPSS.

**Results**
In total, 283 eyes (145 infants) with conbercept treatment and 916 eyes (480 infants) with ranibizumab treatment were enrolled. In zone I ROP and aggressive posterior ROP (APROP), the recurrence prevalence was 49.09% (108/220 eyes) and 28.57% (10/33 eyes), and the recurrence interval was $7.87 \pm 0.65$ (5.5±9.5) weeks and 10.6 ±1.53 (10.5±13) weeks in the ranibizumab and conbercept groups, respectively. In zone II ROP disease, the recurrence prevalence was 23.56% (164/696 eyes) and 13.31% (33/248 eyes), and the interval of recurrence was $8.40 \pm 0.88$ (6±10.5) weeks and 11.4±1.35 (11±13.5) weeks in the ranibizumab and conbercept groups, respectively. The recurrence prevalence was significantly higher with ranibizumab in Zone I ROP and APROP (p = 0.006) and Zone II ROP (p < 0.001), and the recurrence interval was significantly longer in the conbercept group than that in the ranibizumab (p < 0.001). There was no significant difference in the rate of retinal vascularization (p = 0.441).

**Conclusions**
Conbercept and ranibizumab are effective for treating ROP. Compared with ranibizumab, conbercept resulted in less recurrence and longer treatment intervals.
Is Diabetic Macular Edema a More Advanced Stage of Diabetic Retinopathy?

**Purpose**
To assess optical coherence tomography angiography (OCTA) metrics of eyes with diabetic macular edema (DME) and compare them with OCTA findings in eyes with diabetic retinopathy (DR) without DME.

**Setting/Venue**
Rassoul Akram Hospital, Tehran, Iran

**Methods**
In this retrospective case series, macular optical coherence tomography angiography (OCTA) images were obtained from eyes with DR with and without diabetic macular edema. Foveal avascular zone was delineated using a previously described deep learning approach. In addition to vascular density (VD), different complexity indices including vascular tortuosity index (VTI), fractal dimension (FD), vessel diameter index (VDI), vascular complexity index (VCI) and vessel diameter index (VDI) were measured using an automated method. The area of capillary non-perfusion (CNP) and geometric perfusion deficit (GPD) in superficial capillary plexus (SCP) and deep capillary plexus (DCP) was measured using an automated approach after excluding the foveal avascular zone.

**Results**
One-hundred-fifty-five eyes of 105 diabetic patients were included in the study; of those 59 eyes (38.1%) had diabetic macular edema. Fifty-two eyes (33.5%) had PDR and the remaining eyes were categorized as NPDR. The mean±SD age of the patients was 60±11.3 years. The mean central foveal thickness (CFT) was 420.1±115.4 and 257.1±31.4 in eyes with DME and without DME, respectively (p value = 0.000). The mean CNP and GPD in both SCP and DCP were significantly higher in eyes with diabetic macular edema than eyes without DME. In multivariate analysis after adjusting for stage of diabetic retinopathy, the presence of diabetic macular edema was associated with GPD in SCP (B= -1.587, p value=0.006), VD of SCP (B= -0.729, p value=0.000), VDI in SCP (B= 16.76, p value=0.000), GPD in SCP (B= 0.839, p value=0.006) and VD of DCP (B= 0.444, p value=0.004). Moreover, in eyes with DME, central foveal thickness was associated with VD ratio (VD in SCP/DCP) (B= -369.53, p value=0.001) and FAZ area (B= -393.49, p value=0.001) after adjusting for stage of diabetic retinopathy.

**Conclusions**
Eyes with diabetic macular edema have significantly different microvascular changes compared to those without macular edema. DME may be considered a more advanced stage of diabetic retinopathy.

**Financial Disclosure**
No conflict of interest to report.
## Title
In vivo assessment of associations between photoreceptors structure and macular perfusion in type 1 diabetes

## Purpose
To explore the potential relationships between macular vascular network and different adaptive optics (AO) metrics in patients with type 1 diabetes mellitus with no or early signs of non proliferative diabetic retinopathy (NPDR).

## Setting/Venue
Observational cross-sectional study

## Methods
Consecutive DM1 patients with no or early signs of NPDR and healthy age matched control subjects were enrolled at the Department of Ophthalmology of IRCCS-Fondazione Bietti, Rome. All patients and controls were imaged by using AO retinal camera (rtx1; Imagine Eyes, Orsay, France) and PLEX Elite 9000 OCT angiography (OCTA, Carl Zeiss Meditec Inc., Dublin, CA, USA). The main AO outcome measures to evaluate cone mosaic characteristics were: i) Cone density (CD), ii) linear dispersion index (LDi), and iii) heterogeneity packing index (HPi). The main OCTA outcome measures were: i) SCP perfusion (PD) and vessel length densities (VLD) (ii) DCP PD and VLD (iii) SCP and DCP vessel diameter index (VDI) (iv) the CC flow deficit (FD).

## Results
The multiple regression analysis revealed that the NPDR group was characterized by a close relationship between cone metrics and CC FD. Notably, there was a positive relationship between FD and LDi ($P= .035$). On the contrary, a negative relationship was found between FD with both the CD ($P=.042$) and the HPi ($P= .017$). The OCTA parameters for retinal circulation, including PD and VLD, displayed a significant negative correlation with CD. In the analysis investigating the parafoveal subfields, the NPDR temporal sector was characterized by a higher negative correlation between AO metrics and OCTA variables.

## Conclusions
In conclusion, using a combination of SS-OCTA and AO, our study assessed the relationship between macular perfusion (both retinal and choroidal) and AO metrics in patients with DM1 diabetes. In particular, in NPDR eyes photoreceptor damage was strongly associated with choriocapillaris insufficiency even in the early stage of the disease.
Title
Long-term Visual Outcomes and Morphologic Biomarkers of Vision Loss in Eyes with Diabetic Macular Edema treated with Anti-VEGF Therapy

Purpose
Diabetic macular edema (DME) represents a frequent complication of diabetes as it occurs in nearly 12% of patients with diabetic retinopathy (DR). Although anti-vascular endothelial growth factor (VEGF) therapy has significantly improved visual outcomes in these patients, a group of subjects is still characterized by worse visual acuities even after successful treatment. The aim of this study was to perform a qualitative and quantitative analysis on structural optical coherence tomography (OCT) images from DME eyes obtained more than 5 years after the initiation of anti-VEGF treatment to characterize morphologic characteristics correlating with good and poor long-term visual outcomes.

Setting/Venue
Retrospective study at San Raffaele Scientific Institute, Milan, Italy.

Methods
In this study, subjects 18 years of age and older with center-involved DME in at least one eye were identified from the medical records. Subjects were required to have a long-term follow-up (≥5 years) and evidence of resolved DME (i.e., restoration of the foveolar depression with a central macular thickness (CMT) <315 µm) in at least one visit after 5 years of follow-up visits following the initiation of anti-VEGF therapy. The last visit with OCT evidence of resolved DME was considered as the study visit and was used for morphologic analysis. OCT images at the study visit were graded for qualitative features previously proposed as reflecting a distress of the neuroretina in patients with DME, as follows: (i) integrity of the ellipsoid zone (EZ) and external limiting membrane (ELM) bands within the foveola; (ii) integrity of the retinal pigment epithelium (RPE) within the foveola; (iii) presence of disorganization of retinal inner layers (DRL) in the 1 mm central fovea. A quantitative topographical assessment of the inner (combination of nerve fiber and outer plexiform layers) and outer retinal (combination of the outer plexiform and outer nuclear layers) thicknesses was also provided.

Results
Sixty-one eyes (50 patients) were included and divided into two subgroups according to the visual acuity (VA) at the inclusion visit, yielding a group of 24 eyes with a VA<20/40 (“poor/intermediate vision” group), and 37 eyes with a VA≥20/40 (“good vision” group). The ELM and RPE bands were more frequently disrupted/absent in the “poor/intermediate vision” group (P=0.003 and P=0.019). Similarly, DRL was more prevalent in the “poor/intermediate vision” group (P=0.013). The foveal and parafoveal outer retinal thicknesses were reduced in poor/intermediate vision eyes (P=0.022 and P=0.044). No differences in perifoveal outer retinal thickness and inner retinal thicknesses were detected between groups. Multivariate stepwise linear regression analysis demonstrated that the strongest associations with BCVA were with appearance of the RPE (P<0.0001), parafoveal outer retinal thickness (P=0.035), foveal outer retinal thickness (P=0.046), and appearance of the ELM (P=0.048).

Conclusions
In a real-world setting, long-term visual outcomes are generally favorable, and many eyes maintain better than 20/40 vision after >5 years from the initiation of anti-VEGF therapy. More importantly, this longitudinal study provides OCT biomarkers associated with long-term visual outcomes in eyes with DME treated with anti-VEGF. Our findings may be employed to guide the optimal anatomic target in patients with this disorder.

Financial Disclosure
I have no financial disclosure
Anatomical and functional results of dexamethasone intravitreal implant in diabetic macular edema patients.

Purpose
To assess functional outcomes of intravitreal dexamethasone implant in eyes with diabetic macular edema (DME), naïve or without adequately respond to antivascular endothelial growth factor inhibitors (AntiVEGF).

Setting/Venue
Department of Ophthalmology, Complejo Hospitalario Universitario de Albacete (CHUA), Spain

Methods
Retrospective real-world study conducted on consecutive DME patients who underwent treatment with a dexamethasone implant injection and were controlled at 2, 6 and 12 months. Subjects were divided in groups: naïve patients and non-responders to previously treated eyes with antiVEGF injections. Primary endpoints were best-corrected visual acuity (BCVA) and central retinal thickness (CRT).

Results
A total of 128 eyes (31 naïve) were finally included in the study, with a mean age of 64.07 ± 10.24 years. At baseline, there were no statistically significant differences between gender, BCVA, CRT, type of diabetes mellitus, DME subtype and state of the lens. At month 2, the BCVA (logMAR) changed from 0.4 ± 0.61 to 0.3 ± 0.37 and 0.52 ± 0.50 to 0.52 ± 0.4 in naïve and previously treated, respectively (p<0.05). At month 6 and 12, there is no difference between groups with final visual acuity of 0.52 ± 0.4 and 0.52 ± 0.7 in naïve and previously treated group, respectively (p=0.15). CRT improved at month 2, 6 and 12 in both groups (p<0.05). 21 eyes (72.41%) and 62 eyes (71.26%) improved in 20% the CRT in naïve and previously treated group, respectively, without differences between groups at 2 months. 40% of patients improved in 20% the CRT in both groups at month 6 (p=0.68) and 12 (p=0.83).

Conclusions
In our study, there were no differences in functional and anatomical response to dexamethasone implant in naïve patients versus previously treated patients.

Financial Disclosure
We have no financial interest.
Purpose
Patients with macular edema due to retinal vein occlusion (RVO) have a high treatment burden which results in the majority of the patients requiring long-term treatment with frequent clinic visits for monitoring and injections to ensure vision gains are maintained over the long term. Real world evidence indicates that patients with branch or central RVO require an average of 8 injections of anti-vascular endothelial growth factor (VEGF) in the first year of therapy. Therefore, an unmet need exists for both improved vision outcomes, and for more durable treatments (requiring less frequent monitoring and fewer injections). Dual inhibition of angiopoietin (Ang)-2 and VEGF-A with faricimab, the first bispecific antibody designed for intracocular use, has shown excellent visual acuity gains with strong durability in Phase 3 studies in patients with diabetic macular edema (DME) and age-related macular degeneration (nAMD). The strong durability findings in patients with DME and nAMD suggest that faricimab may meet the unique needs of patients with RVO by potentially reducing the number of injections required to maintain visual acuity. Our goal was to design a study to investigate the effects of faricimab on visual acuity and treatment durability in patients with RVO.

Setting/Venue
High levels of Ang-2 have been observed in RVO and Ang-2 has been implicated in RVO pathology; including pathologic neovascularisation, endothelial destabilisation, vascular exudation, and retinal inflammation. Unlike DME or nAMD, patients with RVO less frequently have underlying chronic systemic or ocular disorders that further promote the progression of the disease. Thus, the benefits of dual Ang-2/VEGF inhibition may be more pronounced in patients with RVO than other retinal diseases. We designed the phase 3, multicenter, randomized, double-masked, active comparator-controlled BALATON (NCT04740905) and COMINO (NCT04740931) trials, to compare faricimab with aflibercept in patients with macular edema due to RVO.

Methods
Anti-VEGF treatment-naive patients with foveal centre-involved macular edema due to branch RVO (BALATON; n=570) or central/hemiretinal RVO (COMINO; n=750), best-corrected visual acuity (BCVA) 73—19 letters (20/40—20/400 Snellen equivalent), and central subfield thickness (CST) ≥325 μm (Spectralis/Zeiss) or ≥315 μm (Cirrus/Topcon) will be included. Patients with prior macular laser/pan-retinal laser ≥3 months before screening, prior steroids (intravitreal/implants), amodate non-proliferative diabetic retinopathy, and advanced nAMD, will be excluded. Both studies will compare 6x monthly injections of faricimab 6.0 mg with aflibercept 2.0 mg (Part 1). All patients will roll over to faricimab 6.0 mg administered in up to 16-weekly intervals using a personalized treatment interval (PTI) dosing regimen (Week 24—72; Part 2). PTI adjustments are based on changes in CST and BCVA from reference values at previous dosing visits via an interactive (voice-/web-based) response system (IxRS). PTI allows adjustment of dosing in 4-week increments up to a maximum 16-week interval, and down in 4 or 8 week decrements to a minimum 4-week interval if needed. To maintain masking, at study visits without faricimab injection sham injections will be administered, and CST and BCVA values will be collected for safety/efficacy purposes (not considered by the IxRS system for PTI interval determination).

Results
The primary endpoint is non-inferiority of faricimab versus aflibercept, with the potential to demonstrate superiority, in the mean change from baseline in BCVA at Week 24. Secondary endpoints include mean change from baseline in BCVA, CST, and NEI VFQ-25 composite score, and proportion of patients gaining/avoiding a loss of ≥15, ≥10, ≥5, or ≥0 letters through Week 24. Additional secondary endpoints measured through Week 72 will include change from baseline in BCVA and CST, proportion of patients on a 4-weekly (Q4W), 8-weekly (Q8W), 12-weekly (Q12W), or 16-weekly (Q16W) treatment, number of study drug injections received from Week 24 through Week 72, and assessment of the other Week 24 secondary endpoints. Imaging assessments will include spectral domain or swept-source optical coherence tomography, color fundus photography, and fundus fluorescein angiography. Incidence and severity of ocular and non-ocular adverse events, plasma concentration of faricimab over time, and the development of anti-drug antibodies will be assessed.

Conclusions
BALATON and COMINO are designed to evaluate whether dual inhibition of angiopoietin-2 and VEGF-A with faricimab may improve outcomes beyond anti-VEGF monotherapy in patients with macular edema due to RVO. The PTI phase is designed to examine the potential for individualized faricimab therapy, tailored according to patient needs, to reduce treatment burden while maintaining efficacy.

Financial Disclosure
Consultant: Novartis, Bayer, Pharm Allergan, Roche; Participation in study: Novartis, Bayer, Roche, Apellis, Chengdu Kanghong
Diabetic retinopathy in Greece: prevalence and risk factors studied in the medical retina clinic of a Greek tertiary hospital

**Purpose**
Diabetic retinopathy comprises one of the most devastating microvascular complications associated with diabetes mellitus. Among the large number of risk factors influencing the pathophysiology of the disease, ethnicity has been shown to play a significant role in terms of the prevalence and progression of diabetes. Mediterranean populations are known to have a healthier profile as far as cardiovascular mortality rate is concerned. Thus, the effect of ethnic background should also be taken under consideration in the context of microvascular entities, including diabetic retinopathy. The aim of this study was to report the prevalence of diabetic retinopathy and maculopathy in a cohort of Greek diabetic patients and identify patient characteristics as possible risk factors associated with this entity.

**Setting/Venue**
This is a population-based, non-interventional, cross-sectional study conducted in diabetic Greek patients who attended the medical retina clinics of Hippokration General hospital of Athens during a period of one year.

**Methods**
Clinical and imaging data, including OCT scans were obtained. Retinal photographs were graded based on the newest modification of the International Clinical Disease Severity Scale classification system for diabetic retinopathy. Statistical analysis was performed using Statistical Package for the Social Sciences, version 2019 (SPSS Inc, Chicago, IL). Categorical data was described as absolute numbers and percentages while numerical variables as mean and ± standard deviation. Normality was tested with Q-Q plots. Confidence intervals (CI) at 95% and statistically significant p values ≤0.05 were set.

**Results**
A total of 300 diabetic patients were included. Of these patients, 21 (7%) were diagnosed with diabetes mellitus type I and 279 (93%) with diabetes mellitus type II. The average duration of diabetes was 15 ± 9.4 years (95% CI, 13.9-16.1%) and the mean level of HbA1c was 7.2 ± 1.3 (95% CI, 7.1-7.4). Prevalence of diabetic retinopathy was 38.7% (116 patients), only 15 patients (5%) had proliferative diabetic retinopathy and cystoid macular oedema was detected in 19 patients (6.3%). Good glycemic control was recorded in 157 patients (52.3%), while 16 patients (5.3%) and 21 (7%) were previously subjected to panretinal photocoagulation and intravitreal anti-VEGF treatment, respectively. Patients diagnosed with any stage of diabetic retinopathy had statistically significant longer history of diabetes (p=0.000), poor glycemic control (p=0.009) and were more likely to be on medication for hypertriglyceridemia (p=0.000) compared to those with no diabetic retinopathy. Binary logistic regression analysis identified duration of diabetes (p=0.000), HbA1c levels (p=0.033) and hypertriglyceridemia (p=0.001) as risk factors for the development of diabetic retinopathy, while age, gender and other co-morbidities, including hypertension and hypercholesterolemia did not present any statistically significant association with the presence or stage of diabetic retinopathy.

**Conclusions**
The current study is the first attempt to present the extend and severity of diabetic retinopathy in Greek diabetic patients and also identify risk factors associated with this entity. The prevalence of diabetic retinopathy in this cohort was 38.7% and the majority (93%) had diabetes mellitus type II. Longer duration of diabetes, poor glycemic control and hypertriglyceridemia were identified as risk factors for the development and progression of diabetic retinopathy. Given the absence of a national screening program in Greece, our findings highlight the need for such a program in order to facilitate early diagnosis of diabetic retinopathy with special consideration to susceptible patient groups.

**Financial Disclosure**
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**Title**
Fluocinolone acetonide 0.19mg intravitreal implant for retinal vein occlusion treatment: a case series

**Purpose**
To analyze visual outcomes and safety of a fluocinolone acetonide (FA) sustained drug delivery implant (ILUVIEN®, Alimera Sciences Ltd, Hampshire, UK) for eyes with chronic macular edema due to central (CRVO) or branch retinal vein occlusion (BRVO).

**Setting/Venue**
Ophthalmology department of Centro Hospitalar Universitário do Porto (CHUPorto), Oporto, Portugal.

**Methods**
Patients with central or branch retinal vein occlusion who were submitted to FA implant were included. The main objectives were to assess the changes in Best Corrected visual acuity (BCVA) and central macular thickness (CMT) six months after intravitreal injection. Secondary outcomes included the occurrence of ocular hypertension and cataract. Demographic data, time without edema after implant and the need for additional intravitreal injections during follow-up were also recorded. All patients were previously submitted to intravitreal anti-VEGF and steroids injections with dexamethasone implant or triamcinolone.

**Results**
Eight eyes were enrolled. Mean age at diagnosis was 63±10.6 years-old. The mean±SD follow-up prior to FA implant was 4.75±2.73 years. Mean BCVA improved from 20/125 to 20/63 (p=0.154). Mean±SD CMT decreased from 567±144 to 455±191 micrometers (p=0.023). Ocular hypertension occurred in 2 patients (25%) and both were medically controlled. Of the four phakic patients before FA implant, 3 (75%) developed cataract within 6 months and were submitted to phacoemulsification. The mean±SD period without recurrence of macular edema was 4.0±3.3 months [1;10]. One patient (12.5%) remained without macular edema until the last follow-up (10 months after injection). Two patients (25%) were submitted to 4 monthly anti-VEGF injections immediately after FA implant. In these patients, the FA implant was used as an adjuvant treatment and they remained without macular edema until the last follow-up (18 and 9 months after last intravitreal injection, respectively). In four patients (50%), there was a recurrence of macular edema after a period without treatment: in three patients (37.5%) regular anti-VEGF injections were reintroduced and one patient (12.5%) was treated with dexamethasone implant. One patient (12.5%) didn’t respond to monthly treatment with anti-VEGF and lost follow-up. Mean follow-up after FA implant was 17.4±12.8 months.

**Conclusions**
Fluocinolone acetonide (FA) sustained drug delivery implant can be an option as an adjuvant or single therapy to treat chronic and unresponsive macular edema related to retinal vein occlusion, after partial response to other shorter action intravitreal steroids. According to our results, this therapy seems to be safe, since only two patients developed ocular hypertension controlled with topical medication. Prospective, randomized studies are necessary to understand the benefits of this implant in retinal vein occlusion’s macular edema.

**Financial Disclosure**
The authors have nothing to declare.
Early complications of dexamethasone intravitreal implant in diabetic macular edema patients.

__Purpose__

To assess early complications outcomes of intravitreal dexamethasone implant in eyes with diabetic macular edema (DME).

__Setting/Venue__

Department of Ophthalmology, Complejo Hospitalario Universitario de Albacete (CHUA), Spain.

__Methods__

Retrospective real-world study conducted on consecutive DME patients who underwent treatment with a dexamethasone implant injection and were controlled at 2 months. The spectral domain optical coherence tomography images were quantitatively and qualitatively analyzed. Subjects were divided in groups: naïve patients and previously treated eyes with antiVEGF injections. Primary endpoint were complications after dexamethasone implant.

__Results__

A total of 128 eyes (31 naïve) were finally included in the study. At baseline, there were no statistically significant differences between gender, best-corrected visual acuity, type of diabetes mellitus, DME subtype and state of the lens. At month 2, 43 (33.59%) eyes developed ocular hypertension (8 and 35 eyes in naïve and previously treated, respectively) after dexamethasone implant (p=0.42). Ocular hypertension was defined as a single measurement of ≥25 mmHg, or an increase of ≥10 mmHg from baseline. It was no necessary glaucoma surgery. There were association between ocular hypertension and diabetic retinopathy grade, presence of disorganization of the inner retinal layers and the ellipsoid zone and/or external limiting membrane alterations with statistically significant differences (p=0.002, p=0.008 and p=0.02, respectively).

__Conclusions__

Complications after dexamethasone implant are similar in both groups. Ocular hypertension increases in patients with advanced diabetic retinopathy.

__Financial Disclosure__

We have no financial interests.
# Title
Macular perfusion significantly affects mesopic and scotopic function in eyes with treatment-naïve mild diabetic retinopathy

## Purpose
The detection of alterations in an early clinical phase could help in the prompt identification of patients at higher risk of diabetic retinopathy (DR) progression and in a better understanding of disease pathogenesis. The aim of this study was thus to evaluate the correlations between retinal blood flow alterations and scotopic and mesopic macular sensitivity in patients with treatment-naïve mild DR.

## Setting/Venue
A prospective cross-sectional study was performed at IRCCS San Raffaele Scientific Institute. The study was approved by the local Ethical Committee and was conducted in accordance with the declaration of Helsinki.

## Methods
In this prospective cross-sectional study 5 patients (10 eyes) classified as mild DR underwent a comprehensive multimodal imaging evaluation including swept-source optical coherence tomography angiography (SS-OCTA; PLEX Elite 9000, Carl Zeiss Meditec Inc., Dublin, CA, USA). OCTA imaging of the macula included a 3x3-mm field of view area centered on the fovea (300 A-scans x 300 B-scans). En face OCTA images of the superficial capillary plexus (SCP) and deep vascular complex (DVC) were obtained and imported in ImageJ for analysis. For each result image, the perfusion density and vessel length density (PD and VLD) were measured. Furthermore, all subjects underwent mesopic and scotopic examinations of the central retina using the modified Macular Integrity Assessment device (S-MAIA, CenterVue Spa, Padova, Italy). While the mesopic testing was conducted under light-adapted conditions, the scotopic examination was performed following dark adaptation for 30 minutes. Spearman’s correlation coefficient was used to assess correlations.

## Results
Mean±SD best corrected visual acuity was 20/20 Snellen in all the examined eyes. Mean±SD mesopic and scotopic macular sensitivities were 23.7±2.2 dB and 21.2±1.4 dB, respectively. The PD was 23.9±4.2 % at the SCP level and 37.2±2.3 % at the DVC level. The VLD was 3.5±0.9 % and 5.7±0.7 % within the SCP and DVC slabs, respectively. Both PD and VLD at the DVC level were correlated with mesopic (P=0.030 and P=0.041) and scotopic (P=0.045 and P=0.040) macular sensitivities. Conversely, PD and VLD at the SCP were not correlated with macular sensitivity (P=0.256 and P=0.350 for mesopic and P=0.299 and P=0.828 for scotopic macular sensitivities, respectively).

## Conclusions
In eyes with early signs of DR, scotopic and mesopic macular sensitivities are significantly correlated with macular perfusion at the deep vascular complex. Assuming that perfusion at the DVC is known to contribute to photoreceptors’ function, our results may suggest that an early impairment of perfusion at this level may result in both cone and rod injuries.

## Financial Disclosure
None
Title
The Prognostic Role of Optical Coherence Tomography in Diabetic Macular Edema Patients Undergoing Early Dexamethasone Implant Shift

Purpose
To determine the prognostic features of optic coherence tomography (OCT) parameters by evaluating diabetic macular edema (DME) patients with dexamethasone (DEX) shift in the early period.

Setting/Venue
Retrospective, observational study

Methods
Fifty-four eyes of 34 patients who had DEX implant after three doses of ranibizumab (RNB) were included in this study. Baseline OCT values and factors before Ranibizumab treatment affecting best corrected visual acuity (BCVA) and central macular thickness (CMT) response 3 months after DEX implant were analyzed with logistic regression analyses.

Results
The presence of subretinal fluid and hyperreflective spot (HRS) >20 were found to be a negative predictive factor for anatomical response. (p=0.009, p=0.001, respectively) Low initial BCVA creates a positive effect on visual gain. (p=0.041) Giant outer nuclear layer cysts, completely disrupted inner segment-outer segment and HRS>20 have a negative effect on visual gain. (p=0.025, p=0.043, p=0.023, respectively) According to the receiver operating characteristic analysis, the subretinal fluid volume threshold at which >20% reduction in CMT occurs was determined to be 0.85 mm³. (sensitivity 70%, specificity 84% area under the curve 0.817 p=0.021).

Conclusions
The presence of high number of HRS and high subretinal fluid volume at the baseline negatively affect prognosis even in patient groups with early DEX shift.

Financial Disclosure
none
## Purpose
Hard macular exudates in diabetic retinopathy represent deposits of lipid and proteinaceous material that settle in the outer retinal layers. They often cause significant visual loss when deposited in the foveal region and substantially impacts patient’s quality of life. Fenofibrate is a fibric acid derivate that is currently used to treat high triglycerides and low HDL or as adjunct to statin therapy. It regulates the expression of many genes that work against lipids, inflammation, angiogenesis and cell apoptosis. Purpose of our study was to assess whether long-term lipid-lowering therapy with fenofibrate could reduce the number and extension of massive macular exudates in type 2 diabetes patients.

## Setting/Venue
This study was performed at the International Clinic, Orhei, Moldova in 2018-2020.

## Methods
There were 97 person (194 eyes) with type 2 diabetes, dyslipidemia and moderate nonproliferative diabetic retinopathy with hard exudates included in this study. Age ranged from 42 to 82 years. All patients had relatively well compensated diabetes with HbA1C ranging from 6% to 8%. The mean visual acuity on presentation was 0,3 ± 0,1. Patients were divided into 2 groups - main (52 person) and control (45 person). Exclusion criteria: patients who were already on lipid lowering drugs or glitazones, females taking oral contraceptive pills or hormone replacement therapy or pregnant, familial hypercholesterolemia, hypothyroidism, chronic liver disease, kidney disease. All patients in the main group received fenofibrate 145 mg once a day for 8 months, patients in control group had conventional therapy. All patients had undergone standard ophthalmological examination, fundus photos and OCT imaging on presentation and during follow up visits. Patients were followed at 2, 6,12 and 18 months after the start of the treatment.

## Results
In the main group anatomic result expressed by the reduction of number and extension of hard exudates, decrease in central retinal thickness was achieved in 88% of patients (46 patients, 92 eyes). Central retinal thickness in the main group decreased from mean 382 mkm to 250 mkm ± 30 mkm. Good functional result was achieved in 67 % of patients (70 eyes), where visual acuity increased from 0,3 to 0,5 ± 0,1. This effect was stable for the whole follow up period. In the control group 75 % of patients had no anatomic neither functional changes. In 15 % of patients mean visual acuity slightly improved from 0,3 to 0,4 ± 0,05 with decrease in central retinal thickness from mean 382 mkm to 320 mkm ± 30 mkm due to better compensation of the main disease. In 10% the number and extension of hard exudates increased with further vision deterioration. No fenofibrate side effects were noticed in either group.

## Conclusions
Fenofibrate in type 2 diabetic patients diminishes number of macular hard exudates, reduces macular edema, improves visual acuity with stable effect over the time.

## Financial Disclosure
n/a
Intravitreal injections of vascular endothelial growth factor inhibitors, one of which is aflibercept, have replaced macular laser photocoagulation as the mainstay treatment for diabetic macular edema (DME). Although clinical trials have demonstrated the effectiveness of aflibercept treatment, the outcomes may differ in a real-world clinical setting. The aim of this study was to evaluate the outcomes of aflibercept treatment for DME in a real-world clinical setting.

Setting/Venue
The study took place at the Hospital of Lithuanian university of health sciences Kauno klinikos department of Ophthalmology.

Methods
This retrospective monocenter study involved the analysis of medical records of patients who started aflibercept treatment for DME at the Hospital of the Lithuanian University of Health Sciences Kauno klinikos between October 2017 and November 2019. Anonymized data regarding follow-up visits, aflibercept injections administered and best-corrected visual acuity (BCVA) were collected. Snellen BCVA measurements were converted to approximate Early Treatment Diabetic Retinopathy Study letter scores. The Wilcoxon signed rank test was used to compare BCVA values at baseline with values at different time points during the follow-up period. Baseline BCVA subgroups were compared using the Kruskal-Wallis test. P value <0.05 was considered statistically significant.

Results
89 eyes of 68 patients were included in the study. The median follow-up duration was 469 days (min 276; max 764). Over the first year, all eyes received a median of 5 injections (min 1; max 9). Among eyes with at least 24 months of follow-up and ≥1 injection over the second year, a median of 3 injections (min 1; max 6) were administered over the second year of the treatment. 87.6 % of eyes were treatment-naive prior to the study while 12.4 % of eyes had been previously treated with laser photocoagulation. The median baseline BCVA was 82 letters (min 30; max 100). BCVA improved by a median of 3 letters 365 ± 60 days and 730 ± 60 days after baseline. At the first visit ≥365 days after baseline, 9.2 % of eyes gained ≥15 letters from baseline while 10.1 % of eyes lost ≥15 letters. For 67.4% of eyes, BCVA improved (gain of ≥5 letters) or remained stable (gain/loss of ≤4 letters). Although the changes in BCVA were less noticeable among eyes with better baseline BCVA (>68 letters), their BCVA remained better than of eyes with worse baseline BCVA throughout the two years of follow-up (p<0.001).

Conclusions
Injections were administered less frequently than in randomized prospective clinical trials. BCVA outcomes were also inferior to those reported in clinical trials. The improvement in BCVA was maintained throughout a year of follow-up. Among eyes with worse baseline BCVA, the change in BCVA was more noticeable but not sufficient to reach the BCVA of eyes with better baseline BCVA.

Financial Disclosure
We have no financial relations with any company.
Long-term outcomes and OCT-biomarkers after fluocinolone acetonide intravitreal implant in diabetic macular edema: a real-world study

Purpose
The first endpoint of this study aimed to evaluate long-term visual, anatomic and safety outcomes in patients with diabetic macular edema (DME) treated with fluocinolone acetonide intravitreal implant [FAc] in a real-world clinical setting. The second endpoint intended to investigate the change of OCT prognostic and predictive biomarkers.

Setting/Venue
Retrospective, single center analysis conducted at the Ophthalmology Department, Centro Hospitalar Universitário Lisboa Central - Lisbon, Portugal.

Methods
Retrospective data collection and analysis of consecutive 13 eyes (11 patients) treated with ILUVIEN® (190µg FAc intravitreal implant) for DME insufficiently responsive to previous treatments (persistent/recurrent DME despite treatment). Standard measurements included: visual acuity (BCVA; ETDRS letter score), central macular thickness (CMT; µm), macular volume (MV; mm³), intraocular pressure (IOP; mmHg), IOP related events. All parameters were assessed at baseline, and months 1,3 and 6, and then semesterly afterward. The mean follow-up period was 31.85±6.19 months (mean±standard deviation) (range, 18 to 36 months) and all results are reported at the last observation. Prior treatments were recorded. Additional assessments were performed to determine the percentual change of specific retinal OCT biomarkers (disorganization of the retinal inner layers [DRIL], ellipsoid zone [EZ] disruption, subfoveal neuroretinal detachment [SNL], number of hyperreflective foci [HRF] >30 and intraretinal cysts graduation [severe, moderate, mild and absent]) at baseline, 12 months, 24 months and 36 months post-FAc. Imaging biomarkers were assessed by SD-OCT, based on the 1-mm diameter central region. Regarding statistical analysis, T-test and Fisher’s exact Chi-squared test were performed using SPSS (version 25.0); statistical significance was taken as p-value<0.05.

Results
At baseline, patients had a median(±SD) age of 73±7.2 years and had been diagnosed with DME for 5±1.54 years. Seventy-seven percent of eyes were pseudophakic and 69% were male. All eyes had received laser and anti-VEGF intravitreal treatment before FAc implant, 85% were treated with short-acting corticosteroid intravitreal therapy and none of the eyes had prior vitrectomy. The baseline median(±SD) BCVA, CRT, MV and IOP were 55±20.91 ETDRS letters, 691±207.88µm, 12.72±2.74mm3 and 12.72±2.72mmHg, respectively. At last observation, visual acuity stabilized/improved in 85% of eyes (median(±SD) BCVA of 35±23.12 ETDRS letters [p=0.12]), anatomical reduction of CRT and MV in -435µm (>35% reduction from baseline [p=0.08]) and -3.4 mm3 [p=0.04], respectively. IOP increased slightly to 15mmHg [p=0.97] and 38% of eyes were being treated with IOP-lowering medication. Thirty-one percent of eyes received supplemental DME treatment. In terms of OCT biomarkers, at baseline, 92%, 85%, 8% and 77% of eyes had DRIL, EZ disruption, SND and HRF>30, respectively. 54%, 39%, 8% and 0% had severe, moderate, mild and absent intraretinal cysts. All the imaging biomarkers improved during treatment.

Conclusions
This real-world study examines the FAc implant effectiveness as a long-term option in treating DME that persists or recurs despite treatment. The high rate of poor functional prognostic OCT biomarkers before FAc implant led to no significant gains in visual acuity in most patients. Despite this bad baseline prognosis, 85% of eyes had their visual acuity stabilized or improved during the follow-up period. Reduction of the central macular thickness by >35% from baseline and an improvement of imaging biomarkers during the treatment was also observed in this cohort.

Financial Disclosure
None
Impact of treatment with fluocinolone acetonide implant (FAC; 0.2 µg/day, ILUVIEN®) on diabetic macular edema patients: treatment burden reduction

João Ramalhão
Portugal

Purpose
Treatment of Diabetic Macular Edema (DME) with intravitreal (IV) injections can be associated with a high appointment burden for patients, which has the potential to affect patient’s quality of life in a multitude of ways. The IV implant of fluocinolone acetonide (FAc, 0.19 mg, ILUVIEN®) is an injectable corticosteroid implant approved for the treatment of diabetic macular edema (DME), with continuous and sustained release of FAc for up to 3 years. The aim of this study was to evaluate the effectiveness of ILUVIEN®, comparing the 24 months after treatment with FAc implant with the previous 24 months, in patients with persistent and recurrent DME.

Setting/Venue
This study compares the response to treatment, 2 years before and 2 years after the injection of the FAc implant, in patients with diabetic macular edema, carried out at Centro Hospitalar e Universitário do Porto, Portugal.

Methods
Retrospective and observational study which included 45 eyes from 33 patients with DME that persisted or recurred despite treatment. All patients received an injection of FAc implant between April 2015 and June 2017. Different ophthalmic parameters were measured for 24 months after the FAc implant compared to the same pre-FAc period: best corrected visual acuity (BCVA), central macular thickness (CMT), intraocular pressure (IOP) and number of IV and / or laser treatments performed. After FAc implant, the variation of BCVA, CMT and IOP was evaluated at month 1, 3 and then quarterly until the end of follow-up.

Results
The mean age of patients was 69.6 ± 8.4 years. Before the FAc implantation, 93.3% underwent panretinal photocoagulation and 28.9% macular LASER. The average number of IV treatments in the 24 months prior to ILUVIEN® was 6.8 (4.3 anti-VEGF and 2.5 short-acting steroids). At the moment of the FAc implant injection, 42.2% of the eyes were medicated with hypotensive drops (IOP 15.6 ± 2.9 mmHg), BCVA was 42.1 ± 18.4 ETDRS letters and CMT was 538.4 ± 190.0 µm. After a 2-year follow-up, 51.1% of the eyes were medicated for IOP (16.4 ± 4.0 mmHg) (p<0.001), BCVA was 52.9 ± 21.7 ETDRS letters (p=0.000) and CMT was 381 ± 239.2 µm (p=0.000) [greater reduction in eyes without need of additional treatment during follow-up (p > 0.05)]. After FAc implant, 24 eyes required additional treatment, on average, 283.8 ± 188.3 days after FAc: 10 eyes (22.2%) underwent laser therapy, 17 eyes (37.7%) received anti-VEGF and 4 eyes (8.8%) received short-acting steroids. The average number of IV treatments in the 24 months after FAc implant was 2.6 treatments (2.5 anti-VEGF, 0.1 short-acting steroids) (p=0.002). In 3 eyes, an additional FAc implant was required, on average 491 ± 111.3 days after the first one.

Conclusions
This study shows that the injection of the FAc implant has great efficacy in the treatment of recurrent and persistent DME, evidenced by the significant improvement in the increase in the BCVA, a high reduction in the CMT, without significant variations in the IOP during the follow-up. It also shows that this therapy leads to a significant reduction in the burden of treatment with clear benefit for the patients. Although there was a need for additional treatment in some eyes, there was a considerable decrease in the number of treatments per eye (6.8 pre-FAc vs 2.6 post-FAc) and in almost 50% of the eyes, no additional treatment was needed during the 24 months of treatment follow-up.
Title
Intravitreal Dexamethasone Implant (Ozurdex®) versus Anti-VEGF Injection in Branch Retinal Vein Occlusion: An Optical Coherence Tomography Angiography study

Purpose
To evaluate and compare changes in retinal vasculature after intravitreal dexamethasone implant (Ozurdex) insertion and antiangiogenic factor (anti-VEGF) injection in patients with branch retinal vein occlusion (BRVO) using optical coherence tomography angiography (OCT-A).

Setting/Venue
Department of Ophthalmology of the Military Hospital of Tunis, Tunisia

Methods
We retrospectively analyzed 20 patients with unilateral BRVO. Subjects were divided into two groups according to the treatment agent: Ozurdex (n = 8) and anti-VEGF (n = 12). Spectral domain (SD) OCT and OCT-A 6 x 6 mm scans of the superficial (SCP) and deep capillary plexus (DCP) were analyzed in all eyes. Intravitreal implant and anti-VEGF injections were performed following a PRN regimen. The specific anti-VEGF agent used was chosen among bevacizumab and aflibercept.

Results
Of the 20 patients (mean age 60 ± 8.9 years; 11 male and 9 female) with unilateral BRVO, there was a greater vascular reperfusion of the choriocapillaris in the intravitreal Ozurdex implant group than in the anti-VEGF group (p = 0.011). The mean baseline VD of the SCP and the DCP was similar between groups in all quadrants. At 12 months, the parafoveal VD of the SCP and DCP was significantly higher in the Ozurdex group than in the anti-VEGF group (p < 0.05 for all). Further, there was a statistically significant positive correlation between the improvement of visual acuity and increased VD in both groups (R = 0.648, p = 0.022 and R = 0.544, p = 0.032, respectively for Ozurdex and anti-VEGF).

Conclusions
Our findings suggest that the intravitreal Ozurdex implant induced higher retinal vascular reperfusion compared with anti-VEGF injection. Macular VDs can be used as biomarkers to evaluate the visual prognosis in long-term follow-up for the treatment of BRVO.

Financial Disclosure
The authors declare no conflict of interest.
**Purpose**
To present the short-term effects of intravitreal bevacizumab, ranibizumab and aflibercept on diffuse diabetic macular edema (DME) with real life data under varying payment conditions.

**Methods**
One hundred and four eyes of 86 patients with DME were included in the study. In the groups in which 3 doses of intravitreal treatment is planned for DME; before the treatment, best corrected visual acuity (BCVA), central macular thickness (CMT), fundus angiography (FA) and complete ophthalmologic examination were performed. The examinations were repeated at 1, 2 and 3 months.

**Results**
The mean age of the patients was 63.19 ± 7.8. The mean BCVA before injection was 0.43 in the bevacizumab group, 0.52 in the ranibizumab group and 0.53 logMAR in the aflibercept group (p = 0.258). CMT before injection was 540 ± 75, 497 ± 70, 517 ± 105 (p = 0.117) in the bevacizumab, ranibizumab and aflibercept groups, respectively. After three doses of injection, BCVA was 0.30 in the bevacizumab group, 0.23 in the ranibizumab group and 0.30 logMAR in the aflibercept group (p = 0.397). After three doses of drug injections, CMT values were found to be 429 ± 90 μm in the bevacizumab group, 348 ± 48 μm in the ranibizumab group, and 338 ± 61 μm in the aflibercept group (p <0.001). The least decrease in CMT was in the bevacizumab group (111 μm, p = 0.012). In the aflibercept and ranibizumab groups, a decrease of 178 μm and 166 μm was found in CMT, respectively, and there was no statistically significant difference between the two agents (p = 0.862).

**Conclusions**
Significant improvement was observed in BCVA and CMT. The improvement in CMT was greater in the aflibercept and ranibizumab groups than in the bevacizumab group.

**Setting/Venue**
This study retrospective study conducted at Kütahya Health Science University School of Medicine
Volume rendered OCTA assessment of macular ischemia in patients with type 1 diabetes and without diabetic retinopathy.

Domenico Grosso, Italy

Purpose
To measure macular perfusion in patients with type 1 diabetes and no signs of diabetic retinopathy (DR) using volume rendered three-dimensional (3D) optical coherence tomography angiography (OCTA).

Setting/Venue
IRB-approved multicenter, retrospective observational case series

Methods
We collected data from 35 patients with diabetes and no DR who had OCTA obtained. An additional control group of 35 eyes from 35 healthy subjects was included for comparison. OCTA volume data were processed with a previously presented algorithm in order to obtain the 3D vascular volume and 3D perfusion density. In order to weigh the contribution of different plexuses’ impairment to volume rendered vascular perfusion, OCTA en face images were binarized in order to obtain two-dimensional (2D) perfusion density metrics.

Results
Mean±SD age was 27.2±10.2 years [range 19-64 years] in the diabetic group and 31.0±11.4 years [range 19-61 years] in the control group (p=.145). The BCVA was 0.0±0.1 LogMAR in the diabetic group and 0.0±0.0 LogMAR in healthy eyes (p=.871). The 3D vascular volume was 0.27±0.05 mm3 in the diabetic group and 0.29±0.04 mm3 in the control group (p=.020). The 3D perfusion density was 9.3±1.6 % and 10.3±1.6 % in diabetic patients and controls, respectively (p=.005). Using a 2D visualization, the perfusion density was lower in diabetic patients, but only at the deep vascular complex (DVC) level (38.9±3.7 % in diabetes and 41.0±3.1 % in controls, p=.001), while no differences were detected at the superficial capillary plexus (SCP) level (34.4±3.1 % and 34.3±3.8 % in the diabetic and healthy subjects, respectively, p=.899).

Conclusions
Eyes without signs of DR of patients with diabetes have a reduced volume rendered macular perfusion compared to control healthy eyes.

Financial Disclosure
-
**Title**
Prediabetic early microvascular changes detected by optical coherence tomography angiography

**Purpose**
To determine early microvascular changes in patients with prediabetes using optical coherence tomography angiography (OCT-A).

**Setting/Venue**
Tertiary referral center FOSCAL International in Colombia

**Methods**
Single-centre retrospective case-control study. Macular OCT-A images of superficial capillary plexus (SCP) and deep capillary plexus (DCP) were analyzed in non-diabetic controls, prediabetic and diabetic subjects. A quantitative analysis was performed using the ImageJ software of the foveal avascular zone (FAZ) area, acircularity index (AI), perfusion density (PD) and vascular density (VD).

**Results**
A total of 94 eyes of 53 patients were included in this study. The global mean age was 57.7 years, 39.6% men and 60.4% women. In SCP, mean PD was 0.283±0.15, 0.186±0.720 and 0.186 ± 0.07, in non-diabetic controls, prediabetics and diabetic groups respectively. Mean VD was 8.728 ± 3.425 in non-diabetic controls, 6.147 ± 1.399 in prediabetics, and 6.292 ± 1.997 in patients with diabetes. The comparison of prediabetic patients and controls show statistical differences between PD and VD in both plexus SCP (p=0.002 and p=0.001 respectively) and DCP (p=0.005 and p=0.002 respectively). The mean area of FAZ in the SCP in patients with diabetes and normal individuals was 0.281 mm² and 0.196 mm² respectively (p<0.001). AI was higher in the control group (0.87 ± 0.14) and prediabetic (0.80 ± 0.17) compared to diabetic patients (0.64 ± 0.19). There were no differences in FAZ area and AI between prediabetics and non-diabetic controls.

**Conclusions**
PD and VD demonstrated to be early microvascular changes in prediabetic patients evaluated by OCT-A. On the other hand, alterations of FAZ were not evidenced.

**Financial Disclosure**
Coauthor Juan David Arias is a consultant for Topcon
**Title**
Changes in the VEGF-A concentration in the intraocular fluid of rats with alloxan model of diabetes at different durations of insulin therapy

**Purpose**
To study the changes in the VEGF-A concentration in the intraocular fluid of rats with alloxan model of diabetes at different durations of insulin therapy.

**Setting/Venue**
The experiment was carried out on 212 outbred rats. In 197 rats, the alloxan model of diabetes was simulated by a single intraperitoneal injection of 100 mg/kg alloxan hydrate.

**Methods**
7 days after administration of alloxan hydrate, the animals were divided into 3 groups. The main group consisted of animals with alloxan model of diabetes, which started single daily intraperitoneal injection of prolonged-acting insulin at a dose of 0.9 U/kg of body weight. The comparison group included animals with an alloxan model of diabetes, which did not receive specific therapy. The control group consisted of healthy animals that did not receive therapy. The experimental animals were withdrawn from the study 1 and 4 months after the start of insulin therapy. The concentration of VEGF-A was determined in 80—90 μl of intraocular fluid collected from both eyes of each animal.

**Results**
At a 1-month period of insulin therapy, the VEGF-A concentration in the intraocular fluid in the study group (n = 17; 140 {136; 210} pg/ml) was statistically significantly higher than in comparison group (n = 20; 72 {58; 86} pg/ml; pm-u <0.0004), and in control group (n = 16; 76 {62.5; 88} pg/ml; pm-u = 0.0045). The comparison group did not have statistically significant differences when comparing the indicators of the control group (pm-u = 0.9979). At 4-months period of insulin therapy, the VEGF-A concentration in the intraocular fluid in the study group (n = 18) was 84.8 {61.1; 93.2} pg/ml, in comparison group (n = 16) - 66.4 {54.4; 73.75} pg/ml. The VEGF-A concentration in the intraocular fluid in the study group at the 4-month period of insulin therapy was statistically significantly lower than in the study group at the 1-month period of insulin therapy (pm-u <0.0044).

**Conclusions**
Insulin therapy during 1 month causes an increase in the concentration of VEGF-A in the intraocular fluid of rats with an alloxan model of diabetes, but after 4 months of insulin therapy, the VEGF-A concentration reduced to the initial values.

**Financial Disclosure**
Authors do not have any financial interest in the subject matter. The study was funded by the Russian Foundation for Basic Research grant no. 18-315-00029.
# Title
Retinal vascular disorders in a patient with phacomatosis pigmentovascularis

## Purpose
Phacomatosis pigmentovascularis (PPV) is an uncommon sporadic genetic syndrome characterised by the coexistence of a capillary vascular malformation and a congenital pigmented skin lesion (epidermal nevus, nevus spilus or dermal melanocytosis). There are various groups of PPV that depend on the type of nevus associated with the vascular lesion. Patients can present only the skin condition or have systemic manifestations, including traumatic, neurologic and ophthalmologic manifestations. We report a case of phacomatosis cesioflammea with relevant ophthalmologic involvement.

## Setting/Venue
A recently born female patient was diagnosed with type IIb phacomatosis pigmentovascularis and was treated with pulsed dye laser sessions for right hemifacial capillary malformation since birth. Follow-up was conducted by paediatric ophthalmology since the age of 3 years, and the patient was diagnosed with bilateral oculodermal melanocytosis (nevus of Ota).

## Methods
At the age of 13 years, the patient was referred to a retina consultation for a lesion in the left eye fundus. Her vision with correction was 1 in both eyes. The eye fundus examination revealed a pigmented choroidal naevus in the superior temporal retina of one optic disc diameter with defined edges. We requested fluorescein angiography and optical coherence tomography angiography.

## Results
The angiography showed no disorders in the right eye but revealed a lack of perfusion in the peripheral temporal and inferior retina of the left eye, with areas of diffuse vascular leakage. We also found a retinal macrovessel possibly related to the aberrant retinal vessels described in the patient’s condition. The naevus showed no angiographic signs of interest. The optical coherence tomography angiography ruled out disorders of the foveal avascular zone.

## Conclusions
PPV constitutes an uncommon entity that can be accompanied by various ocular manifestations. An eye fundus study using various imaging techniques is essential for detecting retinal and choroidal disorders.

## Financial Disclosure
NO FINANCIAL RELATIONS
The effect of intravitreal bevacizumab dose on retinal vascular progression in retinopathy of prematurity.

Objective
Peripheral vascular immaturity is a challenging problem encountered in clinical practice after anti-vascular endothelial growth factor (VEGF). It has not been clear whether the incomplete retinal vascularization is due to the nature of the disease or secondary to anti-VEGF in babies who received anti-VEGF injection. However, the effect of different bevacizumab doses on peripheral retinal vascularity is not yet known. The dose of intravitreal bevacizumab (IVB) in the randomized comparative prospective study was 0.625 mg. Since the vitreous volume in premature babies is about a quarter of adults, there are many retrospective studies using 0.3125 mg bevacizumab injection and reporting successful results. In Phase 1 dosing study conducted with a limited number of eyes, it has been reported that it is effective in ROP treatment in doses as low as 0.031 mg. The aim of the presented study is to investigate the effect of drug dose on the progression of retinal vascularization in eyes treated with different doses of IVB.

Methods
Retrospective, comparative, case series. Between May 2018 and December 2019, the patient charts of 142 babies who were administered 0.3125 mg or 0.625 IVB as primary therapy for type 1 ROP or aggressive posterior ROP (APROP) and pre-treatment fundus photographs were retrospectively reviewed. One hundred and four eyes of 52 babies who were treated with the same dose in both eyes, who had fluorescein angiography (FA) at their follow-up and who did not undergo additional IVB, laser, or vitreoretinal surgery until FA, were included in the study. Fifty-six eyes of 28 babies treated with 0.3125 mg bevacizumab were grouped as low dose group, and 48 eyes of 24 babies treated with 0.625 mg bevacizumab were grouped as high dose group. Quantitative measurements were made with the Image J program on the recorded wide-angle images. Horizontal optic disc diameter (HODD), optic disc fovea distance (ODFD), temporal retinal vascularization distance (TRVD) were measured on recorded pre-treatment and FA session images. TRVD is the measurement of the length starting from the optic disc, passing through the fovea to the vascular-avascular border. The plus severity of the pre-treatment photos was scored from one to five.

Results
The mean of week of the first treatment and FA were 36.2 ± 2.2, 65.1 ± 13.8 weeks respectively. In the low dose and high dose group, the pre-treatment TRVD / ODF ratio was 2.40 ± 0.51 and 2.39 ± 0.58 (p = 0.290), respectively. The final TRVD / ODF ratio was 4.13 ± 0.52 and 4.10 ± 0.68, respectively (p = 0.183). The TRVD / ODF ratio increased by 80.49 ± 50.87% and 79.81 ± 49.82%, respectively (p = 0.587). The percentage of increase in the TRVD / ODF ratio was significantly and positively correlated with severity of plus, presence of APROP, FA week, and vascular progression rate of the fellow eye (p = 0.003, r = 0.286; p = 0.000 r = 0.417; p = 0.004 r = 0.280 p = 0.000, r = 0.697). The percentage of increase in the TRVD / ODF ratio was significantly and negatively correlated with treatment week and pre-treatment TRVD / ODF ratio (p = 0.000, r = -0.343; p = 0.000, r = -0.708). There was no significant correlation between vascularization growth rate and dose of IVB (p = 0.938, r = 0.008).

Conclusions
The severity of the plus disease, the presence of APROP, the increased week of FA, and vascular outgrowth rate of the other eye were positively correlated with the vascular outgrowth. The presence of pre-treatment advanced retinal vascularization and advanced treatment week resulted in a lower rate of vascular outgrowth. Our study shows that treatment with different doses of bevacizumab in ROP did not affect the progression of vascularization and final vascularization.

Financial Disclosure
We declare that we have no financial relationship with companies.
Title
Bull in a China Shop? Fluocinolone acetonide implant results in central retinal vein occlusion induced macular edema in eye with glaucoma

Purpose
To report efficacy, safety and management of fluocinolone acetonide implant administration in central retinal vein occlusion induced macular edema (CRVO-ME) in an eye with glaucoma.

Setting/Venue
Hospital do Espírito Santo de Évora, Évora, Portugal

Methods
Case report of a 60-year-old patient with glaucoma followed in our department for unilateral CRVO-ME. Baseline best-corrected visual acuity (BCVA) was counting fingers (5.00 logMAR) with intraocular pressure (IOP) of 18mmHg under timolol+dorzolamide bid. SD-OCT registered central subfield thickness (CST) of 578mcm, cube volume (CV) of 12.1mm3 and mean cube thickness (MCT) of 337mcm.

Results
Patient was submitted to loading dose of 3 intra-vitreal administrations of ranibizumab 0.5mg with insufficient response in increasing BCVA (<+0.1), in reducing CST (reduction<20%) and intra-retinal fluid. The IOP value remained fluctuating between mild elevation and borderline values, under maximum therapy (timolol+dorzolamide and brimonidine bid). Faced with the dilemma of refractory CRVO-ME and borderline IOP values in glaucoma, we took the controversial decision of administering a fluocinolone implant. On 1st month, BCVA rised to 1.0, CST reduced to 243mcm (-48%), CV reduced to 8.9mm3 (-12%), MCT reduced to 248mcm (-12.5%) and there was no residual intraretinal or subretinal fluid. IOP climbed from 20 to 28mmHg and we took another controversial decision of adding travoprost. Follow-up appointments during 8 months showed stable BCVA values, maintained absence of intraretinal or subretinal fluid and IOP reduction to 22-24mmHg without structural or functional glaucomatous progression. From the 8th month onwards, BCVA started to progressively decline due to cataract progression until 0.4 at 12 months. After uneventful cataract surgery, BCVA returned to 0.9 and IOP value lowered to 18 mmHg. Until 20 months of follow-up, BCVA has remained stable at 0.8, without any residual fluid and without any glaucomatous functional or structural progression.

Conclusions
Fluocinolone acetonide implant proved effective in reversing CRVO-ME and in restoring BCVA in an eye with glaucoma. However, the IOP rise was difficult to control with hypotensive drugs and requires more frequent monitoring for signs of structural or functional glaucoma progression. Despite this risk, after 20 months of follow-up, BCVA has remained high and the eye has not suffered structural or functional glaucomatous progression.

Financial Disclosure
None
Efficacy of intravitreal injection of conbercept on non-proliferative diabetic retinopathy: a retrospective study

Purpose
This study assessed the efficacy of conbercept for patients with non-proliferative diabetic retinopathy (NPDR).

Setting/Venue
Department of Ophthalmology, Qilu Hospital, Shandong University

Methods
In this retrospective clinical study, 54 patients with NPDR (54 eyes) were treated with intravitreal injection of conbercept using a 3+ pro re nata regimen and followed up for 12 months. Best corrected visual acuity (BCVA), central foveal thickness (CFT), area of hard exudate (HE), and number of microaneurysms (MAs) were used as indicators of therapeutic effects. Systemic adverse reactions were recorded to assess safety.

Results
During the 12-month follow-up period, the mean number of injections was 6.12±1.89 on demand. From baseline to the 12-month follow-up, the BCVA of patients with NPDR increased from 0.71±0.20 logMAR to 0.43±0.16 logMAR, CFT decreased from 424.26±64.89 lm to 269.27±44.79 lm, and the number of MAs declined from 79.53±27.18 to 33.34±16.53. Moreover, the area of HE was significantly reduced after 9 months of treatment. There were no serious systemic adverse events during the follow-up.

Conclusions
Intravitreal injection of conbercept has a stable and robust effect on patients with NPDR over a 12-month follow-up period. Thus, conbercept is an effective and feasible treatment for NPDR.

Financial Disclosure
none
**Title**

Effect of intravitreal ranibizumab on serous retinal detachment in diabetic macular edema

**Purpose**

The aim of this study was to evaluate the functional and anatomical results of intravitreal ranibizumab in the treatment of diabetic macular edema (DME) with and without serous retinal detachment (SRD).

**Setting/Venue**

Retrospective

**Methods**

Fifty-one eyes treated with three intravitreal injections of ranibizumab for DME with and without SRD were retrospectively analyzed. Patients were divided into two groups according to spectral-domain optical coherence tomography (SD-OCT). Group 1 was consisted of 25 DME patients with SRD, Group 2 was consisted of 26 patients without SRD. After three consecutive intravitreal ranibizumab injections, changes in best-corrected visual acuity (BCVA) and central macular thickness (CMT) were analyzed and compared between groups.

**Results**

The mean age was 64.16 ± 6.43 and, 68.77 ± 7.19 years, respectively (p=0.036). Initial BCVA was 0.55 ± 0.36 logarithm of the minimum angle of resolution (LogMAR), 0.62 ±0.39 LogMAR, respectively (p:0.613). Initial CMT was 548.76 ± 111.62 µm, 446.04 ± 104.10 µm in groups, respectively and it was significantly higher in Group 1 (p=0.001). After three consecutive intravitreal injections of ranibizumab, mean BCVA improved from 0.55 ± 0.36 LogMAR to 0.47 ± 0.30 LogMAR (p=0.281) and CMT decreased from 548.76 ± 111.62 µm to 331.68 ± 165.12 µm (p= 0.000) in Group 1. Mean VA improved from 0.62 ± 0.39 LogMAR to 0.40 ± 0.34 LogMAR (p=0.005) and CMT decreased from 446.04 ± 104.10 µm to 287.25 ± 148.82 µm (p= 0.000) in Group 2. While the decrease in CMT values were similar between the groups, the increase in BCVA was more pronounced in Group 2 after ranibizumab treatment.

**Conclusions**

Although functional results were not sufficient in DME with SRD; adequate anatomical results could be obtained in DME with and without SRD.
Benefit of injection of fluocinolone acetonide (FAC, 0.19 mg, ILUVIEN®) implant in eyes with less chronic diabetic macular edema

Miguel Afonso

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Purpose
The ILUVIEN® implant (fluocinolone acetonide, FAC 0.19 mg), due to its unique sustained micro-dosing technology allows treating diabetic macular edema (DME) continuously, up to 36 months. In Europe, it is indicated for the treatment of persistent and recurrent Diabetic Macular Edema (DME) considered insufficiently responsive to first-line therapies. According to the IRISS study, patients with chronic short-term DME, injected with ILUVIEN® implant, achieved greater visual gains compared to patients with long-term chronic DME. The purpose of this study is to determine the degree of functional and anatomical improvement considering the chronicity of edema following ILUVIEN® implant.

Setting/Venue
This study evaluates the functional and anatomical improvement considering the chronicity of edema following ILUVIEN® implant, performed at Centro Hospitalar e Universitário do Porto, Portugal.

Methods
This is a retrospective and comparative analysis of 34 eyes of 28 patients diagnosed with DME who were treated with ILUVIEN® implant after an insufficient response to previous treatments. The eyes were divided into 2 groups according to the duration of edema: ≤3 years, i.e. short-term edema (group 1; n = 18) and> 3 years, i.e. long-term edema (group 2; n = 16). Best Corrected Visual Acuity (BCVA) reported in ETDRS letters, number of previous intravitreal anti-VEGF and short-acting steroids, duration of edema and Intra-Ocular Pressure (IOP) as well as assessment of Central Macular Thickness (CMT), by Spectral Domain Optical Coherence Tomography (SD-OCT) were recorded at baseline. The results reflect the mean variations in BCVA, CMT and IOP, recorded at month 1, 3 and then every 3 months up to 3 years.

Results
At baseline, the mean age of group 1 was 68.9 ± 7.2 years and of group 2 69.9 ± 8.5 years (p>0.5); the mean duration of DME was 2.6 ± 0.4 months in group 1 and 4.5 ± 0.9 months in group 2 (p<0.001). The mean follow-up for groups 1 and 2 was 32.8 ± 3.6 and 32.1 ± 5.6 months, respectively (p>0.5). Prior to ILUVIEN®, all eyes received intravitreal injections of anti-VEGF (group 1: 2.9 ± 1.6 injections and group 2: 5.4 ± 3.6 injections (p<0.01) and / or short-acting steroids (group 1: 2.6 ± 4.0 injections and group 2: 4.0 ± 4.5 injections (p>0.5). Mean BCVA, in group 1 increased 13.7 ETDRS letters at last observation and in group 2, mean BVCA increased 6.9 ETDRS letters at last observation (p<0.05). CMT decreased by 248.3 μm in group 1 and by 201.8 μm in group 2 (p>0.5), from baseline to last observation. IOP remained stable and without significant variations over 36 months, in both groups (p>0.5).

Conclusions
This study not only demonstrated greater visual gains in patients with less chronic DME - which is in line with the IRISS study results - but also revealed superior morphological results in this group of patients, with increased edema reduction although without statistical significance. As such, this analysis once again highlights the clinically significant anatomical response to ILUVIEN® and functional benefit of early treatment with ILUVIEN® in eyes with persistent and recurrent diabetic macular edema.

Financial Disclosure
The authors don’t have any financial relations with specific companies.
**Title**
Panretinal photocoagulation versus intravitreal bevacizumab versus a proposed modified combination therapy for proliferative diabetic retinopathy treatment; a randomized 3-arm clinical trial

**Purpose**
To compare the safety and therapeutic effect of panretinal photocoagulation (PRP) alone versus intravitreal bevacizumab (IVB) alone versus a modified combination of IVB and laser photocoagulation on naïve proliferative diabetic retinopathy (PDR).

**Setting/Venue**
Ophthalmic Epidemiology Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran

**Methods**
In this randomized 3-armed clinical trial, 153 eyes with PDR were included and divided randomly into 3 groups: PRP group (51 eyes) that underwent full PRP in 2 or 3 sessions and then rescue IVB; IVB group (52 eyes) that received 4 monthly IVB injections and then rescue IVB, and modified combination group (50 eyes) that received 2 bimonthly IVB injections and a modified laser (1 session anterior to the equator) and then rescue IVB or laser. Diabetic macular edema (DME) was treated independently. Primary outcome was best corrected visual acuity (BCVA) at 1-year follow-up. Additionally, area of neovascularization leakage on retinal angiography, central macular thickness (CMT), mean deviation (MD) of visual field (VF) sensitivity on 30-2 pattern test, and the number of examinations and injections were compared.

**Results**
The difference of final BCVA was not significant between the groups. Modified combination group had lower final leakage area compared with PRP (P=0.003) and IVB group (P=0.001). Eyes in IVB group experienced the lowest decrease of neovascularization (P=0.006). The difference of MD of VF was insignificant between IVB and modified combination groups, while PRP group had lower final MD of VF compared to IVB (P=0.001) and modified combination group (P=0.001). The rate of new-onset DME was the highest in RPP group (P=0.01). There was no difference in the rate of new-onset DME between IVB and modified combination groups. The difference of final CMT was insignificant between the groups. The median of total IVB injections were 3.5, 7.5, and 6 for PRP, IVB, and modified combination group, respectively (P=0.002). The median of IVB injections for DME were 3, 2.5, and 2.5 for PRP, IVB, and modified combination group, respectively (P=0.11). Patients in IVB group underwent more visits (P=0.001). For the eyes with baseline DME, final leakage was the lowest in modified combination group (P=0.005). In final BCVA and CMT, however, the difference was not significant. For the eyes without baseline DME, there were no difference in final BCVA and leakage area.

**Conclusions**
This trial showed that all treatment protocols were similarly effective in improving BCVA and CMT. However, modified combination protocol was more effective in PDR regression, overall and in the presence of baseline DME. Since the numbers of intravitreal injections and laser adverse effects were fewer in modified combination protocol, this protocol would be recommended for PDR treatment, especially in cases with baseline DME.

**Financial Disclosure**
There is no financial interest to declare.
**Title**
Case report: Recurrent and persistent Diabetic Macular Oedema after multiple intravitreous treatments: Iluvien® to the Rescue!

**Presenter**
Renato Correia Barbosa
Portugal

**Purpose**
Vascular endothelial growth factor inhibitors (anti-VEGF) and intravitreal corticosteroids are the current main therapeutic strategies to manage Diabetic Macular Edema (DME). Treatment goals include resolution of the edema, stabilization or improvement of vision, and a reduction in morbidity translated by reduced frequency of injections and adverse events. In this case report, we present a clinical case of recurrent DME, despite treatment with multiple anti-VEGF, triamcinolone and dexamethasone implants, which was then submitted to a fluocinolone acetonide 0,19mg, ILUVIEN® implant.

**Setting/Venue**
The diagnosis and treatment of this recurrent DME case took place in the department of ophthalmology of Hospital Pedro Hispano – Unidade Local de Saúde de Matosinhos, Portugal, in 2020.

**Methods**
Clinical case of an unilateral recurrent DME, previously treated with multiple intravitreal anti-VEGF and corticosteroids, and subsequent stabilization after fluocinolone acetonide 0,19mg, ILUVIEN® implant during the 39 month follow-up period, without further need for treatment.

**Results**
A 77-year-old female patient, diagnosed with Diabetes Mellitus type 2 for 32 years, developed bilateral non-proliferative diabetic retinopathy and DME in the right eye (OD). OD was treated with panretinal photoocoagulation and 3 ranibizumab intravitreal injections, achieving a best corrected visual acuity (BCVA) of 79 early treatment diabetic retinopathy study (ETDRS) letters. Although responsive to treatment, DME in the OD recurred after 8 months, and she underwent an intravitreal injection of triamcinolone, with temporary anatomical and functional improvement, which relapsed again, after 3 months. She was then injected with 3 successive dexamethasone implants, with temporary improvement, but DME relapsed 4-6 months after each procedure. Due to the multiple recurrences, the next treatment strategy consisted on fluocinolone acetonide 0,19mg, ILUVIEN® implant, which preserved normal macular thickness and function (84 ETDRS letters) during the 39 months of follow-up after the procedure. Intra ocular pressures remained stable, without need for hypotensive drugs usage.

**Conclusions**
The sustained release fluocinolone acetonide implant effectively restored and preserved macular thickness, which resulted in improved visual function, prevailing during the 39 months of follow-up. There were no visual adverse events during this period. This treatment demonstrated to be a therapeutical option in cases of corticoid responsive DME with successive relapses.

**Financial Disclosure**
There are no financial relations with any company.
Title

Purpose
Diabetic Macular Oedema (DMO) remains a cause of irreversible vision loss in the United Kingdom (U.K.). The first-line treatments for centre-involving DMO in the U.K. are intravitreal anti-vascular endothelial growth factor (anti-VEGF) Aflibercept and Ranibizumab. The recent outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) led to the declaration of a global COVID-19 pandemic in March 2020 following which the U.K. government declared a national lockdown effective from the 23rd of March 2020. Subsequently, the Royal College of Ophthalmologists (RCOphth) published recommendations for the management of ophthalmic conditions during the pandemic. A majority of DMO patients were unable to receive their scheduled anti-VEGF injections during the first wave of the pandemic, which were deferred for 4 months as recommended by RCOphth. Therefore, the objectives of this study were to investigate the effects of the COVID-19 lockdown on the visual and anatomical outcomes of patients receiving intravitreal Aflibercept for DMO, identify demographic or ocular factors that influence functional outcome with deferred treatment and to explore any influence of self-perceived eating habit, physical activity, and psychological well-being on these outcomes.

Setting/Venue
This study was conducted at Central Middlesex Hospital (CMH) in London, United Kingdom. The ophthalmology department is situated in the borough of Brent, which has one of the highest prevalence of diabetes in the United Kingdom. The first-line treatment of choice for centre-involving DMO at CMH is intravitreal Aflibercept.

Methods
This was an observational, retrospective study. Four data time-points were pre-defined: the pre-lockdown period spanned 17th of September 2019 to 22nd of March 2020, lockdown spanned 23rd of March to 7th of June 2020, the post-lockdown visit (PLV) was the first visit attended by the patient after the clinic re-opened to patients with DMO (8th of June 2020), and the follow-up visit, which was the last visit before the clinic again deferred non-urgent patients with DMO on the 6th of January 2021 due to a resurgence of COVID-19 cases nationally. Patients with centre-involving DMO on a course of intravitreal Aflibercept during the pre-lockdown period were identified, and demographic, clinical and optical coherence tomography (OCT) data were collected from these patients at all four pre-defined time-points. In addition, a short telephone questionnaire incorporating the short version of the validated Psychological General Well-Being Index (PGWBS) was administered to patients to enquire about their psychological well-being during lockdown. Descriptive statistics are presented and differences between time-points were tested using a t-test and Mann-Whitney test as appropriate, with a p-value of less than 0.05 considered statistically significant. Linear regression analysis was used to investigate correlations.

Results
178 eyes of 129 patients met the inclusion criteria. The mean age was 65.8±11.3, mean best-corrected visual acuity (BCVA) pre-lockdown was 0.23±0.26 (LogMAR) and mean central subfield thickness (CSFT) was 329µm±89. Fifty-one eyes (29%) had BCVA ≥0.3, whilst 21 of 168 eyes (13%) had CSFT ≥400µm. The median duration between the last pre-lockdown visit and PLV was 168 days [IQR: 140-199]. There was a significant mean decrease in BCVA of 0.09 (0.05-0.13; p<0.001) between the two visits. The proportion of patients with BCVA ≥0.3 increased from 29% pre-lockdown to 42% at PLV (p<0.001). 31% of patients lost at least one line of vision at PLV (BCVA change ≤0.1), whilst 17% lost at least two lines of vision (BCVA change ≤0.2). There was a mean increase in CSFT of 38µm (39-77; p<0.001). The proportion of patients with a CSFT ≥400µm increased from 14% to 30% (p<0.001) between the two visits. Of those who lost ≥0.2 BCVA at PLV, only 27.6% achieved pre-lockdown level or better by end of follow-up. Demographic factors, ocular factors, eating habit, physical activity or PGWBS scores did not correlate with change in BCVA at PLV or by end of follow-up.

Conclusions
The COVID-19 lockdown significantly impacted the functional and anatomical outcomes of patients being treated for DMO, as was predicted. We demonstrated that a third of patients lost at least one line of vision and almost one in five lost two lines of vision. This was associated with recurrence of significant retinal fluid on OCT after deferral of treatment due to lockdown. Importantly, only about a third of those who lost vision had regained it before resurgence of the pandemic necessitated further deferral of treatment. We sort to determine any factors that may predict those likely to sustain significant visual loss with deferred treatment or less likely to regain lost vision, but no correlations achieved statistical significance. Our study confirms the significant and ongoing morbidity sustained due to COVID-19 lockdown in patients with centre-involving DMO. Given the ongoing disruption to services globally during the current pandemic and the significant backlog many healthcare services are facing, mitigating strategies are needed to prevent increasing morbidity in the event of pandemic resurgence. Longer-acting therapeutic agents may reduce the risk of visual loss in the event of future pandemic resurgence or interruption to healthcare.

Financial Disclosure
C.D. has served on advisory boards for Novartis, Allergan and Apellis. She has also received lecture fees from Novartis
Purpose
To describe 2 unusual cases with epiretinal membrane from uncontrolled gliosis that was seen after multilayered inverted ILM flap technique for full thickness macular hole (FTMH).

Setting/Venue
We describe 2 eyes with full thickness macular hole that developed postoperative ERM following an uneventful surgery with multilayered ILM flap technique. Both patients had Metamorphosia and one of these eyes underwent re-surgery for ERM. ERM can be a rare and undesirable effect of excessive gliosis induced by ILM flaps.

Methods
We examined 2 eyes with FTMH who have undergone surgery with inverted ILM flap technique. Serial OCT scans were done to evaluate the course of foveal hyperreflective lesions observed in these eyes. OCT features analyzed were architecture of inner retinal layers and restoration of outer retinal layers. We also retrospectively analyzed the postoperative OCTs of 38 consecutive eyes with FTMH that were operated by inverted ILM flap technique by same surgeon (DVS).

Results
Both eyes demonstrated multiple layers of ILM flap visible as hyperreflective structures over fovea. On serial follow up, we observed excessive uncontrolled gliosis from these hyperreflective ILM flaps that resulted in ERM formation. Both patients reported worsening of Metamorphosia and decline in best corrected visual acuity (BCVA). Case 1 had to undergo a repeat surgery for removing ERM. We could also observe similar hyperreflective ILM flaps over fovea in 34 out of 38 eyes. The ILM flaps in all but the 2 eyes described above were stable and did not show progression or gliosis at final follow up period not less than six months.

Conclusions
We report excessive uncontrolled gliosis as a rare complication of multilayered inverted ILM flap technique for FTMH that resulted in ERM formation and adversely affected visual outcome following surgery.

Financial Disclosure
NO FINANCIAL DISCLOSURE
Assessment of retinal function and structure in patients after scleral buckling surgery for macula on rhegmatogenous retinal detachment

Purpose
To compare the retinal sensitivity, vessel density (VD) and thickness of the inner retinal layers (IRL) between normal eyes and eyes after scleral buckling surgery for rhegmatogenous retinal detachment.

Setting/Venue
Department of Ophthalmology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Poland, Oftalmika Eye Hospital in Bydgoszcz, Poland

Methods
We enrolled to a cross-sectional study 21 patients that underwent in one eye scleral buckling surgery with episcleral implant due to macula-on rhegmatogenous retinal detachment. All participants were examined bilaterally at least 6 months after the operation using optical coherence tomography angiography (OCT-A) to assess VD and Spectral domain OCT (Sd-OCT) to assess thickness of IRL. Retinal sensitivity was tested with microperimetry (MP). A direct comparison of the retinal sensitivity, VD and IRL thickness between the operated eye and the fellow normal eye was received by normalizing the obtained values as percentage loss.

Results
The intereye comparison showed that the most significant changes after scleral buckling surgery were observed in OCTA in the radial peripapillary capillaries VD (13.9%) then in the deep and superficial vascular plexus (11.5%). It was observed difference in the retinal ganglion cell complex thickness (8.6%) in Sd-OCT, as well as decreased retinal sensitivity (7.6%) in MP. The percentage reduction in relation to the fellow eye was statistically significant for all tested parameters.

Conclusions
After the scleral buckling surgery for macula on rhegmatogenous retinal detachment adverse functional and structural changes in the macula are observed in comparison to the fellow eye. The disturbances in retinal microcirculation are more advanced than in retinal sensitivity, which may indicate the vascular pathomechanism of functional dysfunction.

Financial Disclosure
Authors do not have any financial relations to disclose.
### Title
Silicone oil-related complications as intraocular tamponade: A systemic review and meta-analysis.

### Purpose
Silicone oil (SO) still represents the main choice for long-term intraocular tamponade in complicated vitreoretinal surgery. This review compared the complications associated with the use of SO and other vitreous substitutes after pars plana vitrectomy in patients with different underlying diseases.

### Setting/Venue
1. Department of Ophthalmology, University Clinical Hospital of Valladolid, Valladolid, Spain
2. Institute of Applied Ophthalmobiology (IOBA), University of Valladolid, Valladolid, Spain
3. Faculty of Medicine. University of Valladolid, Valladolid, Spain
4. Department of Statistics. Faculty of Medicine. University of Salamanca. Salamanca Biomedical Research Institute (IBSAL), Salamanca, Spain.
5. Cooperative Health Network for Research in Ophthalmology (Oftared), Carlos III National Institute of Health, ISCIII, Madrid, Spain

### Methods
This meta-analysis was conducted in accordance with the PRISMA guidelines. We retrieved retrospective case-control studies and randomized clinical trials (RCTs) evaluating the risk of SO published between 1994-2020, conducting a computer-based search of the following databases: PubMed, Web of Science, Scopus, and Embase. The primary outcome was the rate of complications such as intraocular hypertension, retinal re-detachment, unexpected vision loss, or hypotony. The secondary outcome was to compare the rate of adverse events of different SO viscosities, including particularly emulsification.

### Results
Forty-two articles were included. There were significant differences in intraocular hypertension (P=0.0002, OR=1.66; 95% CI=1.27-2.18) and the rate of retinal re-detachment (P<0.0009, OR=0.65; 95% CI=0.50-0.64) between SO and other agents, including placebo. However, there were no differences in other complication rates. SO-emulsification rate is non-significantly higher in low than high SO viscosity and results from other complications were comparable in both groups.

### Conclusions
The high quality of most of the studies included in this study is noteworthy, which provides some certainty to the conclusions. Among them, the high variability of the residence time of the SO. The fact that ocular hypertension and not hypotension are related to SO use. That a clear relationship is not found for the so-called unexplained vision loss, which affects a significant percentage of eyes. That the cases of re-detachment are less if SO is used and that surprisingly there does not seem to be a relationship in the percentage of emulsification between the low and high viscosity silicones. All these data warrant more standardized prospective studies.

### Financial Disclosure
The author CAI receives funding from AJL Ophthalmic S.A. The authors JCP and CAI are members of the ISO Technical Committee involved in ISO 16672:2020 “Ophthalmic Implants – Ocular endotamponades”.

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Presenter

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Purpose

In previous studies, we proved that preliminary YAG-laser retinotomy of the horseshoe tear area with vitreoretinal adhesion (VRA) significantly increases the efficacy of pneumatic retinopexy (PnR) in the treatment of rhegmatogenous retinal detachment. The aim of the study is to evaluate the single operation success rate (primary anatomical success) and functional outcomes of radial scleral buckling (SB) versus pneumatic retinopexy with preliminary YAG-laser retinotomy.

Setting/Venue

S. Fyodorov Eye Microsurgery Federal State Institution, 59а, Beskoudnikovsky blvd, Moscow, 127486, Russian Federation.

Methods

The current study was a prospective randomized clinical trial. 84 eyes from 84 patients with macula-on RRD were included in this study. The patients were randomly allocated into a treatment group (43 patients who undergo PnR with preliminary retinotomy) and control group (41 patients who undergo SB). All patients of the treatment group underwent wide-field optical coherence tomography (Spectralis HRA+OCT; Heidelberg Engineering Inc., Germany) to determine the length and localization of VRA. The obtained data were used to perform YAG-laser retinotomy (Ultra Q Reflex; Ellex Inc., Australia). After YAG-laser retinotomy (on the same day), 12% C3F8 was injected. The final step of surgical treatment was laser photocoagulation (LPC) around the peripheral retinal hole after retinal attachment (2-3 days after pneumatic retinopexy). The follow-up was 3, 6, 12, 18, 24 month after treatment. We compared uncorrected (UCVA) and best corrected (BCVA) visual acuity, intraocular pressure (IOP), corneal astigmatism, the spherical component of the refraction and axis.

Results

The single operation success rate in the control group was 95% and 93% in the treatment group. Two years after treatment the stable anatomical result in the control group was 85 % and 86% in the treatment group. Comparative analysis of functional outcomes revealed the absence of statistically significant changes after surgery in patients undergoing pneumatic retinopexy with preliminary YAG-laser retinotomy and in patients after SB - statistically significant changes in UCVA, cylindrical and spherical components of refraction.

Conclusions

Preliminary YAG-laser retinotomy in the horseshoe tear area in patients with macula-on RRD allows to relieve vitreoretinal traction and increase anatomical efficacy of treatment. Combined laser surgical treatment (YAG-laser retinotomy + PnR + LPC) showed the same single operation success rate and significantly higher functional outcomes compared to SB.

Financial Disclosure

no
Title
Intraocular Pressure Compensation Performance for 25 Gauge Dual-Cutting and Single-Cutting Beveled Vitrectomy Probes Comparison

Purpose
To understand intraocular pressure (IOP) compensation performance for 25 Gauge (Ga) dual-cutting, 20K cuts per minute (cpm) beveled vitrectomy probes under different system settings; to compare IOP compensation performance for 25 Ga dual-cutting, 20 K cpm beveled vitrectomy probes with previous generation 25 Ga single-cutting, 10 K cpm beveled vitrectomy probes.

Setting/Venue
Various laboratory bench tests

Methods
Both 25 Ga dual-cutting 20K cpm beveled and single-cutting 10K cpm beveled vitrectomy probes were driven by a dual-pneumatic vitrectomy system with IOP control to aspirate sterile irrigating solution in a hollow acrylic eye model. A digital transducer (OMEGA, PX409-001GUSBH) was connected to the bottom of eye model to detect IOP change during aspiration. Six samples were tested under core duty cycle and vacuums of 250 mmHg, 450 mmHg and 650 mmHg. Cut rate ranged from 2500 cpm to 10,000 cpm for 10K probes and 2500 cpm to 20,000 cpm for 20K probes. Both system IOP compensation enabled and disabled settings were used. The average IOP during aspiration was calculated for each test setting and statistical analyses were performed using Welch’s t-test with statistical significance level of p<0.05.

Results
Without IOP compensation, changing the cut rate did not generate a significant difference for 20K probes (p>0.05). IOP ranged from 21.80 ± 0.59 mmHg to 21.96 ± 0.60 mmHg for 250 mmHg, 13.93 ± 0.96 mmHg to 14.32 ± 1.11 mmHg for 450 mmHg and 7.19 ± 1.36 mmHg to 7.47 ± 0.98 mmHg for 650 mmHg. However, IOP level for 10K probes was statistically different when the cut rate changed. IOP ranged from 25.07 ± 0.26 mmHg to 27.63 ± 0.30 mmHg for 250 mmHg, 19.86 ± 0.29 mmHg to 24.14 ± 0.53 mmHg for 450 mmHg, and 14.85 ± 0.41 mmHg to 17.81 ± 0.49 mmHg for 650 mmHg. When IOP control was enabled, IOP for 20K probes and 10K probes were not significantly influenced by cut rate changes. 20K probes’ IOP at maximum cut rate significantly increased to 32.32 ± 1.07 mmHg for 250 mmHg, 33.25 ± 1.55 mmHg for 450 mmHg and 37.12 ± 4.04 mmHg for 650 mmHg compared with result without IOP compensation (p<0.05). With IOP compensation, IOP of 10K probes was similar to that of 20K probes.

Conclusions
25 Ga dual-cutting 20K cpm vitrectomy probes have a more constant IOP when cut rate changes without IOP control compared to the previous generation single-cutting 10K cpm vitrectomy probes. Using IOP compensation can help surgeons to keep the eye at stabilized IOP ranges during aspiration of 25 Ga dual-cutting 20K cpm vitrectomy probes and maintain the efficiency of aspiration.

Financial Disclosure
The study is funded by Alcon Research. Ying Zhu, Val Kolesnitchenko and Vara Wuyyuru are employees of Alcon.
### Title
Rhegmatogenous retinal detachment in choroidal melanoma

### Purpose
To ascertain demographic, clinical features, prognostic factors, safety, rate of success of surgery and visual outcomes in patients with rhegmatogenous retinal detachment (RD) and choroidal melanoma (CM)

### Setting/Venue
Moorfields Eye Hospital NHS Foundation Trust, London, UK

### Methods
A retrospective, observational case-series of 20 patients with rhegmatogenous retinal detachment or combined tractional-rhegmatogenous retinal detachment in patients with choroidal melanoma over a period of 20 years (2002-2020)

### Results
There were 18 patients of age (mean+SD) 61.3 (13.9) years included in the final analysis. CM location was mid-periphery in 10 eyes and posterior pole in 8 eyes (mean tumour elevation 4.0 (1.7) mm; largest diameter 11.0 (2.4) mm. In 14 eyes the RD was rhegmatogenous and in 4 eyes combined rhegmatogenous/tractional. The timing of the RD occurred after the CM treatment in 14 eyes at mean interval of 44.2 (58.3) months; concurrent with the CM in 2 eyes, found during RD surgery, and in 1 eye suspicious melanocytic lesion before surgery was later confirmed as CM. 2 eyes had previous tumour biopsy for diagnosis or cytogenetic testing. Other features were macula-on RD in 6 eyes, PVD in 12 eyes and PVR in 6 eyes (100% PVR-C). RD repair was by vitrectomy in 15 eyes, and 1 each of barrier laser, scleral buckle and observation. Silicone oil was used in 8 eyes and gas in 7 eyes. LogMAR BCVA at presentation was 0.6 and final BCVA was 1.5 (P=0.003). Final retinal status was retina attached in 14 eyes (9 under oil) and detached in 4 eyes (3 under oil and 1 no surgery). No intraocular or extraocular tumour dissemination occurred

### Conclusions
Retinal detachment in patients with choroidal melanoma is uncommon but requires multidisciplinary management. Anatomical results are favourable but visual outcomes are poor due to a combination of factors related with melanoma treatment as well as retinal detachment. Vitrectomy as a surgical intervention for RD appears to be safe in terms tumour dissemination.

### Financial Disclosure
N/A
Baseline visual acuity as the main predictor of functional success after macular hole surgery

**Purpose**
Idiopathic macular hole (MH) is a disease from the vitreoretinal interface whose treatment is surgical and requires pars plana vitrectomy (PPV). This study aims to evaluate which clinical factors may be predictors of anatomical and functional success after PPV in patients with idiopathic MH.

**Setting/Venue**
Department of Ophthalmology, Hospital de Braga, Braga, Portugal.

**Methods**
This retrospective study included patients aged ≥ 45 years with idiopathic MH submitted to primary PPV in a tertiary Portuguese ophthalmology department. The minimum postoperative follow-up time was 6 months. The main outcomes were the anatomical success defined by the complete closure of MH and the functional success defined by the postoperative best-corrected visual acuity (BCVA). The parameters evaluated included age, gender, preoperative BCVA, MH size, time until surgery, surgical technique, presence of epiretinal membrane (ERM), or presence of posterior hyaloid attachment.

**Results**
A total of 67 eyes of 67 patients were included. The mean time until surgery was 88.0 ± 118.0 days. The surgical technique employed was internal limiting membrane peeling in 22 (32.8%) eyes, inverted flap in 37 (55.2%) eyes and internal limiting membrane transplant in 8 (11.9%) eyes. Preoperative BCVA was 1,00 ± 0,60 logMAR and postoperative BCVA was 0,60 ± 0,60 logMAR (p<0,001). Anatomical success was achieved in 71.4% patients. None of the variables – age (p=0,15), gender (p=0,93), preoperative BCVA (p=0,24), MH size (p=0,13), time until surgery (p=0,44), surgical technique (p=0,63), concomitant ERM (p=0,77), or posterior hyaloid attachment (p=0,25) – were predictors of anatomical success. The preoperative BCVA was the only predictive factor for postoperative BCVA (p<0,001). None of the variables – age (p=0,15), gender (p=0,41), MH size (p=0,25), time until surgery (p=0,28), surgical technique (p=0,07), concomitant ERM (p=0,19), or posterior hyaloid attachment (p=0,08) – were predictors of functional success.

**Conclusions**
PPV is anatomically and functionally efficient for the treatment of MH leading to structural and functional recovery of the retina. The baseline BCVA was found to be the main predictive factor of functional success in patients with MH submitted to PPV.

**Financial Disclosure**
This research received no financial support. The authors declare no financial, institutional nor commercial interests related to the research.
Demographic And Clinical Characteristics of Recurrent Rhegmatogenous Retinal Detachment Cases Treated With Retinectomy

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Purpose
To report the demographic and clinical characteristics of recurrent rhegmatogenous retinal detachment cases treated with retinectomy.

Setting/Venue
Vitreoretinal Surgery Unit, Ophthalmology Department, Marmara University Pendik Training and Research Hospital, Istanbul, Turkey.

Methods
This retrospective, noncomparative, interventional case series included 15 eyes of 15 patients that had undergone retinectomy for recurrent rhegmatogenous retinal detachment. We assessed demographic and clinical features, including age, sex, follow up time, best-corrected visual acuity (BCVA, logMAR), the time between symptoms and the surgery, macula status (on and off), type of first surgery, number of surgeries before retinectomy, proliferative vitreoretinopathy (PVR) grade, the operative technique (including relaxing retinectomy, intraocular tamponade, and laser photocoagulation), silicone oil tamponade duration, retinal status with silicone oil tamponade, the period between silicone oil removal, and recurrent detachment.

Results
Of the 15 patients included (74% male and 26% female), the mean±SD age was 56.5±8.7 years (range, 40–75). The mean follow-up time was 16.7±10.4 months (range 6–48), and the mean preoperative BCVA was 1.64±0.8 logMAR. The time between symptoms and the first surgery was 18.6±20.3 days (range, 1–103). The PVR grades of the cases were PVR-A in two (13.3%), PVR-B in six (40.0%), and PVR-C in seven (46.7%) patients. The macular status of the patients was macula-on in four (26.7%) and macula-off in eleven (73.3%) patients. Five patients (33.3%) received a 360-degree laser retinopexy in the first surgery. Five patients (33.3%) had recurrent detachment under silicon oil tamponade, while the remaining ten patients (66.7%) had recurrent detachment after silicone oil removal. The time between silicone oil removal and detachment recurrence was 95.1±99.4 days (range, 21–330). The mean operation count before retinectomy was 1.53±1.1 (range, 1–5). All patients underwent a minimum 100-degree retinectomy at the last surgery, and the retina remained attached with silicone oil tamponade.

Conclusions
Recurrent detachments can also be seen under silicone oil tamponade. Retinectomy may be effective in achieving anatomical success in recurrent detachments.
Phakic versus pseudophakic primary rhegmatogenous retinal detachments: phenotype and outcomes.

**Purpose**
To compare phakic and pseudophakic primary rhegmatogenous retinal detachments (RD) and, within phakic RD, eyes with and without cataract, in terms of clinical features and anatomical and functional outcomes.

**Setting/Venue**
Online database of prospectively collected data.

**Methods**
We performed a retrospective comparative clinical study. The data for this analysis were extracted from the Britain & Eire Association of Vitreoretinal Surgeons (BEAVRS) RD audit database in May 2018, including patients aged ≥ 50 years who had undergone RD repair of any type (i.e. vitrectomy, buckling, pneumatic retinopexy or combinations thereof) from March 2011 to March 2018. The data included baseline demographic and clinical features, surgical details, anatomical and functional outcomes. Univariate analysis was performed to compare pseudophakic with phakic RD, and phakic RD with and without cataract. Age and gender dependency of variables was analysed and the association of preoperative variables with final visual acuity was assessed using multivariate analysis. The main outcomes measured were preoperative features, intraoperative management, postoperative outcomes, association of preoperative features with postoperative outcomes.

**Results**
Out of a total of 4231 eyes, 1332 were pseudophakic and 3019 phakic, amongst which 310 were phakic with cataract. Pseudophakic RD were found to exhibit significant differences compared with phakic RD, including older age, higher prevalence of male gender, foveal detachment, grade C proliferative vitreoretinopathy (PVR), inferior retinal breaks, inferior retinal involvement and greater RD extent. Although pseudophakic RD showed more advanced clinical features, pseudophakia was a positive factor for visual outcome. Contralateral RD was more frequent in pseudophakic than phakic RD eyes (p<0.0001). Within phakic RD, phakic RD with cataract showed multiple similarities with pseudophakic RD, including greater age, more frequent foveal detachment, PVR and greater RD extent.

**Conclusions**
Pseudophakic RD showed significant differences compared to phakic RD in terms of presenting features and RD distribution, with greater occurrence of inferior retinal breaks and inferior retinal involvement in particular. Phakic RD with cataract shared several features in common with pseudophakic RD. The greater age of pseudophakic RD and phakic RD with cataract could contribute to the these finding. Despite having a more severe presentation, and clinical features traditionally associated with worse anatomical and functional outcomes, the success rate of pseudophakic RD repair is high and visual outcomes generally good.

**Financial Disclosure**
None
Purpose
To determine the demographic, etiological, and clinical features of surgically treated pediatric traumatic macular holes and to evaluate the surgical results.

Setting/Venue
Beyoglu Eye Training and Research Hospital, University of Health Sciences, Istanbul, Turkey.

Methods
All patients under the age of 18 who were diagnosed with traumatic macular hole (TMH) between January 2015 and February 2021 in our retina department were evaluated. Retrospectively, gender, age at presentation, etiology, initial examination findings, and optical coherence tomography (OCT) findings were evaluated. In addition, best-corrected visual acuity (BCVA) and OCT findings at the last control were recorded. BCVA was evaluated using the Snellen visual chart. All patients with TMH underwent surgical repair with a three-port vitrectomy. After induction of posterior vitreous detachment vitrectomy with internal limiting membrane (ILM) peeling and gas tamponade.

Results
Fifteen eyes of 15 patients were included in this study. The mean follow-up time was 20.8 ± 15.0 months. The mean age was 12.8 ± 3.1 (7-17) years, and all of the patients were men. 53.3% of the cases were right eye while 46.7% left eye. Etiology was blunt trauma in all eyes. The narrowest hole diameter was 590 ± 264μm at the beginning. The initial BCVA was 0.12 ± 0.15. In the OCT images, 66.6% of the patients had a pseudocyst in addition to the macular hole. Pars plana vitrectomy was performed in all patients and the internal limiting membrane was peeled off. All had achieved hole closure. Final BCVA was 0.32 ± 0.23 and was found to be increased after surgery and was statistically significant (p = 0.01). However, of the 4 patients who underwent surgery and could not provide visual enhancement despite anatomically closing the hole, 3 had accompanying retinal pathologies such as choroidal rupture.

Conclusions
Spontaneous closure may be observed in cases with small hole diameter in some traumatic pediatric macular holes. In cases that do not close spontaneously, pars plana vitrectomy is a safe method for treatment TMH. However, the increase of visual acuity remains limited in the presence of retinal pathologies accompanying secondary to trauma.

Financial Disclosure
none
Amniotic membrane graft to promote macular hole closure

**Purpose**
To study the effectiveness of the human amniotic membrane plug for the treatment of persistent macular hole (MH) in patients that already underwent pars plana vitrectomy with internal limiting membrane peeling and gas endotamponade. (Sin posicionamiento)

**Setting/Venue**
Macular hole patients who did not respond to a pars plana vitrectomy with internal limiting membrane peeling were chosen to undergo a novel intervention to promote macular hole closure. The patient sample was collected from the Consorci Sanitari de Terrassa (Terrassa, Spain).

**Methods**
Four patients with MH (two females and two males) underwent pars plana vitrectomy and internal limiting membrane peeling. After surgery the closure of the MH was not achieved. Given these results, a 25-gauge pars plana vitrectomy was performed. A cryopreserved human amniotic membrane plug implant was placed in the MH before air-fluid exchange, with the stromal layer facing down in order to minimize the risk of graft dislocation. C3F8 was used as endotamponade gas without positioning after surgery.

**Results**
The closure of the MH was observed in all patients four weeks after the surgery confirmed by optical coherent tomography. No human amniotic membrane plug dislocation was observed at the end of the follow-up. Best-corrected visual acuity remained unchanged in two patients during the 12-month follow-up. The third patient improved from 2/370 to 20/240 six months after surgery, and the fourth patient improved from 20/63 to 20/32 four months after surgery. Interestingly, a progressive restructuring of the outer retina layers was observed in the fourth patient. No adverse events, intra-operative or postoperative complications were reported.

**Conclusions**
The amniotic membrane plug has been used recently to promote the closure of MH refractory to a first surgery or in high myopic patients, achieving good anatomical and functional results. Being considered as a safe and easily reproducible surgical technique it can be considered as an option for those refractory cases in which pars plana vitrectomy with Inner Limiting Membrane (ILM) peeling has not been successful.

**Financial Disclosure**
The authors declare lack of funding sources.
Title
Spontaneous closure of an idiopathic full-thickness macular hole: a literature review

Purpose
Full-thickness macular hole (FTMH) is defined as an opening through all of the layers of the retina at the fovea. These holes are mostly idiopathic, also known as primary. Idiopathic FTMH may close spontaneously, prompting discussion regarding observation without surgery. FTMH closure incidence, factors influencing closure, closure mechanism, and post-closure outcomes are controversial. Optical coherence tomography (OCT) has made the classification, diagnosis, and observation of FTMH more precise. The purpose of this study was to review the literature regarding incidence, clinical characteristics, outcomes, and mechanisms of spontaneous closure of idiopathic FTMH to consolidate our understanding in the context of modern classification.

Setting/Venue
Literature review.

Methods
Literature on patients with spontaneous idiopathic FTMH closure was reviewed via Ovid MEDLINE, EMBASE, and PubMed until July 16, 2020. Only English-language articles were included. The search strategy was the following: “idiopathic” and “macular hole” and “spontaneous”. Twenty-seven out of 66 identified articles were included. Studies were included if they reported one or more cases of spontaneous idiopathic FTMH closure with detailed description of clinical characteristics including patient age, sex, hole size, and hole classification. The majority of studies used OCT to characterize their cases. Exclusion criteria were history of ocular surgery in affected eye, or any intervention in affected eye at any time from hole diagnosis to resolution.

Results
Sixty-eight eyes of 66 patients had spontaneous closure. Patients were 62.7% female and average age was 67.5±8.35 years old (range 26-81). Best-corrected visual acuity (BCVA) improved by -0.37±0.27 (range -1.3 - 0.12) after closure: initial BCVA was 0.59±0.33 logMAR (range 0 - 1.78) and post-closure BCVA was 0.22±0.20 logMAR (range -0.12 - 1). Final BCVA, available for 18 eyes, was 0.11 ± 0.11 logMAR (range -0.12 - 0.3). Average hole diameter was 176.8±81.8 μm (range 60 - 350). Most holes were Stage 2 according to Gass and OCT-modified Gass or small (≤ 250 μm) according to International Vitreomacular Traction Study Group (IVTS) staging. The predominant classification system in recent literature is IVTS staging. Average OCT-observed closure time was 4.5±4.9 months (range 3 weeks - 24 months).

Conclusions
Based on our review, we can define important characteristics that clinicians may use in daily practice. No demographic subgroup is more likely to have spontaneous closure than others. Closure is associated with favourable visual outcomes with early recovery of the ellipsoid zone line being the most important factor. There is evidence supporting various proposed mechanisms of spontaneous closure, but retinal bridge formation via glial cells appears to be most critical based on OCT-based observations. Spontaneous closure rate for all holes, regardless of stage or size, is 2.9% based on two OCT-based retrospective case series with a sample of 652 eyes and 12.3% based on two OCT-based randomized controlled trials with a sample of 73 eyes, which are more reliable than studies without OCT observation. Our review is the first to comprehensively assess Gass and IVTS staging via in-depth analysis of hole sub-classifications. Holes in earlier stages according to Gass staging are more likely to close. Small holes (≤ 250μm) have higher closure rates (22.2%) than medium (250-≤400μm) (13.3%) and large (>400μm) (0%) holes according to two OCT-based prospective studies with a combined sample of 36 small, 30 medium, and 7 large holes. This highlights the utility of the IVTS system, which may provide more insight for practitioners into whether FTMH can be safely observed before considering elective surgery. However, this determination is hindered by the lack of OCT-based studies, which is a limitation of this review.

Financial Disclosure
None
Comparison of intravitreal C3F8 and SF6 gas injections in the treatment of vitreomacular traction syndrome

Ahmet Altun, Turkey

**Purpose**
To compare the treatment efficacy of intravitreal C3F8 and SF6 gas injections in eyes with vitreomacular traction syndrome (VMT) syndrome.

**Setting/Venue**
In this prospective and comparative study, eyes of patients with symptomatic and idiopathic VMT syndrome were included and randomly divided into two groups.

**Methods**
C3F8 and SF6 gases were injected into the eyes in Group 1 and Group 2, respectively. VMT grade and macular anatomy were followed by optical coherence tomography for 2 months. Characteristics of the groups and complete ophthalmologic examination findings were investigated and compared.

**Results**
A total of 42 eyes of 42 patients were included in the study. There were 21 eyes of 21 patients in both groups. There was no statistically significant difference between the groups in terms of age, gender and VMT grade before injection. During the two-month follow-up period, VMT released in 11 and 6 eyes in Group 1 and Group 2, respectively.

**Conclusions**
Intravitreal gas injection may be a minimally invasive method in the treatment of idiopathic VMT syndrome without epiretinal membrane. The more successful C3F8 gas may be due to its longer stay in the vitreous cavity.

**Financial Disclosure**
The authors declare that they have no financial or non-financial relationship or commercial interest with any of the materials discussed in this manuscript.
Anatomical and Functional Outcomes of Indirect Ophthalmoscopy versus Chandelier Illumination in Scleral Buckling Surgery

Purpose
To investigate the anatomical and functional outcomes of indirect ophthalmoscopy versus chandelier illumination in scleral buckling surgery due to rhegmatogenous retinal detachment (RRD).

Setting/Venue
University of Health Sciences, Ankara Ulucanlar Eye Education and Research Hospital.

Methods
A retrospective observational includes 50 RRD patients who underwent scleral buckling surgery. Conventional surgery with indirect ophthalmoscopy was performed for 30 patients (Group 1) and retinal examination under chandelier illumination was performed for 20 patients (Group 2) during the conventional surgery. The anatomical and functional outcomes of the two groups were compared.

Results
The demographic characteristics of the groups were similar (p > 0.050). The preoperative clinical characteristics of the groups including preoperative time, visual acuity, intraocular pressure, presence of associated risk factors (complicated cataract surgery, trauma, pathological myopia), extensity of attached retina, presence of macular involvement, and retinal tear number and localization, were also similar (p > 0.05). There was no difference between the groups in terms of postoperative visual acuity, intraocular pressure, the rate of re-operation, and the time of re-operation (p > 0.05). On the other hand, a total of post-operative complications including epiretinal membrane, glaucoma, proliferative vitreoretinopathy, foveal atrophy, gaze restriction, cystoid macular edema, and macular hole occurred more common in Group 1 (p = 0.001).

Conclusions
Despite postoperative visual acuity is similar, using chandelier illumination in addition to conventional scleral buckling surgery techniques has lowering effects on the postoperative complication rate.

Financial Disclosure
None
Purpose
To present long-term results of macular hole surgery without vitreous cavity tamponade with gas or another vitreous substitute in post-op period.

Setting/Venue
IRTG Eye Microsurgery Ekaterinburg Center, Ekaterinburg, Russia

Methods
Thirty-four eyes of 34 patients were operated on for full-thickness macular holes 100 to 932 (558.5 ± 50.9) microns in diameter without vitreous cavity tamponade. BCVA was 0.02 to 0.25 (0.11 ± 0.02). The operation included 3-port 25-27 G vitrectomy, separation of posterior hyaloid. ILM was stained and removed, BSS – air exchange was performed, hole edges were passively pulled towards the center with extrusion cannula and air supply into the vitreous cavity under a pressure of 20-25 mm Hg without mechanical closure. Immediately 0.05 ml of platelet rich plasma (PRP) was applied to macular hole zone. In 2 minutes, fibrin film was formed at the place of application which was pressed to the retina by injection of 0.3 ml of PFCL into the vitreous cavity. PFCL exposure was 5 minutes, then PFCL was passively aspirated with exchange for air. The operation was finished by air exchange for BSS. High specific weight of PFCL facilitated tight adhesion of fibrin film to the retina; due to this the film was attached to the retina during PFCL exchange for air and then for BSS. Follow-up period made from 1 to 20 months (7.9 ± 0.8).

Results
No intraoperative and postoperative complications were seen. In the result of surgery complete closure of the macular hole and anatomical restoration of the macula was achieved in 32 of 34 cases (94.1%). Mean age of the patients was 69±1.2 years (range, 57-84). Mean parameters were: minimum diameter 558.5 ± 50.9 µm (range, 100 – 932); base diameter 990 ± 57 µm (range, 599 – 1740 µm); fovea thickness 403 ± 28 µm (range, 300 – 520 µm); parafovea thickness 383±17 µm (range, 338 – 424 µm); macular volume 7.65 ± 0.22 mm³ (range, 7.12 – 8.36 mm³). Thirty patients (88.3%) were phakic. Two eyes (5.8%) had Stage 1 macular holes, one eye (2.9%) had Stage 2 macular hole, five eyes (14.7%) had Stage 3 macular holes, twenty-six eyes (76.4%) had Stage 4 macular holes (Optovue RTVue). First day after surgery IOP was 7 to 15 mm Hg (11 ± 0.46). Postoperative IOP (one year after surgery) was 10 to 20 mm Hg (15 ± 0.78). First day after surgery BCVA was 0.08 to 0.35 (0.2 ± 0.02). Postoperative BCVA (one year after surgery) was 0.3 to 0.7 (0.5±0.05). None of the patients needed cataract surgery at 12-month follow-up (30 patients – 88.3%). Three patients (8.8%) who could get home only by plane flew away at the first day after surgery. A recurrence in two cases was associated with a violation of operation technology when a partial mechanical displacement of the fibrin film with a cannula during PFCL exchange for air occurred.

Conclusions
The suggested method of macular hole surgery without postoperative tamponade of the vitreous cavity with gas or another vitreous substitute may be used in routine clinical practice: the patients get rather high visual acuity at the first day post-op (which is especially important for monocular persons) without face down positioning, reduced risk of cataract and increased IOP, and possibility of air flights and height climbing in the early post-op period.
**Title**
Comparison of the Intraocular Pressure Control Performance with 27 Gauge Dual-Cutting and Previous Generation Single-Cutting Beveled Vitrectomy Probes

**Purpose**
To evaluate intraocular pressure (IOP) control performance of 27 Gauge (Ga) dual-cutting, 20K cuts per minute (cpm) beveled vitrectomy probes under different system settings; to compare IOP control performance for 27 Ga dual-cutting, 20K cpm beveled vitrectomy probes with previous generation 27 Ga single-cutting, 10K cpm beveled vitrectomy probes

**Setting/Venue**
Various laboratory bench tests

**Methods**
27 Ga dual-cutting 20K cpm beveled and single-cutting 10K cpm beveled vitrectomy probes were driven by dual-pneumatic vitrectomy system with IOP control to aspirate sterile irrigating solution in a hollow acrylic eye model. A digital transducer (OMEGA, PX409-001GUSBH) was connected to the bottom of eye model to detect IOP change during aspiration. Six samples were tested under core duty cycle and vacuums of 250 mmHg, 450 mmHg and 650 mmHg. Cut rates ranged from 2,500 cpm to 10,000 cpm for 10K probes and from 2,500 cpm to 20,000 cpm for 20K vitrectors. Both system IOP compensation enabled and disabled settings were used. Average IOP during aspiration was calculated for each test setting and statistical analyses were performed using Welch’s t-test with statistical significance level of p<0.05

**Results**
Without IOP compensation, IOP for 27 Ga 20K probes was similar for all cut rates. IOP ranged from 22.71 ± 0.30 mmHg to 22.81 ± 0.37 mmHg for 250 mmHg, 15.46 ± 0.33 mmHg to 15.62 ± 0.33 mmHg for 450 mmHg and 7.93 ± 0.46 mmHg to 8.33 ± 0.32 mmHg for 650 mmHg. However, IOP for 10K probes was significantly different when cut rates changed (p<0.05). IOP ranged from 25.47 ± 0.38 mmHg to 27.46 ± 0.43 mmHg for 250 mmHg, 20.51 ± 0.54 mmHg to 24.32 ± 0.73 mmHg for 450 mmHg, and 16.14 ± 0.77 mmHg to 19.30 ± 0.77 mmHg for 650 mmHg. When IOP control was enabled, there was no significant difference of IOP when using different vacuum and cut rate for 20K probes and 10K probes (p>0.05). IOP for 20K probes at maximum cut rate significantly increased to 29.24 ± 0.75 mmHg for 250 mmHg, 28.43 ± 1.71 mmHg for 450 mmHg and 27.42 ± 2.64 mmHg for 650 mmHg as compared with results without IOP compensation (p<0.05). IOP of 10K probes was similar to that of 20K probes with IOP compensation.

**Conclusions**
27 Ga dual-cutting 20K cpm vitrectomy probes provide a more constant IOP level compared to the previous generation single-cutting 10K cpm vitrectors under different cut rates without IOP compensation. Using IOP compensation and 27 Ga dual-cutting 20K cpm vitrectomy probes can help surgeons keep the eye at stabilized IOP ranges and have an efficient aspiration.

**Financial Disclosure**
This is Alcon funded study. Ying Zhu, Val Kolesnitchenko and Vara Wuyyuru are employees of Alcon
### Title
Comparative study of success of various techniques of ILM peel in management of RRD with PVR with concomitant macular hole.

### Purpose
To assess the anatomical & functional success in patients with rhegmatogenous retinal detachment (RRD) with Proliferative Vitreoretinopathy (PVR) \( \geq C1 \) with coexisting macular holes (MH) using different management strategies.

### Setting/Venue
Sarakshi Netralaya, Nagpur, Maharashtra, India

### Methods
It is a prospective, non-randomised, interventional study in 23 eyes of 23 patients (Male : Female = 15:8) diagnosed with RRD with PVR \( \geq C1 \) with MH. Patients were divided into 3 groups according to the technique. Group 1: Pars Plana Vitrectomy (PPV) without (Internal Limiting Membrane) ILM peel, Group 2: PPV with ILM peel & Group 3: PPV with inverted ILM peel technique.

### Results
The closure of MH was confirmed on SD-OCT. Of the total 23 eyes, 19 patients had attached retina with closed macular hole during a follow up period of 6 months. Out of 4 cases of recurrent RD, 3 patients belonged to no peel group & 1 to ILM peel group. In no peel group, 2 patients had recurrence with re-opening of macular hole, & out of these 2 cases, 1 patient had additional break in periphery. While, 2 other cases, each from No peel & ILM peel group had recurrence due to PVR changes in periphery. Visual acuity (VA) improvement to LogMar

### Conclusions
The results suggest that ILM flap technique without encirclage band can be effectively applied to the treatment of MH with RD with more severe PVR changes and that the hole closure results in improved postoperative BCVA.

### Financial Disclosure
No financial relations
Digital Filters Improve Visualization of Important Retinal Landmarks During Heads Up Retinal Surgery

**Purpose**
Precise identification and subsequent delamination of pre-retinal membranes is a core skill required for almost every retinal surgery. It is also important to minimize toxicity of high concentrations dyes used to stain these membranes. Manipulation of the digital image in real time has the potential to both improve edge detection and decrease dye concentration.

**Setting/Venue**
Retrospective image analysis of different digital filters used during macular surgery in a private practice setting.

**Methods**
This is a retrospective review of images captured during retinal surgery for patients who underwent epiretinal membrane delamination. Still image captures during DAVS retinal surgery were taken with either standard constellation visualization filter, yellow thumbnail, green or blue enhancing filters, and the images to be compared were captured within 3 seconds of each other. The image pairs were converted to grey scale or CIELab Color Space for calculations of contrast and color difference, respectively. A linear sample taken perpendicular to edge of peeled and unpeeled tissue was analyzed for gray scale and color difference calculations.

**Results**
The blue enhancing digital filter effectively increased both the gray scale contrast by approximately 40% and the CIE color difference by 9, at the edge of peeled and unpeeled retina after staining with TissueBlue®. Both of these signals were highly significant, p < 0.05. Less of a signal difference was observed with the yellow thumbnail setting, NGENUITY Version 1.4, but a significant difference in CIE color difference is anticipated based on the trend and the relatively low number of eyes analyzed. The green enhancing digital filter effectively increased both the gray scale contrast by approximately 15% and the CIE color difference by 2, at the edge of peeled and unpeeled retina after staining with ICG. Both of these signals were highly significant, p < 0.05. Relatively dilute ICG 0.1% was used and the stain was applied for less than 30 seconds. Similar to that observed with TissueBlue®, the yellow thumbnail did show a trend for contrast and CIE color difference enhancement.

**Conclusions**
Digital filters significantly enhance edge detection of peeled and unpeeled retina by increasing both gray scale and CIE color difference. In addition, this enhanced signal permits lower exposure to ICG dye to achieve adequate visualization. These data show promise that digital visualization during retinal surgery will ultimately minimize dye exposure and trauma to the retina.

**Financial Disclosure**
Alcon Consultant and Grant Support AsclepiX Consultant Scanoptix Consultant ForwardVue Pharma Founder
Surgical treatment of large macular holes with bacterial collagenase and plated reach plasma

**Purpose**
To study the possibility of treating large macular hole (MH) with bacterial collagenase and plated reach plasma.

**Setting/Venue**
S.N. FEDOROV NMRC "MNTK "EYE MICROSURGERY"

**Methods**
25 patients with MH were examined and treated. Diameter of macular hole was from 400 to 850 µm. The BCVA before surgery ranged from 0.03 to 0.1. The result of treatment was evaluated by BCVA, OCT and microperimetry. The follow-up period was 12 months after surgical treatment. Surgical technique. 25G pars plana vitrectomy, fluid-to-air replacement, application of bacterial collagenase solution to the macula, application with platelet-rich blood plasma to the MH, final tamponade with gas at MH diameter from 400 µm to 650 µm or silicone at MH diameter more than 650.

**Results**
In all cases MH closure was achieved. Silicone was removed in 1 to 3 months. In 3 months after the operation, BCVA was 0.2 to 1.0. In all cases, anatomical repair of the macular profile was achieved. There was no decrease of retinal sensitivity according to microperimetry during 1, 3, 6 and 12 months after surgery. There was no retinal nerve fiber layers damage like DONFL in 1, 3, 6 and 12 months after surgery.

**Conclusions**
Our results demonstrate the possibility of surgical treatment of large macular with bacterial collagenase and plated reach plasma. Excluding the ILM peeling reduces the risk of iatrogenic damage to the retina, as well as the decrease of the vision quality associated with DONFL.

**Financial Disclosure**
no financial relationship
Title
Intravitreal Tissue Plasminogen Activator Injection for the Treatment of Proliferative Vitreoretinopathy in a Rabbit Model

Purpose
To evaluate the effect of intravitreal injection of tissue plasminogen activator (tPA) on proliferative vitreoretinopathy (PVR).

Setting/Venue
Felsenstein Medical Research Center, Tel Aviv University, Israel.

Methods
Experimental PVR was induced in the right eye of rabbits by intraocular injection of dispase (0.05 U/0.1 mL). Progression of PVR was followed by indirect ophthalmic examination. Six weeks after Dispase injection, animals were divided to receive intravitreal injection of either 25 µg/0.1 mL tPA or balanced salt solution (BSS). Animals were euthanized at 48 hours following tPA/BSS injection and eyes were enucleated for histological evaluation. Immunostaining for fibroblasts using Mouse Monoclonal anti Rabbit α-smooth muscle actin (αSMA) and staining for collagen using Sirius Red were performed.

Results
: Five PVR model eyes were injected with tPA and four with BSS. Following tPA injection, one eye had a reduction in PVR from grade 2 to 1, three eyes remained stable and in one eye the severity of PVR couldn't be assessed due to limited view. In the BSS group, PVR grade was unchanged in three eyes and couldn't be visualized in one eye. Staining of histological specimens with αSMA showed a reduced presence of fibroblasts in eyes injected with tPA compared with those injected with BSS. In addition, collagen type I and III, demonstrated by Sirius Red staining, was reduced in the tPA group in comparison to controls.

Conclusions
Our results suggest that intravitreally injected tPA may show an inhibitory effect on PVR progression. This experiment provides a scientific rationale for further exploration of the use of intravitreal tPA for the treatment of PVR in clinical trials.

Financial Disclosure
NONE
Title
Some aspects of early vitreous surgery with active retinopathy of prematurity

Purpose
The observed widespread increase in the number of premature infants at birth with ultra-low birth weight and their high survival rate contributes to an increase in severe cases of retinopathy of prematurity (ROP) requiring compulsory treatment [1,4]. Late detection, as well as untimely treatment of severe stages of active ROP do not allow to achieve regression of the disease, its further progression occurs [2,3,5]. Such cases require vitreoretinal surgery. Purpose is to estimate the effectiveness and safety of vitreoretinal surgery as the primary stage of the treatment of active ROP, as well as in cases of its progression after laser coagulation of the retina (LC).

Setting/Venue
Kaluga branch of the S. Fyodorov Eye Microsurgery Federal State Institution, Russia

Methods
138 children (198 eyes) with active ROP who were undergone vitreoretinal surgery were divided into 3 groups: 1-st group - 66 children (87 eyes) – an early primary vitrectomy was performed (gestational age at birth (GA) 25-29 weeks, post-conceptual age (PCA) by the time of vitrectomy 39-41 weeks); 2-nd group - 45 children (69 eyes) - an early vitrectomy with progression after LC no later than 2-3 weeks (GA 23-30 weeks, PCA by the time of LC 33-36 weeks, PCA by the time of vitrectomy 36-39 weeks); 3-rd group - 27 children (42 eyes) vitrectomy with progression after LC in the late 2-3 weeks (GA 24-29 weeks, PCA by the time of LC 33-36 weeks, PCA by the time of vitrectomy 44-46 weeks). A standard 3-port transscleral 27-G lens-sparing primary vitrectomy using a Constellation device (Alcon, USA) was undergone for patients of 1st and 2nd groups. During primary vitrectomy after complete removal of the fibrovascular tissue, retinal endolaser coagulation was performed along the pre-existing proliferation ridge and in the avascular zone of the retina. For patients of 3rd group: lens-sparing vitrectomy was undergone for 13 patients; lensvitrectomy for 19 patients; phacoaspiration without IOL and vitrectomy for 10 patients.

Results
For patients of 1st and 2nd groups, surgical intervention was completed with silicone tamponade at 7 cases, for patients of 3rd group - at 31 cases. At the postoperative period, the results of vitrectomy were estimated by the anatomical attachment of the retina: in 1st group - 92% (80 eyes), in 2nd group - 75% (52 eyes), in 3rd group - 41% (17 eyes). In 1st group, after 3 months: greater percentage of cases to complete retinal adhesion in 1st group. This facilitated to the correct formation of the vitreoretinal interface, the normalization of morphometric parameters, and the growth of blood vessels into the previously avascular retinal zone. In general, 1 year after surgical treatment, favorable anatomical results were achieved in 1st and 2nd groups. However, dystrophic changes of the retina and disruption of the course of the vascular arcades were more pronounced in 2nd group. Late vitrectomy at 3rd group is characterized by a high complication rate and failure in terms of anatomical attachment. Patients of 3rd group are the severest: high vascular activity, pronounced retinofibrosis, gross changes in the vitreous body, the initial significant area and height of retinal detachment lead to less anatomical success.

Conclusions
Laser treatment of the III active stage of ROP and aggressive posterior ROP is effective only if the LC is performed at timely implementation no later than 34-35 weeks of PCA. During the severe course of III active stage of ROP and aggressive posterior ROP with the presence of pronounced fibrovascular proliferation, when laser coagulation of the retina was not performed at the optimal time, the pathological process continues to progress with the development of advanced stages. This requires vitreoretinal surgery no later than 2-3 weeks from the beginning of disease progression after LC. Early vitrectomy performed for children with active stages of ROP, both primary and having progression after previously performed transpupillary LC (no later than 2-3 weeks), allows in one intervention to eliminate vitreoretinal traction, remove fibrovascular tissue, carry out dosed endolaser retinal coagulation. This creates conditions for the stabilization of the pathological process, the formation of the correct vitreoretinal interface and the development of visual functions.

Financial Disclosure
No
Intravitreal fluocinolone acetonide implant (FAc, 0.19 mg, ILUVIEN®) in the treatment of patients with recurrent cystoid macular edema after pars-plana vitrectomy: A case series

Mário Lima Fontes, Portugal

Purpose
Cystoid macular edema (CME) is a well-known postoperative macular complication of several ocular procedures, including pars-plana vitrectomy, and its pathogenesis after surgery is attributed to the breakdown of the blood–aqueous barrier due to an exaggerated inflammatory reaction and to the release of cytokines. Recurrent CME is difficult to treat, and many strategies have been employed with varying degrees of success. The purpose of this case series is to evaluate the effectiveness and safety of fluocinolone acetonide intravitreal implant (FAc, 0.2 μg/day; ILUVIEN®) in the treatment of refractory CME after successful pars-plana vitrectomy (PPV).

Setting/Venue
Retrospective observational case series, that evaluates the effectiveness and safety after fluocinolone acetonide implant in patients with recurrent CME that underwent PPV or PPV combined with phacoemulsification, at Centro Hospitalar Universitário São João, Porto, Portugal.

Methods
Retrospective case series with consecutive eyes of patients with recurrent cystoid macular edema after vitrectomy and treated with a single implant of fluocinolone acetonide. Mean follow up after FAc implant was 36.4 ± 17.6 months. Demographics, previous treatments, best-corrected visual acuity (BCVA, ETDRS letters), central macular thickness (CMT, μm), intraocular pressure (IOP, mmHg) and IOP lowering medication needed before FAc implant were recorded at baseline. Highest BCVA and IOP values and lowest CMT values registered throughout study were recorded as well as time to edema recurrence and the need of hypotensive drops. Total macular edema resolution was defined as CMT < 300μm or reduction > 20% and partial macular edema resolution was defined with a reduction >10%.

Results
Nine eyes from 9 patients with mean age of 68.7 ± 10.8 years were included. Eight patients were female, 4 underwent phacoemulsification simultaneously with PPV, while the remaining were already pseudophakic previously to PPV. Prior to FAc implant, all eyes received intravitreal short-action corticosteroids (triamcinolone and Ozurdex®), that led to macular edema resolution but with quick relapse 1 to 5 months later. At baseline, BCVA was 55.0 ± 10.6 letters, CMT was 514.9 ± 165.6 μm and IOP was 15.4 ± 2.4 mmHg with 4 eyes under IOP lowering medication. After FAc implant, all eyes achieved edema resolution (8 total and 1 partial resolution) with a peak gain of 17.2 letters and a maximum decrease of 208.2 μm in CMT. During follow-up (36.4 ± 16.6 months), 66.7% of the eyes kept their macula dry and 3 showed recurrence after 11, 14 and 18 months post-FAc implant, respectively. Maximum IOP registered was 17.0 ± 6.0 mmHg (9.0 ± 11.2 months after FAc implant). From the 4 eyes under hypotensive drops at baseline, the IOP lowering strategy was increased in 1 and maintained in the remaining during follow-up. Other 2 eyes started IOP-lowering medication, and 3 remained without need of IOP-lowering drops.

Conclusions
Intravitreal corticosteroid injections have shown to be an effective treatment option for recurrent CME after PPV. This case series showed that FAc implant not only maintained an anatomical dry macula but also provided visual improvement. These results demonstrate that FAc implant is an effective treatment option, and it reduces the need for repeated treatments. Significant IOP increase was observed in one third of the patients and it was effectively managed with topical treatment.

Financial Disclosure
None.
Title
Features of the natural history of lamellar macular holes with epiretinal proliferation.

Purpose
To establish the features of the course and the possibilities of the SLO in the diagnosis of lamellar macular holes with the presence of epiretinal proliferation.

Setting/Venue
The question of natural history of LMH (favorable or progressive) remains controversial to this day. It is relevant to study the role of epiretinal proliferation (EP) on the natural course of the disease, as well as the value of the method of scanning laser ophthalmoscopy (SLO) in the diagnosis of EP.

Methods
Clinical and instrumental monitoring was carried out in 48 patients with LMH in two groups: with the presence of EP (27 patients) and its absence (21 patients). The follow-up period was 15.9 ± 2.3 months. The dynamics of the best corrected visual acuity (BCVA), mean retinal sensitivity (MRS) of the retina in 2 and 4 degree zones, subjective complaints were assessed; according to OCT data - the main morphometric and morphostructural parameters of the retina. SLO was performed in 21 patients with LMH with the presence of EP.

Results
Patients with LMH and presence of EP had an initial lower BCVA, as well as according to OCT, disruption of the ellipsoid zone and the presence of a central foveal bump (37% and 22.2% of patients, respectively). During the follow-up, patients with EP showed an increase in subjective complaints, a statistically significant decrease in the retinal MRS in the 2-degree zone, and a decrease of the minimum retinal thickness. In all cases, the SLO made it possible to visualize the EP.

Conclusions
LMH with EP are characterized by an unfavorable course, which is confirmed by a decrease in functional parameters and a deterioration in anatomical parameters.

Financial Disclosure
No
**Title**
Surgical Management of Complex Retinal Detachment Associated with Retinal Capillary Hemangioblastoma in von Hippel-Lindau Disease

**Presenter**
Remzi Avci

**Co-Author 1**
Aysegul Mavi Yildiz

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Sami Yilmaz

**Purpose**
Retinal capillary hemangioblastoma (RCH) are rare benign tumours, usually associated with von Hippel-Lindau (VHL) disease. Various treatment options including; argon laser photocoagulation, cryotherapy, plaque radiotherapy and vitreoretinal surgery have been suggested for the management of RCH. However, no consensus exists regarding the ideal treatment method. The aim of our study was to assess results of vitreoretinal surgery with excision of retinal capillary hemangioblastomas in von Hippel-Lindau (VHL) disease.

**Setting/Venue**
Retrospective, interventional, case series

**Methods**
An electronic database search was performed. We identified 23 patients who underwent 23 G vitrectomy and tumor resection for retinal detachment (RD) associated with RCHs between January 2001 and January 2020. Primary outcome measures were anatomic success rate and final visual acuity (VA).

**Results**
The mean age was 32.04±12.08 (range 12-58) years and mean follow up was 20.7±12.68 (range 4-44) months. Of the patients, 30.4% (n=7/23) got unilateral onset and 69.5% (n=16/23), suffered bilaterally. Ten of the patients had multiple RCHs whereas 13 had solitary tumor. The size of the tumor ranged from 2 disc diameters (DD) to 5 DD. The location of the tumor was classed into 3 groups; preretinal (n=8/23), intraretinal (n=17/23) and subretinal (n=7/23). All of the patients (n=23/23) had exudative retinal detachment, %78.2 (n=18/23) also had severe proliferative vitreoretinopathy and 4.3% (n=1/23) had a full thickness macular hole. Of the 23 patients/detachments; 47.8% (n=11/23) were total and 52.1% (n=12/23) were subtotal. 43.7% (n=10/23) of the patients had undergone non-surgical treatments (argon laser photocoagulation: n=6/23, photodynamic treatment: n=3/23, intravitreal anti-VEGF injection: n=6/23, and plaque radiotherapy: n=1/23) preoperatively. All patients underwent 23 G pars plana vitrectomy, tumor resection and endolaser photocoagulation. In addition, relaxing retinectomy (n=8/23) and proliferative membrane removal (n=18/23) was performed if needed. Silicone oil was used in 9 cases, %14 C3F8 gas was used in 13 cases and air tamponade was used in one case. The mean preoperative and postoperative VA were; LogMAR 1.78±1.14 (range LP-0.1) and LogMAR 1.04±1.11 (range LP-0.0) respectively (p=0.002). Visual acuity improved in 18 patients (mean 0.58±0.84 LogMAR; 1.35±1.07).

**Conclusions**
Vitrectomy with RCH excision is a safe and effective method for the treatment of large tumors complicated with exudative and/or tractional retinal detachment. Surgical resection of large retinal hemangioblastomas and complete removal of proliferative membranes are the most important points of surgery. However, life long follow-up is recommended to diagnose and treat recurrences.

**Financial Disclosure**
We have no financial relationships
Free Internal Limiting Membrane Transplantation for Large or Persistent Idiopathic Macular Holes

Purpose
To report anatomical and functional results in cases where we applied free internal limiting membrane (ILM) flap assisted with the perfluorocarbon liquid (PFCL) as primary or secondary surgery in large or persistent idiopathic full-thickness macular holes (FTMH).

Setting/Venue
Trakya University, School of Medicine, Edirne, Turkey

Methods
Ten eyes of 10 consecutive patients who underwent free ILM flap combined with pars plana vitrectomy (PPV) surgery due to idiopathic large or persistent FTMH (diameter > 400 μm), and who used silicone-oil as an endotamponade were reviewed retrospectively. A full ophthalmic examination and optical coherence tomography (OCT) were performed at each visit. The patients were followed up on the first month, the third month, the sixth month, and twelve months after the surgical treatment. The rates of anatomical closure, best-corrected visual acuity (BCVA) values, and ellipsoid zone (EZ) disruption values were compared within the preoperative and postoperative periods.

Results
The mean age of the patients was 69.20±4.94 years. Seven patients (70.0%) were female, and 3 patients (30.0%) were male. Anatomical closure was achieved in the FTMHs of all eyes postoperatively. The mean BCVA values increased compared to baseline (0.95±0.27) at postoperative 1 month (0.93±0.34), and 3 months (0.87±0.32), but this increase was not statistically significant (p=0.809, p=0.237, respectively). The mean BCVA values significantly improved compared to baseline at postoperative 6 months (0.54±0.28), and 12 months (0.47±0.21) (p=0.000, p=0.000, respectively). The mean EZ disruption diameter significantly decreased compared to baseline (1177.30±266 μm) at postoperative 1 month (495.90±349.49 μm), 3 months (385.20±21.35 μm), 6 months (286.80±316.23 μm), and 12 months (273.70±276.70 μm) (p=0.005, p=0.000, p=0.005, p=0.000, respectively). No complications were observed.

Conclusions
Free ILM flap transplantation and the use of silicone-oil as an endotamponade provide an increase in BCVA levels, high anatomic closure rates, and improvement in ellipsoid zone defects in the 1-year follow-up of large or persistent macular holes.

Financial Disclosure
No financial relationship with any of the commercial products or vendors in this presentation.
The Effect of Silicone Oil Tamponade on Optical Coherence Tomography Findings in Patients with Rhegmatogenous Retinal Detachment

Ömer Özer, Turkey

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Purpose
The aim of this study was to evaluate optical coherence tomography (OCT) findings in eyes that underwent pars plana vitrectomy for rhegmatogenous retinal detachment (RRD) and using silicone oil tamponade.

Setting/Venue
Forty-two eyes of 42 patients who were used pars plana vitrectomy and silicone oil tamponade for rheumatogenic RD between March 2017 and March 2020 in Department of Ophthalmology, Faculty of Medicine, Mersin University were included in the study.

Methods
Cases with ocular pathology other than cataracts, those who had undergone surgery for any reason other than cataract surgery, those who had membrane peeling and whose anatomical success could not be achieved, those who did not come for regular controls or whose records could not be reached were excluded from the study. Anatomical success was defined as retinal attachment after vitrectomy for RD and removal of silicone oil tamponade. File records and optical coherence tomography sections (OCT) (Heidelberg HRA-OCT Spectralis®, Heidelberg Engineering GmbH, Heidelberg, Germany) of all patients included in the study were retrospectively scanned and examination findings, macular thickness, presence of degeneration in the inner retinal layers, ellipsoid zone/external limiting membrane (EZ / ELM) continuity, presence of subretinal fluid and accompanying vitreomacular pathologies were recorded. In addition, the time elapsed between the onset of symptoms and surgery was evaluated. The first and sixth months after silicone oil injection and the first and sixth months after removal of silicone oil were re-evaluated, and OCT findings obtained from the operated eyes were compared with the data obtained from fellow eyes.

Results
The patients in this study 29 were male (69%), 13 were female (31%), and the mean age was 62.1 ± 9.09 years. At admission, 20 eyes (47.6%) were phakic and 22 eyes (52.4%) were pseudophakic. Macular involvement was detected in 23 eyes (54.76%) and was not detected in 19 eyes (45.24%). When the anatomical locations of the tears were evaluated, found that the most common localization was in the supertemporal with 42.5%, followed by the inferotemporal with 22.7%, the superonasal with 22.7% and the inferonasal with 6.9%. The mean follow-up period of the patients included in this study was 18.09 ± 8.24 months, and the mean duration of silicone oil tamponade in the operated eyes was 253.21 ± 113.32 days. Preoperative BCVA was 0.09 ± 0.16, 0.14 ± 0.1 at first month postoperatively, 0.29 ± 0.23 at first month after silicon oil removal, and 0.32 ± 0.25 at the sixth month after silicon oil removal. Visual acuity increased significantly compared to before surgery (p <0.0001 for each parameter). In addition, an antiglaucomatous drop was required in 20 (47.6%) eyes that underwent surgery. The central retinal thickness (CRT) in fellow eyes was 289.54 ± 33.45 µm, in silicone oil injected eyes 268.42 ± 62.95 µm in the first month and 291.64 ± 65.09 µm in the sixth month. After silicon oil removal, CRT was 286.04 ± 68.54 µm in the first month and 322.06 ± 64.91 µm in the sixth month. The difference between the CRT values of the eyes injected with silicone oil in the sixth month and the CRT values in the sixth

Conclusions
This study shows that the use of silicone oil in patients with rhegmatogenous RD has effects on central retinal thickness, visual acuity and OCT findings. However, many of these effects were not found to be related to the duration of silicone oil tamponade. However, in cases where silicone oil is used as a tamponade, thought that it may be beneficial to remove this oil from the eye in the early period. In addition, it would be appropriate to evaluate the possible effects of silicone oil on retinal tissue with larger patient series and longer patient follow-up.

Financial Disclosure
There are no financial conflicts of interest to disclose.
Title
Management of combined tractional and rhegmatogenous retinal detachment, due to diabetes. A case report.

Purpose
To point out the technique that was used to treat a case of combined tractional and rhegmatogenous retinal detachment in a diabetic patient.

Setting/Venue
“Diathlasis” Day Care Unit, Thessaloniki, Greece

Methods
A 42 year-old diabetic woman presented with bilateral visual acuity loss (VAre: cf and VAle: 1/10). Fundoscopy revealed severe proliferative diabetic retinopathy and retinal detachment due to tractional and rhegmatogenous etiology. The findings were bilateral. We performed pars plana vitrectomy, removal of the membranes and tractional elements, sealing of the retinal tears with endolaser and finally silicone oil infusion. One month later, the patient underwent the same procedure for the other eye.

Results
Postoperatively we noticed the lysis of the tractions, restoration of the anatomical structures and visual acuity improvement.

Conclusions
The vitrectomy system of small incision and bimanual technique offers specific advantages, concerning the management of demanding cases of combined tractional and rhegmatogenous retinal detachment. In cases of bilateral appearance, the timing of the second eye surgery is co-decided by the doctor and the patient.

Financial Disclosure
None
Quality Assessment and Comparison of 2D and 3D YouTube Videos as an Additional Educational Source about Vitreoretinal Surgery

Purpose
To analyze 3D YouTube videos as an additional educational resource about vitreoretinal surgery, and compare them with 2Ds.

Setting/Venue
Samsun Bafra State Hospital, Department of Ophthalmology, Turkey

Methods
Using a YouTube search using the keyword "vitreoretinal surgery", "retinal surgery" and "vitrectomy", 2D and side-by-side 3D surgery videos in the search results were included in this retrospective, cross-sectional and register-based study. The video length, time since upload, number of views, number of likes, number of dislikes, type of surgery and visualization system were recorded. Video popularity and interaction was calculated using the video power index (VPI) and interaction index (II). Videos were watched and evaluated by two ophthalmologists. 3D videos were watched on 4K TV, using the side-by-side 3D option on, with polarized 3D glasses. 2D videos were also watched on same screen with a bare eye. A modified usefulness score system was devised as "1=useless", "2=slightly useful", "3=useful", "4=very useful" and "5=definitely useful" to categorize for evaluate video quality and content. Interrater reliability was assessed using Kappa’s coefficient.

Results
We screened 258 videos, of which fifty in 2D, fifty in 3D were found eligible for this study. Median VPI was 100 (range, 92.30-100) in 2D, and 100 (range, 66.66-100) in 3D videos (p=0.781). Median II was 0.71 (range, 0.21-4.88) in 2D, and 0.0 (range, 0.0-12.50) in 3D videos (p<0.001). The modified usefulness score was 3.27 ± 0.42 in the 2D video group, and 3.49 ± 0.55 in the 3D video group (p=0.209). A strong agreement of interrater reliability was confirmed using Kappa's coefficient (κ value=0.84).

Conclusions
While YouTube videos involving vitreoretinal surgery are certainly not a method of learning surgery from beginner level, they can be used as a resource to reinforce learned surgery, see new techniques, and remember old ones. In the present study, 2D and 3D vitreoretinal surgery videos were found similarly "useful" by specialists. Since 3D video viewing requires special equipment such as an imaging system and polarized glasses, 2D videos may have been watched/liked more and the interaction index level determined higher. Further studies are needed in this relatively new technological field on the 3D learning effects, especially in ophthalmology residency.

Financial Disclosure
Financial Disclosure: No
Title
Full thickness macular hole formation preceded by lamellar macular defects in the context of complete posterior vitreous detachment

Purpose
To describe the morphology of the vitreoretinal interface preceding full thickness macular hole (FTMH) formation in relationship to the posterior vitreous detachment (PVD) status with optical coherence tomography (OCT).

Setting/Venue
Retrospective cohort study

Methods
The clinical and morphological data of 47 consecutive patients with a diagnosis of FTMH were retrospectively screened for fellow eye involvement. OCT images of fellow eyes were reviewed at baseline and all available follow-up exams for: evidence of tractive maculopathy (e.g. epiretinal membrane, vitreomacular traction, FTMH), evidence of lamellar macular defects, irregularities of foveal contour, irregularities of inner and outer retinal layers and the status of vitreopapillary adhesion (VPA).

Results
The mean follow-up time was 26.76 (SD 47.92) months. In 6 of 47 fellow eyes (12.77%) a FTMH developed over the time range of 6-27 months after the first presentation. In 3 of these cases (50%) the FTMH developed in the presence of an attached posterior vitreous and was preceded by either vitreomacular adhesion or vitreomacular traction. In the other 3 cases (50%) the FTMH developed after complete PVD and was preceded by lamellar macular defects in all cases. Lamellar macular defects in the fellow eye, if present, were in all 3 cases (100%) associated with later FTMH development.

Conclusions
The study of the fellow eye makes it possible to study vitreoretinal pathologies at a point of time, when patients may still be asymptomatic. This retrospective cohort study describes the pathophysiological role of lamellar macular defects in the formation of full thickness macular holes, especially in the context of complete PVD and prior fellow eye involvement.

Financial Disclosure
J E Klaas has received speaker honoraria for Novartis. No conflicts of interest.
Correlation between outer nuclear layer thickness and visual acuity with duration of retinal detachment

Purpose
To correlate outer nuclear layer thickness and visual acuity with duration of detachment. Primary outcome measure was outer nuclear layer thickness and ONL restoration post rhegmatogenous retinal detachment repair and correlation with duration of detachment. Secondary outcome measure were other structural changes seen in optical coherence tomography such as IS-OS disruption, ELM disruption, persistent sub retinal fluid and correlation of above with duration of detachment. Correlation of best corrected visual acuity with ONL and duration of detachment

Setting/Venue
it was a prospective, observational and comparative study, conducted at Vitreoretinal services of Gurunanak eye Centre, Maulana Azad Medical College, Delhi, India. We enrolled patients diagnosed and treated for retinal detachment from September 2015 to December 2017. A written informed consent was taken from each patient.

Methods
Patients were divided into three Groups, Group A patients operated within 1 month of RRD; Group B RRD repaired 1-3 months, Group C RRD repaired after 3 months. Each group had 15 patients with total of 45 patients (90 eyes). The OCT parameters and BCVA were noted 4 months post operative. To measure the mean outer nuclear layer, we chose the OCT image with the steepest foveal excavation from the radial scans across the foveal area. The outer nuclear layer thickness is the distance between the inner limiting membrane and the external limiting membrane at the central foveal. This was compared with patient’s normal eye to give the ONL restoration in percentage. Patients underwent either buckling surgery or parsplana vitrectomy depending upon the indication.

Results
The difference in ONL thickness was significant between Group A and C (p=0.001), Group B and C (p=0.049) but insignificant between Group A and B (p=0.246),The ONL restoration was significant between Group A and C (p=0.001), Group B and C (P=0.025) but insignificant between Group A and B (P=0.197). The difference in BCVA was significant between Group A and B (p=0.028), between Group A and C (p=0.001) and insignificant between Group B and C (P=0.052). With each day of RD there was 0.004 logMAR loss of vision. IS-OS disruption was significant between Group A and B (p=0.02) and Group A and C (p=0.001) and insignificant between Group B and C (p=0.05). Similarly, ELM disruption was significant between Group A and B (P=0.027) and Group A and C (p=0.001) but insignificant between Group B and C (p=0.104)

Conclusions
Our study reemphasis the need for early repair of RRD within 1 month. Beyond 1 month, though ONL restoration occurred the BCVA was worse in patients operated after 1 month. Most microstructural changes go hand in hand with the chronicity of detachment. With an increase in duration of detachment more number of patients had IS-OS junction disruption and ELM disruption. However, ERM, persistent SRF and intraretinal fluid had not correlation with duration of detachment and final BCVA. Longer follow up is required to give better idea about the ONL restoration, and other OCT parameters like IS-OS junction disruption, ELM disruption, intraretinal and sub retinal fluid, ERM formation.

Financial Disclosure
no financial interest
The impact of COVID-19 pandemic on primary retinal detachments: presenting characteristics, timings and surgical decisions

André Ferreira
Portugal

Purpose
To describe the impact of COVID-19 pandemic on the presentation characteristics, timings and surgical decisions for primary rhegmatogenous retinal detachment (RD).

Setting/Venue
Retrospective consecutive cohort of rhegmatogenous RD that were submitted to surgery at a tertiary center, Centro Hospitalar Universitário do Porto (CHUPorto), during the year preceding the pandemic and the pandemic year.

Methods
All patients who presented to the Surgical Retina Section at CHUPorto, over a 2-year period were recruited and divided in 2 groups: pre-COVID group, from March 20, 2019 to March 19, 2020; and pos-COVID group, from March 20, 2020 to March 19, 2021. The onset of the COVID-19 pandemic was recorded as starting on March 20, 2020, the same day the first pandemic-related lockdown came into effect in Portugal. Patients were identified by the ICD-9 and ICD-10 codes. Patients were only included if they presented between the specified dates with a primary rhegmatogenous RD and had at least 6 weeks after pars plana vitrectomy (PPV), scleral buckle (SB), or combined PPV and SB given the use of long-acting gas in most surgical cases. Patients were excluded if the affected eye was treated with laser retinopexy for a retinal tear only, or if the affected eye had pre-existing maculopathy, retinopathy, amblyopia, or prior history of serous, tractional or rhegmatogenous RD in the affected eye.

Results
This study enrolled four hundred and forty-nine eyes of 443 patients: 272 in the pre-COVID groups and 177 in the post-COVID one. Of the patients, 63.6% were male and the mean±SD age was 63.0±13.2y (range 13 to 92y). Of the eyes, 55.5% (n = 151) presented with macular detachment in the pre-COVID group compared with 66.9% (n = 119) in the pos-COVID group (odds ratio [OR] 1.62; 95% confidence interval [CI], 1.09-3.86; p=0.016). The time from symptoms onset to hospital admission was longer in the pos-COVID era (median [interquartile range (IQR)]: 7 [3-10] vs 7 [3-15], p=0.021). As well, the time from hospital admission to surgery was also longer during the pandemic year (median [IQR]: 0 [0-2] vs 2 [1-4], p<0.001). PPV was performed in 97.6% of cases and the overall success of interventions (PPV and SB) was 84.2%; no differences between groups. In the pos-COVID, silicone oil (OR 2.03, 95%CI 1.09-3.79, p=0.025) and C3F8 gas (OR 2.42, 95%CI 1.57-3.71, p<0.001) were used more often. No differences were found regarding baseline visual acuity, lens status, trauma or relapse.

Conclusions
The lockdown due to COVID pandemic affected the epidemiology of rhegmatogenous RD, including the macular status at admission and the time since symptoms onset and hospital admission until surgery. Moreover, silicone oil and C3F8 gas were used more often during the pos-COVID year. Despite these contingencies, our Service revealed a quick adaptation to the new scenario as demonstrated by the time of waiting since hospital admission until surgery in the pos-COVID period.

Financial Disclosure
None
Results of pars plana vitrectomy with inferior retinotomy in inferior rhegmatogenous retinal detachments with inferior retinal breaks and proliferative vitreoretinopathy grades B or C

**Presenter**
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**Purpose**
To report the surgical outcomes of pars plana vitrectomy (PPV) with inferior retinotomy without the need for scleral buckling in primary inferior rhegmatogenous retinal detachment (RRD) with inferior retinal breaks and Proliferative vitreoretinopathy (PVR) grades B or C.

**Setting/Venue**
Department of Ophthalmology - Centro Hospitalar de Vila Nova de Gaia e Espinho

**Methods**
A retrospective, consecutive series, single-center study of patients that underwent PPV with inferior retinotomy for primary inferior RRD with inferior retinal breaks (4:00 to 8:00 clock hours) and PVR grades B or C. Data was obtained from patients’ medical records from October 2014 to November 2020. The primary outcomes of the study were retinal reattachment and visual acuity improvement. Data collected before and after surgery was compared between groups using chi-square analysis and paired samples t-test. The resulting p-values significance level was set at p=0.05.

**Results**
Thirty-two patients (32 eyes) met the inclusion criteria. PVR in stage B was present in 19 patients and stage C in 13 patients. Macula-off RRD was diagnosed in 25 patients while the other 7 patients had RRD with the macula attached. Regarding primary outcomes, 31 out of 32 (97%) patients achieved retinal reattachment with no differences between PVR groups (p=0.406). The best-corrected visual acuity (BCVA) improved significantly in eyes with macula-off RRD at presentation (p<0.001). Although macula-attached RRD eyes had higher final BCVA, its improvement was not statistically significant (p=0.370). Besides one retinal redetachment, no other significant complications were reported after surgery.

**Conclusions**
Inferior retinal breaks are associated with surgical failure following PPV for inferior RRD repair, especially if advanced PVR is present. Our results suggest that, in these less common and more challenging cases, PPV with an inferior retinotomy is associated with very favorable anatomic and visual outcomes.

**Financial Disclosure**
None
# Title

Enface Optical Coherence Tomography as a Screening Test for Outer Retinal Folds and Subretinal Fluid Blebs

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## Purpose

To investigate enface optical coherence tomography (OCT) as a screening tool for the detection of outer retinal fold (ORF) and subretinal fluid (SRF) blebs after successful rhegmatogenous retinal detachment (RRD) repair in eyes undergoing pneumatic retinopexy versus pars plana vitrectomy.

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## Setting/Venue

Cross-sectional study within a prospective cohort study were conducted on St. Michael's Hospital which is a clinical teaching hospital affiliated with the University of Toronto based on Toronto, Ontario, Canada.

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## Methods

Patients with RRD were followed prospectively following treatment. All patients had a 6x6 macular cube optical coherence tomography (OCT) scan within 1 to 4 months of surgical intervention. Enface slabs used for detection of ORF were between the ellipsoid zone and interdigitation zone with a thickness of 22 microns. For the detection of SRF blebs enface slab were 73 microns thick and extended from the outer nuclear layer to the ellipsoid zone. We assessed the sensitivity, specificity, positive predictive value (PPV) as well as the negative predictive value (NPV) of enface OCT in comparison to cross-sectional OCT, the current gold standard.

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## Results

We assessed 316 eyes for the presence of ORFs and SRF blebs on enface and cross-sectional OCT. On Enface OCT 50% (158/316) had ORFs and 28.16% (89/316) had SRF blebs. On cross-sectional OCT, 25% (79/316) had ORFs and 28.48% (90/316) of eyes. For ORFs sensitivity was 100%, specificity 66.67%, PPV 50% and NPV 100%. For SRF blebs sensitivity was 100%, specificity 71.84%, PPV 48.55% and NPV 100%.

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## Conclusions

Enface OCT is a useful screening test for the detection of ORFs and SRF blebs after successful rhegmatogenous retinal detachment repair. The presence of ORFs and SRF blebs detected on enface OCT should be confirmed with review of the cross-sectional OCT volume scan.

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## Financial Disclosure

Non/Applicable No financial relations to be disclosed
**Title**
Persistent subretinal fluid in Pneumatic Retinopexy vs Pars Plana Vitrectomy for Rhegmatogenous Retinal Detachment Repair: Post Hoc Analysis from PIVOT

**Purpose**
To assess the incidence of post-operative persistent subretinal fluid (PSRF) in pneumatic retinopexy (PnR) vs pars plana vitrectomy (PPV) with en face and cross-sectional spectral-domain optical coherence tomography (SD-OCT) following rhegmatogenous retinal detachment (RRD) repair and to determine the association of persistent subfoveal fluid (PSFF) with functional outcomes.

**Setting/Venue**
This is a post hoc analysis of the PIVOT randomized trial at St Michael's Hospital/Unity Health Toronto, Toronto, Canada. The trial was registered at ClinicalTrials.gov (identifier, NCT01639209). This study was approved by the Research Ethics Board at St. Michael's Hospital/Unity Health Toronto in Toronto, Canada, and adhered to the Declaration of Helsinki.

**Methods**
Eyes with gradable en face and cross-sectional SD-OCT at 1-month postoperatively were included in the study. Two masked graders assessed the images, and any disagreement was adjudicated by a third senior masked grader. The primary outcome was the proportion of patients with PSRF following PnR versus PPV at 1-month postoperatively. Secondary outcomes included the association of PSFF with functional outcomes (ETDRS letter score & quantitative metamorphopsia score with MCHARTs).

**Results**
92.04% (81/88) in PnR and 87.5% (77/88) in PPV group had gradable month 1 post-operative OCT scans. Baseline characteristics were similar between groups. Intergrader agreement (Cohen's Kappa) for PSFF and PSRF were 0.870 and 0.905, respectively. The incidence of PSRF was 30.9% (25/81) in the PnR group and 24.7% (19/77) in the PPV group (p=0.386; OR=1.36, 95% CI 0.68-2.75). Similarly, proportion of eyes with PSFF was 16% (13/81) following PnR and 10.4% (8/77) after PPV (p = 0.295; OR=1.65, 95% CI 0.64-4.23). PSFF gradually resolved over time with no significant difference between groups at any time point. The median ETDRS letter score at 3 months postoperatively between eyes with and without PSFF was 65 (IQR=26) and 78 (IQR=14), respectively (difference=13 letters, p=0.037). At 6 and 12 months postoperatively this difference was 6 letters, (p=0.478) & 1.5 letters, (p=0.37), respectively. The median metamorphopsia scores in patients with vs without PSFF was, horizontal: 0.2 (IQR=0.5) versus 0 (IQR=0.2) (difference=0.2, p=0.228) and vertical: 0.3 (IQR=0.5) versus 0 (IQR=0.3) (difference=0.3, p=0.148) respectively.

**Conclusions**
The proportion of eyes with PSRF was similar in PnR and PPV. Eyes with PSFF had delayed visual recovery, although there was no significant impact on functional outcomes at one year.

**Financial Disclosure**
None
**Title**
Plasma rich in growth factors membrane in the treatment of MacTel Type 2 related full thickness macular holes: A Pilot Study

**Purpose**
To showcase a regenerative approach using plasma rich in growth factors membrane (PRGFm) as a useful adjuvant in surgical treatment of full thickness macular holes (FTMH) associated to macular telangiectasia (MacTel) Type 2

**Setting/Venue**
Single center institutional vitreoretinal surgery practice

**Methods**
FTMH is a rare complication in MacTel Type 2 patients that has no definitive treatment. Anatomic closure rates after standard pars plana vitrectomy (PPV) have been reported to be around 25-30% and functional outcomes have a guarded prognosis. PRGFm has been shown to increase tissue regeneration and is used in other atypical or large FTMH with good results. Recent characterization of MacTel Type 2 as a neurodegenerative disorder with secondary vascular changes suggest a role for regenerative modalities. This is an observational consecutive case series report. We reviewed electronic medical records from 2018 to 2021 and included patients with MacTel Type 2 who underwent PPV + PRGFm for FTMH with or without previous surgical interventions. Data was collected for BCVA, Swept Source OCT (SS-OCT) imaging with preoperative macular hole size using minimal diameter (MD), anatomic closure rates and length of follow up. Data was reported qualitatively or using descriptive statistics were appropriate.

**Results**
103 patients with FTMH were identified of which 7 had concomitant MacTel Type 2 and only 3 eyes were treated with PPV + PRGFm with SS-OCT follow up. One surgeon (JA) performed 2 cases and another (CR) the remaining one. Case 1 was a 63 year-old female with no history of previous surgery with a 677 µm FTMH on his right eye that improved from 20/100 to 20/30 after surgical treatment without internal limiting membrane (ILM) removal. Case 2 was a 72 year-old female with a 628 µm recurrent macular hole on his left eye that improved from counting fingers (CF) vision to 20/300 after treatment with ILM removal. Case 3 was a 70 year-old female presenting with a 624 µm FTMH on his right eye that improved from 20/200 to 20/100 after treatment with ILM removal. Median follow up was 6 months (range 6-18 months), anatomic closure rate was 100% and median LogMar change 0.5 (range 0.3-0.8). No PRGFm related complications were registered.

**Conclusions**
The use of PRGFm appears to be useful and safe as an addition to PPV in the treatment of MacTel Type 2 related FTMH. It can be used safely and provides stimulation for tissue regeneration and closure due to its biological characteristics. The technique is reproducible and does not require complex ILM manipulation. The regenerative properties of PRGFm within this tissue preserving approach could be key in addressing the neurodegenerative component of this disease.
Displacement of Submacular Hemorrhage with Tissue Plasminogen Activator and Subretinal Air

Alicia López de Eguileta, Spain

Jaume Crespí

Jose Ignacio Vela

Jesus Díaz

Nuria Torrell

Purpose
To assess our surgical experience of using subretinal air injection in combination with recombinant tissue plasminogen activator (rtPA) at the time of pars plana vitrectomy (PPV) to displace submacular hemorrhage (SMH).

Setting/Venue
Retrospective, noncomparative, interventional case series.

Methods
Chart review of patients who underwent displacement of SMH with PPV, subretinal injection of air (0.2 ml) and rtPA (125 mg/mL), with partial fluid air-exchange with gas tamponade, and preoperative, intraoperative, or postoperative intravitreal injection of anti-vascular endothelial growth factor agent. The main outcomes measured were visual acuity (VA), the displacement of SMH from the fovea and the macular thickness.

Results
Twenty eyes of 20 patients were included (11 men; mean age 77.95) with a follow-up of 12 months.*SMH was due to age-related macular degeneration (AMD) in 16 patients, retinal arterial macroaneurysm in 3 patients and blunt ocular trauma in 1. One week after surgery, complete displacement from the foveal center was achieved of SMH was achieved in 19 no displacement was found 1 eye (5%). Residual subretinal pigment epithelial hemorrhage was seen in 13 eyes (65%). Mean preoperative VA was 1.96 (logMAR). Mean best corrected VA postoperative 1 week later was 2.07, and 1 and 3 months after surgery was 1.4 and 1.17 logMAR respectively. Mean central macular thickness (CMT) was 689.5 µm before treatment, and after 1 month it improved until 472.74 µm. Complications as retinal detachment, vitreous hemorrhage, and macular hole appeared in 25% of cases.

Conclusions
PPV with subretinal injection of rtPA and subretinal injection of air is an effective treatment of SMH in terms of complete displacement of the hemorrhage and VA recovery.

Financial Disclosure
No one
**Title**
Effect of Demographics and Ethnicity on laser retinopexy in preventing retinal detachment in a tertiary eye hospital in 812 eyes.

**Purpose**
To investigate different baseline characteristics, clinical indications, repeat retinopexy rate, and six-month detachment rate of primary laser retinopexy across different ethnicities.

**Setting/Venue**
The Birmingham and Midland Eye Centre, United Kingdom

**Methods**
Retrospective, single centre, consecutive comparative study, looking at all patients who had primary laser retinopexy between January 2017-2020. Multivariate Cox survival (reporting Hazard Ratio [HR]) and binary logistic regression (reporting Odds Ratio [OR]) analyses were performed to investigate differences between ethnicities with age, gender, operator level (vitreo-retinal or general ophthalmologist) and high myopia status (≥ -6.0Dioptres) as covariates.

**Results**
We report on 812 patients in three ethnicities: Black (69[8.5%]), South Asian (SA, 156[19.2%]) and White (587[72.3%]) with overall six-month detachment rate of 31 (3.8%). Rate for subsequent retinopexies were Black:12 [17.4%], SA:15 [9.6%] and White:131 [22.3%], p=0.002. Multivariate Cox Survival regression analysis found no difference in detachment rate between ethnicities. SA had lower repeat retinopexy rate than White patients (HR0.40 [95%CI 0.22-0.71,p=0.002). Multivariate binary logistic regression found that Black and SA patients compared to White, have: i) higher proportion of round holes relative to horseshoe tears (OR2.31[95%CI1.19-4.49,p=0.014] and OR2.06[95%CI1.25-3.40],p=0.004 respectively), ii) higher proportion of high myopia (OR2.99 [95%CI1.20-7.46,p=0.019] and OR2.35[95%CI1.11-4.96],p=0.025 respectively). Ethnic minorities were younger than White patients: SA [43,IQR28-61], Black [49,IQR35-57] and White [61,IQR54-67] years, p<0.001) and had more indirect and 360-retinopexy compared to slit-lamp (p<0.001).

**Conclusions**
We demonstrate a significant difference in baseline characteristics, retinal tear morphology and treatment course between the ethnic groups. Further studies are necessary to investigate the genetic and biological differences that may influence these variations and may help to allow for more targeted healthcare.

**Financial Disclosure**
no

### Co-Authors
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### Purpose
To leverage micro-PIV experiments and validated computational fluid dynamics simulation models to define and compare sphere of influence (SOI) extent and pulsatile motion around vitrectomy probes.

### Setting/Venue
Laboratory study using Micro-PIV (Particle Image Velocimetry), CFD (Computational Fluid Dynamics)

### Methods
The micro-PIV experiments and simulation models of three probes, namely, 25+® Advanced UltraVit 10,000 cuts per minute (cpm), 25+® HyperVit 20,000 cpm flat and beveled tips were used to compare flow velocity around the probe tip. Vitrectomy system parameters such as applied vacuum settings of 650 mmHg, 50/50 duty cycle setting on the CONSTELLATION® Vision System were applied for both micro-PIV and CFD simulations in a BSS filled beaker. Further CFD simulations were conducted with matched flow rates to compare performance. For micro-PIV, a thin sheet of laser (PurePoint at 525mW) was used to illuminate Polyamid particles dispersed in the beaker. The movement of particles was captured using a high-speed CCD camera. For CFD simulations, a dynamic mesh was used to simulate the motion of the cutter. Flow was assumed to be incompressible and laminar. All products are made by Alcon, Fort Worth, TX.

### Results
The micro-PIV results indicate higher fluctuation magnitude for the Advanced UltraVit Bevel probe as compared to the HyperVit probes. There was a slight fluctuation in the velocity profile between consecutive cycles, which may be resulting due to the minor pressure fluctuations inside the probe. Both HyperVit cutters, beveled and flat tips demonstrated a similar behavior. The Reynolds number (representing flow velocity) and Intensity of Root Mean Square (RMS) of the velocity were used in CFD simulations to define extent of SOI and intensity of pulsatile motion, respectively. They were measured on spheres of increasing radii from probe tip and maximum values were recorded. In a quantitative agreement with micro-PIV results, the intensity of velocity fluctuations in CFD simulations was significantly reduced for both HyperVit Probes compared to Advanced UltraVit probe. The Beveled tip of the probe contributed to lowering the flow velocity close to the probe tip (at a distance of r=1 mm) for HyperVit Probes. Such observations hold true for matched-vacuum condition and matched-flow condition. In addition, under matched-flow, the maximum SOI size of HyperVit Probes was smaller compared to that of AdvUltraVit Probe.

### Conclusions
Micro-PIV experiments and CFD simulations were used to compare flow dynamics in nearfield of the Vitrectomy probe tip. The flow performance of 25 gauge HYPERVIT probes had more stable aspiration, which was shown by the reduction in the intensity of pulsation of velocity during fluid aspiration. The HyperVit probes showed a smaller SOI compared to advanced UltraVit probes under matched-flow conditions. A smaller SOI and a reduced pulsatile motion may enhance safety of the vitreoretinal surgery. Simulations may help surgeons better understand differences in probe performance and optimize instrument selection.

### Financial Disclosure
Research funding: Alcon, Bayer, DORC Consultancy: Gyroscope, Roche
**Title**
Microstructures of the foveolar region after surgery for idiopathic macular ruptures

**Purpose**
To study the features of regenerative processes occurring in the microstructures of the foveolar region after successful surgery of the primary full-thickness macular holes (FTMH) by the method of "temporal inverted ILM flap".

**Setting/Venue**
Department of eye diseases of Samara State Medical University; Ophthalmic clinic "Eye Surgery", Samara, Russia

**Methods**
Using spectral optical coherence tomography (SOCT), the features of regenerative processes in the microstructures of the foveolar region were studied in 31 patients (32 eyes) with stage II-IV FTMH according to J. Gass (1995), who were successfully operated on for this reason.

**Results**
Regenerative processes of gradual restoration of microstructures of the foveolar region began from the first days after surgery and continued for 1 year. As a result, the U-shaped foveolar contour was restored, the central retinal thickness changed (from 399±61.4 to 195±61 microns, p<0.05); the external limiting membrane (ELM) and the ellipsoid zone (EZ) were completely restored in 27/32 (84.4%) and 23/32 (71.8%) eyes, respectively.

**Conclusions**
Regenerative processes in the microstructures of the foveolar zone are of a step-by-step nature and are traced for one year after the surgery of the primary FTMH by the method of "temporal inverted ILM flap". The essence of the processes: overlapping FTMH with flaps of ILM, filling its lumen with a "glial plug", restoring the ELM, EZ and interdigitative zones.

**Financial Disclosure**
no
## Title
An analysis of changes in retinal layers after rhegmatogenous retinal detachment treatment with silicone oil and gas tamponade

## Purpose
To evaluate retinal layers after treatment with silicone oil (SiO) or gas endotamponad in eyes with macula-off rhegmatogenous retinal detachment (RRD)

## Setting/Venue
Health Science University, Kayseri City Training And Research, Department Of Ophthalmology, Kayseri, Turkey

## Methods
Forty-one patients who underwent vitrectomy for rhegmatogenous retinal detachment were included in the study. There were 20 eyes treated with silicone tamponade and 21 eyes treated with gas tamponade (C3F8, SF6). OCT imaging was performed at least 6 months after surgery. Central macular thicknesses were evaluated and automatic retinal segmentation analyzes were performed. Retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL) in OCT analyzes at least 6 months after surgery, photoreceptor layer thickness, retinal pigment epithelium, inner retina, outer retina layers were evaluated. In terms of retinal layer thickness, the operated eyes and the fellow eyes were compared. It was also associated with the type of tamponade used in surgery.

## Results
Eight women and 33 men were included in the study. The mean ages in the silicone group and the gas group were 59.8 ± 12.23, 62.20 ± 11.37 years, respectively (p=0.530). The mean central macular thickness was 237.2 ± 32.5 µm, 244.7 ± 34.4 µm in the operated and fellow eyes, respectively (p = 0.014). At 6 months postoperatively, central macular thickness was 234.19 ± 36.60µm, 239.25 ± 38.9 µm in the silicone group and the gas group, respectively (0.424). Best corrected visual acuities were 2.64 ± 0.48 and 2.72 ± 0.52 logMAR at baseline, 0.70 ± 0.31 and 0.60 ± 0.34 logMAR at 6 months, respectively, in the silicone oil tamponade and gas tamponade group (p = 0.48 and p = 0.32, respectively). Fovea NFL, GCL, IPL, INL, OPL, ONL, RPE, IRL and ORL layers were all statistically significantly thinner in the silicone oil tamponade group (p = 0.02, p = 0.012, p = 0.028, p = 0.015 ve p = 0.017 p=0.03 p= 0.001, p=0.025 p=0.006, respectively).

## Conclusions
Our study showed changes in retinal layers after vitreoretinal surgery for RRD at least 6 months of follow-up. However, the type of tamponade used can have different effects on retinal layers. In particular, the use of silicone tamponade significantly affects the thickness of the retinal layers.

## Financial Disclosure
No
### Title
Aerosol levels during vitreoretinal surgery and the role of secondary protective drapes

### Purpose
A pilot study to measure the level of aerosol particles PM 2.5 generated during pars plana vitrectomy and to establish the role of secondary adhesive drapes as an extra protection measure against aerosols.

### Setting/Venue
**Princess Alexandra Hospital, Essex, Harlow, CM20 1QX**

### Methods
A purpose build particle detector equipped with GP2Y1014AU aerosol sensor made by Sharp corporation was used to count aerosol particles PM 2.5 trapped within the closed environment under secondary surgical drape (Sterikit COB: 130025) which is typically attached to the edge of the lower surface of the microscope and tents over the surgical field. The measurements were taken during a case of pars plana vitrectomy for a dislocated intraocular lens implantation and iris fixed artisan lens without phacoemulsification.

### Results
Mean aerosol recorded throughout the procedure within the closed environment under the secondary drape was 506.37 Particles/0.01L3 compared to 491.47 Particles/0.01L3 recorded in open environment within the theatre but outside the secondary drape. Mean aerosol recorded within the closed environment under the secondary drape tent during the initial half of the procedure was 501.87 Particles/0.01L3 compared to 510.88 Particles/0.01L3 recorded during the second half of the procedure. Mean aerosol recorded in open environment in the theatre and outside the secondary drape during the initial half of the procedure was 490.12 Particles/0.01L3 compared to 492.83 Particles/0.01L3 recorded during the second half of the procedure. All the differences were statistically significant (p<0.05).

### Conclusions
Sharp GP2Y1014AU sensor could be used to monitor aerosol during ophthalmic procedures. Clinically minor but statistically significant increase in aerosol is detected at close vicinity to pars plana vitrectomy procedure, the increase is mostly within the closed environment under the secondary drape and during the second half of the procedure.

### Financial Disclosure
None
Comparison of inner limiting membrane removal vs. non-peeling in the treatment of epiretinal membrane

**Purpose**
To compare the removal of inner limiting membrane (ILMp) with not peeling in the treatment of epiretinal membrane (ERM).

**Setting/Venue**
International FOSCAL, Floridablanca, Colombia.

**Methods**
Case-control study. Patients were treated either ILMp (group 1) vs. not peeling (group 2). The change of best corrected visual acuity (BCVA), average macular thickness (AMT), recurrence of ERM, presence of dissociated optic nerve fiber layer (DONFL) and persistence of ectopic inner foveal layers (EIFLs) and disorganization retinal inner layers (DRIL) were evaluated.

**Results**
One hundred sixty eight eyes of 138 patients were included. There was not difference in the change of BCVA (p=0.26). The change of AMT was 16.54 μm (SD±31.3) and 24.79 μm (SD±31.2) in group 1 and 2 respectively (p=0.44). The rate of recurrence was 8.1% in group 2 and 0% in group 1. DONFL was identified in 29.41% of all sample, being significantly higher in group 1 (90%) (p<0.05). There were not differences in the persistence of EIFLs (p=0.64) and DRIL (p=0.34) between groups.

**Conclusions**
The ILMp demonstrated a high development of DONFL and less ERM recurrence compared to not peeling. There was not difference in change of BCVA, AMT, EIFLs and DRIL.

**Financial Disclosure**
Juan D. Arias: Topcon consultant
# Real world outcomes for the use of recombinant tissue plasminogen activator in the management of submacular haemorrhage.

**Presenter**
Haneen Jasim
United Kingdom

**Type**
Free Paper

**Purpose**
To assess the standards of management, outcomes and complications of submacular haemorrhage (SMH) displacement with tissue plasminogen activator (TPA).

**Setting/Venue**
Tertiary referral centre.

**Methods**
Retrospective analysis of the electronic patient records and OCT database for consecutive patients treated with intravitreal or subretinal TPA for any indication between 01/01/2017 and 01/01/2020. The main outcome measurement was best-corrected visual acuity (BCVA) at 6 months. Secondary measurements were mode and degree of displacement, BCVA at 3 and 12 months post treatment and complications. Displacement was offered to all patients who had lost vision from SMH in under 2 weeks. SMH was categorised as <5DD, 5-10 DD, >10DD. Displacement was defined as complete if there was no residual SMH within 750µ of the fovea; partial if the SMH shifted but not beyond 750µ from the fovea. Patients not completing follow-up visits were excluded from analysis.

**Results**
Fifty-eight patients were included in this study. The mean age was 82 years and 57% were female. The aetiologies of SMH were age-related macular degeneration (AMD) in 49/58 (84%) cases; retinal macroaneurysm (RMA) in 7/58 (12%) and polypoidal choroidal vasculopathy (PCV) in 2/58 (4%). SMH was the initial presentation of AMD in 60% if patients. Of the 58 patients, 49 (84%) were treated with intravitreal TPA + gas and 7/58 (17%) underwent pars plana vitrectomy with subretinal tPA + gas injection. The mean delay from diagnosis to treatment was 1.3 days (SD± 2.5). SMH was <5DD in size in 27/58 (47%), 5-10 DD in 10/58 (17%) and >10DD in 6/58 (10%). The remaining 15 patients had SMH of unknown size due to lack of preoperative retinal imaging. At six months, 21/43 (49%) AMD and PCV patients had improvements in BCVA of >=0.3 lines, and 24/43 (56%) had BCVA of 1.0 or better. Their mean presentation BCVA was 1.3±0.6 improving to 0.98±0.5 at 3 months; then 1.0±0.6 at 6 months and 1.1±0.7 at 12 months (p=0.06). For RMA patients, the average presentation BCVA was 1.7±0.5 evolving to 1.2±1.1, 1.2±1.1, and 1.0±1.1 at 3, 6, and 12 months postoperatively (p=0.81). In AMD, complete displacement lead to mean VA of 0.6±0.3, partial displacement to 1±0.6 and no displacement to 1.5±0.7 (p=0.003). Smaller SMH were more likely to be displaced (p=0.06) and had better BCVA (p=0.07). There was no difference in the rate of displacement between intravitreal and subretinal TPA (p=1.0).

**Conclusions**
A significant number of patients had BCVA improvements yet the outcomes of SMH displacement in our group were poor. There was a statistically significant association between degree of displacement and BCVA, suggesting a benefit for treatment. We found no advantage in performing vitrectomy surgery for this indication.

**Financial Disclosure**
No financial disclosures
Effectiveness of immediate vitrectomy and intravitreal antibiotics for post-injection endophthalmitis

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Purpose
To show that an immediate vitrectomy with an intravitreal injection of antibiotics can be an effective approach for the treatment of acute endophthalmitis following intravitreal injections.

Setting/Venue
Eye Clinic Sulzbach, Knappschaft Hospital Saar.

Methods
We reviewed all cases of clinical endophthalmitis caused by an intravitreal injection that were treated in our department between March 2012 and November 2019. Only patients that underwent a vitrectomy within 6 h after presentation to the clinic and with a documented visual acuity shortly before the causative event were included. Baseline best-corrected visual acuity (BCVA) before the causative event was compared to BCVA measured within a follow-up period of 8 months (up to 14 months).

Results
In total, 30 eyes of 30 patients were included. The BCVA before the intraocular infection was a mean value of 0.55 logMAR, and the BCVA on the day of the endophthalmitis decreased significantly to 1.66 logMAR. Within 2 months following the pars plana vitrectomy (PPV), the mean BCVA improved to 0.83 logMAR. Eight months following PPV (mean value, 8.20 months; SD, 3.59 months), the mean BCVA was 0.63 logMAR. In the last follow-up interval most of the eyes recovered, and the BCVA did not differ significantly from baseline. Two eyes underwent further pars plana surgery during the follow-up period. No enucleation was required.

Conclusions
In this study, we have shown that an immediate vitrectomy with subsequent intravitreal injection of antibiotics is an effective option for treating post-injection endophthalmitis and frequently results in recovery of vision; thus, it should be performed as early as possible, where available.

Financial Disclosure
none
### Title
Minimally Invasive Surgery for Retinal Detachment - Circular Scleral Buckling with Endoilluminator Control

### Purpose
Rhegmatogenous retinal detachment (RRD) is the most common form of retinal detachment, occurring in about 1 in 10,000 people a year. (1) The ideal procedure should involve break closure with minimum trauma and maximum primary retinal attachment. Long-term success and functional results depend on technique and patient-related conditions. In the last few decades, Primary Posterior Vitrectomy (PPV) has been the method of choice to manage RRD but it may not be the best procedure for every patient. (2) (3) (4) Circular Scleral Buckling (SB) offers a minimally invasive solution to treat RRD and is usually preferred in the context of isolated retinal break, young phakic patients and absence of vitreo-retinal proliferation (VRP). (5)

### Setting/Venue
All surgeries were conducted at the Ophthalmology Department of Hospital de Santa Maria - Centro Hospitalar Universitário Lisboa Norte (HSM - CHULN), Lisbon, Portugal, with explicit informed consent and following the Portuguese medical legis artis.

### Methods
Case-series description of the surgical technique used for minimally invasive surgery in the setting of RRD. Patients underwent minimally invasive retinal detachment surgery at HSM-CHULN between April 2020 and November 2020. Preoperatively, all the patients underwent a complete ophthalmologic examination including assessment of best-corrected visual acuity (BCVA), Goldmann® tonometry and standard fundus dilated ophthalmic examination. All patients underwent surgical repair upon a week after holes or retinal tears were identified. A circular scleral buckling with scleral tunnels was performed and cryotherapy was applied ab externo to the areas of retinal tears, under direct visualization with an endoilluminator (Alcon® Laboratories, FW, TX) through a BIOM®5 microscope system (OCULUS® Surgical, Inc., FL, USA) coupled with a surgical microscope (Zeiss® OPML Lumera T). No further drainage or tamponades were performed.

### Results
A total of 6 eyes of 4 patients underwent this procedure. The surgery was performed under direct visualization with a 25-G endoilluminator intraoperatively. All patients presented with inferior detachment, either with macula on or with macula off, and all patients presented good retinal apposition upon surgical completion and maintained this result through serial ophthalmologic examinations. Residual subretinal fluid was reabsorbed in the first 24 hours postoperatively as observed by fundus examination combined with Optic Coherence Tomography (OCT), which also showed anatomical chorioretinal apposition in every patient enrolled in this study. Upon 6 months follow-up, all patients maintained anatomical chorioretinal apposition and presented an improved best-corrected visual acuity (BCVA) when compared to the pre-operative status. No patient developed cataract or ocular hypertension during the 6-month follow-up so far.

### Conclusions
Scleral buckling is still an important procedure in selected eyes, producing good visual outcomes. When combined with recent technologies such as endoilluminators, it may provide an optimal control over chorioretinal apposition and cryotherapy application delivery, therefore avoiding the need for PPV and its most common complication in phakic eyes.

### Financial Disclosure
There are no conflicts of interest to report.
Persistent Subretinal Fluid Following Diabetic Tractional Retinal Detachment Repair: Risk Factors, Natural History, and Management Outcomes

Ahmed Algethami, Saudi Arabia

Purpose
To study the natural history, anatomical and functional outcomes of persistent subretinal fluid (SRF) after pars plana vitrectomy (PPV) for diabetic tractional retinal detachment (TRD) and combined traction-rhegmatogenous retinal detachment (TRRD)

Setting/Venue
King Khaled eye specialist hospital, Riyadh, Saudi Arabia.

Methods
METHODS: Retrospective interventional case series of 43 patients (46 eyes) with persistent SRF following PPV for diabetic TRD or combined TRRD from January 2010 to December 2017 at single tertiary institution. Primary outcomes included best corrected visual acuity (BCVA) and central foveal thickness (CFT).

Results
RESULTS: Thirty-one eyes (67.4%) had macula-off TRD, 5 (10.9%) had fovea-threatening TRD and 10 (21.7%) had combined TRRD. The mean (±SD) duration of decreased vision was 48.0±58.2 weeks. The mean follow-up duration was 21±13.2 months. Residual macular SRF was detected by optical coherence tomography in all eyes at 3 months and in 10 eyes (23.8%) at 12 months after surgery. Only 3 eyes (6.5%) had persistent SRF at final follow up. The mean time to resolution was 10.6 ±4.1 months [range 6.0-23.0]. 13 eyes received additional intervention to address SRF. The mean CFT gradually improved until final follow up (P-value <0.001). The mean BCVA improved from 1.62 ±0.88 LogMAR at presentation to 1.05 ±0.76 LogMAR at final follow up. No statistically significant difference in final BCVA was found between eyes that had intervention and eyes that were observed (P value= 0.762).

Conclusions
Conclusion: persistent SRF after diabetic vitrectomy resolves slowly over time with gradual improvement in visual acuity. Additional drainage of persistent SRF may not be necessary.

Financial Disclosure
None
Heavy silicone oil Densiron-68 as an intraocular tamponade for retinal detachments associated with inferior retinal breaks: 10-year study of outcomes and complications

**Purpose**
To report the anatomical and functional outcomes and complications of Densiron-68 as an intraocular tamponade after vitrectomy in eyes with retinal detachments (RDs) associated with inferior retinal breaks.

**Setting/Venue**
Retrospective, non-comparative case series from the University Hospitals of Derby and Burton NHS Foundation Trust.

**Methods**
All cases that underwent vitrectomy surgery with Densiron-68 between 31 December 2010 and 31 December 2020 were included. The primary outcome measure was the rate of anatomical reattachment of the retina. Secondary outcomes included the pre- to postoperative change in visual acuity and complication rates associated with Densiron-68.

**Results**
140 eyes of 139 patients were included in the study. Anatomical success rate with one operation was 66.4% and with further surgery 79.3%. Visual acuity improved from mean LogMAR of 1.07 (SD 0.90) to 0.82 (SD 0.82), p = 0.0150. Postoperative complications included cataract formation (63.3%), rise in intraocular pressure (IOP) ≥30mmHg (42.2%), cystoid macular oedema (10%), epiretinal membrane (10%), uveitis (3.6%), glaucoma (2.1%) and emulsification (2.1%).

**Conclusions**
Good anatomical and functional success rates can be achieved with Densiron-68 for eyes with primary RDs and eyes with complex retinal re-detachments after prior retinal surgery. Patients should be counselled appropriately about the postoperative complications, most notably a rise in IOP with Densiron-68 in-situ and after its removal, which may lead to the development of secondary glaucoma or progression of pre-existing glaucoma.

**Financial Disclosure**
No financial disclosures
**Title**
Internal Limiting Membrane Peeling Effect in Eyes with Major Diabetic Fibrovascular Proliferation to Prevent Mid-term Post-vitrectomy Epiretinal Membrane Development

**Purpose**
Post-operative proliferation with epiretinal membrane development is a major complication after vitrectomy for complex diabetic retinopathy. Prompt surgical treatment with internal limiting membrane (ILM) peeling seems to have an important prognostic value in these cases, preventing postoperative proliferation and epiretinal membrane (ERM) development. The effect of ILM peeling during vitrectomy in diabetic macular edema has been subject of several publications, but its role to prevent mid-term post-vitrectomy ERM development is not well established. The authors’ purpose is to evaluate the morpho-functional results after ILM peeling, particularly with respect to its effect on the prevention of post-vitrectomy ERM development in patients with a major diabetic fibrovascular proliferation.

**Setting/Venue**
Department of Ophthalmology in Beatriz Ângelo Hospital.

**Methods**
Retrospective, comparative study including 50 eyes from 50 diabetic patients that had undergone pars plana vitrectomy (PPV) for fibrovascular proliferation. Eyes were divided in two groups according to surgical treatment: group 1 performed PPV with ILM peeling in the macular area and group 2 performed only PPV. Best corrected visual acuity (BCVA), central retinal thickness (CMT) and the presence of epiretinal membrane (ERM) documented by optical coherence tomography were evaluated at 6 months postoperatively. The reliability of the sample size was tested at 95% power and 0,05 significance level (95% CI) using statistical software Stata/MP version 14.1. Continuous variables were evaluated with t-Student test.

**Results**
The study cohort was comprised of 27 eyes of 27 patients in group 1 with a mean age of 51,0±3,15 years and 23 eyes of 23 patients in group 2 with a mean age of 52,1±3,63 years. There were no significant differences between groups regarding pre-operative variables (age, gender, preoperative BCVA, CMT and phakic/pseudophakic status). At 6 months postoperatively, ERM was documented in 4 eyes (14,8%) in group 1 and 10 eyes (43,5%) in group 2 (p<0,05) and CMT was 189,90±42,3 µm and 265,40±77,1 µm respectively (p<0,05). Although visual improvement had been observed in both groups, it was not statistically different (0,35±0,05 in group 1 and 0,28±0,05 in group 2 p>0,05).

**Conclusions**
This study supports the idea that complete ILM peeling around macular area during PPV may avoid postoperative proliferation and ERM development in eyes with major diabetic fibrovascular proliferation, with additional significant reduction of CMT, resulting in better anatomic and functional prognosis for these patients.

**Financial Disclosure**
The authors have no financial interests to disclose.
Comparison of 27-gauge to 23-gauge pars plana vitrectomy for the treatment of vitreous amyloidosis in hereditary transthyretin amyloidosis – an experimental trial

**Purpose**
A 27-gauge trocar pars plana vitrectomy (PPV) system has been used successfully in surgery for epiretinal membrane and retinal detachment. The advantages of a smaller sclerectomy in these cases is reduced need for scleral sutures and reduced postoperative hypotony. In hereditary transthyretin amyloidosis (hATTR) patients, amyloid fibrils are formed in the ciliary body and retinal pigmented epithelium and they aggregate in the vitreous humor. Clinically, vitreous opacities in amyloidosis can lead to significant symptoms of floaters and reduced visual acuity. Current systemic treatments are ineffective for vitreous amyloidosis in hATTR and the only available treatment is PPV. We aim to explore the use of 27-gauge PPV in the treatment vitreous amyloidosis.

**Setting/Venue**
Ophthalmology Department, Centro Hospitalar Universitário do Porto

**Methods**
Ten eyes from ten patients undergoing PPV for treatment of vitreous amyloidosis because of decreased visual acuity were randomized 1:1 to either 27-gauge (27G) or 23-gauge (23G) systems with 7500 cuts-per-minute probes (Constellation Vision System, Alcon Laboratories, Inc., USA). Surgery time, intraoperative and postoperative complications, improvement in best-corrected visual acuity (BCVA) from preoperative to week 1 postoperative and intraocular pressure (IOP) at week 1 postoperative were compared. A video showing central vitrectomy with each one of the probes is also available. Values are shown as median [minimum – maximum].

**Results**
Median age was 52 [44-54] years in 27G and 53 [46-64] years in 23G. In the 27G group, 3/5 cases had to be converted to 23-gauge trocars because vitrectomy was not effective and / or posterior vitreous detachment was impossible. No other complications were noted. No case in the 27G group that was not converted to 23-gauge system (0/2 cases) required sutures, whereas three patients that end up using 23-guage (3/8 cases) needed scleral sutures for proper wound closing. Surgical time was 55 [40-100] min in 27G and 45 [38-60] min in 23G groups. Postoperative IOP was 20 [44-54] years in 27G and 20 [46-64] years in 23G groups. Best-corrected visual acuity improved from 0.3 [0.2-0.4] to 0.8 [0.6-1.0] and from 0.3 [0.2-0.6] to 0.8 [0.6-1.0] in 23G and 27G groups, respectively.

**Conclusions**
Comparing to a 23-gauge system, 27-gauge probes may difficult vitrectomy and posterior vitreous detachment in hATTR patients. We observed longer surgery time and the need to convert to 23-gauge in a substantial number of cases. Mutant transthyretin forms amyloid fibrils that attach to the vitreous matrix, namely to collagen and proteoglycans, probably making it harder to cut and aspirate. The fact that these patients undergo vitrectomy at young age may also be a contributive factor. Despite the small sample of this work, our work suggests that 27-gauge vitrectomy must be optimized in hATTR patients. New probes with higher cutting rates may show different results.

**Financial Disclosure**
No financial disclosures
Role of microperimetry in observation and treatment in patients with macular holes

Purpose
To assess the role of microperimetry in dynamic observation and treatment of patients with macular holes.

Setting/Venue
S.N. Fedorov NMRC "MNTK "Eye Microsurgery", Volgograd Branch

Methods
Retrospective study of the microinvasive vitrectomy results using 25G or 27G technologies in 29 patients (29 eyes) with idiopathic macular holes (IMH). The examination included the determination of the best corrected visual acuity (BCVA), tonometry, perimetry, ultrasound biometry, optical coherence tomography, fundus photography, microperimetry.

Results
After surgical treatment all patients showed a significant improvement in BCVA and retinal photosensitivity (p<0.001). A formula was derived for the dependence of BCVA after treatment on the initial retinal photosensitivity and the minimum IMH size, which can be applied to predict the results of surgical treatment.

Conclusions
Microperimetry is a modern non-invasive examination method that allows with a higher density and resolution to localize central defects of the visual field and to carry out thorough monitoring before and after surgical treatment. The study of the retinal photosensitivity in the macular region and the minimum IMH size before treatment allow to predict BCVA in the postoperative period.

Financial Disclosure
none
Title
Comparison of Short Term Results of Dexamethasone Intravitreal Implant for Retinal Vein Occlusion in Vitrectomised and Non-vitrectomised Eyes

Purpose
Macular oedema (MO) is characterized by the accumulation of extracellular fluid between the retinal layers. MO may be associated with many pathological conditions such as diabetic retinopathy, retinal vein occlusion and inflammatory diseases. Intravitreal dexamethasone implant (DEX; Ozurdex, Allergan, Irvine, CA, USA) is widely used in MO treatment. It has been shown that the efficacy and half-life of intravitreal drugs are reduced due to increased drug clearance in vitrectomised eyes. Our aim is to compare the short-term results of intravitreal dexamethasone implant for retinal vein occlusion (RVO) in vitrectomised and non-vitrectomised eyes.

Setting/Venue
Retrospective, consecutive, interventional case series / Ordu University, School of Medicine, Department of Ophthalmology

Methods
The records of 28 pseudophakic eyes with or without vitrectomy but receiving DEX for RVT after poor response to anti-vascular endothelial growth factor were analyzed retrospectively. Central macular thickness (CMT) measurement by optical coherence tomography, intraocular pressure (IOP) and best corrected visual acuity (BCVA) examinations were performed before, 1 and 3 months after implantation.

Results
The BCVA, CMT and IOP measurements were evaluated to compare the effectiveness of the dexamethasone implant between the age and sex-matched vitrectomized group (12 eyes) and the non-vitrectomized group (16 eyes). In the nonvitrectomized group, logmar VA improved from mean 1.39 ± 0.27 at the beginning to 0.85 ± 0.18 and 1.05 ± 0.24 after 1 and 3 months, respectively. In the vitrectomized group, the initial logmar VA improved from mean 1.52 ± 0.41 to 1.11 ± 0.49 and 1.19 ± 0.43 after 1 and 3 months, respectively. In the non-vitrectomised group, the CMT was mean 666.75 ± 170.81 before DEX implantation, 244.75 ± 74.44 and 288.70 ± 62.44 after 1 and 3 months, respectively. In the vitrectomised group, the CMT was mean 662.25 ± 202.30, 380.25 ± 42.35, and 398.37 ± 100.98 at before, 1 and 3 months, respectively. In both groups, BCVA and CMT significantly improved at 1 and 3 months after DEX implantation. IOP increased in 2 eyes in the vitrectomized group and 3 eyes in the nonvitrectomized group. However, it was controlled with IOP lowering medication. There was no statistically significant difference in BCVA, CMT and IOP between the two treatment groups at any time point.

Conclusions
The short-term effectiveness of the DEX implant is not affected by previous vitrectomy surgeries in eyes with RVO. The effects on SMT, IOP and BCVA in the first 3 months were similar to eyes without vitrectomy. Studies evaluating the long-term effects of dexamethasone multiple injections in vitrectomized eyes will be guiding in this regard.

Financial Disclosure
NONE
Post-Vitrectomy Endophthalmitis: An eye-devouring consequence

**Purpose**
To study the clinical profile and outcome of patients developing endophthalmitis after vitrectomy

**Setting/Venue**
Tertiary Eye Care Centre

**Methods**
The study was initiated after approval from the Institutional Ethics Committee to retrospectively analyze the data from a series of 3100 consecutive vitrectomy surgeries performed from January 2015 to January 2109. The tenets of the Declaration of Helsinki were followed and informed consent was obtained from the patients for use of their data from medical records for research purpose. Endophthalmitis developing after vitrectomy was defined as presence of unusual inflammation in the vitreous cavity or anterior chamber within a period of 6 weeks after surgery along with microbiological evidence of bacterial/fungal infection. All cases of endophthalmitis in this study was culture-positive. All patients taken up for vitrectomy were prescribed antibiotic eye drops (gatifloxacin 0.3%) 4 times per day for application from 3 days prior to surgery. Pre-operatively 5% povidone-iodine solution was instilled in the conjunctival sac and was allowed a contact period of 3 minutes followed by periocular cleaning with 1% povidone iodine solution before draping. Following the surgery the patients were put on oral antibiotics and anti-inflammatory agents, topical antibiotics and topical steroids routinely. The cases were followed up the very next day before being called for the next follow up at 1 week interval. For the patients who developed endophthalmitis data such as age of the patient, sex of the patient, indication for surgery, which eye was affected, as well as pre-operative visual acuity were obtained. The mean age of the patients was 21.12 years. The mean interval from surgery to diagnosis of endophthalmitis was 7.37 days. 3 of the patients were known diabetics (37.5 %), one patient was on oral steroids for associated systemic illness (12.5 %).

**Results**
In our series of 3100 consecutive vitrectomies 8 patients (0.26%) developed endophthalmitis in the post-operative period. All of them developed the dreaded complication within a period of 15 days from the vitrectomy surgery. All the surgeries performed in our series were 23 Gauge trans conjunctival vitrectomies. The indication for surgery in the cases which developed endophthalmitis were proliferative diabetic retinopathy (PDR) in 3 cases (37.5 %), traumatic vitreous haemorrhage in 2 cases (25 %), vasculitis related vitreous haemorrhage in 2 cases (25 %) and a traumatic retinal detachment in 1 case (12.5 %). The mean visual acuity on presentation was 1.4 LogMAR. Six of the patients were male (75 %) and 2 were female (25 %). The mean age of the patients was 21.12 years. The mean interval from surgery to diagnosis of endophthalmitis was 7.37 days. 3 of the patients were known diabetics (37.5 %). One patient was on oral steroids for associated systemic illness (12.5 %). Two of the patients presented with ocular motility restriction along with the acute signs of inflammation (25 %). Intravitreal injection of antibiotics vancomycin and amikacin was given to 2 patients (25 %) and 1 patient received a combination of the above antibiotics and steroid intravitreal injection (12.5 %). Repeat vitrectomy was performed for 4 (50 %) of the cases with 1 patient out of them having to undergo repeat surgery.

**Conclusions**
Endophthalmitis after vitrectomy, though rare, usually ends in a grave clinical picture with very poor visual and structural prognosis. Extreme caution with regard to asepsis in the peri-operative period is essential to reduce the incidence and morbidity of this condition.

**Financial Disclosure**
Not Applicable
### Title
Management of intraocular foreign bodies in the posterior segment – analyses of the last 10 years

### Purpose
Intraocular foreign bodies (IOFBs) are a serious form of ocular injury that can cause direct mechanical damage to the eye but can also have a significant risk of associated post-traumatic endophthalmitis. Pars plana vitrectomy (PPV) is the most commonly used technique to remove IOFBs from the posterior segment. The purpose of this study was to evaluate the management of posterior segment IOFB in our service, as well as the clinical characteristics, complications, visual outcomes, and globe survival after IOFB extraction via PPV.

### Setting/Venue
Tertiary ophthalmology center and surgical retina reference center, in Portugal.

### Methods
Patients that suffered a penetrating eye injury with IOFB retained in posterior segment who underwent PPV for IOFB extraction between 2010 and 2020 were included. All patients were operated by the same surgeon. Patients with IOFB in the anterior segment or lens were excluded. We collected data from patients’ archives, namely patient’s demographic data, diagnostic tools, pre-surgical complications, and management. Timing of the first ophthalmologic examination and timing of PPV, surgical procedures, post-surgical complications, visual outcome, and globe survival were also collected. All statistical analyses were performed using SPSS statistical software (SPSS, Inc., Chicago, IL, USA). Non-parametric Mann-Whitney test was used to evaluate differences between groups. A p value of 0,01 or less was considered statistically significant.

### Results
38 eyes were included, 86,8% males and 13,2% females with mean age of 48,68 years old. 59,5% came to the ophthalmology emergency at the same day of the accident, but 16,2% took 3 days or more. The diagnosis of IOFB was confirmed by CT-scan (83,3% of the cases), radiography (8,3%), ultrasound (5,6%), or MRI (2,6%). The most common complications on initial examination included traumatic cataract (52,6%), retinal lesions (34,2%) and hyphema (23,7%). Also, 42,1 % of patients developed endophthalmitis before IOFB extraction. Most patients (84,2%) had systemic antibiotics before IOFB extraction and 71,1% received intravitreal antibiotics. Primary closure of the wound was done on 45,9% of eyes. All had a PPV to extract the IOFB, performed on a median of 6 days after first ophthalmological contact. 84,2% also had a combined cataract surgery. Comparing the 15,8% of eyes that ended developing phthisis bulbi with those who didn’t, the only statistically significant difference (p<0,01) was the time between first ophthalmological contact and VPP, that was superior on the phthisis bulbi group, with a median of 13 days. The development of endophthalmitis was not significantly related to a superior time before surgery, nor to the use of intravitreal or systemic antibiotics.

### Conclusions
Ocular trauma with IOFBs can have serious ocular complications, such as RD and endophthalmitis that can greatly affect the visual outcome. Most of our patients had traumas that occurred in an agricultural setting which usually gives rise to dirty wounds and probably contaminated IOFBs. This fact could possibly justify our rather high rate of 42% of endophthalmitis (which is, nonetheless, within what is described in the literature). We had a significant number of eyes that ended up developing phthisis bulbi which was related to a superior time delay to PPV. We conclude that our service could benefit from a protocol for IOFB suspicion cases, and it would be beneficial to find a solution to diminish the delay of PPV.

### Financial Disclosure
The authors have no financial interests
Silicone oil tamponade for persistent macular holes

Purpose
The debate about the best re-treatment approach for post-operatively persistent or recurring macular holes is ongoing. To allow for a comparison with alternative surgical therapies, we assessed the anatomical and functional outcome of a temporary tamponade with conventional silicone oil in persistent or recurrent full-thickness macular holes.

Setting/Venue
Retrospective clinical study

Methods
Patients with full-thickness macular holes that persisted or recurred following vitrectomy with internal limiting membrane peeling and gas tamponade that received re-treatment by temporary silicone oil tamponade without postoperative positioning were included. Retrospective assessment of anatomical closure rate by optical coherence tomography and change of best-corrected visual acuity (BCVA) was performed.

Results
A total of 33 eyes of 33 consecutive patients were included. Macular hole closure following silicone oil tamponade was achieved in 30 of 33 eyes (90.9%). Median BCVA improved from 1.00 logMAR (interquartile range, 0.60–1.00) to 0.65 logMAR (0.49–1.00; p = 0.010) after silicone oil removal. In patients with macular hole closure, 61.3% showed functional improvement with median BCVA changing from 1.00 logMAR (0.70–1.00) to 0.60 logMAR (0.49–1.00; p = 0.0005). Mean minimal linear diameter of macular holes before ILM peeling was 391.0 µm (±137.8; range 133–630), and 48.5% of macular holes were 400+ µm in diameter.

Conclusions
Treatment of persistent or recurrent full-thickness macular holes by temporary conventional silicone oil tamponade without postoperative positioning results in a high closure rate and a significant mean improvement of visual acuity.

Financial Disclosure
JQL has nothing to disclose. RB has nothing to disclose. FGH reports personal fees from Acucela, grants and personal fees from Allergan, grants and personal fees from Bayer, personal fees from Bioeq, personal fees from Boehringer Ingelheim, grants and personal fees from Carl Zeiss Meditec, grants and personal fees from Genentech, grants and personal fees from Heidelberg Engineering, personal fees from Merz, personal fees from NightstarX, grants and personal fees from Nonius, personal fees from Optikon, personal fees from Zeiss, and personal fees from Carl Zeiss Meditec.

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The use of microperimetry in assessing visual function after vitrectomy with endotamponade due to rhegmatogenous retinal detachment (RRD).

**Purpose**
To evaluate changes in retinal sensitivity after vitrectomy with gas and silicone oil tamponade due to rhegmatogenous retinal detachment.

**Setting/Venue**
N. I. Pirogov National Medical and Surgical Center of the Ministry of Healthcare of the Russian Federation.

**Methods**
20 cases of surgery treatment of patients with primary macula-off RRD were enrolled. All cases were divided in two groups depending on the type of endotamponade. In the 1st group (10 eyes) a vitreoretinal surgery with silicone oil tamponade (1300 cSt) was performed. The 2d group (10 eyes) included only cases with a gas (C2F6) tamponade. The control group included contralateral eyes without ophthalmic pathology. An outcome was best-corrected visual acuity (BCVA) and retinal sensitivity. The examination was performed 30 days after silicone oil removal for the 1st group and 30 days after a primary surgery with a gas tamponade for the 2d group. The participants underwent microperimetry in the expert mode 10°. The mean sensitivity threshold was calculated for each ring (zone I-IV) of the scanning grid, where zone I corresponded to 0°.

**Results**
The duration of the detachment did not differ between the groups ($p=0.23$). The mean macular sensitivity threshold in the 1st group was significantly reduced ($19.7 \pm 2.7\* dB$), both in comparison with the 2d group ($p=0.007$) and the control group ($p=0.003$). Differentiation by zones in the 1st group revealed a decrease in each analyzed zone in comparison with the control group and a decrease in zone II ($p=0.031$) and in zone IV ($p=0.038$) in comparison with the 2d group. In zone I of the 1st group the relative scotoma was revealed in 5 cases out of 15 (33%). The mean macular sensitivity threshold in the 2d group was significantly reduced in each zone in comparison with the control group. A strong direct correlation was found between BCVA and mean macular sensitivity threshold in the 2d group ($r=0.87$).

**Conclusions**
There is a decrease in the functional parameters of the retina after vitrectomy with silicone oil in comparison with gas tamponade. This decrease is in the form of a reduction of retinal sensitivity in the 10° zone according to microperimetry data. Microperimetry is the preferred research method when assessing the dynamics of the functional parameters of the retina after vitrectomy with various types of tamponade.

**Financial Disclosure**
The authors received no specific external funding.
**Title**
Case Series: Anatomical and Functional outcomes after Lamellar Hole Surgery

**Purpose**
Lamellar hole (LH) surgery remains controversial and evidence for long term outcomes is scarce. This study aimed to evaluate anatomical and functional outcomes after LH surgery with pars plans vitrectomy (PPV) in a local cohort of patients over a 12 month follow up period.

**Setting/Venue**
This study retrospectively reviewed the medical records of 41 patients who underwent PPV for LH between February 2015 and February 2020 in Great Western Hospital NHS Foundation Trust.

**Methods**
Baseline demographics included ocular and systemic co-morbidities, operation details and LH characteristics. Primary outcome was LH closure. All analyses were carried out using SPSS and GraphPad Prism.

**Results**
Forty-seven eyes of 41 patients were operated on from 16th February 2015 to 18th February 2020. Seventy-three percent of patients (n=30) were diagnosed with tractional LH, compared to 27% (n=11) with degenerative LH. All patients underwent 23G PPV, 98% (n=40) of patients underwent internal limiting membrane (ILM) peel and 71% (n=29) underwent ERM peel. Mean LH volume and surface area were 0.126±0.118mm³ and 2.32±1.9mm² respectively. In 93% (n=38) of patients anatomical resolution of the lamellar hole was achieved. In one patient the LH was still present and in one patient their LH progressed to a macular hole (MH). Two patients experienced complications post-operatively: one developed glaucoma and one required re-operation with PPV. Foveal thickness increased from 198±54μm pre-operatively to 324±77μm at 1 month post-operatively (P<0.0005) and then decreased to 312±81μm at 3 months (P<0.0005) and 296±62μm at 12 months (P<0.0005). Binary logistic regression did not demonstrate any predictors for LH closure. Multiple linear regression analysis (Rsq = 0.6126) with 9 anatomical variables at baseline significantly predicted the foveal thickness at last follow-up (P<0.001).

**Conclusions**
PPV is a safe treatment for LH and is effective in terms of anatomical outcomes with a low risk of complication. Measurement of anatomical variables at baseline can accurately predict the final outcome.

**Financial Disclosure**
N/A
Intraretinal Hyperreflective Lines in Eyes with Vitreomacular Adhesion

**Purpose**
To investigate the prevalence of intraretinal hyperreflective lines (IHL) in eyes with vitreomacular adhesion.

**Setting/Venue**
A retrospective study in Ophthalmology Consult - Ophthalmology Department of the University of Health Science, Ankara Ulucanlar Eye Education and Research Hospital, Ankara, Turkey.

**Methods**
49 eyes of 49 patients with VMA were included. Spectral domain optical coherence tomography (SD-OCT) volume scans were analysed for the presence of a central vertical hyperreflective line. The sequential OCT images of the fellow eyes of patients with IHL were further studied to analyse the changes in vitreous interface status during the follow up period.

**Results**
IHL was observed in 10 of 49 eyes (20.4%) of patients with vitreomacular adhesion (VMA). The vitreous interface status of patients with IHL included VMA (eight eyes) and posterior hyaloid detachment on foveal region (two eyes). In fellow eyes, 5 VMA, 2 vitreomacular traction (VMT), 2 full thickness macular hole (FTMH), 1 full thickness macular hole – rhegmatogenous retinal detachment (FTMH-RRD) were detected. At later periods, in the 2 eyes with VMA, lamellar and full-thickness macular hole developed. 5 of fellow eyes displayed IHL in the course of time.

**Conclusions**
The presence of IHL detected by SD-OCT in patients with VMA may indicate that posterior hyaloid firmly attached to the fovea. This in turn may reflect the onset of foveal dehiscence due to the structural changes on foveal architecture. The increase in the prevalence of vitreomacular interface disease (VMID) in fellow eyes of patients with IHL may require close follow up.

**Financial Disclosure**
None
Vitrectomy surprise hit hard

**Purpose**
To report the management of occult posterior globe rupture which was detected during vitrectomy

**Setting/Venue**
Ophthalmology Department, National University of Malaysia, Jalan Ya'acob Latif, Bandar Tun Razak, Cheras 56000 Kuala Lumpur Malaysia

**Methods**
A case report

**Results**
A 54 year-old gentleman presented with history of poor vision for 3 months with unnoticed prior history of trauma. Anterior segment was normal. He was diagnosed with subtotal bullous RRD with no apparent tear seen. Vitrectomy was commenced and upon exploration, there was posterior globe rupture with retinal and vitreous incarceration. Suturing of the scleral wound was done with heavy liquid in situ in the same setting. Orbital imaging post-surgery revealed the presence of hyperdense intraorbital foreign body. We will be sharing our video of intraoperative management.

**Conclusions**
This is an unusual presentation of posterior globe rupture. Not only it was unnoticed by the patient but lack of evidence on the anterior segment findings. Detection of posterior globe rupture remained a challenge which require high index of suspicion with appropriate management.

**Financial Disclosure**
Ophthalmology Department National University of Malaysia Postgraduate Master Student in Ophthalmology
### Title
Efficiency of phacoemulsification of primary cataract by the second stage after vitreoretinal surgery of PDR patients.

### Purpose
Evaluation the efficacy of phacoemulsification of primary cataract by the second stage after vitreoretinal surgery of PDR patients.

### Setting/Venue
National Medical and Surgical Center named after N.I. Pirogov of the Ministry of Healthcare of the Russian Federation.

### Methods
67 cases of surgery treatment of patients with PDR and complicated primary cataract were enrolled. This patients were divided into two groups depending on the treatment tactics. In the 1st group patients were subjected to a two-step surgical procedure: vitreoretinal surgery with silicone oil tamponade performed as the 1st step in their treatment; followed by the 2d step, phacoemulsification surgery and silicone oil removal, and the IOL implantation, respectively. In the 2d group phacoemulsification performed simultaneously with vitreoretinal surgery: phacoemulsification, IOL implantation, vitreoretinal surgery with silicone oil tamponade. The second step included the removal of silicone oil from the vitreous cavity.

### Results
Visual functions improved in 88.6% of cases in group 1, and in 68.7% in group 2. Frequency of postoperative complications: the severity of inflammatory reactions on the 2nd day after the 1st step surgery was significantly higher in patients of group II. The development of neovascular glaucoma was significantly more frequent in patients of group II (n=9; 28,1%) than in patients of group I (n=3; 8,6%), p=0.037.

### Conclusions
Outcomes of the preliminary studies suggest that it is more viable to perform phacoemulsification surgery sometime later along with silicone oil removal on PDR patients with complicated primary cataract. This sequence of treatment procedure ensures a more gentle approach to the anatomic structures of the eye during the first stage (vitreoretinal surgery) and contributes to the reduction in the number of intraoperative and postoperative complications.

### Financial Disclosure
No author has a financial or property interest in any material or method mentioned.
Minimum linear diameter measurements of macular holes using horizontal linear and radial OCT scans

Purpose
To assess repeatability and reproducibility of measuring the minimum linear diameter (MLD) of macular holes (MH) using horizontal linear and radial scan modes in optical coherence tomography (OCT).

Setting/Venue
Department of Ophthalmology, Hospital Rechts der Isar, Technical University of Munich (TUM), Germany

Methods
Patients with concurrent sets of radial and horizontal linear OCT volume scans were included. The MLD was measured twice in both scan modes by six raters of 3 different experience levels (groups). Outcome measures were the reliability and repeatability of MLD measurements.

Results
Fifty patients were included. Mean MLD was 317.21(±170.63) µm in the horizontal linear and 364.52 (±161.71) µm in the radial mode, a difference of 47.31 (±26.48) µm (p<0.001). The intra-group coefficients of repeatability (CR) for the horizontal linear mode were 23µm, 33µm and 45µm, and for the radial mode 25µm, 44µm and 57µm for group 1, 2 and 3, respectively. The inter-group CR, taking group 1 as reference standard for groups 2 and 3, were 74µm and 71µm for the linear mode, and 62µm and 78µm for the radial mode. For both the horizontal and the radial mode, there were no significant differences in MLD measurements, either within raters (p≥0.22 and p≥0.16) or groups (p=0.91 and p=0.31), or between raters (p=0.98 and p=0.97) and groups (p=0.76 and p=0.81). For both the linear and the radial mode, however, there was a significant increase in variability from group 1 to group 2 (p<0.01, p<0.01), group 1 to group 3 (p<0.01, p<0.01) and from group 2 to group 3 (p=0.015, p=0.003). In the radial scan mode, the MLD was identified within 15° of the horizontal meridian in 27% and within 15° of the vertical meridian in 26.7%, with the remainder (46.3%) in oblique meridians.

Conclusions
The radial mode provides comparably good repeatability and reproducibility to the horizontal mode for measurement of MLD size of MH. The variability of measurements decreases in both modes as the experience of the raters increases. In a majority of cases the MLD does not lie in the horizontal meridian and would be underestimated using a horizontal OCT mode.
Analysis of the activity of vitreoretinal surgery in metropolitan France in 2016: Impact on training capacities

**Purpose**
To describe vitreoretinal surgery activity and vitreoretinal surgeons in private or public practice in metropolitan France over the year 2016 in order to anticipate surgical training needs.

**Setting/Venue**
We identified all medical procedures carried out in 2016 using the French National Healthcare System database, on behalf of the French Council of professors in Ophthalmology (COUF).

**Methods**
The study investigated the entire population aged 20 years and older on 1 January 2016 that had undergone vitreoretinal surgery, alone or combined with cataract surgery. We calculated the incidence of surgeries per 100,000 inhabitants 20 years of age and older in metropolitan France performed by ophthalmologists carrying at least 50 procedures during the year, the number of surgeons doing these surgeries, the mean age of these practitioners, and the number of surgeons older than 55 years.

**Results**
The study population included 57,947 posterior segment surgeries, 40% in the public sector and 49% in the private sector for private surgeons and/or public centers performing at least 50 surgeries/year. Private surgeons and/or public centers performing less than 50 surgeries/year yielded the remaining 11% of surgeries. The analysis included 356 vitreoretinal surgeons with a mean age of 41 ±10 years (39% female) in the public sector and a mean age of 47 ±10 years (14% female) in the private sector. The majority of urgent surgeries were for retinal detachment in 50.3% of cases (n = 29121). This study identified the university regions with the least number of surgeons and regions with surgeons older than 55 years of age, thus anticipating the training of new surgeons. Within the next 10 years, in order to maintain surgical activity, it will be necessary to train 56 vitreoretinal surgeons for regular activity in the field of surgical retina in France.

**Conclusions**
This study demonstrates the strong disparities in the geographic distribution of vitreoretinal surgery in France, and identifies regions that need training capacities to ensure a sufficient number of surgeons.

**Financial Disclosure**
None
Intravitreal Aflibercept Injection Therapy in Silicone Oil Filled Diabetic Eyes

Purpose
To investigate the effect of monthly intra-silicone Aflibercept injections on visual acuity (VA) and anatomical outcomes in eyes with diabetic tractional retinal detachment (RD) repair.

Setting/Venue
This was a single-hospital (Section of Surgical Sciences, Department of Ophthalmology, Faculty of Medicine, Giresun University), retrospective, case-control study of 10 eyes of 9 patients (study group) and 9 eyes of 9 patients (control group).

Methods
A retrospective evaluation of monthly intravitreal Aflibercept injection treatment that was performed in 10 eyes of 9 patients (study group) who had undergone diabetic tractional RD surgery (from August 1, 2018 through March 1, 2021) and received silicone oil was done. Intra-silicon injection of Aflibercept was performed intraoperatively and at 1, 2 and 3 months postoperatively. Silicone oil was removed 3 months after surgery in eyes with attached retinas. The main outcome measures were the logarithm of the minimum angle of resolution (logMAR) VA, central macular thickness (CMT), retinal reattachment rate, rate of epiretinal membrane (ERM) formation at 4th month.

Results
The study group was compared to a control group composed of age- and sex-matched controls (9 eyes of 9 patients- from August 1, 2018 through March 1, 2021) who had undergone diabetic tractional RD surgery and were not received intravitreal anti-vascular endothelial growth factor treatment. In the study group, logMAR VA improved from mean 1.88 ± 0.64 to 1.33 ± 0.45, (P =0.04), CMT improved from mean 478.92 ± 205.63 to 293.00 ± 68.8 (P=0.03), retinal reattachment was achieved in 7 of 10 eyes (70%), and ERM formation was observed in 3 of 10 eyes (33%) at 4 months. In the control group, logMAR VA improved from mean 1.52 ± 0.55 to 1.44 ± 0.56, P=0.55), CMT improved from mean 493.12 ± 199.87 to 335.00 ± 89.65 (P=0.6), retinal reattachment was achieved in 6 of 9 eyes (66%), and ERM formation was observed in 3 of 9 eyes (33%) at 4 months. A significant difference was observed in CMT improvement (P=0.03) and final VA (P=0.046), no significant difference in retinal reattachment rate (P= 0.65), or ERM formation (P=0.41) was observed between groups. Ocular adverse events associated with intra-silicone aflibercept injection were not observed.

Conclusions
The outcomes of vitreoretinal surgery using silicone oil for diabetic retinal detachment repair may be improved by monthly injection of intra-silicone aflibercept. Further prospective studies on larger numbers of patients are recommended for clarifying intra-silicone anti-vascular endothelial factor injection efficacy.
The Pit Evolution Story: A tale of 4 pits

**Purpose**
To report anatomical and functional outcomes of four cases of optic disc pit which underwent surgical intervention using four different techniques and to discuss variations in techniques as they have evolved over time.

**Setting/Venue**
A tertiary ophthalmic care and research centre

**Methods**
A retrospective interventional case series of 4 cases of optic disc pit maculopathy who underwent surgical intervention where four different surgical approaches were studied: • Case 1 - A 42 year old man underwent vitrectomy with standard arcade to arcade ILM peeling and gas tamponade followed by laser to edge of disc. • Case 2 - A 36 year old man underwent vitrectomy along with macular sparing ILM peel, stuffing of the disc pit and gas tamponade followed by laser. • Case 3 - A 6 year old boy was taken up for vitrectomy with ILM peel (macula sparing), SRF drainage via 39 GAUGE soft tip needle and gas tamponade. • Case 4 - A 15 year old female underwent vitrectomy with hAMG grafting and macular sparing ILM peel with gas tamponade.

**Results**
Anatomical and functional outcomes of these four varying techniques were studied. A successful procedure was defined as complete resolution of the neurosensory detachment on OCT with improvement in vision.  
Case 1 - The BCVA improved to 6/60 from 6/120 at 6 weeks with slight decrease in NSD. Unfortunately, 6 months down the line the NSD increased with drop in vision to 3/60.  
Case 2 - Preoperative BCVA of 6/18, showed mild decrease in NSD at 6 weeks. Patient was observed and followed up regularly. At 3 months post op, after undergoing laser to edge of disc, with complete resolution of the NSD, the BCVA improved to 6/12.  
Case 3 - The BCVA improved to 6/12, from 2/60 at 6 weeks with resolution of the NSD. Six months the fluid reappeared with drop in BCVA to 6/60 followed by spontaneous resolution of fluid and BCVA of 6/12 in the next 4 months and puzzling waxing and waning of SRF.  
Case 4 - A dramatic complete resolution of the NSD on day 1 with visual improvement to 6/18, from a preop BCVA of 6/24. The status 3 months postoperatively was satisfactory and no fluid noted on OCT.

**Conclusions**
Optic disc pit surgical management has always been controversial with various techniques being described over the years. Persistent Fluid or late resolution and recurrences have always lead to doubts on the optimal procedure for disc pits. In this series of 4 cases we describe the surgical variations in management of optic disc pit maculopathy. The hAMG Grafting technique seems promising with a more complete closure of the pit with fast and complete resolution of the NSD leading to better anatomical and functional improvement.

**Financial Disclosure**
NONE
### Title
Management of macular hole with concurrent retinal detachment

### Purpose
To present an interesting case of macular hole with concurrent retinal detachment and discuss the surgical challenges in such cases.

### Setting/Venue
Vitreo-retinal service, 2nd University eye clinic of Aristotle University of Thessaloniki. Papageorgiou General Hospital, Thessaloniki, Greece

### Methods
An 82 year-old woman with high myopia, retinal detachment and macular hole in her right eye attended the eye emergency clinic of our department. Complete ocular history, ophthalmic clinical examination and imaging (fundus colour photography and optical coherence tomography) were performed before and after the surgery. The surgical procedure was recorded: a 25G pars plana vitrectomy, ILM peeling was performed and the hyaloid cavity was filled with C3F8 20%. Postoperative instructions for face-down positioning were given to the patient.

### Results
Best corrected visual acuity was improved from hand movement to 1/10 after surgery. Complete closure of macular hole and successful re-attachment of the retina succeeded after surgery.

### Conclusions
In rare cases, a macular hole can co-exist with retinal detachment. Standard vitrectomy with ILM peeling and injection of internal tamponade gas could be an suitable surgical approach to address these challenging cases.
### Title
A new treatment method for hemorrhagic retinal detachment by drainage sclerotomy combined with subretinal and submacular injections of tPA

### Purpose
To evaluate the effect of a new drainage sclerotomy method combined with subretinal and submacular injections of recombinant tissue plasminogen activator (tPA) in treatment of hemorrhagic retinal detachment (RD).

### Setting/Venue
case-series report

### Methods
Eight eyes underwent vitrectomy combined with the evacuation of subretinal hemorrhage from the site of the sclerotomy. Among them, 2 eyes received subretinal injections of tPA, 3 eyes received intraoperative submacular injection of tPA, and the other 3 eyes received both subretinal and submacular injections of tPA. The regression of subfoveal hemorrhage was monitored after operation.

### Results
The submacular hemorrhages and the most of the subretinal hemorrhages were removed successfully in all eyes. The subfoveal hemorrhage was resolved between 1 day to 1 month postoperatively in the eyes with either subretinal injection or submacular injection or both. There was no vitreous or anterior chamber hemorrhage or elevated intraocular pressure observed after operation.

### Conclusions
Our results suggest that the external drainage of subretinal hemorrhages from the site of sclerotomy combined with subretinal and submacular injections of tPA, was an effective and safe therapeutic strategy for treating hemorrhagic RD.

### Financial Disclosure
no
Feasibility of internal limiting membrane peeling in epiretinal membrane surgery

Maximilian Gabriel
Austria

Purpose
To assess the feasibility of internal limiting membrane peeling in vitrectomies for idiopathic epiretinal membranes.

Setting/Venue
Explorative, prospective, single-center case series.

Methods
Patients with idiopathic epiretinal membranes were operated using 27-gauge vitrectomy. Exclusion criteria were myopia over 6 diopters, glaucoma, diabetes, idiopathic macular holes or pseudoholes, previous vitrectomy, patient age under 18 and other pathologic ocular conditions except cataract. Epiretinal membrane (ERM) peeling was performed with the aim to leave the internal limiting membrane (ILM) intact. Surgical success was therefore defined as ILM nonpeeling and evaluated by the surgeon intraoperatively. The presence of intraretinal hemorrhages in the peeled area and the inability to stain the ILM with a blue dye were defined as criteria for accidental ILM peeling. Metric parameters were descriptively summarized using mean and standard deviation (SD).

Results
25 eyes of 25 patients (14 men; 56%) were recruited and mean patient age at the time of surgery was 69.7 years (range 55 - 80, SD 6.7). ILM nonpeeling was achieved in 10 patients (40%). The patient group in which ILM nonpeeling was achieved showed no statistically significant differences in preoperative visual acuity (nonpeeling mean 0.52 Snellen, range 0.1 - 0.8, SD 0.2; peeling mean 0.45 Snellen, range 0.2 - 0.8, SD 0.16), axial eye length (nonpeeling mean 23.08 mm, range 21.02 - 24.14, SD 0.92; peeling mean 23.58 mm, range 21.98 - 25.12, SD 0.95) or preoperative spherical equivalent (nonpeeling mean 0.7 diopters, range -0.25 to +2.5, SD 0.2; peeling mean 0.18 mm, range -3.5 to +3.25, SD 1.76) compared to the ILM peeled group.

Conclusions
ILM nonpeeling was attainable in less than half of the cases in our series. Future trials should include more patients, determine preoperative anatomic or functional factors that could influence ERM/ILM adherence and compare anatomic and functional results of ILM peeled and nonpeeled eyes using multimodal imaging.

Financial Disclosure
None.
Lyophilized amniotic membrane patch combined with autologous blood covering in the treatment of refractory macular hole

Purpose
To observe the effect of lyophilized amniotic membrane patch combined with viscoelastic agent or autologous blood covering in the treatment eyes with refractory macular hole, including unclosed macular hole, high myopia macular hole, large diameter macular hole (> 700um).

Methods
Fifteen patients with refractory macular hole were performed with 23g or 25g vitreoretinal surgery. After liquid-gas exchange, according to the size of the macular hole, the lyophilized amniotic membrane patch (slightly larger than the macular hole) was selected to cover the surface of the macular hole, then covered with viscoelastic or autologous blood. Air tamponade were performed in all eyes, and all of them were asked to remain in the prone position for 1 weeks after the surgery.

Results
compared with lyophilized amniotic membrane patch combined with viscoelastic covering group, lyophilized amniotic membrane patch combined with autologous blood covering group, had a little amniotic patch deviation, but less amniotic patch shedding after operation. For the refractory macular hole with good amniotic membrane covering position, the macular hole was closed, and the postoperative visual acuity was improved.

Conclusions
Lyophilized amniotic membrane patch combined with autologous blood covering group has proven to be safe and effective of treatment refractory macular hole and the outcome needs further observation.

Financial Disclosure
no
Choroidal Vascularity Index and Choriocapillary Changes After Epiretinal Membrane Surgery

Purpose
To study the structural changes in the choroid after idiopathic epiretinal membrane (ERM) surgery via optical coherence tomography angiography (OCT-A) and enhanced depth imaging optical coherence tomography (EDI-OCT).

Setting/Venue
Gazi University School of Medicine, Ophthalmology Department, Retina Service.

Methods
Changes in the structure of the choroid after ERM surgery were studied in sixty-six eyes of thirty-three patients with unilateral idiopathic epiretinal membrane using optical coherence tomography (OCT) with enhanced depth imaging (EDI) and OCT-angiography (OCT-A). Choroidal vascularity index (CVI), Haller layer/choroidal thickness (H/C) ratio, and choriocapillaris flow density (CF) were used to compare the structural characteristics of the choroid with fellow eyes. OCT and OCT-A measurements were obtained at the baseline and six months after the ERM surgery.

Results
The mean CVI (0.60±0.04) and H/C values (0.69±0.08) of the ERM group at the baseline were higher than the mean CVI (0.58 ± 0.03) and H/C values (0.64 ± 0.09) of the control group (p: 0.009 and p:0.04 respectively), while postoperative mean CVI (0.58±0.03) and H/C values (0.63±0.08) of the ERM group were found to be similar to CVI (0.58 ± 0.03) and H/C values (0.63 ± 0.09) of the fellow eyes. (p: 0.761 and p:0.827 respectively) In addition, CVI and H/C ratio were decreased after surgery in the ERM eyes (p:0.009 and p:0.001, respectively) while no change was found in the fellow eyes between the baseline and postoperative measurements. (p:0.161 and p:0.827, respectively). The mean CF (0.88 ±0.28) of the ERM eyes was lower than the mean CF (1.09 ± 0.07) of the fellow eyes while no difference was found between the mean CF of ERM eyes(1.08 ± 0.1) and fellow eyes (1.11 ± 0.09) at the postoperative measurements. (p:0.001 and p:0.463, respectively). In addition, CF was increased after surgery in the ERM eyes while no difference was found between baseline and postoperative measurements in the fellow eyes. (p:0.041 and p:0.507, respectively)

Conclusions
The CVI and H/C ratio decreases while CF increases following the epiretinal membrane removal in contrast to the fellow eyes. Decreased H/C ratio and increased CF suggest structural changes especially in the small-sized vascular layers of the choroid. Epiretinal membrane appears to alter the hemodynamic properties of the choroid which might be reversible by surgery.

Financial Disclosure
We have no conflict of interest to disclose.
Title
Functional and morphological outcomes of the inverted internal limiting membrane flap technique in small and medium sized macular holes <400 µm

Purpose
To assess the effect of an internal limiting membrane flap (IF) in macular hole surgery on best-corrected visual acuity (BCVA) and integrity of the external limiting membrane (ELM) and ellipsoid zone (EZ).

Methods
Patients were included who had successful surgery for macular holes <400 µm with or without an IF. Main outcome measures were BCVA and restoration of the ELM and EZ at 12 months.

Results
Sixty patients were included, 36 with conventional peeling and 24 with an IF. BCVA improved from 0.74 (±0.30) to 0.26 (±0.20) logMAR in patients without and from 0.77 (±0.32) to 0.18 (±0.12) logMAR in patients with an IF, respectively. There was no difference in the integrity of the ELM and EZ in patients with or without an IF at either 3 (p=0.58, p=0.20), 6 (p=0.81, p=0.10), or 12 months (p=0.60, p=0.20) or in the BCVA at 3 (p=0.24), 6 (p=0.18) and 12 months (p=0.11). In the multivariable model, only pre-operative BCVA (p<0.01), EZ integrity (p=0.001), and age (p<0.01) were associated with the post-operative BCVA.

Conclusions
In patients undergoing surgery for macular holes <400 µm, the use of an IF did not affect the BCVA or the integrity of the ELM and EZ.

Financial Disclosure
no financial relations
**Purpose**
Pars plana vitrectomy (PPV) and scleral buckling (SB) are two of the most common surgical treatments for rhegmatogenous retinal detachments (RRD). This meta-analysis aimed to compare the efficacy and safety for PPV and SB in RRD repair.

**Methods**
A systematic literature review was performed using Ovid MEDLINE, EMBASE, and Cochrane CENTRAL from January 2000 to June 2020. Randomized controlled trials (RCTs) and observational studies reporting on the efficacy and/or safety of PPV and SB for the primary surgical management of RRDs were included. Categorical outcomes were reported as risk ratios (RR) and continuous outcomes were reported as weighted mean differences (WMD) with 95% confidence intervals (CI). A random effects model was used for all analyses. Number needed to treat (NNT) and number needed to harm (NNH) were reported. Risk of bias assessment was conducted with the Cochrane criteria for RCTs and the ROBINS-I tool for observational studies. The primary outcome was final best corrected visual acuity (BCVA). Secondary outcomes were primary and final reattachment rates and the incidence of adverse events.

**Results**
Across 38 studies, 5225 SB and 9473 PPV eyes were included. Median final follow up was 6 months (range: 1–60). Final BCVA significantly favored SB over PPV (WMD, 0.06 logMAR; 95%CI, 0.01 to 0.11; P=0.03). Compared to SB, PPV was associated with a higher incidence of cataracts (10.4% vs. 39.8%, respectively; RR, 3.48; 95%CI, 2.48 to 5.16; P<0.00001; NNH, 4) and iatrogenic breaks (0.5% vs. 7.9%, respectively; RR, 6.58; 95%CI, 2.98 to 14.52; P<0.00001; NNH, 12.5). However, PPV was associated with a lower incidence of subretinal/choroidal hemorrhage (0.6% vs. 5.5%, respectively; RR, 0.24; 95%CI, 0.09 to 0.67; P=0.0007; NNH, 20), choroidal detachment (0% vs. 4.1%, respectively; RR, 0.14; 95%CI, 0.04 to 0.54; P=0.004; NNH 12.5), and residual subretinal fluid (3.6% vs. 28.4%, respectively; RR, 0.18; 95%CI, 0.10 to 0.35; P<0.00001; NNH 3.85) compared to SB. PPV and SB had similar primary (86.2% vs. 85.0%, respectively; P=0.62) and final (96.7% vs. 97.8%, respectively; P=0.10) reattachment rates. There were no significant differences in operation time (P=0.52) and adverse event rates including diplopia (P=0.24), anterior chamber inflammation (P=0.27), elevated intraocular pressure (P=0.13), ocular hypertension (P=0.19), iris capture (P=0.84), proliferative vitreoretinopathy development (P=0.81), macular edema (P=0.86), macular hole (P=0.59), and epiretinal membrane formation (P=0.48).

**Conclusions**
For RRD repair, SB was associated with a better final BCVA compared to PPV. Primary and final reattachment rates were similar between the two procedures. PPV was favored for reduced choroidal detachment, choroidal/subretinal hemorrhage, and residual subretinal fluid while SB was favored for fewer iatrogenic breaks and reduced cataract formation.
Surgical approaches to optic disc pit maculopathy: seven case reports

**Purpose**
To evaluate the clinical outcomes of 7 patients with optic disc pit maculopathy submitted to different surgical procedures.

**Setting/Venue**
Noncomparative, retrospective, interventional case series at the University Hospital of Coimbra.

**Methods**
Seven patients aged 13 to 74 years were submitted to vitreoretinal surgery at the University Hospital of Coimbra throughout 2005 and 2020. Decreased visual acuity (VA) form baseline and macular detachment confirmed with OCT imaging were important criteria for surgical intervention and these were also the main postoperative outcomes. Vitrectomy, posterior hyaloid detachment, and gas tamponade were executed in all cases. Endolaser photocoagulation on the temporal margin of the optic pit, ILM peeling and inverted flap technique were successfully executed in 4 cases and stuffing of the pit with a free autograft of ILM was performed in 2 cases. Follow-up time ranged from 1 to 13 years.

**Results**
All surgeries consisted in pars plana vitrectomy with posterior vitreous detachment and gas tamponade with either 14% C3F8 or 20% SF6. Low-fluence argon endolaser was applied to the temporal margin of the optic pit in all but 2 cases; ILM peeling and inverted flap technique were successfully executed in 4 cases and stuffing of the pit with a free autograft of ILM was performed in 2 cases. There was VA improvement in 6 out of the 7 patients, within 4 months to 3 years after surgery. Complete macular reattachment was achieved in 5 cases. Three patients had recurrence of the macular detachment and one was submitted to reoperation. There were no surgical complications besides a cataract.

**Conclusions**
Vitrectomy with posterior vitreous detachment combined with either endolaser photocoagulation, ILM peeling and ILM stuffing techniques were safe and effective procedures for surgical treatment of OPM. Most patients had VA improvement and nearly complete macular reattachment with no recurrence.

**Financial Disclosure**
No financial interests or relations to declare.
Short-term progression of macular holes in patients awaiting surgery

**Purpose**
To determine a cutoff for progression of macular hole (MH) size.

**Setting/Venue**
Ophthalmology Department, Hospital rechts der Isar, Technical University of Munich (TUM), Ismaninger Str. 22, 81675 Munich, Germany

**Methods**
Patients were included who were waiting for MH surgery. Two observers performed 3 repeat sets of MH size measurements on optical coherence tomography (OCT) high-density radial scans at baseline and at 4 weeks. Main outcomes were change in minimum linear diameter (MLD) size and best-corrected visual acuity (BCVA).

**Results**
Fifty-one patients were included. The cutoff for an increase in MLD size calculated as the outer confidence limit for the 99.73% limits of agreement was 31 µm. This was independent of MH size. Using this cutoff, MLD size increased in 9/34 (26.5%) of patients without and in 14/17 (82.4%) of patients with vitreomacular traction (VMT) (p<0.001). Mean BCVA deteriorated in patients in whom the MH had progressed from 0.62 (±0.23) logMAR (20/83 Snellen) to 0.82 (±0.29) (20/132 Snellen) (p<0.001), while there was no significant change in BCVA in patients without MH progression (p=0.25). In 31% (16/51) of patients, classification of their MHs changed over the 4 week period.

**Conclusions**
Using a cutoff discriminates change from measurement error. A significant proportion of MHS progressed by 4 weeks, particularly in the presence of VMT, accompanied by a deterioration in BCVA.
Title
Lens densitometry for assessment and prediction of cataract progression after pars plana vitrectomy with C3F8-gas for retinal detachment

Purpose
Lens opacification is a common complication after pars plana vitrectomy (PPV) and knowing its progression would facilitate consulting patients. This study quantified and predicted the effect of PPV with C3F8-gas on the lens status after surgery in patients of various age and lens densitometry (LD) treated for rhegmatogenous retinal detachment (RRD).

Setting/Venue
Prospective study conducted between March 2018 to March 2020. The study followed the tenets of the Declaration of Helsinki and was approved by the Medical Institutional Review Board of Hamburg.

Methods
Data between March 2018 and March 2020 were evaluated retrospectively. The Pentacam® Nucleus Staging mode (PNS) was used to quantify lens opacification. A mixed effect regression model was created that is capable of predicting LD for any time after PPV by using age and baseline LD as dependent factors. Six random patients were excluded from the creation process of the model to test its power afterwards.

Results
34 patients (male 19 [55.9%], female 15 [44.1%]) have matched the inclusion criteria. Average age was 58.5 years (32-77;±4.3), average follow-up was 7.2 months (3.4-23.1;±1.8) and mean baseline LD was 10.9% (8.7%-14.8%;±0.8). Within 6 months after surgery mean LD increased by 0.8% (10.3%→11.1%) for patients under 50 years of age (n=5) and by 3.1% (11.0%→14.1%) for patients over 50 years of age (n=29). Using the prediction model, LD values for these six previously selected patients closely match the observed data with an average deviation of 1.07%.

Conclusions
Age and baseline LD were enough adequate factors to predict LD at any time in a clinically acceptable way for cases of RRD treated with C3F8-gas. It might be a useful tool for consideration when consulting about cataract surgery.

Financial Disclosure
no financial relations
Post-operative Intravitreal Methotrexate Injections Reduce Reoperations in Eyes with Proliferative Vitreoretinopathy and Diabetic Retinopathy

**Purpose**
Fibrous and glial proliferation is one of the largest surgical challenges that present to retinal specialists. Studies have indicated a potential role for postoperative intravitreal methotrexate after previous failed retinal detachment surgery. We included previously unoperated eyes at high risk for failure because of pre-existing advanced proliferative vitreoretinopathy or diabetic retinopathy.

**Setting/Venue**
This is a retrospective review of outcomes in a private practice setting in eyes with advanced proliferative diabetic retinopathy, trauma associated pathology, or proliferative vitreoretinopathy. Outcome measures are examined and compared amongst patients with or without postoperative intravitreal methotrexate injections.

**Methods**
This is a retrospective chart review of patients who underwent retinal detachment surgery for the following reasons: 1) Failed previous retinal reattachment surgery, 2) Advanced Proliferative Diabetic Retinopathy, 3) Initial surgery for retinal detachment associated with trauma, or 4) Primary retinal detachments associated with Grade C proliferative vitreoretinopathy. Methotrexate, 200µg, was administered intravitreally via the inferotemporal par plana at post op weeks 1, 2, 4, 7, and 11. Data including reoperation rate, visual acuity, physical exam, and OCT biomarkers were analyzed.

**Results**
A total number of 112 eyes were evaluated in this study. 14 eyes received intravitreal methotrexate and 98 eyes did not. The average number of reoperations among eyes treated with methotrexate was 0.57, compared to an average number of 1.12 among those who did not, \( p < 0.05 \). Many eyes had previously underwent multiple operations for proliferative vitreoretinopathy, and required no further operations after postoperative intravitreal methotrexate. Similarly, many patients with advanced proliferative diabetic retinopathy who required surgery in both eyes required less operations in the eyes that received postoperative intravitreal methotrexate compared to the fellow eye that was not injected. On exam, eyes injected with methotrexate had less postoperative epiretinal membrane proliferation compared to uninjected eye. Initial analysis also suggests a trend in better visual acuity for eyes that underwent intravitreal methotrexate. OCT biomarker analysis is pending.

**Conclusions**
We report that 5 postoperative intravitreal injections of methotrexate reduce reoperation rates in both eyes that have failed previous retinal reattachment surgery and eyes that are higher risk to fail primary surgery because of advanced proliferative vitreoretinopathy or diabetic retinopathy. Less postoperative epiretinal membrane formation is also evident in eyes injected with methotrexate.

**Financial Disclosure**
Alcon Consultant and Grant Support AclepiX Consultant Scanoptix Consultant ForwardVue Pharma Founder
Reliability of OCT Biomarkers for Idiopathic Epiretinal Membranes

OCT biomarkers are specific presurgical changes in retinal morphology with possible influence on postsurgical outcome. Aim of our study was to calculate reliability in diagnosing OCT biomarkers for epiretinal membranes and their influence on postsurgical visual acuity.

Methods
A retrospective analysis of patients scheduled for pars plana vitrectomy with membrane peeling due to idiopathic epiretinal membranes. All patients were pseudophakic at the follow-up 3 months after surgery and occurrence of the following OCT biomarkers (yes/no) was assessed in the presurgical OCTs: ectopic inner foveal layer (EIFL), disorganization of retinal inner layers (DRIL), intraretinal cystoid changes, defects of the ellipsoid zone, cotton ball sign, hyperreflective foci (HR-foci), and epiretinal membrane rips (ERM rips). Intra- and interobserver reliability, calculated with the Kuder-Richardson 20 test, was assessed from two independent readers and influence of OCT biomarkers on postsurgical DCVA (EDTRS charts) was calculated for each of the mentioned OCT biomarkers and central subfield thickness (µm) independently and for all of them together in a multiple regression analysis.

Results
In total, 136 patients were included into the analysis. Intraobserver reliability values were higher than interobserver reliability values (EIFL: 0.889/0.703; DRIL: 0.823/0.528; intraretinal cystoid changes: 0.926/0.888; defects of the ellipsoid zone: 0.835/0.782; cotton ball sign: 0.837/0.716; HR-foci: 0.676/0.582; ERM rips: 0.554/0.467) and only DRIL and central subfield thickness resulted in significant influence on postsurgical DCVA.

Conclusions
Intra- and interobserver reliability showed variability between OCT biomarkers with at least acceptable to good values for EIFL, DRIL, intraretinal cystoid changes, defects of the ellipsoid zone, and cotton ball sign. Central subfield thickness and DRIL showed significant association with DCVA 3 months after surgery.

Financial Disclosure
O. Findl is a scientific advisor for Alcon, Croma, Carl Zeiss Meditec AG and Merck. All authors declare, that there are no conflicts of interest.
Title
Natural history and surgical outcomes of lamellar macular holes

Purpose
To assess the natural history, and the surgical outcomes of lamellar macular holes (LMH).

Setting/Venue
Clinical charts and optical coherence tomography features of patients with LMH from multiple tertiary care centers were reviewed in this retrospective study.

Methods
The natural history of eyes that were observed, and the functional and anatomical outcomes of eyes that underwent surgery were analyzed. Within the operated group, surgical outcomes were compared between eyes that had epiretinal proliferation (ERP) peeled off from the surface of the retina with those that had peeling surrounding the foveal center with preservation of the central ERP (referred to as ERP perihole peeling).

Results
178 eyes were included, of which 89 underwent surgery and 89 were monitored. In the observation group, the mean visual acuity (VA) decreased from 0.25 +/- 0.18 to 0.28 +/- 0.18 logMAR (20/35 to 20/38 Snellen equivalent) (P = 0.079) over 45.7 +/- 33.5 months of follow-up. Nine eyes (10.1%) spontaneously developed a full-thickness macular hole. In the operated group, the mean VA increased from 0.47 +/- 0.23 to 0.36 +/- 0.28 logMAR (20/59 to 20/45 SE) (P = 0.0001) after a mean follow-up of 21.5 +/- 28.6 months. ERP was peeled off in 65 eyes (73.0%) while 24 eyes (27.0%) had ERP perihole peeling. Mean visual acuity gain was significantly greater in eyes that had ERP perihole peeling (-0.22 +/- 0.20 logMAR) compared to those that had proliferation peeled off (-0.07 +/- 0.30 logMAR) (P = 0.013). Eight eyes (8.5%) developed a postoperative full-thickness macular hole, of which all but one had proliferation peeled off.

Conclusions
Patients with LMH may benefit from surgery, while monitored patients develop a progressive loss of visual acuity. Perihole peeling of epiretinal proliferation contributes to a better surgical outcome than conventional macular peeling, and reduces the risk of postoperative full-thickness macular hole development.

Financial Disclosure
None
Title
Vitreoretinal Emergency Service at County Durham and Darlington Hospitals NHS Foundation Trust during COVID-19 Pandemic

Purpose
To study the Vitreoretinal (VR) emergency service during the first wave of COVID-19 Pandemic. To highlight additional processes needed in order to provide emergency VR service. To also compare the VR emergency procedures and post-operative complications during COVID to a similar time period in the previous year (2019).

Setting/Venue
Retrospective case study of VR emergencies during COVID-19 Pandemic lockdown. Emergency Eye Clinic (EEC), Darlington memorial hospital (DMH), County Durham and Darlington Hospitals NHS Foundation Trust (CDDFT) UK. Pre-operative assessment: DMH, Bishop Auckland Hospital (BAH) CDDFT. Operating theatre: General Anaesthetics at DMH, Local Anaesthetics at BAH. Post-operative care and visits: EEC DMH, outpatients eye clinic BAH. Personal protective equipment (PPE) fitting and training: DMH, BAH.

Methods
This is a retrospective case study of primary VR emergencies during initial COVID-19 pandemic lockdown at CDDFT catering for approximately 600,000 population in North-east of England. A total of 55 primary VR patients (55 eyes)(28 males and 27 females) treated from 25/03/2020 to 31/07/2020 were included. Of the 55 patients, 22 had retinal detachment (RD) who underwent RD Surgery, 23 had retinal breaks treated with retinopexy (22 laser-retinopexy, 1 cryoretinopexy) and 10 had diabetic-related vitreous haemorrhage/tractional RD (TRD) who underwent vitrectomy/delamination. Work-up and management of patients was undertaken with full PPE. All patients tested COVID negative before the procedure. A single VR surgeon (KO) performed all RD procedures. We compared VR emergencies managed during the same time-period in 2019 which included 57 eyes of 57 patients (33 males, 24 females) of which 31 had retinal breaks treated with laser/cryoretinopexy, 13 had RD who underwent RD surgery and 13 had vitrectomy/delamination for vitreous haemorrhage/TRD secondary to diabetes mellitus. Two VR surgeons performed vitreoretinal procedures in 2019.

Results
During COVID-19 pandemic in 2020, of the 22 patients who had RD surgery, 21 patients had better post-operative Snellen visual acuity (VA) with 15 patients 6/9 or better, 5 between 6/12 to 6/24 and one less than 6/24. One had drop in VA from immediate post-op VA of 6/9 to 6/18 due to cataract. One patient had post-operative macular edema which resolved with topical therapy and one hypotony, needing reinjection of gas. During 2019, of the 13 patients who underwent RD surgery, all 13 patients had better post-op VA, with 8 patients 6/9 or better and 5 patients had VA less than 6/24. Three cases has retinal redetachment needing further surgery. Although there was no significant difference in the overall number of VR cases during COVID 2020, the primary RDs needing surgery increased by 169%. Lesser number of retinal breaks were seen during COVID 2020 as compared to the same period in 2019. Anatomical success rate of retinal attachment with first surgery was 100% (22 eyes) during COVID 2020. In 2019 anatomical success rate of retinal attachment with first surgery was 77% and with second surgery was 92%. There were no COVID related complications encountered in our patients.

Conclusions
Total number of primary VR patients seen during COVID lockdown in 2020 was similar to previous year. Increased number of RD and retinal detachment procedures by 169% during COVID maybe because of patients failing to present early at the stage of retinal breaks for prophylactic retinopexy. Our cohort of patients did not have any COVID related complications.

Financial Disclosure
No financial disclosure for all authors
Title
Filtered-air versus long-acting gas tamponades in pars plana vitrectomy treatment for primary rhegmatogenous retinal detachment.

Purpose
In the Radboud University Medical Center, Nijmegen, the use of 20% SF6 and 14% C3F8 gas has gradually been replaced by filtered-air tamponade between 2014 and 2020. We have compared treatment success of filtered-air versus other gas tamponades in pars plana vitrectomy treatment of primary rhegmatogenous retinal detachments (RRDs), and analyzed whether the choice of tamponade affects treatment success in inferior located retinal tears.

Setting/Venue
This retrospective cohort study was conducted with all consecutive rhegmatogenous retinal detachment cases treated at the tertiary referral center, the Radboud University Medical Center, Nijmegen, the Netherlands, between June 2014 and May 2020.

Methods
We identified 1272 patients searching for ‘RRD’ in our vitreoretinal surgery database treated by a single vitreoretinal surgeon. Cases were excluded in which no pars plana vitrectomy was used, or a retinal re-detachment was treated. We defined an inferior located retinal tear as a defect involving clock hours 4, 5, 6, 7, and/or 8. Primary treatment success was defined as a retinal reattachment without re-detachment within six months after initial treatment. We built a univariate multivariable binary logistic regression model to analyze the effect of tamponade choice on treatment success. The model-building process was executed using the ‘purposeful selection method’ approach.

Results
Pars plana vitrectomy was in 1023 eyes indicated for a primary rhegmatogenous retinal detachment. We used intraocular gas tamponades in 872 cases with PVR grade B or lower: 414 eyes were treated with filtered-air tamponade and 458 eyes with 20% SF6 or 14% C3F8 gas tamponade. The first years, we primarily chose filtered-air tamponade in superior located retinal tears. Gradually, retinal detachments with defects at 4 and 8 o’clock were also treated with filtered-air tamponade. In 2020, filtered-air tamponade was the only type of gas tamponade used. Primary treatment success was achieved in 96.9% (n=845). We found no significant difference in re-detachment rate between filtered-air and other gas tamponades (risk difference; 95% confidence interval -1.0% and 4.1%). Additionally, the subgroup of RRDs with retinal defects located inferiorly showed no significant difference in primary treatment success between tamponade groups (p=0.54 Fisher’s exact). Candidate variables for the univariate multivariable binary logistic regression model were tamponade and all parameters that were univariably associated with treatment success. The final multivariable model included tamponade, PVR grade, a retinal detachment involving clock hour six and age as covariates, and showed no significant effect of tamponade choice on treatment success (OR 0.5, 95% 0.2-1.0, p=0.10).

Conclusions
We found no significant difference in pars plana vitrectomy treatment success between filtered-air and SF6 or C3F8 gas tamponades in primary rhegmatogenous retinal detachments with a PVR grade B or lower. Filtered-air tamponade also resulted in similar treatment success compared to other gas tamponades in inferior located retinal tears.

Financial Disclosure
None
Causes of low vision after endovitreal interventions with anatomical effect in rhegmatogenous retinal detachment

Purpose
To study the postoperative dynamics of visual acuity in relation to changes in the morphological structure and chorioretinal microcirculation in the macula at the stage of completion of silicone tamponade after endovitreal surgery in case of rhegmatogenous retinal detachment (RRD).

Setting/Venue
The work was performed in the S.N. Fyodorov NMRC «MNTK «Eye Microsurgery», Khabarovsk, Russia

Methods
The retrospective study included 21 patients (21 eyes) with anatomical retinal fit after endovitreal surgery, aged 25 to 56 years (mean age 46.5±15 years). Mild myopia (15 people) prevailed in the structure of refraction, emmetropia (3 people) and hyperopia (3 people) were less common. The duration of RRD varied from 8 days to 3 weeks; the period of macular detachment was calculated from the moment of decrease in central vision and ranged from 4 to 10 days. Preoperative visual acuity (VA) varied from light perception with correct light projection to 0.15 rel. The exclusion criteria from the study were patients with diabetes mellitus, glaucoma, and myopia over 3 diopters. All patients underwent a standard three-port vitrectomy with tamponade of the vitreous cavity with silicone oil. 3 months after the operation, by the time of the formation of strong chorioretinal adhesions in the area of retinal ruptures, the silicone oil was removed from the vitreous cavity. Standard ophthalmological examination included: visometry, computerized perimetry, tonometry, biomicroscopy, ultrasound A- and B-scanning. The analysis of changes in the macular region was performed by OCT: the central foveal thickness (CFT, μm), the thickness of the photoreceptor outer segments (POS, μm), the state of the layer of outer and inner segments of photoreceptors (IS / OS, abs.), defects of the outer boundary membrane (OBM, abs.) and internal boundary membrane (IBM b )

Results
Before the completion of the silicone tamponade, VA on average was similar to 0.28±0.05 in the 1st group of patients and 0.27±0.03 in the 2nd group (p<0.05). In the 1st group after removal of the silicone there was a rapid recovery of VA. During the first 7-10 days after surgery, VA averaged 0.69±0.04, and reached its maximum by the final follow-up period (3 months after surgery) and was 0.72 ± 0.05. Analysis of tomograms in postoperative dynamics revealed minimal changes in morphological structure of retina in macula in the first 1-3 days after surgery, which were limited to an increase in CFT to 361.2±9.0 μm at 250.0±5.7 μm in the control and in 2 cases (8.3±0.7%) with minimal signs of disorganization of the IS / OS and OBM lines. Restoration of the normal structure of the retina in the macula in patients of the 1st group was observed 7-10 days after removal of the silicone. According to OCT-angiography 3 months after surgery, patients in this group showed a tendency towards normalization of chorioretinal blood flow in the macula. So, by the final follow-up period, the area of nFAZ was 0.41±0.02 at 0.39±0.05 in the control group, DSCN was 53.9±3.0% at 54.4±4.5% in the control group and CT 285.0±8.1 at 290.5±7.0 in the control group (p>0.05). In patients of the 2nd group, there was no significant improvement in VA after surgery. During the first 7-10 days after the surgical intervention, VA averaged 0.23±0.01, and by the final follow-up period (3 months after the operation) it improved

Conclusions
1. As a result of a retrospective analysis of the postoperative dynamics of VA in operated patients with RRD at the stage of completion of silicone tamponade, according to tomograms, it was found that the main cause of low VA is structural changes in the neuroepithelium in the macula, disorganization of the IS / OS line, defects in the OBM and IBM, and the presence in the macula signs of the epiretinal membrane. 2. During OCT-angiography, a relationship was revealed between the degree of decrease in VA, morphological changes in the macula and the severity of disturbance of chorioretinal blood flow in the macula. Operated patients with low visual acuity are characterized by: prolonged and pronounced capillary hyperperfusion, which ends 3-10 days after removal of the silicone with a persistent deficit of chorioretinal microcirculation in the macula.

Financial Disclosure
No
Title
“ILM Peeling”- searching hope in ERM associated Ectopic Fovea

Purpose
To determine the anatomical and functional impact of internal limiting membrane (ILM) peeling in cases of Idiopathic epiretinal membrane (ERM) associated Ectopic Fovea

Setting/Venue
Tertiary Eye Care Centre, Kolkata, India

Methods
A retrospective, interventional case series of 39 eyes with Idiopathic epiretinal membrane (ERM) associated with Ectopic Fovea at presentation. The study period was between January 2016 and December 2019. Relationship between Pre-operative and Post-operative logMAR BCVA, Pre-operative and Post-operative Central Foveal thickness (CFT) evaluated. Effect of ILM peeling on Post-operative logMAR BCVA and Post surgery Ectopic fovea evaluated. Relationship of presence of Ellipsoid Zone (EZ) disruption and Recurrence of Epiretinal membrane (ERM) compared with Post-operative logMAR BCVA. Parametric and non-parametric tests are used to compare categorical and non-categorical variables and with appropriate significance (p<=0.05)

Results
Thirty-nine patients with mean age of 58.34 years and mean duration of complain of 8.97 months were included. Mean duration of follow up was 20.74 months and mean duration of Ectopic fovea resolution was 2.97 months. Treatment options included Pars plana Vitrectomy and ERM removal with or without ILM peeling. Post-operative BCVA noted to be better than pre-operative value, which was statistically significant also (p value = 0.001). CFT noted to be reduced after surgery and that too was statistically significant (p value = 0.001). ILM peeling not noted to have a statistically significant relation with absence of post-operative ectopic fovea (p value = 0.256). ILM peeling noted to have good impact on logMAR BCVA but that was not statistically significant (p value = 0.456). Absence of EZ disruption noted to have significant positive association with post-operative logMAR BCVA (p value = 0.001). Faster resolution of ectopic fovea was not consistent with ILM peeling (p value = 0.196). Post-operative logMAR BCVA was also not noted to be consistently poor in case of recurrence of ERM (p value = 0.146)

Conclusions
In our study internal limiting membrane (ILM) peeling noted to have significant good impact on anatomical as well as functional outcomes in Idiopathic epiretinal membrane (ERM) associated with Ectopic Fovea, though results was not statistically significant. So ILM peeling is not essential in treating cases with Ectopic fovea

Financial Disclosure
Not Applicable
Structural and functional macular changes after retinectomy for retinal detachment complicated by proliferative vitreoretinopathy. Anatomical and functional outcomes of non-primary retinectomy

Purpose
To report anatomical and functional outcomes of non-primary retinectomy for rhegmatogenous retinal detachment (RRD) with grade C proliferative vitreoretinopathy (PVR-C), and to assess the structural and functional macular changes in eyes with anatomical success.

Setting/Venue
Vitreoretinal Service, Ophthalmology Department, the Royal Hallamshire Hospital, Sheffield, United Kingdom.

Methods
Retrospective single-centre cohort study: one hundred-one consecutive retinectomies of 101 previously vitrectomized eyes (101 patients) affected by RRD with PVR-C between January 2014 and February 2020 were included. The mean postoperative follow-up was 36.18±19.53 months (12-75 months).

Results
Mean preoperative best corrected visual acuity (BCVA) was 1.48 ± 0.71 logMAR. Anatomical success rate was 78.2% after one retinectomy and 83.1% after two retinectomies. Final BCVA ≥ 20/200 was achieved in 29% of cases, 8% gained ≥ 20/80. Final mean postoperative BCVA of successes with oil in situ was 1.68 ± 0.59 compared with 1.07 ± 0.63 logMAR of successes after oil removal (p=0.00005). Post-operative macular Optical Coherence Tomography (OCT) was obtained from 60/84 successes (71%). Normal macular profile was found in 3%, while majority demonstrated exudative maculopathy (51.5%), macular atrophy (22%), tractional maculopathy (21.5%), macular disciform scar (2%). Bivariate linear relationship between final central foveal thickness (CFT) and BCVA was statistically significant (p=0.000013).

Conclusions
Satisfactory anatomical and functional outcome is possible following retinectomy for PVR-C. Positive prognostic factors include removal of oil without re-detachment, normal macular status and lower CFT. Normal macular profile was rarely found (3% of cases), while majority demonstrated exudative maculopathy, macular atrophy, tractional maculopathy. Functional outcome was influenced by macular changes, as final BCVA and CFT correlated.

Financial Disclosure
Financial Disclosures: The authors have no proprietary or commercial interest in any material discussed in this article.
Autologous anterior lens capsule flap transplantation with serum application in managing idiopathic full thickness macular holes

Purpose
Overall the incidence of full thickness macular holes (FTMH) has been estimated at 0.1 - 0.8% in individuals aged over 40 years old. The current primary gold standard treatment is pars plana vitrectomy (PPV) with internal limiting membrane (ILM) peel and gas tamponade. Several adjuncts have been described in current literature to address refractory FTMHs to varying levels of anatomical and visual success. Here we described the results of six patients who have undergone PPV +/- ILM peel alongside phacoemulsification and intraocular lens (IOL) implantation with autologous anterior capsule flap transplantation and serum application to the FTMH as both a primary treatment for idiopathic FTMHs or a secondary procedure for refractory idiopathic FTMHs. Main outcome measure: Closure rate of FTMHs and change in best-corrected visual acuity (BCVA)

Setting/Venue
King’s College Hospital NHS Trust, a tertiary hospital in South-East London

Methods
A retrospective case series review was undertaken of six patients who received this procedure between August 2019 and July 2020. Each case alongside relevant spectral domain optical coherence tomography (SD-OCT) images were analysed in depth; we describe demographics, BCVA in early treatment diabetic retinopathy study (ETDRS) letters, presenting macular hole characteristics and International Vitreomacular Traction Study Group grading, surgical treatment, complications, and status of macular hole following treatment.

Results
Presenting median FTMH diameter was 478um interquartile range(IQR) 432. Final median FTMH hole diameter was 0.00um, IQR 239.25. Mean FTMH size decrease was -355.17 standard deviation(SD) 515.80 (p=0.173, Wilcoxon Signed-rank test). 66.67% had large holes, 16.66% medium and 16.66% small. Median presenting BCVA was 42.50 letters IQR 35.00. Median final BCVA 57.50 letters IQR 53.74. Mean BCVA improvement was 9.16 SD 11.14 (p=0.068, Wilcoxon Signed-rank test). This was the primary procedure for four of the six cases. 75% (three patients) achieved FTMH closure within six weeks and the fourth patient in eight weeks with additional serum application. Visual improvement was experienced in 50% (two patients) and BCVA was maintained in the remainder. Two patients underwent this combination procedure following failure with standard PPV, ILM peel and octafluoropropane(C3F8) tamponade. Closure rate was 50%; one patient underwent this procedure six weeks following initial surgery for a large FTMH and three weeks later closure was achieved with BCVA improvement. The second case underwent this intervention four weeks after the primary procedure for a medium FTMH. The FTMH failed to close after two weeks and a further PPV with C3F8 was carried out. Unfortunately, improvement was subsequently limited by a rhegmatogenous retinal detachment (RD).

Conclusions
Previously this autologous capsule transplantation had been reported largely in East Asian, mainly myopic populations with large refractory holes. Here we describe PPV with ILM peel alongside phacoemulsification and intraocular lens (IOL) implantation with autologous anterior capsule flap transplantation and serum injection as a viable treatment option for both primary and refractory FTMHs of various sizes; hole closure was achieved in all except one case which was limited by a subsequent RD. Further work on a larger scale should be undertaken with longer follow-up periods to see if there are any long-term transplantation implications. Furthermore, this method should be trialed in different populations, in FTMHs of different sizes and presentations to further validate its use. Additionally, more research should be employed to investigate an optimum adjunct for capsule incorporation to FTMHs. We used autologous serum obtained from perioperative centrifugation effectively for its fibrocellular adhesive and proliferative properties but success has also been reported without serum or with whole blood instead.

Financial Disclosure
All authors have none to declare
**Title**
Three Dimensional Digitally-Enabled Intraoperative Optical Coherence Tomography Compared with Conventional Microscope-Integrated Intraoperative Optical Coherence Tomography in Vitreoretinal Surgery: A Post Hoc Analysis of the DISCOVER Study

**Purpose**
The recent technological evolution in surgical microscopes has brought new digitally-enabled options for high-definition, heads-up stereoscopic visualization during posterior segment surgery. Surgical efficiency, ergonomics, patient safety, and new surgeon education in vitreoretinal surgery may be enhanced with this technology but there is limited literature in this area. In this analysis, a comparative assessment of surgeon experience between conventional microscope-integrated intraoperative optical coherence tomography (iOCT) and a digitally-enabled microscope-integrated iOCT surgical platform in vitreoretinal surgery was performed.

**Setting/Venue**
This study was conducted at a single, academic institution with multiple vitreoretinal surgeons involved.

**Methods**
This was a post-hoc case-control analysis from the DISCOVER study - a prospective, multi-surgeon case series - comparing the use of two different microscope-integrated OCT (iOCT) platforms. One group consisted of eyes that underwent surgery with a conventional microscope-integrated iOCT (Rescan 700 Prototype; Carl Zeiss Meditec, Oberkochen, Germany), while the second group of eyes underwent surgery with a digitally-enabled iOCT (Artevo 800; Carl Zeiss Meditec, Oberkochen, Germany). When feasible, the two groups were matched for surgeon and preoperative diagnosis (i.e., surgical indication). Standardized surgeon questionnaires were collected immediately following surgery. Variables examined included patient demographics, indication for surgery, endoillumination levels, utilization and visualization of iOCT, surgeon feedback on viewing quality, and impact of iOCT on surgical decisions. Visualization and review of the iOCT dataset were evaluated based on the following options: surgical-field based visualization (i.e., ocular heads-up display in the conventional group, 3D screen-based visualization in the digitally-enabled group) and non-surgical field-based (i.e., review on the external monitor (Callisto)). Inclusion criteria included age of 18 years or older and planned vitreoretinal surgery. Statistical analysis included t-tests to compare continuous variables and Chi-square and Fisher’s exact tests to compare categorical variables.

**Results**
173 eyes from 173 patients were analyzed. 78 patients (mean age 64.8 ± 10.9 years) composed the conventional iOCT group and 95 (mean age 64.1 ± 14.2 years) composed the digital iOCT group. The most common indications for surgery were epiretinal membrane (conventional iOCT = 29.5%; digital iOCT = 33.7%) followed by retinal detachment and full thickness macular hole (conventional iOCT = 26.9%, 17.9%; digital iOCT = 23.2%, 19.0% respectively). Surgical field-based visualization of iOCT datastream was significantly higher in the digitally-enabled group compared with conventional iOCT group (85.2% vs 11.4%, p <0.0001). The required endoillumination level was significantly lower in the digital iOCT group (34 % vs 37.1 %, p = 0.0007). Surgeon-perceived utility of iOCT was similar between groups (conventional iOCT = 50%; digital iOCT = 58.9%, p = 0.234). The direct impact of iOCT on surgical decision-making was also similar between both groups (12.8% vs 21.1%, p=0.155) although there was a trend towards greater impact in the digital iOCT group.

**Conclusions**
Digitally-enabled microscope-integrated iOCT resulted in greater surgical visualization efficiency with a significantly higher proportion of cases with surgical-field based visualization of the iOCT datastream compared to the conventional system. The digital iOCT display also appeared to require a lower illumination level for performance of surgical tasks. Surgeon-perceived utility of iOCT was high in both groups.
National Emergency Department Trends for Endogenous Endophthalmitis: Findings from the United States

Purpose
Endogenous endophthalmitis (EE) is a rare entity with potentially devastating visual consequences from systemic infection. Large-scale analysis is scant regarding predictors of systemic outcomes for patients specifically with EE. The goal of this study is to characterize incidence rates and identify risk factors for admission and mortality with EE in the United States (US).

Setting/Venue
A nationwide, retrospective cohort study was conducted from the National Emergency Department Sample. Study participants received care at any US emergency department (ED) between 2006–2017.

Methods
Patients with EE were identified by requiring diagnoses of both endophthalmitis and septicemia using contemporary International Classification of Diseases diagnosis codes. Main outcome measures were nationwide EE incidence rates and risk factors for admission and mortality.

Results
A total of 6,400 patients with EE were identified. Incidence increased from 0.10 (95% confidence interval [CI]: 0.07-0.12) per 100,000 in the US civilian population in 2006 to 0.25 (95%CI: 0.21-0.30) in 2017 (p<0.05). Most were female (55.4%), insured with Medicare (53.5%), had first income quartile earnings (29.3%) [bottom 25% income bracket], lived in South (40.5%), and presented to metropolitan teaching hospital (66.6%) (p<0.05). Mortality increased from 8.6% (95%CI: 3.8%-18.3%) in 2006 to 13.8% (95%CI: 9.7%-19.2%) in 2017 (p=0.94). Factors predicting admission included older age (odds ratio [OR] 32.59; [95%CI 2.95-359.78]) and intravenous drug use (OR 14.90 [95%CI: 1.67-133.16]). Factors associated with increased mortality included: human immunodeficiency virus infection/immune deficiencies (OR 2.58 [95%CI: 1.26-5.28]), heart failure (OR 2.12 [95%CI: 1.47-3.05]), and hepatic infections/cirrhosis (OR 1.89 [95%CI: 1.28-2.79]). Pneumonia, renal/urinary tract infections (UTI) were associated with both increased hospital admission [(pneumonia OR 9.64 (95%CI: 1.25-74.35, p=0.030), renal/UTI OR 4.09 (95%CI 1.77-9.48)) and mortality [(pneumonia OR 1.64 (95%CI: 1.17-2.29, p=0.030), renal/UTI OR 1.87 (95%CI 1.18-2.97)]. Patients with type 2 diabetes mellitus (DM) had decreased odds ratio for mortality (OR 0.49 [95%CI: 0.33-3.73]).

Conclusions
EE has increased in incidence throughout US. The two systemic factors that conferred both an increase in mortality and admission were pneumonia, and renal/UTI. Additional exploration of the potential protective association of DM with decreased mortality in this context is needed.

Financial Disclosure
Ophthalmology Times (Honorarium), techspert.io (Ad Hoc Consultant)
Sequelae of posterior segment complications after implantation of scleral fixated intraocular lens using Yamane technique- a case series

**Purpose**
To report the possible sequelae of posterior segment complication following Yamane technique scleral fixated intraocular lens (SFIOL) implantation.

**Setting/Venue**
Universiti Kebangsaan Malaysia Medical Centre

**Methods**
Reporting 3 cases of complication in using Yamane technique SFIOL implantation

**Results**
Case 1: 64 years old man with a history of bilateral pseudophakia presented with a bilateral subluxated intraocular lens (IOL). Right eye pars plana vitrectomy, lens explantation, scleral fixated intraocular lens implantation was done using Yamane technique. Post-operative patient developed cystoid macula oedema and with treatment, his vision improves to 6/18 pinhole 6/12.  
Case 2: 60 years old man with a history of cataract surgery presented with dislocated right eye intraocular lens (IOL). The IOL was then removed by an anterior segment surgeon without posterior vitrectomy and scleral fixated IOL implanted using Yamane technique. Immediate post-operatively noted vitreous haemorrhage. One-week follow-up noted vitreous haemorrhage has reduced but revealed large retinal tear superiorly. Patient then underwent an emergency vitrectomy and endolaser. Case 3: 64 years old man with a history of right eye cataract surgery complicated with corneal decompensation. The patient underwent Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) and vision improves. Two years later the patient had right IOL dislocation which was explanted by the anterior segment surgeon without posterior vitrectomy and scleral fixated IOL implanted using Yamane technique. Two months post-surgery patient developed macula hole.

**Conclusions**
- To note the possible sequelae of posterior segment complications after the implantation of scleral fixated intraocular lens with Yamane technique.
- Extensive manipulation in implanting a scleral fixated intraocular lens may lead to complications especially without proper posterior vitrectomy as most of the vitreous gel is still preserved.

**Financial Disclosure**
nil
Outcomes of 27 gauge pars plana vitrectomy for simple and complex vitreoretinal diseases in Pakistan

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Purpose
To evaluate outcomes of 27 gauge (27g) pars plana vitrectomy (PPV) for simple and complex Vitreoretinal-retinal diseases in Pakistan.

Setting/Venue
Single center, retrospective, large cohort study that included all the patients who underwent 27g PPV.

Methods
Retrospective analysis of the medical records of all the eyes that utilized 27g PPV system at a single tertiary care hospital from July 2015 to June 2019 was done. A total of 665 eyes of 574 patients of both genders and all age groups were included in our study. This study has been approved by the Institutional Review Board of the hospital. All the surgeries were performed by a single vitreo retinal surgeon (MAA). Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21.0 (IBM SPSS Statistics, Armonk, NY). For qualitative measures, frequency and percentage was used while mean and standard deviation was calculated for quantitative measures.

Results
Mean age was 55 ± 16.9 years (median, 58; range, 2 months-99 years). There were 355 (62%) males and 219 (38%) females. Common surgical indications included; Diabetic tractional retinal detachment (n= 196, 29.5%), vitreous haemorrhage (n= 191, 28.7%), full thickness macular hole (n= 80, 12%), epiretinal membrane (n= 66, 9.9%), endophthalmitis (n= 26, 3.9%), tractional diabetic macular edema (n= 14, 2.1%), ectopia lentis (n= 11, 1.7%), dropped lens matter (n= 13, 2%) and others (n= 68,10.2%). Modified retrobulbar anaesthesia was utilized in 617 (93%) eyes and 48 (7%) eyes required general anesthesia. No anesthesia related complications were noted. Among 665 eyes, 305 also had concurrent phacoemulsification with intraocular lens implantation.  Mean operating time was 62 ± 37 minutes.  Per-operative complications included; iatrogenic retinal tear (2 eyes, 0.3%) and supra choroidal silicon oil migration (1 eye, 0.15%). Regarding tamponade agents, 338 eyes (51%) were left on air, SF6 gas in 32 eyes (5%), C2F6 gas in 109 eyes (16%), C3F8 in 5 (0.8%) and silicon oil in 104 eyes (16%). Seventy seven (12%) of the eyes were left with a fluid filled vitreous cavity.  None of the patients developed ocular hypotony on first postoperative day. Post-operative complications were raised IOP (7 eyes, 1%), endophthalmitis (1 eye, 0.15%), hemorrhagic occlusive retinal vasculitis (1 eye, 0.15%) and retinal detachment (2 eyes, 0.3%). Mean postoperative visual acuity improved from 1.62 ± 0.68

Conclusions
27g PPV has proved to be a safe and effective system for both simple and complex retinal pathologies requiring significant surgical manipulation in any age groups. It requires less use of accessories in tractional retinal detachment due to small gauge and there is no significant increase in operative time.

Financial Disclosure
None
Purpose
Purpose: This study aims to identify the average axial length (AL) of patients with rhegmatogenous retinal detachment (RRD) treated within Dunedin, New Zealand and compare the results to patients without RRD.

Methods
Patients and methods: This is a retrospective study exploring patients treated for RRD by vitrectomy at Dunedin Eye Department. The diagnosis of RRD was confirmed through the patient’s medical records. Patients had to have biometry data with the AL of the affected eye after the surgery with the Zeiss IOL Master 500. The mean AL of the eyes treated for RRD was compared to the AL of patients without RRD from a previous publication.

Results
Results: This study included 108 eyes of 105 patients with RRD (60% male and 40% female). The mean AL of patients with RRD was 24.30 ± 0.33mm, males had a greater mean AL of 24.60 ± 0.41mm compared to women who had an average of 23.84 ± 0.53mm. The difference in AL between RRD patients and the control group was 0.82 ± 0.23mm, p < 0.0001.

Conclusions
Conclusion: Patients treated for RRD in Dunedin have a greater mean AL compared to patients without RRD, representing myopia as a risk factor. The mean AL of males and females differed; indicating males may be at greater risk of RRD.
Title

Silicon Oil Complications descriptive retrospective study

Purpose

Principal Objective The objective of this study is to describe the characteristics, outcomes and complications of eyes after vitreoretinal surgery using SO as endotamponade. Secondary Objective To compare the complication rates after vitreoretinal surgery using 1000- vs 5000-centistoke SO. There has been multiple based on literature search in other articles reporting complications and outcomes after the use of 1000 cSt SO. Nonetheless, based on a literature search of the MEDLINE database there has been limited number of published reports comparing the complications and outcomes rates after the use of 1000 cSt and 5000 cSt,. Most these studies includes a reduced sample size giving results which could not be statistically proven. Even though the Silicon Study group proved SO to be a very useful tool in the treatment of complicated retinal detachments, questions and indications for selecting SO viscosity for use in clinical settings still remains unanswered. Hence this warrants additional studies with a larger sample size, like this one, to compare and validate a true associations between complications and SO viscosity.

Setting/Venue

In this retrospective study, the records of 362 eyes undergoing PPV with injection of SO for complicated vitreoretinal conditions followed in the Hospital Universitario Valladolid (n=22) and the IOBA's (n=340) vitreoretinal clinic and presenting between May 2006 and November 2019 were reviewed.

Methods

All eyes had a complete preoperative examination, including best corrected visual acuity (BCVA), IOP by applanation tonometry, biomicroscopic and fundus examination. Postoperative follow-up evaluations took place at 1 week, 3, 6 and 12 months. At each follow-up visit, a complete ocular evaluation was performed, including BCVA, IOP, slit lamp and fundus examination. A database was created with multiple characteristics. These variables were subsequently analyzed. Comparison between complication rates when using SIOTAL 1000 cSt and 5000 cSt (AJL, Alava, Spain) was then performed. BCVA was measured using Snellen and ETDR charts and converted into logMAR units for statistical purposes. Ambulatory vision was defined as a BCVA of 4/200 (logMAR 1.7) or better. According to a modified scale of Avery and colleagues, non-numerical vision was arbitrarily assigned a logMAR value (counting fingers (CF) logMAR 2.0, hand motion (HM) logMAR 2.1, light perception (LP) logMAR 2.3, no light perception (NLP) logMAR 2.8). Increase intraocular pressure above 28 mm Hg was categorized as Ocular hypertension. Besides, we defined hypotony as having IOP ≤5 mmHg, the same cut off as in the Silicone Study.

Results

Our study group included 230 patients [91 males (39.6 %), 138 females (60.4 %)]. Mean age was 58.2±18.4 years. Visual acuities (logMAR) were 1.8±0.6, and intraocular pressures (mmHg) were 15.6±7 at baseline, 15.7±6 at last follow-up. Mean residence time of SO in the eye was 9.109 ± 7.7068 months (median, 7 months, range 01-30 months). Ninety six (47.6%) surgeries were performed with SO 1000 cSt and one hundred thirty four (58.3%) using SO 5000 cSt. The indications for SO use included: previous re-RD (n=152); complicated primary RD (n=126); PDR (n=24); history of previous trauma, and/or intraocular foreign body and/or scleral rupture (n=19); and 28 surgeries had various etiologies including subretinal hemorrhage secondary to wet AMD, choroidal hemorrhage, Melanoma, CMV retinitis and Uveitis. The main silicone-oil-related complications observed were: SO emulsification 22.51%, redetachment 21.35%, ocular hypertension 19% of which 25% developed secondary glaucoma, band keratopathy 5.56%, hypotony 3.51%. Most of the complications, (45%) appeared < 4 months post-operative being acute ocular hypertension being the most common with a 14.86%.

Conclusions

This study provides evidence that there is a higher incidence of complications in the 1000 cSt group than in the 5000 cSt. Regardless, of our results the final visual outcome did not differ much but we must take into consideration that a higher rate of complications can result in recurrent visits to the hospital, more expenses, as well as additional nuisances to the patient therefore lower quality of life. There is much to be investigated for the predilection of SO used in surgery, there are not enough literature comparing this two SO.