

**F008**

**Comparing the mid-term efficacy and safety of the Stegmann Canal Expander Canaloplasty with the prolene suture Canaloplasty in cases of open angle glaucoma**

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**Purpose**

To examine the mid-term efficacy of the Schlemm's canal Canaloplasty with Stegmann Canal Expander (Ophthalmos GmbH, Schaffhausen, Switzerland) in comparison to prolene suture Canaloplasty in OAG.

**Methods**

203 eyes of 184 consecutive patients with POAG or PEX glaucoma. 96 eyes of 86 patients underwent primary Canaloplasty with Stegmann's Expander and 107 eyes of 98 patients underwent primary Canaloplasty with prolene suture. All eyes were operated by the same surgeon (GSM) using a standardized Canaloplasty procedure by the insertion either of two 9mm long and 240µm wide polyimide stents into both surgically created Schlemm's ostia or either by the insertion of a 9.0 prolene suture.

**Results**

The mean age for Canaloplasty with Stegmann's Expander was  $74.65 \pm 9.73$  years; the mean follow-up was  $33.3 \pm 10.89$  months (range: 7-52). Mean IOP decreased from  $20.95 \pm 6.14$  mmHg before surgery to  $12.75 \pm 3.34$  at 24 months. Number of medications dropped from 2.91 presurgery to 0.55 postsurgery ( $p < 0.01$ ). Canaloplasty with prolene suture mean age at the time of surgery was  $72.66 \pm 13.55$  years, the mean follow up was  $26.75 \pm 19.06$  months (range: 3-58). Mean IOP decreased from  $19.36 \pm 5.24$  mmHg before surgery to  $12.87 \pm 3.99$  at 24 months. Number of medications dropped from 2.86 presurgery to 0.48 postsurgery ( $p < 0.01$ ). No surgery related complications were reported in 40 eyes (42%) and in 54 eyes (51%) for Stegmann's Expander and prolene Canaloplasty respectively.

**Conclusions**

Significant IOP reduction is observed in both surgical techniques. Both techniques seem safe and provide satisfactory mid-term IOP lowering resuming OAG. Although there was no statistically significant difference there was a trend towards lower IOP with the Stegmann Expander.

**1743**

**Microglial response to optic nerve injuries**

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**Summary**

Microglial cells are the sentries of the central nervous system. They maintain tissue homeostasis and upon injury they become activated, release inflammatory mediators and become phagocytic. Here, we will discuss the

microglial response after optic nerve trauma. Optic nerve axotomy, either crush or transection, causes the direct death of retinal ganglion cells (RGC) and, in turn, the activation of the resident microglial cells that become phagocytic and engulf the dead RGCs. The appearance of phagocytic microglial cells (PMCs) in the axotomized retina of mice and rats is inversely proportional to the loss of RGCs both numerically and topographically. However, RGC death occurs earlier than RGC clearance by PMCs. In mice, but not in rats, there is a PMC response in the contralateral non-injured retina. This contralateral response involves as well regulation of inflammatory proteins.

#### **S046**

##### **Impact of preserved and preservative-free latanoprost on the survival of conjunctival goblet cells**

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##### **Purpose**

To isolate and cultivate goblet cells from human donor conjunctival tissue and determine the influence of available latanoprost generics, brand name latanoprost, and preservative-free latanoprost, on goblet cell survival.

##### **Methods**

Human goblet cells were isolated from explant cultures established from donor tissue. Cells were cultivated in culture medium supplied with 10% Fetal Bovine Serum. Goblet cells were identified by morphology and Periodic Acid Schiff (PAS) staining. Cell survival was determined by LDH assay after exposure to the diluted latanoprost products. The latanoprost products consisted of preserved latanoprost (Xalatan® and generics from Pfizer, Stada, Sandoz, and Teva) and the preservative-free latanoprost (Monoprost® - Laboratoires THEA). pH and osmolarity of the eye drops were evaluated by a standard laboratory pH meter and a Cryoscopic Osmometer, respectively.

##### **Results**

The pH of the preserved latanoprost compounds (average pH = 6.8) were higher than Xalatan® (pH = 6.1) ( $p < 0.0001$ ) and lower than Monoprost® (pH = 7.0) ( $p < 0.001$ ). No difference in osmolarity values of Xalatan®, preserved latanoprost products, and Monoprost® were found. Survival of goblet cells exposed to preserved treatments was generally reduced to: 71.3 +/- 3.7% for Xalatan®, 74.1 +/- 3.9% for Pfizer, 70.3 +/- 3.6% for Stada, 71.2 +/- 3.6% for Sandoz, and 70.1 +/- 1.5% for Teva. A significant higher goblet cell survival was found in cells treated with Monoprost® compared to all preserved latanoprost drugs (98.8 +/- 9.1) ( $p < 0.001$ ). There was no significant difference in cell survival between controls (treated with growth media) and Monoprost® treatment.

##### **Conclusions**

Significant differences in the impact of Xalatan®, latanoprost generics, and Monoprost® were found on goblet cell survival. Monoprost® caused no significant goblet cell death.

#### **1423**

##### **Phaco iStent**

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## Summary

Glaucoma and cataracts are still the biggest cause of irreversible and reversible causes of sight loss worldwide respectively. And many glaucoma patients will go onto develop cataracts.

Cataract surgery for glaucoma patients is now seen as a useful window of opportunity in which additional glaucoma procedures can be performed to reduce both intra-ocular pressure and the number of glaucoma medications.

MIGS (Minimally Invasive Glaucoma surgery) devices have a good safety profile, and cause less ocular trauma than traditional glaucoma surgery, as well as significantly reducing eye. The iStent GTS100 is marketed as a device that can be used in conjunction with cataract surgery to reduce intra-ocular pressure in mild to moderate glaucoma patients.

The original iStent, GTS100, was the first commercially available MIGS device. The Western Eye Hospital Glaucoma department were early adopters of the device in the UK and started using them in 2012 and to date have implanted over 150.

We will present our real world long term results and experiences and videos of using the first MIGS (minimally invasive glaucoma surgery) device- the iStent G100 (Glaukos). Practical advice on surgical technique will also be discussed as well as patient selection.

**2651**

## New approaches to study retinal pericytes

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## Summary

Pericytes are contractile cells that wrap along the walls of capillaries. Pericytes have been proposed to regulate the capillary diameter and vascular blood flow in response to metabolic demand, a process defined as neurovascular coupling. Due to their small size, it has been a challenge to perform in-vivo single pericyte imaging in the retina, which has greatly limited our knowledge about the contribution of pericytes to microvascular dysfunction in the retina. Moreover, the particular requirements for postmortem fixation to preserve the subcellular components in capillary pericytes have yielded controversial results. Here, we show novel histological methods, genetic tools, and minimally invasive two-photon microscopy to monitor retinal pericytes and capillaries in the mouse retina. We report pericyte-dependent vascular dysfunction in several models of neurodegeneration including glaucomatous and ischemic optic neuropathies. Our data identify pericytes as important cellular targets to maintain microvascular function and preserve vision.

**F113**

## The effect of sustained eye rotation upon central and peripheral axial length in young, adult myopic subjects

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## Purpose

Previous work has shown that the ocular globe is less rigid in myopia, and a recent study showed that this can alter the characteristics of saccadic eye movements. It is also well established that the eye in myopia has relatively hyperopic peripheral refraction. The aim of this study is to determine whether ocular movement can affect the shape of the globe and lead to measurable change in axial length (AL).

## Methods

Ten subjects aged 18 to 30 years old (6 Male/4 Female) participated in the study with informed consent. No subject had a history of ocular or systemic disease, and the mean spherical equivalent (MSE) refractive error was  $\leq -1.00$ DS with cylindrical refraction  $< -1.50$ DC. One drop of tropicamide hydrochloride 1% was instilled 20 minutes prior to measurement to induce mydriasis and mild cycloplegia. Using IOL Master mounted on a rotating platform, AL was measured centrally and temporally (30 degrees off-axis) in two different eye positions. Subjects fixated centrally and then rotated their eye 30 degrees in the temporal direction for 10 minutes, and the same measurements were repeated.

## Results

Prior to rotation, the group mean temporal AL was significantly shorter than the central AL (mean difference =  $-0.667 \pm 0.367$ ;  $t=5.694$ ,  $df=18$ ,  $p<0.0001$ ). There was no significant variation in central or temporal AL due to off-axis fixation, either after the initial eye rotation, or after 10 minutes fixation at the off-axis point. The difference between central and temporal AL was maintained after ten minutes of temporal fixation (mean difference =  $-0.693 \pm 0.370$ ;  $t=5.918$ ,  $df=18$ ,  $p<0.0001$ ).

## Conclusions

Temporal AL was shorter than central AL showing the prolate shape associated with myopia. The action of the extraocular muscles on the globe has no effect upon the retinal shape assessed by off-axis AL in myopic subjects.

## S045

### The effect of eliminating tear evaporation on tear osmolarity

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## Purpose

To assess the effect of eliminating tear evaporation on tear osmolarity using two methods: eye closure or retarding tear evaporation using a very high relative humidity (95% RH). In the first method it can be hypothesised that when the eye is closed, the tear fluid is replaced with basal tears with no loss to evaporation. In the second, tear evaporation would be suppressed. In both instances, it is hypothesised that the tear osmolarity will drop to near plasma osmolarity.

## Methods

20 subjects ( $n=10$  dry eye (DE);  $n=10$  normal) age ( $38.9 \pm 9.4$  years) were enrolled. DE subjects had: tear stability ( $<10$  secs), Schirmer ( $<10$ mm in 5 min) and symptoms ( $\geq 13$  symptoms by OSDI). The study consisted of two visits: one visit was conducted in normal environmental conditions ( $\sim 21^\circ\text{C}$  and 40% RH) where tear osmolarity was measured before and after 20 minutes of eye closure. The other visit was in a controlled environmental chamber ( $23^\circ\text{C}$  and 95% RH) where tear osmolarity was measured before and after 20 minutes of open-eye exposure.

## Results

There was a significant decrease in tear osmolarity after eye closure ( $p<0.05$ ) (Mean  $\pm$  SD) (before:  $313.90 \pm 11.30$  mOsm/l; after:  $304.15 \pm 10.71$  mOsm/l). There was also a significant decrease in tear osmolarity after exposure to 95% RH ( $p<0.05$ ) (before:  $315.05 \pm 10.40$  mOsm/l; after:  $304.15 \pm 8.42$  mOsm/l). There was no significant difference in the reduction in tear osmolarity between dry eye and normal groups ( $p>0.05$ ).

## Conclusions

There was a significant decrease in tear osmolarity after exposure to both situations. The findings demonstrate the effect of eliminating tear evaporation on tear osmolarity and suggest that elevated tear evaporation may be

responsible for tear hyperosmolarity in DE patients. In addition, they display the likely impact of patient behaviour and ambient environment on clinical tear osmolarity measurements.

**S087**

**New nature-inspired hybrids activating the Nrf2-HO1 pathway in retinal pigment epithelial cells and their potential use in pathologies featured by oxidative stress**

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**Purpose**

Among the earliest factors triggering Age-related Macular Degeneration (AMD) is the degeneration of retinal pigment epithelium (RPE). A primary system used by RPE to neutralize oxidative stress and maintain cellular homeostasis is the nuclear factor E2-related factor 2 (Nrf2) pathway. We aimed to further test some novel Nature-Inspired Hybrids (NIH) endowed with anti-oxidant properties, in order to evaluate their capability to activate Nrf2-pathway and to promote protection in RPE cells.

**Methods**

ARPE-19 cells were exposed to NIH (5µM) for increasing times (from 3 to 48 hours). Dimethyl-fumarate (DMF; 10µM), a well-known Nrf2 activator, was used as a positive control. The Nrf2-pathway activation was evaluated by studying Nrf2 protein nuclear translocation and Heme-Oxygenase 1 (HO-1) expression (mRNA and protein, with real time PCR and Western blotting, respectively). Cell viability of ARPE-19 exposed to the NIH in the presence/absence of AMD-related stressors was evaluated by various techniques (MTT, LDH and PrestoBlue® assay).

**Results**

The NIH are well tolerated by ARPE-19 cells. The NIH presenting in their structure the chemical active group(s) responsible for the Nrf2-pathway activation (catechol group and/or Michael acceptor) induce Nrf2 nuclear translocation, suggesting an interference in Nrf2 protein degradation process. The same NIH upregulate HO-1 expression, although with entities and/or time-courses that vary among molecules, with potential outcomes on the cellular stress response.

**Conclusions**

A positive modulation of Nrf2-pathway by NIH may be protective in RPE cells, encouraging further studies on their potential use in pathologies featured by oxidative stress.

**1863**

**Animal Case**

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### Summary

We present mouse mutants with ocular findings identified in the German Mouse Clinic screen. The *Uqcrh* gene deficiency in mouse shows alterations in the development of the eye structures. For the homozygous *Uqcrh* mouse OCT evidences abnormal retinal structure with early signs of retinal detachment and inner nuclear layer defects with additional observation of pathologies in the anterior chamber. The ubiquinol:cytochrome c oxidoreductase hinge protein (UQCRH) plays an important role in the formation of the complex between the cytochromes c and c1 in the complex III (CIII) of the oxidative phosphorylation system. A disease linked to UQCRH has yet not been described.

2111

### Peripheral ischemia in diabetes: anti VEGF, PRP?

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### Summary

Peripheral ischemia in diabetic retinopathy (DR) is a sight threatening condition especially in the presence of disc or preretinal neovessels. Based on the ETDRS studies, peripheral laser photocoagulation (PRP) has been recognized for more than 30 years as the gold standard treatment for peripheral ischemia in DR. Recently, the widespread use of repetitive anti VEGF injections in the management of diabetic macular edema revealed an additive favourable effect on the regression of diabetic retinopathy severity scale.

The goals of this talk are two-fold : first, to review the published evidence for the use of PRP and anti VEGF injections independently in the management of peripheral ischemia in DR; second, to discuss the associated characteristics of DR, socio economic issues that could guide the clinician into his therapeutical decision.

At the end of the talk, participants should be able to take a thorough decision to guide an evidence based treatment for peripheral ischemia in DR.

F131

### Does the presentation of orbital cellulitis exhibit seasonality?

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### Purpose

Seasonality is known to affect both immune function and stress related diseases. This study aims to investigate whether seasonality is related to presentations of orbital cellulitis.

### Methods

Electronic patient records from the eye casualty were retrospectively examined between January 2008 and December 2017 for all new presentations of orbital cellulitis. Presentations were grouped according to season. The Chi Squared test was used to compare the observed and expected frequencies of presentation.

## Results

Sixty two new presentations of orbital cellulitis were identified during the ten year study period. Of these, 23 (37.1%) presentations were in spring, 11 (17.7%) were in summer, 8 (12.9%) were in Autumn and 20 (32.3%) in Winter. This is insufficient evidence to suggest a seasonal relationship to the presentation of orbital cellulitis ( $p>0.99$ ). Comparing Summer Months to Winter months yielded no significant difference ( $P>0.99$ )

## Conclusions

No seasonal relationship with the presentations of orbital cellulitis has been found. Seasonal variations in immune function are complex and it has not been possible to demonstrate that this may affect the presentations of orbital cellulitis.

1822

### **micropulse diode laser trabeculoplasty- subthreshold is the new threshold**

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## Summary

Micropulse laser trabeculoplasty: subthreshold is the new threshold. S Ameen

In the past, laser treatment was only considered as a treatment option in the glaucoma- the very mild & end stage. This is due to the belief that the outcome is unpredictable and short lived. With the move towards less invasive interventions, the options of the laser treatment modalities available have expanded. One of those is Micropulse Laser Trabeculoplasty (MLT). MLT uses a specific diode laser with a much longer pulse length to target the trabecular meshwork. The temperature rises slowly, because laser energy is delivered in short microbursts over an extended time. This prevents scarring and helps to minimize the intraocular pressure (IOP) spikes. MLT is suitable with patients with open angle ocular hypertension/glaucoma. There has been a number of prospective and retrospective studies assessing the efficacy and safety of MLT and all have shown promising results of it being as effective as a single topical medication without the side effects. This is not only cost effective but also has a great impact on improving the patient's quality of life. Therefore, MLT should be considered as a first line treatment in the stepwise treatment regime of glaucoma.

S105

### **Calcium signaling in ex vivo cultured human anterior lens epithelial cells after mechanical stimulation**

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## Purpose

The purpose of this study is to explore and identify intra- and inter-cellular calcium ( $\text{Ca}^{2+}$ ) signaling in primary cultures of human lens epithelial cells (LECs) upon local mechanical stimulation, to understand better the role of  $\text{Ca}^{2+}$  in intercellular communication related to posterior capsular opacification (PCO), lens regeneration and cataract.

## Methods

The explants of anterior portion of the lens capsule consisting of monolayer of LECs were obtained from uneventful cataract surgery and were cultivated under adherent conditions. LECs were stained with Fura-2 dye, the fluorescence of which was imaged to monitor spatio-temporal changes in cytosolic free  $\text{Ca}^{2+}$  concentrations in response to localized, micropipette induced mechanical stimulation.

## Results

Local mechanical stimulation of primary LECs culture induces a Ca<sup>2+</sup> transient that propagates from the stimulated cell to other cells. In general, the amplitude of the Ca<sup>2+</sup> signal decays with increasing distance from stimulation, whereas the duration increases. The Ca<sup>2+</sup> signal propagation speed and its extent increase with the degree of confluency, but both parameters are lower in comparison to the postoperative lens capsules. In confluent culture LECs are in size similar to postoperative lens capsules LECs, whereas in non-confluent culture the LEC are up to several times larger. Moreover, Ca<sup>2+</sup> wave within the cell travels faster than between the cells.

## Conclusions

The modifications of Ca<sup>2+</sup> homeostasis in ex vivo cultured LECs, which are associated with different degrees of LECs confluency, affect Ca<sup>2+</sup> signaling upon the local mechanical stimulation. With increasing level of confluency, LEC's cultures have more developed Ca<sup>2+</sup> signaling capabilities. Establishing intercellular communication and Ca<sup>2+</sup> signaling might be reflected on lens regeneration and PCO.

## S098

### **Cenupatide is an effective antiangiogenic in a novel mouse model of rubeosis iridis associated with neovascular glaucoma**

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## Purpose

Puncture-induced iris wound healing in mice is associated with upregulation of inflammatory factors and iris neovascularization (rubeosis iridis; RI). Here, we investigate the anti-angiogenic and anti-inflammatory effectiveness of cenupatide (aka Uparant) in a new model of rubeosis iridis associated with neovascular glaucoma (NVG).

## Methods

BALB/c mouse pups of either sex were subjected to uveal puncture to stimulate RI or injected with ARPE-19 hypoxia-conditioned media to mimic NVG. Cenupatide effectiveness in reducing RI and NVG was determined by noninvasive in vivo iris vascular densitometry, and confirmed in vitro by quantitative vascular-specific CD31 immunostaining. Angiogenic and inflammatory related factors were assayed by quantitative PCR at the transcript level and by semi-quantitative western blot at the protein level.

## Results

Our data comparatively analyses antiangiogenic effects of cenupatide to a mouse equivalent of aflibercept (VEGFR1 Fc chimera). Intravitreal administration of cenupatide successfully and rapidly reduced iris vasculature to control (non-induced) level, in both RI and NVG models, while VEGFR1 Fc chimera displays a slower antiangiogenic effect that is not reduced to control levels. Molecular analysis revealed that cenupatide antagonizes formyl peptide receptors (FPR) through a predominantly anti-inflammatory response, accompanied with significant reduction of IL1 $\beta$ , IL6, CXCR4, CCL2, MMP2, MMP9, PAI-1, and uPAR. Furthermore, similar results were observed when cenupatide was administered systemically by subcutaneous injection.

## Conclusions

The tetrapeptide cenupatide is superior to anti-VEGF in the treatment of RI and RI associated with NVG in this novel mouse model. In addition, cenupatide displayed systemic effectiveness in reducing both RI and NVG, which could provide improved therapy for proliferative ocular diseases.



3155

### Hypoxia and eye: from bench to bedside

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#### Summary

The retina is the most metabolically active tissue and, therefore, the retina is highly sensitive to reduction in oxygen tension. All the hypoxia-dependent events in cells appear to share a common denominator: hypoxia-inducible factor (HIF), which is a heterodimeric transcription factor, a protein. Oxygen plays the key role in stabilizing HIF and its function. When the oxygen tension is normal, HIF is rapidly oxidized by hydroxylase enzymes, but when cell become hypoxic, HIF escapes the degradation and starts to accumulate. A large number of genes will be activated, among those are VEGF and EPO. The downregulation of HIF has a pivotal role if we are to inhibit neovascularization, as in the wet form of AMD or in proliferative diabetic retinopathy. HIF is a remarkable example of a single transcription factor that can be regarded as a "master switch" regulating all the oxygen-dependent retinal diseases. Clinical trials have shown that VEGF antagonists provide benefits for the patients with retinal neovascularization and several ongoing studies related to the oxygen metabolism of retina have been registered on the site of ClinicalTrials.gov. To combine basic and clinical research will increase job satisfaction among ophthalmologists.

3164

### Whole genome analysis of inherited retinal disease patients reveals non-coding mutations intractable to other detection strategies

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#### Summary

Purpose:

To identify pathogenic non-coding mutations using whole genome sequencing (WGS) in inherited retinal dystrophy (IRD) patients unsolved by prior exonic variant analysis.

Methods:

599 IRD singletons and 250 families underwent WGS. Non-coding variants in a panel of 224 IRD genes were investigated focusing on those patients in whom there was evidence for a single gene. Candidate intronic variants underwent *in silico* cryptic splicing analysis and likely pathogenic alleles were selected for functional testing.

Results:

225/599 families remained unsolved after exonic variant analysis and together harbored 91,758 ultra-rare variants (MAF <0.0005) across the entire gene panel. Likely pathogenic intronic variants identified included a *CRB1* variant (c.3879-1203C>G) found in trans with previously reported coding mutations in 2 unrelated families. This variant may activate a cryptic splice site leading to a 559bp pseudoexon. Additional likely pathogenic intronic variants were found in *ABCA4*, *USH2A*, *PRPF31* and *BEST1*.

#### Conclusions:

We identify potential pathogenic mutations in IRD genes intractable to other detection strategies. *In silico* and *in vitro* functional investigation (where possible) can confirm the pathogenicity of these mutations.

#### T024

##### **The EYE-MI pilot study: a prospective acute coronary syndrome cohort evaluated with retinal optical coherence tomography angiography**

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#### **Purpose**

To evaluate the association between retinal microvasculature (vascular density) on Optical Coherence Tomography-Angiography (OCT-A) and the cardiovascular profile of patients hospitalized for acute coronary syndrome (ACS).

#### **Methods**

EYE-Myocardial Infarction (EYE-MI) study is a prospective cross-sectional study in the Cardiology Intensive Care Unit of Dijon University Hospital. Retinal OCT-A was performed for each patient within 2 days after admission. Superficial retinal capillary plexus (SCP) vascular density was measured. The population was divided into tertiles according to OCT-A data.

#### **Results**

Overall, 237 cases were retained for analysis. Patients in the tertile with the lowest retinal vascular density (RVD) were older, and more frequently had systemic hypertension and diabetes. Moreover, AHA (American Heart Association) risk and GRACE (Global Registry of Acute Coronary Events) scores were higher and left ventricular ejection fraction (LVEF) was lower in these patients. In multivariate analysis, the AHA risk score (OR, 1.06; 95% CI, 1.04-1.09;  $P < 0.001$ ) and LVEF (OR, 0.95; 95% CI, 0.93-0.98;  $P = 0.001$ ) were significantly associated with the lowest tertile of RVD. The association between RVD and a high-risk cardiovascular profile was confirmed by a significant correlation with the GRACE scores (Spearman  $r = -0.33$ ,  $P < 0.001$ ).

#### **Conclusions**

SCP density measured on OCT-A was associated with the cardiovascular risk profile and with impaired LVEF in patients with a high-risk cardiovascular status. In the future, quantitative retinal microvascular data could be considered a good surrogate of the cardiovascular risk profile and could improve cardiovascular risk assessments.

#### F060

##### **Macular and papillary morphometric evaluation with SD-OCT in children affected by mild-severe refractive errors**

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#### **Purpose**

To evaluate macular and papillary parameters by spectral domain optical coherence tomography (SD-OCT) in children affected by mild-severe refractive errors.

## Methods

310 eyes of 155 children (mean age: 9.04 years) were divided into 3 groups: group 0 (223 eyes with spherical equivalent (SE) between  $-3$  D and  $+3$  D); group 1 (31 myopic eyes with  $SE \leq 3$  D); group 2 (56 hypermetropic eyes with  $SE \geq 3$  D). All the subjects were assessed for retinal nerve fiber layer thickness (RNFLT), optic nerve head (ONH) parameters, ganglion cell complex thickness (GCCT) and macular thickness (MT) at 3 and 5 mm from the fovea by Optovue iVue SD-OCT. Axial Length (AL) evaluation was assessed by optical biometer Zeiss IOL Master. Two-sided  $p$  values  $<0.05$  were considered statistically significant.

## Results

Average, superior and inferior RNFLT were higher in group 2 compared to group 1, with values of 95, 98 and 92.5  $\mu$ m (group 1) and 106, 107 and 104  $\mu$ m (group 2) ( $p<0.001$ ). Rim and disc area were higher in group 2 compared to group 1, with values of 1.72 and 2.17 mm<sup>2</sup> (group 1) and 2.16 and 2.48 mm<sup>2</sup> (group 2) ( $p<0.001$ ). Average, superior and inferior GCCT were higher in group 2 compared to group 1, with values of 96, 97 and 97  $\mu$ m (group 1) and 101, 100 and 101  $\mu$ m (group 2) ( $p<0.001$ ). MT was higher in group 2 compared to group 1, in the quadrants superior (S), inferior (I), temporal (T) and nasal (N), both at 3 and 5 mm from the fovea, with values of 274 and 303  $\mu$ m (group 1) and 305 and 318.5  $\mu$ m (group 2) (S), 266 and 303  $\mu$ m (group 1) and 295.5 and 315.5  $\mu$ m (group 2) (I), 254 and 297  $\mu$ m (group 1) and 254 and 307  $\mu$ m (group 2) (T), 291 (group 1) and 317 (group 2) (N, 3 mm from the fovea) ( $p<0.001$ ). AL was significantly different between the groups ( $p<0.00001$ ).

## Conclusions

Mild-severe refractive errors affect morphometric parameters of the ONH and of the macula assessed by SD-OCT.

2721

## Neuroprotective efficacy of a multi-loaded micro particulate drug delivery system in an ocular hypertension model of glaucoma

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## Summary

### Purpose

To evaluate the neuroprotective efficacy of a multi-loaded drug delivery system (PLGA microspheres (MSs)) after intravitreal injection in an experimental glaucoma model.

## Methods

Dexamethasone (DX), Melatonin (MEL) and Coenzyme Q10 (CoQ10) were selected as neuroprotective active substances. MSs loaded with the three drugs were prepared according to the O/W emulsion solvent extraction-evaporation technique. Multi-loaded MSs (ML-MSs) were characterized in term of morphology, encapsulation efficiencies and *in vitro* release studies. Bioactivity of the encapsulated drugs was performed in a retinal cell line (R28). To assess *in vivo* neuroprotection of ML-MSs, a well-established rodent model of ocular hypertension was employed.

## Results

MSs (20-30 $\mu$ m) showed spherical shapes. Encapsulation efficacies were higher than 60% and DX/MEL/CoQ10 were released in a controlled fashion up to 30 days. The multi-loaded system promoted a significant rescue of retinal cells from glutamate excitotoxicity ( $p<0.05$ ) compared to non-loaded-MSs. ML-MSs were able to significantly ( $p<0.05$ ) reduce RGC loss per integral IOP regarding non-treated animals.

## Conclusions

The developed drug delivery system demonstrated both *in vitro* and *in vivo* neuroprotective activity.

## T067

### Syphilitic placoid chorioretinitis: Clinical features and therapeutic response in two cases

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## Purpose

Ocular syphilis is a clinical manifestation that can occur at any stage of syphilis. Ocular syphilis can involve almost any eye structure, but posterior uveitis and panuveitis are the most common. Acute syphilitic posterior placoid chorioretinitis (ASPPC) is an uncommon manifestation of ocular syphilis. Our purpose is to present two clinical cases of ASPPC.

## Methods

We report two cases of unilateral ASPPC. Patient 1: A 54-year-old man presented with acute visual loss in his left eye. Best corrected visual acuity (BCVA) was 20/200 in his left eye and 20/25 in his right eye. Funduscopy examination of the left eye showed a yellow placoid lesion at the posterior pole. Patient 2: A 44-year-old man presented with 1 day of decreased vision in his left eye. Visual acuity was 20/70 in the left eye and 20/25 in the right eye. Dilated fundus examination also revealed a yellow lesion that involved the macula.

## Results

Optical coherence tomography angiography (OCTA) showed the placoid lesion at the level of the choriocapillaris. Fundus Autofluorescence (FAF) imaging demonstrated an area of hypoautofluorescence corresponding to the placoid lesion. Serologic tests were positive for syphilis in both cases. The patients were admitted and treated with intravenous infusion of Penicillin G with complete recovery of vision and disappearance of the lesions in the OCTA and fundus autofluorescence images.

## Conclusions

The manifestations of ocular syphilis are diverse and can simulate different pathologies. A proper diagnosis of ASPPC is important to perform the appropriate treatment. OCTA and FAF show characteristic outer retinal abnormalities that allow early diagnosis and follow-up of patients with disappearance of lesions with appropriate treatment.

## T048

### Carotid-cavernous fistula in a patient with diabetic macular edema. A case report

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## Purpose

Carotid-cavernous fistula (CCF) is an abnormal communication between the cavernous sinus and the carotid artery. CCF can develop either because of trauma or spontaneous causes. Common symptoms and signs on presentation include chemosis, pulsatile exophthalmos, ocular bruit, proptosis, diplopia, and visual loss.

## Methods

Observational case report of a diabetic patient that presented a spontaneous CCF.

## Results

We report a case of a 54-year-old man with a 40-year history of type 1 diabetes with cystoid macular edema (CME) due to diabetic retinopathy. He had persistent macular edema despite having good glycemic control and had poor response to treatment in spite of receiving multiple doses of intravitreal antiangiogenic injections. He presented a spontaneous CCF that was treated with endoscopic embolization. It was observed that the macular edema had almost completely reverted after this treatment.

## Conclusions

CCF is a rare condition and occurs mainly secondary to head trauma. Although spontaneous fistulas are usually of low flow and indirect and can revert without intervention in the majority of cases, in our patient it was decided to perform embolization due to decreased visual acuity and macular edema.

S068

### Morphological and refractive consequences of traumatic loss of LASIK corneal flap

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## Purpose

A 54-year-old woman came to our Emergency Department complained of pain and acute visual loss in her left eye after being hit with a projection of a chair. She had observed the fall of some tissue from her eye. As ophthalmological history she reported LASIK refractive surgery in both eyes fifteen years ago to correct a moderate myopia (6 diopters).

## Methods

A slit-lamp examination demonstrated a complete corneal abrasion with edema and Descemet membrane folds. At that time the patient had a visual acuity (VA) of 1/10 in her left eye. A traumatic flap amputation was suspected and to confirm it we decided doing an anterior optical coherence tomography (OCT). That image showed a flap loss with corneal thickness decrease until 300 micrometres. We decided to place a therapeutic contact lens (CL) and schedule treatment with vigamox three times a day, fluorometolone once a day, cyclopentolate three times a day, ophthalmic matrix therapy (Cacicol) every forty-eight hours, ocular hydration with artificial tears and doxycycline 100 mg for seven days. After that, the CL was maintained as well as the fluorometolone, vigamox and hydration twice a day for 2 weeks. By then she had already noticed a great improvement.

## Results

When we removed the CL we also performed an ORBSCAN, an Aladdin, a refractometry and an OCCAS. In that moment her VA without correction was similar in both eyes (6/10) in spite of the flap loss.

## Conclusions

The use of CL in addition to matrix therapy (Cacicol), antibiotic protection and ocular hydration has shown good results in cases of traumatic corneal flap loss. The loss of the corneal flap reduces the pachymetry without significant refractive affection with VA preserved.

2152

### OCT angiography in myopia

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#### Summary

Pathological myopia (PM) is a major cause of legal blindness in many developed countries. The increased axial length may lead to development of macular complications, including posterior staphyloma, retinoschisis, lacquer crack formation, chorioretinal atrophy, and myopic choroidal neovascularization (CNV). Moreover, various morphologic changes in the optic disc, such as  $\beta$ -peripapillary atrophy ( $\beta$ -PPA), optic disc tilt and rotation, have been demonstrated in myopic eyes.

Different techniques, such as fluorescein and indocyanine green angiography as well as Colour Doppler imaging, have been used to study retinal and choroidal blood flow in myopic eyes, revealing vascular changes which may be related to the pathogenesis of PM and the increased glaucoma susceptibility in myopic eyes.

Optical coherence tomography angiography (OCT-A) is an advanced and noninvasive imaging technique that provides depth-resolved visualization of the retinal and choroidal microvasculature without the need for dye injection. We will give an update on the role of OCT-A in the diagnosis of myopic CNV, as well as the analysis of the superficial and deep vascular density in macular and optic disc regions.

2921

### Influence of eyesight difficulties in the late work of the Spanish painter Francisco de Goya (1746-1828)

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#### Summary

The Spanish painter Francisco de Goya (1746-1828) has been admired for his use of colour, his energetic loose brushstrokes, his disregard for details and his bold compositions, as well as for his different artistic styles throughout his life. The evolution of Goya's style of painting in his later works seems to have been the consequence of an eyesight condition, probably age-related cataracts at an advanced stage. The faded dark backgrounds, which become blurred with the silhouette of the person portrayed, could indicate a certain degree of eye strain. This can be traced in the late works, but is especially evident in the unfinished portrait of *Pío de Molina* (1827-28), as well as in the portraits of *Mariano Goya* (1827), and *Jacques Galos* (1826). It has been considered that the late and isolated Goya's sight problems were a belated consequence of his severe illness of 1792. Nevertheless, this is a simplistic explanation and, given the painter's age, it is logical to presume that their cause could be age-related lens opacities. This article argues that Medicine may become a subsidiary science to Art History, as it can provide empirical evidence of the way painters' illnesses may have a strong impact on their art works.

2764

### Transcriptional networks regulating timing and differentiation of the retinal pigmented epithelium

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#### Summary

The retinal pigmented epithelium (RPE) reside between the blood vessels of the choroid and the photoreceptors and is required for the development and function of these adjacent cell types. Accordingly, mutations in RPE genes cause monogenic as well as multifactorial retinal diseases. The RPE is readily generated from stem cells, and these stem cell-derived RPE cells are currently being tested in clinical trials for transplantation in cases of retinal dystrophies; they also constitute an important model to study developmental processes in vitro. To elucidate the molecular mechanisms regulating RPE differentiation and mediating interactions with adjacent photoreceptors and choroid blood vessels, we conducted functional and biochemical studies of transcription factors in vivo in mice, and in stem cell-derived RPE. The results reveal early and late gene regulatory networks of RPE-expressed genes and point to the signaling pathways mediating interactions with adjacent choroidal vasculature. These findings contribute to uncovering gene regulatory networks that control the gradual and coordinated differentiation occurring during organogenesis of the eye and further advance research of retinal disorders.

**2963**

#### **Classification of ocular anterior dysgenesis: new insights**

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#### **Summary**

Ocular anterior segment dysgenesis may be associated with a variety of systemic and ocular conditions. Anterior segment structures are very important in visual system development as the anomalies can result in corneal opacities that obstruct visual axis or can cause angle defects that increase intraocular pressure and cause glaucoma. Clinical manifestations can be variable according to the involved tissue. Embryologically, neural crest mesenchymal cells and the neuroectoderm of the optic cup and the surface ectoderm also have role in development of anterior segment structures. Recent advances in genetics help us to better understand the underlying mechanisms. Clinically there is a large spectrum of findings from posterior embryotoxon to more severe forms such as aniridia, Peters anomaly or sclerocornea, or congenital glaucoma.

**017**

#### **Inherited disease: from diagnosis to treatment**

**018**

#### **Macular edema**

**F124**

#### **On the day cataract operation cancellations: A prospective audit**

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### **Purpose**

A prospective audit was undertaken to establish the rate of cancellation of elective cataract surgery cases on the day of planned surgery and the reasons for these cancellations in a large district general hospital in the UK.

### **Methods**

A record was kept of all cancellations made on the day of surgery over a consecutive five-month period.

### **Results**

During the audit period there were 1730 elective cataract surgeries performed and 59 on the day cancellations of surgery, giving a cancellation rate of 3.3%. The leading cause of cancellation was co-existing eye problems (30.4%), followed by other medical illnesses in 28.9%. Other causes for cancellation included high INR, inappropriate listing for surgery, unavailable intraocular lens (IOL), inappropriate surgeon allocation and patient transport failure.

### **Conclusions**

Although the cancellation rate was found to be relatively low, this still represents a significant loss of income, waste of resources and source of concern for patients and staff.

### **S081**

#### **Improved wound resolution for Entropion Surgery using a microscope-assisted 8'0' vicryl suture technique.**

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### **Purpose**

Most entropion surgery is performed using loupes and 6.0 vicryl. However, vicryl sutures cause granulomatous reaction within the eyelid and tarsal plate. Use of finer sutures may reduce this reaction, but it is unknown as to whether they are strong enough to prevent wound dehiscence.

### **Methods**

A retrospective case series was performed to investigate whether microscope-assisted entropion surgery performed using 8.0 vicryl was a safe alternative to conventional surgery using larger sutures. Rates of recurrence of entropion, wound infection and dehiscence were investigated. Success was defined as normal eyelid position and complete or significant resolution of preoperative symptoms at the last postoperative follow-up visit.

### **Results**

6 months or more of follow up was achieved. Of 26 procedures performed between August 2013 and August 2016 for involutional entropion using a 'microscope assisted' approach there was a 96.2% (25/26) success rate (defined by complete resolution of symptoms). No skin lumpiness or notch was seen in 84.6% (22/26) of cases. No residual lid laxity was found in 96.2% (25/26). In the 1 patient who had a recurrence of symptoms 6 months after surgery, it was found that they had a negative cheek vector and residual laxity, and required increased lid tightening. Notably, as early as 1-week post-operative review, many patients reported minimal residual inflammation and pain.

### **Conclusions**

These preliminary results form part of a larger ongoing study and demonstrate that microscope-assisted entropion repair using 8.0 vicryl is a robust technique for entropion repair, achieving high success rates and good cosmetic outcome. These results demonstrate non-inferiority to reported success rates for conventional entropion surgery and suggests reduced recovery times and reduced incidence of granulomatous reactions.



2526

### TFOS DEWS II Management and Therapy Report

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#### Summary

The members of the Management and Therapy Subcommittee of TFOS DEWS II undertook an evidence-based review of current dry eye therapies and management options. We present management options reviewed in detail including treatments for tear insufficiency and lid abnormalities, as well as anti-inflammatory medications, surgical approaches, dietary modifications, environmental considerations and complementary therapies. Reflecting on all available evidence, a staged management algorithm that presents a step-wise approach to implementing the various management and therapeutic options according to disease severity will be presented.

2362

### Retinal vascular changes in mitochondrial optic neuropathy

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#### Summary

Advances in ocular imaging, particularly the introduction of new imaging techniques and software analysis, have enabled to visualize in detail retinal, choroidal and vascular structures. Recent studies evaluated macular and peripapillary choroidal thickness changes in asymptomatic, acute and chronic stage of LHON and in DOA. Moreover, the vascular supply of the optic nerve, the macula and the choriocapillary has been detected by using the optical coherence tomography angiography technique in LHON. Peripapillary microangiopathy has been documented in the acute phase of LHON and a progressive peripapillary vascular reduction is detectable starting from the temporal and inferotemporal sectors as the disease progresses, then spreading to all the other peripapillary vessels in the chronic phase. The study of the vascular supply and of the vessel density using algorithms able to quantify optic nerve head, peripapillary, choroidal and macular perfusion may become a useful biomarker to monitor the disease process, evaluate therapeutic efficacy and elucidate pathophysiology.

3522

### Biomarkers in optic neuritis

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#### Summary

OCT has emerged as a potential metric for axonal loss in patients with multiple sclerosis (MS), both those with optic neuritis (MS-ON) and those without optic neuritis (MS-non-ON). Retinal nerve fiber layer (RNFL) thinning is detectable about 2 months after optic neuritis, with most loss occurring within 3 to 6 months. Peripapillary RNFL thinning is also reported in patients with MS-non-ON, thus suggesting subclinical axonal damage in the anterior visual pathway. A thinning of all the macular layers (mostly of the inner retina) is reported in patients with MS-ON. Thinning of the macular RNFL, but not of the ganglion cell-inner plexiform layer (GC-IPL) can also be detected in patients with MS-non-ON. The temporal and spatial associations between axonal injury and ganglion cell loss have

yet to be determined, although retrograde degeneration of the RNFL has been implicated as the most important mechanism leading to macular damage. Reduction of peripapillary RNFL, macular RNFL, GCL-IPL thickness is associated with 1) loss of visual function, 2) function disability as measured by the Expanded Disability Status Scale, and 3) vision-specific quality of life in MS patients. New promising data about OCT angiography will be discussed.

**3421**

### **Scattered light and retinal sensitivity to contrast**

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#### **Summary**

The Light Scatter (LS) function of the eye was measured in 40 subjects (21 to 68 yrs old) using a new version of the City University 'Light-Scatter' test which measures with greater sensitivity and accuracy both the amount and the angular distribution of forward LS in the eye. This function was then used for each subject to predict how retinal illuminance in the very centre of the fovea is expected to increase due to LS when a small 'Glare Source' (GS) is present at a known eccentricity in the visual field.

Retinal sensitivity to contrast was measured using Landolt ring targets for 5°, 10° and 15° GS eccentricities, 3 background luminance levels (1, 2.6 and 26 cd/m<sup>2</sup>) and 3 pupil plane GS illuminance levels (0, 1.35 and 19.2 lm/m<sup>2</sup>). Measured increments in contrast thresholds due to forward LS were then compared against predicted changes in retinal image contrast caused by the 'veiling' luminance of the GS. Performance was better than predicted, particularly in the mesopic range. These findings will be discussed in relation to the expected improvement in retinal sensitivity to contrast as a result of increased retinal illuminance caused by the GS, internal scatter within the eyeball and the directional sensitivity of cones.

**S005**

### **Processed human umbilical cord lining as transplant for sclera defect: an in vivo study**

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#### **Purpose**

Umbilical cord lining (UCL) is composed of 2 layers : amnion and wharton's jelly. To be use as graft, UCL undergoes a viral-inactivating, freeze-drying and sterilizing patented treatment (tUCL). An *in vivo* study is performed in order to investigate the regenerative potential of scleral defect with tUCL.

#### **Methods**

16 male rabbits are included in this study and distributed in 4 groups with sacrifice on day 7, 14, 30 or 45 after surgical act. Deep sclerectomies (4x4mm) are performed on every left eyeball in the dorsolateral area. 3 eyeballs per group have been implanted with tUCL and 1 eyeball per group have been sutured with the scleral excision part (sham). Post surgery clinical follow-up have been performed on days 3, 7, 10, 14, 21, 30 and 45. Sclera regeneration assessment have been performed macroscopically and microscopically (histopathological analysis) after sacrifice.

#### **Results**

Clinical monitoring shows no difference between animal implanted with tUCL and sham. Almost all clinical signs disappeared at day 21. Macroscopic and histological evaluation shows no difference between treated animals and sham. Histopathological analysis reveal good tolerance and integration of tUCL. At day 45, no biomaterial residue have been detected which approve its biodegradability, each animal had its sclera fully reconstructed with a similar

thickness compared to adjacent sclera and there was a complete return to normal aspect of the subconjunctival space. The overall quality and kinetic of reconstruction of tUCL-implanted animals for scleral defect was similar to sham-operated animals.

### Conclusions

The patented treatment applied on UCL provides a safe, biocompatible and biodegradable graft. The human umbilical cord lining derived tUCL happens to be as efficient as an autologous transplant for scleral defect which make it a good candidate for scleral transplant.

### S006

#### Development of secured amniotic membranes as ophthalmologic allografts

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### Purpose

The objective is to develop an AM treatment process with a chemical treatment, freeze-drying and gamma sterilization to produce a safe product stored at room temperature (RT) with structural characteristic and growth factors preservation

### Methods

Viral inactivation (2 baths) is evaluated by spiking a wide range (DNA, RNA enveloped or not) of viruses into spongy layer before each bath and quantifying potential remaining viruses extracted by titration. Disinfection by chemical baths is evaluated by bioburden assessment before sterilization, and endotoxin. Sterilization is evaluated by spiking 107 radioresistant and vaginal strains. Biocompatibility is assessed by ISO 10993 and cell culture with mesenchymal stem cell (MSC). Structure preservation is based on immunostaining of major proteins and quantitative analysis of TGF- $\beta$ 1, KGF and EGF on final product compared to fresh membrane.

### Results

Chemical treatment showed a viral reduction > 4 Log of each virus. *B. pumilus*, *S. pyogenes*, *C. albicans*, *E. coli* et *E. faecalis* strains inoculated inside the membranes were not present after irradiation. Bioburden, endotoxin are very low. MSC were viable and strongly attached to both sides of the membrane. Final structure contains collagen I, elastin and laminin V at the same range than fresh AM. TGF- $\beta$ 1 levels are similar for fresh and processed AM (around 10 ng/g), EGF level is 7 time less (0.73 ng/g fresh vs 0.11 ng/g processed) and KGF levels are close (0.48 ng/g fresh vs 0.2 ng/g processed).

### Conclusions

Treatment applied to AM gives an effective viral-inactivation, disinfection and sterilization. Final products show good biocompatibility with similar structure and presence of growth factors. The treatment can provide safe AM easy to manipulate, storable at RT, with same biological structure than fresh tissue.

### T019

#### Macular thickness and volume related to vascular macular capillary in OCTA in patients with Type 1 diabetes with no retinopathy

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## **Purpose**

neuronal changes in diabetic patients can be study indirectly using spectral domain OCT thickness and volume. OCT angiography (OCTA) allows studying the macular vascular plexus in a non-invasive way. The purpose of our study was to evaluate changes in the macular vascular density changes using OCTA, and to examine its correlation with OCT macular thickness diminution over 8 year follow-up in patients with type 1 diabetes and no signs of diabetic retinopathy.

## **Methods**

eighteen eyes of 9 diabetic patients with no retinopathy were studied by SD-OCT at 2009. The patients were reexamined by SD-OCT looking for changes in macular thickness and volume; all eyes underwent angio OCT. FAZ was manually measured. Macular thickness and volume changes over these 8 years were correlated with finding at the OCTA and FAZ area.

## **Results**

mean age of the patients was  $35.32 \pm 14.23$  years (range 23-54). Mean time of diabetes evolution was  $15.96 \pm 11.46$  years. Best corrected visual acuity (BCVA) was comprised between 0 and -0.3 logMAR. 16 eyes showed no signs of diabetic retinopathy. One patient had mild-moderate diabetic retinopathy with macular edema in his LE. Eyes with OCTA changes showed modification in both superficial and deep plexus. Vascular changes included reduced capillary density, regions of capillary dropout and foveal avascular enlargement. Patients with OCTA changes displayed a diminished macular volume over the 8 years of follow up (excluding the one with diabetic retinopathy).

## **Conclusions**

despite we are not able to find signs of diabetic retinopathy, type 1 diabetic patients develop changes at the vascular level that are related to a diminution of the OCT macular volume.

## **T023**

### **Optical coherence tomography findings after retinal artery occlusion**

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## **Purpose**

The purpose of our study is to demonstrate the importance of OCTA in the evaluation of the retinal vessels in two cases of retinal occlusion.

## **Methods**

We report two cases of retinal occlusion

## **Results**

A 57-year-old man presented with sudden painless loss of vision in his left eye for 1 hour, with no other symptoms. His best corrected visual acuity (BCVA) was 20/40 and perception of light in his RE and LE respectively. Detailed fundusoscopic examination showed diffuse whitening of his macula, except for the nasal parafovea and perifovea with cilioretinal artery sparing with orange perfused retina in its distribution, cherry-red spot. OCTA was performed in both eyes demonstrated a severe nonperfusion in superficial and deep retinal capillary plexus in the macular area except for the nasal parafovea where we could see a spider-web pattern of vessels which corresponds to the cilioretinal artery without reaching the fovea region.

A 61-year-old woman diagnosed with monoclonal gammopathy IgG kappa and arterial hypertension, came to the emergency room complaining of a superior visual field defect in her RE 7 days before. Her BCVA was 20/20 in both eyes. Detailed fundusoscopic examination revealed a white thrombus in the beginning of the inferotemporal retinal artery. OCTA showed a lower capillary density in her inferior zone both in superficial and deep capillary plexus. We could observe macular edema that hides vascularization in the inferior paramacular sector and vessels with many small, discontinuous segments.

### Conclusions

OCTA is becoming an important tool in all retinal and choroidal vascular diseases. In retinal arterial occlusion OCTA assesses the real macular ischemia and give us new information of the retinal status to evaluate blood changes during a vascular disease such as CRAO.

### F044

#### Amniotic membrane transplantation and conjunctival autograft for repair of leaking glaucoma filtering bleb

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### Purpose

We report the case of amniotic membrane transplantation and conjunctival autograft to repair a late leakage bleb that occurred long time after a phacotrabeculectomy with mitomycin C.

### Methods

A 65-year old woman, with a history of bilateral open angle glaucoma, she had undergone a combined cataract and trabeculectomy surgery with mitomycin C in both eyes 10 years before. In 2011 she came to the Emergency Service of our hospital and presented with a leaking bleb in her right eye, her best corrected visual acuity was perception of light in her right and 20/100 in her left eye. Slit-lamp examination revealed an avascular filtering bleb with leakage in the middle and necrotic conjunctiva around it. Intraocular pressure (IOP) was 4 and 7 mmHg respectively.

### Results

After local anesthesia, the necrotic avascular conjunctiva around the bleb was dissected and a sample of amniotic membrane was used to repair the bleb and finally an autologous conjunctival graft from the other eye was sutured above the amniotic membrane. During the follow up the leak remained successfully repaired and the IOP stayed in 12 mmHg without medication and best-corrected visual acuity improved to 20/50 in her right eye.

### Conclusions

Conjunctival autograft placed over a sample of amniotic membrane seems to be an effective and safe technique in the management of late-onset bleb leakage.

#### F040

##### **Comparison of vessel diameters during hypoxia in patients with low tension glaucoma, ocular hypertension and age-matched control**

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##### **Purpose**

The pathogenesis of glaucoma is not fully known. Poorly regulated auto regulation is thought to be one of the risk factors for development and progression of glaucoma. The purpose of this study was to investigate differences in retinal vessel diameters in low-tension glaucoma patients (LTG), ocular hypertension patients (OHT), and age-matched controls before, during and after universal hypoxia.

##### **Methods**

Ten controls, ten patients diagnosed with LTG and nine patients diagnosed with OHT underwent normobaric hypoxia (10% O<sub>2</sub> and 90% N<sub>2</sub>) for two hours. Fundus pictures were taken at baseline, one-hour hypoxia, two-hours into hypoxia, and 30 minutes after hypoxia. Diameters of the upper temporal artery and vein were measured.

##### **Results**

Consistent with a previous study, we found a significantly smaller arterial vessel diameter at baseline in patients with LTG compared to controls  $-1,33 \pm 0,63$  (mean  $\pm$  sd, n=20, p=0,04). Relative arterial vessel diameters increased significantly in both patients with LTG ( $2,126 \pm 0,752$ , p=0,01) and patients with OHT ( $-3,547$  to  $-0,2015$ , p=0,02). Vein vessel diameter did not change significantly from the control group in neither the LTG group nor the OHT group.

##### **Conclusions**

Reduced arterial vessel diameter at baseline was identified as a potential marker for LTG. Moreover, patients with LTG tend to have the biggest variation in vessel diameters in response to universal hypoxia. This indicates retinal vascular dysregulation as a potential LTG marker. Vessel diameters among patients diagnosed with OHT had a pattern similar to patients with LTG, but to a lesser extent. This study suggests that better auto regulation is a protective factor against optic neurodegeneration. Overall, our study suggests a link between dysfunctional auto regulation and LTG.

#### T065

##### **Acute endophthalmitis after intravitreal injections of corticosteroids or anti-vascular growth factor agents. A nationwide study in France from 2012 to 2015**

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### **Purpose**

The number of patients affected by retinal diseases treated with intravitreal injections has resulted in a rapidly growing number of procedures. One of the most dreaded complications following these injections is endophthalmitis. The objective of this study was to evaluate the incidence of acute endophthalmitis after intravitreal injections of corticosteroids or antivascular endothelial growth factor (VEGF) agents.

### **Methods**

The French Medical-Administrative Database was used to assess the incidence rate of endophthalmitis at a nationwide level and its risk factors between 1 January 2012 and 31 December 2015.

### **Results**

From January 2012 to December 2015, 1,811,977 intravitreal injections of corticosteroids or anti-VEGF agents performed on 254,927 patients were analyzed. We recorded 444 acute endophthalmitis cases (0.0245%). In multivariate analysis, the risk of endophthalmitis was lower in males (incidence rate ratio (IRR), 0.78; 95% CI, 0.63–0.96;  $P=0.02$ ), higher for corticosteroids than for anti-VEGF agents (IRR, 3.21; 95% CI 2.33–4.44;  $P<0.001$ ) and higher for non-prefilled syringes of anti-VEGF medications than prefilled syringes (IRR, 1.63; 95% CI, 1.15–2.30) for ranibizumab and (IRR, 1.82; 95% CI, 1.25–2.66;  $P<0.001$ ) for aflibercept.

### **Conclusions**

A national database confirmed the low incidence rate of acute endophthalmitis after intravitreal injections of corticosteroids or anti-VEGF agents. The risk for acute endophthalmitis after intravitreal injections was higher for corticosteroids compared with anti-VEGF agents. A significantly lower risk of endophthalmitis was observed with prefilled syringes of anti-VEGF medications.

3442

### **Automated analysis of eye tumor MR-images for an improved treatment determination**

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### **Purpose**

MR-imaging has become a valuable additional imaging modality for Uveal Melanoma (UM). The capability to image the eye in 3D is of the main advantages of MRI over conventional ultrasound imaging. Although 3D images allow for a more accurate assessment of the tumor geometry, the analysis of these images can be quite time-consuming, especially for tumors with a complex shape. We therefore propose an automatic framework to segment these MR-images and measure tumor thickness accurately.

### **Methods**

The automatic segmentation was performed in MevisLab. Initially, the sclera was detected on the T2-weighted image and this mask was used to register the T2- and T1-weighted images using ElastiX, with normalized mutual information as a similarity metric. Vitreous body, lens and tumor were subsequently segmented on the T1-weighted image. Finally, tumor thickness was determined by calculating the maximum distance between the tumor and sclera. The method was evaluated on 7 patients who were examined on a Philips 7-Tesla MRI using a dedicated eye-coil. Eye-motion artefacts were minimized by a cued-blinking protocol.

### **Results**

The proposed automatic method successfully detected the different tissues. In two patients, MRI artefacts caused a small error in the sclera segmentation, but this did not influence the subsequent steps. The benefit of the automatic analysis was clearly illustrated in the patients. For example, for tumours consisting of multiple lobes the plane and location for the distance measurement are not known a priori. As this method calculates the distance for the complete tumor boundary, it results in more accurate measurements.

### Conclusions

The proposed automatic analysis pipeline for MR-images for UM enables an accurate and fast 3D assessment of the tumor dimensions, which directly improves the therapy planning.

002

### Blood retinal barrier

2523

### TFOS DEWS II Pain & Sensation Report

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### Summary

Discomfort in DED is a particular type of somatic pain and can be nociceptive, i.e. caused by actual damage to tissues, or neuropathic due to a lesion within the pain sensory pathways. Pain signals activated by DED are transmitted via the peripheral axons of trigeminal ganglion neurons. Functionally, TG neurons belong to the polymodal nociceptor, mechano-nociceptor and cold thermoreceptor sensory categories. They project primarily into the trigeminal brainstem nuclear complex, which mediate sensory-discriminative aspects of ocular pain, and lacrimation and blinking control through the modulation of sympathetic and parasympathetic pathways. In experimental DED, reduced tearing leads to inflammation which sensitizes moderately polymodal and mechano-nociceptors and nerve terminal injury which causes prominent, abnormal impulse activity in cold thermoreceptors, suggesting that cold nerve terminal injury dominates over inflammation effects. Long-lasting, abnormal peripheral nerve activity in DED may cause functional and anatomical alterations at higher levels of eye pain pathways. This evokes neuropathic pain largely independent of the original cause which persists without an obvious relationship with the peripheral nociceptive input.

T080

### The incidence of rhegmatogenous retinal detachment in France from 2010 to 2016: seasonal and geographical variations

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### Purpose



To investigate the annual and monthly incidence of rhegmatogenous retinal detachments (RRD) from 2010 to 2016 in France at the national and departmental levels.

### Methods

We identified hospital and clinic admissions for a first episode of RRD in France from 2010 to 2016 by means of billing codes from the national administrative database. Patients admitted for a RRD in the two previous years were excluded. The annual and monthly incidence of RRD per 100 000 inhabitants was calculated for the whole country and for each department. The number of inhabitants in France and in each French department was obtained from the French National Institute of Statistics and Economic Studies.

### Results

We identified 101 085 admissions for a first episode of RRD in France between 2010 and 2016. The average annual national incidence of RRD was 21.97 per 100 000. The annual national incidence of RRD was the lowest in 2010 (20.91 per 100 000) and increased until 2015 (23.55 per 100 000). The average monthly national incidence was the highest in June (2.03 per 100 000) and July (1.99 per 100 000) and the lowest in August (1.60 per 100 000) and February (1.67 per 100 000). The average annual departmental incidence was the highest in Lot (34.54 per 100 000) and in Finistère (32.52 per 100 000) and the lowest in Guyane (10.05 per 100 000) and in La Réunion (13.52 per 100 000). There was a tendency toward a higher RRD incidence in southern and western France.

### Conclusions

This national population-based study allowed us to identify 101 085 admissions for a first episode of RRD in France between 2010 and 2016. Annual national incidence of RRD increased from 2010 to 2015. Incidence of RRD varied with seasons and geographical location.

## F054

### Orbital exenteration with superficial temporalis muscle flap: an innovating approach

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### Purpose

Usual reconstruction approach after eyelid and conjunctiva-sparing orbital exenteration consists of the transfer of a temporalis muscle pedicle flap for orbital socket reconstruction or the transfer of fascia temporalis only. We describe an innovating approach to transfer only the superficial third of the temporalis muscle.

### Methods

We report the case of a 6-years-old boy operated in our pediatric center for a relapsing left orbital rhabdomyosarcoma staged IRS 3. After biopsy and confirmation of the tumor, initial treatment consisted in chemotherapy (Ifosfamide, vincristine, actinomycine) and protontherapy. The RMS recurred 18 months after the end of treatment, with an intraorbital RMS extending to the medial, lateral, upper rectus muscles and the latero-orbital ridge. A second line of rescue chemotherapy (IV Etoposide and Cyclophosphamide Adriamycine Vincristine) was begun before exenteration. A partial temporalis muscle flap reconstructed cavity.

### Results

Flap technique. The muscle is supplied by 3 pedicles: the deep, the middle and the superficial temporal artery. This flap is supplied by the middle and superficial pedicles. The flap is harvested through an hemicoronal and preauricular approach. The deep layer of deep temporalis fascia is incised in a vertical direction, and the underlying temporalis muscle is exposed. The superficial and middle temporal vessels are identified. The middle part of the

muscle and the fascia superficialis provided a good volume for a suitable prosthesis and minimizes the usual deformity of temporalis fossa. The flap was transferred through a lateral orbital wall osteotomy.

### Conclusions

The use of this flap allowed facilitating the rehabilitation process and postoperative treatment. Compared to a temporal muscle flap, it avoids temporal depression; compared to fascia temporalis flap, it provides more tissue.

## T089

### Retinal biomarkers for Alzheimer's and Parkinson's diseases

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### Purpose

The use of the retina as a window into the brain is a promising avenue of research when it comes to the identification of imaging biomarkers that can assist in the early diagnosis of neurodegenerative disorders such as Alzheimer's (AD) and Parkinson's (PD) disease. In this work, optical coherence tomography data were used to compute macular images of the six innermost retinal layers and classify eyes into the AD, PD and healthy control groups.

### Methods

Computed fundus images were analysed by applying local and global texture metrics, to identify criteria that distinguish between healthy controls and patients diagnosed with any of the two neurodegeneration states mentioned above. The possibility of distinguishing between the two disorders themselves, that is, between the AD and PD eyes, was also investigated. The identification of the most significant features and their use in classification models was performed using support vector machines with radial basis function kernel.

### Results

Median results after 100 consecutive runs of the classification process, with 10-fold cross-validation, are 88.7%, 79.5% and 77.8% for the sensitivity and 84.9%, 92.5% and 97.8% for the specificity in identifying, respectively, healthy control, AD and PD eyes. Notably, when the same subject has their two eyes attributed to the same class, 94.4% (median) of the classifications are correct. Furthermore, when using texture features, only 1.4% (median) of the eyes do not show any difference among the three groups.

### Conclusions

Achieved results reveal that a significant amount of information concerning AD and PD states is conveyed by optical coherence tomography imaging of the human retina. The diagnosis of the two most common neurodegenerative disorders in the developed world can thus benefit from the information provided by this non-invasive in-vivo imaging technique.

## 1233

### Optical Coherence Tomography – Machine Learning

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### Summary

Machine learning is a method of data analysis. It gives computers the ability to learn from data and to build models from which predictions can be made. Even though OCT is mainly used to visualize retinal structures and compute thickness maps, it conveys information on subtle changes within the retina before structural ones can be identified. Exposing the machine learning model to a set of examples allows it to build a model from which predictions can be made on new data and explain differences between groups. This lecture will explain the underlying principles of machine learning and discuss potential applications in ophthalmology and CNS disorders through the imaging of the retina.

**2634**

#### **Link between genetic and functional analyses in pseudoexfoliation glaucoma**

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#### **Summary**

Pseudoexfoliation (PEX) syndrome is an age related systemic disorder characterized by deposition of abnormally crosslinked, extracellular material in various ocular tissues. It often results in PEX glaucoma (PEXG), the most common identifiable form of secondary glaucoma, accounting for 25-70% of open angle glaucoma. Besides various environmental conditions, e.g. UV radiation and oxidative stress, several genome wide associations studies (GWAS) and functional analyses revealed *LOXL1* as the major genetic and pathophysiologic risk factor for this complex disease. However, all associated *LOXL1* risk variants identified to date, show frequent occurrence in healthy subjects and significant allele reversal between Caucasians and other ethnic populations. This presentation will highlight the necessity of worldwide, large scale genomic studies in combination with precise functional gene characterization to elucidate the pathogenesis of complex multifactorial diseases like PEX syndrome/glaucoma.

**T088**

#### **Is that a torpedo near the fovea? Torpedo maculopathy a case report**

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#### **Purpose**

Torpedo maculopathy is a benign maculopathy, characterized by hypopigmentation of the pigmentary retinal epithelium. It is not related with other systemic diseases.

The best corrected visual acuity depends in the foveal affection. The patients can suffer of a scotoma Diagnosis depends on fundoscopy and macular OCT.

#### **Methods**

Slit lamp examination, best corrected visual acuity, indirect fundoscopy, OCT swept source.

#### **Results**

The patient showed in the first examination (4 years old) a BCVA of 0,4 in the right eye. The fundus examination showed a hypopigmentary macular lesion temporal to the fovea. Te infectious etiology was dismissed due to the normal serologies. In the next examinations when the patient was 5 year old the visual acuity was 0,5 in the right eye and 10/10 in the left eye. the patient showed a good stereopsis.

#### **Conclusions**

Torpedo maculopathy is a characteristic pathology that we have to take into account in pediatric patients with macular lesions. The patients present a good prognosis and don't need treatment.

**1422**

#### **Phaco ECP**

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#### **Summary**

Lasers have been used extensively in glaucoma treatment. Nowadays surgical options include transcleral photocoagulation (TSC) and endoscopic cyclophotocoagulation (ECP) of the ciliary body. ECP is a purely inflow procedure which is used to ablate the ciliary body. With ECP there is a direct view of the ciliary processes with the help of an endoscope. Unlike TSC the treatment is targeted in the ciliary body and there is no absorption of the laser energy from adjacent tissues. Commonly it is used along with cataract surgery after the implantation of the IOL through the main incision. ECP belongs to the MIGS category since it is an ab interno procedure, it is combined with cataract extraction and it is ocular surface friendly. Unlike TSC the post-operative complications are few and the reduction of the IOP can be up to 30%. Previous studies have also shown that it is a cost-effective treatment compared to other MIGS devices. Even though ECP is mostly used along with cataract surgery, it can be performed after pars plana vitrectomy in pseudophakic eyes (through the pars plana) but it can also be done in phakic eyes.

**1823**

#### **ALPI- Post EAGLE to PI or not to PI**

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#### **Summary**

Laser peripheral iridoplasty (LPI) is an alternative treatment for opening an appositionally closed angle. Unlike peripheral iridotomy the aim of LPI is to tighten the peripheral iris and widen the anterior chamber angle. The treatment consists of a series of burns applied in the peripheral iris which are of low energy, small duration and large spot size. In that way there is a shrinkage of collagen and the iris is pulled away from the angle. Traditionally LPI is performed with an Argon laser but it can also be done with Pascal laser. LPI can be applied in an acute angle closure attack where a peripheral iridotomy is more difficult or even in chronic angle closure glaucoma. ALPI can also be used in plateau iris syndrome where the angle remains occludable despite a patent iridotomy. Other indications include lens-induced glaucoma and the widening of the angle prior to laser trabeculoplasty. Although it is a safe procedure sometimes there is recurrence of the angle closure, especially in plateau iris syndrome.

**1451**

#### **New technologies in proteomic research**

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#### **Summary**

Proteomics and the closely related area of metabolomics provide insights into the status of a chronic disease process such as dry eye while metabolomics is more immediate with snapshots of the ongoing cell physiology. Thus, the two types of data will show long term tissue pathology which can potentially be used for predicting outcomes and stratifying patients for treatment cohorts. Metabolomics can reveal within the same sample population the changing contribution of the physiology of cells to treatment or worsening of the pathology. The information represents gene expression at the highest level which in fact feedback to the genome producing a new proteome and metabolome. It is generally accepted that the correlation between gene expression and changes in the proteome or metabolome are only 40-50%, and not 1:1. New technologies such as pathway mapping, proteomic characterization in the development of antibody treatments, and the very exciting area of imaging proteomics/metabolomics are receiving a great deal of attention.

**1853**

#### **Large data sets in Proteomics and new insights into eye disease**

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#### **Summary**

In recent years proteomic technology, largely using time of flight mass spectrometry, TOF/MS with MALDI as an initial step, has progressed beyond what was expected. Although, interest in understanding the relevance of certain constituents of the tears and their correlation with disease states especially inflammation and dry eye was active studies usually examined pooled tears from a number of patients and used crude protein extracts or antibody techniques to examine no more than 8-12 constituents at a time. Now studies routinely progress with tear samples of 1-2µl and accurate quantitation approaching that of ELISA.

The results show that the tear proteome in a normal eye has more than 1200 identifiable proteins. However, a great advantage of the approach over genomics is that the exact source for each protein does not need to be specified rather they are present at quantifiable levels characterizing a disease or a stage of the disease or treatment. Bioinformatics analysis of these large data sets continue to require new approaches due to the necessity of interpretation as well as statistical rigor.

**1722**

#### **UK Trainee Trabeculectomy Outcomes incorporating Simulated Surgery**

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#### **Summary**

Multiple research articles, 30 randomised controlled trials and a Cochrane review on simulation in surgery and training emphasize the interest and wide application of simulated methods that can be utilised. Simulated practice often occurs now as a component of undergraduate training. Easing the learning curve of complex tasks is obviously beneficial for trainees and patients and this has shown to be the case with the use of simulation models. A practical guide to implementation of the use of simulation surgery in training will be outlined, with emphasis on glaucoma surgical training.

**S083**

#### **Effect of Pseudomonas and Acanthamoeba infection upon inflammation produced by human cornea epithelial cells**

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## Purpose

The cornea epithelial cells are the first line of defense and physical barrier of the eye against infectious agents, capable of producing cytokine response. We aimed to study the effect of *Pseudomonas aeruginosa* (PA) and *Acanthamoeba polyphaga* – trophozoite form (AP) infection – two devastating ocular surface pathogens, and the inflammatory response induced by them on human corneal epithelial cells (HCECs) derived from limbus.

## Methods

Human limbal tissue explants were isolated from cadavers following the Guidelines of the Declaration of Helsinki and approved by the Regional Ethics Committee (Oslo, Norway). *Ex vivo* cultivation produced HCEC cultures maintained in complex medium (DMEM/F12, anti-biotics/mycotics, 5% FBS, EGF, insulin, transferrin and Na-selenite, cholera toxin A, DMSO and hydrocortisone). 300000 cells/well were plated in 12-well plates. 24 hours before infection, serum-free medium was applied, and cells treated with TNF $\alpha$  accordingly. Thenafter, HCECs were incubated with PA at multiplicity of infection (MOI) 1:1, and AP at MOI 1:10, 6hrs, 37 °C. Secreted cytokine concentration from the HCECs (IL-1 $\beta$ , IL-6, IL-8) was measured using commercial ELISA kits; LDH release was measured by commercial cytotoxicity assay kit.

## Results

HCECs treated by PA and AP infection and primed by TNF $\alpha$  treatment had an enhanced IL-1 $\beta$  secretion compared to TNF $\alpha$ , PA and AP treatment alone; this induction of the inflammasome pathway was not related to the cell death. In addition, there was a clear differential response of IL-6 and IL-8 secretion between the two pathogens over the treatment period.

## Conclusions

The study shows a specific pathogen-induced inflammatory response in HCECs, which can be used in devising more specific treatments for ocular surface infection by PA and AP in the future.

## S032

### Prevalence and clinical patterns of ocular complications associated with anti PD-1/PDL-1 anticancer immunotherapy

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## Purpose

Immune checkpoint inhibitors targeting programmed cell death protein 1 (PD-1) pathways are the mainstay of metastatic cancer treatment. Patients receiving these treatments develop many immune related adverse events (irAEs). The aim of this study is to describe and estimate prevalence of ocular irAEs.

## Methods

This is a retrospective, observational case series that includes patients recruited via the Registry of Severe Adverse Events of Immunomodulating Monoclonal Antibodies in Oncology (REISAMIC) at Gustave Roussy cancer centre (Villejuif, France). All consecutive patients with ocular irAE grade  $\geq 2$  following anti PD-(L)1 agents were included. Patients underwent a comprehensive ophthalmological assessment by an ophthalmologist based on history, examination, and ocular/orbital imaging. The severity of adverse events was graded according to the Common Terminology Criteria for Adverse events (CTCAE), that was the main outcome measure.

## Results

5 females, 2 men aged  $64,2 \pm 12.8$  were included. They received either anti-PD1 (pembrolizumab, nivolumab) or either anti-PD-L1 (atezolizumab) for metastatic cancers. Overall patients receiving anti PD1/PD-L1, the prevalence of ocular irAEs was 0,67%. Five patients over seven presented intra ocular inflammation, one developed ocular surface disease and one pseudo myasthenia gravis. These side effects occurred with varying frequency (after the 2nd to the 36th cure). Five patients experienced extra ocular manifestations. Treatment by local and/or systemic corticotherapy permitted resolution of the symptoms in the most cases.

## Conclusions

As immunotherapy is increasingly used for a range of malignancies, clinicians should be aware of the potential adverse events this treatment may elicit, including rare events like ocular and orbital inflammatory conditions.

## T118

### Efficacy of a colloidal silver-based topical solution on microbial biofilms

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## Purpose

It is known that the lid margin is an ideal surface for biofilm formation and this could play a crucial role in developing chronic infections such as blepharo-conjunctivitis. The aim of this study was to evaluate the activity of colloidal silver-based topical (CST) solution on preformed biofilms at different maturation state.

## Methods

The CST solution used to soak gauzes for periocular hygiene (Silverix<sup>®</sup>, Alfa Intes present in Italian market; Ocusilver<sup>®</sup> available soon in foreign market) was tested. Standard ATCC strains of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *S. epidermidis* and *Candida albicans* were studied. The strains grown on polystyrene microplates as early (6 h) and late stages (14 h and 24 h) biofilms were treated with the CST solution for different exposure times (5, 15, 30, 60, 120 min). After each treatment time, the CST solution was removed and the biofilm cell viability was evaluated and expressed as logarithm of colony-forming units (log CFU).

## Results

The results showed that the CST solution was active on microbial biofilms with a different effect related to maturation state. At 5-15 min exposure, the CST solution caused a more log CFU reduction in the early stage biofilm than that detected in the late stage biofilm. Specifically, at 15 min exposure a 3.1-4 log CFU decrease for all bacteria was revealed. In contrast, for *C. albicans* a 0.3 - 3.1 log CFU reduction occurred at a much slower rate,

from 5 to 60 min. Regarding the late stage biofilm, a significant effect (2-3 log CFU drop) was achieved only after prolonged exposure times (60 - 120 min).

## Conclusions

The present study demonstrated the efficacy of the CST solution on microbial biofilms, particularly on early stage biofilms. These findings suggest the potential of CST solution to prevent the ocular biofilm-related infections.

1252

## Methods to study mitochondrial DNA damage

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## Summary

Mitochondrial quality control (MQC), a complex mechanism ensuring the balance between mitochondria functioning, biogenesis and clearance involves DNA damage reaction (DDR). DDR in mitochondria seems to be limited as compared with its nuclear counterpart, but it has a unique feature that highly damaged mitochondrial DNA (mtDNA) can be degraded along with entire mitochondrion in the process of mitophagy. Therefore mitophagy can be considered as an important element of DDR in mitochondria. Damage to mtDNA can be studied with quantitative real-time PCR (qPCR), in which DNA polymerase abandons DNA synthesis at DNA damage. This procedure can be enforced by a supercoiling-sensitive approach. Immunofluorescence methods can be applied to quantify oxidative modifications to mtDNA bases, including 8-oxo-guanine. mtDNA can have many deletions, which are associated with premature aging and diseases. Quantitative detection of these deletions can be performed by qPCR with fluorescence quenching probes and single-cell single-molecule PCR. Therefore, many procedures and tools to study damage to mtDNA are available, which can be combined to give more informative results.

1424

## Phaco Cypass

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## Summary

The patient-related burden of long-term eye drop therapy is underestimated. Minimally Invasive Glaucoma Surgery (MIGS) devices are altering surgical treatment of mild/moderate glaucoma, offering reasonable efficacy and may be safer than conventional surgery. MIGS intervention is now advocated earlier in the treatment paradigm than traditional techniques; earlier surgical intervention may delay disease progression and improve quality of life.

The Cypass stent (Alcon, USA) is a new MIGS device that diverts aqueous to the suprachoroidal 'space', an approach described recently as ... 'converting a potential space into a space with potential'. This unique approach could prove important, as suprachoroidal outflow may be additive to the effects of 'conventional' therapies on; (a) outflow (drops +/- sub-conj drainage), (b) inflow (drops +/- ECP) and conceivably (c) trabecular drainage restoration (iStent). This may inform a new approach to surgery, with MIGS procedures performed in sequence or in combination, much like we now use medications.

This presentation will consider indications, techniques (using videos), post-op management and complications of this innovative implant, with reference to published and real-world clinical data.



## T069

### Post-hoc comparison of best-corrected visual acuity improvement in study and untreated fellow eyes with active non-infectious uveitis of the posterior segment in the SAKURA program

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#### Purpose

The Sirolimus Study Assessing Double-masked Uveitis TReAtment (SAKURA) Program, which consisted of two Phase III multinational randomized clinical trials, compared the effects of intravitreal (IVT) sirolimus 440 µg vs 44 µg (low dose) in subjects with non-infectious uveitis of the posterior segment (NIU-PS). A post-hoc comparison of study eyes (SEs) and untreated fellow eyes (FEs) in the SAKURA Program was performed to evaluate the impact that absence of a placebo control had on the estimation of the effect size of IVT sirolimus on best-corrected visual acuity (BCVA).

#### Methods

Subjects with active NIU-PS (vitreous haze [VH]  $\geq 1.5+$ ) in the study eye who were randomized to every-other-month IVT sirolimus 44 or 440 µg (n=208 in each group) and 96 FEs with baseline VH  $\geq 1.5+$  from all treatment groups were included in this analysis. Post-hoc comparisons of  $\geq 1$ -line and  $\geq 2$ -line improvements (5 and 10 letters, respectively) in BCVA at Month 5 were performed in SEs and FEs with baseline BCVA  $\leq 70$  letters ( $\leq 20/40$ ).

#### Results

A total of 253 SEs (n=127, 44 µg; n=126, 440 µg) and 52 FEs were analyzed. The proportion of SEs with  $\geq 1$ -line improvement in BCVA at Month 5 (44 µg, 44.9%; 440 µg, 48.4%) was significantly greater than that in the FE group (21.2%; p=0.003 vs 44 µg, p<0.001 vs 440 µg). The proportion of SEs with  $\geq 2$ -line improvement (44 µg, 35.4%; 440 µg, 31.0%) was also significantly greater than that in the FE group (13.5%; p=0.003 vs 44 µg, p=0.015 vs 440 µg). The mean change in BCVA from baseline in SEs was greater than that in FEs at all analysis time points up to Month 5.

#### Conclusions

Post-hoc comparison of BCVA response rates of untreated FEs with 440 µg treated SEs in the SAKURA Program suggests that the effect size of the 440 µg dose could have been greater if a placebo had been used instead of a low-dose control.

## S101

### Epiretinal membranes in a db/db model of diabetic retinopathy

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#### Purpose

Epiretinal membranes (ERMs) are excrescences of fibrocellular tissue that proliferate on the inner retinal surface and that frequently occur during diabetic retinopathy. This secondary complication of diabetes can be divided in two phases, characterized by retinal edema and neovascularization, respectively. The outgrowth of new vessels can be extended into the vitreous forming a neovascular ERM that, eventually, can distort retinal anatomy and cause severe alterations. For the first time we observed vascular structures in the vitreous of a db/db mouse model and our purpose was to determine whereas these structures were persistent hyaloid vessels or ERMs and if other retinal lesions could be triggered by the presence of ERMs.

### Methods

Eight weeks old diabetic (db/db) and control (db/+) mice were used in this study. Immunohistochemistry analyses on paraffin sections were performed against GFAP, Col IV, and MMP9. Transmission electronic microscopy studies were executed to assess other retinal lesions.

### Results

Dual immunostaining with GFAP and Col IV, a known marker of vascular basement membrane, pointed out the presence of glial cells surrounding intravitreal vessels of db/db mice. Furthermore, the expression of MMP9 in the wall of intravitreal vessels suggested their angiogenic nature. The transmission electron microscopy analysis revealed areas of edema in db/db retinas.

### Conclusions

Altogether, these findings suggest that intravitreal vascular structures observed in db/db mice could be ERMs, because persistent hyaloid vessels are never covered by glial cells and/or express MMPs. Additionally, db/db mice suffer from retinal edema, which might contribute in ERM formation, and vice versa. The relation between retinal edema and the development of ERM remains unclear and further studies must be performed to understand their interaction.

### F114

#### Indications for electrostimulation method in the treatment of children with concomitant non-accomodative strabismus

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### Purpose

The aim of the study was to increase the effectiveness of ocular motility disorders treatment in concomitant strabismus by detecting the indications for the use of the muscles electrostimulation method studying the peculiarities of the biopotentials of oculomotor muscles by surface electromyography (SEMG).

### Methods

44 children (80 eyes) with concomitant strabismus aged 11-16 were observed. Surface electromyography (SEMG) under local anaesthesia with suggested electrode proper to the anatomical muscles and insertion size was conducted. The main parameters of the horizontal muscles SEMG potentials were defined: the total electrical activity frequency, maximum and average signal amplitude.

### Results

It was suggested to use the ratio coefficient of the SEMG frequency of the medial rectus muscle (MRM) bioelectric activity to the lateral rectus muscle (LRM) in patients with esotropia and the frequency ratio of the SEMG bioelectric activity of the LRM to the MRM at the exotropia (Kv). It was found that if the ratio coefficient of the frequency of the SEMG (Kv) was  $1,9 \pm 0,3$  – the deviation angle decreased and if the ratio coefficient of the SEMG frequency was  $Kv = 1,42 \pm 0,04$ , ( $p = 0,0009$ ) – no changes of deviation was observed.

## Conclusions

If the ratio of the SEMG frequency is more than 1,5, this is an indication for conducting electrostimulation and achievement of the deviation angle decrease.

## S017

### Verification of splicing alteration caused by a novel *SLC4A11* intronic mutation using an autologous induced pluripotent stem cell-derived corneal endothelial-like cell model

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## Purpose

To develop an autologous induced pluripotent stem cell-derived (iPSCs) corneal endothelial-like cell model (CEC) in order to evaluate the effect of intronic *SLC4A11* variants on pre mRNA splicing.

## Methods

Ophthalmic examination was performed in the proband with congenital hereditary endothelial dystrophy, three unaffected siblings and parents. Direct sequencing of the *SLC4A11* coding region was performed. Peripheral blood mononuclear cells isolated from the father of the proband were reprogrammed using the Sendai-virus delivery system. Differentiation into CECs was achieved by modifying a previously published two step protocol originally used for human embryonic stem cells. iPSC cells were cultured for 48 hours in dual Smad medium containing inhibitors Noggin and SB431542 followed by cultivation in a medium enriched by B27 supplement, platelet derived growth factor-BB and Dkk-2 for 8 days. cDNA was reverse transcribed from total RNA extracted from CECs. PCR using primers spanning exons 15-17 was performed and the product was Sanger sequenced.

## Results

The proband was a compound heterozygote for a novel variant c.2240+5G>A evaluated in silico as potentially affecting splicing, and a previously reported mutation c.625C>T. Segregation analysis revealed that c.2240+5G>A was inherited from the father. iPSC derived CECs expressed *SLC4A11*, and stained positive for corneal endothelial markers ZO-1, N-Cadherin and CD166. Transcript analysis confirmed aberrant splicing of *SLC4A11* with an insertion of six nucleotides leading to a premature stop codon (p.Thr747\*).

## Conclusions

iPSC derived CECs represent a useful model in the assessment of functional effect of intronic *SLC4A11* mutations. Supported by GACR 17-12355S and UNCE 204064.

## 2961

### What's new in ocular anterior dysgenesis imaging?

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## Summary

The classification system of congenital corneal opacification is best described as kerato-irido-lenticular dysgenesis and other secondary causes including infection, iatrogenic, developmental anomalies of the iridotrabecular system

or lens or both, and developmental anomalies of the adnexal. The appropriate classification may help determine prognosis of any surgical intervention. Peters' anomaly is too imprecise and this term has to be better defined. New imaging systems completely changed the approach of Ocular Anterior Dysgenesis. Genotype/phenotype correlation is enhanced by anterior segment imaging (OCT or high-frequency ultrasound) or histology or both. Practical cases will be described for a better understanding of these rare anterior segment diseases leading to a better surgical management.

**003**

**Introduction**

**006**

**Panel**

**004**

**Introduction**

**005**

**Introduction**

**S007**

**Effects of a hydrocortisone plus sodium hyaluronate solution on wound healing and inflammatory biomarkers in corneal epithelial cells**

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**Purpose**

To evaluate the effects on wound healing and inflammation of hydrocortisone plus sodium hyaluronate solution on rabbit corneal epithelial cells.

## Methods

SIRC cells were obtained from ATCC® and were cultured in EMEM plus with 10% of FBS and incubated at 37°C in 5% CO<sub>2</sub>. Scratch-wound assay and hyperosmotic stress model were used to assess the effects of a solution containing a low concentration of hydrocortisone (0.001%) and sodium hyaluronate (0.2%) on wound closure and inflammatory process, respectively. Forty-eight hours after wounding, the percentage of wound closure by SIRC in response to treatment was compared to control at T0, images were obtained and the mean area was determined using an image analysis system (Image J Software). In a separate set of cells, SIRC cultured in iso-osmolar medium (300 mOsm/L) were switched to hyperosmotic media (450 mOsm/L), with or without incubation with the hydrocortisone/sodium hyaluronate solution and the release of inflammatory biomarkers (TNF- $\alpha$ , IL-1 $\beta$  and IL-8) was evaluated by ELISA.

## Results

Hydrocortisone/sodium hyaluronate solution significantly ( $p < 0.05$ ) enhances the re-epithelialization of SIRC scratched. Hyperosmolar media significantly ( $p < 0.05$ ) stimulated protein expression of pro-inflammatory biomarkers such as TNF- $\alpha$ , IL-1 $\beta$  and IL-8. Treatment with hydrocortisone/sodium hyaluronate significantly ( $p < 0.05$ ) reduced the expression of these biomarkers in corneal cells.

## Conclusions

Altogether these data suggest that 0.001% hydrocortisone+0.2% sodium hyaluronate has a relevant anti-inflammatory effect on corneal epithelial cells exposed to the hyperosmolar stress and improve re-epithelialization of corneal wound.

## S043

### Effect of a new ophthalmic hydrocortisone and sodium hyaluronate formulation on two experimental dry eye models

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## Purpose

To evaluate the efficacy of a new hydrocortisone and sodium hyaluronate eye drops (Idroflog® Alfa Intes) in two rabbit models of dry eye.

## Methods

Dry eye was induced in rabbit by topical administration of atropine sulfate or by concanavalin A (ConA), an inflammation-mediated dry eye paradigm. Animals in both models were treated with low dose of hydrocortisone (0.001% w/v) plus sodium hyaluronate (0.2% w/v) (Idroflog®) or with vehicle. All experiments were carried out according to the ARVO (Association for Research in Vision and Ophthalmology) guidelines on the use of animals in research. Tear levels of TNF- $\alpha$ , IL-8 and MMP-9 were assessed by ELISA. Tear volume was evaluated by the Schirmer test. TBUT was determined after instillation of sodium fluorescein.

## Results

Topical treatment with Idroflog® significantly reduced the tear levels of TNF- $\alpha$  ( $p < 0.05$ ) and IL-8 ( $p < 0.01$ ) vs. vehicle in ConA dry-eye model. No statistical differences were observed between groups (CTR vs. treated) in terms of MMP-9. Moreover Idroflog® significantly ( $p < 0.05$ ) maintain the tear volume and tear integrity measured by Schirmer test and TBUT in both paradigms.

## Conclusions

In conclusion, the present data demonstrate that, due to the presence of 0.001% hydrocortisone, the new ophthalmic solution Idroflog® is effective to counteract the inflammation in an inflammation-mediated dry eye

model, and thanks to the combination with sodium hyaluronate, it is able to maintain the physiological tear volume level as well as tear integrity.

### **S033**

#### **Ocular pharmacokinetics profile of different hydrocortisone ophthalmic formulations**

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#### **Purpose**

To evaluate the ocular pharmacokinetics profile of different eye drops based on hydrocortisone plus sodium hyaluronate (0.2%) in rabbit eye.

#### **Methods**

Four formulations containing hydrocortisone (FA=0.001%, FB=0.003%, FC=0.005% and FD=0.33%) were topically administered in the conjunctival sac 4 times every 2 hours. Aqueous humor samples were collected after 15, 30, 60 and 90 minutes from the last instillation and hydrocortisone detected by LC-MS/MS. All experiments were carried out according to the ARVO (Association for Research in Vision and Ophthalmology) guidelines on the use of animals in research.

#### **Results**

No levels at any time of hydrocortisone were detected in the aqueous humor in the group treated with the formulation containing the lowest concentration of drug (0.001%). On the contrary, the aqueous humor samples obtained by the other groups (0.003%, 0.005% and 0.33%) showed a remarkable amount of drug (C<sub>max</sub> ng/ml = 10.6, 24.0 and 69.1, respectively; T<sub>max</sub> min. = 30, 60 and 30, respectively; AUC<sub>0-90</sub> ng×min/ml = 535, 1526 and 4510, respectively).

#### **Conclusions**

The present findings showed the ocular PK profile of four ophthalmic formulations containing different concentrations of hydrocortisone. As regards the formulations FB (0.003% hydrocortisone), FC (0.005% hydrocortisone) and FD (0.33% hydrocortisone) the data demonstrated that the drug crossed the corneal barrier and that the bioavailability of the drug in the aqueous is dose-dependent. No levels of hydrocortisone were detected in the aqueous after topical administration of formulation A containing 0.001% of drug, suggesting that at this low concentration the molecule did not cross the corneal barrier, staying in the ocular surface to carry out its anti-inflammatory effect.

### **T113**

#### **EYS606 for the Treatment of Non-Infectious Uveitis (NIU)**

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#### **Purpose**

Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is an effective target for the treatment of NIU. While uveitis models demonstrate the efficacy of intravitreal TNF- $\alpha$  inhibition, the benefit in patients remains unclear. Eyevensys is developing non-viral gene therapies utilizing a proprietary electrotransfection system to deliver plasmids to the ciliary muscle allowing sustained therapeutic protein expression in the eye. EYS606, our lead product, encodes a

recombinant fusion anti-TNF- $\alpha$  protein linking the TNF- $\alpha$  p55 receptor 1 to the human IgG1 Fc domain. We present the first-in-human study of EYS606 in patients with NIU.

### Methods

EYS606-CT1 is a 24-week multicenter, open-label, phase I/II study investigating the safety and tolerability of EYS606. In Part 1, end stage NIU patients are assigned to treatment with escalating EYS606 doses. In Part 2, patients with less severe, active NIU will receive the maximally tolerated EYS606 dose. The primary endpoint is adverse events with longer term safety and clinical activity assessed as secondary endpoints. EYS606 protein in the aqueous humor will be analysed as a potential efficacy biomarker.

### Results

The study is enrolling in the United Kingdom and France. To date, 4 patients have been treated with EYS606. Reported adverse events include headache, eye pain, keratitis, foreign body sensation, subconjunctival hemorrhage, vitreous floaters and corneal abrasion. An update including enrollment, demographics, preliminary safety and efficacy results will be presented.

### Conclusions

EYS606 is the first gene therapy for the treatment of NIU inducing sustained intraocular expression of a potent TNF- $\alpha$  inhibitor. The EYS606-CT1 study will further clarify the risks, potential benefits and duration of sustained therapeutic protein expression in the eye resulting from treatment with EYS606.

### S097

#### Prevention of glutamate-induced retinal ganglion cell death by UCCB01-144 treatment

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### Purpose

Glutamate excitotoxicity, through the NMDA receptor, causes neuronal cell death in both neurodegenerative diseases in brain and retina. Recently, the administration of the UCCB01-144, a dimeric inhibitor of the PSD-95, has undergone clinical trial for prevention of neuronal cell death in patients with stroke and has shown promising effects. Thus, we aimed to test whether UCCB01-144 protects retinal ganglion cells (RGCs) from glutamate-induced cell death.

### Methods

RGCs were exposed to 1 mM of L-glutamate to ensure toxicity. Afterwards, cells were exposed to 3 or 30  $\mu$ M of UCCB01-144 for 24 hours. The experiments were performed with and without 6 mM of glucose in the media. Survival was assessed by the commercially available viability assays, MTT and LDH.

### Results

Neither 3 nor 30  $\mu$ M of UCCB01-144 were toxic for the RGCs. On an average glutamate exposure reduced RGC survival by 17 %. The presence of 3  $\mu$ M UCCB01-144 reduced RGC death (90.73 % survival), while 30  $\mu$ M UCCB01-144 enhanced cell survival in cultures exposed to glutamate (105.9%).

### Conclusions

The present study reveals that the dimeric inhibitor of the PSD-95, UCCB01-144, has a neuroprotective effect on glutamate induced RGC death. Hence, UCCB01-144 administration may be a potential new strategy to sustain RGCs, ultimately preventing visual disability as a consequent of RGC death.

\*Both authors contributed equally

## F123

### Ocular manifestations in S77T transthyretin-related familial amyloid polyneuropathy

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#### Purpose

Transthyretin-related familial amyloid polyneuropathies (TTR-FAP) are associated with ocular manifestations including dry eye, anterior chamber and vitreous amyloid deposits, secondary glaucoma and retinal angiopathy, which have been extensively described for V30M mutation. S77T is the second most frequent mutation in France and is associated with a severe neurologic and cardiac phenotype. However, ocular manifestations of this form of TTR-FAP have been scarcely described.

#### Methods

This monocentric observational study was conducted at the french national reference center for TTR-FAP. Genetically confirmed S77T-TTR-FAP patients had a standardized neurologic and ophthalmologic evaluation. Sensorimotor polyneuropathy was staged using the Polyneuropathy Disability (PND) score. Ophthalmological examination included best corrected visual acuity, Schirmer test, intraocular pressure, slit lamp photographs, fundus examination.

#### Results

Eighteen S77T-TTR-FAP patients (11 males, 7 females), aged 31-71 years, (mean 58.2±11.1 years), originating from France, were included. None of them presented with anterior chamber/vitreous amyloid deposits nor secondary glaucoma. Conjunctival lymphangiectasia were present in both eyes in 9 patients (50%) and associated with a more severe neurologic disease (PND = 2.5±1.0 vs 1.2±1.2; p<0.05). Retinal ischemic amyloid angiopathy was found in one patient. Dry eye was found in one third of patients.

#### Conclusions

Our results suggest that anterior chamber deposits, secondary glaucoma and vitreous deposits do not occur in S77T-TTR-FAP. Conjunctival lymphangiectasia occur in patients with severe neurologic disease and were not described in TTR-FAP associated with other TTR mutations, suggesting a genotype-phenotype correlation in TTR-FAP ocular manifestations, with conjunctival lymphangiectasia being a specific feature of S77T-TTR-FAP.

## F096

### Accommodative convergence pupillary eye system and psychological status of healthy school aged children

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#### Purpose

To estimate the functional state of the accommodative-convergence-pupillary system of the eye and psychomotor status of healthy school children.



## Methods

Visual acuity at the distance and near, autorefractometry, accommodative reserves by Dashevsky method, Haidinger test (maculotest), binocular vision test, stereovision test, computer pupillography: pupil fluctuations number per 30 sec, presence of anisocoria, speed of pupil narrowing, time of pupil area renewal.

Psychological tests: kinematometric test, sensomotor reactions, reaction on the moving object, critical frequency of light flashings, tapping-test (speed of right and left hand movement).

## Results

Weak type of nervous system, choleric, makes 64.8% of children (quick learning and quick tiredness).

Middle type of nervous system, normosthenic, makes 29.6%.

Strong type of nervous system, melancholic, makes 5.6% (long learning, low tiredness).

Children were divided into 2 groups according to accommodative reserves (AR):

1st group consists of 31 children with mean AR  $4.7 \pm 1.9$  D. There were weak type 64%, middle type 28.9%, and strong type 6.1%.

2nd group consists of 10 children with mean AR  $1.36 \pm 0.72$  D (between groups  $P = 0.0001$ ). There were weak type 50%, middle type 40%, and strong type 10%.

## Conclusions

The biggest part of healthy children has normal reserves of accommodation (75.6%) and weak type of the nervous system (64.8%). Groups of healthy children with the normal visual acuity with high and low RA differ on the state of visual and psychomotor functions. In a group with high RA stereovision is higher, indices of psychomotor functions are better; the nervous system is stronger. The renewal of pupils after accommodation is considerably longer in a group with high RA.

1852

## Ocular surface disease and dessicating stress

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## Summary

Dry Eye (DE) is the ocular surface disease most importantly affected by a prolonged exposure to adverse environmental conditions, both outdoor (climate-related conditions) and indoor (controlled environmental conditions). The 3 environmental factors with the highest impact are high temperature, low humidity, and air flow. These factors negatively affect the ocular surface of not only DE patients, but also contact lens wearers and even healthy subjects.

The influence of adverse environment has been successfully used to develop experimental models (*in vitro*, *ex vivo*, and *in vivo*) of DE, fundamental to unravel DE physiopathology and to help to test new therapies.

Accordingly, controlled-environment equipment (laboratories, chambers or special goggles) is used to study the influence of environmental variables (i.e. temperature, humidity, air flow, barometric pressure) on human DE, to discover new biomarkers of this disease, and to perform clinical trials that can show efficacy of potential therapies

under the adverse desiccating environmental stress in which people spend a considerable amount of time. This approach will hopefully help to develop more successful clinical trials in DE disease.

## **S067**

### **Effect of laser-assisted subepithelial keratectomy with mitomycin C on corneal optical density measured with confocal microscopy**

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#### **Purpose**

To study the changes on corneal optical density with confocal microscopy using the Heidelberg Retina Tomograph II in combination with the Rostock Cornea Module (HRTII/RCM) in eyes treated with laser-assisted subepithelial keratectomy (LASEK) with intraoperative mitomycin C (MMC) to correct myopia

#### **Methods**

We performed a prospective study of 14 consecutive myopic eyes that underwent surface ablation with the adjuvant use of MMC and a control group of 14 non-treated eyes. Optical density was measured using the images provided by the confocal microscopy (HRTII/RCM) 3 months, 15 months and 3 years after surgery; and compared with controls. For the analysis, we selected the first image under the epithelium in each group and to obtain the mean reflectivity we used the histogram of the Image J software. The values were obtained in a gray scale, between 0 (black) and 255 (white).

#### **Results**

The mean values of optical density for the LASEK group were  $81,74 \pm 9,7$ ;  $78,64 \pm 11,73$  and  $73,56 \pm 18,7$  for 3 months, 15 months and 3 years respectively, and  $61,80 \pm 8,21$  in controls. We found a statistically higher optical density 3 months after LASEK with MMC compared to controls ( $p=0,01$ ). On the contrary, no differences were found when comparing the control group and 15 months ( $p=0,063$ ) and 3 years ( $p=0,15$ ) post-op.

#### **Conclusions**

Our study suggests that after LASEK with MMC the anterior corneal stroma has higher optical density than controls which can be related to mild and subclinical haze, but seems to return to normal values 15 months post-op and remains stable until 3 years after surgery.

## **S050**

### **Corneal Sub basal nerve plexus 10 years after LASIK**

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### **Purpose**

In LASIK, the flap created with a microkeratome cuts the sub-basal nerve fiber bundles and the superficial stromal nerves, although nerves that run through the hinge are spared. This disruption is thought to contribute to dry eye and alterations in the tear film after these procedures.

### **Methods**

We analyzed the nerve morphology (number of nerves, density of nerves, density of nerve branches) and the density of dendritic cells from the confocal images obtained with the Heidelberg Retina Tomograph II (HRTII). The number of nerves (n/ image) and the density of nerves (um/mm<sup>2</sup>) were measured using the plugin NeuronJ from the ImageJ software, which allows semi-automated tracing of nerve fibers and provides quantification. Nerve branches and dendritic cells, were manually counted and the density calculated (n/mm<sup>2</sup>).

### **Results**

In this study were included 47 eyes divided in two groups. One group of 20 eyes without refractive surgery and other group with 27 eyes that underwent LASIK at least 10 years before. We didn't found statistically differences in the density of nerves, density of dendritic cells and nerve branches between groups.

### **Conclusions**

In summary, the corneal nerves that are lost during LASIK slowly regenerate, and appear to return to preoperative densities by 10 years after LASIK surgery. The return is characterized by variations in the regeneration rate, with a decrease in number during the early post operative.

## **S039**

### **Failure to validate the fluorescein breakup patterns classification in an italian sample of dry eye patients**

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### **Purpose**

A recent Japanese research on Dry Eye patients proposed 5 different fluorescein break-up patterns(FBUPs),related to different pathophysiologies.The aim of our cross-sectional study was to test the FBUPs classification in an Italian sample of Dry Eye patients

### **Methods**

We included 210 eyes of 105 Dry Eye patients diagnosed on the basis of the TFOS DEWS II recommendations.Exclusion criteria were eyelid disorders, history of ocular surgery, ocular surface co-morbidities and Meibomian Gland Dysfunction.Each patient underwent an examination including accurate anamnesis, standardized assessment of symptoms, ocular surface inspection, FBUPs classification (strictly based on the methodology described by Yokoi N and colleagues),FBUT, corneal and conjunctival staining, and Schirmer test without anesthesia. FBUPs' inter-observer and inter-visit reproducibility and relationship between FBUPs and clinical manifestations were investigated

### **Results**

FBUPs showed almost perfect inter-observer agreement and inter-visit reproducibility. We classified 102 eyes (48%) into spot break, 70 eyes (33%) into line break, 30 eyes (14%) into dimple break, and 8 eyes (4%) into random break. No eyes were classified into area break. BUPs showed poor agreement between the right and the left eye of the same patient.Ocular Surface Disease Index, symptoms Visual Analogue Scales, FBUT, corneal and conjunctival staining and Schirmer test showed no significant BUPs-related differences

## Conclusions

We failed in validating this FBUPs classification in our sample of dry eye patients. Differences between our results and those reported by Yokoi N and colleagues might be due to several factors, including ethnicity, diagnostic dry eye criteria, and sampling and procedural errors. However, although its intriguing rationale, this BUPs classification doesn't seem to be ready for use in clinical practice

## S037

### Clinical signs in dry eye: a multicentric cross-sectional study

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## Purpose

Several clinical signs of Dry Eye may be evaluated by minimally invasive and most accessible methods. However their clinical utility is limited by lack of knowledge of their diagnostic value and by poor association with symptoms. The aim of this exploratory research was to investigate low-tech clinical signs profiles in Dry Eye patients.

## Methods

We performed a multicentric cross-sectional study, collecting clinical data from patients with Dry Eye who underwent eye examination in 26 Italian Ocular Surface Second-level Referral Centers between July 2017 and October 2017. Collected data included systemic co-morbidities and treatments, ocular therapies, ocular surface symptoms and signs. We assessed and graded 19 eyelid, 29 conjunctival, 28 corneal, and 12 tear film abnormalities.

## Results

We included 707 eyes of 397 patients. The most frequent systemic co-morbidities were cardiovascular (45.4%) diseases;  $P < 0.01$ , Chi-Square test. 16.5% of our patients were taking 5 systemic drugs or more. 72.4% of patients were using topical therapies (artificial tears in 83.2% of cases). Burning and foreign body sensation were the most frequently reported symptoms (54.8% and 47.6%, respectively;  $P < 0.001$ ). The most frequent eyelid abnormalities were hyperemia (72.3%) and bridge vessels across the margin (66.2%), in each case  $P < 0.01$ . The most frequent conjunctival abnormalities were nasal staining (46.2%) and conjunctivochalasis (43%); in each case  $P < 0.01$ . The most frequent corneal abnormality was inferior staining (38.8%;  $P < 0.001$ ). The most frequent tear film abnormalities were reduced break-up time (71.3%) and reduced tear menisci (63.2%). Cluster analysis based on clinical signs allowed us to identify homogeneous groups of patients.

## Conclusions

Low-tech examination of Dry Eye patients can provide several important information and it allowed us to identify clusters of patients.

## F064

### Inner retinal layers of the retina predict visual cortical thickness and structural connectivity in early Alzheimer's Disease

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## **Purpose**

This study aims to investigate the relationship between the retina and grey and white matter integrity in the brain, in early Alzheimer's disease (AD).

## **Methods**

Seventeen AD patients (mean age =  $66.5 \pm 6.6$  years) and 23 healthy controls ( $63.4 \pm 7.5$  years) were recruited. We combined optical coherence tomography (OCT), structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) – to assess the association between individual retinal layers and both grey and white matter dysfunction in early AD. Macular retinal layers were segmented, and thickness measurements were obtained from individual layers. Moreover, average thicknesses were computed for the primary visual area (V1). DTI images were analyzed with a data-driven approach to evaluate whole-brain diffusion metrics, using tract-based spatial statistics. Diffusion metrics, such as fractional anisotropy (FA), are sensitive markers for white matter integrity. Multivariate and partial correlation analyses evaluating the association between individual retinal layers, thickness, diffusion metrics and V1 cortical thickness were performed, controlling for age.

## **Results**

We found that axial diffusivity was significantly reduced in AD ( $p=0.004$ ) while in the retina only a marginally significant difference was found for the OPL ( $p = 0.057$ ). A significant correlation ( $p<0.035$ ) was found between inner plexiform layer (IPL) thickness and cortical thickness in V1, in AD. Furthermore, a positive association was found in the AD group between fractional anisotropy and inner nuclear layer thickness ( $p<0.05$  corrected for multiple comparisons by controlling family-wise error rate).

## **Conclusions**

Our findings suggest inner retinal atrophy reflects brain integrity and structural connectivity in early Alzheimer's disease. Moreover, layer-specific changes might reflect different disease mechanisms in AD.

1235

## **Retinal Imaging – a Window into Brain Mechanisms**

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## **Summary**

The retina is increasingly being recognized as a window to brain neurodevelopment, ageing and degeneration. This non-invasive window to vascular and neural function has shown promise to modify disease diagnosis, follow-up and management. Here we review imaging evidence reflecting critical interactions between ageing, systemic disorders (diabetes) and neurodegenerative diseases. We will also address neural and vascular compartments and their critical interfaces, blood-retinal and blood-brain barriers. It remains to be clarified how brain neuroinflammation and amyloid deposition can be mirrored by surrogate markers at the level of the retina. We also address the intriguing link with diabetes as a systemic disease where all these factors are important in relation to barrier function and neurodegeneration associated with normal/pathological ageing. The association between abnormal retina and brain development will also be discussed, in relation to imaging approaches using the retina as a window into the brain.

**3438**

**Outcomes of patients with conjunctival squamous cell carcinoma treated with proton beam therapy**

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<sup>1</sup>

**F111**

**Pattern electroretinogram steady-state in dyslexia and normal readers**

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**Purpose**

Dyslexia is a condition characterized by impairment of reading skills in subjects without alteration of visual acuity and with normal intelligence. The etiology of dyslexia is still under discussion even if an alteration of the magnocellular pathway in particular of the magnocellular-dorsal pathway (M-D). This deficit would seem to be confirmed by recording of pattern evoked visual potential (PVEP) and frequency doubling illusion visual field test (FDT). We studied a group of dyslexic patients using pattern electroretinogram steady-state (PERG-SS) to evaluate the presence of a deficit also in M-Y retinal ganglion cells.

**Methods**

Fifteen subjects with dyslexia (10 females and 5 males) mean age  $28.7 \pm 5.9$  yrs and 15 non-dyslexic subjects (8 females and 7 males) with mean age  $27.8 \pm 4.1$  yrs were enrolled in the study. All participants had normal binocular vision with random-dot stereopsis and absence of retinal and optic nerve diseases. The PERG-SS stimulus, similar to the one used in the FDT, was first presented as a full-screen black-and-white vertical bar pattern with contrast: 20%; spatial frequency: 0.3 cycles per degree/cpd; temporal frequency: 15 Hz. The number of samples acquired were mediated and processed with Discrete Fourier Transform (DFT).

**Results**

We found a significant decrease in the amplitude of the wave of the second harmonic of PERG-SS in dyslexic readers when compared to the non-dyslexic subjects ( $0.600 \pm 0.121$   $\mu$ V vs  $1.250 \pm 0.297$   $\mu$ V;  $p=0.0001$ )

**Conclusions**

Our study demonstrates an abnormal activity of M-Y retinal ganglion cells in dyslexic adult readers, thus confirming the involvement of M-pathway in the clinical expression of this learning disability. Further studies are needed to determine if the damage of M-Y retinal ganglion cells is primary or secondary to damage of the M-D pathway in the lateral geniculate nucleus.

**T003**

**Effect of raising in complete darkness on pathological and functional readouts in the mouse blight light exposure model**

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### **Purpose**

The bright light exposure (BLE) model is commonly used to model photoreceptor degeneration associated with the dry form of age-related macular degeneration. Retinal degeneration is induced by exposing rodents to bright light (2,500 – 10,000 lux). Previous studies have shown that 7.5 months-old mice have thinner retinas than 3.5 months-old mice and that BLE caused a significantly exacerbated phenotype of retinal degeneration in aged vs. young mice. The purpose of this study was to determine whether exposure to light or age is the primary determinant of reduced photoreceptor viability in the BLE model.

### **Methods**

Control mice (3.5 months of age, n = 15) were housed under regular light conditions in a 12/12h light/dark cycle, while another age-matched cohort was kept in complete darkness from birth until used in the experiment. Both cohorts were exposed to BLE (10,000 lux) for 16 hr. The functional response of retinal cells was evaluated using flash electroretinography (fERG) and total retinal thickness was measured using spectral-domain optical coherence tomography (SD-OCT) the day prior to BLE and 7 days after BLE. Mice were euthanized on day 7, eyes enucleated, embedded into paraffin and sectioned. Retinal sections were stained in hematoxylin and eosin (H&E) for histological assessment.

### **Results**

No statistically significant differences were observed in retinal thickness (Control  $0.126 \pm 0.013$  mm vs. Bred in darkness  $0.129 \pm 0.020$  mm, n = 15,  $P > 0.05$ ) as quantified by SD-OCT. Furthermore, there were no differences between functional fERG parameters at baseline and after BLE between young mice bred in darkness and control mice.

### **Conclusions**

Our data suggest that standard light conditions do not cause retinal degeneration and do not affect photoreceptor sensitivity to BLE in young mice. A similar study with 7.5 months-old mice is currently underway.

### **F021**

#### **Prevalence of unknown ocular hypertension, pre-perimetric glaucoma and glaucoma in patients seen in primary refraction center in France**

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### **Purpose**

The rate of unknown glaucoma is around 50% in the general population. The purpose of our study was to estimate the prevalence of unknown cases of ocular hypertension, pre-perimetric glaucoma and glaucoma in patients consulting for refractive disorder in France.

### **Methods**

This was an observational, retrospective and monocentric study conducted between June 2015 and June 2017 in France. The identification of unknown ocular hypertension or glaucoma was defined by the discovery of ocular hypertension and/or suspicious papilla followed by a visual field assessment with Octopus® field analyser and structural assessment by Optical Coherence Tomography. Glaucoma was defined as the association of a

glaucomatous papilla and 2 successive pathological visual fields. Pre-perimetric glaucoma was defined as the association of a glaucomatous papilla and a normal visual field.

## Results

66068 patients consulted for a refractive visual assessment during the study period, 189 had at least an unknown diagnosis among ocular hypertension, pre-perimetric glaucoma or glaucoma. The number of unknown cases was 177 ocular hypertension, 51 pre-perimetric glaucoma and 33 glaucoma, representing a prevalence of unknown cases of 2.7, 0.8 and 0.5 per 1000 consultants, respectively. Patients in glaucoma group were significantly older than those in isolated hypertension group and pre-perimetric glaucoma group (65 years (53-69) vs. 52 years (43-61) and 53 years (37-62), respectively,  $p = 0.0003$ ). Glaucoma patients were diagnosed at a moderate stage as the median Mean Defect was 7.2 (5-10.5) dB.

## Conclusions

The prevalence of unknown cases of glaucoma was lower in our study compared to population studies that focus on older subjects from the general population. Our study highlights the importance of glaucoma screening as early as 40 years or even earlier for pre-perimetric glaucoma screening.

## T078

### The effect of internal limiting membrane peeling in treatment of idiopathic epiretinal membrane

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## Purpose

To investigate the changes of macular thickness and visual acuity in patients undergoing internal limiting membrane (ILM) peeling in eyes with idiopathic epiretinal membrane (ERM).

## Methods

A retrospective analysis of 35 eyes of 35 patients who were diagnosed with idiopathic ERM and received pars plana vitrectomy, membrane peeling and ILM peeling from March 2015 to March 2017 was performed. The results consisted of the measurements of best corrected visual acuity (BCVA, logMAR), central macular thickness (CMT), and macular volume (MV), which were taken before surgery and 1 month, 6 months, and 12 months after surgery. We investigated the recurrence rate of ERM and the occurrence of macular edema.

## Results

The mean age of the patients was  $64.20 \pm 6.60$  years old, and 11 patients were male and 24 patients were female. 5 pseudophakic eyes of 35 eyes underwent only ERM surgery and 30 phakic eyes underwent simultaneous ERM and cataract surgery. The mean follow-up period was  $17.80 \pm 8.41$  months. The BCVA (logMAR) was 0.38 before surgery and 0.27, 0.20, 0.13, 0.10 at postoperative 1, 3, 6, 12 months, respectively, and a statistically significant improvement after 1 month ( $P < 0.05$ ). The CMT was  $468.54 \mu\text{m}$  before surgery and  $433.74, 393.83, 376.09 \mu\text{m}$  at postoperative 1, 6, 12 months, respectively. The MV was  $10.86 \text{ mm}^3$  before surgery,  $10.04, 9.36, 9.12 \text{ mm}^3$  at postoperative 1, 6, 12 months, respectively. Both CMT and MV were statistically significantly improved compared with preoperative values ( $P < 0.001$ ). There was no recurrence of ERM during the follow-up period of 12 months or more. Macular edema which improved within 6 months occurred in 2 eyes.

## Conclusions



We confirmed the improvement of visual acuity and reduction of macular thickness after ILM peeling in eyes of idiopathic ERM. And, ILM peeling is thought to be an effective surgical method for lowering the recurrence rate of ERM.

#### **F075**

##### **Ganglion cell layer complex measurement in the evaluation of an optic chiasm compression**

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##### **Purpose**

To assess the macular ganglion cell layer complex analysis (GCA), on current practice, in the detection of visual pathway involvement by a pituitary tumor compression, compared to Goldmann visual field and retinal nerve fiber layer (RNFL).

##### **Methods**

This unicentric prospective and observational study included consecutively 56 eyes of 28 patients with pituitary adenoma (17 were already operated and 11 non operated). All patients underwent Goldmann Visual Field, Humphrey Visual Field (CVH 24-2) by HFA II-i (Carl Zeiss Meditec Inc.), RNFL thickness measurement and GCA measurement by CirrusTM HD-OCT (Carl Zeiss Meditec Inc.), which was the main outcome. Patients were divided into two groups according to the CVG normality (preperimetric) or not (perimetric).

##### **Results**

There were 37 eyes (18 patients) in the preperimetric group and 19 eyes (10 patients) in the perimetric group. There were no significant difference in age, sex distribution, intraocular pressure, pachymetry and best corrected visual acuity between the two groups. The prevalence of GCA thinning in the preperimetric group was 28%, and was earlier and more frequent than the RNFL thinning (19,6%). The mean and the minimum GCA thickness were thinner in the perimetric group than in the preperimetric group ( $p < .05$ ), as a witness of the optical fibers loss severity. Furthermore, the thickness map showed typical chiasmatic compression pattern with binasal GCA thinning associated with a bitemporal RNFL thinning.

##### **Conclusions**

Thinning of the GCA may be detected before the RNFL thinning and the CVG defect in chiasmatic compression. GCA analysis may be useful in the early detection of optic nerve fibers loss in pituitary adenoma assessment, and may be a part of the surgical decision to prevent visual field deficit.

#### **T050**

##### **Coexistence of diabetic retinopathy and age-related macular degeneration: Epidemiology and management**

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##### **Purpose**

To investigate the coexistence of diabetic retinopathy (DR) and age-related macular degeneration (AMD) with regards to epidemiology and treatment.

##### **Methods**

Participants in the study were 972 consecutive patients with diabetes mellitus, who were examined in the specialized department of our clinic during 2015-2017. We recorded demographic data for patients with coexistent DR and AMD, as well as the therapeutic approach we followed.

### **Results**

The coexistence of DR and AMD is not common. In cases with diabetic macular edema (DME) and dry AMD, treatment with anti-VEGF agents was shown to retard the progression of AMD, while in cases of neovascular AMD (nAMD), there was a statistically significant anatomical and functional improvement along with the regression of DME. Furthermore, in cases of DR and dry AMD coexistence, patients were observed conservatively and when nAMD was present, patients were treated with anti-VEGF agents.

### **Conclusions**

Since the coexistence of DR and AMD is not common, the investigation of their correlation is interesting. In all cases of coexistence, there was anatomical and functional improvement or stabilization, following the guidelines of DR and AMD management accordingl

### **T071**

#### **Risk Factors for Central Serous Chorioretinopathy: Multivariate Approach in a Case-Control Study**

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### **Purpose**

The purpose of this prospective study was to investigate the potential risk factors associated independently with central serous retinopathy (CSR) in a Greek population, using multivariate approach.

### **Methods**

Participants in the study were 183 consecutive patients diagnosed with CSR and 183 controls, matched for age. 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. Univariate and multivariate analysis was performed.

### **Results**

Univariate analysis showed that male sex, high educational status, high income, alcohol consumption, smoking, hypertension, coronary heart disease, obstructive sleep apnea, autoimmune disorders, H. pylori infection, type A personality and stress, steroid use, pregnancy and hyperopia were associated with CSR, while myopia was found to protect from CSR. In multivariate analysis, alcohol consumption, hypertension, coronary heart disease and autoimmune disorders lost their significance, while the remaining factors were all independently associated with CSR.

### **Conclusions**

It is important to take into account the various risk factors for CSR, so as to define vulnerable groups and to shed light into the pathogenesis of the disease.

### **T047**

#### **Fundus autofluorescence changes in diabetic retinopathy**

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### **Purpose**

The purpose of this study was to investigate fundus autofluorescence (FAF) changes in patients with diabetic retinopathy (DR) and compare these findings with color fundus (CF) imaging.

### **Methods**

The purpose of this study was to investigate fundus autofluorescence (FAF) changes in patients with diabetic retinopathy (DR) and compare these findings with color fundus (CF) imaging.

### **Results**

FAF showed more retinal alterations related to DR than CF imaging. FAF signal intensity was associated with DR status. In patients with DME, there was significantly lower FAF signal intensity in the parafoveal subfields compared to patients without DME. The FAF intensity was correlated with retinal thickness in the corresponding subfields.

### **Conclusions**

FAF in the parafoveal subfields has diagnostic significance and is clinically relevant in DME, while FAF signal intensity was correlated with DR status and retinal thickness in the corresponding subfields.

**3112**

### **OCT angiography can replace fluorescein angiography in clinical practice - Against**

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### **Summary**

Optical coherence tomography angiography (OCTA) is a non-invasive technique, which can detect blood flow without the use of dye and has gained interest for the imaging of retinal diseases. However, there are some limitations of OCTA versus the gold-standard fluorescein angiography (FA) for retinal imaging. Various artifacts (motion, segmentation, projection artifacts) can occur during OCTA and may affect its interpretation. In addition, although the technique is quick and easy to be performed, the interpretation seems to be difficult and time-consuming. Another challenge pertains to the management of OCTA findings. For example, in cases of subclinical choroidal neovascularization, which is only detected on OCTA without any evidence on OCT, it is really difficult to decide whether treatment should be initiated or not and when. As a result, since there are no guidelines based on OCTA large trials, the clinical decision for treatment remains controversial. Finally, the major limitation of OCTA is the limited field of view, which is concentrated on the macular area, compared to the wide-field FA, showing the far periphery. Taken as a whole, OCTA cannot replace FA for the time being.

**T061**

### **Comparison of the efficacy of intravitreal Bevacizumab and Dexamethasone implant in patients with macular edema by branch retinal vein occlusion according to macular perfusion type**

*C.W. CHOI<sup>1</sup>*

### **Purpose**

The purpose of this study is to evaluate the difference in treatment efficacy between intravitreal bevacizumab injection and dexamethasone implant according to macular perfusion type in patients with macular edema due to branch retinal vein occlusion.

### **Methods**

We analyzed retrospectively the medical records of 104 patients with 104 eyes who had been diagnosed branch retinal vein occlusion. Patient with macular edema undergone intraocular injection therapy and who were able to be followed up and further study(Fundus photo, FAG, OCT) for more than 6 months after treatment. We classified 43 eyes of the non-ischemic type and 61 of the ischemic type according to the type of perfusion of the macula using fluorescein angiography. Intraocular injections were performed with intravitreal anti-VEGF, dexamethasone implant, and mixed treatment by randomized assignment. We analyzed the changes of BCVA and CMT during the period at least 6 months after treatment

### **Results**

In non-perfusion type, there were significant difference between the three groups of injection in the change of CMT and BCVA(P <0.025, p <0.012). In the precision analysis of each group, dexamethasone implant showed a significant difference in the CMT change compared with the intravitreal anti-VEGF. (p <0.008) And dexamethasone group has a significant difference compared to the other two groups in the change of BCVA (p <0.005). In the analysis of the perfusion and non-perfusion treatment effects of dexamethasone implant, the changes in CMT were  $437.20 \pm 54.84 \mu\text{m}$ ,  $251.00 \pm 34.88 \mu\text{m}$ (p <0.030, p <0.018).

### **Conclusions**

Intravitreal dexamethasone implant is considered to be as effective as intravitreal anti-VEGF in BRVO patients with macular edema. Especially, when the ischemia of the macula is observed, Intravitreal dexamethasone implant is effective for structure and function of retina.

## **T074**

### **Histopathologic analysis as a tool for understanding the pathogenetic mechanisms in posterior pole pathologies**

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### **Purpose**

To investigate the pathogenetic mechanisms that lead to vitreoretinal interface alterations in various conditions.

### **Methods**

Epiretinal membrane and internal limiting membrane specimens, from 17 eyes of 17 patients were peeled. These patients had various conditions such as idiopathic epiretinal membrane (iERM- 4 eyes), tractional retinal detachment (TRD- 4 eyes), diabetic macular oedema (DMO- 2 eyes), vitreous haemorrhage due to proliferative diabetic retinopathy or branch retinal vein occlusion (PDR- 2 eyes, BRVO- 1 eye), rhegmatogenous retinal detachment (RRD- 2 eyes) and other vitreoretinal interface pathology such as full thickness macular hole or vitreomacular traction syndrome (FTMH- 1 eye, VMT- 1 eye). Specimens were examined by light microscopy and immunochemistry (GFAP, CLA, CD 68).

## Results

Epiretinal membranes are identified in light microscopy as cellular membranes whereas in cases of proliferative disease there are also discrete vascular features and even more numerous cells. Internal limiting membrane specimens are non cellular but depending on the co-existing condition of the vitreous cavity they may carry various inflammatory factors or cellular components.

## Conclusions

The structural variations among epiretinal membranes in different conditions are related to the inflammatory cells and agents found in the specimens. Internal limiting membranes obtained from proliferative disease are thicker compared to those in other conditions. A variety of cells, especially inflammatory ones, are found adhered to the inner surface of the ILM. The correlation of these results with other clinical findings or markers is essential for more effective treatment strategies.

## T025

### Vascular features of surgical macular pathologies in OCT-A imaging

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## Purpose

To study the features of superficial and deep capillary plexus in cases of idiopathic epiretinal membrane (ERM) and macular hole, using optical coherence tomography angiography (OCT-A).

## Methods

OCT-A (Zeiss) was performed in 21 eyes of 21 patients, with macular pathologies (idiopathic ERMs and macular holes) 12 women and 9 men. The mean age was 70.6 years  $\pm$ 1.6. All patients had a thorough ophthalmic examination. Best corrected visual acuity (logMAR) was 0.55  $\pm$ 0.30. OCT-A 3x3 and 6x6 analysis of superficial retinal layer (between ILM and IPL) and deep retinal layer (between IPL and OPL) as well as (en face) OCT were performed in all eyes. The acquired data of the two plexuses were compared accordingly to those of age-matched healthy controls.

## Results

Tractional forces apply mainly to the superficial capillary plexus. As a result the superficial layer becomes thicker and the vessels are more tortuous. This effect seems to be diminished after vitrectomy for ERM and ILM peel. The results are discussed.

## Conclusions

Assessing the vascular features of surgical pathologies by OCT-A may serve as an important tool. Firstly, for the understanding of the extent and depth of foveal capillary architecture distortion, due to tractional forces applied to the retina, and secondly to measure the extent that this distortion is related to BCVA.

## F059

### Retinal layer thinning in Parkinson's disease: a meta-analysis of optical coherence tomography studies

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## Purpose

Patients with Parkinson's disease experience visual symptoms, partially originating from retinal changes. Spectral domain optical coherence tomography (SD-OCT) enables the study of retinal layer thicknesses. Since 2011, multiple case-control studies have been published, with different outcomes. The aim of this study was to determine the occurrence and extent of retinal degeneration in Parkinson's disease by performing a meta-analysis.

## Methods

SD-OCT case-control data were collected by performing a search in PubMed and Embase with search terms: "optical coherence tomography" and "parkinson", up to December 31, 2017. Studies with fewer than 10 patients or controls were excluded. We performed a random effects meta-analysis. Heterogeneity was evaluated with I<sup>2</sup> statistics; publication bias with Egger regression and Begg's test.

## Results

Out of 66 identified studies, 29 were included, totaling 1636 patients and 1790 controls. A significant thinning of the peripapillary retinal nerve fiber layer ( $d = -0.37$ ; 95% confidence interval  $-0.51$  to  $-0.23$ ) and the combined ganglion cell layer and inner plexiform layer ( $d = -0.31$ ;  $-0.61$  to  $-0.02$ ) was found. The inner nuclear layer and outer plexiform layer did not show significant changes. Heterogeneity ranged from 3 to 92%; no publication bias was found.

## Conclusions

Parkinson's patients show significant thinning of the inner retinal layers, which resembles the changes found in glaucoma and other neurodegenerative diseases like multiple sclerosis and Alzheimer's. Retinal degeneration seems to be a robust biomarker for neurodegeneration, irrespective of the pathophysiological nature. Degeneration could be related in Parkinson's to disease progression, including motor and non-motor symptoms.

## F024

### Long term postoperative refractive outcomes of combined cataract and glaucoma surgery

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## Purpose

To compare the long-term postoperative refractive outcomes following phacotrabeculectomy and phacoemulsification with posterior chamber intraocular lens implantation.

## Methods

In this retrospective cross-sectional study, we compared the postoperative refractive outcomes between uncomplicated phacotrabeculectomy in eyes with concurrent cataract and open angle glaucoma ("combined" group, 51 eyes) and phacoemulsification alone ("phaco-only" group, 74 eyes). The refractive prediction error (RPE), mean absolute prediction error (MAE), and median absolute prediction error (MedAE) were compared between groups. Subgroup analysis based on the preoperative axial length (AL) was performed (medium:  $> 22.0$  to  $< 24.5$  mm, medium-long:  $\geq 24.5$  to  $< 26.0$  mm, and long:  $\geq 26.0$  mm).

## Results

The mean interval between surgery and refraction measurement was  $14.70 \pm 10.80$  months (median, 13.0 months) in the "combined group," and  $4.81 \pm 4.97$  months (median, 2.0 months) in the "phaco-only" group. The "combined" and "phaco-only" groups showed no statistically significant differences in terms of refractive outcomes: RPE,  $-0.05 \pm 0.64$  vs.  $-0.04 \pm 0.52$  ( $P = 0.905$ ); MAE,  $0.46 \pm 0.44$  vs.  $0.38 \pm 0.36$  ( $P = 0.258$ ); MedAE, 0.32

(interquartile range: 0.17, 0.67) vs. 0.28 (interquartile range: 0.13, 0.54) ( $P = 0.297$ ). Furthermore, subgroup analysis also did not show significant differences between the two groups (all,  $P > 0.05$ ).

### Conclusions

The long-term postoperative refractive outcomes of phacotrabeculectomy and phacoemulsification alone were not significantly different, regardless of the preoperative axial length in eyes with open angle glaucoma.

### T072

#### Spironolactone in the treatment of central serous chorioretinopathy

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### Purpose

To evaluate the effect of spironolactone, a mineralocorticoid receptor antagonist for nonresolving chronic central serous chorioretinopathy with intravitreal bevacizumab injections.

### Methods

This prospective clinical trial was conducted on patients with chronic central serous chorioretinopathy, who had remaining subretinal fluid (SRF) after intravitreal bevacizumab injections. Eleven patients were treated with spironolactone 25 mg twice daily (Aldactone film coated tab 25 mg, Pfizer Pharmaceuticals Korea) for up to 3 months. BCVA and OCT were performed at baseline, 1 and 3 months after starting the treatment.

### Results

Patients were administered 3.54 intravitreal bevacizumab injections before receiving spironolactone. The mean SRF decreased from 91  $\mu\text{m}$  at baseline to 46  $\mu\text{m}$  at 3 months after treatment. Total central retinal thickness (CRT) decreased from 264  $\mu\text{m}$  to 227  $\mu\text{m}$ . The BCVA(logMAR) increased from 0.42 baseline to 0.36 at 3 months.

### Conclusions

In chronic central serous chorioretinopathy which SRF did not resolve after intravitreal bevacizumab injections, spironolactone can be useful reducing CRT and SRF.

### T049

#### Dipeptidyl peptidase-4 inhibitors and risk of diabetic retinopathy progression in patients with type 2 diabetes: a population-based cohort study

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### Purpose

The antidiabetic effect of dipeptidyl peptidase-4 inhibitors (DPP4i) is based on the glucose-lowering activities of the gastrointestinal hormone, glucagon-like peptide-1. DPP4i seems to be protective in cardiovascular events as well as in nephropathy through previous studies, while few investigations have been performed on diabetic retinopathy (DR). Accordingly, we investigate the effects of DPP4i as add-on medications to metformin on progression of DR in patients with type 2 diabetes, compared with sulfonylureas (SU) or thiazolidinedione (TZD).

## Methods

We identified 4,447 patients with DPP4i, 6,136 with SU, and 617 with TZD in addition to metformin therapy from the database of Korean National Health Insurance Service. We first extracted type 2 diabetic patients who had received metformin monotherapy for at least 90 days between January 2009 and December 2012. The second line antidiabetic medications implied DPP4i, SU, or TZD, and those initiated second line antidiabetic therapy from January 2013 to December 2015 were included. Cox proportional hazards regression models were used to calculate hazard ratios (HR) for DR aggravation.

## Results

The age and sex-adjusted HR of DR aggravation was 0.74 for DPP4i add-on group compared with SU add-on group (95% confidence interval (CI) 0.62 – 0.89). This lower risk of DR aggravation remained significant after additional adjustments for comorbidities, duration of metformin therapy, intravitreal injections and calendar index year (HR 0.80, 95% CI 0.66 – 0.97).

## Conclusions

This population-based cohort study showed that the use of DPP4i was associated with lower risk of DR aggravation compared to SU. This suggests that DPP4i can be considered as second line antidiabetic medication preferentially in patients with DR, along with its protective effect in DR aggravation.

1713

### The functional results after Argus II implantation

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## Summary

The Argus® II Retinal Prosthesis System (Second Sight Medical Products, Inc., Sylmar California) is an epiretinal device with a 60 electrodes epiretinal array approved for the treatment of blind patients affected by end stage Retinitis Pigmentosa. The purpose of this study is to report the functional results after Argus II implantation. Thirtysix eyes of 36 patients received the Argus II Retinal Prosthesis System in the worst eye from October 2011 to November 2017 at the Pisa and Florence hospital. Only 29 eyes were included in this study as they have follow-up longer than 12 months.

At each follow-up visit (1 day, 1 week, and 1, 3, 6, 12, 24 and 36 months), a complete ophthalmologic examination was performed including Visual Function Tests, OCT, retinal fundus photography and ECO B-scan.

Five patients abandoned the study for personal reasons. Out of a total of 24 patients, 4 have gone through postoperative serious adverse events. Nine eyes had non serious adverse events without deterioration in their visual performance. The rest 11 eyes resulted uncomplicated with a good improvement in visual acuity assessed by visual function tests.

In conclusion serious adverse events were uncommon and the system seems to have visual effectiveness.

T044

### Retinal measurements in type 2 diabetic patients without diabetic retinopathy using Spectralis Optical coherence tomography

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## Purpose



To evaluate retinal thickness and retinal nerve fiber layer (RNFL) changes in type 2 diabetes mellitus (DM) patients without diabetic retinopathy compared with healthy subjects using Spectralis Optical coherence tomography.

### Methods

Sixty healthy and 60 DM eyes were studied and underwent examination of retinal measurements using Spectralis Optical coherence tomography (Heidelberg Engineering). Macular and peripapillary retinal thickness were analyzed with different protocols: fast-macular (which analyzed nine macular ETDRS areas), RNFL-glaucoma and RNFL-N axonal protocol (which analyzed six peripapillary RNFL thickness sectors and average thickness). The RNFL-N protocol scans the peripapillary area from and to the nasal sector obtaining reliable information of the temporal sector (which is affected first in neurodegenerative diseases). Additionally, the RNFL-N protocol provides measurements of the papillomacular bundle and the nasal/temporal sector index.

### Results

All retinal ETDRS areas measurements were significantly thinner in the DM group ( $p < 0.05$ ). A significant reduction of the RNFL thickness was observed in patients in the average, temporal (T), inferotemporal (TI), inferior (I) (RNFL-glaucoma, RNFL-N) and inferonasal (RNFL-N) sectors. A reduction of thickness of the papillomacular bundle was also observed in patients compared to controls.

### Conclusions

Type 2 Diabetes mellitus produces subclinical macular and RNFL thinning in patients without diabetic retinopathy. OCT Spectralis is a useful tool to detect early neurodegenerative retinal changes in these patients.

### T046

#### Retinal measurements in type 2 diabetic patients without diabetic retinopathy using Swept-Source Optical coherence tomography Triton device

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### Purpose

To evaluate retinal thickness and retinal nerve fiber layer (RNFL) changes in type 2 diabetes mellitus (DM) patients without diabetic retinopathy using Swept Source Optical coherence tomography (SS-OCT) Triton device.

### Methods

Sixty healthy and 60 DM eyes were included in the study and underwent evaluation of retinal measurements using Triton 3DH wide scan. Macular and peripapillary retinal thickness was analyzed. Automated segmentation by Triton OCT evaluated the different retinal layers in both areas (total retinal thickness, retinal nerve fiber layer [RNFL] and Ganglion cell layer [GCL+: between the RNFL and inner nuclear layer; GCL++ : from the inner limiting membrane to the inner nuclear layer]). Macular volume and macular choroidal thickness were also evaluated.

### Results

Patients with DM2 presented with significant reduction in all retinal measurements of the ETDRS macular areas except in the outer temporal and central thickness ( $p < 0.05$ ). The different macular layers (including the choroid) showed significant thinning in DM2 patients compared to controls. Significant reduction of peripapillary RNFL and GCL was found in the patients group ( $p < 0.05$ ).

### Conclusions

Type 2 Diabetes mellitus produces a subclinical thinning of the RNFL in patients without diabetic retinopathy signs. Swept source OCT Triton is a useful tool to detect early neurodegenerative retinal changes in these patients.

### **T123**

#### **Visual electrophysiological assessment in birdshot chorioretinitis treated with anti-TNF- $\alpha$**

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#### **Purpose**

To evaluate the efficacy of anti TNF- $\alpha$  in birdshot chorioretinitis (BSCR) using full-field electroretinography (ERG) as an assessment tool.

#### **Methods**

A retrospective cohort study of patients with BSCR treated with anti-TNF- $\alpha$  attending Ghent University Hospital from 2002 till 2018.

#### **Results**

49 patients (98 eyes) were diagnosed as BSCR based upon clinical suspicion, the presence of hypofluorescent dark dots on early frames of indocyanine green angiography (ICGA) and HLA-A29 antigen positivity. ERG was performed on 47 patients (95,9%) at presentation. 45 (91,8%) patients were treated with steroids, immunosuppressive agents and biologics. 24 (49,0%) patients were treated with anti-TNF- $\alpha$  of whom 4 received infliximab and 20 received adalimumab. 20 (83,3%) patients were regularly monitored by ERG with a mean follow up of 1,6 electrophysiological assessments every year. In the 30Hz photopic 3.0 Flicker the implicit time is the key parameter which is delayed in 91,7% of patients at baseline. 75% patients showed an significantly improvement of the implicit time since the start of the treatment with anti-TNF- $\alpha$ .

#### **Conclusions**

This study confirms ERG as an important tool in the diagnosis and the follow-up of BSCR. Anti-TNF- $\alpha$  is known to be an effective treatment in patients with BSCR. This report confirms the role of ERG in the management and monitoring of the disease activity in BSCR. The improvement of the implicit time provides essential information of the retinal function. More electrophysiologic analysis is necessary as these results could be important in the therapeutic strategy of BSCR.

### **3134**

#### **Toric phakic IOL implantation in keratoconus: indications and outcomes.**

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#### **Summary**

Although Phakic implantation is not under control or accepted by all ophthalmologists, it should find legitimacy in refractive surgery, when cornea cannot be safely treated by laser surgery. Beyond high ametropia, where photoablation would expose the cornea to a weakening and a deterioration in quality of vision, it is also justified in the field of keratoconus. In this area, the indication will be discussed in case of primitive or secondary ectasia combining sphere with astigmatism, when measure of refraction is accessible; this with or without cross linking, or prior ring segments. Moreover, phakic implants can be proposed after keratoplasty, for induced ametropia, in pre-crystalline situation or as a piggy back in front of a pseudophakic IOL after cataract. In any case, the toric version is the model of choice. Whether it's an anterior chamber iris fixated IOL, or a posterior chamber implant, rules for

calculation must look for a customization of the sizing based on intraocular imaging. An annual follow-up is necessary to verify the absence of corneal, crystalline or iris complications. The reported series are based on small cohorts but demonstrate the interest of this surgical option in the keratoconus indication niche.

**1223**

### **A model to quantify retinal ganglion cell loss in patients**

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#### **Summary**

Apoptosis is an early event in glaucoma - and highlights the impending loss of retinal ganglion cells. Using DARC in vivo experimental models and in patients, we have been able to look at the possibility of apoptosis being a surrogate of glaucomatous neurodegeneration. This suggests that DARC could be used to help model disease processes and assess the efficacy of new treatments.

**3525**

### **New and emerging ocular biomarkers**

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#### **Summary**

Biomarkers are increasingly used in medicine as indicators of a disease and treatment response. The eye lends itself to providing different biomarkers as structural indicators of pathology. Examples of ocular and neurological disease biomarkers are discussed, including OCT, and we review new and emerging technologies which may be used as clinical outcome measures

**2663**

### **PAX6 non-coding regions variants leading to aniridia spectrum**

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#### **Summary**

Congenital aniridia is a panocular genetic disease with autosomal dominant inheritance. It is characterized by complete or partial absence of the iris and foveal hypoplasia. Up to 90% of aniridia patients carry loss-of-function or copy number variants causing haploinsufficiency of PAX6, a highly conserved transcriptional regulator that plays a key role in normal ocular development. Here, we describe non-coding PAX6 variants in two cohorts of French and Spanish aniridia patients without mutation identified in the coding sequences.

In a total of 47 patients, we analyzed the entire PAX6 locus, including coding, untranslated regions and cis-

regulatory sequences by using custom targeted approaches for resequencing and/or CGH arrays. We found non-coding single nucleotide variants or copy number variations in 62% (29/47) of the patients, revealing an outstanding mutation pattern in non-coding *PAX6* regions. *In silico* and *in vitro* analysis using minigene constructs for mutant and wild-type alleles were performed to assess the impact of 5' UTR variants on splicing. Our new analysis strategy brings molecular diagnosis to more than 95% of aniridia patients. This study confirms that *PAX6* remains the major gene for aniridia.

## T018

### Quantitative OCT-Angiography for neovascular age related macular degeneration: Six months follow-up study

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#### Purpose

To compare quantitative Optical Coherence Tomography Angiography biomarkers in treatment-naïve and inactive choroidal neovascularization (CNV) in neovascular age-related macular degeneration (nAMD) on a six-month follow-up.

#### Methods

Prospective, observational study conducted between January 2017 and March 2018. Enrolled patients with treatment-naïve nAMD (group 1) and nAMD in remission phase (group 2) after intra-vitreous injections. Eyes were scanned by a high-speed (100 000 A-scans/seconds) 1050-nm wavelength swept-source OCT-A. The macular scan covered a 4.5x4.5mm area, blood flow was identified in outer retina angiograms and delineation performed automatically using algorithms developed in MATLAB. Quantitative parameters (surface area, vessel density, aspect-ratio, fractal dimension (FD) and lacunarity) were analyzed at baseline and 6 months later. At baseline, all the patients performed two consecutive OCT-A acquisitions for reproducibility analysis. Wilcoxon signed-rank test was used to compare the average of consecutive acquisitions. A level of significance  $\alpha=0.05$  was considered.

#### Results

Inclusion of 60 patients at baseline (28 in group 1 and 32 in group 2) and 40 patients at the 6-month follow up (18 patients from group 1 and 22 patients from group 2). Automatic surface area delineation was not different on consecutive acquisitions ( $p = 0.23$ ). At the 6-month follow-up visit, surface area and FD were lower in group 1 ( $p<0.01$ ) and not statistically different in group 2. LAC, density and aspect-ratio were not statistically different.

#### Conclusions

OCT-A can be used to perform quantitative analyses of CNV lesions. Short-term follow up of active and remission CNV reveal blood flow area and fractal dimension modifications related to different vessel maturation status. OCT-A may provide biomarkers of neovascular activity useful for nAMD follow-up.

## 1812

### Structural versus Angiography OCT in AMD

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## Summary

**Purpose:** To evaluate the performance of different optical coherence tomography angiography (OCT-A) quantitative parameters in predicting the likelihood of neovascular age-related macular degeneration (nAMD) remission on structural OCT.

**Methods:** Eyes were analyzed using SD-OCT and high-speed swept-source OCT-A. Speckle noise removal and CNV blood flow delineation were automatically performed. Quantitative parameters analyzed included blood flow area, vessel density, fractal dimension (FD) and lacunarity. All algorithms and graphical user interfaces were built as a unified tool in Matlab coding language.

**Results:** One hundred and seven patients of whom 74 (74 eyes) were in Group 1 (active nAMD) and 33 (33 eyes) in Group 2 (remission nAMD) based on SD-OCT qualitative morphology. Blood flow area had the highest discriminative power (AUC = 0.87) while the association of blood flow area and FD had the highest predictive performance (Hosmer-Lemeshow test  $p = 0.97$ ).

**Conclusions:** Blood flow characteristics on OCT-A can accurately predict the exudative signs on structural OCT. In the future, analyses of OCT-A quantitative parameters could potentially help assess CNV activity status.

## S080

**The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): an innovative ex vivo model of human herpetic keratitis**

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## Purpose

Our university lab BiiGC patented 2 versions of a bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé. Aim: to present an innovative ex vivomodel of human herpetic keratitis (HSV-1).

## Methods

By restoring IOP and medium renewal, the BR maintained the viability of human or animal corneas over a prolonged period. Its transparency allowed characterizing the tissue with existing or customized devices without compromising its sterility. Corneas discarded after organculture (OC) were placed in the BR for 14 days at 21mmHg and 5µL/H medium renewal. We previously showed that these 2 weeks allowed restoring a multilayered epithelium. The BR lid was opened for HSV inoculation: the epithelium was scarified and immersed for 1H in a solution of 105 to 106 Plaque-Forming Unit/mL HSV-1. The active storage was then continued for 48H. Anti-HSV labeling was done on whole corneas maintained in the BR by incubating primary and secondary antibodies only with the epithelium. Observations: on the whole cornea by slit-lamp and a macroscope, and, after flat-mounting, by epifluorescence and confocal microscopy.

## Results

Immunostaining revealed infected epithelial cells and several areas with ulcers. Outside these spots, the epithelium remained multilayered. In several infected areas rounded and desquamating cells were observed. Controls without HSV remained unstained.

## Conclusions

The OBSERV platform is an efficient tool to store and maintain a multilayered epithelium on corneas discarded after OC, and allows HSV inoculation in more physiologic conditions than on a desquamated epithelium. The BR can complete or replace animal experimentation for academic or industrial research.

## S042

### All-in one automated measurement of ocular surface parameters: interferometry, tear meniscus, non-invasive break-up time and meibography

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## Purpose

To present a new device that simultaneously measures four parameters of the ocular surface indicated for the diagnosis and monitoring of dry eye disease (DED).

## Methods

First use in a volunteer patient with known DED. The device sequentially performed: 1/ interferometry that provided quantitative and qualitative analysis of the lipid layer of the tear film depending on its thickness and regularity; 2/measurement of the height of tear meniscus that is a surrogate criterion for the tear volume; 3/ non-invasive break-up time (NIBUT) consisting in a non-invasive, fluorescein-less measurement of the stability and regularity of the tear film; 4/ meibography consisting in taking an infrared picture of Meibomian glands and quantifying glands area.

## Results

The 4 parameters were obtained on both eyes in 10 minutes. The device identified: an unstable lipid layer, shortly visible due to severe tear deficiency; a discontinuous and thin lacrimal river; a very slight decrease of the NIBUT; a low level of Meibomian glands loss. The device allowed diagnosing a DED mainly due to aqueous deficiency without significant Meibomian gland dysfunction. A graphic presentation provided clear information liable to help ophthalmologists explaining the disease to the patient.

## Conclusions

To the best of our knowledge, this new device is the first to perform the 4 measurements simultaneously. Non-invasive measurements are in conformity with the recent Dry Eye Workshop II recommendations.

## S063

### In vivo biocompatibility of a new intrastromal inlay for spherical ametropia and presbyopia correction, in a rabbit model

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## Purpose

Intrastromal inlays (ISI) are a promising technique for spherical ametropia and presbyopia correction. Aim: to assess the biocompatibility and efficacy of an innovative ISI in rabbits

## Methods

Twelve 6 month-old NZW rabbits were used. A stromal pocket (diameter 5.2mm, depth 250µm) was cut with a Z8 femtosecond laser (FSL) (Ziemer) after manual docking. Nine rabbits were implanted with the new ISI (Cristalens Industrie) and 3, not implanted, served as control. ISI consisted in lenticules (diameter 5mm, thickness 120µm) made of a soft hydrogel permeable to nutrients. Dexamethasone eyedrops was instilled twice daily for 2 weeks. Monitoring: slit-lamp and corneal thickness (CT) + keratometry by OCT (Casia 1), weekly during 1 month, every two weeks until M3, then monthly until M6. Three rabbits were euthanatized at M1, 3 at M3 and 3 at M6 for cross section histology (hematein-eosin-saffron) and transmission electron microscopy (TEM).

## Results

All ISI were well tolerated without clinical or histological inflammation, fibrosis or scarring. Corneas and ISI remained transparent. In TEM, collagen layers in the FSL cut plan were slightly disorganized in implanted as well as in control corneas. A few vacuolized keratocytes, presumed activated, were present only in the 50µm around the ISI. Outside, the stroma, epithelium and endothelium were normal. All ISI remained intact. Central CT was 51+/- 28µm higher with the ISI than for controls (P=0.006). The mean central keratometry in front of the ISI was 5.8+/- 2.7D higher than for controls (P=0.0002).

## Conclusions

The new ISI is fully biocompatible in rabbits after 6 months and induces significant geometric and optical corneal modifications.

## S072

**The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorization): study of a new intrastromal inlay for presbyopia**

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## Purpose

Our university lab BiiGC patented 2 versions of a bioreactor (BR): one for long-term eye banking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Intrastromal inlays (ISI) are promising

techniques for spherical ametropia and presbyopia correction. Aim: to assess the biocompatibility and efficacy of an innovative ISI.

### Methods

By restoring IOP and medium renewal, the BR maintained corneal viability over a prolonged period. Its transparency allowed characterizing the tissue in live with existing or customized devices without compromising its sterility. A stromal pocket was cut with an Alcon Wave-Light femtosecond laser after docking on the opened BR. ISI consisted in lenticule made of a soft hydrogel permeable to nutrients. Implanted cornea and control were stored for 4 weeks. Monitoring: before implantation, D1, W1 to 4: transparency (slit-lamp), modulation transfer function (custom-made transparometer), corneal thickness and keratometry (OCT), endothelium/epithelium (specular microscopy). At W4: histology and ultrastructure by transmission electron microscopy (TEM).

### Results

The ISI remained transparent, intact, well tolerated without histological fibrosis, scarring or necrosis. The cornea remained transparent with a normal endo and epithelium. Thickness and keratometry were modified in front of the ISI. In TEM, collagen layers in the femtosecond laser cut plan were slightly disorganized but normal outside the ISI.

### Conclusions

The OBSERV platform is efficient to study the biofunctionality of an ISI. It complements and/or replaces animal experimentation for industrial research.

### S074

#### **The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): study of a retro-corneal implant for corneal edema**

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### Purpose

Our university lab BiiGC patented 2 versions of a bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to study an innovative retro-corneal implant developed to treat corneal edema

### Methods

By restoring intraocular pressure and medium renewal, the BR maintained the viability of cornea (human/animal) over a prolonged period of time. Its transparency allowed characterizing the tissue with existing or customized devices without compromising its sterility. A 7mm Descemetorhexis was performed on 5 edematous human corneas. For 3 of them, a 7mm diameter silicone implant (EndoArt, EyeYon) was applied to the endothelial side. Controls: 2 corneas without EndoArt. The 5 corneas were then stored for 4 weeks in the BR at 37°C, in organoculture medium, 21mmHg and 5µL/Hour. Corneal thickness (CT) was measured by OCT at D0, W1, 2, 3, and 4. At W4, an eye-rubbing mimicking pressure was applied to the centre of the epithelium at 37°C.

### Results



At D0, central CT was approximately 1100µm in all corneas. The 3 EndoArt were adherent. By W1, CT was stabilized and was significantly lower with the EndoArt: 606+/-50µm versus 881+/-57 for the controls (P=0.009). One EndoArt spontaneously detached at D25 followed by CT increase. At W4, the 2 others detached only after the rubbing test.

### Conclusions

The OBSERV platform is efficient for the study of a retro-corneal implant. It could complement or replace animal experimentation for academic or industrial research.

1441

### Structure of the human fovea: from the microscopy to the OCT

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### Summary

Optical coherence tomography has been a technological breakthrough in the diagnosis and treatment of many ocular diseases. The structure of the foveola is different from that of the rest of the laminated retina and consists of a unique layer with a high concentration of cones. Until now, several controversies have been arisen about the specific histological structures that represent the bands observed in the OCT, especially for the four hyperreflective outer retinal bands. The aim of this study was to correlate these hyperreflective bands observed in the OCT with the retinal structures using human sections and immunocytochemistry at the fovea level. We provide demonstration that the bands 1 and 2 correspond to the outer limiting membrane and the ellipsoids respectively. The band 3 corresponds to the cone phagosomes zone, located into the apical portion of the RPE. The 4 band may be the reflection of the basal mitochondria of the RPE and the hyporeflective band between 3 and 4 correspond to the melanosomes and nuclei. This work proposes a new interpretation of the 4 outer retinal bands that leads to a more accurate interpretation of OCT images and could help to a better understanding of retinal diseases diagnosis and progression.

3523

### Structural Biomarkers in neurodegeneration

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### Summary

The aim of this study is to compare macular retinal layers and choroidal thicknesses of patients with Alzheimer's disease (AD) with those of patients without other known ophthalmological pathology, using spectral domain optical coherence tomography (SD-OCT). Fifty eyes of 50 patients (mean age 73.10; SD=5.36 years) with a diagnosis of mild AD and 152 eyes of 152 patients without AD (mean age 71.03; SD=4.62 years) were included. There was a thinning in the peripheral ring of the ganglion cell layer (GCL) in the AD group (S6 p < 0.001; T6 and N6 p = 0.001). In the superior sectors of the inner plexiform layer (IPL), differences between the two groups also remained statistically significant after Bonferroni correction (S3 p = 0.001 and S6 p < 0.001). Patients with AD showed a significant reduction in retinal layers and choroidal thickness. The thinnest macular measurements were found mostly in the inner layers, GCL and IPL, at superior pericentral and peripheral rings. This thinning may represent a possible retinal biomarker of AD, related with both primary retinal lesion and transsynaptic retrograde

degeneration and the choroidal thinning probably reflects the importance of vascular factors in the pathogenesis of this disease.

**2164**

#### **Cholesterol and the extracellular deposits of age-related macular degeneration (AMD)**

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#### **Summary**

AMD is a prevalent cause of central vision loss in older persons worldwide. The best documented intraocular risk factor for progression is drusen, i.e., extracellular deposits between the RPE basal lamina and the inner collagenous layer of Bruch's membrane. Clinicopathologic correlation, histochemistry for esterified and unesterified cholesterol (EC, UC), lipid-preserving ultrastructure, gene expression, and lipid profiling indicating enrichment in linoleate combine to suggest that the major component of soft drusen in central macula are large apolipoprotein B,E lipoproteins secreted by the RPE. This theory has received strong experimental support with a primary RPE cell culture system that lays down sub-RPE deposits without supplementation with outer segments. Through histologically-validated clinical imaging, a second layer of deposits between the photoreceptors and RPE, called subretinal drusenoid deposits is now recognized (SDD, originally called reticular pseudodrusen). Drusen have both EC and UC, and SDD have only UC. Further, soft drusen are abundant in central macula and SDD are abundant in the perifovea, thus linking distinctive cholesterol-containing deposits to the physiology of cone and rod photoreceptors.

**2761**

#### **Gene regulation and lens development: Insights from single-cell RNA-seq analysis**

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#### **Summary**

Lens progenitor cells emerge from a common pool of anterior pre-placodal cells located at the border between the neuroectoderm and surface ectoderm. Multiple lines of evidence exist to support critical roles of BMP and FGF signaling in this process. Our goal was to elucidate the complete transcriptome of lens progenitor and precursor cells. Human ES cells were differentiated into lens cells using noggin/BMP+FGF/FGF). In the second stage, BMPs were added +/- FGF2. The system was analyzed at between days 6-21 using single cell RNA-seq, using a PDMS co-flow microfluidic droplet generation device. Each cell was barcoded and sequenced using HiSeq2500 rapid mode. A total number of 25-30,000 of cells were captured and data were analyzed using tSNE. The proteomes of mouse lens were analyzed using tandem MS. DLX5 and FOXG1 expression are first activated followed by SIX1 and DLX2 expression. Evidence for common lens/olfactory is supported by the identification of ALDH1A3+/PAX6+/GATA3+ cells. Collectively, these studies show that lens cells are formed between days 12-18 of the cultures. Ongoing experiments are aimed to identify how BMP and FGF signaling direct formation of the lens progenitor cells.

**T016**

#### **Study of macular and optic disk blood flow by angio-OCT in Glucose-6-Phosphate Dehydrogenase (G6PD)**

## deficient men and age-related G6PD-normal subjects

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### Purpose

The reported prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency in Sardinia, Italy, ranges from 8% to 15%. Hemizygous males have totally deficient erythrocytes. Evidence indicates that patients with G6PD deficiency are protected against ischemic heart and cerebrovascular disease, colorectal cancer, retinal vein occlusion, and nonarteritic anterior ischemic optic neuropathy. The purpose of this study was to study the macular and optic disk blood flow by angio-OCT in G6PD-deficient men and age-related G6PD-normal subjects and ascertain whether, or not, there are statistically significant differences between the two groups

### Methods

22 G6PD-deficient men and 22 perfectly age-matched G6PD-normal controls were examined at the Ophthalmology Unit, University of Sassari, Sassari, Italy. A complete review of the medical history and a complete ophthalmological examination, including ETDRS best corrected visual acuity, slit-lamp biomicroscopy of the anterior segment, applanation tonometry, and fundus examination, was carried out. An HD 6-mm Angio-Retina and a 4.5-mm Angio Disk (RT-Vue, Optovue XR-100 with Angio Vue, CA) examination were also performed

### Results

Only 1 eye per patients was included in the analysis, for a total of 22 eyes in each group. All the exported parameters about retinal and disk flow were evaluated. No statistical differences between the two groups were found, even after controlling for the effects of age, hypertension and hypercholesterolemia ( $p=0.9$ ).

### Conclusions

Results suggest that G6PD-deficient and G6PD-normal men have similar macular and optic disk blood flow. Larger scale studies are necessary to confirm these findings.

## S104

### Comparison of collagen and alpha smooth muscle actin distribution in in-vitro and in-vivo developed posterior capsule opacification

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### Purpose

To compare the expression of collagen and alpha smooth muscle actin ( $\alpha$ SMA) in lens capsule samples after a short and long term post cataract surgery.

### Methods

Twenty-four human donor eyes were obtained, and separated in to three different groups: IOL capsules (n=12): lens capsules with IOLs and varying degrees of Soemmering's ring formation, Cultured capsules (n=6): emptied

capsular bags, cultured for 1-month and Intact lenses (n=6). All samples were stained with H&E,  $\alpha$ SMA and Picro Sirius Red for collagen I, III and IV.

### Results

All Cultured capsules except one, expressed  $\alpha$ SMA which tended to concentrate near the capsule. IOL capsules only expressed  $\alpha$ SMA in areas where the capsules adhered to each other. Intact lenses did not express  $\alpha$ SMA. All samples expressed collagen I and IV in the lens capsules, and collagen I and III in the ciliary muscles. None of the Intact lenses or Cultured capsules expressed collagen in any other areas. Seven of the twelve IOL capsules expressed collagen I and III in their Soemmering's rings where the anterior rhexis and posterior capsules contacted the IOL. These areas were also the only ones that expressed  $\alpha$ SMA.

### Conclusions

In the short term after cataract removal (Cultured capsules),  $\alpha$ SMA was found throughout all cells, adhering the capsules together. In the long term (IOL capsules), both  $\alpha$ SMA and collagen were found near the IOL, creating a type of seal.

### F125

#### The 100,000 Genomes Project and the Western Eye Hospital Experience

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### Purpose

Genetic eye diseases are extremely heterogeneous both in terms of possible phenotypes and related molecular causative defects.

Any part of the visual system can be affected with an extremely high number of conditions that recognize a genetic defect as the primary cause. To date at least 600 genes are considered as involved in both isolated and syndromic forms of genetic eye diseases, but yet the genetic cause remains unidentified in a significant percentage of patients.

Despite the high number of identified genes causing ophthalmologic diseases and the new available advanced sequencing facilities, a consistent percentage of patients will not have access to molecular genetic diagnosis.

### Methods

At the Western Eye Hospital an integrated diagnostic pathway has been created in collaboration with the 100,000 Genomes Project, a UK Government project, aiming at the identification of genetic defects related to cancer and rare diseases (including ophthalmological) through whole genome sequencing in National Health Service (NHS) patients.

### Results

Patients are given the opportunity to receive a one-stop care including clinical and instrumental investigations (including imaging and electrophysiology), counselling and genetic testing. Results from genetic testing are related to phenotype and discussed in a multidisciplinary context. Segregation studies are then carried out both to validate results and as a diagnostic tool to family members.

### Conclusions

The identification of causative genes and eventually novel genes and pathogenic mechanisms leads to multiple benefits, from the precise definition of clinical entities, to the possibility to provide focused genetic counselling to patients and their family members. Finally, this is a crucial step towards patients' recruitment in possible experimental therapeutic strategies.

**2133**

**Confocal microscopy for diagnosis of infectious processes in the cornea**

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**Summary**

Confocal microscopy has been focusing on imaging the retina and optic nerve head for the past decades. It has been the reference technology for imaging of the endothelium before the invention of specular microscopy. For the anterior segment of the eye it is mostly used for investigation of corneal pathologies such as corneal dystrophies, corneal inflammatory processes/infections or localization of opacifications. It offers a very high axial resolution in contrast of complementary technologies such as optical coherence tomography. In this talk we will present an overview on different fields of applications with a high resolution confocal microscope for assessment of corneal pathologies.

**2335**

**Mycotic keratitis – the threat of today?**

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**Summary**

Mycotic keratitis is a comparatively rare but serious ophthalmological disease, that can possibly lead to a severe loss of vision up to blindness. Over the last two decades an increase of cases with mycotic keratitis has been noticed, which is possibly caused by an increased use of soft contact lenses. In this talk we would like to give an overview on the typical clinical signs, symptoms, diagnostics and therapy as well as new diagnostic methods of keratomycosis.

**2934**

**Intracorneal ring segments (INTACS) – long-term results of the first 100 keratoconus patients**

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**Summary**

Implantation of intracorneal ring segments (ICRS) using a femtosecond laser represents a reliable option to widen the spectrum of the stage-related therapy of keratoconus in patients with contact lens intolerance, post-LASIK-keratectasia, or pellucid marginal degeneration (PMD).

Between August 2011 and February 2018, ICRS (Intacs-sk, Addition Technology, Inc.) were implanted in 101 eyes of 81 patients with clear central cornea. The patients had to fulfill the corneal diagnostic criteria required for

implantation. Tunnel creation should nowadays only be carried out by femtosecond laser, in order to avoid intra- and postoperative complications.

Two years after surgery, the patients showed an increase in uncorrected (logMAR) from  $0.9 \pm 0.1$  to  $0.4 \pm 0.1$  and bestcorrected distance visual acuity (logMAR) from  $0.4 \pm 0.2$  to  $0.2 \pm 0.1$ .

Uncorrected and corrected distance visual acuity can be improved by implantation of the ICRS. Progression of ectasia seems to be retarded. Complications after ICRS implantation are rare due to strict patient selection and modern surgical techniques.

#### **T104**

##### **Retinal response to hypoxia: new insight on the functional role of beta3 adrenoceptors**

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##### **Purpose**

Beta adrenoceptors ( $\beta$ -ARs) play an important role in retinopathy of prematurity (ROP) as demonstrated by experimental models and clinical trials assessing safety and efficacy of propranolol, a  $\beta$ -AR blocker, in preterm newborns with ROP. Among  $\beta$ -ARs,  $\beta_2$ -ARs are mainly involved in the retinal response to hypoxia as their blockade reduces neovascular tuft formation and recovers visual damage. However,  $\beta_2$ -ARs are not regulated by oxygen levels, while  $\beta_3$ -ARs are upregulated at the neovascular tufts in response to hypoxia, suggesting their role in angiogenesis. However,  $\beta_3$ -AR blockade is ineffective in counteracting retinal neovascularization. We attempted to reveal the elusive role of  $\beta_3$ -ARs in a mouse model of oxygen-induced retinopathy (OIR) mimicking ROP. To this aim, we used the 129S mouse strain, which exhibits higher  $\beta_3$ -AR upregulation in response to hypoxia as compared to the C57 strain.

##### **Methods**

The time course of  $\beta_3$ -AR, HIF-1 and VEGF expression was assessed in normoxia, hyperoxia and hypoxia by Western blot. The effect of  $\beta_3$ -AR blockade on HIF-1/VEGF axis, retinal angiogenesis and retinal function was studied by Western blot, immunohistochemistry and electroretinogram.

##### **Results**

Retinal  $\beta_3$ -ARs were highly expressed in the embryo and their expression progressively decreased during postnatal development. In respect to normoxia,  $\beta_3$ -ARs were downregulated by hyperoxia, while they were upregulated by hypoxia indicating a role as oxygen sensing receptors.  $\beta_3$ -AR blockade reduced HIF-1/VEGF upregulation with consequent reduction of neovascular responses to hypoxia, which was correlated to recovered retinal function.

##### **Conclusions**

The present results demonstrate that  $\beta_3$ -ARs play an important function in hypoxic diseases of the retina, but their role may be unraveled depending on the level of their expression in response to hypoxia.

#### **T105**

##### **VEGF-induced VEGF release in the retina in response to oxidative stress**

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### **Purpose**

Vascular endothelial growth factor (VEGF) influences both neural and vascular physiology in the retina. Oxidative stress (OS) is a sort of final common pathway of pathological mechanisms in retinal diseases such as diabetic retinopathy (DR). Our working hypothesis is that in early phases of the disease VEGF would be released as a neuroprotectant, while, in the following period, increasing VEGF expression and release would lead to the typical DR vasculopathy. We tested the possibility that retinal cells express and release VEGF in response to OS and that further VEGF expression and release are sustained by VEGF itself.

### **Methods**

Human Müller MIO-M1 cells and *ex vivo* mouse retinal explants were subjected to OS for 24h. Untreated MIO-M1 cells and explants were exposed to exogenous VEGF at various concentrations. Untreated MIO-M1 cells were also exposed to conditioned medium (CM) from OS-stressed MIO-M1 cells. VEGF expression was measured with qPCR and VEGF release with ELISA.

### **Results**

Both in MIO-M1 cells and in explants, OS significantly increased VEGF expression and release, indicating an early VEGF response to retinal stress. In untreated MIO-M1 cells or explants, 1 ng/ml exogenous VEGF induced significant VEGF expression and release, indicating that VEGF regulation may be influenced by VEGF itself. CM induced VEGF expression in untreated MIO-M1 cells, suggesting that factors released in response to OS may be sufficient to cause further VEGF expression. Finally, adding a VEGF trap to the CM abolished VEGF expression by untreated MIO-M1 cells, demonstrating that the component of CM inducing VEGF expression was indeed VEGF itself.

### **Conclusions**

These observations reveal a novel mechanism of VEGF regulation and support the hypothesis of a positive feedback that maintains elevated retinal VEGF levels for a long period.

## **F063**

### **Spectral-Domain Optical Coherence Tomography findings in 64 patients with aniridia : a retrospective study**

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### **Purpose**

To evaluate foveal anomalies on spectral-domain optical coherence tomography (SD-OCT) in aniridia patients.

### **Methods**

Consecutive patients presenting with aniridia between September 2015 and April 2018 were retrospectively reviewed. Clinical and genetic characteristics and SD-OCT finding were analyzed. Foveal hypoplasia was classified according to Thomas et al. as grade 1 to 4. The Spearman coefficient was used to assess correlations.

### **Results**

Charts of 145 patients with aniridia were reviewed. SD-OCT could not be performed in 81 patients because of young age, corneal or lens opacification. Sixty-four aniridia patients (36 females and 28 males) with SD-OCT records were included. Mean age was 22.3±20.3 years. 91% of patients presented with isolated aniridia and 9% with syndromic aniridia. PAX6 mutation was confirmed in 47% of patients. SD-OCT was performed bilaterally in 49 patients and unilaterally in 15 patients. A total of 113 eyes were analyzed. The majority of eyes showed grade 4 hypoplasia (n=90, 79.6%). Grade 3 hypoplasia was found in 2 eyes (1.8%), Grade 2 in 8 eyes (7.1%) and grade 1 in 8

eyes (7.1%). Three patients (n=5, 4.4%) presented with normal foveal characteristics on SD-OCT. LogMar BCVA was significantly correlated with the degree of foveal hypoplasia on SD-OCT ( $p < 0.001$ ,  $r = 0.5$ ).

### Conclusions

The majority of aniridia patients presented severe foveal hypoplasia on SD-OCT, that was associated with lower visual acuity. Genetic alterations such as PAX6 mutations may explain the co-existence of foveal and iris developmental defects.

3161

### Antisense therapy for Fuchs endothelial corneal dystrophy ameliorates TCF4 repeat-expansion mediated toxicity

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### Summary

Fuchs endothelial corneal dystrophy (FECD) is a common disease for which corneal transplantation is the only treatment option in advanced stages; alternative treatment strategies are urgently required. Expansion ( $\geq 50$  copies) of a non-coding trinucleotide repeat in *TCF4* confers  $>76$ -fold risk for FECD in our large cohort of affected individuals. We have developed an FECD subject-derived corneal endothelial cell (CEC) model to probe disease mechanism and investigate therapeutic approaches. The non-coding repeat expansion leads to the occurrence of nuclear RNA foci, with the sequestration of splicing factor proteins (MBNL1 and MBNL2) to the foci and altered mRNA processing. Antisense oligonucleotide (ASO) treatment led to a significant reduction in the incidence of nuclear foci, MBNL1 recruitment to the foci and downstream aberrant splicing events, suggesting functional rescue. This proof-of-concept study highlights the potential of a targeted ASO therapy to treat the accessible and tractable corneal tissue affected by this repeat expansion-mediated disease.

F047

### Neuroprotective Activity of Curcumin Nanocarriers in Rodent Models of Retinal Injury

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### Purpose

Curcumin (1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5dione) is a polyphenol extracted from turmeric that has long been advocated for the treatment of a variety of conditions including neurodegenerative and inflammatory disorders. Despite this promise, the clinical use of curcumin has been limited by the poor solubility and low bioavailability of this molecule.

### Methods

In this study, we describe the development of a novel and highly stable curcumin nanocarrier formulation that successfully solubilized high concentrations ( $> 4$  mg/mL) of curcumin. Characterisation with x-ray diffraction and *in vitro* release assays localized curcumin to the nanocarrier interior, with each particle measuring  $< 20$  nm diameter. Resulting nanoparticles were stable for over 60 days when stored at room temperature.

### Results

Curcumin-loaded nanocarriers (CN) were found to significantly protect against cobalt chloride induced hypoxia and glutamate-induced toxicity *in vitro*, with CN treatment significantly increasing R28 cell viability in a dose-



dependent manner. Using established glaucoma-related *in vivo* models of ocular hypertension (OHT) and partial optic nerve transection (pONT), topical application of CN twice-daily for three weeks was found to significantly reduce retinal ganglion cell loss compared to controls as determined histologically using whole-retinal retinal ganglion cell counts.

## Conclusions

Collectively, these results suggest that our novel topical CN formulation has potential as an effective neuroprotective therapy in glaucoma and other eye diseases with neuronal pathology.

2121

## RGC cell size and susceptibility to loss in rodent glaucoma models

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## Summary

Although multiple mechanisms have been proposed to describe the processes leading to glaucoma, it is widely accepted that glaucoma principally results from the loss of RGCs involving apoptotic cell death. A more controversial topic is whether some RGC subpopulations are more susceptible to glaucomatous degeneration than others. Cell morphology has previously been used to stratify RGC population in retinal histological samples based on cell size. Early work in this field suggested that larger RGCs and their axons were more susceptible to early loss than smaller RGCs. More recently, however, RGC soma and axon size have been suggested to be dynamic and change in response to injury. To address this controversy, we sought to apply recent advances in maximizing information extraction from RGC populations to evaluate the changes in RGC size distribution over the natural history of two rodent models of optic nerve injury. In contrast to previous studies based on sampling approaches, we sought to evaluate the change in size of the (brn3a+) RGC population over the natural history of these models. To achieve this, the morphology of over 4 million RGCs were assessed from 65 retinæ in order to glean new novel insights from this dataset.

2724

## Evaluation of topical curcumin nanoparticles in rodent glaucoma models

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## Summary

Curcumin is a polyphenol extracted from turmeric recently advocated for the treatment of a variety of conditions including neurodegeneration and inflammation. Amongst several issues limiting its clinical applicability and widespread use, key challenges have been its poor solubility and low bioavailability. Several methodologies including nanotechnology have been proposed to overcome these problems. Here, we describe a novel nanocarrier curcumin formulation which can solubilize high concentrations of curcumin. Characterisation with x-ray diffraction and *in vitro* release assays localize curcumin to the micelle interior, with each particle measuring < 20 nm diameter. Curcumin-loaded nanocarriers (CN) were found to significantly protect *in vitro* retinal cell viability. Using established glaucoma-related *in vivo* models of ocular hypertension (OHT) and partial optic nerve

transection (pONT), topical application of CN twice-daily for three weeks significantly reduced retinal ganglion cell loss compared to controls. Collectively, these results suggest that our novel topical CN formulation has potential as an effective neuroprotective therapy in glaucoma and potentially all eye diseases with neuronal pathology.

**3163**

### **The non-coding morbid genome of inherited retinal diseases**

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#### **Summary**

Inherited retinal diseases (IRD) are a major cause of early-onset blindness, having an overall prevalence of 1/3,000. Whole exome sequencing (WES) revealed the underlying coding mutations in ~60% of cases, but few novel candidate genes are identified in the remaining cases. Missing heritability of IRD is assumed to reside in non-coding regions harboring cis-regulatory elements (CREs) affecting expression of a target gene.

Thus far, several non-coding variants have been linked to IRD, the majority of them affecting cis-acting splicing, exemplified by a recurrent deep-intronic CEP290 mutation in LCA. Other deep-intronic mutations have been reported in ABCA4, CHM, OFD1, PROM1, and USH2A, typically resulting in the inclusion of pseudo-exons into the mRNA and amenable to antisense oligonucleotide-mediated rescue. Examples of cis-regulatory variants can be found in CHM, LCA5, NMNAT1, PRDM13 or IRX1 implicated in North Carolina macular dystrophy, and more recently in ABCA4 in Stargardt disease. The integration of genomic and transcriptomic data and epigenomic datasets generated in retinal cells provide interesting tools for addressing the gap between disease-associated non-coding variants and their target genes.

**2125**

### **Image analysis and data science for vessel network analysis in the retina**

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#### **Summary**

The retinal blood vessel pattern can be used as a proxy to characterize microvascular pattern changes of the central vascular system. In addition, the retina develops from the brain. Hence, retinal vessels changes can also be used as a true window to the brain. Epidemiological research shows that deviating retinal blood vessel patterns can predict the risk and progression of chronic diseases. There are already indications for risk of hypertension, myocardial infarction and stroke. Retinal vessel analysis can be performed with computer algorithms. Our lab develops software for quantification of the blood vessel pattern. Recently, a shift occurred from computer vision technologies to machine learning to extract in an automated way more information from retinal images. The presentation will give an overview of the current application possibilities of retinal vessel analysis for classification and prediction of diseases. The possibilities of machine learning and artificial intelligence for improved retinal vessel analysis will be discussed. Examples will be given from our lab about progress in segmentation of vessels and simultaneous segmentation of arterioles and venules using state-of-the convolutional network architectures.

**T039**

### **Topical Treatment for Ocular Diseases of the Posterior Segment: Non-Invasive Delivery of Large Therapeutics such as Bevacizumab and Ranibizumab**

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## **Purpose**

To investigate the use of novel cell penetrating peptides (CPP) to deliver a range of therapeutics to the posterior segment of the eye without the need for intravitreal injection.

## **Methods**

Ranibizumab, bevacizumab and other therapeutics were applied topically to ex-vivo porcine eyes and to in vivo rodent and rabbit eyes. CPP were mixed with therapeutic and a 50 µL drop applied to the ocular surface. Animals were grouped into 1) CPP+therapeutic, 2) CPP alone, 3) therapeutic alone, 4) negative control. The animals were sacrificed and the ocular tissues dissected and homogenised in sterile PBS. The levels of therapeutic were determined using ELISA or fluorescence.

## **Results**

Utilising the CPP to deliver therapeutics, the CPP could successfully deliver  $1.7 \pm 0.4$  µg/mL (ranibizumab),  $1.1 \pm 0.3$  µg/mL (bevacizumab),  $15 \pm 10$  µg/mL (Bovine Serum Albumin),  $0.5 \pm 0.1$  µg/mL (Ovalbumin) to the eye. All of these are significantly higher than the therapeutic applied without CPP, CPP and saline controls  $p < 0.05$ . The levels of therapeutics in the eye in both rodents and rabbits demonstrated a clearance profile over 24 hours in rodents and 7 days in rabbits. The CPP also demonstrated high antimicrobial activity against *S. aureus*, *P. aeruginosa* and *E. Coli* removing the need for preservatives in eye drops.

## **Conclusions**

The CPP can be used to deliver a range of therapeutics in rodents, rabbits and porcine eyes. The endurance of the therapeutic in the eye was dependent on the size of the eye, informing a clinical dosing regime in humans. The antimicrobial efficacy of the CPP also removes the need for preservatives in the eye drops, which often lead to ocular irritation and damage to the ocular surface.

## **2722**

### **Evidence for MMP-3 as neuroprotection target at the crossroad of inflammation and neurodegeneration**

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## **Summary**

Although matrix metalloproteinase-3 (MMP-3) has been associated with many neurodegenerative diseases, via its role in glial activation and neuronal apoptosis, its involvement in optic neuropathies remains largely elusive. In this study, we investigated the role of MMP-3 in glaucomatous retinal degeneration, and found an interplay of neurodegenerative and neuro-inflammatory processes orchestrated by MMP-3.

The study was initiated by the findings that MMP-3 expression follows a tightly regulated spatiotemporal expression pattern in the mouse retina following optic nerve crush, and that the brief peak in MMP-3 expression at 4 days post injury is essential to neuroprotect retinal ganglion cells. A comprehensive study of inflammatory cytokines, cell adhesion molecules and blood-retinal barrier proteins, using qPCR, western blotting, immunohistochemistry and bioplex assays, next pointed out that this is likely linked to a role for MMP-3 in the initial phases of the neuro-inflammatory response. Indeed, our findings suggest that MMP-3 is essential to the recruitment of inflammatory cells to the site of injury and that the increased neurodegeneration in MMP-3 null mice is linked to an uncontrolled immune response and cytokine imbalance.

#### **F038**

##### **Bilateral activation of retinal microglia: quantitative analysis of the microglia cell number at different time points after laser-induced ocular hypertension in mice**

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#### **Purpose**

To quantify the number of retinal microglial cells in different retinal layers at different time points (1, 3, 5, 8 and 15 days) after unilateral laser-induced ocular hypertension (ULOHT) in OHT-eyes and their contralateral-eyes.

#### **Methods**

Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=30, six mice by each time-point analyzed). Retinal whole-mounts were immunolabeled with anti Iba-1 to quantify: i) number of Iba-1 + cells (Nibac) in outer segments (OS), outer plexiform layer (OPL) and inner plexiform layer (IPL).

#### **Results**

With respect to naïve-eyes: i) in OHT-eyes, there was a significant increase in the Nibac in all retinal layers and in the different time-points analyzed except at 1d. ii) In contralateral-eyes, the significant increase of the Nibac was restricted to OS at 3d, 5d and 8d, and in IPL at 8d. The comparison of Nibac between the different time-points after ULOHT showed: i) In OS, there was a significant Nibac increase at 5d with respect to 1d and 3d, and a significant decrease from 5d to 8d and 15d in OHT-eyes. In contralateral-eyes, the significant increase of Nibac was at 3d and decreased significantly at 15d. ii) In plexiform layers, in OHT-eyes there was a significant increase of Nibac at 3d and 5d with respect to 1d. From then, there was a significant Nibac decrease until 15d. iii) In contralateral-eyes at 8 days, only in the IPL there was a significant Nibac increase with respect to naïve.

#### **Conclusions**

ULOHT produces a reactive proliferative microgliosis response both in OHT-eyes and in contralateral-eyes since 3d. In OHT-eyes, this microglial proliferation was produced in all retinal layers analyzed, while in contralateral-eyes it was restricted to OS and IPL. This microglial proliferation could be associated with an inflammatory process occurring in glaucomatous neurodegeneration in both eyes.

#### **1442**

##### **Visual perception in the human fovea: functional evaluation of cone diseases by neurophysiological methods.**

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### Summary

We describe the principles behind the pattern electroretinogram (pERG) as a useful technology to evaluate the function of the central retina. The pERG may be recorded from the human cornea under light-adapted conditions. By using a black/white checkerboard pattern, the central retina is stimulated at different temporal frequencies. Stimuli elicit the retinal response which may be recorded as positive- and negative deflections. Since the overall luminance of the pattern stimulus remains constant, the linear responses of the flash ERG are suppressed, leaving only nonlinear responses corresponding to retinal ganglion cells. The pERG has been used clinically to assess RGC function in diseases that affect their integrity. However, not much information is available about the capacity of the pERG to evaluate the foveal cone function in health and disease. By the use of different stimuli parameters (contrast, size, frequency, wavelength, ...) we tested the pERG responses both in healthy humans and those affected of dyschromatopsia or AMD. We will show the effectiveness of this electrophysiological technique to address the central retinal function.

1244

### Molecular genetics in clinical practice II (Retina)

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### Summary

Using a case presentation format, this presentation will illustrate how molecular genetics is used in the inherited retinal disease clinic. It will focus on phenotypes, and how molecular genetic testing is chosen, and subsequently how the results are interpreted. All consequences of such an approach will be highlighted.

1864

### Human Case

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### Summary

This presentation will illustrate the challenges of making the correct diagnosis in a case with inherited ocular disease.

S108

### Prediction of postoperative spherical equivalent after cataract surgery using a machine learning approach

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### Purpose

To compare the accuracy of prediction of the postoperative spherical equivalent after cataract surgery between the SRK-T formula, the Haigis formula, and a machine learning approach using the gradient-boosted three algorithm XG-Boost.

## Methods

2697 eyes that underwent cataract surgery at Rothschild Foundation, Paris, were analysed. Preoperative clinical and biometric data, power and model of implanted intraocular lenses, and postoperative refractive results were retrieved. The XG-Boost algorithm was trained to predict the postoperative spherical equivalent on 2022 eyes. Data from the 675 remaining eyes, unknown to the model, were used to assess the algorithm predictions in comparison with Haigis formula and SRK-T formula predictions. Python programming language version 3.6 and the machine learning library Sci-kit Learn were used to code the model and the formulas.

## Results

The machine learning approach had a root mean squared error (RMSE) of 0.53, compared to a RMSE of 0.58 using the Haigis formula and a RMSE of 0.62 using the SRK-T formula.

The XGBoost model was more accurate in predicting the postoperative spherical equivalent than the SRK-T formula (+ 17.4 %,  $p < 0.01$ ) and the Haigis formula (+ 13.6 %,  $p < 0.05$ ).

## Conclusions

This study confirms the great potential of data-based approaches to increase the accuracy of intra-ocular lenses calculus in cataract surgery. A larger study focused on intraocular lenses power prediction is currently in progress at the Rothschild Foundation.

## F023

### Modeling the circadian pattern of intra-ocular pressure

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## Purpose

To investigate if modelling the circadian patterns of IOP could have a relevant impact on the design of glaucoma studies, particularly on the number of subjects needed.

## Methods

Data was used from a database where patients with glaucoma were treated with prostaglandin analogs. IOP was measured 3 times per day and treatment with prostaglandins was initiated as of the third visit. A nonlinear mixed model was fitted including an intercept and the circadian pattern with a 24-hour cycle period, amplitude and phase. The intercept represents the overall mean IOP while the circadian pattern is characterized by its amplitude (maximum deviation from the mean) and phase (time when the maximum deviation from the mean is reached). Mean IOP, amplitude and phase were allowed to be different by type of glaucoma and by treatment, and patient-level random effects were also taken into account.

## Results

Modelling the circadian pattern in the data provided a good fit with a significant circadian pattern. The mean IOP value is higher in patients with primary open angle glaucoma (POAG) vs ocular hypertension (OHT), lower after treatment with prostaglandins and patient-level variation is also present. The amplitude is lower in patients with POAG vs OHT, whereas treatment with prostaglandins has no influence on the amplitude of the circadian pattern, and also no patient-level variation in amplitude is found. Treatment with prostaglandins moves the IOP peak forward.

## Conclusions

The design of clinical studies in glaucoma should take into account the circadian pattern and also patient specific factors like the type of glaucoma. With more IOP time points, deeper analysis of circadian IOP patterns may have an impact also in reducing sample size.

**3436**

**Challenge in eyelid melanoma combined with conjunctivitis melanoma challenge**

**019**

**Detachment of pigment epithelium**

**2313**

**Macroaneurysms and their photocoagulation in other diseases**

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### **Summary**

The control of the duration of macular edema is a key-factor to prevent irreversible neuro-retinal lesions. Pharmacological studies have demonstrated the interest of early intravitreal treatments (either anti-VEGF or dexamethasone) to control vascular macular edema, especially in retinal vein occlusions. However, in some cases, pharmacological therapy fails to control retinal exudation, either at once or after a while. The remodeling of the retinal capillary network secondary to chronic vascular disturbances can indeed maintain the exudation. Capillary macro-aneurysm (CMA) is one of the modifications of the vascular network that can be involved in persistent or recurrent vascular edema. CMAs may be identified on the fundus as dark-reddish round lesions often with white borders. CMA may be either isolated or gathered in clusters. In some cases, however, CMA remains barely visible. ICG-angiography remains the most efficient imaging mode for CMA detection, enabling to precise the number of CMA(s) and their location towards the fovea. Our presentation will focus on clinical presentations of such CMAs in vascular diseases outside diabetes: retinal vein occlusions, Coats' disease... Both management and outcomes will be discussed.

**F042**

**ISY (satISfaction surveY): First real-life data of use of a preservative-free multidose glaucoma device (EasyGrip® delivery system) in 5 European countries**

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### **Purpose**

Preserved eye drops can cause local side effects, some of which appear more rapidly, that can impact the patients' quality of life. The new availability of the first Preservative-Free (PF) Dorzolamide/Timolol (DT) Fixed Combination (FC) in a new MD bottle (EasyGrip®) could improve patient satisfaction, treatment compliance and ultimately treatment efficacy.

### **Methods**

ISY is an International, multicentre, observational and cross-sectional study. 1880 glaucoma patients, treated and stabilised for at least 28 days with the PF-MD DTFC (Duokopt®/Dualkopt® - Laboratoires Théa - France), were planned to be recruited in 7 European countries. A two-part questionnaire is completed independently by the ophthalmologist and the patient during one routine visit. The primary endpoint was the prevalence of patients satisfied with the PF-MD vial. Other parameters was: patient age, year of glaucoma diagnosis, IOP, visual acuity, QuickDASH® score [0=very good dexterity to 100=very low dexterity], physical function and symptoms, easiness of use of the vial; ophthalmologist satisfaction; use of tear substitutes and adherence.

### **Results**

The results of the first 493 patients from 5 countries (SP:189, FR:163, GE:110, DK:23, FI:8) are presented. Patients were previously using 70% MD vial and 30% unidose format. 82.2% of patients have a QuickDASH® score from 0 to 25, 14.8% from 25 to 50 and 3.0% from 50 to 75. 97.3% of ophthalmologists are satisfied/very satisfied to prescribe the PF-MD DTFC. 81.7% of patients are satisfied enough to continue with the PF-MD device.

### **Conclusions**

The results confirm the interest of both ophthalmologists and patients (even an elderly population) of switching to the PF-MD EasyGrip® delivery system whilst keeping the efficacy of DTFC.

**2644**

### **Management of epithelial malignancies ( radiotherapy and local chemotherapy)**

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### **Summary**

Ocular surface neoplasia includes in situ carcinomas and invasive epidermoid carcinomas. Surgical removal of the lesion is always necessary with pathological examination unless the patient has previously been treated for in situ carcinoma and the aspect is typical of recurrent in situ carcinoma. Surgery must be done after careful clinical examination and slit lamp photographs, under topical or general anesthesia. In case of in situ carcinoma, if the surgical resection is complete on pathology and there is no visible residual tumor, a simple observation can be proposed. Residual tumor or recurrent in situ carcinoma can be treated by several antimitotic drops including mitomycin, 5 FU and interferon. Treatment protocols and results will be described. Invasive carcinoma of the conjunctiva must be treated by surgical excision followed by radiotherapy. Proton beam radiotherapy is the most precise irradiation and plaque brachytherapy is also an option in selected cases. Protocols and results will be given.

**T103**

### **Microglial cell inhibition improves photoreceptor survival in two animal models of inherited retinal degeneration**



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### **Purpose**

To analyze the effects of the inhibition of microglial cells and bFGF administration during the early period of retinal degeneration in two animal models with different mechanisms of degeneration.

### **Methods**

Homozygous albino P23H-1 (n=6 per group) and pigmented Royal College of Surgeons (RCS) rats (n=6 per group) received daily intraperitoneal (IP) injections of minocycline, one intravitreal injection (IVI) of bFGF or a combination of both starting at post-natal (P) day 10 in P23H-1 rats and at P33 in RCS rats. Retinas were cross-sectioned at P21 or P45 for P23H and RCS rats respectively and immunoreacted to label the outer segments of cones and rods and the microglial cells. Retinal morphology was analyzed qualitatively. The numbers of nuclei rows in the outer nuclear layer (ONL) and of microglial cells in each retinal layer were manually quantified in eight standard areas per retinal section in three sections per animal.

### **Results**

In both models, minocycline administration decreased microglial cell activation and migration from the inner to the outer retinal layers and significantly increased photoreceptor survival. bFGF also increased significantly photoreceptor survival in both models in similar proportions. The combination of minocycline and bFGF had an additive effect.

### **Conclusions**

Minocycline and bFGF increase photoreceptor survival in both animal models through two different, microglial cells mediated or not, mechanisms, and their effects are additive. Thus, photoreceptor cell rescue in inherited retinal degenerations may be augmented using combined targeting of cell death mechanisms.

**2322**

### **Seeing is believing : live imaging of microvascular pathology in glaucoma**

*A. DI POLO<sup>1</sup>*

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### **Summary**

Vascular deficits have been shown to contribute to glaucoma pathogenesis. However, the cellular and molecular basis of microvascular defects in ocular hypertension, a major risk factor in glaucoma, is poorly understood. Pericytes, the contractile cells that wrap around capillaries, have emerged as key regulators of blood flow in response to metabolic demand. We implemented a minimally invasive, two-photon microscopy approach to monitor retinal capillaries and pericytes in a mouse glaucoma model. Ocular hypertension was induced by microbead injection in mice expressing genetically encoded calcium indicators selectively in pericytes. Two-photon imaging demonstrated that ocular hypertension results in early capillary constriction at pericyte locations, prior to retinal ganglion cell death. Narrowing of capillaries correlated with progressive accumulation of intracellular calcium in pericytes and reduced blood flow. Intriguingly, pharmacological reduction of eye pressure was not sufficient to reverse pericyte contraction, capillary constriction, and impaired blood flow. Our data suggest that glaucoma management should focus not only on controlling ocular hypertension but also on resolving microvascular dysfunction to preserve vision.

**008**

### **Immune tolerance and its alteration**

**1311**

**Ocular Inflammation**

**Summary**

The management of Ocular Inflammation until recently has lacked high level clinical trial evidence despite years of experience with DMARDs and Biologics. On the backdrop of this data, I will be discussing future approaches no longer quixotic, through our understanding of the immunobiology of experimental models, advances in experimental medicine in man and our increasingly elegant imaging technologies to develop our future approaches that through endophenotypes of uveitis we will target patients appropriately, at the right time and with the right drugs.

**013**

**Introduction**

**1734**

**Triple procedure for treating advanced AAK with cataract**

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**Summary**

Results of keratoplasty combined with cataract surgery (triple procedure) in aniridia show, that surgery should be considered, if central stromal haze coexists with cataract involving visual axis. Treatment is usually proceeded, when VA has dropped to hand movements. Stage of aniridia keratopathy is very important. Limbal deficiency with local involvement is the best option. In other cases, pannus removal with amniotic membrane application or transplantation of cultivated oral mucosa epithelium is offered to the patient, as a primary treatment. PK in aniridia is a difficult procedure with high risk of conjunctival invasion. Last therapeutic procedure to consider is keratoprosthesis implantation.

**S082**

**Increased TRAIL and TRAIL receptor expression in rat corneal stroma exposed to chemical burn damage**

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### **Purpose**

To study the expression levels of TRAIL and TRAIL receptor in the rat cornea after alkali burn.

### **Methods**

A 2 mm<sup>2</sup> filter paper embedded with a 0,5 M NaOH solution was applied in the centre of cornea for 30 seconds, then we followed healing process up to 14 days. Immunostainings were done for TRAIL and TRAIL receptor. For western blot analysis, corneal epithelial cells from 5 different rats were pooled.

### **Results**

The immunostaining showed a strong up-regulation of TRAIL and TRAIL receptor in the nuclear and perinuclear area of corneal stroma and limbal cells. The intensity of the staining regained baseline levels few days later. After 14 days the central corneal stroma appeared to be as in the control eyes.

In corneal epithelial cells, the chemical burn seems to not sensibly affect the expression of TRAIL. The chemical burn slightly upregulated the TRAIL receptor in corneal epithelial cells between 3 and 7 days following the healing of the tissues.

In conjunctival cells alkali burn slightly raised up TRAIL from day 1 to 14. Instead, the expression of TRAIL receptor does not present a significant difference between treated and control eye.

### **Conclusions**

TRAIL may be a novel regulator and therapy target to treat chemically damaged cornea.

**2914**

### **Adaptive optics in the eye as window to brain function**

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### **Summary**

Growing evidence suggests that disruptions in microvascular function are responsible for neurological conditions including Multiple Sclerosis, Alzheimer's and Parkinson's. The retinal and cerebral circulations are morphologically and physiologically similar. Therefore the retina can be used as a surrogate for the brain. Several previous techniques have investigated retinal blood flow. However they have only detected signals in large vessels, or relied on arbitrary units as surrogates for flow. Most importantly, these techniques have not characterised individual erythrocytes movements, the basis for O<sub>2</sub> dispersion. Adaptive optics aided imaging facilitates accurate measurement of large vessel flow dynamics and quantification of erythrocyte movement at rest and during retinal stimulation. This talk will focus on AO imaging techniques developed to study the inner retinal circulation as a surrogate for systemic disease. Data on pre-clinical, vascular changes associated with diabetes, cardiovascular disease and multiple sclerosis will be presented as well as evidence that the retina may act not only as a "window to the brain" but also as a surrogate tissue for investigation of systemic vascular condition.

**1241**

### **Introduction to molecular genetics**

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## Summary

The presentation will provide basic information on the human genome, DNA and genes structure, principles of building proteins, modes of inheritance as well as basic mechanisms of genetic diseases in order to understand some of the terms and topics discussed in the rest of the course.

## S114

### Molecular genetic analysis in three cases with syndromic cataracts

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## Purpose

To identify disease-causing mutations in three female probands with bilateral congenital or juvenile cataracts associated with a range of systemic findings.

## Methods

Based on careful phenotype evaluation promoter of the *FTL* (ferritin light chain) gene was directly sequenced in proband 1 with hyperferritinemia. Whole exome sequencing (WES) was performed in case 2 suffering from bilateral deafness, hepatomegaly and decreased kidney function. In case 3, with microhematuria, mild hypotony and congenital cataract, MLPA (Multiplex Ligation-dependent Probe Amplification) analysis of *COL4A5* and *COL4A6* genes followed by whole genome sequencing was performed. Only variants with minor allele frequency of 0.005 as per gnomAD were further assessed for pathogenicity. The Decipher database was used for evaluation of copy number variations. Segregation analysis of the identified mutations was performed using direct sequencing.

## Results

*De novo*, previously reported, heterozygous mutation c.-167C>T in 5' untranslated region of *FTL* was found in proband 1 aged 8 years, confirming the clinical diagnosis of "hyperferritinemia cataract syndrome". *De novo* novel heterozygous variant c.512T>G; p.(Leu171Trp) in *MYH9* (myosin-9) was detected by WES in proband 2 aged 16 years, supporting the clinical diagnosis of *MYH9*-related disorder. In proband 3, aged one year, a unique ~233,336 bp heterozygous deletion, encompassing *COL4A5* exons 1-37 and first two exons of *COL4A6* was identified, corroborating the diagnosis of X-linked Alport syndrome.

## Conclusions

Molecular genetic investigation has been proven to be a valuable tool corroborating clinical diagnosis in syndromic patients with congenital or juvenile cataracts and no family history of disease. Supported by AZV 17-30500A.

## 2312

### Laser photocoagulation of macroaneurysms; clinical cases in DME

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### Summary

Prevalence of capillary macro-aneurysms (CMA) is estimated to be around 30% of cases in patients with diabetic macular edema (DME). CMA may be occult, or barely visible on fundus, because they are frequently associated with haemorrhages, exsudates or because of their transparency. CMA can take several appearances : round light red lesion, surrounded by a white ring (corresponding to a thickened wall), or isolated dark red lesions. They can be isolated, or multiple, and are predominant in the macular area.

ICG-angiography allows the detection of the CMA, and precise their location compared to larger retinal vessels. Media opacities (such as cataract), or eye movements, or non visualization of CMA on fundus, might prevent from efficient photocoagulation.

Baseline laser parameters to start with are: spot size 60µm, spot duration : 30 ms, power : 100mW. Several shots can be performed. If the targeted CMA is missed, a white burn is visible on the retinal pigmentary epithelium. The CMA to close to the fovea (ie, located < 500µm from the center) should not be treated.

We will present several clinical cases to illustrate the photocoagulation technique of CMA associated with DME

### 2743

#### Biopsy of orbital inflammation

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### Summary

Orbital inflammation comprise a whole series of different conditions: Myositic Idiopathic Orbital Inflammation (IOI), Nonmyositic IOI, Specific autoimmune orbital inflammatory manifestations like Graves' orbitopathy, Sarcoidosis, Granulomatosis with Angiitis.... and IgG4 related diseases (IgG4-RD). Some of them present with specific manifestations so that they can be diagnosed without biopsy (Graves'disease). A Delphi approach of experts of orbital disease showed that myositic IOI can be diagnosed without biopsy to the following rank of clinical and radiologic imaging indicators: painful eye movement and orbital pain, enlarged muscle tendon, acute or subacute unilateral onset and limited eye movement. The basis of nonmyositic IOI is a biopsy and serum diagnostic. Symptoms which lead to the decision of biopsy are: orbital pain, acute or subacute unilateral onset, intact orbital bone and no history of orbital-related systemic disease. Differential diagnosis between nonmyositic IOI and IgG4-RD is made by the combined presence of IgG4 positive cells in tissue and plasma in IgG4-RD. Experts on orbital disease agreed that nonmyositic IOI is more likely if less than 30 IgG4-positive plasma cells can be count per high-power field.

### T022

#### OCT-angiography: Deep irregular vascular network predictor of neovascular complication in angioid streaks

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### Purpose

To evaluate the risk of neovascular complication in presence of deep irregular vascular network in eyes with angioid streaks.

### Methods

This prospective study recruited 3 eyes with angioid streaks (AS) involving the macula. These eyes showed a deep irregular vascular network (IVN), without choroidal neovascularization (CNV).

All patients underwent fundus examination, fluorescein angiography (FA), Swept Source structural B-Scan OCT, en face OCT and OCT angiography (OCTA). They were followed up during 18 months to detect possible neovascular complication.

### Results

The IVN was detected on OCTA as a peripapillary hypersignal lesion, visible in the outer retina (OR) slab. One of the patients complained at the 18 months control about functional worsening as visual decline and metamorphopsia. Fundus examination showed subretinal hemorrhage. Repeated OCTA could detect a « medusa head » shaped CNV, emerging from the IVN. The CNV was seen as a hypersignal rich anastomotic vascular network in the OR slab, with a perilesional dark halo.

The patient received three intravitreal injections of Bevacizumab. Control OCTA could show a decreased CNV area with a lower density and a vascular rarefaction.

### Conclusions

Our results demonstrate the usefulness of OCTA in detecting IVN in asymptomatic eyes with AS, during a routine examination.

This IVN could be predictor of neovascular complication, needing a close surveillance and more frequent follow up.

To our knowledge this is the first prospective report of CNV complicating IVN in AS.

The limitation of this study is the small number of eyes included and a larger series of patients is required for the validity of the conclusion.

## F118

### Phenotype in homozygous and heterozygous carriers of BEST1 mutations in autosomal recessive Bestrophinopathy

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### Purpose

Autosomal recessive Bestrophinopathy (ARB) is part of the diverse spectrum of retinal diseases caused by mutations in the *BEST1* gene. We report the phenotype and genotype results in a family including a patient with ARB and we present phenotype characteristics of heterozygous carriers.

### Methods

We performed a clinical and molecular genetic study of a consanguineous Tunisian family with one patient affected with ARB. DNA sample from the index patient was subjected to whole exome sequencing (WES). Variants localized in homozygous regions were validated by Sanger sequencing. Familial segregation was performed.

### Results

The index patient was 50 years old and reported visual loss from the second decade of life. Visual acuity was limited to 3/10 RE and 2/10 LE. Fundus examination revealed macular central vitelliform lesions with yellow flecks and dots surrounding the arcades, extending to the midperiphery. Electroretinogram showed a moderate reduced response in both scotopic and photopic conditions. Electrooculogram revealed reduction in the EOG light rise.

We found in this patient a novel homozygous mutation p.[L31M],[L31M] in *BEST1*. A brother of the proband showed some yellow autofluorescent deposits in the posterior pole with severe reduction in the EOG light rise. Two other brothers had normal fundus appearance with also reduction in the EOG light rise. All brothers were heterozygous carriers of the *BEST 1* mutation.

### Conclusions

We identified a novel mutation in a Tunisian family with ARB. This mutation expands the mutation spectrum of *BEST 1* and helps to further study molecular pathogenesis of ARB. Contrary to what is known, we had affected patients carrying mutations heterozygously with a reduced EOG light rise in all of them.

### F119

#### Clinical and Genetic Characteristics of Leber Congenital Amaurosis in the Tunisian Population: experience of the oculogenetic laboratory LR14SP01

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### Purpose

Leber Congenital Amaurosis (LCA) is a rare retinal dystrophy causing severe visual impairment before the age of 1 year.

Our aim was to study the genotype-phenotype characteristics of LCA in the Tunisian population based on the experience of our oculogenetic laboratory LR14SP01.

### Methods

Descriptive retrospective clinical and genetic study including patients with inherited retinal dystrophies who consulted the oculogenetics laboratory LR14SP01, at Hedi Rais Institute of ophthalmology.

### Results

370 patients from 294 families were studied. LCA was found in 36 patients (9,7%). Genetic analysis was contributive in 15 of them and revealed mutations in *RPE65*, *RDH12*, *CRB1*, *RPGRIP1*, *CEP290*, *PROM1* and *CUCY2D*. Mutations in *RPE65* gene were the most frequent (6 patients). Many phenotype-genotype correlations were established. Patients with *RPE65* mutations showed white deposits in the mid periphery, mild optic atrophy, narrowing of the vessels with no clumped pigmentations. *RDH12* patients had diffuse pigment deposits and retinal disorganization, better visualized on optic coherence tomography. *CRB1* patients had preserved para-arteriolar retina and *CEP290* patients had large area of atrophy in peripheral retina. *GUGY2D* patient had normal fundus appearance.

### Conclusions

These results confirm the involvement of a large number of genes in ACL in the Tunisian population with predominance of *RPE65* mutations. Phenotype-genotype correlations are very contributive in ACL. They are helpful for genetic diagnosis of each entity and for selecting candidates for gene therapy.

### T055

#### Combining sub threshold laser therapy and anti-VEGF injections in diabetic macular edema

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### **Purpose**

To evaluate the therapeutic impact of combining intravitreal injections of Bevacizumab (IVB) with the micropulse laser (MP) in diabetic macular edema (DME) during a follow-up of 12 months and to study the predictive factors of visual prognosis.

### **Methods**

This prospective study included 49 naive eyes with clinically significant DME treated with 3 monthly consecutive IVB associated with a macular grid session performed with MP laser (duty cycle: 5%; No spacing application of spots, mean power 400 mW, using a 2x2 grid on the edematous area). Visual acuity (VA) and central macular thickness (CMT) were evaluated. According to their therapeutic responses, patients were classified as "good " or "poor" responders at 4 , 8 and 12 months. The "poor responders" were retreated while the "good responders" were monitored.

### **Results**

BCVA improvement was not significant at both 4 and 8 months ( $p = 0.90$ ,  $p = 0.08$ ). At 12 months, the improvement was statistically significant ( $p = 0.01$ ). The average letter gain in VA was 9.57 letters at 12 months. 69.4% of "good responders" were identified at 4 months, 94% at 8 and 12 months. The mean decrease CMT was significant at 4, 8, and 12 months ( $p < 0.01$ ). The mean number of IVB at 12 months was  $4.1 \pm 1.58$ . We found a statistically significant correlation ( $r = 0.610$ ,  $p < 0.01$ ) between initial and final VA. A statistically significant correlation ( $r = 0.536$ ,  $p = 0.01$ ) was noted between initial CMT and final VA. The grade of the ellipsoid zone and outer limiting membrane was correlated with final VA ( $r = 0.883$ ,  $p = 0.01$  and  $r = 0.730$ ,  $p = 0.01$ ). No systemic or local effects were noted in all patients, in particular no visible retinal scar.

### **Conclusions**

Combining IVB and MP laser in the treatment of naive DME resulted in statistically significant functional and anatomic improvement at 12 months.

## **F120**

### **Novel C8ORF37 mutation causing cone rod dystrophy**

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### **Purpose**

To identify the disease-causing mutation in a one family with cone rod dystrophy (CRD).

### **Methods**

We performed a clinical and molecular genetic study of three individuals affected with CRD. DNA sample from the index patient was undergone to whole exome sequencing (WES).

### **Results**

The index patient was 30 years old and reported night blindness at the age of ten. Visual acuity was limited to 1/10 in right and left eyes. Fundus examination revealed beaten-bronze aspect of the macula, peripheral retinal pigment epithelium atrophy, mild optic atrophy and narrowing of the vessels. Electroretinogram showed altered scotopic and photopic responses. The sister, aged 32, had the same fundus presentation. An affected cousin had on fundus examination gliosis of the posterior pole with diffuse retinal atrophy. Molecular analysis shown that the



index patient carry novel homozygous splice-site mutation (NM\_177965: c.470+1G>T) in C8ORF37. The missense variant located in the donor splice side of intron 6 was not reported in the ExAC and genomAD.

### Conclusions

We describe a novel mutation in *C8orf37*, coding to a ciliary cytoplasmic protein. Our patients showed phenotype variability depending on age; at the third decade patients had beaten-bronze aspect of the macula, peripheral RPE atrophy, mild optic atrophy and narrowing of the vessels. At the fifth decade, we found gliosis of the posterior pole better visualized on OCT with diffuse retinal atrophy.

### F121

#### NMNAT1 mutation causing retinitis pigmentosa

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### Purpose

The aim of this study was to describe an unexpected gene causing retinitis pigmentosa (RP) in a Tunisian family.

### Methods

Two members of a consanguineous family were clinically examined. DNA sample from the index patient was subjected to whole exome sequencing (WES).

### Results

The index patient was 21 years old and reported hemeralopia since 5 years old. Visual acuity was limited to 6/10 right eye and 7/10 left eye. Fundus examination revealed few bone spicule shaped pigment deposits and white dot deposits in the mid periphery with narrowing of the vessels and waxy optic discs. Electroretinogram showed altered scotopic responses with slightly altered photopic responses. We identified a homozygous missense mutation p.[A13T],[A13T] in *NMNAT1*.

### Conclusions

Unexpectedly, in our RP patients, the mutation identified has previously been reported as causing Leber congenital amaurosis but not in patients with RP. Our patients showed preserved visual acuity and RP phenotype with few bone spicule shaped pigment deposits and white dot deposits in the mid periphery.

### T111

#### Fine-Tuning of therapy in stromal choroiditis using indocyanine green angiography (ICGA)

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### Purpose

Investigate indocyanine green angiography (ICGA) in the follow-up of inflammatory activity in stromal choroiditis [Vogt-Koyanagi-Harada disease (VKH) and birdshot retinochoroiditis (BRC)] under treatment and monitor subclinical recurrences requiring therapeutic adjustments.

## Methods

Retrospective data analysis of patients with initial onset disease and/or treatment naive stromal choroiditis (VKH & BRC) quiet under therapy with sufficient follow-up (minimum of 4 years) with both dual Fluorescein (FA) / ICGA angiography and choroidal thickness measurements with EDI-OCT. ICGA scores were correlated with therapy, FA scores and to EDI-OCT choroidal thickness. The number of events leading to therapeutic readjustment as well as subsequent therapy response, were identified.

## Results

Four stromal initial onset or treatment naive choroiditis patients (2 VKH and 2 BRC), were eligible for the study. Pre and post early phase treatment scores were respectively  $7.25 \pm 4.4$  v.  $2.12 \pm 2.5$  for FA, and  $22.87 \pm 7.7$  v.  $3 \pm 2.6$  for ICGA and  $474 \pm 186$  v.  $302.9 \pm 170$   $\mu$ m for EDI-OCT. In the tapering period, 2 patients (both VKH) showed no ICGA recurrences (follow-up  $6 \pm 2.8$  years). For the 2 BRC patients, (follow-up  $6.5 \pm 2$  y.), a total of 7 events (subclinical ICGA recurrences not shown by FA or EDI-OCT and therapy responses to readjusted therapy) were seen after therapy changes due to side-effects or during tapering attempts.

## Conclusions

ICGA was the most sensitive monitoring modality of stromal choroiditis, able to identify subclinical recurrences following changes of therapy and treatment responses after readjusted therapy, events otherwise missed by FA or EDI-OCT. ICGA proved efficient for timely adjustment of therapy in stromal choroiditis.

## T092

### Contribution of multimodal imaging in traumatic maculopathy

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## Purpose

Closed globe injuries can cause severe macular damages. Accurate diagnosis is important to inform the patient about prognosis, follow-up the lesions, and promptly treat.

## Methods

We report 5 cases of different traumatic maculopathies.

## Results

Case 1 : A young man was referred for visual loss (20/50) on his right eye after a public road accident. Fundus examination and Optical Coherence Tomography (OCT) displayed a macular choroidal rupture. Nine months later, OCT-A showed a wound healing process including physiological angiogenesis, complicated few months later by an exudative lesion. Case 2 : a man presented with a visual acuity (VA) limited to hand motion and a central scotoma after a trauma (tensioner). OCT confirmed a full-thickness macular hole. Spontaneous resolution was observed after few months, but VA remained low because of irreversible damage of the photoreceptors and retinal pigment epithelium (RPE). Case 3 : a young man reported visual loss (20/32) and paracentral scotoma after a blunt trauma (capsule) to his right eye. OCT showed a foveal cyst with subretinal fluid (threat of macular hole). This aspect disappeared spontaneously but RPE changes persisted. Case 4 : a man was referred for an expertise, he presented 3 years ago a facial trauma and complained of blurred vision. OCT displayed a sectorial retinal atrophy. OCT-A showed an hypoperfusion in superficial and deep vascular networks in the territory of the cilioretinal artery matching with the defect of the visual field. Case 5 : a 12-year-old boy presented an accidental exposure to laser toy. OCT showed severe alterations of the RPE, leading to a final VA of 20/32 in his right eye.

## Conclusions

Multimodal imaging is useful in traumatic maculopathy for earlier and more accurate diagnosis, better understanding of the physiopathology, helpful for the treatment and the follow-up.

#### **S058**

##### **Dynamics of local antioxidant status in patients with keratoconus after various protocols of ultraviolet crosslinking of the cornea.**

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##### **Purpose**

To determine the dynamics of oxidative activity in the tear in patients with keratoconus after corneal crosslinking

##### **Methods**

38 patients with KC was in order to study the dynamics of the levels of total antioxidant status (TAS) and superoxide dismutase (SOD) in tear. Men - 24 (63.1%), women - 14 (36.9%). The standard UV crosslinking (S-CXL) group was 20 cases and the pulse accelerated crosslinking (A-P-CXL) – 18 cases. Age - 32.4±6.8 years. Control group - 12 fit persons. The observation period 30th days/

##### **Results**

Decrease in the SOD level was determined up to 96.7±11.3, compared to the control - 119.1±16.5 ng/ml. After S-CXL, significant decrease in the SOD occurred: on day 1 - 56.5±12.2, 3rd - 29.1±8.5, 7th - 49.2±9.6, the 14th - 58.7±16.7 and the 30th - 80.2±14.1 ng/ml. After the A-P-CXL, the SOD decreased: on the 1st day - 82.3±18.7, the 3rd - 60.5±11.2, the 7th - 71.4±10.1, the 14th - 93.5±13.2 and the 30th - 106.3±20.4 ng/ml. Decrease was noted only on the 3rd day after the procedure. Decrease in baseline TAS was found from 2.82±0.15 to 1.68±0.21 mmol/L, compared to fit people. The standard CXL procedure induced a sharp decrease of TAS: 1st day - 1.12±0.15, 3rd - 0.81±0.12, 7th - 0.98±0.11, 14th - 1.19±0.15 and the 30th - 1.31±0.19 mmol/l. The accelerated pulse CXL showed a decrease of this index : 1st day - 1.39±0.20, 3rd - 1.03±0.14, 7th - 1.15±0.15, The 14th - 1.47±0.21 and the 30th - 1.80±0.24 mmol/l. On the 30th day the TAS index recovered and was higher than the initial preop level

##### **Conclusions**

The reduction of the local antioxidative status in patients with keratoconus. A sharp decline in the SOD and TAS is observed on the 3rd day, and from the 14th day its gradually recovered and more alternative effect of the standard protocol, expressed in a significant negative dynamics of oxidative indices in the tear in patients with keratoconus

#### **S059**

##### **Riboflavin levels in the aqueous humour of the rabbit's eye with standard UV corneal cross-linking in different Epi-Off areas**

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##### **Purpose**

To investigate the concentration of riboflavin in the aqueous humour of the rabbit's eye for standard saturation of the cornea with solutions for UV cross-linking, depending on the area of its deepithelialization

##### **Methods**

The experiments were carried out on 42 rabbits. Epi-Off with a diameter of 3, 6 and 9 mm was used in all experimental groups. Instillations of riboflavin solutions: 1st group (R) – (28 eyes) 0.1% Riboflavin. 2nd group (RD) – (28 eyes) 0.1% Riboflavin + 20% Dextran. 3rd group (RH) – (28 eyes) 0.1% Riboflavin + 1.0% Hydroxypropylmethylcellulose (HPMC)

### Results

All solutions showed a continuous increase of the riboflavin level of in the AH during 60 minutes. The highest concentration of riboflavin was detected after 30 min using: 0.1% Riboflavin + 1.0% HPMC > 0.1% Riboflavin > 0.1% Riboflavin + 20% Dextran. The larger of Epi-Off area, the higher the concentration of riboflavin: 9 mm > 6 mm > 3 mm. The level of riboflavin in 30 minutes, depending on the Epi-Off area: RH-9 > R-9 > R-6 > RH-6 > RH-3 > R-3 > RD-9 > RD-6 > RD-3. Maximum Riboflavin level is detected: in the 0.1% Riboflavin group for 30-50 min 0.1% Riboflavin + 1.0% HPMC for 50-60 min 0.1% Riboflavin + 20% Dextran for 60 min RH > R > RD or When using a solution of 0.1% Riboflavin, a decrease in the Riboflavin level after 40 min of the experiment was noted. When solution with polymers was used, the effect was prolonged up to 60 minutes of observation: 0.1% Riboflavin + 1.0% HPMC > 0.1% Riboflavin + 20% Dextran.

### Conclusions

A solution of 0.1% Riboflavin + 1.0% Hydroxypropylmethylcellulose the highest efficacy of corneal saturation with riboflavin showed. The optimal time for saturating of the cornea before the start of UV irradiation is 30 minutes. The optimum deepithelization area is 9 mm, because the Epi-Off area forms a zone saturated with riboflavin

## 2134

### Measurement of corneal biomechanics using the high-speed Scheimpflug system CORVIS

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### Summary

The measurement of corneal biomechanical properties gains of importance especially in the detection and management of ectatic corneal diseases. New therapeutic options such as corneal collagen crosslinking or implantation of corneal rings or ring segments can be used to stabilize the corneal architecture in pathologies such as keratoconus, keratoglobus or pellucid marginal degeneration. In these cases, measuring the corneal biomechanical properties is used for monitoring the therapeutic success. In this talk, we show the measurement principle of the high-speed Scheimpflug imager CORVIS and give an overview on the relevant clinical parameters for diagnosing and monitoring ectatic diseases.

## 2933

### Device-based earliest instrument guided diagnosis of keratoconus

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### Summary

Early diagnosis of keratoconus is often supported by computerized diagnostic instrumentation. Apart from the analysis of the corneal anterior surface, new tomography-based diagnostic methods have been evolving. In

addition to these morphologically based methods, the assessment of corneal biomechanical properties gained interest in the community. Starting with the Ocular Response Analyzer and the concept of corneal resistance and hysteresis, new devices such as the Corvis allow a detailed analysis of corneal stiffness. In this talk, we will introduce the available methods and devices for early diagnosis of keratoconus and provide a guideline for the interpretation of the data derived from these devices. In the end we will discuss how to use tomographic alongside with biomechanical data in the diagnosis and followup of keratoconus.

**3542**

#### **Calculation of customized IOLs – from corneal tomography and biometry to the lens shape**

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#### **Summary**

In this talk, we address the calculation process of the lens surfaces of an individual intraocular lens. Based on the wavefront aberrations of the cornea derived from corneal topo- or tomography, we will present a strategy to derive a proper free-form lens surface which corrects for the corneal aberrations in order to get out an aberration-free system of the eye. A theoretical optical model based on clinical data is being used for simulating the imaging performance with different intraocular lens surface profiles. Several clinical examples emphasize the potential of an individual intraocular lens especially in cases such as keratoconus or eyes after refractive surgery.

**T011**

#### **Selected pharmacology of PlGF neutralization over anti-VEGF on retinal gliosis and RGC survival assessed in a diabetic mouse model**

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#### **Purpose**

In this study, the effect of placental growth factor (PlGF) inhibition on retinal inflammation, reactive gliosis and neurodegeneration was investigated by immunohistochemistry in the diabetic streptozotocin (STZ) induced mouse model.

#### **Methods**

Repeated intravitreal injections of an anti-PlGF antibody (5D11D4; 5.4 µg/eye), aflibercept (40 µg/eye) or vehicle were started 7 weeks after diabetes onset in the STZ mouse model (n = 7-30 /group). At 8 weeks after diabetes onset, the retinal inflammation and reactive gliosis was measured on serial 7µm paraffin sections by the quantification of F4/80 positive cells and the vimentin positive area, respectively. The effect on retinal ganglion cell (RGC) density was investigated by Brn3a immunostaining.

#### **Results**

Repeated administration of 5D11D4 and aflibercept both significantly reduced the percentage of inflammatory cells with 51% ± 8% and 59% ± 4%, respectively (P<0.001 vs. vehicle). Retinal reactive gliosis was significantly reduced with 5D11D4 treatment with 51% ± 7% (P = 0.003) in contrast to aflibercept treatment in STZ diabetic mice (33% ± 16%, P = 0.14 vs. vehicle). Anti-PlGF treatment did not alter RGC density, whereas aflibercept injection significantly reduced RGC density with 25% ± 6% (P=0.01 vs. vehicle).

#### **Conclusions**

Repeated administration of 5D11D4 or aflibercept significantly reduced retinal inflammation in a diabetic STZ mouse model. In contrast to aflibercept treatment, neutralization of PIGF has a positive impact on retinal reactive gliosis and does not affect RGC density.

## **F099**

### **New analysis of the Farnsworth D-15 test**

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#### **Purpose**

The Farnsworth dichotomous D15 test has been adopted and continues to be used widely to determine whether an individual meets the colour specification requirements for employment in a given occupation in spite of known difficulties in linking the results of the test to the severity of colour vision loss. The aim of this study was to investigate the variability of the D15 test and the apparent lack of agreement with other tests. The study also investigated the extent to which normal trichromats and subjects with congenital colour deficiency (CCD) can make use of red/green (RG), yellow/blue (YB) and luminance signals to complete the D15 task.

#### **Methods**

RG and YB thresholds were measured with the Colour Assessment & Diagnosis (CAD) test in 590 subjects (325 deuterans, 170 protans and 95 normals). Each subject completed several other tests, including the D15. The spectral radiance of each cap when illuminated with D65 was also measured. These data were then used to model the expected changes in RG, YB and luminance signals in normal trichromats and in subjects with CCD.

#### **Results**

When no crossings or transpositions are allowed on the D15 test, 94% of normal trichromats and 47% of subjects with CCD pass. 26% of the CCDs that pass have RG thresholds above 10 CAD units (one CAD unit describes the RG colour signal strength for young normal trichromats). The modelling work shows that CCD subjects, in particular, can make use of changes in both luminance and YB signals to complete successfully the D15 task.

#### **Conclusions**

47% of colour deficient subjects make no errors on the D15 test. Some of these subjects have severe loss of RG chromatic sensitivity. The large variability in D15 results may be accounted for, at least in part, by the large differences in both luminance and RG and YB colour signals predicted in subjects with CCD.

## **F088**

### **Activation of the phosphoinositide 3-kinase pathway promotes axon regeneration of the optic nerve in vivo**

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#### **Purpose**

We aimed to investigate activation of the phosphoinositide 3-kinase (PI3K) pathway and its effect on axon regeneration *in vivo*. Optic nerve crush (ONC) provides a robust injury model, involving crushing the easily accessible optic nerve. The PI3K pathway converts phosphatidylinositol (3,4)-bis-phosphate (PIP2) lipids to phosphatidylinositol (3,4,5)-tris-phosphate (PIP3). Phosphatase and tensin homolog (PTEN) acts as a pathway regulator, returning PIP3 to PIP2. PIP3 activates a number of pathways, including the mTOR pathway, which others have shown to promote regeneration in retinal ganglion cells (RGCs) and cortical neurons.

## Methods

Two viral vectors were developed: AAV2.PI3K and AAV2.shPTEN.GFP, along with transgenic mouse lines expressing different PI3K isoforms under Cre recombination. Adult wildtype mice were intravitreally injected with either AAV2.PI3K, AAV2.GFP, AAV2.shPTEN.GFP or AAV2.shScram.GFP and transgenic mice with AAV2.Cre.GFP or AAV2.GFP. Retinas were collected 2 weeks post injection. Successful viral transduction was assessed by GFP expression and mTOR pathway upregulation was quantified from immunohistochemistry for pAkt and pS6. To assess regeneration, adult mice received intravitreal injections of the appropriate viral vectors 2 weeks prior to ONC. The retinas and optic nerves were then collected 4 weeks post-crush and assessed for RGC survival and axon regeneration, using cholera toxin-B to visualise axons.

## Results

All viral vectors showed efficient viral transduction across the retina, assessed by spread of GFP expression. In addition, significant upregulation of pAkt and pS6 was found in all treatment groups compared to controls, measured by percentage colocalisation with GFP-labelled RGCs. Finally, a pro-regenerative effect was observed.

## Conclusions

The PI3K pathway may prove to be a useful target in a clinical setting.

## T095

### Morpho-functional relationship and follow up of retinal dystrophy in subjects with Joubert syndrome using OCT and electrophysiology

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## Purpose

To evaluate the structural and functional changes in clinical course of retinal dystrophy in Joubert syndrome.

## Methods

Four patients with Joubert syndrome's retinal dystrophy were periodically submitted to optical coherence tomography study (OCT), electroretinography and visual evoked potentials from 2011 to 2018.

## Results

The full-field ERGs showed marked latency delay and amplitude decrease; pVEPs were altered in all frequencies, mainly in the 30' and 15'; minimal or no variations were observed during the follow up. OCT scan showed, in all cases, alteration of retinal pigmented epithelium, thinning of neuroretina and atrophy of photoreceptors layers which were preserved only in the foveal region; these features remained the same at the end of follow up. We also observed a macular staphyloma in three patients, one developed bilateral macular schisis; the patient without staphyloma developed a monolateral cystoid macular edema.

## Conclusions

Macular staphyloma and cystoid macular edema are unusual findings in Joubert syndrome, follow up with OCT is really helpful because it shows the morphological changes in these subjects. The functional parameters don't change significantly during the follow up and are probably related to the extrafoveal abnormalities of neuroretina.

#### **F116**

##### **Clinical and Genetic Characteristics of enhanced S-cone syndrome in a Tunisian cohort: experience of the oculogenetic laboratory LR14SP01**

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#### **Purpose**

To report the clinical, multimodal imaging and genetic characteristics of patients with Enhance-S-cone syndrome (ESCS) in a Tunisian cohort.

#### **Methods**

Descriptive clinical and genetic study including patients with inherited retinal dystrophies who consulted the oculogenetics laboratory LR14SP01, at Hédi Rais Institute of ophthalmology.

#### **Results**

A total of 9 patients from 6 consanguineous families were diagnosed with ESCS based on typical clinical and ERG abnormalities. All patients complained from hemeralopia since childhood. Visual acuity ranged from light perception to 4/10. Fundus examination revealed variable abnormalities with radial yellow dots in the posterior pole in two patients, nummular yellow dots in one patient, minimal pigmentary changes along the arcades in five patients, nummular pigment clumping in 3 patients and peripheral retinal atrophy in one patient. One patient had macular atrophy and 8 had macular cysts confirmed by SS-OCT. Genetic analysis was contributive in 7 patients and revealed *NR2E3* mutations in 5 patients and *NR2E3+RHO* digenism in two patients from the same family.

#### **Conclusions**

This is to our knowledge the first report on a Tunisian cohort with ESCS. The phenotype in ESCS is highly variable and multimodal imaging may help to the diagnosis in addition to electrophysiology results.

#### **F117**

##### **Novel CDHR1 mutation causing cone rod dystrophy**

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#### **Purpose**

To localize and identify the gene and mutations causing a cone rod dystrophy (CRD) in a consanguineous Tunisian family.

#### **Methods**

We performed a clinical and molecular genetic study of a family with two individuals affected with CRD. DNA sample from the index patient was subjected to whole exome sequencing (WES).



## Results

The index patient was 32 years old and reported night blindness and visual loss at the age of twelve. Visual acuity was limited to light perception in both eyes. Fundus examination revealed few bone spicule shaped deposits in the mid periphery along with atrophy of the periphery retina associated to macular atrophy. Electroretinogram showed reduced scotopic and photopic responses. We report a novel homozygous deletion c.[863-2\_863-1delAG];[863-2\_863-1delAG] in the crucial splice acceptor domain of intron 9 of *CDHR1*.

## Conclusions

Here we describe new frameshift mutation in *CDHR1*. Clinically, the two probands in our family showed CRD phenotype with few bone spicule shaped deposits in the mid periphery along with atrophy of the periphery retina, we noticed also an early macular atrophy.

## S019

### Phenotype-genotype correlation of p.R124S mutation in granular type 1 corneal dystrophy of Tunisian origin

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## Purpose

We report the clinical features and phenotype-genotype correlation in a large Tunisian family with granular corneal dystrophy type I.

## Methods

Twenty-seven members of the Tunisian family underwent a complete ophthalmologic examination. A histopathological examination was performed on corneal specimens of four patients with advanced stage of corneal dystrophy. DNA extraction and direct Sanger sequencing of the exons 4 and 12 of *TGFBI* gene was performed for forty-two members.

## Results

The diagnosis of granular corneal dystrophy type I was clinically and genetically confirmed. Sequencing of exon 4 of *TGFBI* gene revealed the p.Arg124Ser mutation in heterozygous and in homozygous status in patients with different clinical severity. Visual acuity was severely affected in the homozygous patients leading to a first penetrating keratoplasty at 20 years of age in 3 cases, and at 8 years in one case. Recurrence occurred rapidly, began in the seat the corneal stitches and remained superficial up to 40 years after the graft. In heterozygous cases, visual acuity ranged from 6/10 to 10/10. Corneal opacities were deeper and predominating in the stromal center.

## Conclusions

Our study describes for the first time phenotype-genotype correlation in a large Tunisian family with granular corneal dystrophy type I and illustrates clinical presentation of homozygous p.Arg124Ser mutation. These results help to understand pathophysiology of the disease and profile of relapse after keratoplasty.

## 1711

### Intraoperative OCT imaging of the Argus II retinal prosthesis and its clinical significance

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### Summary

**Purpose:** To evaluate imaging techniques of the Argus II retinal prosthesis regarding to its placement on the retinal surface intraoperatively and in postoperative period.

**Methods:** The quality of real-time and post-processed video and optical coherence tomography (OCT) data during and after Argus II implantation were analyzed using the intraoperative OCT (iOCT, Carl Zeiss Meditec RESCAN 700) in the training eye and during surgery.

**Results:** The quality of video imaging of the Argus II prosthesis allowed for tracing all the steps of implantation during surgery. iOCT imaging facilitated a clear view of the prosthesis during its implantation, placement and tacking. In addition the quality of iOCT images in the training eye and during real conditions was comparable. The silicon coating of Argus II appeared to be semitransparent to the OCT signal, with the possibility to assess the underlying retina. The electrodes of the prosthesis created a shadowing effect, which was not clinically significant.

**Conclusion:** The imaging quality of the Argus II prosthesis was depending on the clarity of the optic media, but the natural optic media showed no effect on the reflectivity of the OCT signal obtained from the prosthesis.

2664

**Is the modification of the 13q32.1 regulatory landscape the cause of congenital microcoria?**

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**Summary** Congenital microcoria (MCOR) is a rare autosomal-dominant disorder characterized by inability of the iris to dilate owing to absence of dilator pupillae muscle. Previously, we reported that the disease is due to submicroscopic 13q32.1 deletions encompassing or interrupting *TGDS* and *GPR180*, questioning the role of either or both genes with or without elements regulating the expression of neighboring genes in MCOR. To address these questions, we generated transgenic mouse lines harboring variable deletions of the synthetic region using CRISPR/Cas9 methodology. Preliminary clinical analysis suggest only minor iris dilation dysfunction. In contrast, molecular analysis unambiguously shows iris-specific modification of distant genes expression, suggesting that MCOR deletions modify the 13q32.1 regulatory landscape and the fate of some embryonic cells involved in iris formation.

F034

**Comparison between the 24-2 new grid program of the Compass fundus automated perimeter and the 24-2 program of the Humphrey field analyser**

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## Purpose

To compare the 24-2 New Grid program of the Compass fundus perimeter (CenterVue, Italy) which is equipped with an eye-tracker to the Humphrey Field Analyser 24-2 program. The 24-2 New grid tests 12 additional points in the perifoveolar region.

## Methods

This prospective study included 66 eyes of 66 patients (17 healthy, 14 OHT and 35 glaucoma patients). Visual acuity had to be greater or equal to 8/10, ametropia ranged between -5.00D to +5.00D and less than 2D astigmatism was accepted. The Compass New Grid 24-2 visual field uses a ZEST strategy. Compass examination and HFA SITA Standard 24-2 were performed the same day, after randomization, and with 30 minutes of rest between the two tests. The results were compared via a nonparametric Wilcoxon test. Agreement between the devices was evaluated with Bland Altman plots.

## Results

The mean age of the patients included was  $58.56 \pm 19.14$  years old. The examination times were not significantly different between the two devices :  $327.8 \pm 91.3$  s for the Compass versus  $322.8 \pm 68.7$  s for the Humphrey ( $p = 0.6463$ ). The MD was significantly lower for the Compass at  $-3.27 \pm 3.30$  dB compared to  $-2.47 \pm 3.18$  dB for the Humphrey ( $p < 0.0001$ ). The PSD was also significantly different between the two devices:  $3.95 \pm 3.14$  dB for the Compass  $3.30 \pm 3.16$  dB for the Humphrey ( $p = 0.001$ ). Agreement was good between the devices with the visual evaluation provided by the Bland Altman comparison plots.

## Conclusions

For the same test time as the Humphrey 24-2, the Compass can test 12 more points. Its overall indices are nevertheless different from those of the Humphrey and it therefore seems that these devices are not interchangeable. It would be relevant to study the interest of 24-2 New Grid on patients with paracentral scotoma.

1443

## Macular protection in AMD by Transposon mediated gene delivery

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## Summary

Neovascular age-related macular degeneration (nAMD) deteriorates vision up to blindness. The current treatment is the intravitreal injection of antiangiogenic molecules, which controls choroidal neovascularization in patients. However, effective treatment requires frequent, costly, and life-long injections, and can be associated with side effects, such as endophthalmitis, ocular hypertension, and retinal detachment. We developed a non-viral gene therapeutic approach using the relatively safe and low cost *Sleeping Beauty* transposon (SB100X) mediated system to modify the genome of autologous pigment epithelial cells and justify a protein re-balancing providing a long-lasting effect. An *ex vivo* gene therapy approach based on transgenic overexpression of pigment epithelium derived factor (PEDF) in the eye is assumed to rebalance the angiogenic-antiangiogenic environment of the retina, resulting in growth regression of choroidal blood vessels, the hallmark of nAMD. Here we show the efficacy of a transposon mediated PEDF gene delivery therapy in a rat model of choroidal neovascularisation. In patients, transfection and re-transplantation of the gene modified cells will be performed in one surgical session.

2631

## Nerves in the cornea: proper functioning and healing potential

G. FERRARI<sup>1</sup>

### **Summary**

Corneal nerves have been typically studied for their sensory functions. A significant literature, however, now supports their key role in wound healing. Anatomical and functional integrity of corneal nerves promotes epithelial wound healing, controls corneal neovascularization, and modulates the associated inflammatory response, which are fundamental processes involved in wound closure. Corneal nerves orchestrate such complex processes by modulating secretion of nerve derived peptides/proteins, including Substance P, Nerve Growth Factor, and others. Although the roles of corneal nerves in wound healing have been illuminated mainly locally (i.e. inside the cornea), recent evidence supports that they may act on a larger, systemic scale, by activating specific brain centers (i.e. trigeminal ganglion). A number of questions remains open as to what is the specific contribution of anatomically different fibers, and the specific functional response of these. The observation that corneal nerve density rapidly decreases in highly prevalent disorders, such as infections, dry eye, or surgical procedures, make their manipulation an attractive option for the management of the wound healing process in the cornea.

**1251**

### **Key methods to study mitochondrial function**

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### **Summary**

The mitochondria are the cells primary source of energy, producing ATP through several routes including oxidative phosphorylation (OxPhos), the Citric Acid Cycle (TCA), and  $\beta$ -oxidation. This course will review multiple cell-based methods for studying mitochondrial (Mt) function, content, and cellular distribution. Discussion will include the use of the Seahorse Extracellular Flux Analyzer to measure mitochondria-specific respiration and ATP production during OxPhos and  $\beta$ -oxidation. Also discussed will be fluorescent-based imaging modalities for monitoring Mt membrane potential (TMRM), mitophagy (mKeima), Mt turnover (mitotimer) and Mt reactive oxygen species (mitoSox). Review of luminescent-based assays for evaluating ATP, NADP/NADPH, and NAD/NADH will also be provided.

**1751**

### **Mitochondrial dysfunction in age-related macular degeneration**

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### **Summary**

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries. The dry form of AMD, also known as Atrophic AMD, is characterized by the death of retinal pigment epithelium (RPE) and overlying photoreceptors. While the disease mechanism is not yet known, strong experimental evidence from studies of human donors with AMD supports the hypothesis that defects in RPE mitochondria drives AMD pathology. Evidence supporting the hypothesis includes data showing: (i) disrupted RPE mitochondrial architecture, decreased mitochondrial number and mass, (ii) altered content of multiple mitochondrial proteins, (iii) increased mtDNA damage that correlates with disease severity, and (iv) defects in bioenergetics for primary RPE cultures from AMD donors. These data provide the rationale for targeting the mitochondria in the RPE as a strategy to prevent RPE cell death and vision loss associated with AMD.

3432

### Sebaceous carcinoma highlights

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<sup>1</sup>

T031

### Analysis of choroidal structure changes in diabetic patients without diabetic retinopathy: a longitudinal study

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#### Purpose

To identify changes in choroidal structure in diabetic patients without diabetic retinopathy (DR) after 1 year of follow-up.

#### Methods

Prospective observational cohort study in which 125 diabetic patients without DR were included. Patients received a complete ophthalmologic evaluation including optical coherence tomography scans (SD-OCT) using enhanced depth imaging mode in the first visit (V1) and in a second visit after 12 months (V2). Choroidal thickness (CT) was measured at 13 locations. A 1500µm subfoveal choroidal area (total choroidal area [TCA]) was segmented into luminal area (LA) and stromal area (SA) using an image binarization technique. To assess the vascular status of the choroid, choroidal vascularity index (CVI) was calculated as the proportion of LA to TCA. Generalized linear mixed-effects models were used.

#### Results

Of the 125 patients, 103 completed the study, 9 of which developed DR (8.7%). CT was significantly higher at V2 than at V1, at almost half the locations (500, 1000, and 1500µm temporal; 500 and 1000µm nasal; and 1000µm superior to the fovea) ( $p<0.001$ - $0.003$ ). While SA increased at V2 ( $p=0.01$ ), CVI was significantly lower at V2 than at V1 ( $p=0.03$ ). CVI was positively associated with visible retinopathy ( $p=0.04$ ), axial length and spherical equivalent ( $p<0.001$ ).

#### Conclusions

Diabetic patients without DR appear to have a thicker choroid at the expense of decreased vascularity and stromal thickening, after 12 months of follow-up. These structural changes may be due to ischemic changes in choroidal vasculature, with subsequent hyperpermeability and increased extracellular matrix deposition, and may represent the primary event in diabetes before the onset of DR.

2162

### SLOS, oxysterols and retinal homeostasis

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#### Summary

Smith-Lemli-Opitz syndrome (SLOS) is a recessive disorder of cholesterol biosynthesis involving multiple dysmorphologies and profound neurosensory and cognitive defects. Mutations in the DHCR7 (7-dehydrocholesterol (7DHC) reductase) gene are causative. Oxidation of 7DHC (the immediate precursor of cholesterol) has been implicated in the disease mechanism. 7DHC-derived oxysterols have been found in tissues and bodily fluids of SLOS patients (but not control subjects), as well as in animal models of SLOS (but not controls). A rat model of SLOS has been developed by treating normal rats with the DHCR7 inhibitor AY9944. This model exhibits progressive, irreversible retinal degeneration; retinas derived therefrom contain 7DHC-derived oxysterols and other oxidized molecules. Intense constant light dramatically exacerbates the retinal degeneration; pretreatment with antioxidants suppresses such oxidation and the pathology. Dietary cholesterol supplementation (the current standard of care for SLOS patients) partially ameliorates the severity of the retinal degeneration in the SLOS rat model, while combined cholesterol-antioxidant supplementation prevents it. These findings have translational implications for treating SLOS patients.

2932

### Changes of the subbasal nerve plexus in keratoconus

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#### Summary

Confocal *in vivo* microscopy (CIVM) allows visualizing slightest alterations within the corneal subbasal nerve plexus (SNP). Recent CIVM studies based on the analysis of 3 to 5 confocal *in vivo* images assumed that there might be a reduced SNP density in keratoconus.

The SNP of patients with keratoconus (n=10) and of healthy patients without keratoconus (n=10) was examined by 10 CIVM images of one eye per patient.

SNP density was calculated as the total length of nerve fibres per frame area and the tortuosity of the SNP was quantified by measuring the amplitude of the conical bulges and the area under the curve (AUC) formed by the SNP.

Image analysis with ImageJ® and statistical analysis of the SNP density in 200 images using a Mann-Whitney-U-Test revealed the SNP density to be significantly lower in keratoconus ( $17.4 \pm 2.1$  mm/mm<sup>2</sup>) than in healthy corneae ( $24.9 \pm 3.8$  mm/mm<sup>2</sup>, p<0.05; mean  $\pm$  SD). Values (median with 25th/75th percentile) of amplitudes and AUCs were significantly higher in keratoconus (amplitude 35/25/47  $\mu$ m and AUC 2709/1573/5202  $\mu$ m<sup>2</sup>) than in healthy corneae (amplitude 23/19/28  $\mu$ m and AUC 1510/1262/2085  $\mu$ m<sup>2</sup>, p<0.05).

These alterations in keratoconus might be correlated with the further course of the disease in future.

T059

### Evidences of new risk factors for retinal vein thrombosis

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### **Purpose**

Hypercoagulability and hypofibrinolysis have been implicated in RVO pathogenesis, with possible differences in central and branch RVO. RVO patients have higher Endogenous Thrombin Potential ETP (thus hypercoagulability) and/or higher Clot Lysis Time (thus lower plasma fibrinolytic potential).

### **Methods**

We performed a retrospective and a prospective study on RVO patients referred to our Ophthalmology Unit and Coagulation and Atherosclerotic Diseases Unit. In the retrospective study, we analyzed blood chemistry and thrombolytic factors in 276 consecutive patients. Consequently, we tested these factors in a prospective study involving 127 consecutive patients at RVO diagnosis.

### **Results**

Retrospective study: we found higher ETP in CRVO patients (O.R. 2.13, 95% C.I. 1.66-3.06,  $p < 0.01$ ) and lower fibrinolysis in RVO (O.R. 1.99, 95% C.I. 1.23-2.83,  $p < 0.01$ ). Patients older than 50 (no gender differences) showed positive isolated lupus anticoagulant (LAC), a hypercoagulant factor (O.R. 1.69, 95% C.I. 1.19-2.47,  $p < 0.05$ ) and a strong association with monoclonal gammopathy (O.R. 2.13, 95% C.I. 1.59-3.19,  $p < 0.01$ ), IgG or IgM, 94% of which were  $\lambda$  chains. Prospective study: 56% of our patients were positive for both LAC+ and monoclonal gammopathy at diagnosis (O.R. 4.45, 95% C.I. 3.37-5.98  $p < 0.001$ ). No association with LAC+ or monoclonal gammopathy alone was found.

### **Conclusions**

In our cohort of RVO patients, the association of isolated LAC+ and monoclonal gammopathy appears to be a specific risk pattern. The putative trigger for LAC+ in monoclonal gammopathy may be immunomodulatory dysregulation. Thus, we may consider screening all RVO patients for gamma-globulin disorders and LAC+. If the prospective study, which is still ongoing, confirms these data, we may consider starting specific antithrombotic therapy in patients with monoclonal gammopathy and LAC+.

**2633**

### **Inhibition of apoptosis for the treatment of corneal endothelial diseases**

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### **Summary**

This presentation deals with different strategies to enhance corneal endothelial cell survival. Viral and non-viral vector approaches as well as different therapeutic strategies will be presented.

**2731**

### **Cold plasma - a novel approach to treat therapy-resistant corneal infections**

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## Summary

Application of cold plasma will be presented for the treatment of therapy-refractive corneal ulcerations.

## T054

### Development and validation of a risk-prediction nomogram for good functional response one year after treatment with anti-VEGF in naive-Diabetic macular edema

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## Purpose

To develop and validate a risk-prediction nomogram for good functional response during the first year of treatment with anti-VEGF agents in naive-Diabetic macular edema (DME).

## Methods

This retrospective study included patients presenting naive-DME treated with anti-VEGF agents intra-vitreous injections and followed-up during one year between February 2010 and March 2015 (derivation cohort). We included variables that had significant associations with a good functional response to anti-VEGF agents during the first year of treatment, defined as recovering a best-corrected visual acuity (BCVA)  $\geq$  80 ETDRS letters during the follow-up. We used a program to generate a nomogram based on binary logistic regression predictive model. Then this nomogram was tested on data from a separate cohort of naive patients recruited in a multicenter prospective study (ETOILE study) conducted between January 2014 and June 2015 (validation cohort).

## Results

Data from 141 eyes (99 patients) of the derivation cohort were analyzed. In the final model, the variables age, baseline BCVA and ellipsoid zone (EZ) integrity on spectral-domain optical coherence tomography (SD-OCT) were associated with a good functional response during the first-year treatment and were used to build a nomogram. The resulting nomogram showed excellent discrimination for good functional responders (area under the curve [AUC] 0.906, 95% confidence interval [CI] 0.849-0.964,  $P=0.004$ ). The discriminative power of this nomogram was tested on data from 100 eyes (100 patients) of the validation cohort. The analysis with the nomogram found a good capability to discriminate for good functional responders ([AUC] 0.942, 95% [CI] 0.879-0.978,  $P<0.001$ ).

## Conclusions

This nomogram provides a rapid and simple functional estimation of a good functional response in naive-DME patients treated with anti-VEGF agents.

## S018

### Corneal endothelial follow-up after intracameral injection of lidocaine, tropicamide and phenylephrine for mydriasis during cataract surgery

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## Purpose

To follow the corneal endothelial cell density (ECD) in patients who received simultaneous intracameral (IC) injection of a mixture of tropicamide, phenylephrine, and lidocaine for mydriasis at the beginning of cataract surgery.

## Methods

A non-comparative, single centre, retrospective analysis was conducted in patients who underwent phacoemulsification by the same surgeon (KW), from 2007 to 2010. Pupil dilation was obtained by a single IC injection of a combination of tropicamide 0.5%, phenylephrine 10% diluted in lidocaine 1%. Only patients with preoperative (<6 month before surgery) and postoperative (>15 days and <3 years after surgery) specular microscopy assessments were included. Corneal endothelial images were acquired with a CSO specular microscope SP01. The specular microscopy was calibrated using a certified micrometre (Thorlabs) to obtain the exact ECD. On each image, 50 cells were counted manually with the software ImageJ by drawing cell boundaries. The accuracy of cell recognition was verified by a second observer. Patient demographics, cataract grading (LOCS III), total ultrasound energy, adverse events were recorded.

## Results

Forty-eight eyes (48 patients) were analysed. The mean±SD patients' age was 73±6 (from 59 to 87). The median follow-up after surgery was 96 days (range: 16-903). The mean preoperative ECD was 2592±381 cells/mm<sup>2</sup> and the postoperative ECD was 2333±445 cell/mm<sup>2</sup>, corresponding to a median cell loss of 8.2%. No relationship was found between endothelial cell loss and baseline ECD, cataract grading, or total delivered ultrasound energy. No intraoperative complication was reported.

## Conclusions

IC injection of a solution containing tropicamide, phenylephrine and lidocaine does not seem to affect endothelial cell loss following uneventful cataract surgery. Such IC injection can be used safely in real life setting.

## S076

### The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): study of new lyophilized amniotic membranes

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## Purpose

Our university lab BiiGC patented 2 versions of an ophthalmic bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentation, called OBSERV, supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to study new virus-inactivated, lyophilized, gamma-sterilized amniotic membranes (tLAM, TBF, Mions) stored at room temperature for ocular surface repair, in particular for persistent epithelial and stromal defects.

## Methods

By restoring intraocular pressure and medium renewal, the BR maintained the viability of cornea (human/animal) over a prolonged period of time. Its transparency allowed characterizing the tissue with existing or customized devices without compromising its sterility. Three ulcers (3mm, 250µm depth) were created in each human cornea (n=3). One was filled with 4 layers of a tLAM, one with 1 layer tLAM with its spongy layer (tLSAM), 1 left empty (control). Amniotic membranes were secured by an overlying X-stitch. Corneas were then stored in the BR for 4 weeks (31°C, 21mmHg, 5µL/hour) in CorneaMax. Monitoring was done daily until D4, then weekly by slit-lamp, corneal thickness measurement by OCT and transpachymetry (custom device). At W4: histology, immunolabeling and transmission electron microscopy.

## Results

The OBSERV platform allowed monitoring the stromal and epithelial repair during 1 month. The multi-layered tLAM and the tLSAM allowed epithelial wound healing faster than in controls. In addition, they allowed restoration of the stromal thickness, not observed in controls. tLAM and tLSAM did not trigger fibrosis or necrosis.

## Conclusions

The OBSERV platform is efficient to study the efficiency of new types of AM for corneal repair. It complements or replaces animal experimentation for academic and industrial research.

## T101

### Unilateral optic nerve axotomy at different distances from the optic disk cause the same course of retinal ganglion cells death

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## Purpose

In rats, the course of RGC loss is slower the farther from the optic disk the axotomy is inflicted. Optic nerve axotomy causes the death of retinal ganglion cells (RGCs) in two phases, the first one lasts up to 9 days in mice and 14 days rats, and kills approximately 85% of the RGCs. The main purpose of this work is to evaluate whether, in mice, a lesion in the optic nerve placed at different distances from the cell soma induces a faster or slower death of retinal ganglion cells (RGCs).

## Methods

The left optic nerve of C57BL6 adult mice was crushed at 0.5 mm or 2 mm from the optic disk and flat-mounted retinas were analyzed from 5 to 90 days after the lesion. RGCs were immunodetected with Brn3a and automatically quantified. The percentage of surviving RGCs and their spatial distribution was compared to intact retinas.

## Results

The temporal course of RGC degeneration was similar when the optic nerve was crushed at 0.5 or 2 mm from optic disk. In the first phase of RGC death, 50% and 10% of RGCs survived after 5 days and 9 days, respectively. In the second phase, from 14 to 90 days, only 5% of the RGCs survived after both lesions.

## Conclusions

In mice, the distance at which the axotomy is performed does not influence the course of RGCs loss, at least up to 2 mm from the optic disk.

2654

### Choosing the best marker to identify retinal ganglion cells

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#### Summary

Retinal ganglion cells (RGCs) and displaced amacrine cells (DACs) share their location in the innermost retina, and thus different markers and approaches were developed to differentiate them. Here we assess the specificity and coverage of classic and new mice RGC markers. As control, RGCs were traced from the superior colliculi to label 98% of the population. Nuclear markers (Brn3a and NeuN) and cytoplasmic/axonal markers ( $\beta$ III tubulin, BM88, ERR $\beta$ , NFL, PGP9.5, RBPMS and Y-Synuclein) were immunoidentified in intact flat-mounted traced and non-traced retinas dissected 5 days after optic nerve crush (ONC). Brn3a, RBPMS, and Y-Synuclein are expressed by the vast majority of traced-RGCs (>98%) while  $\beta$ III tubulin, BM88, ERR $\beta$ , NFL, or PGP9.5 were expressed by less than 50% of traced-RGCs. The nuclear staining of Brn3a and NeuN facilitates RGC quantification, although NeuN is also expressed by 15% of DACs. Cytoplasmic/axonal markers are useful to depict the anatomical features of RGCs in health or after an injury, but their axonal expression impairs quantitative analysis in the central retina where RGC axons converge. Finally, none of these markers change their expression pattern by 5 d after optic nerve crush.

S048

### Ocular surface temperature, blinking rate and corneal sensitivity in young contact lens wearers

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#### Purpose

To analyze ocular surface temperature (OST), corneal sensitivity, blink frequency (BF), and discomfort self-perception (DSF) in young contact lens (CL) and eyeglasses (EG) wearers.

#### Methods

Young CL and EG subjects (both sexes; 18-30 years old; 9 each group) with similar refractive errors participated voluntarily. OST was measured from infrared thermography images in central cornea, and nasal and temporal conjunctiva. BF was measured at rest and performing an attentional task. Selective mechanical and chemical 3s-duration pulses of increasing intensities were applied with the Belmonte-CRCERT gas esthesiometer; intensity and irritation components of the evoked sensation were scored with 0-10 VAS. An ad-hoc ocular DSF questionnaire was used to score the frequency and intensity of ocular surface discomfort and dryness sensations.

#### Results

OST was significantly lower during CL wearing, especially in the center of the cornea ( $p < 0.05$ ). OST remained slightly lower after CL removal. BF at rest was significantly higher in CL wearers ( $p < 0.01$ ), and decreased similarly in both groups during attentional tasks. Intensity VAS values to mechanical and chemical stimuli were similar in CL and EG, while the irritation component was scored higher by CL wearers. Mild cold stimulation evoked similar intensity and irritation VAS values. CL users reported higher discomfort and dryness score values in the DSF questionnaire.

#### Conclusions

The ability to determine the intensity of mechanical and chemical stimuli applied to the cornea is preserved in young contact lens users, although stimuli of the same intensity are experienced as more irritant by CL wearers. This may be due to sensitization of corneal polymodal nociceptors and/or to an increased background firing of corneal cold thermoreceptors induced by the lower ocular surface temperature found in young contact lens users.

**S049**

### **Corneal surface temperature decrease during the interblink interval is greater in Sjögren's syndrome**

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#### **Purpose**

To measure corneal surface temperature (CST) by IR video thermography, as an indirect estimation of the degree of activity of cold thermoreceptors to evaluate their contribution to the pathogenesis of dry eye disease (DED).

#### **Methods**

30 patients diagnosed with primary or secondary Sjögren's syndrome (SS) and 30 healthy controls participated voluntarily. Schirmer's test, BUT, meniscus height determined by OCT, corneal staining Oxford scale and McMonnies questionnaire were tested. Corneal surface temperature (CST) was also measured from IR thermography video images. Maximum temperature (TMax), minimum temperature (Tmin), mean temperature (Tm), temperature change ( $\Delta T$ ) and slopes of temperature fall during the interblink interval (IBI) were measured under controlled room environmental temperature and humidity ( $23.3 \pm 0.93^\circ\text{C}$  and  $42.5 \pm 7.1\%$ , respectively).

#### **Results**

SS patients presented clinical parameters indicative of DED ( $p < 0.001$ ) and showed significantly higher TMax ( $34.77 \pm 0.61^\circ\text{C}$  vs  $33.93 \pm 0.84^\circ\text{C}$ , SS vs controls,  $p < 0.001$ ) and Tm values ( $34.23 \pm 0.69^\circ\text{C}$  vs  $33.56 \pm 0.84^\circ\text{C}$ ,  $p = 0.001$ ) than healthy subjects. Tmin was slightly warmer ( $33.63 \pm 0.7^\circ\text{C}$  vs  $33.23 \pm 0.9^\circ\text{C}$ ,  $p = 0.078$ ) and  $\Delta T$  also significantly higher in SS ( $-1.41^\circ\text{C}$  vs  $-0.97^\circ\text{C}$ ,  $p = 0.011$ ). Initial CST decrease during the first 2s after eye opening was slightly faster in SS ( $-0.37 \pm 0.31^\circ\text{C/s}$  vs  $-0.26 \pm 0.2^\circ\text{C/s}$ ,  $p = 0.22$ ). Pearson analysis showed that TMax ( $R = -0.36$ ,  $p = 0.04$ ) and Tmin ( $R = -0.46$ ,  $p = 0.01$ ) decreased with age at a rate of  $-0.02^\circ\text{C/year}$ .

#### **Conclusions**

The warmer corneal surface temperature in SS patients suggests a certain degree of anterior segment inflammation. Together with increased osmolarity, the greater temperature reduction between blinks found in SS may increase corneal cold thermoreceptor nerve activity, inducing dryness and discomfort sensations in these patients.

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**1431**

### **Activity of corneal nerves in health and disease**

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#### **Summary**

During interblink periods, ocular surface temperature decreases rapidly due to tear evaporation, tear film osmolality rises, and thinning and eventual disruption of precorneal tear film apply mechanical stress to the cells

and nerve fibers at the most superficial corneal epithelial layers. All these physical and chemical disturbances are potential stimuli to activate the different types of sensory nerve fibers innervating the ocular surface (polymodal nociceptor, mechanonociceptor, and cold thermoreceptor nerves), being a possible source of discomfort sensation evoked by excessive evaporation and eye dryness.

Activity of corneal nerves is differently modified by inflammation and injury. During ocular inflammatory processes, activity of nociceptive nerves is enhanced and activity of cold nerve fibers is reduced. After corneal lesion and in ocular or systemic diseases accompanied by nerve injury, activity of the different types of corneal nerves is increased. During chronic eye dryness conditions, activity of cold thermoreceptor fibers resembles the injury-evoked neuropathic firing, which seems to underlie the unpleasant sensations experienced by patients with dry eye disease.

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## F010

### Effects of acute ocular hypertension on the adult rat retina: *in vivo* and *ex vivo* retinal analysis.

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#### Purpose

To investigate *in vivo* and *ex vivo* the effects of acute ocular hypertension (AOH) on the adult rat retina.

#### Methods

In adult female Sprague-Dawley rats, the anterior chamber of the left eye was cannulated with a hydrostatic system and the intraocular pressure (IOP) was elevated acutely to 75 mm HG for 90 minutes. Rats were analysed *in vivo* with Ocular Coherence Tomography (OCT) and full-field Electroretinograms prior to and at 1, 3, 7, 15, 25 or 30 days (n=6-8) after AOH. At different survival intervals, naïve and experimental rats were sacrificed, both eyes frozen and horizontal radial sections containing the optic nerve were obtained in the cryostat. Sections were immunolabelled with antibodies against photoreceptor, bipolar and retinal ganglion cells and counterstained with DAPI.

#### Results

Full field ERG showed a significant diminution in the amplitudes of the scotopic threshold response (pSTR, nSTR), and mixed response (a and b-waves) and as early as 24h after AOH (a diminution to 29%, 47%, 100% and 1%, respectively) (n=12). By 15 days there was little change in the amplitudes of the pSTR, nSTR, a and b-waves (28%, 36%, 100 and 12%, respectively) (n=12). When measured with OCT the retina showed a progressive thinning of the inner layers (NFL-OPL) to 75, 55 or 45% of the values found in the contralateral eyes at 3, 7 or 15 days, respectively (n=6). At 25 days, the number of recoverin-labelled bipolar cells had diminished to 49% of their control values (n=4) and retinal thickness (NFL-OPL) had diminished to 59% of their control values (n=4).

#### Conclusions

Acute ocular hypertension results in permanent functional (as measured with full-field ERG and OCT) and structural (as measured with morphometric techniques) alterations of the retina that affect the inner retinal layers.

## T102

### Different aetiologies cause distinct patterns of cone degeneration

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### **Purpose**

To examine the topology of cone degeneration after light-induced retinal degeneration, taurine depletion or both.

### **Methods**

Taurine depletion was achieved by treating albino rats (n=20) with  $\beta$ -alanine (3%) in the drinking water during two months. Half of the animals were light-exposed during 48 hours at 3000lux one month after the beginning of the treatment. All animals were processed one month after light exposure. This same protocol was applied to a control group of animals (n=20) drinking regular water. Retinas were dissected as wholemounts and the populations of S- and L/M-cones were immunotetected.

### **Results**

In control animals, the topology and mean numbers of S- and L/M-cones were similar to those found in previous studies. In control light-exposed animals, in animals treated with  $\beta$ -alanine and in animals treated with a combination of  $\beta$ -alanine and light-exposure there was a significant decrease of both S- and L/M- cones. This decrease was higher when combining both factors, and S-cones were always more affected. Control light-exposed animals also showed rings devoid of both types of mainly in the superotemporal retina. In animals treated with  $\beta$ -alanine, however, cone cell loss was diffuse. In  $\beta$ -alanine treated light exposed animals, there were also similar rings devoid of cones in the superotemporal retina, but they were more extensive and less distinct than in control light-exposed animals.

### **Conclusions**

The different pattern of cone degeneration observed after each insult suggests that cone loss follows localized and diffuse patterns that depend on the insult and also that taurine depletion increases the toxic effects of light.

## **F129**

### **Cornea donation for research versus for transplantation: a one year prospective study of acceptance rates in a French University Hospital**

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### **Purpose**

Obtaining consent to cornea donation specifically for research is essential: this targeted donation is the only way to obtain fresh tissue of the highest quality, similar to grafted corneas. Though, it is not routine and may give rise to reluctance. Aim: to compare cornea donation for Research (R) versus (vs) for Transplantation (Tx) in a tertiary center.

### **Methods**

Ancillary study of 1 year-prospective preclinical randomized study validating a corneal bioreactor for eye banking, authorized by French Biomedicine Agency. Consents were obtained by 3 experienced nurses of hospital transplantation coordination team. Only donors who presented contraindication to Tx were selected for R so as not to reduce number of grafts available for Tx. Based on French legislation, standard protocols face-to-face or phone interviews were used for both eligible donors groups. Research aim was explained, if needed detailed information could be provided.

## Results

For R and Tx respectively, 134 and 244 families were contacted during 1 year, in 70% of cases by phone. Whatever the method used, we obtained consent in 64% for R vs 54% for Tx ( $p=0.06$ ). Acceptance rates were 60% (R) and 50% (Tx) by phone ( $p=0.14$ ) vs 68% (R) and 63% (Tx) face-to-face ( $p=0.64$ ). The main contraindication to donation for Tx was cognitive troubles (65%) followed by hemopathy (12%). Donors age was  $81\pm 12$  for R vs  $71\pm 13$  years for Tx ( $p<0.001$ ). Endothelial cell density at retrieval was  $2541\pm 409$  for R vs  $2641\pm 596$  cells/mm<sup>2</sup> for Tx ( $p=0.052$ ).

## Conclusions

Despite an opt-out system for donation in France, transplantation coordination teams play an instrumental role in obtaining consent for Tx. We found that they are as efficient in obtaining consent for R. This is a key point to obtain numerous research-grade corneas with similar quality to grafted corneas, except for donor age.

## S002

### An innovative bioreactor allows corneal storage for up to 3 months

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## Purpose

Our university lab BiiGC patented a bioreactor (BR) for long-term eye banking that is in the process of industrialization. By restoring intraocular pressure and medium renewal, it maintains the viability of cornea over a prolonged period, without the deswelling step. In addition, tissue controls are possible at any time without deconditioning the cornea. In a previous study comparing OC and BR, we showed that the number of corneas suitable for graft after 1 month of storage was 1.6 times greater with the BR, with 23% more viable endothelial cells. Aim: to assess whether it is possible to extend storage for up to 3 months.

## Methods

12 pairs of corneas with initial ECD  $>2000$  cells/mm<sup>2</sup> and  $<10\%$  difference between both corneas were randomized and stored: one in the BR (21mmHg pressure and 5  $\mu$ L/H of renewal of CMax (Eurobio), the other in OC (sealed bottle of 100mL of CMax, renewed each month). Monitoring: for the BR, no touch specular microscopy through the BR windows at D2, M1, 2, 3; for the OC: standard cell count at M3 by transmitted light microscopy. Final destructive test for all: pancorneal viable ECD by Hoechst/Ethidium/Calcein staining.

## Results

ECD at baseline:  $2718\pm 295$  in the BR vs  $2779\pm 396$  in OC ( $P=0.250$ ). At M1 in the BR, 11/12 corneas were suitable for graft (ECD  $>2000$  cells/mm<sup>2</sup>) and 1/12 suitable for emergency (ECD between 1600 and 2000). At M2, figures were respectively 5/12 and 6/12. At M3, figures were respectively 4/12 and 7/12 versus 0/12 suitable for graft and 4/12 emergency corneas in OC. Viable ECD in the BR remained 27% higher than in OC ( $P=0.015$ ).

## Conclusions

The BR allows storage to be extended up to 3 months with unprecedented viability. With the BR, eyebanks will be able to really optimize grafts' allocation. In addition, it allows to have corneas immediately available with an acceptable ECD, ready to use for emergency situations.

### S109

#### **Correlations between subjective and objective preoperative assessment of cataract severity, and intraoperative ultrasound energy**

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#### **Purpose**

The Optical Quality Analysis system (OQAS, Visiometrics) provides objective measurements of the image formed onto the retina, by combining quantification of medium transparency and aberrations. Aim: to study the correlations between the OQAS, the preoperative clinical parameters and the ultrasound energy during phacoemulsification.

#### **Methods**

Monocentric study of consecutive age-related cataract patients scheduled for phacoemulsification. Preoperative parameters: logMar of the best-corrected visual acuity (BCVA), lens opacity classification system III (LOCS) by 2 independent observers (in blind of each other), objective scatter index (OSI) provided by the OQAS. All patients were operated on by the same senior surgeon (DG) with fixed surgical settings: continuous oZil with grade 2 cataract mode under topical anesthesia. The cumulative dissipated energy (CDE) was the main phacodynamics parameter. Patients with ocular surface diseases impairing OSI were excluded.

#### **Results**

Twenty-two eyes of 21 patients aged 76±9 years were analyzed. There were 19 nuclear, 10 cortical and 1 subcapsular components. Mean LOCS was 5±2 without difference between observers (p=0.51); BCVA was 0.39±0.22 logMAR; OSI was 6.45±3.37; CDE was 10.94±6.25. Correlations were found between BCVA and OSI (r=0.427, p=0.048); BCVA and LOCS (r=0.539, p=0.01); LOCS and OSI (r=0.621, p=0.002); LOCS and CDE (r=0.683, p<0.001). OSI was correlated with CDE only for pure nuclear cataracts (r=0.706, p=0.015). OSI increased with cortical components that did not required more CDE.

#### **Conclusions**

The OQAS may improve the preoperative assessment of cataract patients. When measured in optimal conditions, OSI is correlated with clinical parameters. OSI may also predict ultrasound energy needed, only for nuclear cataracts.

### 3123

#### **Functional imaging of the retina: New way to assess ocular disease**

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#### **Summary**



The fast technical development of retinal imaging allows us now to assess retinal and associated anatomical structures in unprecedented resolution and has now become a mainstay of clinical care and research. However, in the last few years new and sophisticated imaging technologies have been introduced that extend this approach and allow now to gain also information about functional changes of the retina in addition to morphology. These approaches include for example Doppler Optical Coherence Tomography (DOCT), which aims to visualize and quantify ocular hemodynamics. Other imaging approaches allow for the non-invasive measurement of oxygen saturation in retinal blood vessels and thus for the assessment of retinal oxygen metabolism. This talk will focus in the new possibilities to assess functional changes based on recent developments on ocular imaging. Further, it will be discussed how functional imaging may in future be used for the assessment and follow up of ocular diseases.

#### **T096**

##### **Diagnosis of pattern dystrophy in a case with multiple sclerosis (MS) on fingolimod (Gilenya) treatment and progressive dyschromatopsia**

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#### **Purpose**

To present a case with progressive bilateral dyschromatopsia, with a history of MS on fingolimod treatment for previous optic neuritis (ON), diagnosed with pattern dystrophy.

#### **Methods**

A 56 year-old woman with progressive bilateral dyschromatopsia was referred to our department. She had a history of MS on fingolimod treatment with an episode of ON four months ago. As her recent progressive dyschromatopsia was attributed to her optic neuritis, she also received a course of intravitreal steroids for 5 days prior to her visit to our department.

#### **Results**

BCVA was 10/10 bilaterally. Pupillary reflexes were normal but the response to Ishihara was defective. Visual field testing demonstrated central scotoma bilaterally. Macula OCT showed focal atrophic regions bilaterally corresponding to hypoautofluorescence areas on FAF. ISCEV standards PVEPs, PERG and FFERG were normal. mERG responses corresponding to the atrophic areas on OCT were reduced. These findings were compatible with pattern dystrophy. Genetic testing was advised to confirm the diagnosis.

#### **Conclusions**

MS is associated with episodes of optic neuritis that can present with dyschromatopsia. In the case of our patient, the absence of dyschromatopsia with no further signs/symptoms of ON, and the presence of maculopathy may lead to a differential diagnosis of fingolimod retinal toxicity, as this treatment could be complicated with maculopathy and/or macular oedema. However, both the lack of macular oedema on OCT and the short term use of the drug limit the possibility of drug toxicity. Moreover, the atrophic macular changes on OCT and FAF in correlation with the VF and mERG findings are consistent with the diagnosis of pattern dystrophy. In conclusion, ophthalmological assessment remains important in neurological disorders such as MS, before the initiation of ON treatment.

#### **3132**

##### **Intracorneal ring segment implantation in keratoconus: an evidence-based approach**

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## Summary

Intracorneal ring segments (ICRS) are small PMMA devices that are implanted into the cornea, aiming to alter its geometry in a manner that will enhance its refractive properties and thereby improve visual acuity. They act as spacer elements between the collagen fibers of the corneal stroma and induce an arc-shortening effect resulting in flattening of the central corneal area. Implantation of ICRS decreases the keratometric readings, spherical equivalent and cylinder, reduces high-order aberrations and improves visual acuity in patients with keratoconus. Nowadays there are accurate implantation nomograms for customized treatment of each individual case. The use of femtosecond laser technology has further improved the safety profile of this technique.

This talk will present certain indications and contraindications regarding patient selection in order to maximize the treatment's safety and efficacy. It will also highlight intra-operative pearls and pitfalls for young surgeons. Moreover, it will analyse in detail potential prognostic factors that predict success/failure of the treatment and it will report clinical outcomes and complications, as well as options for combined treatment with other therapeutic modalities, such as CXL.

## F082

### Visual function and retinal changes in patients with bipolar disorder

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## Purpose

To evaluate visual function and retinal changes in patients with bipolar disorder and to analyze the correlation between structural changes and visual function parameters.

## Methods

Thirty patients with bipolar disorder and 80 controls underwent visual function evaluation with ETDRS charts at 100, 2.50 and 1.25% contrast, Pelli Robson chart and color vision Farnsworth and Lanthony D15 tests. Analysis of the different retinal layers was performed using Spectralis optical coherence tomography (OCT) with automated segmentation software. Correlation analysis between structural and functional parameters was assessed.

## Results

Patients with bipolar disorder did not show differences in visual function parameters compared with controls, except in Lanthony's color test index which was worse in patients ( $p=0.002$ ). Full macular thickness, the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL) and inner plexiform layer (IPL) were reduced in patients compared to healthy individuals ( $p<0.005$ ). The inner nuclear layer (INL) was significantly thickened in patients ( $p<0.005$ ). No differences were observed in the outer retinal layers. Peripapillary RNFL thickness was reduced in all temporal sectors ( $p<0.005$ ). Significant correlations were found between visual acuity and the RNFL thickness (macular and peripapillary;  $r=-0.43$ ,  $p=0.009$  and  $r=-0.30$ ,  $p=0.006$  respectively), the Pelli Robson score and the IPL ( $r=0.35$ ,  $p=0.001$ ) and between the Lanthony's color index and the GCL thickness (inner nasal,  $r=-0.38$ ,  $p=0.001$ ).

## Conclusions

Bipolar patients present quantifiable thinning of the macular RNFL, GCL and IPL, as well as in the peripapillary RNFL thickness, and increase in the INL. The analysis of the retinal sublayers with OCT may be a useful marker to show degeneration and monitor disease progression in bipolar disorder.

**F066**

**Ability of Swept-source OCT to detect retinal changes in patients with bipolar disorder**

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**Purpose**

To evaluate the ability of Swept-source Optical coherence tomography (SS-OCT) to detect retinal changes in patients with bipolar disorder (BD).

**Methods**

Twenty-three patients with BD and 23 controls underwent retinal evaluation using SS Deep Range Imaging (DRI) Triton OCT. Full retinal thickness, the ganglion cell layer (GCL), the retinal nerve fiber layer (RNFL) and choroidal thickness were evaluated with automated segmentation software

**Results**

Patients with BD presented significant thinning of the macular full retinal thickness in the center ( $p=0.049$ ), inner temporal ( $p=0.045$ ), inner nasal ( $p=0.016$ ) and inner inferior ( $p=0.016$ ) of the ETDRS areas. The macular GCL layer was reduced in patients compared with controls (average,  $p=0.002$ ; superior,  $p=0.009$ ; superonasal,  $p=0.009$ ; inferonasal,  $p=0.003$  and inferior,  $p=0.009$ ). Peripapillary reduction of full retinal thickness (average,  $p<0.001$ ; superotemporal,  $p<0.001$ ; superonasal,  $p=0.003$ ; nasal,  $p=0.005$  and inferotemporal,  $p=0.033$ ), GCL (nasal,  $p=0.025$ ) and RNFL (average,  $p=0.002$ ; superotemporal,  $p<0.001$  and superonasal,  $p=0.045$ ) thickness was observed in patients compared with controls. No significant differences were observed in choroidal thickness measurements.

**Conclusions**

BD patients present quantifiable thinning of full retinal thickness and the GCL in the macular area, as well as a peripapillary reduction of the RNFL and GCL thickness. The analysis of the retinal sublayers with SS-OCT may be a useful marker to show degeneration and monitor disease progression in bipolar disorder.

**3115**

**Intraoperative OCT: Is it of clinical use? - For**

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**Summary**

The integration of Optical Coherence Tomography (OCT) into the automated operating microscope has introduced a new era for the operative viewing systems in ophthalmic surgery. The applications of the intra-operative OCT (iOCT) can cover a broad spectrum of ocular surgery not only for vitreous and retina, but also for anterior segment procedures. However, its significant cost combined with limited evidence-based data supporting its actual utility, has raised a controversy on whether it's worth obtaining or not.

In the majority of cases, the iOCT is significantly *helpful*. By adding a cross-sectional visualization to the traditional en face view of the microscope, it can improve the surgical results, in terms of safety and efficacy. However, there are also various novel and advanced surgical techniques for which the use of iOCT is not just helpful, but *essential* for a successful outcome.

Hereby, we will present numerous applications of the iOCT, both from reports in the literature and from our own experience after 2 years of using it. Showing corresponding surgical videos, we will demonstrate that, often, the usefulness of a device depends on whether or not we have explored its potential uses.

### **T093**

#### **Characterization of Retinal Structure in CNGB3-associated Achromatopsia**

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#### **Purpose**

To investigate retinal structure in *CNGB3*-associated achromatopsia (ACHM), using split detection adaptive optics scanning light ophthalmoscopy (AOSLO) and spectral-domain optical coherence tomography (SD-OCT).

#### **Methods**

Twenty-two ACHM patients underwent ocular examination, SD-OCT and AOSLO imaging. The OCT scans were used for grading the appearance of the fovea and measuring the outer nuclear thickness (ONL). The interpretable split detection AO images were used to quantify peak foveal cone densities (PFD) and inter-cell distance (ICD). The mean and standard deviation (SD) of ICD were used to quantify the coefficient of variation (CV).

#### **Results**

The mean (range,  $\pm$ SD) age was 23 years (5-41,  $\pm$ 12.5). Mean (range,  $\pm$ SD) best-corrected visual acuity (BCVA) was 0.97 LogMAR (0.60-1.52,  $\pm$ 0.21). SD-OCT disruption/loss of the foveal ellipsoid zone (EZ) was graded as; Grade I (continuous ISe): three (13%), II (ISe disrupted): ten (46%), III (ISe absent): one (5%), IV (presence of a hyporeflective zone): seven (32%) and Grade V (retinal atrophy): one (5%) patient. In all the subjects the grade was the same in both eyes. Thirteen patients (59 %) have a variable degree of foveal hypoplasia. The mean (range,  $\pm$ SD) outer nuclear thickness for all 22 subjects was 66.47 $\mu$ m (37.35-92.45 $\mu$ m,  $\pm$ 16.89). The mean ( $\pm$ SD) ONL thickness for: Grade II was 76.44 $\mu$ m ( $\pm$ 11.14) and for Grade IV was 51.52 $\mu$ m ( $\pm$  21.52). AOSLO images were interpretable in 9 of 22 subjects. Mean (range,  $\pm$ SD) PFD was 20,133 cones/mm<sup>2</sup> (3,652-50,909,  $\pm$  13,940) and the CV (mean  $\pm$  SD) was 0.25  $\pm$  0.05.

#### **Conclusions**

The cone mosaic in patients harbouring *CNGB3* mutations was irregular, variably disrupted and with significantly lower peak foveal densities than normal. The ONL thickness was significantly lower than healthy controls. ACHM patients should be assessed on an individual basis for clinical trials.

### **S003**

#### **Using the angular backscattered light to assess transparency of human corneal grafts after treatment by various anti-edematous eye drops**

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### **Purpose**

The loss of corneal transparency and increase of corneal thickness are common symptoms of corneal oedema disease. However, corneal transparency remains a subjective parameter in clinical applications. A new method to quantify corneal transparency has been developed based on the analyses of the angular backscattered light diffusion. The proposed system collects scattered light from all the reflected space aiming to access to a larger range of angle and a smaller scale tissue structure.

The aim of this study is to compare various topical anti-edematous treatments available on the market by assessing their in-vitro efficacy with regards to the corneal transparency of human corneal grafts.

### **Methods**

Human corneal grafts rejected from Eye Tissue Bank are submitted to swelling protocol to simulate corneal edema (120 minutes soaking in hypo osmolar solution). Then, each graft is placed in a chamber with a permanent irrigation of balanced salt solution to prevent graft dehydration. Samples are separately treated by anti-edematous eye drops instillation every 30 minutes for 6 hours (experiments performed in triplicate). Each eye drop is instilled in the anterior part of the chamber and edema evolution is followed all along the test. Variation of corneal transparency is quantitatively assessed by the angular backscattered light method every 2 hours. In parallel, corneal thickness is controlled by commercial Optical Coherence Tomography every 30 minutes.

### **Results**

Based on collected results, the in-vitro effect of each eye drops is compared and allows to bring out the importance of the anti-edematous treatment formula.

### **Conclusions**

Data suggest that components used in the eye drops formulation and their related concentration influence the edema resorption.

### **F101**

#### **Uncorrected refractive error and associated risk factors among socially vulnerable older adult population living in Armenia**

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### **Purpose**

Visual impairment and blindness are major global public health problems. One of the leading causes of avoidable visual impairment is uncorrected refractive error (URE). This study aimed to estimate the prevalence of URE and associated risk factors in socially vulnerable older population living in Armenia.

## Methods

The cross-sectional study recruited 485 socially vulnerable older adults. The survey instrument included questions about demographics, socio-economic status, spectacle coverage and use of ophthalmic services. All participants underwent comprehensive ophthalmic examination. Patients who had Presenting visual acuity (PVA<6/12) but improved  $\geq 1$  line with or without available spectacles after refractive correction in the better eye were defined as having URE. Descriptive statistics and logistic regression were used to analyze the data.

## Results

The mean age of participants was 74.5 (7.27), ranging from 51 to 94 years. Women constituted the majority of participants (86.0%). The prevalence of URE in the better eye was 25.8%. In bivariate analysis those who were older and those who had less than 10 years of education had significantly higher odds of URE than younger and more educated respondents. In multivariate analysis only education maintained significant association with URE (OR = 3.71; 95% CI: 1.10-12.5). PVA with available correction (normal vision  $\geq 6/12$ ) improved from 58.9% to 81.0%, while PVA with available correction (visual impairment <6/12) decreased from 41.1% to 19.0% in the better eye after best correction.

## Conclusions

The prevalence of URE was high in this study population. Eye screening and provision of affordable spectacle correction to the socially vulnerable older population in Armenia could significantly reduce visual impairments due to URE.

## T094

### Mild Cone-rod dystrophy and sensorineural hearing loss with CEP250 mutation in a Japanese family

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## Purpose

CEP250 encodes the C-Nap1 protein which belongs to the CEP family of proteins. C-Nap1 has been reported to be expressed in the photoreceptor cilia and is known to interact with other ciliary proteins. Mutations of CEP250 cause atypical Usher syndrome which is characterized by early-onset sensorineural hearing loss (SNHL) and a relatively mild retinitis pigmentosa. This study tested the hypothesis that the mild cone-rod dystrophy (CRD) and SNHL in a non-consanguineous Japanese family was caused by CEP250 mutations.

## Methods

Detailed ophthalmic and auditory examinations were performed on the proband and her family members. Whole exome sequencing (WES) was used on the DNA obtained from the proband.

## Results

Electrophysiological analysis revealed a mild CRD in two family members. Adaptive optics (AO) imaging showed reduced cone density around the fovea. Auditory examinations showed a slight SNHL in both patients. WES of the proband identified compound heterozygous variants c.361C>T, p.R121\*, and c.562C>T, p. R188\* in CEP250. The variants were found to co-segregate with the disease in five members of the family.

## Conclusions

The variants of CEP250 are both null variants and according to American College of Medical Genetics and Genomics (ACMG) standards and guideline, these variants are classified into the very strong category (PVS1). The criteria for both alleles will be pathogenic. Our data indicate that mutations of CEP250 can cause mild CRD and

SNHL in Japanese patients. Because the ophthalmological phenotypes were very mild, high-resolution retinal imaging analysis, such as AO, will be helpful in diagnosing CEP250-associated disease.

**2915**

### **High speed adaptive optics angiography**

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#### **Summary**

Image-based angiography is a well-adapted technique to characterize vasculature. Because the microvasculature is of particular interest, being the site of exchange between blood and tissue, a high spatiotemporal resolution is required, hence the use of adaptive optics ophthalmoscopes with a high frame rate. Having a decoupled stimulation/illumination light of the retina makes the use of near infrared (NIR) imaging light desirable. However, the computation of angiography maps is based on the variation in contrast caused by the absorption of erythrocytes passing through capillaries, and NIR light is not optimal for this absorption. We have therefore developed a new computational method allowing us to realize angiography with an adaptive optics flood illumination ophthalmoscope (AO-FIO) using NIR light.

In vivo retinal imaging at 200Hz was performed on healthy subjects using an AO-FIO. Temporal standard deviation of each image sequence was computed after enhancing erythrocyte contrast using a specific spatiotemporal filter.

Our high pixel rate enables us to detect erythrocyte flow on capillaries in a large field and at high frequency. The advantages previously mentioned make NIR AO-FIO a relevant technique for stimulation studies.

**T030**

### **Structural analysis and evolution of AMD Drusenoid deposits “L”, Lipid type: study with OCT and Morphology-Structural software**

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#### **Purpose**

To study structural analysis and evolution of AMD drusenoid deposits “L” with OCT and Morphology-Structural software. 5 years follow-up

#### **Methods**

74 eyes of 68 patients, 24 men, 44 women, with AMD drusenoid deposits “L”, Lipid Type (soft Drusen, Drusenoid PED “L”). Deposits were evaluated by OCT (Spectralis HRA-OCT, spectral domain OCT) and Morphology-Structural software (M-S software). M-S software let analyze drusenoid deposit volume and contours, 3D deposit reconstruction, display in 3D space, let drusenoid deposit contents analyze, discrimination, differentiation, let grading (volume and contours analyze), let measurements: volume (in  $\mu\text{m}^3$ ), density (grey levels of deposits), structure (structural measures, texture parameters), composition (density calculation), evaluation and characterization of those “L”, lipid type deposits. Evaluation, comparison for each eye, for each patient, between all studied patients was done every year, so drusenoid deposit structural evolution assessment too. 5 years follow-up.

#### **Results**

AMD Drusenoid Deposits “L”, Lipid Type, are dark grey, homogeneous, translucent, optically empty, as lipid pearl drops, fatty, under the RPE, Low density, well defined / M-S Software. Evolution was: 40% the same/eye, patient, all patients; 35% less volume, higher density, structure/eye, patient, for 75% patients; 25% almost or total all gone/eye, patient, for 85% patients, with abnormal facing Photoreceptor layer and/or Pigment Epithelium layer (granular, irregular, less thick, thinner and thinner) to disappear, to Atrophy

### **Conclusions**

OCT, Morphology-Structural Software contribute to and improve AMD Drusenoid deposits “L”, Lipid type, volume, structural and evolution study, so AMD knowledge, understanding and AMD biomarkers feature

### **T029**

#### **Structural analysis and evolution of AMD Drusenoid deposits “P”, Protein-Cellular Type: study with OCT and Morphology-Structural software**

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### **Purpose**

To study structural analysis, evolution of AMD drusenoid deposits “P”, with OCT and Morphology-structural software. 5 years follow-up

### **Methods**

214 eyes of 174 patients with AMD drusenoid deposits “P”, Protein-Cellular Type: Cuticular drusen, Pseudovitellic AMD, Subretinal drusenoid deposits (SDD), Drusenoid PED “P”. Deposits were evaluated by OCT (Spectralis spectral domain HRA-OCT) and Morphology-Structural software (M-S software). M-S software let analyze drusenoid deposit volume, contours, 3D deposit reconstruction, let drusenoid deposit contents analyze, discrimination, differentiation, let grading (volume, contours analyze), let measurements: volume (in  $\mu\text{m}^3$ ), density (grey levels of deposits), structure (structural measures, texture parameters), composition (density calculation), so evaluation, characterization of those “P” deposits. Evaluation, comparison for each eye, each patient, between all studied patients, was done every year, so drusenoid deposit structural evolution assessment too, 5 years follow-up

### **Results**

AMD Drusenoid Deposit “P” are dense, white, granular, heterogeneous PED, below Pigment Epithelium and/or just above, Medium density, well defined / M-S Software. Evolution was: 25% the same/eye, patient, for all patients; 55% higher volume, higher density, structure/eye, patient, for 85% patients; 80% choriocapillaris change-pigment epithelium involution: more dense, irregular, inhomogeneous, crumbled-inflammation-neovascular signs, to Neovascular Complication; 20% less volume, higher density, structure/eye, patient, for 25% patients; almost all gone/eye, patient, with abnormal facing Photoreceptor layer, Pigment Epithelium layer (granular, irregular, less thick, thinner and thinner) to disappear, to Atrophy

### **Conclusions**

AMD Drusenoid deposits “P” volume, structural and evolution study with OCT and Morphology-Structural Software contribute to and improve AMD knowledge, understanding and AMD biomarkers feature

### **T091**

#### **Age Macular Degeneration - Alzheimer Disease: Ophthalmic exam - MCI in-between correlations. 5 years evolution**

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## **Purpose**

To evaluate AMD-AD correlations after 5 years evolution, their in-between impact

## **Methods**

AMD patients: 240 patients, 3 Groups A, B, C. A: 70 AMD patients with first stage AMD, B: 64 Atrophy AMD patients with predominant atrophic areas, C: 106 Neovascular AMD patients, with Neovascular AMD. Ophthalmologic exam included ETDRS visual acuity (VA), complete ophthalmic examination, Fundus examination, autofluorescence imaging (FAF), (Region Finder Software, for atrophic areas), optical coherence tomography (Spectral Domain OCT) and fluorescein angiography (FA), ICG when Neovascular complication. Cognitive evaluation is done with MMSE: Mini Mental State Examination (Folstein, GRECO), score allow to determine various groups and subgroups. Ophthalmic Exam and Cognitive Evaluation were done T0 and 5 years later, were compared to each one and in between. Own evolution assessment of Ophthalmic Exam and Cognitive Evaluation are done and compared each other.

## **Results**

Cognitive impairment differ in each AMD subgroup: Normal score most in group A (37%), less in group B (23%) than in group C (35%). MCI was predominant (A: 63%, B: 77%, C: 62%) and the most in group B. Early stage AD: 3% only in group C. After 5 years follow-up, similar results were observed in each subgroup, but more moderate cognitive impairment in Group B, few but the most severe worsening in Group C. Normal score: still most in group A (34%), even less in group B (20%) and than in group C (31%). MCI was predominant (A: 66%, B: 82%, C: 65%) and the most in group B. Early stage AD: 7% only in group C. AMD complications, their evolution were correlate with MCI, its evolution, each one and both. AMD ophthalmologic signs are predictive and precursor for AD. Fundus examination, even more (FAF, OCT) are useful, needed to enhance AD screening and follow-up.

## **Conclusions**

The AMD-AD correlations are confirmed, enhance AMD as marker for AD, let improve AMD and AD screening and knowledge.

## **T079**

### **Retinal detachment following elective macular surgery**

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## **Purpose**

Macular surgery has become an increasingly atraumatic procedure for the eye with the surgical methods that have been further developed in recent years. The most common complications include cystic macular edema and retinal detachment, more rarely endophthalmitis. The aim of this retrospective study is to record the number of retinal detachments following elective macular surgery.

## **Methods**

In this study we included all patients who underwent pars plana vitrectomy (ppV, 20 gauge or 25 gauge) in the years 2009-2016. Then it was examined which patients were hospitalised again because of a retinal detachment. For the affected patients the rate of retinal detachment, functional outcomes and possible risk factors were recorded.

## **Results**

A total of 1027 patients were identified, of whom 759 had surgery for epiretinal membrane, 213 for macular hole, and 55 for vitreomacular traction with a 20 gauge or 25 gauge ppV. Of these 1027 a retinal detachment occurred in 18 (1.75%) cases. The mean time between first ppV and second ppV with retinal detachment was 101 days (2-648 days). Four of the 18 patients had at least one retinal break before or during surgery. The retinal break was located inferior in nine cases, superior in four, in three cases a PVR retinal detachment and in two cases the foramina were distributed. Mean visual acuity was 0.25 (decimal) before macular surgery, 0.12 before retinal detachment, and 0.25 at the time of last presentation.

### Conclusions

Modern vitrectomy techniques reduce the complications in elective macular surgery, but do not replace the surgeon's experience.

**3664**

### MBGE - Updates in Ophthalmology

**2912**

### Structural and functional imaging of ocular tissues with full-field OCT

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### Summary

Full field OCT achieves 3D micrometer resolution in ocular tissues, acquiring images in en face slices, using spatially incoherent illumination and microscope objectives in a Linnik interferometer configuration. Here we present FFOCT combined with SD-OCT for in vivo corneal and retinal imaging, and dynamic FFOCT for in vitro tissue explant imaging. FFOCT is a promising new modality for corneal and retinal imaging in patients with increased patient comfort and image resolution compared to existing modalities. In cornea, FFOCT provides micron resolution over a 1.3mmx1.3mm field with non contact operation to reveal micrometric features such as keratocytes, sub basal and stromal nerves, and endothelial cells, through the depth of the cornea. In retina, FFOCT reveals nerve fibers, vessels and photoreceptors without the use of adaptive optics. In tissue explants, FFOCT can probe cell activity and indicate function. By measuring the intracellular dynamics, signal contrast is enhanced. Using image processing methods, FFOCT dynamic data can then produce non invasive cell labeling via color coding according to frequency of intracellular movement. Perspectives include quantification of dynamic FFOCT functional information in disease models.

**3154**

### Rod-specific inactivation of Vhl leads to HIF-dependent retinal degeneration

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### Summary

Reduced choroidal blood flow and tissue changes in the ageing eye may impair oxygen delivery to RPE and photoreceptors and may result in mild but chronic tissue hypoxia. Supporting this notion, we detected increased expression of several hypoxia-inducible genes in the aged human retina suggesting increased activity of hypoxia-inducible transcription factors (HIFs). This activity may affect cell metabolism and survival, and may contribute to retinal pathologies such as AMD.

To model chronically elevated HIF activity in photoreceptors, we inactivated von Hippel Lindau (VHL) protein in rods or cones. The resulting increased HIF activity led to a slowly progressing retinal degeneration in the ageing retina. Degeneration depended on HIF1 as genetic inactivation of *Hif1a* but not of *Hif2a* rescued both rods and cones. This contrasts to the RPE where HIF2 was shown to be responsible for degeneration (Kurihara et al., 2016). Since lack of HIF1 and HIF2 in photoreceptors did not affect retinal function or cell survival, HIF1 may be a therapeutic target to rescue vision. Indeed, an AAV-mediated RNA interference strategy significantly mitigated the degeneration suggesting that this intervention therapy may be applicable to human patients.

## **T112**

### **Treatment of corticosteroid resistant Grave's orbitopathy with tocilizumab**

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#### **Purpose**

Corticosteroid is the reference treatment of active Grave's orbitopathy (GO), however, 40% of patient do not respond to this therapy. Tocilizumab (TCZ) is an anti interleukin-6 receptors monoclonal antibody that specifically binds to the membrane-bound and soluble receptors of interleukin-6, and which is efficient in severe rheumatoid arthritis and used since more than ten years. Its efficiency in active corticosteroid resistant GO has been reported in 2014 in a Spanish study. Aim: to assess tocilizumab as an emergent treatment for corticosteroid resistant active GO and patients with short term sight-threatening complications.

#### **Methods**

We assessed TCZ in eight patients with active corticosteroid resistant GO including three patients with compressive neuropathy. Each patient received intravenous TCZ every four weeks until symptom stabilization. We monitored visual acuity, ocular motility, Hertel exophthalmometry, clinical activity score and thyroid-stimulating immunoglobulin (TSI) for each patient. Humphrey visual field monitoring was performed for patients with compressive neuropathy.

#### **Results**

Seven of eight patients were clinically improved after the first or second pulse. A mean of 3 pulses was necessary to drastically decrease the TSI level. One patient with Graves' neuropathy with a low TSI level was not improved and underwent orbital decompression. No side effect was noticed in any patient.

#### **Conclusions**

As shown by the initial Spanish study, our results confirm an outstanding efficiency of TCZ in active corticosteroid resistant GO including compressive neuropathy, with a large rate of responsive patients. Given its much better tolerance compared to high-dose steroids, its place in first-line treatment in severe forms should be evaluated, as well as the medico-economic consequences of such treatment.

### F115

#### Maximum human objectively measured pilocarpine stimulated accommodative amplitude

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#### Purpose

To measure the maximum, objectively measured, accommodative amplitude, produced by pharmacologic stimulation

#### Methods

Thirty-seven subjects were enrolled, with a mean age of 20.2±1.1 years, corrected visual acuity of 20/20, and mean spherical equivalent refraction (SER) =-0.83±1.60 diopters. For each subject, the right pupil was dilated with phenylephrine 10%. After 30 minutes, the pupil was measured, the left eye was patched, and the right eye was auto-refracted. Pilocarpine 4% was then instilled in the right eye, followed by phenylephrine. At 45 minutes after the pilocarpine, auto-refraction and pupil size were again measured.

#### Results

Mean pupil size pre- and post-pilocarpine was 8.0±0.8 mm and 4.4±1.9 mm, respectively. Pre- and post-pilocarpine, the mean SER was -0.83±1.60 and -10.55±4.26 diopters, respectively. The mean pilocarpine-induced accommodative amplitude was 9.73±3.64 diopters. Five subjects had accommodative amplitudes ≤14.00 diopters. Accommodative amplitude was not significantly related to baseline SER ( $p$ -value =0.24), pre- or post-pilocarpine pupil size ( $p$ -values =0.13 and 0.74), or change in pupil size ( $p$ -value =0.37). Iris color did not statistically significantly affect accommodative amplitude ( $p$ -value =0.83).

#### Conclusions

Following topically applied pilocarpine, the induced objectively measured accommodation in the young eye is greater than or equal to the reported subjectively measured voluntary maximum accommodative amplitude.

### S103

#### Image registration demonstrates central lens thickness minimally changes during accommodation

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### **Purpose**

The purpose was to determine the changes in anterior chamber depth (ACD) and central lens thickness (CLT) during pharmacologically induced accommodation.

### **Methods**

Following pupillary dilation with phenylephrine 10%, baseline auto-refractions and swept-source optical coherence tomographic biometric images (Zeiss IOLMaster 700) were obtained from right eyes of 25 subjects aged 19 to 24 years. Pilocarpine 4% and phenylephrine 10% were instilled into these right eyes. One hour later, auto-refractions and biometric imaging were repeated. Only data from eight of 25 subjects met the following stringent criteria to be included in the study analysis: pre and post-pilocarpine biometric foveal images were registerable, images of the corneal centers were shifted by  $\leq 100 \mu\text{m}$ , pupils  $> 5 \text{ mm}$  and pharmacologically induced refractive change  $\geq -7$  diopters.

### **Results**

The mean auto-refractive accommodative change for the eight included subjects was  $-12.45$  diopters ( $\pm 3.45$  diopters). The mean change in CLT was  $81 \mu\text{m}$  ( $\pm 54 \mu\text{m}$ ) and the mean change in ACD was  $-145 \mu\text{m}$  ( $\pm 86 \mu\text{m}$ ). Superimposition of the registered pre and post-pilocarpine biometric images of the sagittal sections of the whole eye from each subject demonstrated that the position of the whole lens did not shift either anteriorly, posteriorly or vertically during pharmacologically induced accommodation.

### **Conclusions**

A small increase in lens thickness was associated with a large change in accommodative amplitude and no significant change in lens position as predicted by the Schachar theory.

2155

### **Other strategies of Myopia control**

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### **Summary**

In the last 60 years, there has been a marked increase in the prevalence of high myopia in younger generations in developed countries in East and Southeast Asia, and there are signs of similar, but less pronounced increases in North America and Europe. In some parts of the world, 70-90% of children completing high schools are now myopic, and as many as 20% may be highly myopic. High myopia is a major cause of uncorrectable visual impairment.

The high prevalence poses a major public health challenge. With that, myopia is known to be associated with several ocular complications such as retinal detachment, glaucoma, cataract, optic disk changes or maculopathy. It is now clear that myopia results from excessive axial elongation of the eye and this greater rate of axial elongation appears to be, at least in part, environmentally driven. Experimental studies have examined the biochemical mechanisms involved in regulation of axial elongation. From these studies, some options have emerged for preventing the development of myopia or slowing myopic progression, including atropine eye drops, progressive contact lenses, orthokeratology, and more outdoor activity. Some other experimental methods are also being tested.

2922

Tadeusz Krwawicz , MD, PhD – inventor of cryo-surgery

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### Summary

Tadeusz Krwawicz (1910–1988) pioneered the use of *cryosurgery* in ophthalmology. Moreover, he developed techniques for corneal refractive surgery—partial lamellar removal of the corneal stroma and temporary interlamellar introduction of a plastic disc in order to change the corneal curvature. Krwawicz presented other ophthalmic interests—his research concerned immunology, histology, histochemistry, biochemistry of ocular tissue, and mainly corneal and experimental surgery with a particular focus on the pathology of the cornea.

F057

Screening and follow-up of acute ROP: reproducibility and diagnostic accuracy of fluorescein angiography

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### Purpose

To evaluate the reproducibility and diagnostic accuracy of fluorescein angiography (FA) in the screening and follow-up of retinopathy of prematurity (ROP).

### Methods

This is a retrospective study of FA reproducibility and diagnostic accuracy. 106 couples of FA images (early and tardive FA times) of 30 eyes of 15 premature infants with type 2 stage II ROP were evaluated by 5 ophthalmologists: 2 ROP experts, 2 non-experts, and 1 expert in the adult FA. Each operator gave a score ranging from 0 to 2-3 to each one of the following parameters: leakage, ischemic areas, plus disease and vascular anomalies. The images were reviewed twice (the second time after two weeks). Intra-inter concordance among raters of FA findings was evaluated with Kappa Choen (CK) statistic.

### Results

The intra-operator concordance was very good (CK>0.81) for all FA findings. Inter-operator concordance was good (CK>0.41) for all operators and all FA findings. Global concordance was: substantial (intra-inter raters: CK>0.61) in the evaluation of the leakage, size of the ischemic areas, and plus disease; almost perfect (CK>0.81) in the evaluation of the vascular anomalies; moderate (CK: 0.41-0.60) in the definition of the continuity/discontinuity of the ischemic areas. The total FA score was directly correlated to the percentage of treatment: a score ≥7 was correlated with 100% treatment and a score ≤3 with no treatment. Treatment timing (time between FA and laser treatment) was inversely correlated to the FA score: a score ≥8 was correlated with a timely treatment (≤6 days), and a score ≤7 was correlated with a delayed treatment (< 10 days).

## Conclusions

This study showed that FA represents a reproducible imaging technique with a high diagnostic accuracy. It is useful in order to detect ROP progression, and to define the treatment timing and size.

## S077

### **The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): regeneration of corneal and limbal epithelium of stored human corneas**

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## Purpose

Our university lab BiiGC patented 2 versions of an ophthalmic bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentation, called OBSERV, supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to compare the quality of corneal (CE) and limbal (LE) epithelium of human corneas stored in the BR versus in other experimental storage methods.

## Methods

By restoring IOP and medium renewal, the BR maintained corneal viability over a prolonged period. Its transparency allowed characterizing the tissue with existing or customized devices. We analyzed 3 modalities of storage in the BR: 1/air-lifting i.e. alternating air and supplemental hormonal epithelial medium (SHEM); 2/epithelial immersion in SHEM, 3/epithelial immersion in standard organ culture (OC) medium (CorneaMax, Eurobio). For all, OC medium circulated in the endothelial chamber at 21mmHg. The 3 were compared to passive immersion in OC or in SHEM, either complete immersion or epithelial immersion only, with the cornea mounted on agar gel. Criteria after a 14-day storage: histology, ultrastructure (TEM) and immunolabeling for ABCB5, K3/K12, MUC16 and Zo-1.

## Results

The BR with air-lifting was the most efficient to restore a pluristratified, differentiated (K3/K12+) and mature (apical Zo-1 and MUC16 staining; microvilli and mucin-like structure on TEM) CE; in addition, LE was stratified and ABCB5+. The BR with immersion also restored a pluristratified epithelium, but less mature. The passive storage in SHEM and OC led at best to a pauci-stratified CE with reduced maturation.

## Conclusions

The OBSERV platform is an original efficient tool to improve ex vivo epithelial regeneration of human corneas. It can complete or replace animal experimentation for academic or industrial research.

## 3148

### **An “unexplainable” progressive regression of vitreous seeding in advanced retinoblastoma.**

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**Purpose**

to report an unusual regression of vitreous seeding in a retinoblastoma case

**Methods**

: case report .The 3 years old child presented with retinoma in one eye and stage D retinoblastoma in the contralateral eye .

**Results**

An “unexplainable” progressive regression of vitreous seeding in advanced retinoblastoma 9 months after the last intravitreal injection with Melphalan is reported. The child received 3 intraarterial treatments and 11 intravitreal injections

**Conclusions**

We discuss the possible pathogenetic mechanisms of this progressive regression after the end of treatment

**3147**

**Neonatal Retinoblastoma**

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**Purpose**

to identify patients with retinoblastoma diagnosed at the age of 1 month and describe their clinical features and treatment outcome.

**Methods**

a retrospective study of 715 cases of retinoblastoma diagnosed and treated at the Retinoblastoma Referral Center University of Siena between 1980 and 2018 has been performed.

**Results**

thirty-five patients diagnosed within the first month of life have been identified. The majority of them had a bilateral form ; among the unilateral ones some of them developed metachronous tumors in the fellow eye. Family history was positive in most of them. The follow-up range was 1 to 37 years. Management included early enucleation, systemic chemotherapy , bridge chemotherapy followed by intraarterial chemotherapy and focal treatments. None of them developed metastatic disease or second tumors.

**Conclusions**

family history prompted early diagnosis in most cases. However, early diagnosis does not always mean early stage of the disease and better prognosis .

**3131**

**CXL and visual rehabilitation in keratoconus: myths and reality**

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**Summary**



Corneal cross-linking (CXL) has potential to decrease corneal steepness, reduce topographic irregularity indices, improve uncorrected visual acuity (UCVA) and/or best corrected visual acuity (BCVA), or change in the refractive error in patients of any age.

Positive effect of CXL ranges from halting disease progression to improving K values. Mean k values post-CXL can remain similar but equally could be flattened by a mean of 2.0 D. One study observed extreme flattening effect in approximately 0.5% of patients (up to 11.0D). BCVA post-operatively ranges from “no significant differences” to improvement by 1.6 lines.

The visual benefits of CXL varies from individual to another possibly due to the cornea biomechanics and configuration of the cone. Many studies looked at variables that might influence the visual outcomes of CXL, like keratometric apex centricity.

Despite the expanding range of refractive procedures to improve visual functions in stable keratoconus patients, CXL alone could offer some improvement in optical and topographic parameters of the cornea and hence an improvement in UCVA and/or BCVA. The degree of the improvement is difficult to predict and depends on various parameters of the cornea as well as its biomechanics.

### **S073**

#### **The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorization): simulation of a DMEK**

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#### **Purpose**

Our university lab BiiGC patented 2 versions of a bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to reproduce a Descemet membrane endothelial keratoplasty (DMEK) inside the BR.

#### **Methods**

By restoring IOP and medium renewal, the BR maintained corneal viability over a prolonged period and its transparency allowed characterizing the tissue with existing or customized devices without compromising sterility. A 9mm diameter Descemetorhexis was performed open-sky on the recipient human cornea. An 8mm diameter endothelial grafts was dissected with a no-touch technique and transferred using a soft contact lens. The DMEK-bearing cornea was installed in the BR with an air bubble in the endothelial chamber and endothelium facing down. IOP was set to 21mmHg. The bubble was removed after 3 days. Implanted corneas and controls (rhexis alone) were stored for 1 to 4 weeks in a custom-made medium. Monitoring: D-1, D1, W1 to 4: transparency (slit-lamp and customized transparometer), OCT corneal thickness, endothelium/epithelium (specular microscopy). Final test: triple Hoechst/Ethidium/calcein-AM staining to determine endothelial viability and Alizarin red staining.

#### **Results**

The DMEK adhered to the stroma. Implanted corneas were thinner than controls. Endothelial cell survived normally and started to migrate outside the donor Descemet onto the bare recipient stroma from W1.

#### **Conclusions**

The OBSERV platform is efficient to study the biofunctionality of a DMEK. It will be useful for preclinical assessment of next generation bioengineered endothelial grafts.

#### **S078**

##### **The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorization): simulation of the endothelial cells injection therapy for corneal edema**

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#### **Purpose**

Our university lab BiiGC patented 2 versions of a bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to reproduce the injection of cultured endothelial cells (EC) inside the BR.

#### **Methods**

By restoring IOP and medium renewal, the BR maintained corneal viability over a prolonged period and its transparency allowed characterizing the tissue with existing or customized devices without compromising sterility. It is also equipped with injection and sampling sites that do not interrupt flow or pressure regulation. EC were totally removed from the recipient cornea, leaving the Descemet membrane intact. Primary cultures of corneal EC with normal karyotype were obtained from a 55 year-old donor using the Kyoto-protocol with some modifications. 500000 EC were injected with rock-inhibitor into the endothelial chamber maintained at 21 mmHg and placed endothelium facing up. After 6H the medium flow was set at 5 µL/H. Injected corneas and controls (EC scrapping alone) were stored for 1 to 4 weeks in a custom-made medium. Monitoring: D-1 before injection, D1, W1 to 4: transparency (slit-lamp and custom device), OCT corneal thickness, specular microscopy. Final test: triple Hoechst/Ethidium/Calcein-AM to measure EC viability and Alizarin red staining.

#### **Results**

Cultured EC adhered to the recipient Descemet membrane and formed a neo-endothelium. Injected corneas were thinner than controls.

#### **Conclusions**

The OBSERV platform is efficient to study the biofunctionality of primary EC cultures. It is complementary to animal experimentation, which encounters the difficulties of xenogenic rejection. The BR will be useful for preclinical assessment of next generation bioengineered EC.

#### **S051**

##### **Immunolabeling of nerves by anti-neurofilament and anti-βIII-Tubulin in the different compartments of the human ocular surface**

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## Purpose

To provide new insights on the microanatomy of ocular surface innervation by using immunolabeling of 2 proteins of the neuronal cytoskeleton: neurofilaments (NF) and  $\beta$ III-Tubulin ( $\beta$ III-T), and their co-staining with other corneal structures.

## Methods

60 fresh human corneas were used: 37 normal ones (body donation to Science) and 23 post-surgical buttons for: 13 regrafts, 4 Fuchs, 3 keratoconus, 2 lattice dystrophy and 1 post-herpetic scar. Optimized protocols for flat mounted whole corneas were used. Nerves were stained for  $\beta$ III-T and NF (pan- and subunits). Epithelium, Bowman's membrane, limbus, conjunctival vessels, nerve sheath and Schwann cells were respectively stained for CK12, Laminin5, CK15,  $\alpha$ SMA, CollagenIV and NCAM. Epifluorescence, macroscope and confocal microscopy were used.

## Results

Expression of NF and  $\beta$ III-T was not strictly superimposable. In all healthy tissues, the large conjunctival nerve bundles were NF++,  $\beta$ III-T+. The thickest corneal subbasal fibres were NF+,  $\beta$ III-T+ and divided into several thin fibres and Nerve endings that were NF-,  $\beta$ III-T+. Two NF+ mechanoreceptor-like structures (presumed to be tactile receptors) were also identified in the limbus. NF and  $\beta$ III-T expression was altered in all pathological specimens: NF-,  $\beta$ III-T+ structures were systematically less numerous. In regrafts, hypertrophic NF+ nerve bundles were identified at the host-donor interface.

## Conclusions

The double NF and  $\beta$ III-T immunolabeling identifies different neuronal structures at the ocular surface. In corneal epithelium, NF-,  $\beta$ III-T+ axons seem to be predominantly affected during various corneal diseases and could serve as biomarker.

## T052

### Automatic Detection of Diabetic Retinopathy using Jointly Trained CNNs

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## Purpose

The purpose of this study is to evaluate the performance of the RetinOpTIC-v3 algorithm for referable diabetic retinopathy (DR) and diabetic macular edema (DME) detection using fundus photography. Its performance for fully-automatic detection is assessed quantitatively on a publicly-available dataset (Messidor-2). Its use for semi-automatic DR and DME grading is also discussed.

## Methods

Following state-of-the-art artificial intelligence (AI) solutions, referable DR and DME are detected using an ensemble of convolutional neural networks (CNNs). These CNNs take one full retinal image at the input and produce one referral decision. Unlike competing AI solutions, CNNs are trained jointly in such a way that they are complementary with one another. The proposed ensemble is trained on more than 80,000 images. Thanks to a proposed heatmap generation method, the patterns that each CNN detects in images can then be overlaid on images.

## Results

Referable DR and DME can be detected with an area under the ROC curve of 0.987 in the Messidor-2 dataset, using the University of Iowa's reference standard (sensitivity = 99.0%, specificity = 87.0%). This is better than previously reported systems, evaluated under the same conditions. Interestingly, we found that each co-trained CNN specializes in one lesion type or category. Therefore, the system can produce lesion-specific heatmaps, while previously reported CNN heatmaps do not allow lesion differentiation.

## Conclusions

The proposed jointly trained CNN ensemble improves fully-automatic detection of referable DR and DME: it provides more accurate predictions in a few milliseconds only. It is also useful in a semi-automatic setup: by providing very accurate lesion detection and categorization, it is expected to help human readers grade DR and DME, by reducing false negatives in particular.

## F094

### Sarcomere remodeling following strabismus surgery

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## Purpose

To investigate the extent and time axis of sarcomere remodeling following muscle resection in an animal model of strabismus surgery.

## Methods

The right superior rectus muscles (SR) of 16 adult New Zealand white rabbits were resected 4 mm and reattached to the sclera, with ethical permission and following the animal care directives. The SR of 4 rabbits respectively were collected 1, 2, 4 and 6 weeks after surgery. The SR of 4 control rabbits were also collected. The muscles were divided longitudinally into two pieces and one half was directly frozen for RNA extraction and the other half was stretched, fixed in 2% paraformaldehyde and frozen after sucrose cryoprotection. Serial longitudinal sections comprising both layers and the whole muscle length were processed for immunohistochemistry with antibodies against desmin. For each muscle section, the area comprising exclusively longitudinally sectioned myofibers was evaluated and the number of dividing sarcomeres present within that area was determined.

## Results

One week after surgery, the number of sarcomere divisions was 86.5/mm<sup>2</sup> (range 30.9-152.7), after two weeks 72.0/mm<sup>2</sup> (42.5-95.9) and after 4 weeks 95.7/mm<sup>2</sup> (37.4-161.3). After 6 weeks the number of sarcomere divisions (26.8/mm<sup>2</sup>, range 9.2-60.7) was similar to that of the control samples (26.0/mm<sup>2</sup>, range 6.0-66.9). The values at 2 and 4 weeks were statistically significantly higher compared to week 6 and to the controls (p=0.02 and p=0.03).

## Conclusions

Signs of sarcomerogenesis were present during the first 4 weeks after resection of the superior rectus muscle, suggesting that sarcomerogenesis plays a role in surgical failure due to recovery of muscle length. We suggest that medical approaches to limit this mechanism may be a desirable complementary therapy to strabismus surgery in the future.

## 2733

### Trace elements in glaucoma

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## Summary

Glaucoma is one of the leading causes for blindness in the world, yet pathophysiology is widely unknown up to now. It is assumed that it is a multifactorial disease with the main risk factor of an elevated intraocular pressure and other pathogenetic factors like vascular dysregulation or ocular ischemia. Additionally, oxidative stress seems to be a key player in glaucoma pathogenesis, resulting of an imbalance between oxidants and antioxidants. Trace elements (e.g. iron, zinc) were seen to influence the balance between oxidants and antioxidants. As altered concentrations of trace elements were seen open-angle glaucoma patients, it is assumed that trace elements are involved in the pathogenesis of glaucoma.

## F003

### The Role of the $\alpha\text{v}\beta 3$ Integrin in Lamina Cribrosa Cells and the Possible Role in Glaucoma Pathogenesis

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## Purpose

Stiffness is the ability of a material to resist deformation, ECM changes occur with stiffness increasing with age. In glaucoma fibrotic changes occur in both the optic nerve head (ONH) and trabecular meshwork (TM) these changes are associated with cellular and molecular events which drive progressive tissue fibrosis and stiffening. The  $\alpha\text{v}\beta 3$  Integrin is expressed in the ONH. Connecting the extracellular matrix (ECM) to the cytoskeleton, integrins allow for bidirectional signal transduction. We propose that  $\alpha\text{v}\beta 3$  is activated by and transmits mechanical signals from the lamina cribrosa (LC) ECM and is central to the pathogenesis of glaucoma. We have previously shown that production of profibrotic ECM genes is raised when cultured on a stiff substrate. Elevated stiffness drives ECM production.

## Methods

Human LC cells were cultured in substrates of varying stiffness, approximating physiological (4kpa) or glaucomatous (100kPa) for 96 hours.  $\alpha\text{v}\beta 3$  integrin gene transcription were assessed with quantitative RT-PCR.  $\alpha$ -SMA expression was assessed using an immune-fluorescence technique.

## Results

The presence of  $\alpha\text{v}\beta 3$  genes were confirmed by quantitative RT-PCR. Cells grown on the stiff substrate proliferate faster and were more firmly adhered to the substrate than those cultured on the softer substrate. We have previously shown that in normal LC cells  $\alpha$ -SMA staining is more pronounced in cells grown on the stiff substrate.

## Conclusions

The  $\alpha\text{v}\beta 3$  integrin's role in mechanotransduction is proven in other cell lines. This integrin could represent a more specific potential treatment target than others previously investigated (including TGF $\beta$ 1 and TGF $\beta$ 2) to break the cycle of stiffness causing excessive profibrotic ECM production. The increase in expression of  $\alpha$ -SMA signal and the observed change in cellular morphology demonstrates the effect of increased stiffness.

## T064

### Endophthalmitis rate following intravitreal injection of anti-VEGF and the impact of post-injection topical

## antibiotics

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### Purpose

To compare the incidence of endophthalmitis following intravitreal anti-vascular endothelial growth factor (VEGF) injection, with and without post-injection topical antibiotic drops.

### Methods

This retrospective audit was undertaken at Birmingham and Midlands Eye Centre (United Kingdom) between December 2013 and December 2017. On 3rd December 2015 prophylactic topical antibiotic drops stopped being given routinely after every intravitreal anti-VEGF injection. We therefore compared the incidence of endophthalmitis for the two years prior to this (Dec2013-Dec2015) to the incidence in the two years since the change (Dec2015-Dec 017). Cases of endophthalmitis (following anti-VEGF injections administered only at this hospital) were identified by review of records of intravitreal biopsy and inpatient admission for endophthalmitis. Electronic records were then reviewed to determine if there was an association with anti-VEGF injection.

### Results

Over the 4 year period, overall there were 7 cases of endophthalmitis following 33,277 injections (0.21%). The incidence with topical antibiotic use was 4 per 15,545 injections (0.026%), and without topical antibiotics was 3 per 17,732 injections (0.017 %). There was no difference between these groups. Median number of days between injection and diagnosis of endophthalmitis was 4.0 [range 4-14]. Causative organisms included 6 cases of *Staph. Epidermidis* and one case *Staph. Auerus*.

### Conclusions

The incidence of endophthalmitis overall was found to be consistent with the literature. There was no increase in the number of cases of endophthalmitis when routine use of antibiotics was stopped, which would suggest that there is no benefit from topical antibiotics in this situation.

## F007

### Incidence and prevalence of glaucoma in native and immigrant groups living in Denmark

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### Purpose

To describe the prevalence and incidence of glaucoma in Denmark in the period from 1996 to 2015 with a methodological focus on the use of different register-based definitions of glaucoma. Furthermore, we investigate the prevalence within immigrant groups living in Denmark.

### Methods

All Danish citizens were included, covering around 5.4 million individuals. We define glaucoma in three ways based on the type of prescription pattern. Furthermore, we compared the results with alternative indications for glaucoma, namely in-hospital ICD-10-diagnosed glaucoma and in-hospital operation for glaucoma. Finally, we estimated the prevalence and incidence of glaucoma based on an individual having three claimed prescriptions, being diagnosed in hospital or having undergone glaucoma operation.

## Results

We estimated the total prevalence in 2015 to be around 1.6% but potentially in the range 1.4-1.9% depending on the definition. The prevalence increased during the investigated period, whereas the age-specific incidence rate seemed to be constant and even decreasing in ages over 80 years. Africans and Asians living in Denmark have significantly higher risk of glaucoma compared to Danish non-immigrants and with similar frequencies when compared with the world-wide data from their home world regions. Furthermore, Asians tend to get glaucoma at a significantly lower age, on average, compared to Danish non-immigrants, whereas Africans have a similar age-pattern. Finally, we find a high sensitivity of 80% using glaucoma medication prescription as a marker for the amount of primary open-angle glaucoma (POAG) whereas it has a lower sensitivity for primary angle closure glaucoma.

## Conclusions

This study is the first to verify anti-glaucomatous medicine prescriptions as a useful tool for glaucoma frequency estimations, with a particularly high sensitivity for POAG.

3423

### Is bigger better? Glistenings, forward light scatter and visual performance

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## Summary

Glistenings, fluid-filled microvacuoles within an intraocular lens, are a source of light scatter from particles much larger than the wavelength of light. They were first described over 30 years ago but have become much more common following the development of hydrophobic acrylic foldable intraocular lenses in the 1990s. Hydrophobic acrylic lenses have been shown to develop significant numbers of glistenings. Although it has been shown that straylight is increased for high levels of glistenings, there is no clear evidence of an effect on common measures of visual performance such as visual acuity and contrast sensitivity. One explanation could be the relatively simple ways a number of studies have quantified glistenings. Another could be the sensitivity and relevance of the visual function tests used. In this paper the results from a semi-automatic system to quantify glistenings for in vitro studies will be discussed as well as initial results from a clinical trial looking at the association between glistenings and measures of visual function. Results will be presented within the context of recently published literature, which has done much to improve our understanding of large particle light scatter in the eye.

F050

### Just how broken are we? Neck and back pathology among ophthalmologists

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## Purpose

To ascertain the prevalence and severity of neck and back pathology among ophthalmologists working in the Wessex region of the UK.

## Methods

An anonymised online survey was sent to clinicians working in the Wessex area of southern England, encompassing large teaching hospitals and smaller units. The survey was open to ophthalmologists and allied health professionals. Demographic data and basic screening questions related to ophthalmology were followed by specific questions related to neck and spine pathology. These questions were directly taken from the Extended Aberdeen Back Pain Scale, a peer-reviewed method of screening for occupational neck and back pain. The survey also had a free text suggestion box and a pre-selected topic list where participants could identify areas which they felt required improvement.

## Results

Of the 47 respondents, 79% (n=37) suffered from neck or back pain at work. 97% of those who suffered believed their pain was related to work in the Eye Department. Aberdeen Back Scores averaged at 13 points per respondent (range 3-24, where scores >10 indicate likely debilitating pathology and >20 indicate likely severe disabling elements). Results indicated a significant morbidity in terms of chronic pain, limited ADLs, painkiller use and sick leave. This compared to UK average of 0.65% prevalence of self-reported musculoskeletal back problems among health workers. Free text and selections indicated that inadequate seating (patient and clinician), workstation ergonomics and outdated equipment were the most common causes for complaint.

## Conclusions

Ophthalmologists are at very high risk of back and neck problems, more than other clinicians and the public. Early engagement with occupational health services, workplace adaptations and investment in appropriate equipment are essential to prevent injury.

## F048

### Combined phacocanaloplasty for open-angle glaucoma and cataract

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## Purpose

To evaluate efficacy, safety, and success rates of canaloplasty combined with phacoemulsification in patients with open-angle glaucoma (OAG) and visually significant cataract.

## Methods

A prospective interventional case series carried out in Lozano Blesa Clinic Hospital from November 2017 to April 2018 on 10 eyes of 10 patients who had visually significant cataract and primary OAG. All the cases had combined phacocanaloplasty. Preoperative best-corrected visual acuity, intraocular pressure (IOP), and number of antiglaucoma medications were collected and compared to postoperative levels, and complications rates were recorded.

## Results

phacocanaloplasty. Preoperative mean IOP was  $26.30 \pm 1.15$  mmHg. Postoperative IOP decreased to a mean of  $15.30 \pm 0.9$ ,  $14.75 \pm 0.8$ , and  $13.85 \pm 0.7$  mmHg at 3, 6, and 12 months, respectively, with 35% reduction from preoperative IOP level at one year follow-up visit ( $P=0.0005$ ). The number of antiglaucoma medications dropped



from mean of 1.65 preoperatively to 0.45 postoperatively. LogMAR of best-corrected visual acuity improved from  $0.6950 \pm 0.07$  preoperatively to  $0.36 \pm 0.055$ ,  $0.34 \pm 0.056$ , and  $0.033 \pm 0.052$  at 3, 6, and 12 months postoperatively ( $P=0.0005$ ). Complications were limited to anterior chamber hiphema (two cases), corneal edema (one case), that resolved in the first two weeks after surgery.

### Conclusions

Canaloplasty combined with phacoemulsification and intraocular lens implantation may be a safe and effective procedure to lower IOP in adult patients with OAG and visually significant cataract.

### F077

#### OCT- Angiography: perspectives of differential diagnostics of pathology optic nerve

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### Purpose

to estimate the significance of OCT-A in the differential diagnosis of optic nerve head drusen and papilledema.

### Methods

137 people (274 eyes) were examined: the 1st group – 68 patients with optic nerve head drusen, the 2nd group – 37 patients with papilledema and 32 normal controls. OCT-A: CIRRUS HD-OCT, Angiography 6x6mm of the macular zone.

### Results

the study showed decrease in the Full Vessel density (VD) in the 1st group —  $16,4 \pm 0,3 \text{ mm}^{-1}$  (normal controls —  $17,4 \pm 0,2 \text{ mm}^{-1}$ ;  $p=0,003$ ). The reduction in VD was noted in the superior, nasal, inferior quadrants of the outer zone ( $p<0,005$ ). No significant differences in VD between the 2nd and the normal controls diagnosed. In the 1st group, in comparison with the 2nd group, a difference in VD was found in the superior, inferior quadrants of the outer zone ( $p<0,05$ ). The values of Full Perfusion were lower in 1st group —  $0,406 \pm 0,006$  (normal controls —  $0,439 \pm 0,003$ ;  $p=0,005$ ). Perfusion in this group was reduced in the superior, nasal, inferior quadrants of the outer zone ( $p<0,001$ ). Perfusion decreased in the nasal quadrant of the outer zone in the 2nd group -  $0,468 \pm 0,005$  (normal controls  $-0,493 \pm 0,002$ ;  $p=0,03$ ). A difference in Perfusion between the 1st and the 2nd groups was revealed in the superior, inferior quadrants of the outer zone ( $p<0,05$ ).

### Conclusions

OST-A is a promising method in the diagnosis of optic nerve anomalies. The parameters Full Vessel density, Full Perfusion and also Vessel density and Perfusion in the upper and lower sectors of the outer zone of the macula have the greatest diagnostic significance in the differential diagnosis of optic nerve head drusen and papilledema.

### F108

#### Measurement of macular ganglion cell–innerplexiform layer with spectral-domain optical coherence tomography in patients with optic nerve head drusen and papilledema

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### Purpose

to examine measurement of macular ganglion cell–inner plexiform layer (GCL+IPL) with spectral-domain optical coherence tomography in patients with optic nerve head drusen and papilledema.

### Methods

175 people (350 eyes) were examined: the 1st group – 96 patients with optic nerve head drusen, the 2nd group – 47 patients with papilledema and 32 normal controls. The age of the examined persons was  $40,7 \pm 14,5$  years. SD-OCT was performed on CIRRUS HD-OCT 5000 (Ganglion cell OU Analysis: Macula Cube 512x128).

### Results

the Average GCL + IPL Thickness parameter in the 1st group ( $75,1 \pm 1,1 \mu\text{m}$ ) was significantly reduced in comparison with the 2nd group ( $79,2 \pm 1,9 \mu\text{m}$ ,  $p < 0,05$ ) and normal controls ( $82,7 \pm 0,4 \mu\text{m}$ ,  $p < 0,001$ ). Parameter Minimum GCL + IPL Thickness in comparison with the norma ( $81,1 \pm 0,7 \mu\text{m}$ ) was reliably reduced both in the 1st ( $70,5 \pm 1,3 \mu\text{m}$ ) and in the 2nd group ( $75 \pm 2,3 \mu\text{m}$ ). Only in the 1st group, in comparison with the 2nd and normal controls, a significantly significant decrease in the GCL + IPL Thickness parameter in the upper, lower, lower-temporal and upper-temporal sectors was determined ( $p < 0,05$ ).

### Conclusions

Parameter reduction: Average GCL + IPL Thickness, GCL + IPL Thickness (upper, lower, lower-temporal, upper-temporal sectors) are markers in the diagnosis of optic nerve head drusen and are early structural indicators of neuronal loss.

## F109

### Spectral optical coherence tomography with multiple sclerosis. Regression analysis

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### Purpose

To evaluate the value of the S-OCT tomography method in patients with multiple sclerosis using regression analysis

### Methods

Examined 64 patients with optic neuritis due to MS, 14 patients with optic neuritis of inflammatory etiology, and 80 patients with optic atrophy due to MS. The average RNFL thickness - protocol Optic Disc Cube 200x200 with RNFL Thickness Analysis and the thickness of the GCL + IPL complex - a protocol Ganglion Cell Analysis: Macular Cube 512 x 128. The data obtained was subjected to regression analysis.

### Results

It was revealed that for RNFL Thickness, the ROC curve is as follows: AUC = 82.7%, OR = 0.043,  $p < 0.0001$ . If the patient with MS has RNFL Thickness of less than  $62 \mu\text{m}$ , then with a sensitivity of 100% and a specificity of 93%, it can be said about the atrophy of the optic nerve in this eye. For the parameter of the average GCL + IPL thickness, AUC = 98.6%, OR = 0.017,  $p < 0.0001$ ; for the parameter GCL + IPL thickness in the lower segment AUC = 72.1%, OR = 0.107,  $p = 0.063$ ; for the parameter GCL + IPL thickness in the upper segment, AUC = 83.8%, OR = 0.082,  $p = 0.004$ . So, if the patient with MS has an average GCL + IPL thickness of less than  $52 \mu\text{m}$ , the GCL + IPL thickness in the lower segment is less than  $50 \mu\text{m}$ , and the GCL + IPL thickness in the upper segment is less than  $51 \mu\text{m}$ , with a sensitivity of 100% and a specificity of 87, 5 -93%, it can be argued that at this eye there is atrophy of the optic nerve due to MS.

### Conclusions

parameters of RNFL thickness and GCL + IPL thickness of the S-OCT method have high sensitivity and specificity in the early diagnosis of optic nerve atrophy due to MS. The value of the average thickness of the GCL + IPL complex,

determined by the S-OCT method, is a reliable marker of the process of neuroaxonal degeneration both in patients with optic neuritis and in optic nerve atrophy due to MS.

## 1231

### Scanning Laser Ophthalmoscopy – Basic Optical Principles

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#### Summary

Scanning Laser Ophthalmoscopy (SLO) produces an ocular fundus image by moving a focused laser beam via scanning mirrors over the retina in a grid pattern and registering the reflected light from each scanned point. In confocal SLO, a pinhole is placed in front of the detector to cut off scattered or defocused light coming from outside the point of interest, which otherwise can blur the image. This results in a focused, high-contrast image of a single tissue layer located at the focal plane. Tomographic information can be extracted by moving the plane of the pinhole. The use of various wavelengths allows for different applications, such as fluorescein angiography, indocyanine green angiography, and autofluorescence imaging. This lecture will present the basic principles of SLO, as well as discuss notable applications and variants of the technology.

## 1232

### Optical Coherence Tomography – Basic Optical Principles

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#### Summary

Optical Coherence Tomography (OCT) is an optical analogue to ultrasound imaging. The much higher speed of light compared with sound allows for finer cross-sectional views of the retina and anterior segment. Since it is extremely difficult to directly detect the shorter “echo” times it takes light to travel from different structures at axial distances within the eye, interferometry is used. Incident light is thus split into two beams, and the beam backscattered from the ocular tissue is then compared (“interfered”) with the beam that has traveled a known time from the reference mirror. Broadband (i.e., low “coherence”) light sources are used, because they produce a wider band of wavelengths, and thereby enable greater sensitivity in comparing the travel time differences of the two beams. In time-domain OCT, the reference mirror position is altered, so that interference patterns are generated whenever the two beams have traveled almost the same amount of time. In spectral-domain OCT, the reference mirror position is fixed and the mixed interference patterns are separated via spectral wavelength analysis. This lecture will explain underlying concepts of OCT with a discussion of cutting-edge technological developments.

## 1234

### Adaptive Optics – Basic Optical Principles

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#### Summary

Adaptive Optics (AO) refers to a technique to compensate for distortions caused by optical aberrations in the media between the camera and the object being imaged. It was originally developed for use in astronomical telescopes to compensate for optical distortions induced by the inhomogeneous earth atmosphere. It has since evolved to become a powerful clinical tool in ophthalmology. In the eye, a “wavefront sensor” (aberrometer) measures the distortion of incoming light induced by inhomogeneities within the cornea and crystalline lens, which is then “undistorted” via reflection by a deformable mirror. AO thus enables imaging of the human retina with unprecedented resolution *in vivo*, such as revealing individual photoreceptors or the walls of blood vessels. One should note that AO by itself does not provide an image; rather an AO subsystem is incorporated into an existing imaging device. AO subsystems have thus far been successfully integrated into three ophthalmic imaging devices: fundus cameras, scanning laser ophthalmoscopes, and the OCT device. This lecture will introduce the basic principles of AO, illustrate its value with state-of-the-art clinical examples, and discuss potential future applications in ophthalmology.

**3362**

### **Inherited retinal dystrophies and regulated protein clearance**

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#### **Summary**

Autophagy is the homeostatic process through which damaged proteins and organelles are cleared from the cells. Proof-of-concept studies are providing sound evidence for the use of autophagy inducers as therapeutic tools to reduce pathologic accumulation of aggregates in different neurodegenerative disorders in which protein-aggregates are toxic for the neuronal cell lifespan. Inherited retinal dystrophies (IRD), including Retinitis Pigmentosa (RP), are one of the major causes of blindness in industrialized countries. Although more than 60 RP genes have been identified to date, we are still far from an efficient therapy. Recent advances in autosomal dominant RP, which represent up to 30% of all RP cases, have pointed out the role of mistrafficking and accumulation of mutated and unfolded protein in impairing normal cellular function and inducing toxicity in photoreceptor cells. Taking this fact into consideration, we have recently identified miR-211 as lysosomal-autophagic inducer in RPE/PR crosstalks. Most importantly, we showed that pharmacological modulation on miR-211's pathway reduced pathologic accumulation of unfolded proteins and exerted a beneficial effect in a mouse model for adRP.

**F122**

### **A possible novel TGFBI mutation Ser591Phe in a Finnish family with lattice corneal dystrophy**

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#### **Purpose**

To report the phenotype of a lattice corneal dystrophy (LCD) variant caused by a possible novel mutation c.1772C>T (p.Ser591Phe) in the transforming growth factor beta-induced (*TGFBI*) gene in a Finnish family.

#### **Methods**

The index patient, a 71-year-old woman, was referred to the hospital because of bilateral LCD with progressive symptoms. She underwent standard ophthalmological examination, corneal topography, and anterior segment optical coherence tomography. Additionally, six family members (3 siblings and 3 children) were clinically

examined, and blood samples were collected to obtain DNA. Exons 4, 11-14 of *TGFB1* of the index patient and the variant c.1772C>T of the other family members were sequenced using Sanger sequencing.

## Results

Focal corneal stromal lattice lines at inferior midperiphery along with subepithelial fibrosis were noted in biomicroscopic evaluation resulting in mild deterioration of vision. No surgery was planned but annual follow-up was scheduled. Genetic testing revealed a new variant c.1772C>T in *TGFB1* leading to an amino acid change p.Ser591Phe. A daughter presenting with mild attenuation and thickening of stromal nerve fibres along with iron line in corneal stroma exhibited the same mutation as the proband. None of the other family members had similar corneal findings nor carried the mutation.

## Conclusions

Here we report a possible novel mutation in *TGFB1* underlying LCD in Finland. Our finding supplements the knowledge about the spectrum of *TGFB1* mutations related to different phenotypes of LCD.

3444

## MR-Imaging enables accurate diagnosis and follow-up for vitrectomized eyes in uveal melanoma patients

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## Purpose

Serous retinal detachment is a common finding in uveal melanoma (UM) and can be mistaken for a rhegmatogenous detachment. In vitrectomy the original vitreous can be replaced with a silicone oil (SiOil), which hinders ultrasound imaging as the soundwaves reflect at the SiOil-water interface. This severely hinders the diagnosis of the underlying UM and planning of treatment in these patients. MRI could offer the necessary imaging, but the strong off-resonance of SiOil impedes normal MR protocols. We therefore developed a dedicated protocol and evaluated it in three patients.

## Methods

A MRI protocol was developed and subsequently evaluated in three patients. The experiments were performed on a 3T or 7T Philips MRI, using a dedicated eye-coil. The first patient developed a retinal detachment after UM treatment. SiOil hindered follow up so MR scans were used to screen for UM recurrence. The second patient was referred to our hospital after UM was diagnosed during vitrectomy with SiOil tamponade. MR scans were used to plan ruthenium brachytherapy. The third patient underwent vitrectomy during which a small mass was found and an MRI was requested to determine the nature of lesion.

## Results

In all scans, conventional automatic determination of MR scan parameters failed due to the SiOil. The developed protocol resolved these issues and enabled high-resolution MR-imaging. The follow up of the first patient showed reactivity due to radiation but no tumour progression. In the second patient the MR-images showed eligibility for brachytherapy and helped to plan treatment. Finally, in the third patient signs of UM were found and biopsy confirmed the lesion to be UM.

## Conclusions

We developed a MR protocol enabling the use MRI in vitrectomised eyes with SiOil tamponade, inaccessible to conventional imaging with ultrasound.

**3441**

### **Rapid MR Imaging of Ocular Movement for Radiotherapy Planning**

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#### **Purpose**

During ocular movement, the shape and location of orbital structures, such as the optic nerve (ON) change. Currently, this change is not taken into account in the radiotherapy planning of uveal melanoma. In proton therapy for example, the planning is mainly performed in central gaze, while treatment is performed at a gaze angle that positions the tumor in front of the radiation source. This mismatch might result in unnecessary damage to critical structures. To map the location of the orbital structures as a function of gaze angle, the complete orbit needs to be imaged for at least 9 fixation directions. As conventional imaging would take too much time we aimed to develop a fast method to image the complete orbita at nine gaze angles, by combining part of the data between the gaze angles.

#### **Methods**

Both eyes of nine subjects were scanned on a 7T Phillips Achieva MRI after giving informed consent. For each gaze angle, 36% of the conventional data was acquired, resulting in a total scan time of 1 minute. Subsequently, the full images for each direction were reconstructed using shared data. The ON was manually segmented for each gaze direction to evaluate the potential of this technique for radiotherapy planning.

#### **Results**

Execution of the fixation task differed per subject. Some subjects mainly fixated with their dominant eye, while others used their left eye for the left targets and the right eye for the right targets. The average optic nerve movement between the far left and far right gaze was 6.2mm (min:3.6mm, max:8.0mm).

#### **Conclusions**

In conclusion, the location and shape of the orbital structures as a function of gaze angle can be mapped in approximately one minute, making it possible to incorporate this information in the radiotherapy planning for ocular tumors.

**3443**

### **Measuring eye deformation under different patient positions using MRI**

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#### **Purpose**

Proton beam therapy (PBT) for patients with uveal melanoma (UM) is performed in sitting position. However, most of the measurements for the treatment planning are performed in supine position. As a result, gravity works in a different direction, which might deform the eye. As radiotherapy planning for UM is increasing in precision, we aimed to assess the effect of these different positions on the ocular shape.

#### **Methods**

Seven healthy subjects were scanned in two positions on a 3T Philips scanner with a dedicated eye coil in two different positions. Firstly in supine position with the chin on their chest, so gravity works in the superior-inferior direction. Secondly lying flat on their backs, so gravity works in the anterior-posterior position. Additionally, one subject was scanned twice in the same position to assess the reproducibility of the method. The two scans were coregistered using Elastix and subsequently the sclera was segmented using Mevislab. The deformation between both scleras was measured by the Hausdorff distance. The mean and maximum distance was calculated on 95% of the points, to exclude the segmentation outliers on the border of the segmented sclera.

## Results

The maximal difference between the eye was 0.5 mm (range: 0.3mm-0.9 mm) and the mean deformation was 0.2 mm (range: 0.1-0.3mm). The reproducibility measurement showed a maximal deformation of 0.5mm with a mean of 0.2mm. For all subjects, the largest deformation was mostly observed in the nasal and temporal sides of the eye. As for proton beam therapy currently a safety margin of 2mm is used, the effect of gravity is well within these margins.

## Conclusions

Change in gravity direction might affect the shape of the eye up to 0.5mm, which is well within the current safety margins of PBT of UM.

## T005

### Strain differences in the rat streptozotocin-induced model of diabetic retinopathy

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## Purpose

Diabetic retinopathy (DR) is a visual alteration secondary to the development of diabetes, and is the leading cause of blindness. Although several in vivo models of DR exist, all of them need several months to develop complications. We are aiming that by applying various in vivo imaging capabilities with the streptozotocin DR model we would be able to identify novel biomarkers that would provide a model with much shorter follow up.

## Methods

Type 1 diabetes was induced in seven weeks old male rats, Brown Norway, Long Evans and Wistar, by injected intraperitoneally a single dose of STZ. Upon verification of hyperglycaemia the retina structure and the permeability of the blood-retinal barrier were analyzed by spectral domain optic coherence tomography (OCT) and vitrofluorophotometry (FL) as slope and AUC during 11 weeks.

## Results

The blood glucose significantly increased in all three strains. The body weight increased at a slower rate in the STZ groups for the BN and LE. For the WI-STZ group the body weight remained stable during the study, while it steadily increased in the control WI group. No changes were seen in the retina structure analyzed from OCT images as total retinal thickness, inner retinal thickness and outer retinal thickness. The FL slope for the BN and WI STZ groups increased up to week three and remained stable afterwards, the control groups had stable slopes during the whole study. Similarly AUC decreased in the BN and WI STZ groups already at two-three weeks after induction. No remarkable changes were seen in the LE group during the study.

## Conclusions

The results that we have suggest that BN and WI animals might be the ones developing the DR-related complications faster, and therefore more suitable for future studies. Ongoing analysis include: blood vessel diameter; immunohistochemistry for GFAP, IBA-1, BRN3A, VEGF and TUNEL.

**3532**

### **Immunology of conjunctival and uveal melanoma**

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#### **Summary**

Immunotherapy through immune checkpoint inhibitors has become a treatment for many malignancies. For uveal melanoma, only sporadic cases have responded, and little is known about the rare conjunctival melanoma. However, high risk uveal melanoma are known to be highly infiltrated with lymphocytes. TCGA identified four uveal melanoma subtypes, two of which are associated with metastases and a bad prognosis. Tumor types C and D show a loss of one chromosome 3 and are associated with an inflammatory infiltrate in the tumor, consisting of all types of immune cells: CD3, CD4, CD8 cells, macrophages. Macrophages especially belonged to the M2 type, which are considered pro-angiogenic. We noticed an associated between the number of macrophages and high vessel density. This may explain why the presence of an infiltrate is bad: blood vessels are essential for the release of tumor cells into the blood stream, and their transportation to distant organs.

In conjunctival melanoma, the presence of an immune infiltrate was not related to survival. 59% of primary conjunctival melanoma showed PD-L1 expression and 63% PD-1, suggesting that in this tumor, checkpoint inhibitors may be applied.

**F009**

### **Anatomical position of the raphe in the human retina**

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#### **Purpose**

Superior-inferior asymmetry plays a major role in the pathophysiology of glaucoma and other optic nerve disorders. An unbiased assessment of this asymmetry requires a detailed knowledge of the anatomy of the retinal nerve fiber bundle (RNFB) trajectories, and especially the location of the raphe. The aim of this study was to determine the position of the raphe (1) at the 3.46 mm diameter OCT measurement circle and (2) temporal to the fovea.

#### **Methods**

We traced 625 RNFB trajectories in 28 fundus images from 28 Caucasian eyes (median [IQR] spherical equivalent 0.00 [-1.25 to +1.13] D). For the localization of the raphe at the OCT measurement circle, the trajectories were – using predefined criteria - classified as belonging to the superior or inferior retinal hemifield. For the localization of the raphe temporal to the fovea, we compared the coordinates of the endings of the traced trajectories coming from the superior and inferior arcuate bundles, respectively. Results were confirmed in an independent dataset comprising of 1660 traced trajectories from 55 fundus images.

#### **Results**



At the OCT measurement circle, the raphe is located 15 degrees inferior to a horizontal line through the center of the optic nerve head (ONH; that is, halfway between 8 and 9 o'clock for the right eye). The raphe temporal to the fovea follows a horizontal line if the ONH is assumed to be located 15 degrees nasal to and 2 degrees above the fovea.

### Conclusions

At the 3.46 mm measurement circle, OCT brands use either the 9 o'clock position or a straight line connecting the center of the ONH and the fovea as a reference to separate the hemifields. This results in a 15 and 7 degrees misalignment with the anatomical raphe, respectively. The line connecting the center of the ONH and the fovea fails to describe the raphe temporal to the fovea adequately.

### T063

#### Acute Endophthalmitis after Cataract Surgery: 164 Consecutive Cases Treated at a Referral Center in South Korea

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### Purpose

To identify prognostic factors in patients referred with endophthalmitis after cataract surgery, and to evaluate the efficacy of primary vitrectomy as an initial management

### Methods

Over an eight-year study period, we retrospectively reviewed the medical records of 164 patients who were referred with endophthalmitis following cataract surgery. Treatment generally conformed to standard guidelines, although primary vitrectomy was performed in several eyes with a visual acuity of hand motion or better, depending on the patient's status. Using multivariate analysis, we analyzed outcomes to determine the effect on final visual outcome.

### Results

A final visual acuity of  $\geq 20/40$  was achieved in 92/164 (56.1%) cases after treatment. Bacterial cultures showed bacterial growth in 89/164 cases (54.3%). Among the various baseline characteristics, old age ( $P=0.028$ ), poor visual acuity at presentation ( $P=0.004$ ), gram-negative bacterial infection ( $P=0.030$ ), and short time between cataract surgery and signs of endophthalmitis ( $P=0.021$ ) were associated with poor visual outcome. The visual outcome showed no significant difference, in terms of initial treatment feature, between the primary vitrectomy with intraocular antibiotics injection (IOAI) and IOAI-only groups. However, reintervention was significantly less frequent in the primary vitrectomy group than in the IOAI group (12.5% and 32.7%, respectively;  $P=0.002$ ).

### Conclusions

Old age, poor visual acuity at presentation, type of cultured organism (gram-negative bacteria), and early onset of endophthalmitis after cataract surgery were significantly related to poor visual outcome after endophthalmitis treatment. Primary vitrectomy may decrease the need for reintervention to control infection, although the treatment showed no benefits with regard to visual outcome.

### F027

#### Clinical course of prematurity with enlarged cup to disc ratio - 24 months retrospective consecutive case series

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## Purpose

To evaluate the clinical manifestation and management of prematurity with enlarged cup to disc ratio (CDR).

## Methods

This study was a retrospective, consecutive case series study including 139 eyes of 139 subjects with prematurity with enlarged CDR. Gestational age at birth (GA), postmenstrual age, birth weight (BW), vertical CDR, horizontal CDR, and intraocular pressure (IOP) were analyzed. CDR was documented by taking fundus photography with iPhone 5 (Apple Inc., Cupertino, CA). Enrolled all prematurity divided into 2 groups on the basis of mean CDR. Mean CDR more than 0.3 defined as enlarged CDR group and less than 0.3 defined as normal CDR group. We compared demographic and clinical data between 2 groups.

## Results

Among the 139 prematurity, 37 prematurity (26.6%) showed enlarged CDR. Mean vertical CDR of enlarged CDR group was  $3.97 \pm 0.04$ , and mean horizontal CDR was  $3.81 \pm 0.05$ . Mean vertical CDR of normal CDR group was  $0.22 \pm 0.05$ , and mean horizontal CDR was  $0.19 \pm 0.04$ . In enlarged CDR group, CDR has significant negative correlation with BW. In normal CDR group, CDR has significant negative correlation with GA and BW. The baseline IOP of enlarged CDR group was  $13.1 \pm 2.7$  mmHg, and the mean IOP after using anti-glaucoma eye drops was  $10.1 \pm 2.4$ . This result was statistically significant. The baseline vertical and horizontal CDR of enlarged CDR group was  $3.97 \pm 0.04$  and  $3.81 \pm 0.05$ . And the mean vertical and horizontal CDR after using anti-glaucoma eye drops was  $3.96 \pm 0.03$  and  $3.82 \pm 0.04$ . This result was not statistically significant.

## Conclusions

A 26.6% of prematurity has enlarged CDR. Prematurity with enlarged CDR has negative correlation with BW. After using anti-glaucoma eye drops, IOP was significantly decreased and CDR does not changed after using anti-glaucoma eye drops in prematurity with enlarged CDR.

## F001

### Diagnostic accuracy of a new thresholding glaucoma screening programme using temporally modulated flicker

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## Purpose

To determine the diagnostic accuracy of the Accelerator 4-Alternative Forced-Choice Flicker Test prototype (A4FTp) for the detection of chronic open angle glaucoma (COAG) and compare its performance with currently available screening technologies.

## Methods

This prospective study included one eye of 40 participants with COAG and 38 normal controls. Participants were evaluated using the A4FTp, which determines flicker thresholds at specific regions of the visual field with high susceptibility to glaucomatous loss, Frequency Doubling Technology (FDT) (C20-5 supra-threshold programme) and the iVue Spectral Domain Optical Coherence Tomography (SD-OCT) in a random order with test results masked to the clinician conducting the reference ophthalmic examination. The accuracy of each test was evaluated by receiver operator characteristics (ROC) analysis and areas under ROC curves (AUROC) were compared.

## Results

The mean AUROC for the three tests were; A4FTp (0.824, 95% confidence interval (0.726-0.921)), SD-OCT (any RNFL parameter  $p < 1\%$  level) (0.898 (0.830-0.966)) and FDT (one or more locations missed at  $p < 5\%$  level) (0.911 (0.824-0.963)). There was no statistical difference in AUROC between A4FTP and SD-OCT ( $p = 0.181$ ) or FDT

( $p=0.118$ ). The A4FTp test duration averaged just over 2 minutes per eye, taking approximately one third of the time for completion of the HFA SITA 24-2 algorithm and twice the time for the FDT.

### Conclusions

Test accuracy for all index tests was equivalent for the detection of COAG. Time taken to complete the A4FTp was relatively short and initial results are promising. With further refinement, the A4FTp could have a future role in glaucoma detection.

2123

### Neurodegeneration in the Brain – Before or after the retina?

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### Summary

Brain imaging is a big-data science. Functional techniques in particular generate a large amount of information about visual processing but this is rarely systematically compiled to be relevant to eye disease. Functional brain imaging has indicated that the visual cortex can regain some visual function following gene therapy for an inherited retinal condition (Leber Congenital Amaurosis). However, the changes in visual cortical processing occurring as a consequence of field loss are not well understood. We review the use of MRI in examining this problem and identify the key questions to consider when designing interventional trials for inherited retinal disease causing field loss. It is now accepted that there is a greater level of neuroplasticity in the adult brain than previously thought, opening the possibility of incorporating therapeutic techniques specifically targeting the visual cortex if necessary. It is therefore critical to establish baseline changes in visual cortex structure and function caused by retinal disease in order to understand the potential interactions when developing treatments in the future.

1741

### The Spider Effect: Morphological and Orienting Classification of Microglia in Response to Stimuli in Vivo

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### Summary

The presentation will discuss the potential role the retinal microglia plays in retinal physiology and disease.

S021

### Gonococcus: A Rare Cause of Infective Conjunctivitis

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### Purpose

We present a rare case of bilateral gonococcal conjunctivitis in a 26-year-old male, complicated by corneal ulceration, to remind colleagues of the importance of taking a full history, including sexual history, in order to expedite the diagnosis of this potentially sight-threatening bacterium.

## Methods

Observational case report, with corneal photographs and OCT images of the patient's gonococcal shield ulcer.

## Results

Patient presented with two-week history of bilateral painful, red eyes with heavy purulent discharge. On further questioning, he disclosed that during a recent trip he had had 5 different unprotected sexual encounters. On examination, he had bilateral papillary conjunctivitis with purulent discharge, and right corneal shield ulcer, with 80% thinning seen on OCT. An inferior fornix conjunctival swab confirmed the presence of *Neisseria Gonorrhoeae* bilaterally. He was treated with intramuscular Ceftriaxone for 3 days and topical Chloramphenicol for 1 month. Following treatment, the organism was no longer detectable in his conjunctival swabs however his vision from the right eye remained poor.

## Conclusions

Although currently this is a rare cause of ocular infection, incidence of gonorrhoeal infection is increasing, so one might expect this to become a more commonly encountered presentation. This may be a diagnostic challenge due to many patients' reticence to disclose sexual history. Bacterial swabbing to identify bacterial sensitivities is essential in order to instigate the appropriate antibiotic therapy, especially with growing antimicrobial resistance of *N. gonorrhoeae*. This is an important diagnosis to highlight to the ophthalmologist-in-training, as delayed treatment can have catastrophic consequences.

## F076

### Retina, a mirror of the brain: an association between macular and cerebral structural integrity over age

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## Purpose

We intended to evaluate how ageing modulates the structural integrity of brain and retina in a cohort of healthy individuals, by exploring morphologic associations between the two structures.

## Methods

Overall, 56 normally sighted controls, aged between 23 to 79 years old, with no cognitive impairment were enrolled in this study. We resorted to BrainVoyager software to measure the primary visual cortex (BA17) thickness, in T1-weighted MRI structural data. Optical coherence tomography (OCT) images from macula were individualized into 10 layers throughout the *Iowa Reference Algorithms* in an automatic fashion, and an average thickness value was computed for each layer and for all lamina.

## Results

We found a correlated thickness decay of both structures over age. We obtained a negative correlation between age and the BA17 thickness ( $p < 0.0001$ ), and an overall diminished macular integrity across age ( $p < 0.0020$ ). Considering each layer individually we found that GCL ( $p < 0.0034$ ), IPL ( $p < 0.0054$ ), INL ( $p < 0.0038$ ), ONL ( $p < 0.0073$ ) and OPR ( $p < 0.0004$ ) layers decreased significantly with age, whereas OS showed the opposite pattern ( $p < 0.0043$ ). In turn, RNFL ( $p < 0.976$ ), OPL ( $p < 0.288$ ), IS/OS ( $p < 0.437$ ), and RPE ( $p < 0.706$ ) showed no significant alterations with age. Furthermore, a positive correlation between BA17 and all lamina was found ( $p < 0.0124$ ), with a major contribution of the GCL ( $p < 0.00207$ ).

## Conclusions

Our study provides evidence of an age-related decay of primary visual cortical thickness that is significantly correlated with a decrease in retinal thickness. The atrophy of both structures might jointly account for the decline of various visual capacities that accompany the aging process.

**2734**

**Development of antifibrotics for glaucoma surgery - synergy of molecular biology and bioinformatics**

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**Summary**

Glaucoma is a widespread disease in the aging population with an unmet need for effective and low-side-effect therapies. Glaucoma surgery creates an artificial drainage for the aqueous humor. Excessive wound healing processes lead to occlusion of the surgically created drainage pathways. Antifibrotics prevent this scarring (fibrosis) and thus ensure a long-lasting successful outflow. The antifibrotic treatment after glaucoma surgery is currently dominated by cell toxins from cancer therapy leading to serious tissue damage. We are attempting to reposition known drugs by analyzing gene expression data. We have developed a cell culture-based assay for testing antifibrotic agents in vitro. Thus we detected an antibiotic with antifibrotic properties, and which also shows no tissue damage in toxicological tests. We identified the agent bioinformatically from almost 1,000 active compounds, by comparing the gene expression data of known drugs with the gene expression data describing fibrotic processes. Thus, the molecular mechanisms used for the drug repositioning provide molecular biology explanatory patterns of efficacy. Specifically, the antibiotics counteracts inflammation processes underlying the fibrosis.

**F030**

**Association between autonomic dysfunction and retinal nerve fiber layer thinning in healthy subjects**

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**Purpose**

To investigate the association between autonomic dysfunction measured by heart rate variability (HRV) and retinal nerve fiber layer (RNFL) thickness in normal subjects.

**Methods**

Subjects underwent a thorough medical examination including anthropometric and laboratory examinations, heart rate variability, ocular examination, and questionnaires regarding stress, depression, and sleep. Relationship between autonomic dysfunction measured by HRV and RNFL thickness was analyzed. After dividing the subjects into tertiles based on standard deviation of NN interval (SDNN), anthropometric and laboratory examinations and questionnaires were compared among the groups.

**Results**

This study included 153 normal subjects. After adjusting for age, gender, diabetes mellitus, and hypertension, SDNN was positively correlated with temporal RNFL thickness ( $r = 0.182$ ,  $p = 0.038$ ). Subjects in the low HRV group

showed smaller body mass index, muscle mass but higher percent body fat and abdominal fat ratio than those in the high HRV group. Low HRV subjects showed higher systolic blood pressure (BP), BP difference, and higher low density lipoprotein cholesterol. Subjects with low HRV also showed lower sleep quality ( $P = 0.011$ ) and higher depression score ( $P = 0.076$ ).

### Conclusions

Subjects with autonomic dysfunction shown as low SDNN had thinner temporal RNFL. Those with autonomic dysfunction showed different anthropometric measures, lower sleep quality, and higher depression levels.

1453

### From biomarker discovery to proteomic validation using mass spectrometry

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### Summary

Biomarkers are tools of personalized medicine and potentially valuable end points for clinical studies. They can be used to measure a patient's risk to certain disease and the severity of the disease, and to predict and/or measure the patient's therapeutic response to treatment. Mass spectrometry (MS) enables detection and quantification of most proteins in a sample, and therefore has become an attractive method for biomarker discovery in the recent years. It can be used to detect changes in cellular functions and metabolism in a more comprehensive way than the traditional immunoassays. In this presentation, we will demonstrate relative quantification of 780 proteins from single tear sample during a clinical biomarker discovery study and demonstrate the validation of discovered biomarkers using faster and robust MicroLC-MSTrap instrumentation.

S100

### MicroRNA regulation underlines an interplay between autophagy and neovascularization in wet AMD

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### Purpose

VEGF-derived choroidal neovascularization coincides with cellular stress response and autophagy. Pharmacogenetics shows personalized responses to intravitreal anti-VEGF therapy. Recent observations reveal that epigenetic micro RNAs (miRNAs) play an important role in many age-related diseases and may affect treatment response. We investigated the expression of miRNAs, which are involved in the regulation of heat shock stress response, autophagy and choroidal neovascularization in serum of wet AMD patients and controls.

### Methods

TaqMan® Human MicroRNA Array was used to analyze serum samples isolated from 71 wet AMD patients and 70 sex- and age-adjusted controls. A total of 20 miRNAs that regulate HSPA1, SQSTM1/p62, Beclin-1 and VEGF-A were analyzed. The bootstrap-boosted Mann-Whitney U test was used to calculate the Benjamini-Hochberg-corrected P values and for multivariate comparison analysis the bootstrap-boosted Hotelling T test was applied.

## Results

We observed statistically significant differences between wet AMD patients and control groups in the expression of the following miRNAs: miR-34a-5p (HSPA1), miR-30a-5p (Beclin-1) and miR-34a-5p, miR-126-3p, miR-205-5p, miR-361-5p, miR-378-3p (VEGFA).

## Conclusions

The interplay between heat shock stress response, autophagy and neovascularization plays a critical role in wet AMD pathogenesis.

1753

### Antioxidants and mitochondria connection in the regulation of autophagy

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## Summary

Age-related macular degeneration (AMD) pathogenesis involves chronic oxidative stress, dysfunction of mitochondria and impaired protein degradation in retinal pigmented epithelial cells (RPE). The ubiquitin-proteasome pathway and the lysosomal/autophagosomal pathway are the major proteolytic systems in eukaryotic cells. The nuclear factor-erythroid 2-related factor-2 (NRF-2) and peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1 $\alpha$ ) are master transcription factors in the regulation of antioxidant production and mitochondrial respiratory function, respectively. The one year old global NRF-2/PGC1 $\alpha$  double knockout (dKO) mice exhibited age-dependent RPE degeneration, accumulation of oxidative stress marker for 4-HNE, proteasomal ubiquitin and autophagy markers for SQSTM1/p62, Beclin-1 and MAP1LC3A/LC3 together with increased damage of mitochondria. The NRF-2/PGC1 $\alpha$ dKO mouse is a valuable model for investigating the crosstalk of mitochondria and proteasomal and autophagy clearance in the RPE.

F041

### Reactive astrocytosis alters gene expression of ECM components in primary optic nerve head astrocytes

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## Purpose

Glaucoma is a progressive optic neuropathy that manifests in a pathological triad of optic nerve head remodeling, damage to optic nerve axons, and retinal ganglion cell death. Optic nerve head astrocytes (ONHAs) are the primary cell type in the optic nerve head. ONHAs undergo reactive astrocytosis, an activated phenotype characterized by altered gene and protein expression and increased cell migration and proliferation, early in the disease pathology. Reactive astrocytosis is thought to underlie optic nerve head remodeling. The goal of this study was to determine the detailed molecular changes in ECM associated with different methods of inducing reactive astrocytosis in ONHAs.

## Methods

We previously validated three methods for inducing reactive astrocytosis in primary rat ONHAs: hyperbaric pressure (30 mmHg above ambient pressure for 16 hr), mechanical strain (10% static stretch for 16 hr) using a Flexcell® FX-5000 tension system (Flexcell International) and siRNA knockdown of Loxl1, an enzyme involved in the crosslinking of collagen and elastin fibers.

## Results

qPCR analysis revealed a statistically significant reduction in normalized mRNA levels of collagen ( $0.64 \pm 0.04$ ) and elastin ( $0.38 \pm 0.11$ ) due to hyperbaric pressure. Similarly, mechanical strain induced a downregulation of collagen ( $0.58 \pm 0.04$ ) and elastin ( $0.53 \pm 0.14$ ) mRNA levels, while Loxl1 knockdown resulted in significantly reduced elastin mRNA levels ( $0.63 \pm 0.10$ ). Similar decreases were seen in other genes in ECM synthesis pathways, including fibulin 2, fibulin 4, and fibrillin 1. Analysis of ECM protein expression is currently underway.

## Conclusions

The similar changes observed in ECM composition due to various methods of inducing reactive astrocytosis support a unified hypothesis for the pathophysiological changes underlying optic nerve head remodeling in multiple subtypes of glaucoma.

1854

### Standardization of preclinical testing platforms for topical ophthalmic drugs

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## Summary

In this presentation, the latest efforts in the standardization of preclinical testing platforms for topical ophthalmic drugs will be presented. These include *in vitro* and *ex vivo* methods to quantify corneal cytotoxicity and permeability across the cornea, as well as approaches to improve the quantification of *in vivo* readouts from preclinical models for dry eye disease (DED). The development of artificial corneas has been driven by an urgent clinical need for alternatives to human donor tissue in corneal transplant surgery. However, challenges persist in developing artificial corneas for drug development and predicting permeability of experimental compounds. Novel strategies to improve artificial corneas for permeability testing with the ultimate goal of replacing rabbit corneas in preclinical lead identification will be discussed. In contrast, the murine desiccating environment model for DED is a well-established paradigm for testing novel drug candidates that can reduce corneal surface inflammation and prevent T-cell infiltration/leukocyte activation. The validation of our SiccaSystem™ desiccating environment model using FDA- and EMA-approved reference compounds in different experimental paradigms will be presented.

3133

### Corneal surface ablation and CXL for visual improvement in keratoconus: when, what and how.

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## Summary

Didactic approach to the management of progressive cornea ectasia associated with keratoconus and refractive surgery. Several surgical treatment modalities utilized internationally will be presented, including: collagen cross-linking with ultraviolet radiation A in order to halt ectasia, combined in some cases with a customized excimer laser ablation to facilitate visual rehabilitation, These alternatives to intracorneal ring segment implantation,



lamellar grafts as well as penetrating graft techniques will be analyzed. Surgical and medical treatment technique, indications, potential complications and their management as well as clinical experience pearls will be presented.

The participants will share our vast experience in managing progressive keratoconus and post-LASIK ectasia in order to visually rehabilitate these patients. Pearls on indications, patient selection, surgical technique and complication management for safe and effective results will be presented and discussed with the participants.

## **S022**

### **The study of conjunctival bacterial flora isolated in patients undergoing intravitreal injection and cataract surgery**

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#### **Purpose**

The purpose of this study were to investigate the composition of the normal conjunctival flora and to evaluate in vitro susceptibility to ciprofloxacin, levofloxacin and moxifloxacin of *Staphylococcus epidermidis*(SE).

#### **Methods**

From April 2014 to September 2017, conjunctival swabs taken from 374 eyes of 187 patients who underwent intravitreal injection and cataract surgery were inoculated onto 5% blood agar plates. The isolated bacteria were identified using MALDI-TOF MS (Bruker Daltonics GmbH, Germany). Micro-dilution antimicrobial susceptibility test was performed for evaluating in vitro susceptibility to ciprofloxacin, levofloxacin and moxifloxacin of SE in accordance with Clinical and Laboratory Standards Institute Performance Standards.

#### **Results**

Three hundred three microorganisms were isolated from 374 eyes. Gram-positive bacteria were found predominantly (72.94%, 221 of 303 isolates) and SE was the most frequently isolated organism, accounting for 33.7% (102 of the 303 isolates). *Corynebacterium* species was the second most common gram-positive organism in 17.82% (54 of the 303 isolates). Gram-negative organisms were 27.1% (82 of the 303 isolates) and *Ochrobactrum* species was most frequently isolated (10.9%, 33 of the 303 isolates), followed by *Pseudomonas* species (3.6%, 11 of the 303 isolates). For 82 SE isolates, the in vitro resistant rate to ciprofloxacin, levofloxacin and moxifloxacin were 23.2% (19 isolates), 24.4% (20) and 17.07% (14), respectively.

#### **Conclusions**

The percentage of SE was decreased in gram-positive bacteria, but the percentage of *Corynebacterium* was relatively increased. Among the gram-negative bacteria, *Ochrobactrum* species was the most frequently isolated organism. Finally, the quinolone resistance rate of SE was increased and strains resistant to all quinolones were increased.

## **T058**

### **three year real-life outcomes from the use of the fluocinolone acetonide implant (Iluvien) in the treatment of refractory DMO**

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#### **Purpose**

Fluocinolone acetonide (FAc) is a 190 mcg intravitreal implant which has been approved by NICE guidelines for the treatment of persistent chronic diabetic macular oedema (DMO) in pseudophakic patients who have not responded sufficiently to first line treatment. Since the FAME studies, there has been little evidence from the results of the intravitreal implant in a real world setting. This study aims to report three-year real life outcomes of ILUVIEN in patients who received the implant in our hospital

### Methods

Retrospective case series of 25 eyes of 22 consecutive diabetic patients who received the FA implant for the treatment of persistent chronic DME and were followed up for 36 months. Data analysis included the evaluation of best corrected visual acuity in ETDRS letters, central retinal thickness and intraocular pressure at baseline, 12 months, 24 months and 36 months

### Results

All eyes were followed up for at least 36 months. 5 eyes received a second implant at a mean of 24 months (range: 16-30 months). The mean visual gain at 36 months was +3.6 ETDRS letters with 7 eyes (28%) gaining 10 or more ETDRS letters from baseline. The mean reduction in central retinal thickness was 110µm at 36 months compared to baseline. Rescue treatment with a total of 5 intravitreal triamcinolone injections was required for 4 eyes throughout the 36 month period. IOP values of more than 21mmHg were observed in 14/25 eyes (56%), of which 6 eyes underwent glaucoma surgery and 8 eyes were successfully treated with IOP-lowering drops.

### Conclusions

Our results demonstrate positive three year outcomes of the FAc implant on the treatment of chronic diabetic macular oedema. However, IOP monitoring remains essential in patients receiving the implant.

1254

### Mitochondria in the regulation of inflammation

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### Summary

Among various important contributions e.g. to cell cycle, apoptosis, and metabolism, mitochondria produce the majority of energy needed by eukaryotic cells. The production of energy through aerobic respiration generates reactive oxygen species (ROS) as a byproduct. ROS are needed for regulating signal transduction in cells, and they promote also the production of pro-inflammatory cytokines. In normal conditions, cells have various antioxidants keeping the ROS levels in balance. In aged cells, antioxidative systems deteriorate and ROS production accelerates, which together result in excessive ROS levels. This oxidative stress has been associated with numerous inflammatory diseases. Aged mitochondria are efficient in producing ROS, and those organelles should be removed by autophagy. However, aging impairs autophagy, which further enables the excessive ROS production by damaged mitochondria. This creates a vicious circle where impaired autophagy, dysfunctional mitochondria, are inflammation are central players regulating each other.

1463

### How to bare the great imitators

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### Summary

Syphilis and tuberculosis are known as "the great imitators" in internal medicine. These two infectious agents are also responsible for a wide range of ophthalmic conditions, often mimicking non-infectious entities. The differential diagnosis between infectious and non-infectious uveitis is of paramount importance, since the proper treatment of infectious uveitis will often result in complete and lasting cure, whereas immunosuppressive drugs in infectious uveitis often lead to dramatic worsening. The diagnosis of syphilitic uveitis is relatively straight forward: if one suspects the disease a battery of sensitive and specific serologic tests will bare the imitator. Despite the availability of newer tests such as the interferon gamma release assays (IGRA), the diagnosis of tuberculous uveitis remains a difficult one. In doubtful cases a therapeutic trial with antituberculous agents should be considered.

**2624**

#### **Glaucoma, surgical treatment in uveitic and JIA patients**

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#### **Summary**

The proper treatment of uveitic glaucoma depends on the identification of the mechanism(s) responsible for this secondary glaucoma. Both secondary open and closed angle glaucoma occur in uveitis patients. Careful gonioscopy combined with other investigative procedures (anterior chamber OCT, UBM,...) will contribute to identify the pathogenetic mechanism(s). Surgical options for uveitic glaucoma include surgical iridectomy (angle closure), angle surgery e.g. trabeculotomy (steroid glaucoma), filtrating surgery e.g. trabeculectomy or non-penetrating deep sclerectomy with anti-metabolites (mitomycin or 5-FU), diode laser destruction, or setons (Baerveldt or Ahmed).

The indications, results and complications with these different modalities will be discussed. Case presentations of the surgical treatment of uveitic glaucoma in patients with juvenile idiopathic arthritis will illustrate some of the important concepts.

**S055**

#### **Corneal scattering and biomechanical behavior in eyes with Fuchs' endothelial dystrophy**

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#### **Purpose**

To study the light forward and back scatter, the biomechanical properties and ultrasound pachymetry in corneas suffering from Fuchs' endothelial dystrophy (FED) in early stages of the disease.

#### **Methods**

30 eyes from 15 patients diagnosed with mild FED (specular microscopy changes but without clinical corneal edema) were studied. All eyes underwent full ophthalmological evaluation including: light backscatter analysis using the Pentacam® HR with the corneal densitometry map software, forward light scatter analysis using the C-Quant®, biomechanical corneal analysis with Corvis and ultrasound (US) pachymetry.

#### **Results**

We observed an abnormal light backscatter in 92.86% of the eyes, mainly in the central region from 0 to 2 mm (75% of cases). We found no statistical association between forward and backward light scatter ( $p=0.59$ ). In addition, central corneal 0-2mm light backscatter showed an statistically significant association with US pachymetry ( $R= 0.61$ ,  $p<0.01$ ) and Corvis parameters such as pachymetry ( $R= 0.61$ ,  $p<0.01$ ) and deformation amplitude ( $R= 0.55$ ,  $p<0.01$ ).

### Conclusions

We observed structural and functional corneal changes in early stages of FED without clinically relevant corneal edema. Further studies are needed to know if forward or backward light scatter measurement could be a useful tool for the evaluation of FED in early stages.

## S106

### Intraocular lens surface roughness studied by atomic force microscopy in different environments in vitro

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### Purpose

To measure the anterior surface roughness of the of the Envista Bausch and Lomb MX 60 intraocular lens (IOL) using an atomic force microscopy (AFM) in different environments.

### Methods

A single Envista Bausch and Lomb MX 60 IOL (+21D power) was used for this study. We performed a roughness analysis using atomic force imaging with a JPK NanoWizard II® AFM coupled to a Nikon Eclipse Ti-U inverted optical microscope using Olympus OMCL-RC800PSA commercial silicon nitride cantilever tips (0.05 N/m, 18 kHz), with typical 15 nm radius at the end. Vertical accuracy of the instrument is in the order of 0.1 nm. As our aim was to detect differences in the central area of the IOL anterior surface in different environments, we performed our measurements with the IOL immersed in its own buffer carrier, in distilled water and after spontaneous drying. Liquid exchange and evaporation was performed without moving the IOL from its fixation in order to make all measurements in the same exact area. Three different resolution areas were studied:  $2 \times 2 \mu\text{m}^2$ ,  $10 \times 10 \mu\text{m}^2$  and  $50 \times 50 \mu\text{m}^2$ . We measured surface roughness using the root-mean-square (RMS) value within the given areas.

### Results

At  $2 \times 2 \mu\text{m}^2$  RMS increases from air exposure (2,66 nm) to distilled water (3,32 nm) and buffer (3,36 nm). The same increment was found at  $10 \times 10 \mu\text{m}^2$  (3,34 vs 4,13 vs 4,14 nm) and  $50 \times 50 \mu\text{m}^2$  (3,44 vs 4,26 vs 4,28 nm).

### Conclusions

Anterior surface roughness of central area of Envista Bausch and Lomb MX 60 IOL changes depending on the environment it is placed. Further studies are needed to know if this might interfere in its optical performance in vivo.

## S035

### Efficacy and tolerability of Blephademodex® in patients with demodex blepharitis

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### **Purpose**

To evaluate the performance of Blephademodex® in patients suffering from Demodex-associated blepharitis.

### **Methods**

Multicenter, open-label, randomized, 2 parallel group study conducted in patients suffering from Demodex-associated blepharitis. Forty-nine patients were randomly assigned to two different regimes with Blephademodex, once daily application (in the evening, Group1) and twice daily application (morning and evening, Group2), for 29 days. Ocular discomfort, slit lamp examination, corneal fluorescein staining, global ocular performance and tolerance were assessed by investigator. Global ocular tolerance was recorded by the patient at days 8 and 29.

### **Results**

There was no relevant difference between treatment groups in demographics and medical/surgical history. However, Group 2 tended to have a higher cylindrical dandruff count at baseline (mean  $20.0 \pm 12.6$  vs  $15.1 \pm 11.7$  in Group 1,  $p=0.1089$ ) and higher scores for symptoms at baseline. A statistically significant improvement in ocular comfort was seen in both groups compared to baseline, after 8 and 29 days. Eyelid margin redness was also significantly reduced in both groups. Global performance of Blephademodex was considered by the investigators as satisfactory/very satisfactory for 95.7% of patients in Group 1 and 100% for those in Group 2. At Day 29, all patients and investigators considered the ocular tolerance for Blephademodex as satisfactory/very satisfactory in both groups.

### **Conclusions**

Ocular signs and symptoms in patients suffering from Demodex-associated blepharitis were significantly reduced after 29 days of treatment with Blephademodex wipes applied once (morning) or twice (morning and evening) daily. Both treatment regimens were well tolerated and can be chosen according to severity of blepharitis symptoms.

**1462**

### **How to detect a viral retinitis**

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### **Summary**

Viral retinitis is a group of sight-threatening conditions mainly caused by herpes viruses. They may occur as an isolated ocular disease or in association with systemic illness or comorbidities. Early diagnosis of viral retinitis is of utmost importance for prompt initiation of appropriate treatment to prevent ocular and systemic morbidity. Diagnosis of viral retinitis is primarily based on history and a careful and comprehensive clinical examination. Anterior uveitis with fine or granulomatous keratic precipitates and elevated or normal intraocular pressure is common. A dilated fundus examination is mandatory not to miss posterior segment involvement including vitritis, macular edema, optic disc edema, and typical peripheral retinal lesions and retinal vascular changes.

Although the diagnosis of viral retinitis is primarily clinical, PCR applied to aqueous humor or vitreous sample is recommended to confirm the definitive diagnosis, exclude other entities, and identify the causative virus.

**2324**

### **Mitochondrial genetic variation and its implications for glaucoma**

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## Summary

The lecture will cover the following areas:

- • The importance of mitochondria to a healthy optic nerve
- • Well-established mitochondrial optic neuropathies
- • Mendelian versus complex genetics
- • Current evidence for mitochondrial genetic dysfunction in glaucoma
- • New approaches to assessing contribution of mitochondrial processes in complex disease
- • How new evidence will aid the development of new treatments

## S066

### Results of treatment of transient dry eye syndrome with increasing of intraocular pressure in the patient after LASIK

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## Purpose

To estimate the results of treatment of syndrome of dry eye for a patient after LASIK complicated by transient hypertension

## Methods

The article presents a clinical case of treatment of a patient with medium degree myopia, who underwent personalized laser correction of vision (SuperLASIK). Pre- and postoperative examination was performed: biomicroscopy, autorefractometry, pneumotonometry, keratotopography, optical coherence tomography of the anterior eye segment (DRI OCT TRITON, Japan). At the stage of formation of the corneal valve, an automatic microkeratome (Zyoptix, Technolas) with a head of 120 µm was used. The next stage was the excimer laser vision correction system Technolas 217Z100P (Germany).

## Results

After the surgery the patient had a high visual acuity with signs of tear fluid deficiency. Since the 2nd week after the surgery, in addition to a feeling of dryness and discomfort in the eyes, complaints have arisen about the rapidly worsening of vision in both eyes with transient increase in intraocular pressure (IOP) and swelling of the flap. Against the background of the drug therapy, it was possible to stabilize visual functions

## Conclusions

The appearance of transitory edema of the cornea with increasing intraocular pressure occurs within 2 weeks after surgery and against the background of glucocorticosteroid withdrawal and antihypertensive medications the edema of the cornea is stopped, the visual functions stabilize

1844

### **Familial adenomatous polyposis and associated differential diagnosis of RPE lesions**

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#### **Summary**

Pigmented lesions of the retinal pigment epithelium (RPE) are in general benign but can be related to systemic cancer. Familial adenomatous polyposis (FAP) is a genetic disorder resulting from a mutation in the adenomatous polyposis gene (APC) gene, that is characterized by the development of hundreds to thousands of adenomas in the rectum and colon and almost all patients will develop colorectal cancer. APC is a tumour suppressor gene located on the long arm of chromosome 5 in band q21 (5q21). Mutations at specific positions can cause lesions of the RPE that have been described as atypical congenital hypertrophy of the retinal pigment epithelium (CHRPE).

3635

### **Size and chromosomes in uveal melanoma**

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#### **Summary**

The size and location of the uveal melanoma have been shown by several groups to be predictive of survival in patients with uveal melanoma. Within the last decades loss of chromosome 3 and gain of chromosome 8 have also been correlated to increased metastatic death of uveal melanoma. Even though there is a correlation between bigger tumours and chromosome alterations, copy number status of chromosome 3 and 8 can be used to further stratify uveal melanoma patients into low-risk and high-risk groups.

3634

### **Mutations as prognostic factor in uveal melanoma**

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#### **Summary**

Activating hotspot mutations in GNAQ/GNA11 occur in 83–95% of all uveal melanoma (UM) and have been identified as early events in tumorigenesis without any prognostic association.

Hemizygous mutations in BAP1 were found in most of the monosomy 3 UM, resulting in inactivation of BAP1 protein and loss of expression. Overall an aberrant BAP1 is associated with metastatic disease within five years after diagnosis. SF3B1 mutations are correlated with late metastasis with a median of approximately 8.2 years. EIF1AX mutations are associated with favourable prognostic features and prolonged survival.

In general, BAP1 negative UM are characterized by monosomy 3 (95% of cases) and gain of the entire long (q) arm of chromosome 8 (80%). Gain of chromosome 8q is often accompanied by loss of chromosome 8p. SF3B1 mutated UM are characterized by gain of chromosomes 6p (85%) and 8q (73%), and loss of chromosomes 6q (52%) and 11q (45%). EIF1AX mutated UM show gain of chromosome 6p in 65% of the cases. The highest percentages of aneuploidy are found in BAP1 negative UM (11.8%) followed by SF3B1 mutated UM (9.1%). EIF1AX mutated UM

harboured the least percentage of aneuploidy (1.7%). In SF3B1 mutated UM most chromosomal structural variants are found.

## **T007**

### **Functional and histological evaluation in iodoacetic acid induced photoreceptor degeneration feline model**

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#### **Purpose**

To establish the photoreceptor degenerated feline model with IAA(Iodoacetic acid)

#### **Methods**

From January to October 2014, 11 adult feline(22 eyes) over 2 years of age were included. The mean body weight was  $1.61 \pm 0.19$  kg, and sex was 3 males and 6 females. After 12 hours fasting, 20 mg/Kg iodoacetic acid was intravenous injected via femoral vein except two feline for control group. Before injection and at 1st, 2nd, 3rd and 4th week after injection, they were taken with ERG(Electroretinogram). FA(Fluorescein angiography) were done, before injection and 4th week after injection. Then they were sacrificed and enucleation were done. A standard paraffin section, HE(hematoxylin-eosin) and IHC(Immunohistochemistry) stained retinal section was processed. And histologic study was done.

#### **Results**

In ERG, the mean amplitude of b wave was significantly decreased at 1st to 4th week after injection on both rod and cone cell responses compared with baseline examination( $p=0.00, 0.00, 0.00, 0.00$ ). FA study shows no significant change between before injection and after injection. Histologically, both the optical microscope and the fluorescence microscope study showed a significant decrease in the nucleus of the outer nuclear layer of the retina( $p=0.00, 0.00$ ), and there was a significant reduction in rod cell layer( $p=0.00$ ).

#### **Conclusions**

IAA induced feline model shows the decrease of b wave amplitude of ERG in functional evaluation, and reduction of outer nuclear layer and rod cells in histological examination. So they can be used as a useful animal model for retinal degeneration.

## **F026**

### **Clinical implications of reactive epiretinal patches in open-angle glaucoma**

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#### **Purpose**

We elucidated reactive epiretinal patches (REPs) in open-angle glaucoma and investigated associated clinical factors with it.

#### **Methods**

A total of 85 eyes of 85 glaucoma patients were enrolled. Reactive epiretinal patches were defined as mottled, geographic, amorphous, and transparent changes of the retinal surface. The Red-free photography(VX-10; Kowa Optimed) and Spectralis(Heidelberg Engineering) optical coherence tomography(OCT) were used to detect REPs. Peripapillary retinal nerve fiber layer(RNFL) and macular ganglion cell-inner plexiform layer thicknesses(GCIPL)



were measured by the Cirrus(Carl Zeiss Meditec) OCT. For functional evaluation, mean deviation and mean sensitivity of central cluster values were measured using 24-2 standard automated perimetry.

### Results

Reactive epiretinal patches were found to occur in 32 eyes, 37.6 % and 53 eyes did not have REPs in any eyes. The presence of diabetes, hypertension, and disc hemorrhage had a significant influence on the presence of REPs( $p = .038$ ,  $.001$ , and  $.009$ , respectively), and lower central retinal sensitivity was strongly associated with REPs( $p = .024$ ). Group with REPs had a significant lower thickness in inferior peripapillary RNFL quadrant compared with group without REPs( $p = .039$ ), and there were no considerable differences in GCIPL thickness in macular area. In regression, the presence of hypertension and disc hemorrhage were identified as significant clinical factors associated with REPs in glaucoma patients( $p = .015$ , and  $.047$ , respectively).

### Conclusions

Reactive epiretinal patches in open-angle glaucoma are significantly associated with disc hemorrhage and cardiovascular disease and more frequently identified in the eyes with a lower central retinal sensitivity. We carefully suggest that REPs could be one among morphologic variables to detect merged cardiovascular risk factors in glaucoma.

### F083

#### Early prognostic factor for irreversible damage by optical coherence tomography in patients with ethambutol-induced optic neuropathy

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### Purpose

To evaluate the early prognostic factor for irreversible damage by optical coherence tomography(OCT) in patients with ethambutol-induced optic neuropathy(EON).

### Methods

This was a retrospective study of 140 eyes of 76 patients being treated with ethambutol(EMB). Follow up period were at least 2 years and cirrus OCT tests including baseline test were performed more than twice. All patients underwent a neuro-ophthalmologic examination, including best corrected visual acuity(BCVA), color vision test, automated perimetry and fundus photography. Patients were classified into two groups, one was a reversible group, in which patients exhibited the clinical symptom and signs of EON but recover, the other one was an irreversible group that was not recovered at 2 years after cessation.

### Results

There was no significant difference in baseline OCT parameters and demographic factors between two groups except BCVA and mean deviation of automated perimetry at last follow up. Peripapillary retinal nerve fiber layer(RNFL) thickness was initially increased in both groups, it was finally recovered in reversible group but it started to decrease sharply after 12 months in irreversible group. Macular ganglion cell-inner plexiform layer (GCIPL) thickness was also initially increased in both groups, there was no significant change during follow up in reversible group, but in irreversible group, it began to decrease rapidly, and remained thinner than baseline after 4 months. The RNFL/GCIPL thickness ratio calculated from these results was significantly different at 4 months( $P = 0.0013$ )

### Conclusions

The RNFL/GCIPL thickness ratio that maximize difference between two groups can be an early prognostic factor of EON. Especially, GCIPL thickness change within 4 months helps to predict a reversibility of EON.

#### **T014**

### **Repeatability of vessel density measurements using optical coherence tomography angiography in retinal diseases**

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#### **Purpose**

To analyze the repeatability of vessel density (VD) using optical coherence

tomography angiography (OCTA) in patients with retinal diseases

#### **Methods**

Design: A prospective cohort study Methods: Patients diagnosed with retinal diseases (DME, RVO with macular edema, ERM, wet AMD) without history of intraocular surgery were enrolled. Two consecutive VD measurements using OCTA were analyzed. The intraclass correlation coefficient (ICC), coefficient of variation (CV), and test-retest standard deviation of VD measurements were assessed, and linear regression analyses were conducted to identify factors related to repeatability.

#### **Results**

A total of 134 eyes were analyzed. 20 eyes had DME, 44 eyes RVO with macular edema, 50 eyes ERM, and 20 eyes wet AMD. Mean age was 64.9, mean BCVA 0.24, mean spherical equivalent -0.16, and mean axial length 23.7 mm. Mean CMT was 391.6  $\mu$ m and mean GC-IPL thickness was 61.4  $\mu$ m. In all 4 of retinal diseases, ICC and CV of full VD were 0.812, 6.72 % respectively. Univariate analyses showed that the BCVA (B, 8.553;  $p=0.031$ ), mean signal strength (B, -1.688;  $p=0.050$ ), mean CMT (B, 0.019;  $p=0.015$ ), and mean GC-IPL thickness (B, -0.103;  $p=0.001$ ) were significant factors that affected the repeatability. Multivariate analyses of these factors showed that there was significant result for GC-IPL thickness.

#### **Conclusions**

Measurements of VD using OCTA shows relatively good repeatability in various retinal diseases. And BCVA, signal strength, CMT, and GC-IPL thickness can affect the repeatability so we should consider this when analyzing VD.

#### **T056**

### **Analysis of factors related to early macular edema recurrence after intravitreal dexamethasone implant treatment in diabetic macular edema**

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#### **Purpose**

To evaluate factors that affect early recurrence of diabetic macular edema (DME) after intravitreal dexamethasone therapy in DME refractory to bevacizumab.

#### **Methods**

Twenty nine eyes of 24 subjects who had not responded to several injections of bevacizumab for DME underwent dexamethasone implant injection. Changes in best-corrected visual acuity (BCVA) and central macular thickness (CMT) during the one year following dexamethasone injection were evaluated. Additionally, eyes were categorized into early recurrence group and late recurrence group based on whether or not have retreatment due to recurrence within 3 months, and compared between two groups.

## Results

Fourteen eyes were included in early recurrence group and 15 eyes were included in late recurrence group. Statistically significant improvement in CMT was noted at one, three, six, twelve months from baseline after dexamethasone injection in both groups ( $p < 0.05$ ), but there were no significant improvements in BCVA despite the tendency to decrease from baseline in both groups. The initial retinal edema reduction rates during the first month after injection were 48.3 % in early recurrence group and 34.8 % in late recurrence group, respectively ( $p = 0.029$ ). In the early recurrence group, the number of inner retinal cysts and frequency of subretinal fluid were significantly higher than in the late recurrence group ( $p < 0.05$ ).

## Conclusions

Intravitreal dexamethasone implants effectively reduced CMT in DME refractory to bevacizumab, but limited improvement in BCVA. The greater the reduction rate of CMT during the first month after injection, the greater the number of inner retinal cysts, and the presence of subretinal fluid were associated with early recurrence after dexamethasone implant injection.

## T066

### Incidence and Clinical Predictors of Ocular Candidiasis in Patients with Candidemia

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## Purpose

To identify the incidence and risk factors predictive of ocular candidiasis in patients with candidemia and report recent changes in the epidemiology of ocular candidiasis.

## Methods

We retrospectively analyzed the charts of all patients who were diagnosed with candidemia and underwent ophthalmic examinations within 14 days after candidemia onset at Asan Medical Center during January 2007 – December 2015. Data regarding patients' demographics, candida species grown, antifungal agents used, number of initial positive blood culture specimens, the duration of candidemia, visual symptoms, known risks of disseminated candidiasis, and clinical outcomes were noted. Logistic regression analysis was used to determine the factors significantly associated with intraocular candida infection.

## Results

During the 9 year study period, 1,213 patients had candidemia and 634 (52%) patients underwent ophthalmic examinations. Of 634 patients, 60 (9.5%) had ocular involvement, including 17 (2.7%) with endophthalmitis and 43 (6.8%) with chorioretinitis. All of patients with ocular involvement received prolonged systemic treatments and 12 patients (20%) required additional ocular treatments. Of the 37 patients with ocular involvement who could communicate, only 14 (38%) had visual disturbances. In a multivariate analysis, *Candida albicans* species, history of recent gastrointestinal surgery, and long duration of candidemia were risk factors for ocular involvement. The number of patients with candidemia and ocular candidiasis continues to increase in recent years.

## Conclusions

A significant rate of ocular involvement was noted in patients with positive fungal cultures referred for ophthalmologic consultation. Considering increasing incidences of ocular candidiasis and possibilities requiring ocular treatment, meticulous examinations are required for patients at risk.

## T032

### Dietary patterns and age-related macular degeneration in Korean population

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### **Purpose**

To evaluate the association between dietary patterns and age-related macular degeneration risk in the Korean population.

### **Methods**

Food intake frequency and age-related macular degeneration data were collected from Korean National Health and Nutrition examination Survey participants between 2010 and 2011. Diagnosis and the severity of the age-related macular degeneration were determined using fundus photographs. A food frequency questionnaire was used to identify dietary patterns. Logistic regression analyses of the mean intake frequency of food groups were used to assess associations between dietary patterns and the risk of age-related macular degeneration.

### **Results**

Among the participants, 6.8% had early stages of age-related macular degeneration, and 0.6% had late stages. Higher fish intake was associated with 39% reduced odds of early age-related macular degeneration (third vs. first quartile) (odds ratio [OR] 0.61; 95% confidence interval [CI], 0.40-0.92), whereas a higher intake of legumes was associated with 59% reduced odds of late age-related macular degeneration (third vs. first quartile) (OR, 0.41; 95% CI, 0.05-0.09). Adjusted ORs trended downward across quartiles for early age-related macular degeneration in the fruit group and trended upward across quartiles for late age-related macular degeneration in the meat group.

### **Conclusions**

Our data indicate that more frequent intake of fish is associated with lower odds of early age-related macular degeneration, whereas a high intake of legumes is associated with lower odds of late age-related macular degeneration in the Korean population. These results suggest that healthy dietary patterns may protect against early and late age-related macular degeneration.

## **T075**

### **Optical Coherence Tomographic Changes of Subretinal Proliferation in Rhegmatogenous Retinal Detachment with Scleral Buckling**

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### **Purpose**

To observe the time course of subretinal proliferation (SRP) using optical coherence tomography (OCT) in patients who underwent scleral buckling (SB) surgery for the treatment of rhegmatogenous retinal detachment (RRD).

### **Methods**

A descriptive study of ten cases from nine patients who underwent SB with external drainage for RRD with SRP was performed. Fundus photographs and serial OCT images were retrospectively analyzed. Analysis included the shape, preoperative and postoperative locations, invagination, size reduction, heterogeneity of SRP, and absorption of subretinal fluid (SRF).

### **Results**

The mean patient age at the time of surgery was 19.2 years. Mean follow-up period was 66.3 weeks. One patient had a membranous SRP, while the rest had strand-like SRPs. Preoperative SRP locations were beneath the retina in six cases, intraretinal in one case, and between the retina and retinal pigment epithelium (RPE) in one case. One case demonstrated SRP heterogeneity. None of the cases had complete resolution of SRP. Final SRP locations were intraretinal in two cases, on the RPE in seven cases, and beneath the retina in one case. In two cases, the SRP invaginated into the retina while SRF was absorbed.

## Conclusions

Detached retina can be re-attached successfully following retinal break occlusion by SB, although the remaining SRP can disturb the re-attachment. OCT images of SRP demonstrated various features in terms of location, reflectivity, and morphology. Before surgery, the SRPs were typically strand-like types located beneath the retina. Following re-attachment, they were located on the RPE. In some cases, they invaginated into the retina.

## T085

### Pars plana posterior capsulectomy during combined pars plana vitrectomy and cataract surgery

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## Purpose

To evaluate the effect and safety of pars plana capsulectomy during combined pars plana vitrectomy and cataract surgery.

## Methods

Patients (n = 76) who underwent combined vitrectomy and cataract surgery and had followup of more than 2 months were enrolled in this study. The patients were categorized into group A (patients with pars plana capsulectomy during surgery) and group B (patients without pars plana capsulectomy during surgery). The medical records were reviewed and best corrected visual acuity (BCVA), intraocular pressure, intraocular lens (IOL) stability, and inflammation were analyzed.

## Results

Group A included 17 males and 20 females with a mean age of 60.58 years. Group B included 21 males and 18 females with a mean age of 64.3 years. Preoperative diagnoses 106 were epiretinal membrane, proliferative diabetic retinopathy, macular hole, vitreomacular traction, and vitreous hemorrhage. Preoperative BCVA was logarithm of the minimum angle of resolution (logMAR)  $0.65 \pm 0.32$  in group A and  $0.56 \pm 0.21$  in group B. Postoperative BCVA was  $0.32 \pm 0.11$  and  $0.38 \pm 0.14$ , respectively, showing no significant difference ( $P = 0.332$ ). In group A, no case had capsular opacity that needed additional capsulotomy. IOL decentration or gas prolapse to the anterior chamber was not identified in either group.

## Conclusions

Pars plana posterior capsulectomy during combined vitrectomy and cataract surgery is a safe and effective procedure.

## 026

### Pigmented tumor

1843

**BAP1-TPDS: a wide-ranging tumor predisposition syndrome**

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**Summary**

BAP1 tumor predisposition syndrome (BAP1-TPDS) is a new and, thus, still evolving autosomal dominant genetic cause of familial aggregation of certain types of cancer – especially uveal melanoma and mesothelioma (both rare in general population) followed by cutaneous melanoma and renal cell cancer, clear cell type (both frequent also in the general population) – and some related neoplasms – especially atypical Spitz skin tumors. BAP1-TPDS may occasionally contribute to other cancer types. Generally, the median age of onset of cancer is earlier than in the general population, yet many affect older individuals. Exception for mesothelioma, loss of BAP1 is associated with worse survival. As regards uveal melanoma, about 2% of all cases and 20% of familial cases are caused by BAP1-TPDS. This usually can be suspected from a careful family history. Conversely, variants of unknown significance occur in patients whose family members lack typical BAP1-TPDS cancers. BAP1-TPDS is confirmed through identification of a heterozygous germline pathogenic variant. For carriers, yearly dilated fundus examinations from childhood, physical examination including dermatologic screening from early adulthood, and abdominal ultrasonography are recommended.

2742

**Pathology of orbital inflammation**

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**Summary**

A plethora of inflammatory conditions can occur in the orbit. These range from inflammation caused by specific bacterial and fungal infections such as mucormycosis, through known systemic disease such as sarcoidosis and Graves' disease, to so-called idiopathic orbital inflammation (IOI; previously known as "orbital pseudotumor"). The latter diagnostic category is characterized by a mixed inflammatory infiltrate and fibrosis of varying degree, and is in turn divided into subcategories such as IgG4-related ophthalmic disease, eosinophilic angiocentric fibrosis, and various types of xanthogranulomatosis, all of which can share features or overlap with each other. Not infrequently, IOI is a chronic disease, and the histopathologic findings can evolve over time, changing for one diagnostic category to another one. Recently, consensus diagnostic criteria for IOI were published (JAMA Ophthalmol 2017;135:769). The histopathologic criteria consist of: lymphoplasmacytic infiltrate, absence of granulomatous inflammation and vasculitis, absence of necrosis, plasma cell IgG4-positivity of  $\leq 30$  cells/HPF or IgG4+/IgG  $\leq 40\%$ , and presence of fibrosis. These concepts will be exemplified through short cases.

2946

**Intravitreal anti-VEGF for the treatment of intraocular vascular tumors**

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## Summary

Intraocular vascular tumors include choroidal cavernous haemangiomas with and without Sturge-Weber and associated syndromes, retinal capillary and racemose haemangiomas, haemangioblastomas in von Hippel-Lindau disease, and so-called vasoproliferative tumours that histopathologically represent focal retinal gliosis. None of these lesions has a gold standard treatment. Rather, photocoagulation, intravitreal injection of corticosteroids, anti-vascular endothelial growth factor (anti-VEGF) agents, beta-blockers, transconjunctival cryotherapy, transpupillary thermotherapy, photodynamic therapy, brachytherapy, and vitreoretinal surgery all have been tried in individual cases, often sequentially. Anti-VEGF has been administered as a standalone treatment and together with various laser treatments or surgery. It is mostly ineffective for choroidal haemangiomas that are better treated with photodynamic therapy or low-dose irradiation. They are often useful adjuncts to treating haemangioblastomas and larger vasoproliferative tumours with photocoagulation or cryotherapy. Unfortunately, essentially all published experience on use of anti-VEGF for intraocular vascular tumors derives from single case reports and very small case series.

2154

## Myopia control with Atropine in Europe

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## Summary

### INTRODUCTION:

This study explores the 3-year efficacy of atropine 0.5% for progressive myopia in a European setting.

### METHODS:

We performed an effectiveness study of atropine eye drops for progressive myopia in a university clinic in Rotterdam, the Netherlands. Children using atropine eye drops 0.5% daily (N=109) for three years were included. A standardized eye examination, including cycloplegic refraction and axial length at baseline was performed with follow up every 6 months. Logistic regression analysis was used to evaluate risk factors associated with progression of myopia during atropine treatment.

### RESULTS:

At baseline, median age was 9 years, the median spherical equivalent (SphE) -5.56D and median axial length (AL) 25.03mm. Adherence to therapy was 73%. The median annual progression before treatment was -1.1D. The median annual progression over a three year period for SphE was -0.31D(IQR 0.77) and for AL 0.12mm(IQR 0.27). Age at start of therapy was a risk factor, children <10-years had median annual progression of -0.38D/year and ≥10-years -0.25D.(P=0.01)

### CONCLUSION:

In this study, atropine 0.5% was well tolerated and effective for the majority of European children with progressive myopia over a period of 3 years.

057

## Toxoplasmosis

S065

### Central toxic keratopathy after small incision lenticule extraction

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#### Purpose

CTK (central toxic keratopathy) is a noninflammatory postsurgical condition that presents with central corneal opacity and a significant hyperopic shift. Small-incision lenticule extraction (SMILE) is a refractive surgery which a corneal stromal lenticule is formed using femtosecond laser system and removed through a small peripheral corneal incision. The authors present a case of CTK after SMILE.

#### Methods

A 35-year-old male presented with 2 months history of decreased vision of the right eye. He had undergone SMILE surgery 7 months ago. Preoperatively, Manifest Refraction (MR) of his right eye was - 6.75sph - 0.25cyl × 180, with corrected visual acuity of 20/20. Keratometric readings (Pentacam; Oculus, Wetzlar, Germany) were 44.70/44.90 diopters. Central corneal thickness was 565 µm. No anterior and posterior segment abnormalities were observed. The surgery was conducted uneventfully. One day postoperatively, the uncorrected distance visual acuity (UDVA) was 20/50. At 3 months, it was 20/25 and the CDVA was 20/25 with a MR +0.25sph -0.75cyl × 15.

#### Results

Seven months postoperatively, examination revealed the typical central toxic keratopathy triad: corneal thinning, hyperopic shift and a reduction in best corrected visual acuity to 20/50. MR of his right eye was +4.00sph -0.75cyl × 90. Central corneal thickness of his right eye was 373µm.

#### Conclusions

SMILE has been considered as an alternative procedure to conventional laser in-situ keratomileusis (LASIK) because of its benefits of reduced denervation, less post-operative dry eye, and no flap-related complications. Although SMILE has small incision, CTK may be induced. Because SMILE is on the rise, this rare case is important for other refractive surgeons to look up, and as the basis for larger studies.

F006

### Results from an international observatory survey on the management of glaucoma treatments and its impact on the ocular surface disease (OSD), an ECOS-G (European Club of Ocular Surface in Glaucoma) initiative.

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### **Purpose**

To understand the clinical practice of ophthalmologists in the management of glaucoma and OSD.

### **Methods**

702 random ophthalmologists from 19 countries participated in the survey. The inclusion criteria of ophthalmologists were: age  $\leq 65$ , from 3 to 35 years of clinical experience and treating  $\geq 10\%$  of glaucoma patients. The questionnaire Part one was to establish the management of OSD in glaucoma patients in clinical practice, Part two was to describe hypothetical clinical response to two patient scenarios (a newly diagnosed glaucoma patient & a known glaucoma patient with newly diagnosed OSD).

### **Results**

71% of the participants were general ophthalmologists. 47% performed ocular surface examination before starting glaucoma treatment, whereas 43% performed ocular surface exam selectively in patients with OSD. 70% of participants performed “always or often” fluorescein corneal staining, eyelid margin/Meibomian gland examination and T-BUT. According to ophthalmologists, 29% of the patients complained about OSD. Eye dryness and hyperemia were the main ocular surface clinical signs, while dryness sensation and redness were the main symptoms reported by the patients. The three main reasons to change the patients eye drops were lack of efficacy, tolerability, or allergy (45%, 24%, 24%, respectively). 94% of ophthalmologists would prescribe preservative-free glaucoma (PFG) eye drops when asked on a theoretical basis. However, in the two proposed scenarios, 58% prescribed PFG eye drops to newly diagnosed glaucoma patient and 70% prescribed PFG eye drops to a known glaucoma patient with newly diagnosed OSD. Overall, the main reasons to prescribe PF treatment were better tolerance (91%).

### **Conclusions**

This survey highlights that most ophthalmologists are in favor of PF formulations even though the prescription practice does not reflect such preference.

## **T008**

### **Protective Effects of Omega-3 Fatty Acids Supplementation Against Retinal Degeneration in Aged C57BL/6 Mice**

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### **Purpose**

To evaluate the therapeutic effects of omega-3 ( $\omega 3$ ) fatty acids on the retina of aged wild type C57BL/6 mice; when the blood levels of arachidonic acid (AA)/eicosapentaenoic acid (EPA) ratio is between 1 and 1.5.

### **Methods**

Two year-old wild type C57BL/6 mice were allocated to two groups: untreated control and treated with  $\omega 3$ . Three month-old C57BL/6 untreated mice served as a further control.  $\omega 3$  treatment lasted 2 months and comprised of daily gavage administration of EPA and docosahexaenoic acid (DHA) (ratio of EPA:DHA=5:1). Blood and retinal fatty acid analysis was performed using gas chromatography. Eyecups were histologically examined using transmission

electron microscopy and confocal microscopy to evaluate lipofuscin granules and the photoreceptor layer. Mass spectrometry-based proteomics of the retinal tissues was also performed.

## Results

EPA levels increased and AA levels decreased in the blood and retinas of the treatment group. Significantly fewer lipofuscin granules and greater thickness of the outer nuclear layer were observed in the treatment group than in the untreated control. Proteomic analysis indicated significant increase in myelin regulatory factor-like protein, myelin basic protein and myelin proteolipid protein following treatment. Three pathways were significantly affected from  $\omega$ 3 treatment, namely fatty acid elongation, biosynthesis of unsaturated fatty acids and metabolic pathways.

## Conclusions

Two months of  $\omega$ 3 supplementation (AA/EPA  $\sim$  1-1.5) reduces lipofuscin granule formation and may protect the photoreceptor layer in 2 year-old C57BL/6 mice, consistent with slowing the normal age-related degeneration of the retina.

**3116**

### Intraoperative OCT: Is it of clinical use?

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## Summary

During microsurgery, en face imaging of the surgical field through the operating microscope limits the surgeon's depth perception as well as sub-surface anatomy. While Optical Coherence Tomography (OCT) has been integrated into our management of retinal conditions in the clinical setting, its adoption in the operating theater has yet to take full force.

Many published reports presented the benefits of using the iOCT and the impact to the surgical decision. Furthermore they highlighted that surgical decision could be altered in a high percentage of the presented cases. However, various hurdles have halted the transitioning of OCT into the operating room and for many reasons: extreme economic burden in lack of valid cost-benefit analyses, lack of OCT-compatible instrumentation in the already existing set up, lack of optimized surgeon feedback/visualization or software platforms and automated tracking issues. Additionally, there is lack of research validating its utility regarding actual improved patient outcomes.

In summary, while the role of iOCT in ophthalmic surgery has been evolving over the last years, the question if it leads ocular surgery to the next level or it is just another expandable novelty still needs to be answered.

**S015**

### Effects of mesenchymal stem cells on production of cytokines by injured cornea in in vitro and in vivo experimental models

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## Purpose

Approximately 25% cases of blindness are caused by corneal injury or alterations. Corneal transplantation is the first choice of the treatment of such defects. If the damage is more extensive and includes the limbal region, the niche of limbal stem cells (LSCs), cornea cannot regenerate because of LSC deficiency (LSCD). This corneal damage is also associated with the break of immune privilege of the cornea, with harmful inflammatory reaction and production of cytokines. In the case of bilateral LSCD the only option of treatment is limbal tissue or LSC transplantation with a systemic administration of immunosuppressive drugs. As an alternative mesenchymal stem cells (MSCs) turned out to be a suitable source of autologous stem cells.

## Methods

In *in vivo* experiments, mouse MSCs were seeded onto nanofiber scaffolds and transplanted on chemically burned murine corneas. For *in vitro* experiments, mouse MSCs were cultured in 48-well plates for 48 hours. Excised murine corneas were added to the culture and stimulated by pro-inflammatory cytokines. To elucidate cytokine production by MSCs during co-cultivation with corneas, inserts were used to separate MSCs and corneas. After a 48-hour co-cultivation the expression of genes for inflammation cytokines, growth factors and corneal markers in corneas were detected using qPCR. The expression of genes for cytokines and molecules in MSCs were also detected by qPCR.

## Results

The results showed that MSCs have the ability to suppress the expression of genes for IL-1, TNF- $\alpha$ , VEGF and iNOS in damaged cornea in both *in vitro* and *in vivo* mouse models and that transplantation of MSCs inhibits production of pro-inflammatory cytokines and supports corneal regeneration.

## Conclusions

We suggest that the transplantation of MSCs onto injured cornea is a suitable treatment for LSCD and other inflammatory conditions of the cornea.

1432

### Corneal nerves in keratoconus

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## Summary

There is little knowledge about the involvement of corneal nerves in the pathogenesis of keratoconus and only the prominence and visibility of corneal nerves have been reported previously. Reduced density and abnormal morphology of the corneal subbasal and stromal nerves has been described in patients with keratoconus using confocal corneal microscopy. Whether these morphological changes are primary or secondary pathologic manifestations is currently not known. In addition to the sensory and protective functions, corneal nerves are involved in the maintenance of epithelial integrity, the modulation of cell proliferation, and in maintaining normal corneal structure and function. Here we present our results on decreased corneal sensitivity to all stimulus modalities in patients with keratoconus. The significantly impaired sensitivity suggests that axonal damage and/or altered expression of membrane ion channels involved in transduction and membrane excitability affects the different types of corneal nerve terminals in a similar degree. Although the exact mechanism of keratoconus is still unknown, these structural and neural changes may play a role in the abnormal ocular sensations experienced by keratoconus patients.

2762

### The role of Meis family transcription factors in retina development

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## Summary

Meis1 and Meis2 homeobox genes encode evolutionarily conserved transcriptional regulators that are expressed in various eye tissues. Their role in retinal differentiation remains largely elusive due to embryonic lethality between E11.5 and E14.5. To study the role of Meis1 and Meis2 we performed conditional gene targeting in mice. Meis1/2-deficient retina is smaller compared with Meis1-deficient as well as with control retina. EdU/BrdU double labelling shows that the hypocellular phenotype is caused by prolonged cell cycle length. Retinal progenitor cell markers Chx10 and Pax6 are maintained in Meis1-deficient retina, however they are absent in the Meis1/2-deficient retinal cells. Furthermore, ChIP using embryonic retina has shown that Meis transcription factors bind to Pax6 and Chx10 enhancers, which indicates that Meis1 and Meis2 regulate expression of these genes. Additionally, early retinal differentiation markers such as Otx2 and Tbr2 are also significantly downregulated in the Meis1/2-deficient retina. Combined, our data indicate that Meis1 and Meis2 transcription factors redundantly regulate cell proliferation, maintain retinal progenitor cell character, and control retinal differentiation.

## F100

### The Rayleigh equation: reasons for a standard in application

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## Purpose

To explain the need for standardizing the application of the Rayleigh equation in examining red/green color vision

## Methods

The reasons are explained - i) for which Rayleigh spectral emissions deserve careful balancing with cone spectral absorbances, and - ii) for which defined field luminance, field diameter and neutral adaptation are decisive criteria for comparable results of anomaloscopy.

## Results

Basal demands on spectral composition of the red, yellow and green spectral primaries comprise narrow bandwidths, large distance of the red and green primary within the spectrum, and avoidance of blue cone stimulation. Spatial resolution plays a role in color vision, and so does the diameter of the color field. Adherence to a defined level of luminance is a need. In particular in acquired troubles of color vision, fading in low and dazzling in high luminance may occur. By prolonged observation, color vision may fade and the Rayleigh match may shift which is called "Umstimmung". To avoid Umstimmung, neutral adaptation is maintained by regularly switching from the color field to a white field and vice versa.

## Conclusions

Rayleigh spectral matching is a precision diagnostic procedure. For meaningful and comparable results, adherence to standard conditions is inevitable - in terms of defined color stimuli as well as defined conditions of observation. A working group within the German institute of standardization (DIN) is preparing a revision of the standard for anomaloscopes designed for examination of the red/green color sense. The technical realization of such instrument, however, is not the subject of standardization. Subject merely are the optical conditions of stimulation and observation, based on the physiological properties of human color vision.

3146

### **Choroidal osteoma in old age (an unexpectedly difficult diagnosis)**

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#### **Purpose**

To demonstrate a diagnostically challenging case of a choroidal osteoma in an elderly patient and to discuss the differential diagnoses.

#### **Methods**

The common diagnostic features of choroidal osteoma as observed in young patients are well known but differ from findings in old age due to de-calcification and accompanying age related pathology. We report on a female patient of 90 years. Besides visual function, the evaluation of the patient includes various imaging procedures as color fundus photography, IR fundus general view, SD OCT, ultrasound, blue autofluorescence BAF, and fluoresceine angiography FAG.

#### **Results**

The patient presented with a rapid drop in visual acuity OS. This used to be her better eye, because of amblyopia OD. On the IR fundus general view, a uniform area of increased reflectivity showed up, covering a central and paracentral platform-shaped area of the posterior pole in OS. Shown by SD-OCT, BAF and FAG, circumscribed changes attributable in part to age-related macular degeneration appeared as secondary damages. Combined A- and B-scan ultrasound proved sonographic shadowing behind the platform area. Because of lack of prominence, melanoma and metastases were ruled out. The differential diagnosis comprises sclera-choroidal calcifications, however these should be located in more deeper, outer layers.

#### **Conclusions**

Remaining clinically silent for decades, the process had been overlooked by the patient. In old age, the appearance of additional age related changes - presumably facilitated by areolar decalcification of the osteoma - brought the process to the awareness of the patient.

T006

### **A morphological study and expression patterns of iron regulatory proteins in aging Wistar rats retina after iron overload**

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#### **Purpose**

Purpose: Iron is vital for cellular metabolism. In the retina, in excess, it causes oxidative stress. Excess iron is implicated in age related macular degeneration. This study addresses how long-term iron administration modifies retinal structure and expressions of iron regulatory proteins.

#### **Methods**

Male Wistar rats were fed with oral FeSO<sub>4</sub> (500 mg/kg body weight/week) starting from 2 months of age until 20 months. Iron levels in serum and retina were detected by HPLC. Retinal changes were examined by light- and transmission electron microscopy (LM, TEM), funduscopy and electroretinography (ERG). Expression of ferritins, transferrin (Tf), transferrin receptor-1 (TfR-1), ceruloplasmin and hephaestin was analyzed at 8, 14 and 20 months of age (N=40/group; ethics approval No. IAEC/692/2012). One way ANOVA with Bonferroni test was used for statistical analysis.

### Results

Retinal iron levels (N=7), but not serum iron levels, were increased in 20 month iron-fed groups compared to that in age-matched control (61.34±14.82 vs 35.71±7.43 µg/g; p<0.001). There was damage in photoreceptor mitochondria and outer nuclear layer, and necrosis in inner nuclear layer. Fundus photographs indicated optic disk hemorrhages. ERG showed altered amplitude of a- and b- waves. Compared to age-matched controls (N=7), there were increased expressions of Tf, ferritins, and decreased levels of ceruloplasmin, TfR-1 and hephaestin in treated retinas at 20 months of age.

### Conclusions

Long-term iron accumulation with aging causes retinal cellular necrosis. The alterations of a- and b-waves imply damaged photoreceptor and bipolar cells, respectively. Retinal cells in case of iron-overload maintain iron homeostasis via upregulation of Tf-1, ferritins, and downregulation of ceruloplasmin, TfR-1 and hephaestin.(supported by CSIR, New Delhi, 37/1593/13/EMR-II, TCN).

### S093

#### Sitagliptin, a dipeptidyl peptidase-IV inhibitor, attenuates retinal neurodegeneration in rd10 mice

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### Purpose

Retinitis pigmentosa (RP) is an inherited disease characterized by progressive loss of photoreceptors that usually leads to blindness. The dipeptidyl peptidase-IV (DPP-IV) inhibitor sitagliptin has demonstrated neuroprotective effects in type 2 diabetes mellitus. The aim of this work was to establish the neuroprotective effect of sitagliptin in an animal model of retinal degeneration such as RP.

### Methods

Rd10 mice were used as a model of RP. The animals were treated orally with sitagliptin (10mg/Kg/day) or vehicle (PBS) from P18 to P25. Electroretinography (ERG), optomotor test and vertical retinal cryostat sections stained with hematoxylin or immunohistochemistry were used to evaluate the function and morphology of the retina.

### Results

Sitagliptin administration in rd10 mice preserved the functional activity of the retina, with higher amplitudes in a- and b-waves and oscillatory potentials, as well as better visual acuity. Western blot analysis revealed the reduction of DPP-IV levels in the retina of treated animals. The functional findings correlated with a higher number of photoreceptor rows. These photoreceptors presented well defined axon terminals and better preserved outer and inner segments. Furthermore, sitagliptin treatment prevented bipolar and horizontal cells morphology deterioration and preserved presynaptic and postsynaptic elements, as well as synapses between photoreceptors and bipolar or horizontal cells.

### Conclusions

Sitagliptin treatment improves retinal function and preserves photoreceptor number and morphology, as well as their synaptic contacts. The results support sitagliptin as a suitable option for retinitis pigmentosa treatment.

Support

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## T012

### The association between macular thickness and axial length

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#### Purpose

To investigate the relationship between macular thickness and axial length (AL).

#### Methods

We included 415 myopic eyes in this study and measured macular thickness at the fovea and in other macular regions, using optical coherence tomography. We got values of thickness difference by subtracting the foveal thickness from that of each macula sector. We then analyzed the relationships between AL and foveal thickness, and AL and thickness difference values. We also used multiple regression analysis to identify factors associated with foveal thickness.

#### Results

In polynomial regression analyses, foveal thickness slope was relatively flat up to an AL of 25.5 mm, and began to rise from 25.5–26.0 mm. The thickness difference indices were noted as negative slopes that started to steepen at 25.0–25.5 mm. In multivariate regression analysis, foveal thickness was associated with differences in thickness between the fovea and the outer superior macula, and fovea and outer inferior macula ( $p < 0.001$ ,  $p < 0.001$ , respectively).

#### Conclusions

Macular thickness profiles showed appreciable changes at an AL of 25.0–26.0 mm. Foveal thickness was associated with thickness differences between outer macular sectors and the fovea.

## 1732

### Unraveling the pathogenesis of AAK - insights from anterior segment imaging in children

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#### Summary

Congenital aniridia can be recognized by underdeveloped iris, cataract, glaucoma, retinal abnormality and nystagmus, but detailed examination of the cornea is often overlooked unless opacification or Peter's Anomaly is present. Little is known about the development of AAK in the very young. Here, we examined a German cohort of individuals with congenital aniridia with detailed anterior segment imaging. 50 persons with aniridia were examined by anterior segment OCT, 46 with slit lamp photography, and 40 with in vivo confocal microscopy of the

cornea. Half the examined subjects were children under the age of 18 and as young as nine months. Early changes in the corneal thickness, development of cornea, lens, and iris structures, early indicators of AAK development peripherally and cellular-level changes in the central cornea could be detected. Interestingly, phenotypic differences were observed in individuals with different genetic mutations and degrees of iris hypoplasia. We present some of the major findings and discuss the implications for our understanding of AAK and anterior segment development in children with aniridia.

## **T051**

### **Bariatric surgery and its retinal repercussions – a pilot study**

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### **Purpose**

Bariatric surgery improves metabolic profile in type 2 diabetic (T2D) patients. The retinal consequences of bariatric surgery on T2D patients remain unclear. We aimed to evaluate the impact of bariatric surgery in the retina of T2D patients.

### **Methods**

These are preliminary results from a prospective cohort study that has been conducted in two Portuguese Centers for Surgical Treatment of Obesity (CHSJ and CHEDV). Patients that gave their consent to participate were evaluated before and 1 month after bariatric surgery. Ophthalmic evaluations were all performed in the afternoon. We included 10 T2D obese patients and 10 non-diabetic obese patients (control group). Exclusion criteria included any eye disease that can interfere with the evaluations or complicated bariatric surgery. Retinopathy was checked in fundus photographs. Macular thickness (MT) was measured using the automated segmentation algorithm and the follow-up function from the Spectralis® SD-OCT (ART 9, 30°x25°, 61 sections).

### **Results**

We included 20 eyes from 20 patients (right eyes, 30% males, mean age of 47±8 years, mean body mass index before surgery 42±4Kg/m<sup>2</sup>). No patient had/developed retinopathy or macular edema during the study. MT varied from 270±17µm at baseline to 269±19µm one month after surgery in T2D group (p=0.28). MT varied from 282±17µm at baseline to 278±17µm one month after surgery in controls (p<0.001). In T2D group a positive correlation between HbA1c before surgery and variation of MT (r=0.76, p=0.02) was identified.

### **Conclusions**

Our preliminary results demonstrate that bariatric surgery may have an impact on the retinal ultrastructure. This impact seems to be small and may not be relevant in clinical practice. The cohort will be followed for 12 months.

## **S079**

### **The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): an ex vivo model of human Staphylococcus aureus keratitis**



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## **Purpose**

Our university lab BiiGC patented 2 versions of a bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé. Aim: to present a new *ex vivomodel* of human *Staphylococcus aureus* (SA) keratitis.

## **Methods**

By restoring IOP and medium renewal, the BR maintained the viability of human or animal corneas over a prolonged period. Its transparency allowed characterizing the tissue with existing or customized devices without compromising its sterility. Corneas discarded after organculture (OC) were placed in the BR for 14 days at 21mmHg and 5µL/H medium renewal. We previously showed that these 2 weeks allowed restoring a multilayered epithelium. For this work, the endo and the epithelial circuits were independent. The BR lid was opened for SA inoculation: the epithelium was scarified and covered for 1H with a solution of 108 PFU of SA. The active storage was then continued for 72H with a sterile medium. Observations: by slit-lamp, OCT (Casia 1) and a microscope.

## **Results**

Abscess formation was observed only on parts of the epithelial lesions. A strong Tyndall effect was observed in the epithelial chamber at all time points and appeared also in the endothelial chamber at day 3. At D0, the central CT was 520µm and progressively increased to 920µm at 72h. Alongside with the corneal edema, a Descemet detachment occurred as the infection reached the endothelial chamber.

## **Conclusions**

The OBSERV platform is an efficient tool to restore and maintain a multilayered epithelium on corneas discarded after OC, and allows SA inoculation in more physiologic conditions than on a desquamated epithelium. The BR can complete or replace animal experimentation for academic or industrial research.

## **S110**

### **Phacoemulsification and zonular weakness: contribution of the wired capsular tension ring.**

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## **Purpose**

Capsular tension ring brings a proper solution to temporarily consolidate the capsular bag with zonular weakness during all steps of the phacoemulsification. Aim: to describe a surgical tip that secures and facilitates the use of capsular tension rings.

## Methods

Retrospective analysis of 14 consecutive patients presenting with zonular weakness and cataract, who underwent phacoemulsification. Twelve patients suffered from pseudo-exfoliative syndrome and 2 from a post-traumatic cataract. All benefited from the use of a wired capsular tension ring during surgery. The tip consisted in suturing a 7/0 vicryl wire to the extremity of the ring. The ring was introduced normally with the free end of the suture let outside the eyeball. After implantation of the intra ocular lens, the ring could be extracted by gently pulling on the suture.

## Results

All surgeries were successful without complication. The wired capsular tension rings were all removed easily at the end of surgery.

## Conclusions

Dr Oudjani's technique is a cheap, rapid and easy-to-use surgical tip that facilitates and secures the use of tension rings. The suture makes the removal of the ring atraumatic and eliminates the risk of falling into the vitreous.

## F036

### Altered Antioxidant-Oxidant Status in the Peripheral Blood of Patients with Low-Tension Glaucoma and Ocular Hypertension

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## Purpose

Glaucoma is the most common cause for incurable blindness worldwide. The pathophysiology behind glaucoma is unknown, but it has been widely suggested that systemic levels of oxidative stress contributes to the pathogenesis of the characteristic degeneration of the retinal ganglion cells and their axons. The purpose of the present study was to evaluate antioxidants and oxidant markers in the peripheral blood from patients with low tension glaucoma (LTG) and ocular hypertension (OHT) compared with age-matched healthy controls.

## Methods

Patients with LTG (n = 16), OHT (n = 9), and controls (n = 14) were exposed to hypoxia for two hours followed by a 30 minute recovery period. Blood samples were taken prior to hypoxia ("baseline"), during hypoxia ("hypoxia"), and after hypoxia ("recovery"). Plasma samples were isolated for measurements of the total antioxidant capacity (TAC), thiobarbituric acid reactive substances (TBARS) formation, and extracellular superoxide dismutase (SOD3) by commercial kits. Intracellular superoxide dismutase (SOD2) were measured by western blotting in peripheral blood mononuclear cells (PBMCs).

## Results

Patients with LTG presented lower SOD3 protein concentrations at recovery compared to controls. SOD3 levels decreased in healthy controls during hypoxia, and increased during recovery. SOD2 protein concentration in PBMCs decreased in LTG and OHT patients during hypoxia. However, patients with OHT stabilized their levels of SOD2 in the recovery phase. Furthermore, patients with OHT show increased plasma formation of TBARS.

## Conclusions

Overall, our results indicate that patients with LTG present reduced antioxidant status in the peripheral blood. Moreover, patients with OHT show changes in oxidative markers in plasma indicating a tolerance against the high oxidative stress levels.

**2131**

**Placido-based corneal topography and Scheimpflug-based corneal tomography**

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**Summary**

Measuring the curvature of the corneal front surface has a long tradition in ophthalmology. Starting from the Helmholtz keratometer and the hand-held Placido disk, videokeratography and Placido disk based topographers have been developed decades ago. These technologies provide lots of clinically relevant information about integrity or pathology of the anterior corneal surface. In the last decade several tomographers have been developed which work with slit projection technology (e.g. Scheimpflug imaging) and retrieve additional data on cornea thickness and back surface geometry as well as the dimensions of the anterior segment of the eye. This presentation will address the different measurement techniques of topographers and tomographers and their prospects and limitations.

**3541**

**The basic concept behind customized IOLs – optical aberrations and correction options**

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**Summary**

In this presentation we introduce the basic concept of corneal aberrations and their corrections with customized lenses. Starting from the measurement of corneal topo- and tomography we will show how to interpret corneal aberrations and to develop a concept for the compensation of these corneal aberrations using free-form surfaces in an intraocular lens implant. In addition, we will address the reasonable degree of individualization which directly interacts with the robustness of the lens and the manufacturing process.

**S016**

**Comparison of calcium signalling between native and cultured human corneal endothelium after mechanical stimulation**

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**Purpose**

Restoring corneal endothelial integrity by injection of in vitro propagated endothelial cells into the anterior chamber represents the alluring new treatment possibility. The aim of our study was to compare Ca<sup>2+</sup> signalling and intercellular communication in native human corneal endothelium with primary cultures of human corneal endothelium as a model of that potential treatment.

**Methods**

Human corneal endothelial specimens obtained at DMEK surgery and from corneas unsuitable for transplantation were stained with Fura-2 AM fluorescent dye and mechanically stimulated with thin glass pipette. Primary cultures were prepared using suspension enzymatic isolation technique with dual media propagation approach. The changes of intracellular  $\text{Ca}^{2+}$  concentration ( $[\text{Ca}^{2+}]$ ) were detected from 360/380 nm ratio after illumination of Fura-2 AM loaded cells with xenon fluorescent light source. For data acquisition and analysis WinFluor software (University of Strathclyde, UK) was used.

## Results

In all samples we observed radial spreading of  $[\text{Ca}^{2+}]$  changes after mechanical stimulation, with decline of amplitude and increase in rise and activation times with distance. In native human corneal endothelial specimens the changes of  $[\text{Ca}^{2+}]$  after mechanical stimulation were more prominent only in the first and second neighboring cells whereas in cultured specimens, the changes of  $[\text{Ca}^{2+}]$  spread to a larger area. The cells in culture were bigger than in native samples.

## Conclusions

The comparison between native and cultured human endothelial cells showed that  $\text{Ca}^{2+}$  signals after mechanical stimulation seem to spread to a larger area in cell cultures, which deserves further attention.

## F092

### Evaluation of multifocal visual evoked potentials in patients with multiple sclerosis using Retiport device

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## Purpose

To evaluate the electrophysiological topographic distribution of changes in the multifocal visual evoked potentials (mfVEP) of patients with multiple sclerosis (MS) without a previous optic neuritis episode.

## Methods

Thirty-nine eyes of subjects with multiple sclerosis (MS) and eighteen eyes of healthy controls were analyzed by the retiportReti-Port/Scan 21 (Roland Consult, Germany). Multifocal visual evoked potentials (mfVEP) were performed in all subjects. Results were compared between both groups and the spatial distribution of changes was analyzed by concentric rings and quadrants centered in fovea.

## Results

Patients with MS showed a greater latency ( $63 \pm 0.01$  vs  $59 \pm 0.01$  ms;  $p < 0.05$ ) and lower amplitude ( $0.40 \pm 0.38$  vs  $0.69 \pm 0.39$   $\mu\text{V}$ ;  $p < 0.05$ ) of the N1 wave in the mfVEP. The P1 wave showed a greater latency ( $102.6 \pm 12.9$  vs  $100.7 \pm 14.9$  ms;  $p < 0.05$ ) in MS patients. The topographical analysis by retinal rings revealed a higher latency and a smaller amplitude in all rings (except the 3rd ring), with a greater difference observed in the first rings. In the 3rd ring, however, patients with MS showed a shorter latency and a lower amplitude. In the analysis by quadrants we obtained contradictory results: patients with MS showed a lower latency and amplitude of the P1 wave in the upper nasal quadrant, and the N1 wave in the lower nasal quadrant and also a greater latency and greater amplitude in the lower temporal quadrant compared to healthy subjects. However, most of these differences in the quadrant analysis did not reach significance.

## Conclusions

MS produces an alteration of the mfVEP even in patients without a previous optic neuritis episode. A shorter latency of the N1 and P1 waves and a lower amplitude of the N1 can be observed in these patients.

### F093

#### Evaluation of the multifocal electrorretinogram in patients with multiple sclerosis using Retiport device

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#### Purpose

To evaluate the topological distribution of changes in the multifocal electroretinogram (mfERG) of patients with multiple sclerosis (MS) without a previous optic neuritis episode.

#### Methods

Thirty-nine eyes of subjects with multiple sclerosis (MS) and eighteen healthy individuals as a control group were analyzed by the Reti-Port/Scan 21. Multifocal electrorretinogram was performed in all subjects. Results were compared between both groups and the spatial distribution of changes was analyzed by concentric rings and quadrants centered in fovea.

#### Results

Patients with MS presented a lower amplitude in the N1 wave corresponding to the superonasal quadrant compared to controls ( $5.7 \pm 2.11$  vs  $6.90 \pm 4.88$   $\mu$ V;  $p < 0.05$ ). The inferonasal quadrant was most affected in patients, showing lower amplitude and also reduced amplitude ( $22.3 \pm 4.1$  vs  $20.5 \pm 4.1$  ms;  $p < 0.05$ ) of the N1 wave and reduced amplitude of the P1 wave ( $12.19 \pm 4.97$  vs  $14.68 \pm 6.89$   $\mu$ V,  $p < 0.05$ ).

#### Conclusions

MS produces an alteration of the mfERG especially in the inferonasal quadrant of the retina, even in patients without a previous optic neuritis episode.

### 1731

#### Transcriptional analysis of corneal epithelium in AAK and related siRNA-based cell model

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#### Summary

Although it is widely accepted that Aniridia-Patients develop **aniridia**-associated keratopathy(AAK), the pathogenic mechanisms remain unclear. The degeneration of limbal stem cell niche can be observed in aniridia patients in vivo. Additionally, there are a lot of progresses concerning disease models of AAK in mouse and contribution of PAX6 haploinsufficiency to corneal epithelial phenotype. PAX6 and its isoforms seem to regulate the corneal keratin KRT12 expression. Notch1 and Vitamin A metabolism play a role in corneal epithelial cell fate and might act upstream of PAX6. Our purpose is to link these theoretical disease models with human patient data to gain new insights of AAK progression.

We isolated primary epithelial cells from limbus region of patients suffering from AAK. Transcriptional profile was generated and compared to healthy limbal epithelial cell culture. Regulated genes were identified and compared to a siRNA based primary cell model. We could confirm new potential PAX6 regulated target genes, which might explain common disease models. The PAX6- KRT12 dependency was present in patients but not reproducible in our cell model. Further analysis is needed to get more insight in the development of Aniridia.

**1763**

#### **Is there a benefit of nutritional supplementation in the prevention of AMD?**

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#### **Summary**

Oxidative mechanisms are believed to be important in the pathogenesis of AMD and there has been considerable interest in determining whether antioxidant vitamins (beta-carotene, vitamins C and E), carotenoids (lutein and zeaxanthin) and certain minerals (selenium and zinc) are effective in preventing or delaying the onset of AMD. Supplements containing various combinations of these antioxidants are widely available and marketed at the general population for primary AMD prevention. A recent Cochrane review examined the evidence from RCTs that compared antioxidant or mineral supplements with control (placebo or no treatment) for AMD prevention. The review included 5 RCTs with over 75,000 participants who had taken supplements for 4-12 years. There was no evidence that people who take vitamin E or beta carotene supplements reduce their risk of AMD. Although there was less evidence for vitamin C or multivitamins, there was no suggestion that these supplements prevented AMD. Although supplements are generally regarded as safe, they can have harmful effects. For example, beta-carotene increases the risk of lung cancer in smokers and some evidence of a small increased risk of mortality in people who took beta-carotene or vitamin E.

**T106**

#### **Acute high-fat feeding exacerbates retinal degeneration in a mice model of retinitis pigmentosa**

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#### **Purpose**

High-fat diets (HFD) can induce hyperglycemia and metabolic syndrome disorders in rodents and has been associated with diabetic retinopathy. The aim of the current study was to investigate the effects of short-term high-fat diet feeding on retinal degenerative disease such as retinitis pigmentosa (RP).

#### **Methods**

Rd10, a mouse model of RP, and C57BL/6J mice 19 days old were fed either a normal chow (5,5% fat kcal) or high-fat diet (61,6% fat kcal) for 2 or 3 weeks. All the animals were weighed before and after each of the two dietary periods and their blood glucose curve was performed. The function and morphology of the retina were evaluated by electroretinography, optomotor test and vertical retinal cryostat sections stained either with hematoxylin or immunohistochemistry techniques.

#### **Results**

Short-term HFD-fed animals significantly gained weight and developed reversible glucose intolerance. In rd10 mice, high-fat diet produced faster deterioration of retinal responsiveness with decreased a- and b-waves amplitudes and lower visual acuity. This decrease was accompanied with higher reduction in the number of photoreceptor rows and shorter outer and inner segments. Moreover, a worsening of synaptic connectivity was observed with decreased density of presynaptic photoreceptor terminals and retraction of bipolar and horizontal cell dendrites.

### Conclusions

Acute high-fat feeding accelerates pathology progression in retinal degenerative diseases. The results suggest that the consumption of high-fat diet in patients suffering from ocular neurodegenerative diseases could exacerbate the progress of the disease.

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### S047

#### Ocular surface involvement on GVHD patients

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### Purpose

To identify the different complications of GVHD on ocular surface;

### Methods

ocular surface examination on patients with GVHD , referred by the center of bone marrow graft of Algiers, all benefited from OSDI questionnaire, slit lamp examination, fluorescein coloration and Schirmer test,

### Results

127 patients were assessed, the mean age value was 39,3 years+/\_ 7,4; all patients presented different levels of severity of dry eye at slit lamp examination, 5% of them had a very low visual acuity; Mean OSDI score was 76,4+/\_ 10,2 corneal staining was present on 92% of cases (oxford : 6,5+/\_ 2,5) and Schirmer value 10+/\_ 5,4 ),

### Conclusions

Dry eye is the most common ocular complication on GVHD patients, in most of cases it is a severe dry eye with corneal involvement and visual impairment, an early diagnosis and treatment of ocular manifestations of GVHD is essential to prevent severe complications.

### T119

#### Clinical follow-up of uveitis patients treated with TNF-alpha inhibitors and causes of treatment discontinuation

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### Purpose

To study the effectiveness of Tumor necrosis Factor (TNF)- $\alpha$  inhibitors among a cohort of non-infectious uveitis patients. Additionally, to analyze the therapeutic options adopted in patients resistant to anti-TNF $\alpha$  and their clinical evolution after treatment switch.

### Methods

This is a multicenter, retrospective study. We included all anti-TNF $\alpha$  treated patients seen in the department of ophthalmology of CHU St Pierre/ Brugmann with non-infectious uveitis. Anti-TNF $\alpha$  effectiveness was evaluated by clinical inflammatory parameters assessment (visual acuity, anterior chamber cells, vitritis, macular edema, choroiditis, retinitis lesions) and the reduction of the corticosteroid and immunosuppressive drugs doses, over 6 months. In the patients where anti-TNF $\alpha$  was stopped, the same parameters were analyzed after drug discontinuation.

### Results

Twenty-eight patients were included. In all of them, anti-TNF $\alpha$  was introduced in the setting of active disease resistant to conventional therapy. Twenty-one responded well to the treatment. Anti-TNF $\alpha$  treatment was stopped in 7 patients for: lack of efficacy, loss of efficacy, side effects and healed disease. Tocilizumab was given as an alternative treatment to 5 patients. Before Tocilizumab, the mean central foveal thickness was  $384 \pm 109 \mu\text{m}$  and decreased to  $298 \pm 42 \mu\text{m}$  ( $p=0.02$ ) at month 3; mean logMAR best-corrected visual acuity was  $0.17 \pm 0.21$  then  $0.08 \pm 0.09$  at month 3 ( $p=0.29$ ). After 3 months, in tocilizumab patients, all inflammatory parameters were improved and immunosuppressive drugs were reduced.

### Conclusions

The study confirmed that anti-TNF $\alpha$  therapy is efficient in patients with sight-threatening uveitis resistant to conventional immunomodulatory therapy. Lack or loss of efficacy was still the main reason for treatment withdrawal. In those patients, shifting treatment to Tocilizumab seems to be a promising option.

## S113

### Clinical outcomes after cataract surgery with a Precizon Multifocal intraocular lens

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### Purpose

The purpose of this study was to evaluate the visual outcome and optical quality of the Precizon Presbyopic Multifocal Intraocular Lens (MIOL; Precizon Presbyopic IOL<sup>®</sup>, Ophtec BV, Groningen, The Netherlands) in patients undergoing cataract surgery.

### Methods

A total of 9 patients with bilateral cataract received a MIOL implantation. All eyes were evaluated visual acuity at distance (uncorrected distance visual acuity, UDVA 4 m), intermediate (uncorrected intermediate visual acuity, UIVA 50 cm) and near (uncorrected near visual acuity, UNVA 35 cm), manifest refraction spherical equivalent (MRSE) and defocus curve at 1 week and 1, 3 months postoperatively. Information about optical quality was gathered through a questionnaire. Lenses were available in powers ranging from +10.0 D to +30.0 D in 0.5 D increments with add power of +2.75 D.

### Results

The mean intraocular lens power was  $19.80 \pm 1.38\text{D}$  at cataract surgery. At 3 months postoperatively, mean uncorrected visual acuity (logMAR) was  $0.03 \pm 0.02$  at the distance,  $0.13 \pm 0.08$  at the intermediate and  $0.16 \pm 0.07$  at the near distance. The defocus curve showed a peak at 0.0D and -2.5D and a stable visual acuity at the



intermediate distance. Postoperatively, 88.9% of patients were satisfied and 22.2% of patients were complained about glare and halo symptoms.

### **Conclusions**

Bilateral Precizon Presbyopic MIOL implantation showed good uncorrected near, intermediate and distance visual acuity and high satisfaction. It is considered to be an effective intraocular lens at presbyopic cataract surgery in the future.

### **F039**

#### **Visual field changes after epiretinal membrane surgery in glaucomatous eyes**

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### **Purpose**

To investigate visual field (VF) changes after epiretinal membrane (ERM) surgery with internal limiting membrane (ILM) peeling in glaucomatous eyes, identify clinical characteristics associated with VF progression, and determine risk factors related to VF deterioration.

### **Methods**

Glaucoma or glaucoma suspect patients who underwent ERM surgery with ILM peeling during the period from January 2011 to December 2016 and were followed for  $\geq 1$  year after surgery were consecutively enrolled. Variables regarding baseline characteristics and pre- and postoperative ERM and glaucoma related parameters were reviewed for each patient. VF deterioration was defined as VF progression in three clustered points in two consecutive reliable VF tests.

### **Results**

Among total of 38 eyes from 38 patients, 9 eyes (26.3 %) showed VF progression during a mean follow-up period of 2.9 years. There were no differences in pre- and postoperative BCVA and intraocular pressure (IOP) in terms of VF progression ( $P > 0.05$ ). VF progression group had a greater proportion of patients who had dense pigmentation ( $\geq$  Grade 2) of trabecular meshwork (TM), had a pseudoexfoliation material, used a larger number of IOP lowering agents preoperatively, showed VF defects preoperatively, had a greater preoperative central inner retinal layer thickness (CIRLT), and underwent the postoperative IOP spike ( $> 21$ mmHg). In the multivariate analysis, dense pigmentation of TM, the thick preoperative CIRLT, and the postoperative IOP spike were significant risk factors for VF deterioration after ERM surgery.

### **Conclusions**

Some of the glaucomatous patients at risk experienced VF deterioration after ERM surgery with ILM peeling. Therefore, it is important to carefully monitor and timely manage the possible changes to prevent the worsening of glaucomatous VF.

### **T077**

#### **Longitudinal Evaluation of Retinal Structure in Patients with Idiopathic Epiretinal Membrane Using Optical Coherence Tomography**

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## Purpose

To evaluate the change of visual acuity (VA), central foveal thickness (CFT), disruption of external limiting membrane (ELM), disruption of inner/outer Segment junction (IS/OS junction), growth of ectopic inner retinal tissue for idiopathic epiretinal membrane (iERM) without surgery.

## Methods

We tracked 49 patients (49 eyes) with iERM without surgical treatment, retrospectively for over 6 months from January 2016 to January 2018. VA, CFT, disruption of ELM, disruption of IS/OS junction, growth of ectopic inner retinal was reviewed.

## Results

The average follow-up duration was 13 months (range 6-21 months). From first visit to final visit, VA (LogMAR) changed from  $0.18 \pm 0.23$  to  $0.19 \pm 0.18$ , CFT changed from  $350.34 \mu\text{m}$  to  $354.52 \mu\text{m}$  not showing clinically significant changes ( $p = 0.565$ ,  $p = 0.065$ ). Disruption of ELM, growth of ectopic inner retinal tissue did not show clinically significant changes ( $p = 0.083$ ,  $p = 0.317$ ). Disruption of IS/OS junction showed significant difference at follow-up period ( $p = 0.008$ ).

## Conclusions

Clinically significant change of the disruption of IS/OS junction was observed during the average follow-up duration of 13 months. It is known that damage of inner retina is more sensitive indicator than outer retina to surgical results. However, due to the change of outer retina during average of 13 months, early surgical approaches would be recommended for relatively good prognosis.

## T083

### Surgery for macular telangiectasia type 2 with lamellar hole or macular hole in Asians: Affirmative results and mechanisms

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## Purpose

To report the surgical outcomes for macular telangiectasia (MacTel) type 2 with lamellar hole (LH) or macular hole (MH) in Asians.

## Methods

Retrospective observational case review of 329 patients who underwent retinal surgery for LH or MH. Five eyes of 5 patients were classified as definitive MacTel when diagnosed with optic coherent tomography (OCT) and fluorescein angiography (FAG). Five eyes of 5 patients were classified as possible MacTel when no available FAG present, but had MacTel characteristic lesions in the contralateral eye. Each group was divided into LH or MH related groups. (Definitive MacTel with MH : 3 eyes, Possible MacTel with MH : 4 eyes, Definitive MacTel with LH : 2 eyes, Possible MacTel with LH : 1 eye) Postoperative outcomes including best-corrected visual acuity (BCVA) and macular configuration in spectral domain-optical coherence tomography were reviewed.

## Results

BCVA was stabilized or improved by more than 0.2 logMAR (minimum angle of resolution) in 66% of MacTel with LH and 86% of MacTel with MH. The MH occlusion rate was 71% (5/7 eyes) and VA didn't deteriorate in patients with closed MH. In one case with moderate myopia (Spherical equivalent : -4.75 diopter), MH was not closed. In

another case with severe macular telangiectasis, the macular hole was closed 2 weeks after operation, but recurred after 1 month.

### Conclusions

Our surgical results were not as inferior as the previous reports. If the actual outcome is similar to ours, surgical treatment can be valuable as one of the treatment options for MacTel with LH or MH. And when performing surgery on MacTel with LH or MH, widening the internal limiting membrane peeling range to the major vascular arcade can help improve retinal ischemia

2363

### What have metabolism studies taught us about ADOA pathophysiology and possible future therapies?

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### Summary

Autosomal Dominant Optic Atrophy (ADOA) is an inherited blinding condition related to the loss of the retinal ganglion cells (RGCs) that transfer the visual information from the retina to the brain. In most cases, ADOA is related to heterozygous mutations in OPA1, a gene encoding a large dynamin involved in mitochondrial fusion. In the other cases with a molecular diagnosis, the causative genes are also encoding proteins involved in mitochondrial fusion, or eventually fission. Why RGCs are so susceptible to alterations of the mitochondrial dynamics remains an open question that we have addressed by a metabolomics approach aiming at identifying the consequences of mitochondrial shape on the general cellular metabolism. In this respect, we have analysed the organs of an Opa1 mouse model, mouse embryonic fibroblasts deleted for Opa1, rat neurons silenced for OPA1, OPA1 patient fibroblasts and plasma, using either mass spectrometry targeted or untargeted metabolomics approaches. I shall summarize the main common metabolic pathways encountered in these models affected for OPA1 expression, raising novel hypothesis on ADOA pathophysiology and opening eventually novel therapeutic routes to treat this disease.

2635

### TGF- $\beta$ 1 and LOXL1 affect the Pseudoexfoliation syndrome pathology

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### Summary

Pseudoexfoliation (PEX) syndrome is an age related systematic eye disorder and one of the most frequent causes of open-angle glaucoma. PEX is characterized as a genetically determined, complex disorder of the elastic fiber system, associated with the excessive production and abnormal cross-linking of elastic proteins into typical PEX fiber aggregates. Lysyl oxidase-like 1 (LOXL1) encoding a cross-linking matrix enzyme, is identified as a major genetic risk factor for PEX syndrome/glaucoma. Dysregulated expression of LOXL1 is crucially involved in PEX pathophysiology and PEX material formation. Non-genetic factors such as pro-fibrotic cytokines, growth factors and cellular stress conditions may also stimulate the synthesis of abnormal PEX fibrils. The pro-fibrotic growth factor TGF- $\beta$ 1 is a prime candidate, known as a key regulator of expression and activation of lysyl oxidases. TGF- $\beta$ 1 is shown to be significantly upregulated in the aqueous humor and ocular tissues of PEX patients indicating its association with the accumulation of PEX material in the anterior segment of patients. This presentation outlines how the interaction between LOXL1 and TGF- $\beta$ 1 influences the pathophysiological fibrillation process characterizing PEX syndrome.

1243

**Molecular genetics in clinical practice I (Cornea)**

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**Summary**

This session will provide examples of ocular phenotypes associated with different pathogenic mutations implicated in monogenic corneal disorders. The effect of mutations within a single gene *TGFB1* leading to different phenotypes will be given as an example, highlighting the importance of correct variant annotation. The annotation methods required to describe non-coding variants will also be discussed using posterior polymorphous corneal dystrophy 1- and 4-associated mutations as examples.

1861

**Human Case**

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**Summary**

A case of a 4.5 old boy, homoplasmic carrier of m.3460G>A mutation with bilaterally decreased visual acuity, borderline retinal nerve fibre layer measurements and prolonged P100 latency will be presented. Limitations of ocular examination in children with suspected optic neuropathy will be discussed. Supported by AZV 16-32341A.

3162

**Posterior polymorphous corneal dystrophy – a disease caused by dysregulation of transcription factors involved in epithelial-to-mesenchymal transition**

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**Summary**

Posterior polymorphous corneal dystrophy (PPCD) is a genetically heterogeneous disorder transmitted as an autosomal dominant trait. We have shown that promoter mutations in *OVOL2* cause PPCD1. Inappropriate ectopic expression of *OVOL2* in corneal endothelial cells is hypothesised to be the underlying molecular mechanism of disease. *OVOL2* drives mesenchymal-to-epithelial transition (MET) by directly inhibiting epithelial-to-mesenchymal (EMT) inducing transcription factors, such as *ZEB1*. Importantly, loss-of function mutations in *ZEB1*, resulting in *ZEB1* haploinsufficiency, cause PPCD3. Most recently we have mapped a locus for PPCD4 and have demonstrated that *GRHL2* regulatory variants, identified in PPCD4-affected individuals, induce increased transcriptional activity *in vitro*. *GRHL2* is a direct transcriptional repressor of *ZEB1*. Furthermore, although *GRHL2* is not expressed in corneal

endothelial cells in control tissue, we detected GRHL2 in the corneal endothelium of PPCD4 patient-derived tissue. In summary, we and other have demonstrated that PPCD can be attributed to disrupted levels of transcription factors in the corneal endothelium that govern EMT/MET regulation. Supported by GACR 17-12355S.

#### **T038**

##### **Thermo-responsive injectable microgel is able to achieve controlled drug release in the vitreous environment**

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#### **Purpose**

Treatments for many sight-threatening vitreoretinal conditions are delivered via intravitreal injection. However, intravitreal injection leads to an initial period of burst release and an extended period of under-dosing to below therapeutic level. An in situ-forming implants (ISFI) that could deliver drugs with enhanced control of release rate is needed. Thermo-induced microgel poly(N-isopropyl acrylamide) (PNIPAm) is shown to achieve controlled release of encapsulated drugs in agarose gel tissue mimic. Herein, we describe the drug releasing behaviour of PNIPAm-based ISFI in the porcine vitreous model by using micro-computed tomography (MicroCT)

#### **Methods**

PNIPAm microgels were prepared by precipitation polymerisation. Radiographic contrast agents Optiray was used as intravitreal drug mimic. Porcine vitreous humor was pre-warmed to 37 degrees to mimic human intra-ocular condition. PNIPAm microgel incorporated with Optiray were injected into the vitreous model. Diffusion of intravitreal drug mimic was tracked by microCT scanning at serial time points. 1% agarose incorporated with Optiray was used as a control.

#### **Results**

PNIPAm microgel could be injected into pre-warmed porcine vitreous humor leading to rapid aggregation of the particles to form a drug depot. Serial microCT scans for 15 hours showed that the resulting microgel displayed sustained Optiray release at a much slower rate than 1% agarose control. The predicted time for 50% of Optiray to be released from 1% agarose was 3 hours while from PNIPAm was 55 hours.

#### **Conclusions**

PNIPAm microgels could be formulated to form an injectable drug depot in the vitreous environment and provide a long-term sustained release of drugs. These results demonstrated an easily injectable ISFI that provides long-term sustained release of intraocular drugs.

#### **F085**

##### **Maintained treatment with idebenone increases the probability and magnitude of visual acuity recovery in patients with Leber's hereditary optic neuropathy (LHON)**

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#### **Purpose**

LHON, a mitochondrial disorder affecting retinal ganglion cells, leads to progressive and severe central vision loss in both eyes. Idebenone, a potent enhancer of mitochondrial function, is approved for treatment of LHON in the

EU. Here, we report long-term efficacy outcomes following idebenone treatment in real world clinical practice, specifically, recovery of lost visual acuity (VA).

### Methods

As part of a multi center Expanded Access Program, LHON patients within 1 year of disease onset (most recently affected eye) were treated with idebenone (300 mg TID) and monitored as per normal clinical practice. Response was classified as a clinically relevant recovery (CRR), defined as a VA improvement (from Nadir) from off-chart (ETDRS) to 5 letters on-chart, or an on-chart improvement of 10 letters.

### Results

41/87 patients (47.1%) achieved a CRR by last observation, with 28 experiencing a CRR in both eyes. Duration of treatment was longer overall in the responding patient group compared to non-responders (27.7 vs 19.4 months); 41% of which had discontinued treatment within 12 months. The mean time to initial CRR was 10 months, with some patients responding up to 24 months after initiation. The mean magnitude of recovery (vs Nadir) was > 4 lines (ETDRS) at initial CRR, which improved to a mean of > 7 lines with maintained treatment. When separated by mutation, the results yielded some differences.

### Conclusions

The response to idebenone, a CRR, occurred in almost half of all LHON patients, but may only occur after an extended treatment period (up to 2 years). Early interruption of treatment in non-responders may partially explain the lack of visual recovery. Maintained treatment may also increase the magnitude of regained VA. These results suggest that to maximize the probability and magnitude of CRR, a minimum treatment duration of 18-24 months is required.

### F087

#### Long-term maintenance of visual acuity in patients with Leber's hereditary optic neuropathy treated with idebenone

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### Purpose

LHON causes profound bilateral loss of visual acuity (VA). VA deteriorates progressively, and is usually an irreversible process. Three primary mitochondrial DNA mutations cause over 90% of cases. The only approved treatment for LHON is idebenone (150 mg tablets). Data from a multi center Expanded Access Program of idebenone was analyzed for efficacy and safety.

### Methods

Patients diagnosed with LHON, treated with idebenone (300 mg TID) under Named Patient Regulations, were followed (mean: 23.8 months) in routine clinical practice (38 sites, 111 patients); safety and VA data were collected at each visit. Efficacy was assessed as either improvement or maintenance of VA (logMAR, by Best VA and individual eyes). Here we present results on the long-term maintenance of VA.

### Results

The efficacy population consisted of 87 patients (173 eyes) that provided post-baseline (BL) VA data, carried a primary mutation, and were within 1 year of disease onset (mean of 4.6 months). 82% male and median age of onset was 31.4 years. At BL 72.4% patients had severe vision loss (Best VA > 1.0 logMAR), 68.6% of the on-chart patients had no relevant worsening (VA loss < 0.2 logMAR) at last visit (LV) and 41.2% off-chart patients were on-

chart at LV. At LV, from 173 eyes, in 31.7% the change of VA was within  $\pm 0.2$  logMAR. The safety profile of idebenone was consistent with that reported previously.

### Conclusions

In a disease where natural history is mainly towards severe vision loss, idebenone seems to have prevented relevant VA deterioration in a large percentage of patients. No new safety concerns have been observed.

### F004

#### Intravitreal rituximab for the treatment of ocular lymphoma and glaucoma

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### Purpose

Secondary glaucoma refractory to medical treatment is a therapeutic challenge and usually requires surgical intervention. In glaucoma caused by lymphoma with ocular involvement, bleeding caused by dysfunctional platelets poses an additional risk from surgery. Rituximab is a monoclonal antibody derived to target B cells for the treatment of diseases caused by immune dysregulation. We aimed to determine whether intravitreal injection of rituximab would assist in a patient with ocular lymphoma and refractory glaucoma

### Methods

A 71-year old gentleman previously diagnosed and treated for lymphoma involving the central nervous system developed an isolated vitritis, diagnosed as lymphoma following vitrectomy. Unresponsive to topical or systemic steroids the intraocular pressure was elevated despite maximum tolerated medical treatment (34 mm Hg). Best corrected visual acuity was 6/24. With no evidence of relapse elsewhere the oncology team felt that further treatment with systemic chemotherapy or radiotherapy would not be of benefit overall because of side effects.

### Results

After discussion with the patient a course of intravitreal rituximab injections (1 mg) were performed a week apart over a month. The cellular activity reduced to 0.5 cells (Standardization of Uveitis Nomenclature) and eye pressure lowered to 16 mm Hg. Subsequent relapse of lymphoma required further repeat injections and with glaucoma progression Baerveldt tube/plate insertion. At last follow up vision was 6/9 and IOP 18 mmHg

### Conclusions

Intravitreal injection of rituximab may help with controlling ocular lymphoma and temporise glaucoma surgery.

### F014

#### Noninvasive intracranial pressure assessment using otoacoustic emissions: an application in glaucoma

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### Purpose

The theory that glaucoma patients have a lower intracranial pressure (ICP) than healthy subjects is a controversial one. The aim of this study was to assess ICP noninvasively by determining the relationship between distortion product otoacoustic emission (DPOAE) phase and body position and to compare this relationship between patients

with primary open angle glaucoma (POAG), patients with normal tension glaucoma (NTG), and controls. The relationship was also calibrated using published data (Lindén et al 2017) regarding invasive measurements of ICP versus body position.

### Methods

DPOAEs were measured in 30 controls and 32 glaucoma patients (17 POAG, 15 NTG) at the following body positions (assuming 90° as upright): 45, 30, 20, 10, 0 (supine), -10, and -20°.

### Results

DPOAE phase had a clear, nonlinear relationship with body position. The mean DPOAE phase shifts between the two most extreme body positions (45 to -20°) were 73.6, 80.7, and 66.3° for healthy, POAG, and NTG, respectively ( $P=0.73$ ), and the groups showed the same, nonlinear behaviour.

### Conclusions

Based on a noninvasive measurement, there is no evidence that glaucoma patients have a reduced ICP. When calibrated with invasive data, ICP and DPOAE phase were linearly related over an ICP of 3 mmHg. This suggests that, more broadly, DPOAEs could be used in the future to monitor changes in ICP in a clinical setting and to measure dynamic changes in ICP such as diurnal fluctuations or changes induced by certain medications.

Lindén C, Qvarlander S, Jóhannesson G, Johansson E, Östlund F, Malm J, et al. Normal-Tension Glaucoma Has Normal Intracranial Pressure: A Prospective Study of Intracranial Pressure and Intraocular Pressure in Different Body Positions. *Ophthalmology* [Internet]. 2017 Oct 30; Available from: <http://dx.doi.org/10.1016/j.ophtha.2017.09.022>

### S023

#### Bilateral acute corneal melting secondary to nonsteroidal anti-inflammatory drugs

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### Purpose

Currently, nonsteroidal anti-inflammatory drugs (NSAIDs) have multiple uses in ophthalmology and they are often considered a safer alternative to topical corticosteroids. Nevertheless, topical NSAIDs have been associated with delayed epithelial healing, corneal ulceration, melting and corneal perforation.

### Methods

We report a case of an 82 years old woman, with a penetrating keratoplasty in the left eye since 10 years, secondary to spontaneous perforation of a herpetic corneal ulceration. During the last 10 years the corneal graft has been viable without rejection signs, and the patient was stabilized with a chronic treatment with topical cyclosporine and autologous serum tears. Recently, the patient attended the Emergency with bilateral red eyes and burning. Treatment with topic diclofenac and tobramycin was started. Five days later she returned with intense eye pain and blurred vision in both eyes. She presented conjunctival hyperemia, bilateral central ulceration with corneal melt and a reduction of corneal thickness (100 micres in the right eye and 90 micres in the left eye).

### Results

Adverse reaction was suspected as result of NSAIDs toxicity, and diclofenac was discontinued. A contact lens was placed in both eyes and treatment with topical ciprofloxacin and casticin was started. At the follow up



appointments the patient has a significant corneal thinning with resolution of corneal melt and improvement of the conjunctival hyperemia.

### Conclusions

Corneal epithelial toxicity, delayed epithelial healing, and corneal ulceration associated with topical NSAIDs use are infrequent and they often occur in patients affected by systemic or ocular conditions predisposing to corneal melting. Special caution should be exercised with the use of NSAID in patients predisposed to corneal healing.

**S115**

### Orbital cellulitis secondary to malignant neoplasia

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### Purpose

We present an orbital cellulitis secondary to malignant neoplasia.

### Methods

A 63-year-old woman attended the Emergency Department with an ulcerated lesion on the inner canthus of the left lower eyelid, mucopurulent rhinorrhea, epistaxis, left eye proptosis, and weight loss of 6 months of evolution. Treatment with topical tobramycin and oral cloxacillin 500 mg every 8 hours was started. A preferential cranial computerized tomography (CT) was requested to complete the etiological study. One week later, waiting for the execution of the cranial CT, the patient returned to the emergency with a decreased level of consciousness, epistaxis, sphincter dysfunction and dysphasia. Urgent cranial CT was requested.

### Results

The cranial CT revealed a voluminous mass in nasal fossae with extension to paranasal sinuses, orbits and superior cranial fossa, with surrounding cerebral edema, displacement of the middle line. The biopsy of the mass was performed, resulting in a grade III olfactory neuroblastoma according to the Hyams classification. Treatment with intravenous methylprednisolone, ceftazidime and metronidazole was established, with improvement of the clinical manifestations. The patient was discharged with palliative treatment (radiotherapy and chemotherapy). Unfortunately, she died one month later from a bronchio-aspirative pneumoniae.

### Conclusions

Olfactory neuroblastoma, is a slow-growing neuroectodermal malignancy of the nasal cavity, which usually presents with locally invasive disease. Olfactory neuroblastomas have a marked tendency for late local and regional recurrences. Nasal obstruction due to the presence of a mass is the most common symptom. Other manifestations of this malignant tumor include epistaxis, headache, and diplopia. This patient presented some of the symptoms of local extension as eye proptosis, headache, orbital cellulitis and anorexia.

**1814**

### New insight on choroidal vasculature: multimodal morphofunctional approach

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## Summary

Imaging the choroid in vivo using standard modalities is difficult because of light scattering within overlying tissue, particularly the retinal pigment epithelium (RPE). Although the choriocapillaris is composed of relatively large-diameter capillaries, they are interconnected in a dense arrangement. The flow in the choriocapillaris is fast and because of the prominent fluorescein leakage vascular structure is obscured. Indocyanine green dye shows less leakage than fluorescein, but it still leaks from the choriocapillaris and stains Bruch's membrane and the choroidal stroma. Optical coherence tomography angiography has high axial resolution, but the lateral resolution is insufficient to visualize the choriocapillaris clearly in the posterior pole. Nevertheless, it can detect choriocapillaris blood flow, producing contrast between the RPE and choriocapillaris. However, because of signal loss, fringe wash-out, and thresholding used in signal processing, the vessels in Sattler's layer and certainly in Haller's layer appear dark in normal eyes. Purpose of the lecture is to evaluate various choroidal multimodal imaging findings and to allocate them in the context of different macular diseases.

3631

## Occurrence of BAP1 mutations in families

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## Summary

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**Purpose:** To evaluate the clinical phenotype of the BAP1 tumour predisposition syndrome in the Netherlands.

**Methods:** Patients with BAP1 predisposition syndrome are referred to the multidisciplinary clinic in the LUMC. Standard ophthalmological and dermatological examinations are performed, as was imaging of the thorax and abdomen.

**Results:** In total 9 families were identified with in total 35 proven or obligate BAP1 germline mutation carriers. The following tumours were found in one or multiple members of the family; uveal melanoma 56%, cutaneous melanoma 67%, mesothelioma 44%, renal cell carcinoma 11%, MBAITs 89%. Other unconfirmed tumours were found basal cell carcinoma 78%, cholangio-carcinoma of the liver 11% and breast carcinoma in 56%.

**Conclusion:** Patients with a BAP1 germline mutation are exposed to high risk for developing uveal melanoma, cutaneous melanoma, mesothelioma and renal cell carcinoma. Other unconfirmed cancers are basal cell carcinoma, cholangiocarcinoma of the liver. Yearly screening is advised in these patients.

1714

## New tacking forceps for fixation of epiretinal prosthesis

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## Summary

**Introduction:** Array tacking on the right eye using conventional straight forceps shall be performed with the left hand of the surgeon targeting the temporal part of the macula. It creates some difficulties for right-handed surgeons increasing the risks of re-tacking, bleeding and malposition.

**Purpose:** to report the use of modified tacking forceps for Argus II implantation.

**Methods:** The prototype of a new modified tacking forceps was designed to enable the use of surgeon's right hand during the fixation of Argus II epiretinal prosthesis on both eyes. Experimental testing of the forceps was performed using Argus II epiretinal prosthesis and testing eyes of the patient's head simulator.

**Results:** The new tacking forceps with bend design allowed to tack the array with the right hand on the right eye without intrusion into surgical field and without touching the distant lens of the non-contact viewing system. Additionally, array tacking on the left eye was also performed without any complications.

**Conclusions:** The modified tacking forceps can ease and simplify the fixation of the array onto the retina on both eyes using the right hand, which will make this surgical step more controlled and will minimize the risks of the incorrect tacking.

## F055

### Association between myopia and optic nerve head drusen in children

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## Purpose

To evaluate association between myopia and optic nerve head drusen in children.

## Methods

A total of 74 eyes (44 children) with optic nerve head drusen were included. Univariable and multivariable logistic analysis were performed to evaluate associated factors for presence of optic nerve head drusen.

## Results

Mean age of the patients was  $11.86 \pm 2.72$  years (range: 7 to 19) and 21 patients were (44.7%) boy. Unilateral optic nerve head drusen was in 14 (31.8%) children and 30 children (68.2%) were bilateral cases. Mean spherical equivalent by cycloplegic refraction was  $2.65 \pm 1.93$  (range -7.25 to +1.25) diopters. Mean spherical equivalent in eyes with optic nerve head drusen was  $-2.88 \pm 1.83$  and  $-1.21 \pm 1.98$  in eyes without optic nerve head drusen. All children with unilateral optic nerve head drusen demonstrated optic nerve drusen in eyes with more myopia. According to the univariable (odds ratio [OR], 0.535,  $P = 0.004$ ) and multivariable (OR, 0.118,  $P = 0.019$ ) logistic regression analyses, myopia was significantly associated with the optic nerve head drusen.

## Conclusions

Myopia is associated with increased risk of optic nerve head drusen in children. There would be an association between myopia progression in children and optic nerve head drusen which has not been reported.

#### **S060**

##### **The effects of corneal collagen cross-linking and the discrepancy between epithelium on and epithelium off treatment – Results from the Portsmouth population cohort**

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#### **Purpose**

Corneal collagen cross-linking (CXL) was introduced in 2003 and has gained popularity as an early treatment option for corneal ectasias such as keratoconus, pellucid marginal degeneration and post-lasik corneal ectasia. CXL is the only known treatment modality for these conditions and is believed to slow underlying stromal degeneration, halting disease progression. Since its introduction, CXL treatment methods have been modified in order to deliver a more efficient service and improve post-treatment morbidity. The optimum method for longer term stability and need for further intervention continues to be evaluated. We aimed to determine the longer term effectiveness of CXL in our eye unit.

#### **Methods**

A consecutive case series of all CXL procedures performed in a single eye unit. The procedure included a 10-minute riboflavin induction and 10-minute of continuous UV light treatment with epithelium off treatment if corneal thickness was greater than 400 microns. In cases with corneal thickness of less than 400 microns, treatment was applied with the epithelium on. Disease stability, effects on astigmatism, complications and need for further procedure (repeat CXL/progression to penetrating keratoplasty) were determined.

#### **Results**

150 CXL procedures were performed in our department over 4 years. Disease stability was observed in 85% of cases, patients with epithelium on treatment needed repeat procedure in 50% of cases, reduction in astigmatism was not notable in the first year but after 2 years post treatment, our patients had corneal flattening on pentacam and improved visual acuity.

#### **Conclusions**

Our series indicates that a high level of stability can be achieved with a 20 minute CXL application

#### **T107**

##### **Metallothionein-mediated neuroprotection of retinal ganglion cells using FLOREC retinal explants culture**

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#### **Purpose**

To evaluate retinal ganglion cells (RGC) survival under metallothionein-2 (MT2) treatment in FluoroGold-labeled organotypic rat retinal explants culture (FLOREC).

#### **Methods**

Eight Wistar rats received FluoroGold (FG) injection into superior colliculi to retrogradely label RGC. After 5 days, rats were sacrificed by anesthetics overdose, eyeballs were removed, retinas isolated and placed in tissue culture

inserts. Explants (n=32) were cultured in neuronal-specific medium with or without addition of 1 µg/ml of MT2 and/or 1 µg/ml of gentamicin (LDLR2 receptor blocker). The culture medium was exchanged every second day and collected for LDH assay. After 7 days, 16 explants were fixed with 4% PFA and stained with anti-β3-tubulin antibody and TUNEL for apoptotic cells. The RGC density was evaluated for FG labeling using ImageJ. Other 16 explants were utilized for Western Blotting (WB) to evaluate HuR protein content.

## Results

Density of FG-positive cells was significantly higher in explants treated for 7 days with MT2 than without treatment ( $645 \pm 111$  cells/mm<sup>2</sup> vs.  $343 \pm 157$  cells/mm<sup>2</sup>, respectively;  $p < 0.003$ ). The LDH levels presented decreasing trend, however in treated explants the LDH activity decline was significantly slower, suggesting more cells surviving (after 7 days of culture the LDH activity in treated explants was decreased to 22% at day 3 and to 15% in non-treated explants;  $p < 0.01$ ). In WB, the MT2 treatment delayed HuR protein content increase, probably by reducing oxidative stress, which is an enhancer of HuR expression. This effect would not have been present if the megalin receptor (LDLR2) was blocked with gentamycin.

## Conclusions

Treatment with MT2 exerts neuroprotective effect expressed in prolonged survival of RGC in rat retinal explants. The possible mechanism includes suppression of oxidative stress in retinal cells.

3144

### Assessing eye color Inside and out

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## Purpose

Iris color is often used clinically as a surrogate marker for posterior eye (fundus) color. To investigate the hypothesis that iris color corresponds to posterior eye color, we developed a digital imaging approach to quantify continuous iris and fundus color.

## Methods

Digital images of human *post-mortem* irises (n=33), and *in vivo* eye iris and fundus (n=20) were used. Iris color was graded 1 (light blue) to 9 (brown) (Mackey et al., 2011). We quantified continuous iris and fundus color from digitally averaged color images, using a Hue (H), Saturation (S) and Lightness (L) (HSL) color system. H values for images were used for analyses. We examined the relationship between H values for *in vivo* iris and fundus color, and also compared discrete iris grades with continuous H values for iris images.

## Results

Digital averaging of iris and fundus eye color produced quantitative H values for each image; a significant relationship between H values for *in vivo* iris and fundus images was found ( $r=0.7$ ,  $p < 0.005$ ). However, the relationship was complex and non-linear for blue irises. Graded iris color showed minimal inter-observer differences, but varied between observers for irises with heterogeneous features and colors. Applying digital imaging and H values provided a means to quantify continuous iris color.

## Conclusions

Iris and fundus H values (and color) were significantly related, and iris color does provide a surrogate marker of fundus color. However, the iris/fundus digital color relationship for blue irises was complex, and reduced choroid and RPE pigmentation revealed underlying (red) choroid vessels and a corresponding shift in observed H values. We also found that graded iris color is useful clinically, but that digital imaging and H values can quantify the continuous nature of iris color especially for irises with heterogeneous features and colors.

## **T082**

### **Surgical treatment of macular holes using platelet rich plasma**

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#### **Purpose**

On the example of clinical cases, to evaluate the effectiveness of 27G microinvasive surgical treatment for idiopathic macular hole (IMH) using platelet rich plasma (PRP)

#### **Methods**

36 patients (38 eyes) with IMH underwent the surgery. The range of the ruptures was from 400 to 1200  $\mu\text{m}$ . 27G vitrectomy with removal of posterior hyaloid and internal limiting membranes was performed. After air tamponade of the vitreal cavity, 2 drops of PRP, previously prepared from the patient's venous blood, were applied on the macular area. At the end of the surgery, 1.5 ml of SF6 gas was injected into the vitreous cavity.

#### **Results**

After the surgery, blockage of the rupture was achieved in all cases. 2 weeks later, as the gas-air mixture resorbed, the patients experienced a decrease in the phenomena of metamorphopsia and an increase in visual acuity.

#### **Conclusions**

27G vitreoretinal surgery of macular holes using PRP is a highly effective, low-traumatic, cost-efficient method of treatment.

## **T060**

### **Differentiated approach to the management of patients with retinal occlusions.**

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#### **Purpose**

To estimate the efficacy of differentiated approach to the management of patients with retinal occlusions.

#### **Methods**

12 patients with retinal occlusions were treated. Stage 1 - triple intravitreal injection of ranibizumab was performed. Stage 2 - laser coagulation of the retina (RLC) was carried out using Supra Scan 577 nm laser device (Quantel Medical, France). The choice of laser impact depended on the size of macular edema (ME). With the ME less than 400  $\mu\text{m}$ , the subthreshold microimpulse laser therapy technique was used, the applicants were applied to the entire ME area in the pattern mode in the number of 150-450 pieces. When the ME was above 400  $\mu\text{m}$ , the RLC was carried out as a "grating", the spot size was 50-100  $\mu\text{m}$ , the exposure was 0.1s. Panretinal laser coagulation of the retina was performed in patients with neovascularization in the pattern mode.

#### **Results**

Decrease of macular edema to 320 µm and increase in the visual acuity up to 1,0 were observed in all patients.

### **Conclusions**

On the background of differentiated approach to the management of macular edema, caused by retinal occlusions, application of intravitreal injection of angiogenesis inhibitors and laser coagulation of the retina allow achieving maximum decrease in macular edema and recovery of visual acuity.

### **S112**

#### **Implantation of toric intraocular lens and femtolaser arcuate keratotomy as ways for corneal astigmatism correction at single-stage phacoemulsification**

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### **Purpose**

To compare the efficacy of 2 methods for corneal astigmatism correction: phacoemulsification with toric IOL implantation and femtolaser arcuate keratotomy.

### **Methods**

64 patients (80 eyes) with lens pathology combined with corneal astigmatism from 0.75D to 8.0D underwent the surgery. All patients were divided into 2 groups (40 eyes in each group): group 1 – implantation of toric IOL (astigmatism 1.0D - 8.0D), group 2 – femtolaser arcuate keratotomy (astigmatism 0.75D - 4.5D). The operation and postoperative period proceeded without complications. Femtolaser incisions were performed using LensX system, then they were completely opened. Toric IOL was implanted under the control of Verion marker.

### **Results**

On the 1st day visual acuity was 0.8-1.0 in both groups. Keratometry, keratotopography in group 1 didn't differ from preoperative data. Toric IOL position coincided with steep axis. In group 2, the magnitude of corneal astigmatism decreased by 80-90% of the initial value. According to keratotopogram SRI decreased 1.5 times the original value, SAI decreased 2 times the original value. Six months later, in 5 cases of group 1 (12.5%) visual acuity was 0.3-0.4 without correction due to IOL rotation as a result of capsular bag contracture. In 4 cases of group 2 (10%) it was 0.5-0.6 because of residual astigmatism.

### **Conclusions**

Phacoemulsification with toric IOL implantation and femtolaser arcuate keratotomy are effective, modern methods for corneal astigmatism correction. In the long-term postoperative period, stability of functional results remains stable in most cases. Toric IOL tends to rotation both independently after surgery, and because of the contracture of the capsular bag; after femtolaser arcuate keratotomy, decrease of visual function is due to residual astigmatism.

### **F126**

#### **miRNAs as putative biomarkers for recurrent hemorrhage after PPV**

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### **Purpose**

**Identify miRNAs as putative biomarkers for recurrent hemorrhage after PPV.**

## Methods

This study was approved by the regional ethics committee respecting the guidelines of the Helsinki declaration. Undiluted vitreous samples were collected over a two-year's period from patients undergoing PPV for PDR at St. Erik Eye Hospital, Stockholm, Sweden. Vitreouses were grouped into four: Control, non-reoperated, reoperated (both before and after reoperation). Pathway-focused miRNA PCR array allowed profiling the expression of the 84 most abundantly expressed and best characterized human miRNAs in miRBase. Eleven miRNA were selected for the subsequent confirmation analysis. The data was analysed by the  $\Delta\Delta\text{Ct}$  method of relative quantification. Statistics were analyzed by one-way ANOVA followed by Fisher's multiple comparison posttest ( $p < 0.05$  was considered significant).

## Results

miRNA-19a and miRNA-27a are downregulated, whereas miRNA-20a and miRNA-93 are upregulated in PDR patients with recurrent hemorrhage

## Conclusions

miRNA-19a, miRNA-27a, miRNA-20a and miRNA-93 could be biomarkers for recurrent hemorrhage after PPV

## 2712

### Evaluation of small particles in motion in diabetic macular edema

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## Summary

Purpose: To describe hypersignal cystic images (HCI) seen on Optical Coherence Tomography (OCT) Angiography (OCTA) of diabetic patients with diabetic macular edema (DME).

Patients and methods: Retrospective study of DME imaged using OCTA 3X3mm (AngioVue, Optovue, Inc., Fremont, CA) presenting HCI on their angiograms. The capillary density of the plexuses was measured with the AngioAnalytic software.

Results: Over 165 eyes reviewed, 56 eyes had HCI (34%). On OCTA, HCI were roundish images with homogeneous signal, seen in the superficial (57%) or in the deep capillary plexus (95%). HIC matched on OCT B-scan with hyper- (46%), iso- (50%) or hypo- (4%) reflective roundish cysts located in the outer layers of the retina. Multiple hyperreflective foci surrounded HIC in 75% and hard exudates were located in the same area in 68%. These images were considered as flow signal by the AngioAnalytic software and lead to overestimate the macular capillary density. Over 27 eyes followed for a mean time of  $118 \pm 94$  days, HCI totally resolved in 8 eyes. Hard exudates developed in the area of HCI in 2 cases

Conclusion: HCI seen in 1/3 of diabetic patient seem to precede hard exudate and could be due to small particles in motion in resolving DME.

## F046

### Glaucoma drainage devices: making surgery simpler

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## Purpose



Glaucoma drainage devices such as Baerveldt, Molteno and Ahmed tubes are used in complex refractory glaucoma and where previous trabeculectomy surgery has failed. A key step in the implementation of the device is the insertion and positioning of the tube through the sclera. Traditional technique employs the use of a 23 or 25 gauge needle to create a passage, but insertion of the tube subsequently can prove difficult, and the tube may sustain kinks and compression. Furthermore, leaks around the tube can lead to postoperative hypotony.

### **Methods**

We propose creation of a tract with a 23 gauge microvitrectomy (MVR) blade, a blade designed to form fluid-tight incisions & self-sealing wounds in vitreoretinal surgery. Porcine eyes were obtained and sclera were individually pierced with an MVR blade or 23G needle and a sealed tube inserted, at an angle similar to surgery in humans. The surgical sites were exposed to a hydrostatic pressure of 40 cm of water, and leakage from wound assessed with fluorescein dye to look for a Seidel's positive sign.

### **Results**

Creation of a passage using an MVR rather than a needle made tube positioning easier without greater fluid leak at the wound edge, especially after application of a box suture with 10-0 nylon.

### **Conclusions**

MVR blade insertion is a safe and easy way to create a scleral passage for a drainage tube.

## **F053**

### **Ophthalmic Manifestations of Tuberous Sclerosis: A Tertiary Hospital Experience**

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### **Purpose**

To describe the ocular manifestations in patients diagnosed with tuberous sclerosis (TS) at a tertiary hospital in Portugal.

### **Methods**

Retrospective study. Patient medical records evaluated on the Neurophthalmology department at a tertiary hospital were reviewed for TS between 2009 and 2017. Clinical data were analyzed descriptively for ophthalmic manifestations of TS. Multimodal imaging with optical coherence tomography (OCT) and MultiColor (MC) images were reviewed.

### **Results**

A total of 17 patients were included, with a mean age of 13 years. Seven patients (41%) had ophthalmic manifestations. RH were seen in 4 patients, bilaterally in 75% of these, maximum 4 hamartomas per eye. Only 1 eye had a calcified and multinodular hamartoma. The rest of the eyes had smooth, non-calcified RH. RH were better seen at MC and appeared on OCT as dome-shaped hyperreflective masses with retinal disorganization, more pronounced on the multinodular hamartoma. Optic disc hamartoma was observed in 2 patients. One patient had optic disc atrophy due to intracranial hypertension. Two patients had anterior segment (AS) findings that included iris hamartoma, iris coloboma and lenticular opacification. Visual acuity (VA) was not affected in patients who had only RH. The patients who had optic disc atrophy and lenticular opacification, had both low VA. Ocular motility abnormalities in 3 patients were also observed.

### **Conclusions**

According to our study the most frequent ophthalmic finding were RH that did not affect the VA in none of the patients. Nonetheless there may exist other rarer findings, like optic atrophy or AS malformations that may impair the ophthalmic prognosis.

**2115**

**Acute ischemic retinal disease**

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**Summary**

Acute retinal ischemia may show variable presentation ranging from acute central retinal artery occlusion with its catastrophic visual loss to microvascular occlusion known as paracentral acute middle maculopathy leading to relatively minor paracentral scotoma. The presentation gives an overview over shared characteristics and difference, as well as recommended work-up.

Subacute ischemic retinal disorders include the central retinal vein occlusion and ocular ischemic syndrome. The differential diagnosis of these, although important for optimal patient care, may be challenging owing to similar clinical appearance. However, in both the retinal ischemia is a key element for ophthalmic decision making.

**F043**

**Three better than two? A twin study to examine the accuracy of IOP measurement**

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**Purpose**

IOP measurement is imprecise. It is well established in other fields that multiple measures improve accuracy: we have previously shown that heritability of IOP was higher when two readings were used c.f. one per eye, and even higher when all four readings were averaged. The purpose of this study was to examine whether, with three IOP measures per eye, the average of three readings is more accurate than that of two readings, having removed the IOP value furthest from the mean.

**Methods**

IOP was measured with a non-contact tonometer (Visionix, Luneau, France) in an unselected sample of 3392 healthy adults of largely European origin from the TwinsUK cohort: 88% female, mean age 63 years (range 18-90). Given the lack of a "true" gold standard, Pearson product-moment correlations between right and left eyes and twin-twin correlations to estimate heritability were used as measures of accuracy/reliability of IOP.

**Results**

Three IOP measures per eye were available for analysis from 3378 participants, and were available for 964 monozygotic (MZ) and 558 dizygotic (DZ) twin pairs. Taking right eyes as example, mean IOPs were similar for the average of 3 readings (13.3 (SD 3.02) mmHg) c.f. two readings with outlier removed (mean 12.58 (SD 2.81) mmHg), and the right-left correlations were the same for the two measures ( $r=0.766$  and  $r=0.763$  respectively). For the twin modelling, MZ correlations were 0.598 and 0.612 for three vs two readings, and DZ correlations 0.234 and 0.242 respectively.

**Conclusions**

These results suggest little difference between using the average of three IOP readings, or a "cleaned" average of two readings after removing the IOP furthest from the mean. Given there is no perfect IOP measurement technique, it is important to remember that multiple measures of IOP with (non-contact or contact) tonometry allow a more accurate estimation of IOP.

## F058

### Suspecting a goldenhar syndrome: a case report

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#### Purpose

To describe a case of a 14-month-old boy that was found to have bilateral preauricular appendages and a coloboma that involved approximately 50% of the left upper eyelid.

#### Methods

On initial examination the patient presented bilateral preauricular appendages and a upper eyelid coloboma, with near total exposure of the corneal surface and punctate epithelial erosions. Surface lubrication was initiated and he was scheduled for surgical repair. As the coloboma affected almost 50% of the upper eyelid we performed a direct closure with canthotomy and cantholysis, with good results in the next five days. Then the patient suffered a suture dehiscence, and a direct suture was performed again. Finally, after the second intervention no incidences happened, and the surgery had good aesthetic and functional results.

#### Results

Given our patient's signs and symptoms (preauricular appendages and eyelid coloboma) a presumptive diagnosis of Goldenhar syndrome was made, and a systemic examination was performed. Genetic exams are pending. In colobomas of almost 50% of the eyelid affected, performing a direct closure with canthotomy and cantholysis achieve good results.

#### Conclusions

Eyelid colobomas are rare congenital malformations. Colobomas are most commonly idiopathic, but they also can be accompanied by systemic features, as in Goldenhar syndrome. Coloboma are potential threat to vision at an early age and requires close monitoring of the visual development.

## F097

### Acute facial asymmetry as the presentig sign of an underdiagnosed entity

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#### Purpose

The "silent sinus syndrome" is a rare and underdiagnosed entity. Clinical suspicion is provided by its typical manifestations; progressive, unilateral, hypoglobus and enophthalmus. It can be easily interpreted as exophthalmus or proptosis of the contralateral eye or ptosis of the affected eye, delaying the real diagnostic and the treatment.

#### Methods

We present a case of a healthy 35 years-old-woman, who was referred to our hospital with painless enophthalmos, hypoglobus of the left eye and diplopia progressed over four days in the absence of previous trauma or surgery. She had no sinonasal symptoms. A diagnosis of silent sinus syndrome was confirmed when the computerized tomography showed pathognomonic signs of silent syndrome, with downward traction of the orbital floor and implosion of the left maxillary antrum.

## Results

Sinonasal endoscopic surgery (maxillary antrostomy) was performed, and six months after surgery the patient had no diplopia and aesthetic improvements.

## Conclusions

The differential diagnosis of facial asymmetry must include this under diagnosed entity. The clinical suspect is essential for the diagnosis, but it will be confirmed by imaging studies.

## F098

### A software based measurement of horizontal muscles insertion

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## Purpose

To evaluate the reproducibility of a software aided semi-automatic measurement of extraocular muscle insertion from Anterior Segment Swept-Source Optical Coherence Tomography (AS-OCT) images.

## Methods

We conducted a reliability analysis study in 147 horizontal eye muscles: 27 underwent strabismus surgery; 120 eyes of control patients. AS-OCT longitudinal scans were obtained on horizontal gaze at a fixation light. The images were exported as Tagged Image File Format for analysis. Muscle insertion mean gray values were assessed by different observers in a limited area of 400-600 pixels (Fiji, ImageJ). Limbus identification and scleral thickness were performed automatically using custom algorithms. Muscle insertion was selected manually using a graphical user interface (GUI). Manual selection was aided by a color-coded image showing either the average and standard deviation or the k-means algorithm classes. All algorithms and GUI were built as a unified tool in Matlab coding language. The measurement values were obtained automatically and reproducibility was evaluated with the intraclass correlation coefficient (ICC) and Bland-Altman plot.

## Results

Inter-examiner ICC reproducibility value was excellent (0,76 [95% CI, 0,60-0,86]) for the muscle insertion mean gray values obtained. Mean gray values enabled coding a colormap based on densities distribution. AS-OCT measurements had an excellent correlation with intraoperative measurements ( $\delta=0,49$  [0,37-0,61]  $p<0,01$ ) and were within 1 mm of the intraoperative measurements in all cases. Inter-examiner ICC reproducibility values was excellent (0,85 [95% CI, 0,67-0,93]) for automatized limbus-muscle insertion distance.

## Conclusions

Interexaminer reproducibility in a program aided rectus muscle measurements is excellent. Mapping software improves accuracy and reproducibility of measurements.

## F011

### Peripapillary vascular analysis from optical coherence tomography angiography to differentiate glaucoma and normal eyes

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## Purpose

To compare structural, functional and vascular parameters discriminative power between glaucoma and healthy patients.

## Methods

Retrospective study of patients selected from a glaucoma tertiary center consultation. Patients underwent a complete general and ophthalmic examination and Swept Source Optical Coherence Tomography Angiography (SS OCT-A). Glaucoma was defined following a cluster criterion on a visual field (VF) test. ImageJ software was used to demarcate a 0.75mm-width peripapillary ring. Peripapillary vascular density (Vd), fractal dimension (Fd) and lacunarity (Lac) in that ring were computed using an algorithm designed by MATLAB. The models' performance was assessed by the area under the receiver operating characteristic curve (AUC). A p value of  $\leq 0.05$  was considered as statistically significant.

## Results

Inclusion of 133 eyes (71 patients). The mean Mean Deviation (MD) and peripapillary Nerve Fiber Layer Thickness (pNFLT), as well as peripapillary superficial capillary plexus Vd, Fd and Lac values were statistically different ( $p < 0.01$ ) between glaucomatous and non-glaucomatous eyes. Fd alone had the highest AUC (AUC = 0.733; 95%CI: 0.635 – 0.832) followed by Vd (AUC = 0.689; 95%CI: 0.583 – 0.797) and Lac (AUC = 0.685; 95%CI: 0.590 – 0.779). The multivariate model that included both MD and pNFLT attained the best performance considering all assessment criteria (AUC = 0.878; 95%CI: 0.815 – 0.941) although the model including MD and Fd (AUC = 0.873; 95%CI: 0.807 – 0.939) and the model including pNFLT and Fd (AUC = 0.830; 95%CI: 0.754 – 0.906) also had a fairly good performance.

## Conclusions

The peripapillary superficial capillary plexus characteristics on OCT-A are different between healthy and glaucoma subjects. In the future, analyses of OCT-A quantitative parameters could be potentially helpful in glaucoma diagnosis.

3433

## Challenge in squamous cell carcinoma

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<sup>1</sup>

F049

## Implant of micro-stent cypass in glaucoma

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## Purpose

To evaluate the suprachoroidal space by means of Optical Coherence Tomography of the anterior segment after Micropass Stent implantation in patients with open-angle glaucoma.

## Methods

The Micro-Stent is a device that is implanted in the iridocorneal angle in the suprachoroidal space, it is a minimally invasive method that achieves a reduction of the intraocular pressure. Due to its implantation position, CyPass can not be easily visualized, which is why it has resorted to imaging techniques such as the anterior segment OCT. For this we have used the SS-OCT Triton.

After performing these surgeries, a study of the anterior segment was carried out using OCT of the suprachoroidal space, performed one week and one month after the intervention. In these images the CyPass implant was located and the suprachoroidal lake was measured in the two measurements.

### Results

In all cases, both the correct implantation of the CyPass and the suprachoroidal lake were easily identifiable by previous OCT as a hypodense image. In the images obtained both at the week and at the month of surgery, they did not show any significant change in stent position or permeability over time. Just as there were no differences between the combined surgery Faco + CyPass or only CyPass.

### Conclusions

: The CyPass Micro-Stent is designed to reduce the IOP by increasing the suprachoroidal flow through a controlled cyclodialysis, forming a conduit for the aqueous humor from the anterior chamber to the suprachoroidal space. Using anterior OCT images, the accumulation of the aqueous in the suprachoroidal space can be objectified as hypodense areas in all cases and without significant variation in the time of exploration.

**2646**

**Rare conjunctival tumors:( choristomas, neurinomas , sebaceous carcinomas.....)**

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### Summary

Rare conjunctival tumors will be presented, including choristomas, neurinomas, sebaceous carcinomas, and other unfrequent benign and malignant conditions. Aspects of their clinical diagnosis, histopathological characteristics and their clinical relevance, and the most appropriate management strategies will be discussed.

**2947**

**Intravitreal steroids for ocular tumors: indications and limits\r**

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### Summary

A selection of clinical cases, along with data from the literature, will be presented to illustrate the indications of intravitreal steroids, either triamcinolone or sustained-release dexamethasone, for ocular tumors. The limits of these treatment strategies, in term of efficacy and potential complications, will be discussed.

**T002**

**Retinal changes in continuous light: an electron microscopy and NADPH-diaphorase histochemistry evaluation**

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## Purpose

Alterations in photoperiod and light intensities cause damage to retina. Whether retinal synapses are altered after light stress are unclear. Nitric oxide is known to be involved in phototransduction. The aim of this study was to understand the involvement of nitric oxide synthase (NOS) in bright light induced retina.

## Methods

One day-old chicks (*Gallus gallus domesticus*) were reared in normal 12 h light –12 h dark cycle (12L: 12D) for 7 days (400 lux). From day 8 onwards, they were exposed to high intensity light (5000 lux, experimental) and 400 lux (control) at 12L: 12D, 18L:6D and 24L: 0D conditions and sacrificed and their eyes enucleated at 12h, 24h and 168h intervals after light exposure. Retinal changes were examined by transmission electron microscopy (TEM) at 168 h. Cryosections were stained for NADPH diaphorase (NADPH-d), involved in activation of NOS.

## Results

After exposure to 5000 lux, intense NADPH-d staining was found in ganglion and inner nuclear layer (INL) cells, inner and outer plexiform layer at 12h and 24h compared to 400 lux exposed group. TEM analysis revealed cytoplasmic organelle depletion in INL cells after exposure of 5000 lux with respect to 400 lux under 12L: 12D photoperiod for 168 h. There was empty space between INL cells, which was filled by larger Müller cell processes. Synaptic ribbon length was reduced significantly from 0.374 to 0.324  $\mu\text{m}$  in 12L: 12D vs 24L: 0D photoperiod.

## Conclusions

Alterations in photoreceptor synaptic ribbon morphology and intercellular cytoplasmic depletion in INL indicate the adverse effect of light in non- light receptive area. Increased number of NADPH-d positive INL cells after bright light exposure implicate a role for NOS in retinal degeneration.

3361

### Molecular mechanisms underlying retinal degeneration caused by cilia dysfunction

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## Summary

Primary cilia are microtubule based sensory organelles that protrude from the cell membrane. Cilia defects cause a range of human diseases, collectively termed ciliopathies, in which most patients exhibit retinal degeneration (RD). Numerous ciliopathy mouse models have been identified that recapitulate the human RD phenotype. Moreover, a large proportion of genes responsible for non-syndromic RD encode for cilia proteins. The vertebrate retina contains multiple ciliated cell types, most notably the highly modified primary cilium that elaborates to form the photoreceptor outer segment. Until now other ciliated cell types in the eye have been practically ignored and their physiological function is only speculative. One particular cell type that is tightly associated with photoreceptors and essential for their function and survival are the retinal pigmented epithelial (RPE) cells. We have found that the RPE requires a functional primary cilium for complete maturation, and that RPE maturation defects in ciliopathies precede photoreceptor development. We are further characterising the specific role of the primary cilium in the RPE and to which extent its dysfunction can influence the rate of visual decline in ciliopathy mouse mutants.

T013

### In vivo retinal cells visible without adaptive optics using a novel full-field OCT

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## Purpose

Progress in the design of adaptive optics (AO) instruments opened a possibility to view cellular structures of the *in vivo* retina despite presence of eye aberrations. However, complexity of AO devices presents a significant barrier on the way to clinical implementation, as a result, up to this day, no clinical cell-resolution AO instrument reached the market. We created and tested a novel device, called full-field OCT, capable of cell-resolution viewing of the *in vivo* human retina without AO.

## Methods

*In vivo* retinal images were obtained from a healthy human subject using a novel full-field OCT device. Lateral and axial resolutions of the instrument were 4  $\mu\text{m}$  and 7.7  $\mu\text{m}$ , respectively. Images were acquired with a speed of 200 *en face* frames per second, sufficient to freeze the movements of the eye. Registration algorithm followed by averaging procedure was applied to increase signal-to-noise ratio in the images. Eye was illuminated by NIR (near-infrared) LED (light-emitting diode), comfortable for viewing.

## Results

In FFOCT retinal images, the retinal nerve fiber layer (RNFL) and the photoreceptor inner/outer segment (IS/OS) junction layer at retinal near periphery (6°) clearly revealed structural information such as the nerve fiber orientation, blood vessel distribution, and the photoreceptor mosaic. The photoreceptor mosaic spacing showing in FFOCT image agreed with literature.

## Conclusions

FFOCT is a novel tool for imaging *in vivo* human retina with cellular resolution without AO. Dimensions and shapes of the structures observed in FFOCT are in agreement with literature.

S025

## Non-contact millimeter-field imaging of *in vivo* corneal cells by full-field OCT

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## Purpose

Today, confocal microscopy is a single clinical tool providing *en face* images of cornea with cellular resolution. However, it is not exempt from drawbacks, being the small field-of-view and requirement of a contact with an eye. We created and tested a novel non-contact, 1.3 mm X 1.3 mm field-of-view, micron-resolution instrument based on a full-field optical coherence tomography (FFOCT).

## Methods

*In vivo* corneal images from four healthy human subjects were obtained with a new FFOCT imaging instrument. Observation was performed in a non-contact way and did not require introduction of any drugs into the eye.



Illumination of the eye was provided by the pulsating NIR (Near-infrared) LED (light-emitting diode) comfortable for viewing. Images were acquired with a speed of 275 *en face* frames per second with each frame being captured in 3.4 milliseconds. Registration algorithm followed by averaging procedure was applied to increase signal-to-noise ratio in the images.

## Results

*In vivo* corneal epithelium, Bowman's layer, sub-basal nerve plexus (SNP), anterior, middle and posterior stromal keratocytes, stromal nerves, endothelial cells with nuclei were visualized with 1.3 mm x 1.3 mm field-of-view using FFOCT. Nuclei had an oval shape, which was becoming more oblong with depth. Thicknesses of the SNP and stromal nerves were measured to be  $4 \pm 2 \mu\text{m}$  and  $7 \pm 2 \mu\text{m}$ , respectively. Endothelial cells had diameters of  $20 \pm 1 \mu\text{m}$  with their nuclei being  $3.5 \pm 1 \mu\text{m}$ . Cells were hexagonal in shape with a round nuclei. The above results are in agreement with the known confocal microscopy data.

## Conclusions

FFOCT is a novel tool for non-contact imaging of millimeter sections of the *in vivo* human cornea with cellular resolution. Dimensions and shapes of the structures observed in FFOCT are in agreement with those seen in the conventional contact confocal microscopy.

1761

## Overview of the biological rationale for efficacy of nutritional supplements to prevent AMD

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## Summary

In 1965, Bradford Hill introduced the following criteria for the determination of causation in epidemiologic association studies: strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment and analogy. Researchers have consistently demonstrated in epidemiologic studies that low antioxidant intake is associated with increased risk of AMD, and have successfully demonstrated in large randomised clinical trials a decreased risk of AMD progression with antioxidant supplementation. For antioxidant supplementation to successfully prevent AMD progression, oxidative damage must be prevented. The most likely source of the oxidative damage in AMD is cigarette smoking, which has consistently been shown to be the most significant modifiable risk factor for AMD. Purported mechanisms of retinal damage due to cigarette smoking include oxidative damage and cellular changes to the retinal pigment epithelium. Nicotine in cigarettes promotes nitric oxide production. Oxidative stress is thought to be essential in drusen formation, a feature of AMD. The biologic rationale for efficacy of nutritional supplements to prevent AMD will be reviewed.

1222

## Models to study the impact of mitochondrial dysfunction on neurodegeneration

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## Summary

Mitochondrial dysfunction is one of the greatest common factors in ophthalmological diseases characterized by the selective loss of retinal ganglion cells (RGCs). Interestingly, the mitochondrial impairment appears to specifically involve OXPHOS complex I (C-I) inhibition, which correlates with the age of onset and severity of disease. The complex genetics and bioenergetic etiology of these diseases have stalled the development of effective animal models and therapies, until now. We have created mice with mtDNA and nDNA alterations specific to human optic

atrophy. The first, C-I mtDNA *ND6<sup>P25L</sup>* mutant mouse adequately recapitulates LHON. The *ND6<sup>P25L</sup>* mutation causes a ~30% reduction in C-I activity and increased mitochondrial ROS without affecting ATP production. Increased oxidative stress precedes ERG abnormalities in *ND6<sup>P25L</sup>* mice, suggesting RGC death is due to increased oxidative stress. As such, we have developed a noninvasive method for quantitative analysis of oxidative stress *in vivo*, which we propose as a predictive biomarker for optic neuropathy. With these new models and techniques, we are in an unprecedented position to develop preventative mitochondria-targeted therapeutics for direct translation to the clinic.

**3322**

**Lasers**

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#### **Summary**

Since the first laseriridotomy in 1956, the treatment of glaucoma with different laser techniques has been a universally accepted part of the glaucoma management.

The lecture will highlight the newest developments in the different laser techniques and their influence on the glaucoma management, including their use in the glaucoma therapy cascade presented in the EGS guidelines. Besides new studies on laseriridotomie, lasertrabeculoplasty (with different techniques) and laseriridoplasty, also the new developments in microinvasive glaucoma surgery (Eximer Laser Trabeculostomy and Endoscopic and Transscleral Cyclophotocoagulation) will be compared to existing therapeutic options.

We will discuss the results of the newest laser trials, especially the LIGHT trial and how these results can be implemented in our daily practice.

In summary, the lecture gives an overview of the different laser techniques, the newest studies and results of trials and it discusses how we can implement the results in our daily management of glaucoma patients.

**2755**

**Is it possible to run a self-supporting Scleral Contact Lenses practise?**

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#### **Summary**

In recent years, there has been a strong comeback of scleral lenses. Algeria is a keratoconus-endemic country and our center is the main national contact lens center. Since 2012, an average of 1000 eyes are fitted with scleral lens each year and our activity continues to grow. During the presentation, we will share our experience and we will propose the appropriate solutions for the problems we encounter each day to be able to continue to manage this activity which offers a great service to the population.

2955

**After SURGERY CXL or ICRS implantation or after graft (DALK or PK) ?**

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**Summary**

What to do with an unsatisfied keratoconus patient after corneal surgery to stop the disease evolution (corneal collagen cross linking) or to improve his ou her vision (Intracorneal ring segment implantation, phakic intraocular lens implantation, deep anterior lamellar keratoplasty or penetrating keratoplasty)? The contact lenses come back to solve the problem and make patient happy again. We will present these different senarios, how to manage them first psychologically and then with the best contact lens fitting solution.

1721

**The Use of Simulated Ocular Surgery (SOS) eyes in Glaucoma Surgical Training 2 – A U.K. Tertiary Referral Teaching Hospital Experience, One Year Later**

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**Summary**

*The Royal College of Ophthalmologists (RCOphth) sets the curriculum and standards for surgical training in the UK; this receives approval from the General Medical Council. The evolution of surgical training will be presented. A microsurgical skills course, in simulation, prior to commencing live surgery has been mandatory for more than 7 years. A new strategy to increase simulation in all surgical subspecialties was initiated in 2014. This included the development of a curriculum for simulation with recommendations and resources published since 2015. Increasing availability of inexpensive options for simulation has allowed this to be available in all UK regions and to be considered mandatory in the required surgical competencies in the curriculum. Recent developments have included the introduction of Entrustable Professional Activities, or EPAs, to demonstrate the ability to manage an entire surgical list, demonstrating planning, teamwork and communication in addition to surgical technique. This also highlights the importance of considering simulation in communication skills or immersive simulation techniques.*

2913

**Adaptive optics scanning laser ophthalmoscopy: clinical applications**

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**Summary**

Adaptive Optics (AO) has become very popular in recent years, thanks to its capability to measure and correct the aberrations introduced by the optics of the eye when trying to generate retinal images.

The combination of AO with Scanning Laser Ophthalmoscopy (SLO), usually referred to as AOSLO, has been very successful in its clinical applications. Using AOSLO, ophthalmologists have been able to observe individual cones and rods, retinal pigment epithelium cells, the micro-capillary network, or the structure in the retinal nerve fiber

layer or the lamina cribrosa, to name a few. This has been achieved not only in healthy subjects, but also in patients suffering from age related macular degeneration, retinitis pigmentosa, diabetic retinopathy or glaucoma, amongst other.

The clinical applications of AOSLO in the ophthalmology clinic are very broad, and in this presentation we will introduce them along with the concepts behind the technique to give them some context. We will also learn about the results that have already been achieved using this technique, and why AO is having such a great impact in the ophthalmology community.

**2524**

#### **TFOS DEWS II Iatrogenic Dry Eye Report**

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#### **Summary**

Dry eye disease (DED) can be caused by a variety of iatrogenic interventions. Topical medications can induce DED due to their allergic, toxic and immuno-inflammatory effects on the ocular surface. Preservatives, such as benzalkonium chloride, may further aggravate DED. A variety of systemic drugs can also cause DED secondary to multiple mechanisms. Moreover, the use of contact lens induces or is associated with DED. However, one of the most emblematic situations is DED caused by surgical procedures such as corneal refractive surgery and keratoplasty due to mechanisms intrinsic to the procedure (i.e. corneal denervation) or even by the use of postoperative topical drugs. Cataract surgery, lid surgeries, botulinum toxin application and cosmetic procedures are also considered risk factors to iatrogenic DED, which can cause patient dissatisfaction, visual disturbance and poor surgical outcomes. Future directions to address iatrogenic DED, including the need for more in depth epidemiological studies, development of less toxic medications and preservatives, detection of preoperative DED as well as new techniques for less invasive eye surgeries are presented.

**2354**

#### **Refractive development of the lens and it's relation to cataract type**

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#### **Summary**

Cross-sectional and longitudinal population-based studies are reviewed and summarized to quantify and illustrate the changes of the spherical equivalent refractive error by age. Between 35 and 65 years of age an average hyperopic shift of 0.05 diopters (D) per year is found, followed by a stabilization and an average myopic shift of 0.05 D between 75 and 85 years of age.

Spherical equivalent refractive error of 239 patients (age 50-90 years) scheduled for cataract surgery was collected. In order to make the refractive data comparable, the refractive error at an age of 45 years was estimated for all patients, considering the hyperopic and myopic shifts found in the literature. Cataracts were graded and patients grouped into having no relevant cataract, nuclear cataract, cortical cataract or mixed cortical-nuclear cataract. Cases with high myopia and low visual acuity were excluded. Spherical equivalent refractive error (at the age of 45 years) was found to be independent of the degree of nuclear cataract. There was a significant difference between groups with cortical cataract (-0.5 D) and without cortical cataract (-2.6 D).

**S040**

**Developement of a safe and biocompatible powder to be reconstituted as keystone for dry eye syndrome treatment**

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**Purpose**

Umbilical cord lining (UCL) is made up an amniotic membrane and Wharton's jelly (WJ) which is rich in growth factor and 1150 +/- 280 kD hyaluronic acid (HA). HA have the property to be a very efficient moisturizer. The aim is to develop from UCL a safe biologic powder that can be store at room temperature (RT) and moisturizing once rehydrated, to be used as collyrium for dry eye syndrome

**Methods**

Umbilical cords are sampled according to directive 2006/17/CE. Isolated UCL undergoes a viral-inactivating chemical treatment, and is then ground (gUCL), freeze-dried and gamma sterilized (tgUCL). Viral inactivation is assessed by spiking viruses into WJ and quantifying remaining viruses, on treated umbilical veins (tUV). Disinfection by chemical baths is evaluated by bioburden assessment before sterilization, and endotoxin assessment after irradiation on tgUCL. Sterilization is evaluated by spiking 10exp7 radioresistant bacteria before gamma sterilization on the same tissue that did not undergo grinding. Biocompatibilty is assessed by cell culture with mesenchymal stem cell (MSC) on tgUCL. Level of HA and TGF- $\beta$  are performed on gUCL.

**Results**

Chemical treatment showed a viral reduction (>4 Log) of each virus. B. pumilus inoculated inside WJ were not present after irradiation, the product meets ISO 10993 requirements. Bioburden is very low (<1,7 UFC/tgUCL) and so are endotoxins (<0,2 EU/tgUCL). MSC were viable and have colonized the tgUCL. Finally HA is present in gUCL (>2mg/mL of gUCL) and so is TGF- $\beta$ 1 (around 150pg/mL of gUCL).

**Conclusions**

Process applied on UCL can provide a safe, storable at RT and biocompatible powder that contains at least hyaluronic acid and TGF- $\beta$ 1. It is a very promising product due to its biological properties and an innovative alternative treatment for dry eye syndrome

**2647**

**High-throughput sequencing reveals no microbial pathogens in ocular adnexal extranodal marginal zone B-cell lymphoma**

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**Purpose**

To perform a next-generation sequencing (NGS) based analysis of viral and bacterial genetic material in samples from patients with extranodal marginal zone B-cell lymphoma (EMZL) in the ocular adnexa.

**Methods**

We subjected 8 EMZL samples to enrichment of microbial (encapsidated) nucleic acids which included sample homogenization, filtration, and nuclease treatment. Both DNA and RNA were sequenced, and we analyzed the sequencing data for the presence of known as well as unknown viral and bacterial sequences.

### Results

We were not able to identify any pathogenic bacteria or virus likely to be associated with EMZL development in our samples. Furthermore, we found no traces of neither *Chlamydia psittaci* nor *Rickettsia Helvetica*. In one sample, we detected human polyomavirus 7 and traces of Epstein-Barr virus (human herpesvirus 4).

### Conclusions

Applying comprehensive NGS-based methods we did not identify microbial pathogens which could explain ocular adnexal EMZL lymphomagenesis.

### T099

#### Effects of focal light-emitting diode (LED)-induced phototoxicity in the albino rat retina

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### Purpose

To analyse the effects of light-emitting diode (LED)-induced phototoxicity by *in vivo* and *ex vivo* structural techniques and immunohistochemistry.

### Methods

All procedures were performed on anesthetized female Sprague Dawley rats (180-200 gr.). The left eye was exposed for 10 s to 200 Lux of blue light (400nm) emitted by a LED placed at 1mm perpendicular to the corneal apex. Total and outer layer retinal thickness were analysed *in vivo* by optical coherence tomography (OCT) at 1, 3, 7, 14 or 30 days (n=6-8) after LED exposition. At different survival intervals of 1-30 days, retinas were dissected as wholemounts and doubly immunolabeled against S-opsin and Iba-1 to identify S-cones and microglial cells

### Results

After LED-exposure, OCT analysis showed in the left retinas a focal area of lesion located in the superotemporal quadrant of the retina. There was a progressive diminution of the outer layer retinal thickness in the centre of the lesion from 1 to 7 days. Whole-mounted retinas examined under fluorescence microscopy showed signs of reactive microglia IBA1 positive cells in the outer segment layer circumscribed to the lesion at 24 hours that remained until day 14. The morphology of these microglial cells changed along time from a dendritic shape at day 1, to an amoeboid shape at day 3 and returned to a dendritic shape at day 14.

### Conclusions

Focal LED induced photoreceptor phototoxicity results in a focal progressive decrease of outer layer retinal thickness and a microglial reaction located in the outer retina.

### 2331

#### Bacterial keratitis – standard treatment?

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### Summary

With increasing resistance of bacteria to antibiotics, there are changing trends in treatment of bacterial keratitis. We summarize up-to-date diagnostic and treatment options of bacterial keratitis using literature data and some clinical examples. As conservative treatment we use primarily topical moxifloxacin or cephazolin with fortified tobramycin or gentamycin in bacterial infection. In case of early diagnosis and initiation of topical therapy, most cases of infectious keratitis recover successfully. However, beside conservative treatment, crosslinking therapy may be considered in selected cases, moreover, in advanced forms amniotic membrane transplantation and penetrating keratoplasty is necessary.

2916

### Adaptive Optics for inherited retinal disease clinical trials

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### Summary

Since its first use in retinal imaging just over 20 years ago, adaptive optics (AO) imaging has undergone immense growth in its applications amongst vision scientists and clinicians. This technique has allowed imaging of the living retina at a cellular resolution, leading to revolutionary changes in our understanding of retinal diseases, especially those of monogenic aetiology. AO imaging has opened exciting avenues for research, monitoring retinal disease progression and providing new tools for differential diagnosis. To date, nearly 100 publications about cellular anatomy in inherited eye diseases have been published. As we stand at the precipice of new treatments for retinal disease, cellular imaging with AO has assisted with patient selection and guiding potential outcomes. AO imaging can now frequently image not just the cone photoreceptor outer segments, but also rod photoreceptors, cone inner segments and RPE. This talk will highlight several of the cellular structures such as cell density, mosaic organisation, intensity profiles which are likely to prove essential for future work measuring treatment efficacy in clinical trials.

2151

### Myopia epidemiology

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### Summary

There is currently an epidemic of myopia in East and Southeast Asia, where 80-90% of students completing high school are now myopic, with around 20% with high myopia. This may result in an increased prevalence of pathological myopia in the future. In other parts of the world, much smaller increases have appeared. The epidemic of myopia in Orthodox Jewish boys in Israel, but not in Orthodox Jewish girls and the general school-age population, confirms the long-standing idea that intensive schooling plays an important role, although the mechanism is still unclear. In addition, children who spend more time outdoors in bright sunlight are less likely to become myopic, with light-stimulated release of dopamine outdoors inhibiting axial elongation. These two environmental factors provide the basis for primary prevention of myopia. The ability of increased time outdoors to slow the onset and progression of myopia has been demonstrated in school-based trials and is currently the basis of a national program in Taiwan. In China, recent policy statements have emphasized the need to promote

time outdoors and reduce homework demands, particularly in the early school years. These initiatives should have a major effect on the current epidemic.

**2355**

### **Multiple stages of refractive development**

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#### **Summary**

The concept of emmetropisation is supported by the demonstration in animal models that hyperopic defocus stimulates eye growth, whereas myopic defocus inhibits it. These ideas however imply that myopia is a self-limiting condition and that it would be dangerous to correct myopes. Neither of these statements is correct in relation to human refractive development. In fact, the preferred refractive state in humans is mild hyperopia. Human infants are generally born hyperopic, and the Gaussian distribution of refraction is then sharpened into a tightly peaked distribution with a peak at around +1.0D, with reductions in corneal and lens power and axial elongation. After 2-3 years, corneal power stabilizes, but the changes in lens power and axial length continue. Reductions in lens power reduce the myopic shift produced by axial elongation. There is some tightening of the distribution of refraction around approximately 1.0D, with the less hyperopic eyes undergoing hyperopic shifts in refraction if the loss of lens power exceeds the rate of axial elongation. Under environmental conditions which produce myopia, these mechanisms are swamped by excessive axial elongation, and children then proceed to emmetropia and on to myopia.

**2641**

### **Conjunctival tumors: clinics and pathology**

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#### **Summary**

The spectrum of conjunctival tumors is broad including epithelial, melanocytic, stromal, and lymphoid tumors. This course will review the clinical, pathological and molecular aspects of common conjunctival tumors.

**3531**

### **Treatment targets in conjunctival melanoma**

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#### **Summary**

Conjunctival melanoma is still associated with a significant mortality at 10 years. Recent evidences suggest that conjunctival and cutaneous melanoma partially share similar molecular features, notably similar oncogenic driver mutations. We will review the efforts that have been undertaken to delineate the genomic landscape of conjunctival melanoma and inhibit its growth.



### T043

#### Retinal neurodegeneration in patients with type 2 diabetes mellitus without diabetic retinopathy

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#### Purpose

To evaluate the structural changes in the neurosensory retina (NSR) in patients with type 2 diabetes mellitus (T2DM) without diabetic retinopathy (WDR), as measured by spectral-domain optical coherence tomography (SD-OCT).

#### Methods

Cross-sectional, comparative study of patients with T2DM WDR against matched, healthy controls. Subjects underwent ophthalmic evaluation and SD-OCT. Automated retinal segmentation was performed, and overall retinal thickness (RT) and of each retinal layer were measured in all nine Early Treatment Diabetic Retinopathy Study (ETDRS) areas. Enhanced-depth imaging (EDI-OCT) was also performed for measurement of choroidal thickness (CT). Generalized additive regression models were used to analyze the data.

#### Results

A total of 175 subjects were recruited (50 controls, 125 patients with T2DM WDR). Patients were stratified into 3 groups according to disease duration: G1 (<5 years, n=55), G2 (5–10 years, n=39), and G3 (>10 years, n=31). After multivariate regression analysis, no difference in overall RT was found between patient and control groups in all ETDRS areas. The most consistent finding was thinning of the photoreceptor layer (PR). Groups G1 and G3 showed a statistically significant PR thinning compared to the control group ( $P < 0.0007$ ); G3 showed the most significant PR thinning, and G1 showed thinner PR than G2. Thickened retinal nerve fiber layer, inner nuclear layer, and retinal pigment epithelium were also observed. No significant changes were observed in the other retinal layers.

#### Conclusions

Our findings suggest a non-linear retinal thickness profile in patients with T2DM. Although overall RT may be unchanged, retinal neurodegeneration occurs even before the microvascular signs of DR are clinically apparent. PR cells are affected early in the disease process, and may play a role in the early pathophysiology of DR.

### T034

#### A case report of Outer Retinal Tubulations in Age-Related Macular Degeneration - imaging and histologic correlates

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#### Purpose

The authors present a case report of age-related macular degeneration (AMD) and provide a review on the clinical and pathological evidence on outer retinal tubulations (ORT) and the clinical utility of spectral-domain optical coherence tomography imaging (SD-OCT) in the evaluation and follow-up of patients with AMD.

## Methods

Case report analysis of a 81 year-old female patient with diagnosis of advanced AMD with 4 years of follow-up. Her left eye (OS) had "hand-motion perception" (HM) vision and a disciform scar on fundus examination. Clinical and imaging follow-up was performed using SD-OCT.

## Results

During the 4 years of follow-up, vision in the patient's OS remained stable, without significant fundus changes by ophthalmoscopy. SD-OCT documented progressive changes in the outer retinal layers, characterized by the "rolling" of the external limiting membrane (ELM) and formation of multiple ORTs in the outer nuclear layer (ONL). These structures showed different temporal and spatial evolution with time.

## Conclusions

ORTs are a SD-OCT finding that reliably reflects the interesting pathologic process of the latest stages of AMD. They represent a protective gliotic response in macular areas of severe dysfunction and loss of the retinal pigment epithelium (RPE), occurring due to failure of the photoreceptor support system. ORTs are a final, common pathway of retinal neurodegeneration that occurs in a number of disease processes, including AMD. Finally, ORTs have shown to be of prognostic relevance. Outer retinal changes such as ORTs have made OCT imaging and increasingly important tool in the diagnosis and follow-up of patients with AMD.

## F020

### Comparison of 1-year outcomes of XEN implantation alone vs combined phacoemulsification-XEN surgery at a Tertiary Center of Ophthalmology in Portugal

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## Purpose

To compare the 1-year efficacy and safety of the XEN45 Stent (Allergan, Irvine, CA) implantation alone versus combined Xen implantation and phacoemulsification (Phaco-Xen) in patients with medically refractory open-angle glaucoma (mrOAG) at a tertiary center for Ophthalmology in Portugal, reporting the initial experience with XEN nationwide.

## Methods

Retrospective, comparative, interventional case series of patients with mrOAG who underwent XEN surgery (isolated or Phaco-Xen) at our institution with at least 12 months of follow-up post-implantation. Outcomes measured at 12-month follow-up included intra-ocular pressure (IOP) reduction and reduction rate (IOP-RR), number of IOP-lowering drugs, and complications. Success was defined as IOP-RR  $\geq 20\%$  and IOP  $< 18$  mmHg and  $> 5$  mmHg, with (qualified) or without (complete) need for IOP-lowering drugs, without further procedures for glaucoma including needling.

## Results

At 12-month post-XEN implantation, there was a statistically significant reduction in median IOP (5,0 mmHg, p-value = 0,050) in the isolated XEN group, but not in the Phaco-Xen group (median IOP reduction 8,0 mmHg, p-value = 0,123). Nevertheless, no statistically significant differences between both patient groups were observed in IOP-RR (p-value = 0,680) drug reduction (p-value = 0,056), number of successful cases (p-value = 0,605), and number of complications (p-value= 0,457).

## Conclusions

In our study, XEN45 implantation showed good efficacy in medically refractory OAG at 1 year. Combining cataract surgery showed neither added IOP-lowering benefit nor association with inferior success or increased number of

complications. Larger, prospective studies are needed to ascertain whether cataract surgery may have an added IOP-lowering benefit in XEN surgery.

**2741**

### **Clinical features and differential diagnosis of orbital inflammation**

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#### **Summary**

Orbital Inflammatory Disease (OID) may involve one or multiple structures of the orbit as anterior orbit, muscle (myositis), lacrimal gland, and diffuse or posterior orbit. The spectrum of orbital inflammatory disease ranges broadly from specific disease diagnoses, specific to nonspecific. Such mimics of OID must be considered in a comprehensive differential diagnosis and include malignancies (metastasis and lymphomas). Acute diffuse of OID presents with a sudden onset of severe orbital pain with accompanying lid edema and various degrees of erythema, conjunctival chemosis, proptosis and extraocular muscle dysfunction. There is often pain on eye movement and pain on retrodisplacement of the globe. The chronic form may be a sequelae of acute recurrent orbital inflammation or may present insidiously as a sub-acute process.

**F103**

### **Conservative Treatment of Newly Diagnosed Keratoconus**

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#### **Purpose**

To determine if there is statistically significant difference between best corrected visual acuity (BCVA) obtained by spectacles and contact lenses in newly diagnosed keratoconus patients. To determine which type of contact lenses provide better BCVA in keratoconus patients.

#### **Methods**

5-year retrospective study of 2891 patients attending Contact Lens Department for the first time, searching newly diagnosed keratoconus. Data were obtained on gender, age, education level, treated eyes, corneal changes, keratoconus severity, BCVA with spectacles/contact lenses and best fitted contact lens type. All patients underwent standard ophthalmic exam, refractometry and keratometry, spectacles correction and lens fitting. Wilcoxon signed rank test was used for statistical analysis.

#### **Results**

Of all 2891 patients that were examined for the first time, 137 patients (4.74%) have been newly diagnosed with keratoconus. There was male bias (72.26%), mean age 27.7+/-9.9 years. Most patients had high school education (51.11%), 3.70% had present corneal changes, 50.37% had mild keratoconus. Majority had keratoconus on both eyes (36.3%) or keratoconus of right eye (26.67%). There was a statistically significant difference ( $p < 0.001$ ) between BCVA obtained with contact lenses (0.82+/-0.21) rather than spectacles (0.37+/-0.27). BCVA was achieved with RGP lenses in majority of keratoconus eyes (51.85%), with SGP lenses in 43.39%. In 4.23% with PMMA lenses and with "hard-soft" GP contact lenses in 0.53% of keratoconus eyes.

#### **Conclusions**

*There is statistically significant difference in BCVA achieved better with contact lenses than with spectacles. RGP lenses are most frequently used in conservative treatment of keratoconus, but SGP lenses were also shown to be a good option that gives equally satisfying final visual acuity with subjective comfortable feeling of contact lens wear.*

## **S116**

### **Invasive retinoblastoma – case report**

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#### **Purpose**

To present a case of child with invasive retinoblastoma

#### **Methods**

6-year-old patient admitted to our Department for diagnostic evaluation and possible treatment of PHD confirmed invasive retinoblastoma with retrolaminar optic nerve affection. Orbital and brain MRI, skeletal scintigraphy and abdominal ultrasound have been performed, as well as pediatric oncologist examination

#### **Results**

During 1 year patient was followed in another hospital due to suspicious old retinal detachment, then cataract and glaucoma. 3 months before the definitive diagnosis of retinoblastoma, aspiration of lens masses with exploratory vitrectomy, cyclophotoagulation, intravitreal antiVEGF, corticosteroid and antibiotic therapy were done. Further, enucleation with placement of orbital implant and back sclerectomy were performed. Sample was sent to PHD analysis which showed invasive retinoblastoma with retrolaminar spread. Patient was referred to our Department. Skeletal scintigraphy and abdominal ultrasound showed no pathology. After consultation of a pediatric oncologist systemic chemotherapy was started, radiotherapy is planned afterwards

#### **Conclusions**

Retinoblastoma is the most common malignant intraocular child tumor and among most common solid tumors in children, incidence 3.4-42.6 per 106 live births. Most commonly diagnosed during first year in hereditary and bilateral cases, between 1st-3rd year in sporadic and unilateral cases, no gender predilection. By presentation 60% of cases are unilateral, 40% are bilateral. Most commonly presented with leukocoria, strabismus, red eye, preseptal/orbital cellulitis, glaucoma, proptosis, uveitis etc. Mandatory diagnostics include fundus, US, and CT/MRI. Treatment is chemotherapy (systemic, intraarterial, intravitreal), radiation, enucleation. Regular follow-up is mandatory also because of higher risk of other malignancies

## **1716**

### **Innovation and advances in bioelectronic medicine progressing to address atrophic dry AMD with wireless sub-retinal photovoltaic implant**

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#### **Summary**

Several approaches aim to restore some useful vision by electrical stimulation of the retina in patients with degenerated photoreceptors but preserved ganglion cells. The epi-retinal stimulation relies on targeting these cells, bypassing the photoreceptors and the natural processing pathway in the eye. Pixium Vision first developed the epi-retinal IRIS II bionic vision system for retinitis pigmentosa, with 150 electrodes, and successfully presented

positive results at 6 months. To stimulate the retina, the electrode array is inserted into the eye, and is connected via a cable to an extraocular housing containing electronics, hence requiring delicate time consuming surgery. Looking to the future, a new generation miniaturized 2x2mm wireless scalable chip PRIMA (currently with 378 independent electrodes/pixels) has been developed enabling sub-retinal placement. PRIMA was conceived for a minimal invasive surgery, initially targeting dry AMD, a significant unmet need. First clinical study is ongoing in Europe and feasibility study under breakthrough device program is expected to start in the US shortly. Early observations provide confidence with sub-retinal wireless PRIMA chip placed under the macula and elicitation of light perception.

**S089**

#### **Rab 7 characterization and its regulatory role on autophagy in retinal pigment epithelium cells**

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#### **Purpose**

*Background:*

Macroautophagy or autophagy, referred to as a self-eating process performs the critical housekeeping functions in eukaryotic cells. During this process, cytoplasmic materials are delivered to lysosomes for degradation and recycling. Rab 7 belongs to the small GTPase family and has an important role in autophagy. It controls the maturation of endosomes and autophagosomes, directs the trafficking of proteins along the microtubules, and participates in the fusion step with lysosomes. Changes in the inflammatory state along with impaired autophagy are present in the pathogenesis of age-related macular degeneration (AMD).

In this study, we have investigated the regulatory role of Rab7 in human retinal pigment epithelium (RPE) cells with the focus on inflammation.

#### **Methods**

ARPE-19 cells derived from human retinal pigment epithelium were purchased from ATCC and were grown in DMEM medium with 100U/mL penicillin and 100 µg/mL Streptomycin and 2mM L-glutamine. They were incubated at +37°C, 10% CO<sub>2</sub>. The protein levels were detected using western blot and the secretion of inflammatory cytokines using the ELISA method.

#### **Results**

We have used MG-132 to inhibit the proteasomes and AMPK-activator AICAR (5-aminoimidazole-4-carboxamide ribonucleotide) to induce autophagy. Upon the addition of AICAR and MG-132 together, there was a significant increase in Rab7 levels at 24, 48, and 72h. We also observed increased inflammatory response along with higher amounts of Rab7.

#### **Conclusions**

Our results emphasize the importance of Rab7 in the regulation of autophagy and inflammation in RPE cells that play the principal role in the pathogenesis of age-related macular degeneration (AMD).

**3142**

#### **Evisceration with autogenous scleral graft and bioceramic implantation within the modified scleral shell: 133 cases over 17 years**

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### **Purpose**

To present long-term follow-up data on evisceration performed with autogenous scleral grafting and ceramic implantation in a modified scleral shell.

### **Methods**

This was a retrospective analysis of all consecutive eviscerations performed in the department of ophthalmology, Montpellier University Hospital, France, between February 1998 and October 2015. For all patients, the technique used was a conventional anterior evisceration after total keratectomy, desinsertion of the medial rectus muscle, sectioning of the optic nerve and excision of sclera centered on the papilla. The scleral graft was then sutured just behind the sutured keratectomy, and the bioceramic implant was inserted by posterior way in the scleral shell. Demographic characteristics, implant size and type, cosmetic results from pictures of all patients and complications were recorded. This study was performed with Ethics Review Committee Approval, and in compliance with the Declaration of Helsinki.

### **Results**

In total, 133 patients (36.6% women) were identified during the study period. The mean (SD) implant size was 17.32 (1.84) mm. The median follow-up after evisceration was 57.43 (24.7, 68.3) months. Two cases of implant exposure (1.5%) were recorded. For 24 patients (17.9%), additional surgeries were performed for ptosis (2.2%), conjunctival cyst (1.5%) or post-evisceration socket syndrome (6.7%). Cosmetics results were excellent for 50.1% of cases, good for 33.3% and fair for 16.6%; using a grading scale based on the superior sulcus deformity.

### **Conclusions**

Evisceration with autogenous scleral grafting and ceramic implantation can result in a high volume of restoration, good cosmetic results and low risk of exposure of the implant.

**3427**

### **Refractive error and forward light scatter**

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### **Summary**

Despite full refractive correction, visual performance of myopic eyes is often poorer than that of emmetropes. Owing to the strong association between increasing myopia and axial length elongation, the impaired visual response is frequently attributed to structural and neural changes in the posterior aspect of the myopic eye. It has been speculated that reduced retinal function in myopia may include loss of cell function; reduced retinal cell density; and misalignment of photoreceptors. A less well studied cause of retinal image degradation is that of increased forward light scatter.

The light scatter function of the eye was measured using the City University, Light-Scatter test ([www.city.ac.uk/avot](http://www.city.ac.uk/avot)). The preliminary results indicate a significant correlation between increasing myopia and overall amount of forward light scatter in the eye ( $k''$  – a parameter proportional to the ‘volume’ of scattered light in the eye). Due to the paucity of work in this field, the source of variation in light scatter with respect to refractive error remains unclear.

The results of this study will be discussed in the context of previously published data, with particular emphasis on the underlying causes of light scatter changes in myopia.

**S090**

**Ex vivo expansion of human primary RPEs for potential use in clinical transplantation studies**

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**Purpose**

An extended need exists for replacement of retinal pigment epithelial cells (hRPE) in the treatment of retinal disorders, including age-related macular degeneration. We aimed to standardize a protocol for *ex vivo* expansion of human primary hRPEs for future use in clinical transplantation studies in mammalian animal model.

**Methods**

Human primary RPEs were isolated from cadavers following the Guidelines of the Declaration of Helsinki and approved by the Regional Ethics Committee (Oslo, Norway). The cells were cultivated in DMEM Nutrient mixture F12 medium containing 10% FBS, L-glutamine and antibiotic/antimycotic solution and kept at passage 0 throughout the studies. PCR characterization for RPE specific markers (RPE65, ZO-1, ITGAV, ITGB5, PEDF, CONNEXIN43), as well as transmission electron microscopy (TEM) were performed.

**Results**

The hRPEs formed a viable monolayer, which underwent slow proliferation reaching confluency, that could be maintained for longer than half a year. The cells formed spontaneous sheets and produced *de novo* extracellular matrix (ECM) on the basal side. The expression of some of the RPE-specific markers appeared to change *ex vivo*, while maintained expression of ITGAV, ITGB5, PEDF and CONNEXIN43, as well as 100% pigmentation of the cells was achieved. TEM could show the cell-to-cell and cell-to-ECM adhesions.

**Conclusions**

Standardized expansion of hRPE cells with spontaneous sheet formation can be achieved *ex vivo*, which is a necessary step to use such cells in future RPE cell transplantation.

**1454**

**Bioinformatics in tear fluid proteomics – connecting proteomic and clinical data**

*J. NÄTTINEN<sup>1</sup>*

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**Summary**

In precision medicine research, one of the main aims is often to find molecular biomarkers that could indicate e.g. the presence or severity of a given disease or predict a patients response to a given treatment. Biomarkers can include clinical measures but also increasingly, they are molecular expression data obtained from omics studies. Since tears are easy, non-invasive sampling targets, tear proteomics have become a popular field in ophthalmology. However, connecting proteomics and clinical data can be challenging. The aim of this talk is to

discuss about analytical methods, which could be implemented to discover the relevant connections between proteomics data and clinical variables of interest.

**2753**

### **The DOs and DON'T s of Scleral Lens fitting**

A. NAU<sup>1</sup>

<sup>1</sup>Korb & Associates, 400 Commonwealth Ave #2, Boston, United States

#### **Summary**

Scleral lenses, once used only for severe ocular surface disease, are emerging as mainstream therapies for multiple anterior segment conditions. Training clinicians to use this new modality is essential for increasing availability of scleral lenses as a therapeutic option.

The lecture will begin with a brief discussion of the structure of a scleral lens (base curve/sagittal depth/ optic zone/ haptics) and how modifications to these will affect the relationship with the cornea and conjunctiva. Using a patient case, components of evaluating a patient (lid/cornea/conjunctiva/tear film status/refractive status/topical medication use/comorbid conditions/dexterity/living situation) needed to select the appropriate trial lenses will be discussed. Next, elements of trial lens assessment will be covered, with an emphasis on how to make modifications to the fit and lens power. Methods for subsequent evaluation of problems such as lens intolerance, corneal edema, entrapment of conjunctival chalasis, giant papillary conjunctivitis, lid wiper epitheliopathy, and refractive status will be reviewed.

**2954**

### **What do we know of indications and outcome of corneal crosslinking – alternative or in addition to Scleral Lenses ?**

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<sup>1</sup>Korb & Associates, 400 Commonwealth Ave #2, Boston, United States

#### **Summary**

What do we know of indications and outcome of corneal crosslinking - alternative or in addition to Scleral Lenses ?

Keratoconus is a bilateral progressive corneal ectasia. Obtaining useful vision requires the use of highly customized contact lenses. Even small amounts of disease progression requires refitting corneal based contact lenses, causing considerable anxiety for patients. Scleral contact lenses vault the cornea and rest on the relatively stable conjunctiva. While typically relegated to treating advanced disease because of the associated expertise required, time to fit and expense, their use in cases of mild to moderate, but unstable keratoconus patients will be discussed. Collagen crosslinking initiates the formation of reactive oxygen species, causing formation of covalent bonds between collagen molecules thus increasing biomechanical strength of the cornea. The currently meta-analyses on outcomes will be reviewed. Whether crosslinking in combination with scleral lens use could provide better patient outcomes will be debated.

**2752**

### **How do I fit a Scleral contact lens in a specific patient?**

C. NAU<sup>1</sup>

<sup>1</sup>Mayo Clinic, Ophthalmology, Minnesota, United States



### Summary

The two main indications for scleral lens wear are corneal irregularity and ocular surface disease. Ideal fitting parameters may vary depending upon the indication for which lenses are being used. This course will explore basic concepts of scleral lens fitting (eg central corneal clearance, limbal clearance, conjunctival alignment) in the context of various indications. Representative cases of patients fit with lenses for corneal irregularity and ocular surface disease will be reviewed, with specific emphasis on the ways in which fitting goals for particular patients may be driven by the condition being treated.

**2953**

### Which lens fit the best for which patient ?

C. NAU<sup>1</sup>

<sup>1</sup>Mayo Clinic, Ophthalmology, Minnesota, United States

### Summary

In a study of almost 400 keratoconus patients, they were asked their experience and opinions of visual correction, comfort and ease of use with their current correction. Only 11% of these patients (42/389) reported that they were very satisfied with vision, comfort and ease of use with their current correction. However, 25% (101/389) were very satisfied with vision alone. Thirty-one percent were very satisfied with comfort alone (122/389), while another 31% were very satisfied with ease of use alone (121/389). There were very few (3%; 13/389) that were very dissatisfied with vision, comfort and ease of use with their current correction. With the many lens options available to patients, and many different patient expectations, we will review considerations in selecting lenses for the keratoconus patient.

**2353**

### Optical quality of the cornea and its age-related changes

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### Summary

The cornea is the first and most important optical element of the eye. The refractive power of this meniscus lens is about 43 D, about double that of the crystalline lens. Most of that power results from the difference in refractive index between air and corneal tissue at its anterior surface. Despite the role of the tear layer of keeping this surface smooth, the cornea is a highly aberrated lens because its shape is far from ideal. For example the corneal surfaces are misaligned, and show toricity, conicity and other deformations that produce astigmatism, spherical aberration, coma, trefoil, etc. The RMS wavefront error of the average cornea is about 1 wavelength for a 6 mm pupil, which is 14 times higher than that of a perfect lens. The development of the cornea occurs relatively early in life since 6-year-old children already show similar corneal sizes and shapes as young adults. The cornea also shows gradual optical changes with age, with a modest increase in power of 0.75 D between 20 to 75 years of age and an optical quality that changes more dramatically. RMS wavefront error increases by a factor of over 2.5 in the same period, which seems associated to the increase of misalignments and surface deformations.

**F128**

### Mapping of proteomic profile and effect of the spongy layer in the human amniotic membrane

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### **Purpose**

The graft of human amniotic membrane (HAM) contributes to the healing of corneal perforating ulcers and so to save a large number of eyes suffering of severe chemical burns. For clinical use, the HAM is denuded from its spongy layer, but this layer can be an important source of growth factors which promote re-epithelialization. The aim of our study is to provide a general view of protein expression of the HAM, with or without the spongy layer and therefore to determine if the spongy layer and/or mapping patch HAM have a beneficial role in the process of wound healing in patients with corneal ulcers.

### **Methods**

Human placentas were obtained from healthy women after signing the consent form. Mapping of protein expression is done by dividing each placenta in 2 equal parts, one with spongy layer and another without. Each part is divided in 3 zones depending on the distance from the umbilical cord. The proteomic analysis were done by targeting growth factors and pro-inflammatory cytokine.

### **Results**

Our first results show that in general depending on the region of human amniotic membrane no significant difference in expression of proteins levels for KGF, EGF, HGF and TGF- $\beta$ 1 is observed. NGF seems to be expressed at very low level or not in a detectable level. We do not detect TNF- $\alpha$  in the HAM. Interestingly we saw a difference in the expression of those growth factors between different placentas.

### **Conclusions**

These results suggest that the difference in growth factors levels between HAM from different placentas is not due to the suppression of growth factors expression by pro-inflammatory cytokine. We are also performing a comparative evaluation of the mapping in HAM by *label-free* method.

This work is Co-supported by European Union and Normandy Regional Council. Europe gets involved in Normandy with European Regional Development Fund.

### **F091**

#### **Neurodegeneration in non-proliferative diabetic retinopathy: new biomarkers and their relation to vasculopathy and visual function**

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### **Purpose**

To provide non-invasive biomarkers of non-proliferative diabetic retinopathy (DR) based on objective functional parameters of the inner neuroretinal layer and see how they correlate with visual function and structural neurovascular imaging.

## Methods

47 eyes from 25 diabetic subjects were compared to 40 eyes from 20 age-matched controls. Grading of DR from 0 to 3 (no DR to severe) was based on fundus photography. Parafoveal density (PFD) of the superficial vascular plexus on OCTA was correlated to fundus grading. Post-illumination pupil response (PIPR), intended to assess intrinsically photosensitive retinal ganglion cells (ipRGC), was measured by pupillometry. Photonegative response (PhNR) amplitude from RGCs was measured using a skin-electrode full-field portable electroretinogram (ERG). Subjective tests of vision were: best corrected visual acuity (BCVA), low-contrast sensitivity (LCS), color vision and 30° automated perimetry (30°AP). RGC structure was assessed by macular GCL thickness on OCT.

## Results

PIPR and PhNR were significantly reduced in the diabetic compared to control group ( $p<0.0001$  and  $p=0.0046$ ), as were the visual tests: BCVA ( $p=0.0466$ ), LCS ( $p<0.0001$ ), color vision ( $p=0.01$ ), 30°AP mean sensitivity ( $p=0.0004$ ). PIPR and PhNR both correlated with GCL thickness ( $p=0.05$  and  $p=0.015$ ). There was a correlation between the DR grade and PFD on OCTA ( $p=0.046$ ). Both PIPR and PhNR correlated with PFD ( $p=0.028$  and  $p=0.006$ ).

## Conclusions

PIPR and PhNR are reduced in patients with non-proliferative DR. These parameters correlate with decreased visual function and with a thinning of macular GCL as well as vascular rarefaction of the inner plexus. Portable pupillometry and electrophysiology may provide useful biomarkers that quantitatively assess and monitor DR based on neurodegenerative dysfunction in a process that parallels progressive vasculopathy.

## F130

### Vision-Related and Health-Related Quality of Life in Patients with Giant Cell Arteritis

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## Purpose

To assess vision-related quality of life (VR-QoL) and general health-related quality of life (HR-QoL) in patients with giant cell arteritis (GCA). Specific objectives included looking at the relationship between visual acuity (VA), VR-QoL and HR-QoL in GCA patients.

## Methods

Demographic and clinical data were collected prospectively on all patients who presented with symptoms suspicious for GCA. VR-QoL and HR-QoL questionnaires were self-administered to patients on the morning of temporal artery biopsy (TAB). The Vision Core Module 1 (VCM1) and the 36-Item Short Form Health Survey (SF-36) were utilised.

## Results

There were a total of 70 cases with a mean age of 68.9 (SD 9.1) years, and a female to male ratio of 2:1. 24.3% had non-permanent visual disturbance and 20% had permanent visual loss. Median VA in the better eyes of patients was logMAR 0.00 (IQR 0.19) and in the worse eyes was logMAR 0.18 (IQR 0.30). 56.7 % of patients had a VCM1 score of  $>2$ , which indicates 'more than a little' concern about their vision. Worse eye VA correlated with VCM1 score ( $r=0.412$ ,  $p=0.001$ ).

All of the SF-36 subscales except for physical functioning (PF) were significantly ( $<0.05$ ) worse in GCA patients when matched for age and sex. Correlations were found between the VCM1 and the subscales of role emotional (RE), social functioning (SF), mental health (MH), general health perception (GHP) and mental composite score (MCS) ( $r=-0.45$  to  $-0.265$ ,  $p<0.05$  for all). PF was the only subscale in which patients with visual loss scored significantly worse than in those without visual loss ( $z=-2.192$ ,  $p=0.028$ ).

## Conclusions

The majority of patients with GCA do not suffer permanent visual loss. GCA is associated with impairment of HR-QoL in 7 out of 8 subscales of the SF-36 survey when compared with normative data. VR-QoL impairment in GCA correlates to impaired HR-QoL.

## S084

### Effect of trypsin-EDTA on expression of DNA damage repair enzyme APE1 in human conjunctival epithelial cells

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## Purpose

Enzymatic cell dissociation may provide cell-cultures for experimental purposes as well as for tissue engineering. We here examine conjunctival morphology and expression of the DNA repair enzyme APE1 during incubation in trypsin-EDTA, an agent in common use for cell dissociation.

## Methods

Experiments were conducted in accordance with the Declaration of Helsinki and Local Committees for Medical Research Ethics. Post mortem samples of human conjunctiva were incubated in trypsin-EDTA for 0 (control), 1 or 3 hours, fixed, embedded, sectioned and stained with H&E or processed for immuno-histochemistry (IHC) for APE1 detection. Control samples were examined for 8-OHdG (marker for oxidative DNA base damage) and for gene expression of APE1 by *in situ* hybridization (ISH).

## Results

Conjunctival epithelium in control samples was regularly bi- or multilayered and cells were moderately positive for 8-OHdG, while slight expression of APE1 could be detected by ISH. Incubation in trypsin-EDTA for 1 hour was observed to induce slit-like spaces between epithelial cell layers and to promote dissociation of epithelium into single cells and clusters of cells. These patterns were still recognizable in samples after 3 hours of incubation. Semi-quantitative evaluation of APE1 by IHC showed no detectable alteration in its expression during incubation in trypsin-EDTA.

## Conclusions

Damage to the DNA may, when unrepaired, interfere with cell function, differentiation, proliferation and viability. Dissociation of cells by trypsin-EDTA may induce molecular stress and damage. *In vivo*, oxidized DNA bases are normally repaired by base excision repair (BER) enzymes including APE1, and any noticeable changes in the protein levels of this particular repair enzyme could not be observed during incubation in trypsin-EDTA.

## 1263

### Effect of topical glaucoma treatments on OCT Image Quality

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## Summary

the tear film, one of the eye's optical media, can be affected by IOP lowering medications. Its integrity is of paramount importance for generating reliable and reproducible retinal and optic nerve diagnostic images and for the assessment of disease progression.

This presentation will discuss why the ocular surface is so important and how OSD can affect objective imaging parameters for glaucoma progression analysis.

**2122**

### **Improving information extraction from visual field data**

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#### **Summary**

The systematic analysis of longitudinal visual fields is a well-established approach in assessing glaucoma progression. However, current methods are limited by the large variability of individual tests, and the need for a large number of visual fields tests over long follow up periods to eventually demonstrate progression. Perfecting a clinically useful assessment of glaucoma progression remains a great challenge in research and clinical practice. This presentation will discuss novel technology in extracting and analysing visual field data

**2725**

### **Neuroprotection in glaucoma – outstanding challenges**

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#### **Summary**

The rate of ganglion cell loss due to normal aging is approximately 0.4% loss per year, whereas that due to glaucoma estimated as up to 4% per year. Assuming that early visual field defects are identified after a loss of 40% of RGC, this translates to a 10 year delay in picking up abnormalities and potentially start neuroprotective treatments. Novel technologies are now available to assess the early stages of glaucoma and perhaps will help to overcome the current limitations in measuring neuroprotective outcomes. In this presentation we will discuss past present and future of Neuroprotection in glaucoma.

**F035**

### **Changes in circumpapillary retinal nerve fibre layer thickness after phaco surgery only in patients with primary angle closure glaucoma**

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#### **Purpose**

Phaco surgery only can effectively lower intraocular pressure (IOP) in patients with primary angle closure glaucoma (PACG); but there are few studies about the effect of phaco surgery only on the retinal nerve fibre thickness (RNFLT) in patients with PACG.

#### **Methods**

PACG patients who underwent uncomplicated phaco surgery only between June 2016 and December 2017 were enrolled the study. Their medical records were retrospectively reviewed. If both eyes were eligible, only one eye with more glaucomatous damage was selected. Spectral domain optical coherence tomography (SD-OCT) examinations for circumpapillary RNFLT measurement were performed before and after phaco surgery only. PACG

patients who had retinal or neurological diseases affecting RNFLT measurement and had poor quality of OCT images were excluded for analysis.

## Results

During the study period, total of 123 PACG patients underwent phaco surgery. Finally, only 47 eyes of 47 PACG patients (M:F 8:39, mean age at surgery  $73.7 \pm 6.0$ ) were included for analysis. There was no difference in average circumpapillary RNFLT before and after phaco surgery only in PACG eyes ( $76.78 \pm 18.80$  vs.  $77.69 \pm 19.45 \mu\text{m}$ ,  $p = 0.19$ , paired t-test). The average circumpapillary RNFLT, however, decreased 44.7% (21/47) of study population after phaco surgery only. The female gender (vs. male gender) was only risk for RNFL thinning after phaco surgery only in PACG eyes (Odds ratio 22.68,  $p = 0.03$ , logistic regression).

## Conclusions

On average, there was no difference in average circumpapillary RNFLT before and after phaco surgery only in PACG eyes. Some portion of PACG patients, however, had glaucoma progression in circumpapillary RNFLT after phaco surgery only. Especially female gender had a higher risk of thinning of RNFLT than male gender after uncomplicated phaco surgery only.

## T045

### Subclinical alterations in the visual function of type 2 diabetes mellitus patients without diabetic retinopathy

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## Purpose

To evaluate subclinical visual dysfunction in type 2 diabetic mellitus (DM2) patients without diabetic retinopathy.

## Methods

Sixty eyes from 30 patients with DM2 and 60 eyes from 30 healthy subjects were evaluated. Best corrected visual acuity (BCVA) was measured with the 100%, 2,5% and 1,25% saturation ETDRS tests. Contrast sensitivity (CS) was evaluated with the Pelli Robson and CSV100E tests, and color vision with the Farnsworth 15D and Lanthony 15D tests. Automated perimetry was evaluated with the Easyfield perimeter. Endocrin variables such as glycosylated hemoglobin, blood pressure, body mass index, microalbumin, blood cholesterol, age at diagnosis and disease duration were registered.

## Results

Significant differences were found in BCVA (2,50% and 1,25% saturation ETDRS tests,  $p=0.002$  y  $p=0.007$  respectively), in CS as measured with the CSV 1000E (at 12 and 18 cycles per degree,  $p=0.007$  and  $p=0.011$  respectively) and in different indexes of the Farnsworth and Lanthony color vision tests ( $p<0.05$ ). No significant differences were observed in the Pelli Robson results. There was a significant correlation between some of the chromatic evaluation parameters and endocrine variables (age at diagnosis and blood cholesterol levels).

## Conclusions

DM2 patients without diabetic retinopathy present a subclinical visual dysfunction compared to healthy controls. Patients with an early age at diagnosis and/or with higher cholesterol levels present worse color vision parameters.

## T042

### Retinal neurodegeneration exists in type 1 diabetes prior diabetic retinopathy

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## Purpose

To evaluate changes in total retinal and inner retinal layers (IRL) thicknesses in type 1 diabetes (DM1) with no diabetic retinopathy (DR) after 8 years of follow up

## Methods

One hundred and twenty two eyes from 61 DM1 patients that were evaluated by OCT in 2009 have been followed up for 8 years. None of them had signs of DR. Sixty eyes from 30 normal subjects age-matched served as control group. All of them were evaluated with Spectralis OCT. After 8 years all of them were examined again looking for changes in the total retinal thickness and outer retinal and IRL thicknesses, including the retinal nerve fibre layer (RNFL), ganglion cell layer (GCL) and inner nuclear layer (INL) thicknesses in all ETDRS areas.

## Results

Ten patients discontinued from the study and 12 eyes developed DR and were discarded. Ninety eyes from 45 DM1 patients were included. Mean ages were 41 and 45 years from the DM1 and control group respectively. Mean retinal subfoveal thickness was maintained during the 8 years follow up period. The values were  $277.63 \pm 17.96 \mu\text{m}$  vs  $286.60 \pm 23.90 \mu\text{m}$  in control and DM1 group respectively in 2009 and  $279.28 \pm 16.36 \mu\text{m}$  vs  $288.28 \pm 28.59 \mu\text{m}$  in 2017. There was a significant reduction in total retinal thickness in all the ETDRS areas excluding the outer temporal area (T2); the control group showed a thickness decrease only in the inferior areas. The thickness loss was mainly by the thinning of the IRL that was significant in all areas of the DM1 patients excluding the T2. The thickness diminution was in both INL and GCL. The control group showed a significant diminution in the GCL in superior and inferior areas after 8 years of follow up.

## Conclusions

Prior the onset of the DR, DM1 patients experience a diminution of their retinal thicknesses over time, mainly in their IRL, supporting the hypothesis of the retinal neurodegeneration in diabetic patient.

## F110

### Electrophysiology and retinal thickness alterations in patients with multiple sclerosis with and without previous optic neuritis

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## Purpose

To assess differences in visual function, structural measurements and electrophysiological tests between three groups: healthy controls, patients with multiple sclerosis (MS) without previous optic neuritis (ON), and patients with MS and a previous ON episode.

## Methods

18 eyes from 18 controls, 17 eyes from 17 patients with MS without ON, and 22 eyes from 22 patients with MS and previous ON were included in the study and underwent visual function tests, including measure of visual acuity (VA) with ETDRS chart at 100, 2.5 and 1.25% saturation and contrast sensitivity (CS) with the Pelli Robson and CSV1000E tests; structural analysis of the retina with Spectralis Optical coherence tomography (OCT) (macular and peripapillary retinal nerve fiber layer [RNFL] thickness, papillomacular bundle thickness, and the nasal/temporal index) and electrophysiological tests (pattern and multifocal electroretinograms [pERG and mfERG], and multifocal visual evoked potentials [mfVEP]).

## Results

Worse results were observed in the VA and in CS measured with the Pelli Robson test ( $p < 0.05$ ), in patients with previous ON compared to non-ON patients, and in the latter compared to controls. This same trend was also observed in the measurements obtained with OCT; in the amplitude of the N95 wave ( $p = 0.020$ ) obtained with pERG; in the sum of the latency of the N1 wave ( $p = 0.019$ ), the amplitude of the ring 2 of N1 wave ( $p = 0.030$ ) of the mfERG, and in the latency time in ring 5 of P1 ( $p = 0.034$ ) of mfVEP.

## Conclusions

Patients with MS and previous ON present decreased VA and CS compared to non-ON patients, and both groups present lower levels compared to control group. Central macular and RNFL thickness are also decreased in almost all quadrants of the optic nerve in ON patients. Additionally, ON patients present alterations in electrophysiological tests compared to the non-ON group.

2652

## Cell Tracking: The key to understanding the phenomena after photoreceptor transplantation

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## Summary

Fluorescent reporter proteins have been used to track the integration of donor photoreceptors in cell transplantation. Integration was quantified based on the presence of reporter+ cells in the outer nuclear layer (ONL) of recipient retinas post-transplantation. We recently reported that GFP+ cells in the ONL of recipient retinas exhibit mismatched characteristics post-transplant. To investigate this mismatch in donor/host identity, we carefully evaluated GFP+ cells in a series of transplants using multiple transgenic donor and recipient models, including degenerating mouse model (CrxKO). Morphological, synaptic terminal structure, nuclear architecture analysis, fluorescence in situ hybridization, and donor cell DNA pre-labeling indicates that GFP+ signal in the ONL is not a result of cell integration, classical donor/host cell fusion or trans-fating, but rather a consequence of GFP transfer in wildtype and NrlKO mice. In contrast, transplants in CrxKO recipient mice resulted in both cell integration and GFP transfer. Taken together, we identify the need for re-interpretation of previous results in the field of cell transplantation, as stringent standards are required to distinguish between GFP transfer and cell integration.

S094

## Neurogenesis detection in the adult human retina

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### **Purpose**

Adult neurogenesis is well described and characterized in the retina of fish, amphibian and birds, but its existence in mammals has never been proved. In this work, we aim to study the presence of adult neurogenesis in the human and monkey retina.

### **Methods**

Four paraformaldehyde fixed human retinas, ranging from 10 to 40 years old, and two BrdU-treated 10-years-old monkey retinas were employed in this study. Immunohistochemistry in retinal cryosections and wholemounts was performed using proliferation markers (Ki67, BrdU), neural stem cell markers (Pax6, Chx10, Sox2, Rx, Nestin) and mature retinal markers (Recoverin, PKC).

### **Results**

All four human subjects presented Ki67+ cells in the peripheral retina, near the *ora serrata*, what indicates cell proliferation. Many of these cells co-expressed neural stem cell markers like Sox2, Pax6 or Chx10. Monkey retinas also showed proliferating cells that had incorporated BrdU all along the retina, but appearing mainly in the periphery. Mature and immature markers in retinal cryosections showed a gradual morphological maturation of retinal cells from the periphery towards the center: cells in the periphery had an immature morphology, more rounded, without well-established synaptic contacts and lacking mature morphological characteristics.

### **Conclusions**

The existence of a population of proliferating cells together with a maturation process suggest that the peripheral retina may be a niche of neural stem cells and that a neurogenesis process similar to that of fish, birds and amphibians may be occurring in adult mammals.

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### **S010**

**The effect of estrogen and dihydrotestosterone on hyperosmolarity-induced expression and production of IL-1 $\beta$ , TNF- $\alpha$  and IL-8 through MAPK pathway in human corneal epithelial cells**

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### **Purpose**

Hyperosmolarity plays role in pathogenesis of dry eye syndrome by inducing inflammation. However, there is still some controversy about the effect of sex steroids on hyperosmolarity-induced inflammation. Some research suggests that estrogen therapy in postmenopausal women increases risk of dry eye syndrome while some research reports opposite. We aim to put an end to this contradiction by evaluating the effect of not only estrogen but also androgen by showing the link between IL-1 $\beta$ , TNF- $\alpha$ , IL-8 and MAPK pathway.

### **Methods**

Immortalized human corneal epithelial cells (HCECs) were exposed to 500 mOsm media with or without pretreatment with  $10^{-10}$  M estradiol(E2) and  $10^{-10}$  M dihydrotestosterone(DHT) for 48h. After 30 min., 1hr, 3hr and 18hr of treatment cells were harvested and lysed in RIPA to perform Western blot for p-p38, p-JNK, p-ERK and caspase 3. Then, we performed Western blot and RT-PCR for evaluation of the effect of E2 and DHT on IL-1 $\beta$ , TNF- $\alpha$  and IL-8 at both transcriptional and translational levels.

## Results

Our results demonstrated that MAPK pathway (JNK1/2, p38 and ERK1/2) were activated with hyperosmolar media. E2 administration significantly increased activation of MAPK pathway whereas DHT administration suppressed this activation. E2 increased IL-1 $\beta$ , TNF- $\alpha$  and IL-8 expression while DHT showed the opposite effect at both transcriptional and translational levels. The inducing effect of E2 and inhibiting effect of DHT was maximum at third hour after hyperosmolar stress.

## Conclusions

Our findings showed that E2 induced activation of MAPK pathway resulted from hyperosmolarity whereas DHT inhibited this activation in human corneal epithelial cells. DHT showed anti-inflammatory effect, E2 showed proinflammatory effect. These findings may provide additional information about the implication of E2 and DHT in the treatment of dry eye syndrome.

## T062

### Pseudophakic cystoid macular edema responding to the combination of topical and systemic treatment as first-line therapy (case-series study)

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## Purpose

To evaluate the efficacy combination of topical medications (NSAID and steroid) with oral carbonic anhydrase inhibitor as first-line therapy of treatment postsurgical CME.

## Methods

A retrospective review of 8 eyes (8 patients, 7 woman and one male) with postsurgical CME, mean age was 73.6 (63-86). We were analyzed visual function (BCVA) and structural improvements on OCT – mean central foveal thickness (CFT) and central subfield thickness (CST) at baseline and follow-up (9.6 month, 3-24). All patients received a first-line therapy: topical combination of NSAID (nepafenac 0,1%) and corticosteroid (dexamethasone 0,1%) drops with short course of oral CAI (acetazolamide 250 mg/day for 5 days). Sub Tenon or intravitreal injection corticosteroid was performed (triamcinolone 20 mg/0.5 ml or 2 mg/0.05 ml) in cases with the absence of the effect.

## Results

Full resorption of CME with first-line therapy was observed in 6 (75%) patients (average time to treatment was 3.3 months, 1-5). Baseline BCVA was significant improvement from 0,6 ( $\pm 0,37$ ) to 0,22 ( $\pm 0,2$ ) ( $p = 0.012$ , Wilcoxon signed-rank test,  $p < 0.05$ ). Average CFT and CST decreased significantly from 487,2 ( $\pm 82,7$ ) and 482,2 ( $\pm 69,3$ )  $\mu\text{m}$  to 320,1 ( $\pm 139,9$ ) and 356 ( $\pm 105,4$ )  $\mu\text{m}$  ( $p = 0.012$ ). One patient received two times of sub Tenon injection with complete resorption of CME; and one more patient (12.5%) was received intravitreal administration ( $n=4$ , average interval between injections was 4.5 months, 3-6).

## Conclusions

In most cases postsurgical CME was well responds to combination of topical medications with oral CAI as first-line therapy. Refractory cases still require repeated sub Tenon and intravitreal injection of corticosteroids. Our report

can provide anatomical and visual benefit and to be useful as a first-line therapy without corticosteroid-related side and adverse effects.

#### T004

##### **Modulation of oxidative stress in the rod outer segment by diterpene manool and sclareol extracted from *Salvia tingitana***

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##### **Purpose**

Oxidative stress is a primary risk factor for inflammatory and degenerative retinopathies. Exposure to ambient light of isolated rod outer segment (OS) for 1 h was shown to cause an oxidative stress, impairing the extramitochondrial aerobic metabolism of the OS supplying phototransduction. Here we tested the effects of diterpene compounds such as manool and sclareol extracted from *Salvia tingitana* on free radical production as well as on ATP synthase activity of both rod OS and clinical multi-drug-resistant human bacteria.

##### **Methods**

Purified bovine rod OS were utilized. Production of Reactive Oxygen intermediates (ROI) was evaluated by citofluorimetry; ATP synthesis was assayed by luminometry; molecular docking analysis among F1-ATP synthase and manool /sclareol was performed using AutoDockTools v.1.5; structures were defined by IR and 1D and 2D NMR. The antibacterial activity was evaluated by calculating the minimum inhibitory concentrations (MICs)

##### **Results**

Manool and sclareol diminished ATP synthesis activity in rod OS as well ROI production in vitro after exposure to ambient light for 1 h. A strong ligand affinity of both substances with F1 portion of ATP synthase was demonstrated. Manool and sclareol also inhibited ATP synthase activity in bacteria as *E. faecium* and *faecalis* and in *S. aureus* and *epidermidis*.

##### **Conclusions**

Data show for the first time an inhibitory effect of diterpene compounds on ATP synthase in rod OS docking to its F1 portion as well as its beneficial effect as modulator of ROI production, extending the same mechanism of action previously described for polyphenols. Decrease in ATP production after treatment with diterpenes in bacteria may be correlated with their cytostatic effect, confirming ATP synthase conserved structure. Data shed new light on the prevention of the oxidative stress related retinopathies.

#### 2925

##### **Aesthetic blepharoplasty through the ages**

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### Summary

The successful elevation of the relaxed eyelid was always a challenge for the physicians dealing with ptosis patients, as seen from the writings of Celsus and Albucasis. Ancient non-surgical mechanical methods based on scar-related eyelid elevation after application of adhesive slings, metal crutches or cauterization have been described, with rather disappointing results in terms of cosmetic and functional outcomes. Hence, a variety of surgical techniques were developed, based on three sources used to elevate the drooping eyelid: the frontalis muscle, the levator muscle and the superior rectus muscle. Brow suspension by suture was performed during the 19th century, but became popular in the 20th century with the introduction of non-absorbable materials in clinical practice. The procedure gained wide acceptance when the non-absorbable synthetic suture made of polyamide was released in the early 1960s. Since then, several suspension materials, including silicone strips, reconstituted collagen as well as autogenous tissue have been proposed. Levator muscle suspension and suspension from the superior rectus muscle were popular during the first half of the 20th century.

3111

### OCT angiography can replace fluorescein angiography in clinical practice - For

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### Summary

Optical coherence tomography angiography (OCTA) has been changing the diagnostic approach to retinal vascular diseases. Its main advantages consist of repeatable tests in dynamic platforms in combination with an abundance of additional qualitative and quantitative information provided by high resolution cross-sectional and en-face OCT scans in combination with measurements on flow and vascular density. This imaging modality provides insight into pathophysiologic mechanisms of disease and has provided the retinal specialist with new clinical signs decisive for the prognosis and treatment customisation of retinal disease. New further enhancements address successfully the removal of artefacts and wider fields of view expanding the spectrum of information further into the retinal periphery and past the macular area. These advantages are outlined in contradiction to features and restrictions of fluorescein angiography.

2615

### 20 Questions and answers regarding macular interface pathology and surgery

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### Summary

AIM : to answer most of common questions regarding macular interface surgery

METHODS: I will ask a panel of vitreoretinal experts regarding debatable topics in macular interface surgery

RESULTS: I hope to clear as much as possible difficult topics in macular interface surgery

SUMARY: Using question and answers I will explore most of the macular interface surgery topics

3313

### 27g for proliferative diabetic retinopathy

G. PAPPAS<sup>1</sup>

## Summary

AIM: to evaluate the efficacy and safety of 27g surgery in diabetic retinopathy case

METHODS: I present the cons and pros of using a 27g surgical system

Results: I present tips how to get most of the system in proliferative diabetic retinopathy cases

Conclusion: The 27g system is a reliable system to use in diabetic retinopathy cases

## F018

### Retinal blood supply and oxygen extraction as a function of blood pressure status and vascular dysregulation assessed by optical coherence tomography-angiography and dual-wavelength retinal oximetry

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## Purpose

To determine the effect of blood pressure (BP), BP medication, and vascular dysregulation on retinal blood flow (BF) and oxygen extraction (OE) in healthy subjects.

## Methods

One random eye of 31 ophthalmically healthy participants (50-65 yrs) with varying BP status (normotension, treated/untreated hypertension) was imaged with optical coherence tomography-angiography (OCT-A) and scanning laser ophthalmoscopy (SLO). Total sample size on completion will be n=125 divided in 5 age-matched groups (vascular dysregulation, hypotension, normotension, treated/untreated hypertension). BF was approximated with perfused capillary density (PCD) and flux index (FI). OE was approximated with the optical density ratio of the supero- and infero-temporal vessels. Central retinal artery and vein equivalent (CRAE, CRVE) were also calculated. As a secondary outcome we assessed the effect of BP status on retinal nerve fibre layer (RNFL) and macular inner retinal thickness (GCC).

## Results

Kruskal-Wallis test revealed that PCD/FI were not significantly different between the 3 groups (macula: P=0.2/0.1, peripapillary region: P=0.8/0.9). OE was not significantly different (P=0.15), but CRAE was (P=0.026). Post-hoc analysis revealed this was due to the untreated hypertensives (P=0.008). CRVE did not differ significantly (P=0.18). For the secondary outcome, there were significant differences in GCC (P=0.003); post-hoc analysis revealed that normotensives had thicker GCC than both treated (P=0.017) and untreated (P=0.003) hypertensives. For RNFL, this effect was borderline significant (P=0.05).

## Conclusions

There is initial evidence of a complex interaction between BP status, BF and OE in healthy eyes. A larger sample may disentangle the mutual confounding effects. Study completion will provide insight on the effect of low BP and vascular dysregulation.

## 2311

### Capillary macroaneurysms in retinal vascular diseases : an overview

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## Summary

Large microvascular abnormalities developing in chronic microvascular diseases are an increasingly recognized source of chronic macular edema. They most commonly present under the form of capillary macroaneurysms, that can reach several hundred micron size. They are sometime the cause of intravitreal treatment failure. They are highly prevalent in presence of severe hard exudates. Their detection is best done by ICG angiography, and their targeted photocoagulation may be followed by macular edema resolution and/or disappearance of hard exudates. Here we will review clinical presentations and diagnostic strategies of large microvascular abnormalities in retinal vein occlusion, diabetic macular edema, and rare vascular diseases.

**2314**

### Technological developments for improving indocyanine-guided laser photocoagulation

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## Summary

Adaptive optics is a technology that allows to correct in real-time optical aberrations. Coupled with an imaging system, such as a Flood-Illumination Ophthalmoscope or a Scanning Laser Ophthalmoscope, it enables micron scale resolution observation of retinal structures, revealing vessel wall details of red blood cell flow in capillaries. But adaptive optics can also be used to better focus a laser beam inside the retina, for targeted stimulation of a given set of photoreceptors (psychophysics experiments) or for photocoagulation.

Ideed, ocular aberrations prevent a depth selective photocoagulation and probably hinder a stable power delivery. Our project is to use adaptive optics to sharpen a commercial photocoagulation Laser and make it able to target a given macoraneurism in a given retinal layer, while preserving the surrounding tissues. We will present here the latest results obtained with our system.

**2911**

### Clinical use of flood-illumination adaptive optics fundus camera ophthalmoscopy

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## Summary

Adaptive optics imaging of the retina currently resolves cellular-scale structures in humans, in commercially available, user- and patient-friendly systems. Quantitative, micrometric fundus imaging has a great potential in ophthalmology but also in general medicine, since it helps to manage diseases such as high blood pressure, neurological diseases such as multiple sclerosis, vasculitis among others. Hence, not only a true "optical biopsy" is feasible, but also the observation of dynamic pathological processes at a very small scale, revealing for instance that diseases that considered slowly progressive show in fact a highly dynamic behavior such as vasculitis and age-related macular degeneration. We have also been using adaptive optics imaging in a variety of diseases in which the retina may serve as a surrogate marker. The latter includes arterial hypertension, which may benefit from the measurement of the wall-to-lumen ratio of arteriolar wall, a quantitative indicator of the severity of hypertensive microangiopathy. AO ophthalmoscopy hence approaches the goals of precision medicine in several domains.

**T073**

### The effect of eplerenone in chronic central serous chorioretinopathy refractory to PDT therapy

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### **Purpose**

To evaluate the efficacy and safety of oral eplerenone in cases of central serous chorioretinopathy refractory to monotherapy with PDT.

### **Methods**

Eleven patients with persistent subretinal fluid (SRF) received oral eplerenone for a 6-month period. On each patient, the drug dosing increased gradually starting from 25mg/week for 4 weeks, continuing to 50mg/day for 4 weeks and then 75mg/day for 4 months. The examination included BCVA measurement and OCT. FA was performed before treatment. Particularly the level of the SRF, retinal thickness and the presence of intraretinal fluid were assessed using Spectral Domain OCT. Creatinine levels measurement and electrolyte (Na<sup>+</sup>, K<sup>+</sup>) test performed on each patient every 1 month. Two patients with electrolyte and other disturbances were excluded. Patients with other retinal pathology were excluded from the study.

### **Results**

There was a reduction of the SRF in most cases (7/9). In two patients SRF remained stable. BCVA improvement was observed in most cases.

### **Conclusions**

In this study, eplerenone found to be safe and effective in refractory cases of CSR. These results need to be confirmed from a larger scale study.

## **S057**

### **Late onset corneal haze after corneal collagen crosslinking for progressive keratoconus**

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### **Purpose**

To present a case of a patient that underwent corneal crosslinking for progressive keratoconus and the development of clinically significant corneal stromal haze 18 months after treatment.

### **Methods**

A 20-year-old male presented with bilateral progressive visual loss during the last years. *His corrected distance visual acuity (CDVA) OD was 20/30 (-2.75 -1.75 @55) and OS 20/30 (-0.50 -1.75@110).* Corneal topography revealed bilateral keratoconus and the patient underwent corneal crosslinking according to the Dresden Protocol. The postoperative regimen included combined tobramycin and dexamethasone drops along with lubrication until the epithelium healed and then fluorometholone with weekly tapering. At 3 months postoperatively, the topography was stable and his CDVA was 20/25 in both eyes. On slit lamp examination, only clinically insignificant stromal haze was observed. At 18 months postoperatively, the patient reported vision deterioration. On examination his CDVA was 20/25 in right eye, and 20/40 in his left eye. Deep stromal haze was revealed in his central cornea, which was more profound in his left eye. Corneal topography was stable and the CDVA loss was attributed to the notable deep stromal haze. The patient was treated with dexamethasone qid with biweekly tapering.

## Results

One month after dexamethasone treatment his CDVA OS gradually improved to 20/25, and stromal haze was less dense. but still noted.

## Conclusions

Late-onset deep corneal haze is a possible complication of corneal crosslinking in patients with keratoconus.

**3311**

### **Laser or Anti-VEGF for proliferative diabetic retinopathy**

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<sup>1</sup>*Ophthalmiatrico Athens Eye Hospital, 2nd Ophthalmological, Kifissia- Athens, Greece*

## Summary

In high-risk proliferative diabetic retinopathy (PDR), performing panretinal photocoagulation (PRP) has been the standard of care in order to reduce severe visual loss. However peripheral visual loss and macular edema (DME) development remain problems after treatment.

Anti-VEGFs injections are effective for the management of DME. The Diabetic Retinopathy Clinical Research Network randomized clinical trial and similar studies suggest that pharmacotherapy with ranibizumab can be an alternative to PRP. This study had a noninferiority design and suggest that treatment with anti-VEGFs, such as ranibizumab result in visual acuity not worse than PRP at 2 years. The long term implications after pharmacotherapy to PDR remain uncertain and regular follow-up is a critical element for this type of treatment. On the other hand most patients with adequate PRP keep stable retinopathy

Anti-VEGF injections are costly. Cost-effectiveness analysis of ranibizumab compared to PRP revealed that ranibizumab is cost-effective only in eyes with PDR and vision-impairing DME, but not for those with PDR without DME. PRP combined with bevacizumab seem to have superior visual and anatomical outcome than PRP alone in patients with combined PDR and DME.

**1221**

### **Modelling optic neuropathies using human induced pluripotent stem cell- derived retinal ganglion cells**

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## Summary

The molecular profiling of human retinal ganglion cells (RGCs) in normal and diseased ocular tissue is hindered by the lack of non-invasive means of obtaining RGCs from living donors. Patient specific human induced pluripotent stem cells (iPSCs) provide an extremely powerful means by which to investigate the pathogenesis of disease, including of glaucoma. Generating iPSCs directly from patients allows cells to be differentiated into specific, relevant cell types of interest for disease modelling, drug screening, and understanding of fundamental biology. Using an automated cell culture platform, we have generated and characterised over 100 patient iPSCs, developed a reliable protocol for generation of functional RGC-like cells, with the aim of generating functional RGCs for molecular analysis of pathogenesis associated with glaucoma.



3151

### Who's driving? Investigating the role of the HIF-1/PKM2 axis in the Warburg effect in mammalian retina

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#### Summary

The hypoxic inducible factor-1 (HIF-1) regulates an array of target genes to facilitate increased efficiency of oxygen delivery and metabolic adaptation in response to hypoxia. The glycolytic enzyme pyruvate kinase M2 (PKM2) is not only a direct target gene of HIF-1, but it can also function as a coactivator for HIF-1, enhancing HIF-1 activity. Together HIF-1 and PKM2 have been implicated in driving aerobic glycolysis (the Warburg effect) in cancer and other proliferating cells. As the non-proliferating mammalian retina also displays the Warburg effect, here we investigate the hypothesis that this is driven by HIF-1 and PKM2. Using cultured Müller cells as a model, as they display a well-characterised Warburg effect, we demonstrate that primary and immortalised cells express HIF-1 and PKM2. However, shRNA-mediated knockdown of PKM2 fails to alter the Warburg effect, in contradiction to the hypothesis, but PKM2 knockdown does decrease cell number, suggesting a role for PKM2 in Müller cell proliferation and/or survival. Furthermore, while we show that mammalian retinas express PKM2, it is not expressed in Müller cells *in vivo* in most species. We are currently exploring roles for both HIF-1 and PKM2 in other retinal cell types.

T028

### Effect of early age related macular degeneration on the disk halo size produced by a glare source

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#### Purpose

Persons with Age-related Macular Degeneration (AMD) are more likely to experience difficulty in night driving and glare disability compared with those in good retinal health. This study examines disk halo size in response to a glare source in eyes with early to intermediate Age-related Macular Degeneration (AMD).

#### Methods

Measurements were made in 1 eye per control subject (n=24), early AMD (n=15) and intermediate AMD subject (n=17). Eyes had cataract surgery and bilateral implantation of a monofocal intraocular lens 6 to 9 months previously to avoid the light scatter effects of aging lens on halo size. Halo radius was measured using the Vision Monitor (MonCv3) with low luminance (5 cd/m<sup>2</sup>) optotypes presented at a distance of 2.5 m. The visual angle subtended by the radius of the halo was calculated in log minutes of arc (log arcmin).

#### Results

No significant differences in mean halo radii were detected between control ( $2.30 \pm 0.15$  log arcmin), early AMD ( $2.36 \pm 0.12$  log arcmin) and intermediate AMD ( $2.38 \pm 0.13$  log arcmin) groups. However, there were 46%, 47% and 76% of eyes with disk halo radius above the cutoff value (2.30 log arcmin) reported to diagnose cataract in the control, early and intermediate AMD groups respectively.

#### Conclusions

Early to intermediate AMD did not affect the halo size induced by a given glare source. Across all pseudophakic eyes, an increased size of the disk halo would be indicative of altered scattering, transmission and reflection properties of various parts of the aging eye.

## **F090**

### **Silent sinus syndrome: a rare clinical entity**

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### **Purpose**

Silent sinus syndrome is a rare disease characterized by unilateral spontaneous enophthalmos and hypoglobus due to increased orbital volume and retraction of the orbital floor. Obstruction of the maxillary ostium appears to play a critical role in the development.

### **Methods**

Clinical Case: A 32 year-old woman presented with a progressive enophthalmos and without any sinus or nasal symptoms. There was no history of a trauma. The ophthalmology examination showed enophthalmos and hypoglobus with normal visual acuity, unaffected extraocular movements, and no diplopia.

### **Results**

The computerized tomography revealed a collapsed maxillary sinus and a hypoplastic opacified left maxillary sinus with thinning and depression of the orbital floor that led us to the diagnosis.

### **Conclusions**

Silent Sinus Syndrome is an uncommon disease characterized by enophthalmos caused by homolateral atelectasia of the maxillary sinus without nasal nor paranasal symptoms. Although the diagnosis is clinical, the confirmation is achieved by images. The clinical features of silent sinus syndrome are described, as well as the most relevant treatment options.

## **F068**

### **Optical coherence tomography angiography of the foveal avascular zone and vessel density in children: comparison between preterm and full term patients**

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## Purpose

Examination of characteristics of the foveal vascular structure in preterm and full term children by optical coherence tomography angiography (OCTA).

## Methods

This is a transversal observational study on 250 eyes of 133 children (83 eyes of 44 former preterm infants and 167 eyes of 89 former full term infants).

Patients (4-14 year-old) were gathered into 4 groups:

- A) full term infants
- B) preterm infants without ROP (retinopathy of prematurity)
- C) preterm infants with spontaneous regression of ROP
- D) preterm infants with treated ROP

Foveal avascular zone (FAZ) and perfusion density (PD) of superficial and deep plexus were measured using Swept source OCTA. For each patient, vascular density in a 2 X 2 mm sector focused on fovea was analyzed with ImageJ software. Correlation was evaluated with Pearson's coefficient and differences among group were assessed with oneway analysis of variance.

## Results

A correlation between FAZ, birth weight and gestational age proved to be significant ( $r=0,46$  and  $0,53$ , respectively). No correlation was found between FAZ and refraction ( $r=0,1$ ).

The mean FAZ values in group A were  $288,36 \mu\text{m}$ , in group B were  $173,07 \mu\text{m}$ , in group C were  $47,9 \mu\text{m}$ , in group D were  $132,3 \mu\text{m}$ . In preterm infants, FAZ was significantly smaller than in the controls ones (A group) ( $P < 0.001$ ). PD of superficial plexus was  $43,7\%$  in group A,  $43,33\%$  in group B,  $53,7\%$  in group C,  $43,5\%$  in group D. PD of deep plexus was  $63,15\%$  in group A,  $63,69\%$  in group B,  $63,5\%$  in group C,  $62,5\%$  in group D. There are no statistically significant differences among the groups ( $P=0,95$ ).

## Conclusions

OCTA is a novel method for a non-invasive visualization of the retinal vasculature in pediatric patients and improves our knowledge of foveal abnormalities in retinopathy of prematurity. A small or absent FAZ is supposed to be a distinct sign of prematurity.

## S075

**The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): Kinetics of human cornea swelling and deswelling in the bioreactor as a function of IOP and endothelial status**

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## Purpose

Our university lab BiiGC has patented an ophthalmic bioreactor (BR) available in 2 versions: one for long-term eyebanking, the other for preclinical experimentation, called OBSERV supported by the French Agence Nationale de Sécurité du Médicament (ANSM). Aim: to quantify the respective roles of intra ocular pressure (IOP) and endothelial pump in the control of corneal thickness (CT) inside the BR

## Methods

By restoring IOP and medium renewal, the BR maintained the viability of cornea (human/animal) over a prolonged period of time. Its transparency allowed characterizing the tissue with existing of customized devices without compromising its sterility. Human corneas were stored at 31°C in organ culture for 1-3 weeks to reach maximal swelling. After randomization, they were inserted in the BR with (n=3) or without (n=2) their endothelium (scraping respecting the Descemet). All were stored at 21mmHg, 5µL/H of custom-made medium, 31°C for 24H followed by 9H at 0mmHg and 5µL/H. Central CT was measured by OCT every 30mins, except at night. The endothelial viability was finally quantified by Hoechst/Ethidium/Calcein-AM staining.

## Results

At baseline, mean(SD) CCT was 1085(249)µm. In the BR, CCT decreased in both groups. CCT nadir, reached after 7(1) hours in both groups, corresponded to a 36(12)% deswelling with endothelium versus 22(14)% without endothelium. CCT was stable thereafter at 21mmHg. At 0mmHg, CCT increased again to 90(12)% of the initial thickness in 6(3)H.

## Conclusions

The OBSERV platform allows the CCT to be monitored in real time. The IOP initiates deswelling independently of the endothelial pump. In the BR, like in vivo, when IOP is restored, the endothelial pump is efficient but in absence of IOP the pump is almost totally inefficient. IOP and EC are fundamental for corneal hydration control.

## T116

### In vitro antimicrobial activity of a new ophthalmic solution containing povidone-iodine 0.6% (IODIM®)

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## Purpose

To assess the in vitro antimicrobial activity of a new commercial ophthalmic solution containing povidone-iodine 0.6% (IODIM®, Medivis, Catania, Italy).

## Methods

*Staphylococcus aureus* ATCC 4330, *Pseudomonas aeruginosa* ATCC 27853, four ocular bacterial isolates (1 *S. epidermidis*, 1 *S. aureus*, 2 *P. aeruginosa*) and five *Candida species* were used. The bacterial and fungal isolates were sub-cultured onto Columbia blood agar base and Sabouraud-dextrose agar plates, respectively, and incubated overnight at 37°C. Bacterial and fungal suspensions were prepared to an optical density equal to 0.5 McFarland standard (approximately 1,000,000,000 CFU/mL). Suspensions of the different isolates were made in IODIM® solution to obtain a final concentration of 10,000,000 CFU/mL. The suspensions were then distributed in 96-well plates in a final volume of 200 µL and incubated at 37°C. After 24 hours, 10 µL of each suspension was removed, seeded on Columbia blood agar base and Sabouraud-dextrose agar plates and then incubated for 24 hours at 37°C. Positive and negative controls were included in all experiments. Each experiment was performed in duplicate and repeated three times.

## Results

After 24 hours' incubation, there was no microbial growth on any plate.

## Conclusions

IODIM® ophthalmic solution showed in vitro antimicrobial activity against *S. epidermidis*, *S. aureus*, *P. aeruginosa*, and *Candida species*. Results suggests that IODIM® ophthalmic solution may be a potential candidate as an adjuvant for the treatment of ocular surface infections.

3536

#### Treatment of uveal melanoma: an oncologist's view

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#### Summary

From the medical oncologist point of view, uveal melanoma fits several aspects of major interest. This rare melanoma is biologically different from cutaneous melanoma in terms of epidemiology or clinical features. It reveals particular somatic gene alterations associated with a variable prognosis, allowing an active tailored surveillance strategy by a specialist multidisciplinary team and clinical trials investigating novel adjuvant therapies. There is no standard oncological treatment in the metastatic setting, due to the lack of efficacy of drugs already tested, and metastatic patients should be considered for clinical trials wherever possible. Uveal melanoma patients have to face rare cancer issues in a worldwide scale, needing specific management strategies, access to information and to expert centres at all stages, to fight their disease under the optimal conditions. Cross-border collaboration between multidisciplinary teams, researchers and patient association groups through committed networks are essential to improve patient management and care, to accelerate translational and preclinical research, in order to offer uveal melanoma patients strong scientific-based and dedicated clinico-biological studies.

3153

#### Methylation-dependent control of HIF-1/VEGF axis in a mouse model of oxygen-induced retinopathy. Potential role of the glial water channel Aquaporin-4

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#### Summary

The HIF-1/VEGF axis plays a pivotal role in the hypoxia dependent accumulation of VEGF in retinal diseases characterized by neovessel formation. In hypoxia the retinal glial water channel Aquaporin-4 (AQP4) is co-regulated with VEGF through an unknown mechanism.

We investigated whether AQP4 is involved in the hypoxia-dependent VEGF upregulation in the retina.

To this aim a mouse model of oxygen-induced retinopathy (OIR) in presence (WT) and in absence of AQP4 (KO) was used.

The expression levels of VEGF, the hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ), the methylation status of the HIF-1 binding site (HBS) in the *VEGF* gene promoter, the binding of HIF-1 $\alpha$  to the HBS have been determined in the retina of wild WT and KO, in OIR and normoxic conditions.

We found that in KO mice, HBS demethylation in response to the beginning of hypoxia is lower than in WT mice reducing the binding of HIF-1 $\alpha$  to the *VEGF* gene promoter and VEGF upregulation.

These data show for the first time in retina that hypoxia induces HBS demethylation in the *VEGF* promoter, that this mechanism is correlated to HIF-1-mediated *VEGF* transactivation and finally that the AQP4 deletion impairs this mechanism.

**2662**

**FOXE3 mutations correlations between mutation types, inheritance pattern, and phenotype severity**

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**Summary**

Micro-anophthalmia are severe developmental eye anomalies, many of which are likely to have an underlying genetic cause. More than 30 genes have been described, each of which is responsible for a small percentage of these anomalies. Amongst these, the *FOXE3* gene was initially described in individuals with dominantly inherited anterior segment dysgenesis and subsequently, associated with recessively inherited primary aphakia and microphthalmia. To further understand *FOXE3* involvement in this wide spectrum of ocular anomalies with two patterns of inheritance, we collected 8 new *FOXE3* mutated patients and reviewed all individuals with ocular anomalies described in the literature. This allowed demonstrating the presence of genotype-phenotype correlations for *FOXE3* mutations in congenital ocular abnormalities. These correlations will assist both in interpreting the *FOXE3* molecular analysis when the phenotype is known and, in predicting phenotype and inheritance pattern when knowing the genotype in a family. Moreover, these correlations lay the foundations for exploring in more detail the effects of potential modifying factors that could influence the ocular phenotype, improving our understanding of ocular genetic diseases in general.

**F078**

**Woman –ophthalmologists in the past**

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**Purpose**

For centuries women helped to deliver babies and had knowledge of herbs. They produced remedies using herbs, minerals, animal products and clays. In patriarchal societies women received only basic education.

## Methods

The research was based on information obtained from documents, articles in archives, books and journals.

## Results

In the Middle Ages nuns of St. Benedict provided health care for ill. Hildegard of Bingen (1098-1179) was famous for her knowledge of methods of treatment. She wrote several medical books. One chapter in her book was devoted to eyes. Starting from 16th c in Poland women of upper middle class began to educate themselves in natural science. Landladies in villages had a medicine chest containing herbal medicines and collections of notes on the treatment of various disease for home use and to give medical advice to their peasants. Such collections of medical notes was mentioned by Regina Pilsztyn who learned how to treat eyes from her husband and practiced in Istanbul. The first woman – ophthalmologist Isabel Hayes Chapin Barrow studied ophthalmology at the University of Vienna (1870), and practiced in the USA. The first women ophthalmologists Barbara Burbo, Jadwiga Matusewicz, Zofia Wojno studied medicine in Zürich, nostrificated their diploma in Vilnius, Moscow, Petersburg. Leokadia Michniewiczówna was the first ophthalmologist who graduated from Medical Department at Warsaw University in 1926.

## Conclusions

At the beginning of 19thc women were not accepted in the public life but they were active in many ways and wanted to get education equal to men. They struggled to be allowed to study at the universities and were successful about 1860.

## F079

### The development of anatomy of the eye and its optics

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## Purpose

Ancient religions did not allow the dissection of corpses. The knowledge of priest doctors was based on dissection of animals jointed after ritual killing. The functioning of human body was based on the idea of balance of humours or energy.

## Methods

The research is based on information obtained from articles in books, journals and works of scientists mentioned in the article.

## Results

Aristotle investigated natural science in 4thc BC and performed dissections on animals which started the beginning of anatomy in ancient Greece. Claudius Galenus (about 130 AD – 200 AD) performed dissections on animals and formulated his own anatomical theory. In his theory a lens was an organ of vision, it was situated in the center of eye and was considered as *primum visibile*. The eye sent a stimulus from the brain to the object and the picture was returned to the eye. The eye was covered by membranes. The muscle *retractor bulbi* withdrew the eye. This theory was disproved by Gabrielle Fallopio (1523-1562). Advances in optics formed by ancient Greek philosophers Apollonius of Perga, Euclid, Ptolemy were continued by Ibn al-Haytham (965-1040) Arabic mathematician and physicist. He created his theory of eye structure and its functioning, and formed a new theory of vision. He disproved Galen's theory and claimed that rays of light entered the eye from the visible object and this fact was crucial in the act of vision. Christian monks (12th c -13th c) Robert Grosseteste, Witelon, Roger Bacon also contributed to the development of optics.

## Conclusions

Their work was continued by scientists Leonard da Vinci, Johannes Kepler, Rene Descartes, Christopher Schneider and Isaak Newton. Descartes explained how light entered through the pupil of the eye and was refracted by the interior humours. It formed an inverted image on the retina at the back of the eye.

## **F080**

### **Creators of Polish ophthalmology in 19thc and their achievements**

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#### **Purpose**

Ophthalmology became a separate branch of surgery about 1820. Its rapid development was caused by the invention of ophthalmoscope by Hermann von Helmholtz in 1851. During partition of Poland (1795-1918) three centers of ophthalmology were most important: The Institute of Ophthalmology in Warsaw, established in 1827, thanks to the donation in the will of Prince Edward Lubomirski, Teaching Hospital at Jagiellonian University in Krakow and Ophthalmic Hospital at Lvov University.

#### **Methods**

Based on my own the research in archives, articles and books.

#### **Results**

The following ophthalmologists were connected with the Institute of Ophthalmology: Wiktor Feliks Szokalski, Belesław Geppner (technique of iridectomy), Wiktor Jodko-Narkiewicz (the ward head and founder of ophthalmic ward in Jewish Hospital in 1861), Walenty Hieronim Kamocki (diabetic changes in the eyes). The head doctor in Teaching Hospital at Jagiellonian University in 1896 became Bolesław Wicherkiewicz a founder and editor of a first ophthalmic journal in Polish "Przegląd Okulistyczny" ("The Review of Ophthalmology") 1899-1914. His activity was supported by Kazimierz Noiszewski who was an assistant professor at the Military Medical Academy in Petersburg and founded his own hospital. When Poland became independent in 1918 he became a professor at Stefan Batory University in Vilnius and at Warsaw University. When Emanuel Emeryk Machek became the head of the Ophthalmic Hospital at the University in Lvov in 1897 he organized well equipped histological and bacteriological laboratories and prepared his own program of fighting trachoma.

#### **Conclusions**

Thanks to their knowledge and activity in many fields they created the basis of care of the patients suffering of eyes diseases that encompassed almost whole society (about 1924).

## **2923**

### **The System of Fighting Trachoma in Poland (1928-1939)**

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#### **Summary**

##### **Background**

Trachoma, a highly contagious virus disease of the eyelids. It may lead to blindness.



## Methods

The research is based on information obtained from legal documents, registers of trachoma patients from health centers, out-patients and hospitals in the years 1918-1939. These data were analyzed statistically.

## Results

Trachoma was widely spread in Polish population with poor hygiene so the government took steps to eradicate it and issued a legal act in 1928. All doctors working for public health centers were trained in basic methods of diagnosis of trachoma in the national School of Hygiene. They were obliged to register and report all trachoma patients. To limit the spread of trachoma the Government set up a network of health centers, trachoma out-patients in public hospitals and health institutions for isolation and treatment which was free for the patients. The treatment was financed and controlled by District Authorities. Trachoma health centers dealt with diagnosis, registration, treatment education and prophylaxis.

## Conclusion

Trachoma was eradicated in Poland about 1950 but nowadays it may be a serious health hazard due to migration of people from North Africa where this infection is very common.

## F052

### Brushfield spots and Wölfflin nodules unveiled in dark irides using near-infrared light

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## Purpose

To determine if structures such as Wölfflin nodules, or Brushfield spots in Down syndrome, can be established in dark irides.

## Methods

Iris photography of 43 children with, and of 43 control children without, Down syndrome, was taken with standard visible white, as well as with near-infrared light. Main outcome measures: Identification of otherwise unseen iris features using near-infrared light in children with and without Down syndrome.

## Results

Using white light, no child with darkly coloured irides had visible Brushfield spots or Wölfflin nodules. Brushfield spots were seen in 21% of children with Down syndrome, whereas smaller iris spots known as Wölfflin nodules were seen in 12% of controls ( $p<0.001$ ), all noted in those with lightly coloured irides. Using near-infrared light, Brushfield spots could, however, be seen in 58% of those with dark irides. Hence, using near-infrared light, Brushfield spots were detected overall in 67% of children with Down syndrome compared to 21% using white light ( $p<0.001$ ). Peripheral iris thinning was present in 62% of children with Down syndrome but in only 23% of those without ( $p=0.001$ ). Contraction furrows were less frequent in children with Down syndrome (16%) compared to controls (74%) ( $p<0.001$ ).

## Conclusions

Infrared light unveils the presence of Brushfield spots and Wölfflin nodules in dark irides, previously noted in lightly colored irides alone. Clearing this discrepancy should assist in the elucidation of their pathophysiologic origin. A

high prevalence of peripheral iris thinning is also present in children with Down syndrome along with a heretofore unreported reduction in iris contraction furrows.

**2622**

### **The pathophysiology and medical management of uveitic glaucoma**

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#### **Summary**

This basic/intermediate presentation contains a literature review on basics of pathogenesis of uveitic hypertension and uveitic glaucoma. The anatomical, ethiological, pathological and especially the clinical classification will be discussed. The relationship between inflammation and the onset of increased intraocular pressure and its treatment on each stage will be explored. Some more specific types of anterior chamber inflammation like Posner-Schlossman, Fuch's heterochromatic iridocyclitis and herpetic uveitis and the latest guideline for their treatment will be presented. Surgical treatments with special focus on the benefits of MIGS in uveitic glaucoma will be debated. This SIS presentation is adequate for the young ophthalmologists.

**1811**

### **OCT-A biomarkers for the macular surgical pathologies**

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#### **Summary**

Optical coherence tomography angiography (OCT-A) based biomarkers allows the observations of retinal structural alterations, retinal ultrastructural alterations, intraretinal microangiopathic changes and the vitreoretinal interface abnormalities.

OCT is necessary for an accurate diagnosis and guides preoperative decision-making and surgical planning.

Three dimensional imaging along with segmentation techniques and OCT "en face" imaging provided comprehensive evaluation of the vitreoretinal interface surface topography, the anatomical configuration of vitreomacular affection and the associated intraretinal structural modifications along with the microvascular capillaries layers changes. The macular distortion and pseudocyst formation along with the associated intraretinal ultrastructural alterations can help prognosticate the benefit of surgical approaches.

OCT-A imaging-based biomarkers provide a valuable tool for detecting the earlier stages of the macular surgical pathologies, tracking their progression, and monitoring treatment response.

**2715**

### **Multimodal imaging of diabetic retinopathy, the role of OCT angiography**

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#### **Summary**

Changes in the microvascular level, during the different stages of Diabetic Retinopathy (DR), provide important information regarding the perfusion status of the retina and the likelihood of developing more severe retinopathy.

Fluorescein angiography, fundus photographs were the most commonly used imaging modalities in the management of DME as well wide view imaging to quantify the extend of the peripheral ischemia and potentially to observe the peripheral neovascularisation.

SD-OCT and OCT-A are the most widely used instruments in routine clinical practice. The capillaries non-perfusion areas quantification are used as an imaging biomarker to differentiate healthy eyes from eyes of patients with Diabetic Maculopathy without DR. Increased superficial capillaries layer ischemia, may serve as an early indicator for subclinical stages of DR and the significant decline of blood flow in the deep capillaries layer with increasing DR severity. Over all, retinal capillary non-perfusion in OCTA is correlated significantly and linearly with disease severity in eyes with DR.

Technological advances in imaging of the posterior segment of the eye have enabled the monitoring of the disease progression and assessment of the responses to treatment.

**2113**

#### **Techniques of phacoemulsification and vitreoretinal surgeries in ischemic eyes**

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<sup>1</sup>RétinElysée, Vitreoretinal Surgery Unit, Lausanne, Switzerland

#### **Summary**

Cataract surgery and vitreoretinal surgeries are nowadays common surgical procedures performed by high number of ophthalmologists. Understanding the principles of the devices may help surgeons to avoid per and post-operative complications. In ischemic eyes, some recommendations may be applied and will be discussed for both procedures.

**2613**

#### **New Instrumentation**

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#### **Summary**

In the last decade, vitreoretinal instrumentation improved mainly thank to the industry. Introduction of 23G, 25G, and 27G give new perspectives for vitreoretinal surgeons. Panoramic visualization systems offers new possibilities for all surgeons in the peroperative management of patients affected by vitreoretinal disorders. We will focus on main vitreoretinal instrumentation developments.

**3113**

#### **3D vitrectomy can replace conventional vitrectomy - For**

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#### **Summary**

Panoramic visualization systems offers new possibilities for all surgeons in the peroperative management of patients affected by vitreoretinal disorders. Ultradigital 3D heads up surgery offers enhanced 3D visualization with high-definition resolution, image depth, clarity and color contrast while helping to minimize light exposure to the patient's eye. Surgical advantages will be discussed.

**3314**

### **3D surgery for proliferative diabetic retinopathy**

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#### **Summary**

Diabetic retinopathy may lead to severe vitreoretinal complications. In these conditions, panoramic visualization systems offers new possibilities for all surgeons in the peroperative management of patients affected by vitreoretinal disorders. Ultradigital 3D heads up surgery offers enhanced 3D visualization with high-definition resolution, image depth, clarity and color contrast while helping to minimize light exposure to the patient's eye. All surgical or patients advantages will be discussed.

**S091**

### **Contribution of the monocyte-derived macrophages to retinal microglia response after a peripheral nerve injury**

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#### **Purpose**

To characterize the response of microglia and recruited monocyte-derived macrophages (MDM) in the retina after a peripheral nerve injury.

#### **Methods**

In adult C57BL/6J and heterozygote lysozyme M-EGFP-knock-in (LysM-EGFP) mice the tibial and common peroneal branches of the left sciatic nerve were exposed and crushed for 1 minute, or simply exposed (sham). At different survival intervals (ranging 1-14 days), injured, sham, or naïve mice were processed, both retinas were prepared as whole-mounts and analyzed histologically for the expression of microglial markers and LysM-EGFP in mature myelomonocytic cells or quantitative changes in the distribution pattern and appearance of microglia and recruited MDM were performed.

#### **Results**

Morphological signs compatibles with microglia activation and EGFP+ recruited MDM in the innermost retinal layer were evident as early as 1d after injury and persisted along the time-course of study. A population of EGFP+ cells was identified in the peripheral margins, collecting vessels and juxtapapillar area of the retina. Quantitatively the number of Iba-1 immunoreactive cells or EGFP+ cells peaked at 3 days post-lesion and decreased thereafter. At 5d typical activated amoeboid microglial cells were found increased. Sham or naïve animals did not show significant morphological features of microglia activation.

## Conclusions

In response to peripheral nerve injury the retinal microglia population shows significant quantitative and qualitative changes. Moreover, MDM were recruited to the retina and differentiated into microglia.

## S029

### Diclofenac release from LbL coated silicon based contact lenses

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## Purpose

Silicon based contact lenses (SCLs) have raised interest as potential drug vehicles for therapeutic purposes. In this work two polyelectrolytes multilayers coatings were compared as barriers to diclofenac (DCF) release from a SCL material

## Methods

A silicone based hydrogel was produced, loaded with DCF and coated by a layer-by-layer (LbL) process. Two coatings were tested: one double layer coating containing alginate (ALG) and chitosan (CHI), where CaCl<sub>2</sub> and glyoxal were used as cross-linkers, and a two double layer coating with ALG, poly-L-Lysine (PLL), and hyaluronate (HA) as polyelectrolytes, and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride as cross-linker. The release kinetics was investigated in sink conditions. Interaction with lachrymal proteins was evaluated by quartz-crystal microbalance with dissipation (QCM-D). The antibacterial activity of the last coating was tested against *S. aureus* and *P. aeruginosa*. The hydrogels were tested for potential ocular irritation through the chorioallantoic membrane test (HET-CAM test). A simplified mathematical model was used to predict the *in vivo* efficacy of the hydrogels

## Results

The two coatings allowed a controlled release of DCF. QCM-D data revealed no film degradation of the coatings by the lachrymal proteins. The second coating led to a reduction in the growth of *S. aureus* and *P. aeruginosa*. All hydrogels passed the HET-CAM test successfully. The applied mathematical model, estimated a 100% increase in the predicted *in vivo* efficiency due to the presence of the coatings.

## Conclusions

The studied coatings are able to ensure a controlled release of DCF within therapeutic levels during the required period at a controlled rate (2 weeks). The use of a last layer of HA has an antibacterial effect.

**S107**

**Influence of steam and pressure and gamma radiation sterilization on drug loaded intraocular lenses for endophthalmitis prevention**

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**Purpose**

In cataract surgery, the lens is replaced by an artificial intraocular lens (IOL). Endophthalmitis is a severe post-surgical complication. Prevention is sought by frequently applying topical antibiotics and anti-inflammatories. This method leads to low drug bioavailability and low patient compliance. Drug-loaded IOLs can be an interesting alternative. Sterilization of such devices is critical, since its effect on the characteristics and performance of the lenses is yet unknown. Our research focus on the investigation of the effect of two common sterilization methods: steam and pressure (SP) and gamma radiation (GR).

**Methods**

Acrylic IOLs, an antibiotic (moxifloxacin, MXF), and two anti-inflammatories (ketorolac, KTL and diclofenac, DFN) were used. The effect of sterilization on the IOLs properties (swelling, transmittance and Young modulus) and on the drug release was investigated. The IOLs were loaded by soaking in the drugs solution (60°C for 14 days). SP (121°C, 1bar, 1h) was done with hydrated IOLs in the 1<sup>st</sup> or 14<sup>th</sup> day of loading. GR (25 kGy, rate 2.5 kGy/h) was done with dried IOLs after drug-loading. A mathematical model was applied to predict the *in vivo* efficacy of the drug release profile for the best system.

**Results**

SP slightly increased the Young's modulus, while GR slightly increased the transmittance. Concerning the drug release, although SP done in the 1<sup>st</sup> day of loading does not affect the drug release, when done in the 14<sup>th</sup> day decreases significantly the amount of drug released. GR slightly increased the released amount for MXF.

**Conclusions**

The mathematical model suggests that the SP sterilized IOLs at 1<sup>st</sup> day comply with the therapeutic needs. As the IOLs are generally used in hydrated state, SP is the ideal sterilization method for drug loaded IOLs.

**1724**

**Six Essential Steps to Develop a Simulation Based Learning Program**

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**Summary**

Simulation based learning has expanded its scope beyond procedural to behaviour and cognitive skills and has led to new simulation tools and methods. Surgical simulation has been increasingly capturing attention and is widely

valued by surgeons at all levels to meet the patients and the public growing expectations. Learning by simulation has already been formally included in some ophthalmology curricula and require medical educators expert in developing effective simulation-based programs. A simulation center should be an exciting educational platform offering multiple opportunities to develop and practice new procedural, cognitive and behaviour skills in a protected learning environment within an interactive network of medical educators, providers, experts in skills, students and researchers.

By the end of this presentation participants will be able to better recognise the role of the medical educator expert in facilitating learning by simulation, to describe the Kern '6 step approach' to curriculum development, to synthesise how this model can be applied as systematic practice in simulation development and to recognise the simulation center as an interesting research site.

**2713**

### **OCT-A evaluation in glaucoma**

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#### **Summary**

Purpose : To analyse relationship between RNFL thickness and radial peripapillary capillaries (RPC) using OCT angiography for glaucoma patients.

Materials and Methods : We have used OCT-Angiography with Angioanalytics software (Optovue). 4.5mm x 4.5mm HD AngioDisc scan have been performed on 182 Patients (104 female and 78 male), mean age 58,84 (+/- 12,45yr). On this series of 363 eyes, relationship between RNFL thickness and RPC (angioflow density) have been compared by using Pearson correlation test.

Results : Total RNFL thickness(mm) and angioflow density (%) have a positive relationship with Pearson correlation test applied to this 363 eyes. Dividing this series by quadrant (Nasal, Sup Nasal, Inf Nasal, Temporal, Sup Temp, Inf Temp) Pearson correlation test have showned a positive relationship on each quadrant.

Discussion : RPC and RNFL are part of same superficial retinal layer : OCT-A can diagnose reduction of angioflow density. Long term follow-up of RPC and RNFL thickness could help to diagnose primum movens of glaucoma peripapillary alteration.

Conclusion : On this series, OCT-A with Angioanalytics( Optovue), shows a positive relationship between RNFL thickness and angioflow density reduction in case of glaucoma.

**T033**

### **Relationship between Macular Thickness and Mesopic Visual Acuity in Early to Intermediate Age-related Macular Degeneration Subjects**

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### **Purpose**

Impaired mesopic visual acuity (VA) is a risk factor for incident early age-related macular degeneration (AMD). This study examines relationships between macular thickness measurements and photopic or mesopic VA in eyes with early to intermediate AMD.

### **Methods**

In a cross-sectional study 52 age-matched subjects (22 controls, 14 early AMD, and 16 intermediate AMD) older than 63 years of age and with best-corrected distance visual acuity (BCVA)  $\geq 20/25$  were examined. Macular thicknesses were measured through spectral domain optical coherence tomography (Cirrus SD-OCT) across the nine ETDRS subfields centered at the fovea. BCVA was measured using Bailey-Lovie logMAR letter charts (higher logMAR values indicate worse VA) under photopic (100 cd/m<sup>2</sup>) and mesopic (1 cd/m<sup>2</sup>) luminance conditions. In addition, the low luminance deficit in VA (LLD, difference between photopic and mesopic VA) was calculated.

### **Results**

No significant differences in mean macular thicknesses were detected between control, early AMD and intermediate AMD groups. Neither were differences detected between the three groups in mean photopic and mesopic BCVA and mean LLD. Across all subjects, central 1-mm foveal thickness showed positive correlation with mesopic BCVA ( $r=0.32$ ,  $p=0.021$ ) and LLD ( $r=0.34$ ,  $p=0.013$ ). No significant correlations were detected between photopic BCVA and macular thicknesses.

### **Conclusions**

Increased foveal thicknesses on SD-OCT were related to worse mesopic BCVA and LLD in aging and early to intermediate AMD subjects. These structure-function relationships could indicate low-grade inflammation and/or gliosis in early stages of AMD and could be a useful marker of AMD for early detection and monitoring progression.

## **F106**

### **Correlating macular inner retinal layer thickness with photopic and mesopic contrast sensitivity in healthy young and older subjects**

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### **Purpose**

To examine relationships between macular ganglion cell (GC) thickness (GC related layer thickness) and photopic or mesopic contrast sensitivity (CS) in healthy eyes.

### **Methods**

Measurements were made in 38 young and 38 older healthy individuals. Total, inner and outer retinal layer (IRL and ORL) thicknesses were measured in the macula region through spectral-domain optical coherence tomography (SD-OCT) across three subfields, or rings, centered at the fovea: central foveal, pericentral and peripheral. Ganglion cell complex (GCC) and circumpapillary retinal nerve fiber layer (cpRNFL) thicknesses were also measured. Low-spatial-frequency CS for gratings centrally presented were measured through computerized psychophysical tests under photopic and mesopic conditions. Relationships were examined by uni- and multivariate regression analysis.

### **Results**

In the younger subjects, photopic CS showed negative correlation with peripheral IRL thickness ( $p = 0.015$ ), GCC ( $p = 0.001$ ) and cpRNFL thickness ( $p = 0.027$ ). In the older subjects, photopic CS was positively correlated with peripheral IRL thickness ( $p = 0.039$ ), and mesopic CS with peripheral IRL thickness ( $p = 0.0021$ ) and GCC ( $p =$



0.0425) thickness. Peripheral IRL thickness emerged as an independent predictor of photopic CS ( $p=0.0006$ ) in the young group and of photopic ( $p = 0.0257$ ) and mesopic CS ( $p=0.0001$ ) in the older group.

### Conclusions

A thinner GC related layer thickness (IRL) was related to worse CS in healthy older eyes suggesting an age-related loss of retinal GCs. In young healthy eyes, increased macular IRL thickness, likely caused by increased astrocyte reactivity in response to tissue stress, was related to worse CS.

**3426**

### Disk halo size as a measurement of scattering and visual function

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### Summary

Measuring the size of a disk halo in the visual field induced by a bright light has been proposed as a psychophysical test of quantifying quality of vision in subjects such as those with night vision problems following refractive surgery, with cataract or multifocal intraocular lenses. Several methods and testing protocols have been developed to measure halo size. Normal disk halo radius values by age along with intersession repeatability values were provided for measurements made using the Vision Monitor MonCV3 (Metrovision). In healthy eyes, halo size was independent of photopic and mesopic high-contrast CDVA but increased as straylight rose and mesopic low-contrast CDVA worsened. In eyes affected by cataract, the disk halo radius was better able to quantify functional abnormalities than straylight or CDVA. This improved diagnostic capacity may be explained by the fact that both forward light scatter and wavefront aberrations contribute to halo size measured with the MonCV3. Measuring halo size can provide the clinician with additional information, especially when the patient complains of a loss in vision quality despite good VA.

**2525**

### TFOS DEWS II Diagnostic Methodology Report

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### Summary

The key points of the outcome of the recent Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II of the Diagnostic Methodology Subcommittee will be presented. The role of the Subcommittee was to identify tests used to diagnose and monitor dry eye disease (DED). Those which appears to be most appropriate to fulfil the definition of DED and its sub-classifications were identified. The most appropriate order and technique to conduct these tests in a clinical setting, and to provide a differential diagnosis for DED was evaluated. This resulted in a recommendation of a diagnostic workflow, which will be discussed in details. Prior to diagnosis, it is important to exclude conditions that can mimic DED with the aid of triaging questions. The diagnoses consist of a combination of dry eye questionnaires (DEQ-5 or OSDI) and the global tests (ideally non-invasive) tear break-up time, osmolarity and ocular surface staining with fluorescein and lissamine green (cornea, conjunctiva and lid wiper). Meibomian gland dysfunction, lipid thickness/dynamics and tear volume assessment and their severity allow sub-classification of DED (predominantly evaporative or aqueous deficient) which informs the management of DED.

**T010**

**Dose-dependency of intraperitoneally-injected aflibercept in the mouse choroidal neovascularization model**

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**Purpose**

To study the efficacy and dose-dependency of intraperitoneally injected aflibercept (Eylea®) on retinal leakage in the mouse choroidal neovascularization (CNV) model.

**Methods**

Choroidal neovascularisation was induced by penetrating Bruch's membrane using a 532 nm diode laser in 10-week old male C57Bl/6J mice (N=20). Successful rupture was verified by fluorescein angiography (FA) and spectral-domain optical coherence tomography (SD-OCT). Animals received aflibercept (Eylea®, Bayer AG) by injection into the peritoneum at doses of 5 mg/kg, 15 mg/kg and 25 mg/kg, administered one day before CNV induction and every third day thereafter until the end of the 14-day study period. Longitudinal *in vivo* imaging using FA and SD-OCT was performed on days 5, 10 and 14. Mice were euthanized on day 14 and choroidal flatmounts were prepared labelled with Alexa Fluor 594 isolectin GS-IB4. Images were acquired and analysis was performed using ImageJ.

**Results**

Intraperitoneal administration of aflibercept at the highest dose (25 mg/kg) prevented CNV formation and vascular leak on day 5. Whereas a dose 15 mg/kg partially decreased CNV formation and vascular leak (One-Way ANOVA,  $P<0.05$ ), both the lowest dose of aflibercept (5 mg/kg) and saline treatment had no effect on CNV formation at all timepoints. At longer follow-up on day 10 and 14, retinal leak had significantly increased in all aflibercept-treated eyes compared to day 5. Administration of 25 mg/kg aflibercept resulted in a statistically significant reduction of retinal vascular leak compared with saline-treated eyes.

**Conclusions**

Systemically-administrated aflibercept exhibited a strong dose-dependent effect on CNV formation and retinal vascular leak. A dose of 25mg/kg aflibercept administered intraperitoneally successfully prevented CNV formation in mice.

**2661**

**Pathogenic variants in the X-linked BCOR gene cause two different syndromes**

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**Summary**

Pathogenic variants in the X-linked BCOR gene cause two different syndromes that include congenital eye anomalies: OculoFacioCardioDental (OFCD) syndrome, which occurs exclusively in females, caused by various BCOR null mutations, and a severe X-linked recessive microphthalmia syndrome, affecting males, caused by less severe mutations, mainly a specific missense mutation c.254C>T, p.Pro85Leu. Here we describe in further detail the ocular and extra ocular features of these two very interesting syndromes, expanding the phenotype for OFCD, and adding a new male related BCOR condition that does not include eye anomalies. We suggest combining the two conditions under the umbrella term of X-linked BCOR-related syndrome.

**T035**

**Progression of Age Macular Degeneration (AMD) after Cataract Surgery: A Case Series**

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**Purpose**

Age related macular degeneration (AMD) is the leading cause of blindness in people over 50 years of age. Progression AMD after cataract surgery still controversial with the result of the different studies are inconsistent. Multiple epidemiological studies suggest that cataract surgery accelerates the progression of AMD

**Methods**

to report cases of the progression of Age Macular Degeneration after cataract surgery. the macula were evaluated with funduscopy and Ocular Computed Tomography before cataract surgery and more then a year after cataract surgery

**Results**

*Case one, patient with AMD AREDS IV of Right eye with pseudophakic both eye presented worsening blurred of vision in his right eye after about 1 year cataract surgery with best corrected visual acuity (BCVA) is 2/60. OCT macula showed drusen*

*Case two, the patient with AMD both eye with pseudophakic of left eye presented worsening blurred vision about one year and a half after cataract surgery with BCVA 0.2. OCT macula showed drusen*

*Case three, the patient with AMD in both eye with pseudophakic on the right Eye presented blurred vision about one year and a half after cataract surgery with BCVA CFFC. OCT macula showed drusen*

## **Conclusions**

*The patients in this case series showed progression of Age macular degeneration after cataract surgery more than a year.*

## **F081**

### **Pseudo-Foster Kennedy syndrome due to uncontrolled Diabetes Mellitus**

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## **Purpose**

*Pseudo-Foster Kennedy Syndrome is described as unilateral optic disc swelling with contralateral optic atrophy in the absence of an intracranial mass causing compression of the optic nerve. This occurs typically due to bilateral optic neuritis or ischemic optic neuropathy (ION). Diabetes Mellitus (DM) play significant role in pathogenesis of ION which may predispose to optic nerve infarction.*

## **Methods**

*To report a case of Pseudo-Foster Kennedy syndrome due to uncontrolled DM*

## **Results**

*A 43-year-old male patient came to Cicendo Eye Hospital with a chief complaint painless sudden visual field loss on right eye (RE) since 1 week before admission. He has a history of uncontrolled DM since 8 years ago. Visual acuity of the RE was 0.8 and Left Eye (LE) was 0.8. He has relative afferent pupillary defect (RAPD) grade 1 on RE. The funduscopy examination revealed optic disc swelling, peripapillary haemorrhage on RE and optic disc pallor on LE. Laboratory examination revealed hyperglycemia, dyslipidemia, and hypercoagulable state. Humphrey's visual field 30-2 examination revealed inferior altitudinal loss on both eyes. Optical coherence tomography (OCT) showed retinal nerve fiber layer (RNFL) thickening on RE and RNFL thinning on LE. He had treated at Cicendo eye hospital with the same problem on the LE 1.5 years ago. Visual acuity on the RE was 1.0 and LE was 0.8. Funduscopy examination revealed optic disc swelling on LE. OCT examination revealed RNFL thickening in superior, inferior and temporal LE.*

*Visual field examination showed arcuate inferior in LE. Patient was diagnosed as Pseudo-Foster Kennedy Syndrome due to recurrent nonarteritic anterior ischemic optic neuropathy (NAION) with DM with dyslipidemia.*

#### **Conclusions**

*Systemic regulation is required because recurrence of NAION can occurs due to uncontrolled underlying disease.*

#### **F089**

**Statins ameliorate the ultrastructural alterations in the optic nerve in a rabbit model of hypercholesterolemia**

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#### **Purpose**

To analyze by transmission electron microscopy, the possible neuroprotective effects using a low-dosage of statins in optic nerves (ON) from a hypercholesterolemic

### Methods

Three groups of New Zealand rabbits were used for the study: Control (G0; n=10), fed a standard diet; Hypercholesterolemic (G1, n=8), fed a 0.5% cholesterol-enriched diet for 8 months; and Statins (G2; n=8), fed a 0.5% cholesterol-enriched diet for 8 months plus administration of Fluvastatin sodium or Pravastatin sodium at a dose of 2 mg/Kg/day each. The ONs were processed and analyzed by transmission-electron microscopy.

### Results

The cholesterol levels were similar both in G1 and G2. The ON in G1 showed: i) reactive astrocytes with abundant organelles, glial filaments and phagocytosed myelin debris. However other astrocytes were necrotic. ii) Axons with signs of degeneration (hydropic degeneration) and myelin alteration. iii) Necrosis of oligodendrocytes. iv) Vascular alterations, with thickening of the basal membrane and necrosis of the endothelial and muscle cells. However, the ultrastructural changes observed in G2 were less severe than in G1, being intermediate between G0 and G1.

### Conclusions

The use of statins at low-dosage could partly prevent the ultrastructural ON damage associated to hypercholesterolemia, being able to have a certain neuroprotective effect.

## S102

### SIRT1 overexpression induces VEGF expression and pericyte recruitment in the retina

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### Purpose

SIRT1, a key regulator of cell survival, is considered a critical stress-induced protector in retinopathies with aberrant vessel growth such as age-related macular degeneration and diabetic retinopathy. However, SIRT1 expression has also been reported to promote vessel regrowth by controlling the expression of angiogenic factors. Thus, the aim of the study is to clarify the exact role of SIRT1 overexpression in the retina.

### Methods

PCR, western blotting and immunohistochemistry were used to detect VEGF-A, PDGF-B and PDGF-R $\beta$  in the retina of SIRT1-Tg mice and control littermates. Vascular density and pericyte recruitment were analysed by immunohistochemistry in whole-mount retinas.

### Results

As a result of SIRT1 upregulation, VEGF-A mRNA and protein expression were increased in SIRT1-Tg retinas. However, no significant differences were found when comparing vascular density between control and SIRT1-Tg mice retinas. In the view of the absence of neovascularization under VEGF-A overexpression we investigated factors that produce vascular stability, such as pericyte recruitment. The ligand-receptor system PDGF-B/PDGFR- $\beta$ , known to play a critical role in pericyte recruitment, was increased in transgenic retinas. Accordingly, immunostaining with the specific pericyte markers NG2 and PDGFR- $\beta$  demonstrated that SIRT1-Tg mice featured a higher pericyte number and larger capillary surface covered by pericytes than control retinas.

## Conclusions

Our results indicated that although VEGF-A expression is elevated in retinas overexpressing SIRT1, the increase in pericyte coverage induced through the upregulation of PDGF-B/PDGF-R $\beta$  pathway is able to provide blood vessel stabilization protecting thus from the proangiogenic stimuli produced by VEGF-A.

S085

## The role of caspase-8 in inflammasome activation in RPE cells

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## Purpose

Caspase-8 is involved in NLRP3 inflammasome activation and the subsequent secretion of IL-1 $\beta$ . Caspase-8 deletion has been shown to downregulate the expression of pro-IL-1 $\beta$  and decrease the maturation of IL-1 $\beta$  in bone marrow-derived macrophages with RIPK3<sup>-/-</sup> background. Alternatively, other studies have shown that caspase-8 is an downregulator of NLRP3 inflammasome. Since the exact mechanism of caspase-8 is still unknown, our aim was to study the role of caspase-8 on inflammasome signaling in ARPE-19 cells.

## Methods

In this study, the role of caspase-8 on inflammasome signaling was studied in ARPE-19 cells. In order to activate NLRP3 signaling, IL-1 $\alpha$ -primed cells were exposed to MG-132 and Bafilomycin A. Caspase-1 and caspase-8 were inhibited using Ac-YVAD-CMK and Z-IETD-FMK, respectively by adding Z-IETD-FMK one hour prior to IL-1 $\alpha$  or MG-132. Ac-YVAD-CMK was added concurrently with MG-132. IL-1 $\beta$  levels from cell culture medium samples and proIL-1 $\beta$  levels from cell lysates were determined using the enzyme-linked immunosorbent assay (ELISA) method. The metabolic activity of the cells was measured using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and the integrity of the cellular membranes by measuring lactate dehydrogenase (LDH) levels from cell culture medium.

## Results

Caspase-8 inhibition either before the priming or the activation signal lead to decreased secretion of IL-1 $\beta$  along with reduced LDH secretion. The levels of proIL-1 $\beta$  remained high when caspase-8 was inhibited. Concurrent inhibition of caspase-1 and caspase-8 did not have any additional effect on the levels of IL-1 $\beta$ . Reduced LDH levels appeared to depend on caspase-8 but not caspase-1 activity.

## Conclusions

Caspase-8 inhibition prevented the NLRP3 inflammasome activation and had a protective effect on ARPE-19 cells.

3446

## Overall survival after treatment for metastatic uveal melanoma: a systematic review and meta-analysis

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## Purpose

We aimed to compare overall survival (OS) of the treatment options for metastatic uveal melanoma.

## Methods

The study design is a systematic review and meta-analysis. A PubMed search was performed for scientific literature published between January 1, 1980 and March 29, 2017 that assessed the treatment of metastatic uveal melanoma patients. The terms searched were uveal melanoma, choroidal melanoma, ciliary body melanoma, ciliochoroidal melanoma, iridociliary melanoma, iris melanoma, intraocular melanoma, and ocular melanoma. The set of articles identified by this search was evaluated for the additional terms metast\* or stage IV and treatment. Patient-level survival data was required in either Kaplan-Meier form or as numerical information. Kaplan-Meier analyses were manually digitized. The patient-level survivals of each studied treatment were pooled and the median OS was reported. The key endpoint was OS.

## Results

Individual-level data were obtained from 78 peer-reviewed studies involving 2494 patients treated for metastatic uveal melanoma. Significantly better than conventional chemotherapy were isolated hepatic perfusion (HR 0.93 [95% CI 0.87-0.98],  $p=0.006$ ), immunoembolization (HR 0.97 [95% CI 0.95-1.00],  $p=0.009$ ), and surgery (HR 0.94 [95% CI 0.92-0.96],  $p=0.0001$ ). Median OS with conventional chemotherapy was 0.9 years (CI 0.8-1.1), with isolated hepatic perfusion 1.3 years (CI 1.2-1.7), and with surgery 1.4 years (CI 1.3-1.7).

## Conclusions

Our results suggest that there maybe no clinically significant improvement in OS regarding the mode of treatment. Surveillance, selection, and publication bias are likely to explain most of the reported prolongation of survival in the peer-reviewed articles. For few patients with solitary tumour lesions in the liver, surgery might prove more effective than conventional chemotherapy.

1262

### importance of ocular surface for the success of glaucoma surgery

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## Summary

There has been a considerable focus on the ocular surface in recent times, especially since the publication of the DEWS II report. The ocular surface of patients with glaucoma is still an area where more research needs to be carried out to understand the impact glaucoma medications have on the ocular surface, and how to reduce this.

The ocular surface is also an important factor when considering whether glaucoma surgery is appropriate and which surgery is the most suitable. This session will discuss how to assess the ocular surface when considering glaucoma surgery, why this is important and how to optimise the ocular surface, as well as a review of the literature.

2124

### Cortical anomalies in response to RGC damage: how do they affect the visual field and how should we measure them?

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## Summary



It is often assumed that conventional clinical measures of visual field sensitivity are direct measures of retinal ganglion cell (RGC) function. However, the relationship between retinal structure and visual field sensitivity is not straightforward. An enlarged critical area of complete spatial summation (Ricco's area) has previously been found in patients with glaucoma, accounting for disproportionate deficits in visual field sensitivity to a range of perimetric stimulus areas. It has also previously been shown that spatial summation of perimetric stimuli can be accounted for by cortical pooling by numerous spatial mechanisms, but not probability summation across RGCs. Thus, it is likely that perimetric sensitivity loss is a consequence of anomalous cortical spatial pooling resulting from RGC damage, rather than being a direct measure of RGC loss. Recently, it has been shown that stimuli optimised to map to the altered spatial summation function in glaucoma, particularly those that vary in area from a starting value scaled to Ricco's area, offer a greater disease signal, uniform response variability with increasing disease severity, and a greater signal/noise ratio (SNR) than conventional fixed-area stimuli that vary in contrast.

## **T027**

### **Predictive biomarkers in OCT-Angiography of peripheral nonperfusion in retinal venous occlusions**

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#### **Purpose**

To study the association between macular inner vascular layers features assessed by Optical Coherence Tomography Angiography (OCT-A) and peripheral non-perfusion evaluated by fluorescein angiography (FA) on a cohort of patients with retinal venous occlusion.

#### **Methods**

Retrospective review of patients observed between 2015 and 2017 without macular edema. Patients underwent a complete ophthalmic examination, including FA and SD-OCT-A. Significant ischemia was defined as non-perfusion areas superior or equal to one retinal quadrant on FA. Vascular density (VD) and foveal avascular zone were measured using AngioAnalytics software. Fractal dimension (FD) and lacunarity (LAC) were computed using an algorithm designed by MATLAB. Generalized Additive Models were used to study the association between OCT-A parameters and peripheral non-perfusion. The models' performance was assessed by the Akaike Information Criterion (AIC), Brier Score and by the area under the receiver operating characteristic curve (AUC). A p value of  $\leq 0.05$  was considered as statistically significant.

#### **Results**

Inclusion of 48 eyes (48 patients), 19 of which had significant peripheral non-perfusion. Deep capillary plexus FD, VD and LAC were different ( $p < 0.01$ ) between ischemic and non-ischemic eyes. Regarding the association with significant ischemia, LAC alone had the highest AUC (AUC = 0.877) followed by FD (AUC = 0.847) and VD (AUC = 0.731). LAC obtained the best values in the AIC and Brier Score evaluations. The multivariate model that included both LAC and VD attained the best performance considering all criteria (AUC = 0.888).

#### **Conclusions**

Macular deep capillary plexus characteristics on OCT-A may be associated with peripheral non-perfusion on FA. Analyses of OCT-A quantitative parameters could potentially help to dictate the need to perform invasive fluorescein angiography.

**F062**

**Anterior Segment swept-source Optical Coherence Tomography evaluation of patients submitted to lateral recti hang-back recession surgery**

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**Purpose**

To evaluate the reproducibility of extraocular muscle insertion in Anterior Segment Swept-source Optical Coherence Tomography (AS-OCT) and apply the technique to muscles submitted to hang-back recession, correlating findings with one-year post-operative results.

**Methods**

Cross-sectional evaluation of consecutive patients observed between October and December 2016. Anterior Segment Swept-source Optical Coherence Tomography (AS-OCT) longitudinal scans were obtained on horizontal gaze at a fixation light. Muscle insertion was selected using a graphical user interface (GUI) and custom algorithms built as a unified tool in Matlab coding language. Measurement values were obtained intraoperatively and reproducibility was evaluated with the intra-class correlation coefficient (ICC). The correlation between surgical success and the variables of interest was studied using bivariate correlations.

**Results**

Evaluation of 60 normal patients (120 eyes); 18 patients before horizontal recti surgery (27 eyes) and 22 post-operative patients (37 eyes). The reproducibility of the GUI guided limbus-muscle insertion distance measurement was excellent (ICC=0.97). In patients with intermittent exotropia submitted to hang-back recession, the muscle insertion was identified in 21 eyes (57%) and the mean distance to the limbus was 9.95mm [7.52-13.21mm]. There was a strong correlation between normal reinsertion and surgical success ( $r = 0.756$ ,  $p = 0.01$ ) but not with the size of the muscular loop ( $r = 0.56$ ,  $p = 0.75$ ).

**Conclusions**

Inter-examiner reproducibility in a program aided limbus-rectus muscle insertion measurement is excellent. In patients submitted to hang-back recession surgery, abnormal muscular reinsertion is correlated with the surgical success but not with the size of the loop.

**1815**

**3 D OCT angiography in choroid layer**

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**Summary**

**Purpose:** To study the three-dimensional organization of choroidal neovascularization complicating age-related macular degeneration (nAMD).

**Design:** Observational, cross-sectional study.

**Methods:** Eyes were analyzed using high-speed swept-source OCT-A. Raw data was processed automatically to obtain three-dimensional models of choroidal neovascularization blood flow. Quantitative parameters analyzed included blood flow volume, vessel segment length and fractal dimension (FD). Raw data processing algorithms were built in Matlab coding language and model analysis performed using Imaris software.

**Results:** Twenty patients of whom 10 (10 eyes) were in Group 1 (treatment naïve active nAMD) and 10 (10 eyes) in Group 2 (remission nAMD) based on SD-OCT qualitative morphology and multimodal imaging. CNV vessel branches showed statistical self-similarity and a lognormal distribution. Treatment naïve networks were smaller, denser and more disorganized comparing to networks of inactive disease ( $p < 0.01$ ).

**Conclusions:** Blood flow characteristics on OCT-A can be accurately studied using three-dimensional metrics. In the future, volumetric OCT-A quantitative parameters could potentially help assess CNV activity status.

**1735**

### **The use of keratoprosthesis in the treatment of AAK**

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#### **Summary**

**Purpose** To evaluate long-term anatomical outcomes of the Boston keratoprosthesis (KPro) type 1 surgery in patients with corneal blindness due to primary and secondary limbal stem cell deficiency, with special interest for the subset of aniridia patients.

**Methods** Single-center retrospective study evaluating all patients that underwent Boston KPro surgery in the Rotterdam Eye Hospital,

**Results** Thirty-one patients (34 eyes) underwent Boston KPro type 1 surgery since 1994. Preoperative diagnoses were aniridia (n=9), multiple graft failure (n=4), chemical burn (n=7), and other (n=14). Mean follow-up was 54 months (range 2-145 months). Ocular complications leading to KPro explantation were found in 10 (29%) of 34 eyes and mean time to explantation was 26 months (range 3-91). Survival analysis estimated that mean KPro survival time was 8,5 years. The subset of aniridia patients show the same favorable survival as multiple graft failure.

**Conclusions** Boston KPro surgery can be offered to patients with end-stage corneal blindness as an option for temporary restoration of sight. Mean overall anatomical survival time was 8,5 years. This study offers valuable information for patient counselling when considering KPro surgery.

**2333**

### **Aciclovir resistant herpetic keratitis - diagnosis and treatment**

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#### **Summary**

Long-term acyclovir (ACV) prophylaxis, recommended to prevent recurrent herpes simplex virus type 1 (HSV-1) infections, predisposes to ACV-refractory disease due to the emergence of corneal ACV-resistant (ACV-r) HSV-1.

Corneal HSV-1 isolates or quasispecies with >28% ACV-r viruses show clinical behaviour of ACV-refractory disease. 26% of isolates of patients using oral ACV-prophylaxis showed development of ACV-resistance. ACV-susceptibility testing is warranted during follow-up of recurrent herpetic keratitis patients (rHK) .

Treatment of rHK should consist of triple therapy consisting of topical ACV, systemic Famciclovir combined with a thymidine kinase independent drug like topical BVDU, foscarnet or Trifluorothymidine (TFT) .

## **S069**

### **Dropmeter interest in clinical trials**

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### **Purpose**

To describe the different ways to use a dropmeter in dry eye clinical study.

### **Methods**

International, prospective, randomised, and controlled Phase III. In this trial, the dropmeter, a 3G wireless device that records and transmits topical medication use in real time, will be used to count all concomitant drops of saline solution during screening, both 6-month randomised and open clinical phases in addition to the studied drug. As conjunctival cul-de-sac volume is only (7 µL), even if two consecutive instillations in less than 5 minutes was administered, it will be counted as only one.

### **Results**

Two hundred and forty seven patients (494 eyes) suffering from dry eye syndrome were enrolled in 20 countries. In all countries the device works well. A total 247.096 drops, March 9th 2018, have been counted as raw data. The number of instillations is used by investigators as a study inclusion criteria (as no more than "X" instillations permitted), no patients have been excluded till now. Dropmeter can also differentiate patient habits during screening period and we can show different patient patterns according to the daily use of these additional drops need for the different patient categories. Additional subgroup analysis will be done with different dry eye etiologies. In a second time, at the end of the study, we will compare the use of saline solution in both arms (verum vs vehicle).

### **Conclusions**

Dropmeter could be used to follow the patient compliance but also control the use of concomitant treatments in studies (including daily use, preferred drops or tapering period...) or in the real life. This tool is especially interesting to obtain more accurate data concerning patient's instillations and compliance in order to avoid a daily reporting of all instillations witch is often not done.

## T001

### Novel retinal artery pulse transit time measurement shows expected blood pressure dependency in rodents

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#### Purpose

Large artery pulse transit time (PTT) is a marker of arterial stiffness. The retinal vasculature provides unique *in-vivo* access to the microcirculation. This study investigated whether retinal artery PTT decreased with increasing blood pressure (BP) as expected with changes in retinal artery stiffness.

#### Methods

Fundus videos from three Sprague Dawley rats were acquired (high-speed camera, 125 fps, Optronis, Germany on a Zeiss fundus microscope) with simultaneously acquired electrocardiogram and aortic BP. Retinal artery diameter waveforms at proximal and distal sites were extracted using an in-house algorithm. The sinusoidal component of the diameter waveform at the heart rate frequency was isolated. Phase delay between proximal and distal sinusoids defined PTT. PTT was measured across a physiological range of mean arterial pressure (MAP): baseline (90–110 mmHg); 130 mmHg to baseline following systemic phenylephrine infusion (PE, 30 µg/kg/min); 130 mmHg to baseline during PE infusion with simultaneous inferior vena cava occlusion (VO); 70 mmHg to baseline following systemic sodium nitroprusside infusion (SNP); and 70 mmHg to baseline following VO. The correlation between retinal artery PTT and BP was quantified.

#### Results

manipulation	MAP (mmHg)	
baseline	111.8±0.41	84.6±17.39
following PE	118.5±1.77	63.7±5.81
during PE and VO	114.6±3.30	72.3±13.72
following SNP	84.2±3.37	115.3±30.31
following VO	98.5±10.86	104.9±15.98

There was a significant negative correlation between retinal artery PTT and MAP (-1.4 ms/mmHg, R<sup>2</sup>=0.59, p<0.001).

#### Conclusions

The pressure dependency of the measured retinal PTT indicates the measure has utility in *in-vivo* quantification of the impact on microvessels of cardiovascular diseases. Larger cohort and longitudinal studies are required to elucidate the predictive value of screening retinal artery PTT in systemic cardiovascular abnormalities.

## F016

### XEN gel stent to treat intraocular hypertension induced by Dexamethasone-implant intravitreal injections: about 5 cases

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#### Purpose

Intravitreal injections of slow-release dexamethasone are usually well tolerated. The hypertension resulting from single or repeated dexamethasone-implant intravitreal injections is usually successfully managed with intraocular pressure-lowering eyedrops. But high responders, according to Becker's classification, meaning a gain of IOP more than 15 mmHg, have been described with dexamethasone-Implant.

To report the cases of five eyes of four dexamethasone-implant intravitreal injections high-responders patients who benefited from a XEN gel stent.

## Methods

In our cases, anti-VEGF therapy were ineffective. We did not have any other therapeutic alternatives for our patients. The only treatment was DEX-implant intravitreal injection despite of the high pressure raise.

The XEN® Glaucoma Treatment System is available for the surgical management of refractory glaucomas. This implant is a 6-mm tube of collagen-derived gelatin cross-linked with glutaraldehyde. It comes preloaded in an injector. It is implanted ab-interno and it creates a drainage pathway between the anterior chamber and subconjunctival space.

We defined the treatment success rate as as a postoperative IOP below  $\geq 6$  and  $\leq 17$  mmHg without glaucoma medications.

## Results

All of our patients exhibit in this ranges.

We experienced only one complication, an exposure of the implant, easily managed by applying conjunctival sutures and relocation of the implant in the subconjunctival space.

## Conclusions

XEN Gel stent can represent an alternative to trabeculectomy and may be used when corticosteroid therapy is responsible for a severe hypertension but remains the only alternative.

1723

## The Role of Simulators in Cataract Surgery

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## Summary

### The Role of Simulators in Cataract Surgery

The medical training has benefited from technological advances that simulate surgical environments. Recent studies show that surgical simulators' training reduces the complications rate during cataract surgery. This is an invaluable educational benefit with which trainees can gain surgical experience before their first surgery. Performing hundreds of simulated surgeries, including a multitude of simulated complication scenarios allows residents to accumulate surgical experience and refine essential skills, taking the patient out of the learning loop.

2962

## Ocular phenotype of ocular anterior dysgenesis

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## Summary

Ocular anterior dysgenesis (OAD) designates a broad spectrum of malformations, mostly bilateral and mostly resulting from neural crest cell migrations abnormalities, with variable consequences on visual function.

Precisely phenotyping OAD is crucial, as the treatment indications and prognosis depend upon the relative positions and relations of the anatomical structures with each other. This now requires the use of both a slit lamp and an anterior segment ultrasound or OCT in a specialized setting.

From the common posterior embryotoxon to the most severe forms of so-called Peter's anomaly, all peculiarities of the OAD spectrum and practical implications will be reviewed and discussed, with special attention to the terms used to describe the curvature, size, clinical aspect and structure of the cornea, the irido-corneal angle, often not clinically visible, the iris and the lens characteristics.

Only by so doing can the numerous controversies regarding the naming of the OAD varieties be unfold, allowing fruitful discussions on practical therapeutic options.

**3431**

### **Lymphoma highlights**

**T109**

### **Laponite clay for long term delivery dexamethasone intravitreal injections**

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### **Purpose**

To evaluate safety and pharmacokinetics parameters in Laponite clay loaded with dexamethasone for long term delivery intravitreal administrations.

### **Methods**

Sixteen New Zealand rabbit eyes were intravitreally injected with 100 µl Dexamethasone-Laponite suspension (10 mg/ml; 1/10 w/w) in right eyes; left eyes served as controls. Safety study included complete ophthalmological examination by biomicroscopy, intraocular pressure measurements, funduscopy and histological exams by Hematosiline-Eosine and Sirius-Red staining. Pharmacokinetics studies by HPLC method determined Dexamethasone long term release. Time points were 1, 7, 28, 84 and 168 days.

### **Results**

No adverse effects such as inflammation, infection, hyper ocular pressure (range 6-14 mmHg), or retinal damage were detected; even outer retinal layer was better preserved in administrated eyes than control eyes. Laponite was detected in vitreous for up to 14 weeks (98 days) post administration (33% of initial dose administered), and dexamethasone levels remained detectable and stable along studied time periods with a clearance of 0.49 g/day and lengthen the half-live of dexamethasone to 134.75 days (approximately 4.5 months).

## Conclusions

Dexamethasone-Laponite is an intraocular well tolerate formulation, and its gradually long term delivery was demonstrated in this animal study.

## F107

### Different retinal layers thickness measurements change with age in healthy eyes

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## Purpose

To evaluate the physiological changes of the all retina layers thickness in macular and peripapillary areas in healthy subject using standard protocols and grid points of Swept-Source optical coherence tomography (SS-OCT).

## Methods

A total of 480 healthy eyes were analyzed from four different groups of persons (group 1, 2, 3 and 4) divided depending on age, and ranged between 20 to 34 years, 35 to 49 years, 50 to 64 years and 65 to 79 years respectively. All of them underwent Wide protocol (including both macula and optic disc regions, with a field of view of 12x9 cm), using Triton SS-OCT instrument (Topcon Corporation, Japan).

## Results

It is in the transition from group 2 to group 3 where more significant thinning of all layers of the retina occurs, mainly at Temporal-Superior (TS) quadrant at Retina Nerve Fiber Layer (RNFL), Ganglion Cell Layer (GCL) ++ and retina ( $p=0.001$ ,  $p<0.001$  and  $p<0.001$ ), and TS, Temporal Inferior and temporal half at choroid layer ( $p<0.001$ ). Also a significant thickening of RNFL at group 2 when comparing with group 1 at TS quadrant ( $p=0.001$ ), inferior ( $p<0.001$ ) and temporal ( $p=0.001$ ) halves was observed as well as at nasal half at choroid layer ( $p=0.001$ ).

## Conclusions

There is a directly proportional relationship between the thinning of the retina and age, for all layers. Our results suggested that in the third decade of life there is a thickening of the retina and a subsequent thinning that progressed with age.

## 2513

### Laponite clay as a carrier for controlled drug delivery system for intravitreal injections

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<sup>2</sup>

## Summary

To analyze in vitro and in vivo behavior of Laponite clay (LAP) and LAP loaded with dexamethasone (DEX-LAP) and its biocompatibility in ocular tissues, as controlled drug delivery formulation for intravitreal (IVT) injections. In vitro release study of DEX from LAP was performed in saline and hyaluronate solutions, being always < 40% of the initial DEX loaded. A100-μL LAP suspension (15mg/ml) was administered in New Zealand rabbits (NZr) (n=16) by IVT injection for ocular safety study. A complete ophthalmological exam and histological analysis were carried out. No relevant ocular complications, hyperocular pressure or retinal degeneration were detected along the study (1, 7, 28, 84 and 168 days). Single IVT injections of 100-μL DEX-LAP suspension (10mg/ml, 1:10 w/w) were performed in



NZr (n=16) for pharmacokinetic study. Free DEX concentrations in vitreous humor were monitored by HPLC-MS method (1, 7, 28, 84 and 168 days) remaining detectable and stable in vitreous for up to 24 weeks. A significant lower elimination rate was found respecting DEX solution (CL 0.49 vs 315.29 g/day). The administration of DEX-LAP can lengthen the half-life from 0.13 to 134.75 days ( $\approx$  4.5 months).

#### T017

##### Choriocapillaris changes during development of CNV – an OCT Angiography quantitative analysis

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##### Purpose

To study the organization of the choriocapillaris network on active neovascular Age Related Macular Degeneration (nAMD) fellow eyes, using Optical Coherence Tomography Angiography (OCT-A).

##### Methods

Observational, cross-sectional study of 108 patients (108 eyes). Included 59 eyes from patients without known systemic microvascular disorders, and 49 patients with active neovascular Age Related Macular Degeneration (nAMD), in whom the fellow eye was evaluated. The central macula was scanned with a high-speed 1050-nm wavelength swept-source OCT-A. A 10- $\mu$ m slab thickness below the Bruch membrane was considered for choriocapillaris vascular network analysis. Automatic local thresholding of the raw data was issued to differentiate perfusion from non-perfusion regions (flow voids). Flow voids area and indices of morphological complexity (fractal dimension, FD) and structural nonuniformity (lacunarity, LAC) quantified using algorithms designed on MATLAB. All statistical analysis were performed in R.

##### Results

The distribution of flow voids area vs frequency fitted almost perfectly a theoretical power law distribution in all the patients. FD and lacunarity were statistically different ( $p < 0.01$ ) between the two groups. After adjusting for the age effect, we observed a mean increase of 0.011 (CI 95% 0.005 - 0.017,  $p < 0.001$ ) in FD for patients in nAMD fellow eye group and a mean increase in FD of 0.002 (CI 95% 0.001-0.004,  $p = 0.02$ ) for each five years increase in age. Lacunarity was higher ( $\beta = 0.0228$ , CI 95% 0.0150-0.0306,  $p < 0.001$ ) in nAMD fellow eyes than in control patients.

##### Conclusions

Fractal dimension analysis and lacunarity are sensible organization indices able to differentiate late nAMD fellow eyes from sex and age matched control patients. Fractal geometry may be useful in characterizing mechanisms of AMD disease progression.

#### F017

##### Quantitative evaluation of peripapillary microvasculature in Pseudoexfoliation Syndrome

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### **Purpose**

To assess quantitative peripapillary microvasculature changes in Pseudoexfoliation syndrome

### **Methods**

Observational, cross-sectional study. Inclusion of 15 subjects with nonglaucomatous pseudoexfoliation (PXS), 11 patients (11 eyes) with mild or moderate well controlled pseudoexfoliation glaucoma (PXG) and 15 control subjects without any known systemic vascular disorder. Patients in the groups were sex and age matched. All patients underwent complete ophthalmic examination, including visual acuity (VA), blood pressure and intraocular pressure (IOP) measurement and had at least two reliable Standard Automated Perimetry and two Optical Coherence Tomography (OCT) scans in the last 6 months. Peripapillary microvasculature was studied using the swept source Optical Coherence Tomography Angiography (OCTA), scans cover an 4.5x4.5mm area, an automatic segmentation of the superficial vascular plexus and a 0.75 mm circle beyond the optic disc was isolated for quantitative analysis. Vascular mean values: Vessel density (Vd), fractal dimension (FD) and lacunarity (Lac) were computed using an algorithm designed by MATLAB.

### **Results**

Comparing mean values between PXS group and control subjects there were no significant differences in all the microvascular mean values. We found statistically differences regarding Lac ( $p=0.028$ ), Vd ( $p=0.045$ ), FD ( $p=0.06$ ) between PXS and PXG groups, reflecting higher Lacunarity and lower FD values for PXG patients

### **Conclusions**

There were no significant peripapillary microvascular alterations when comparing nonglaucomatous pseudoexfoliation (PXS) and control patients. Microvascular changes were observed only on pseudoexfoliation glaucoma (PXG) group, which may suggest that pseudoexfoliation syndrome by itself may not induce alterations on peripapillary microvasculature.

### **F005**

#### **Peripapillary microvasculature and Lamina cribrosa: is there a role in the diagnosis of primary open-angle glaucoma?**

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### **Purpose**

To evaluate the performance of lamina cribrosa and peripapillary microvasculature in primary open-angle glaucoma (POAG) diagnosis

### **Methods**

Prospective cross-sectional study of 22 eyes with mild or moderate well controlled POAG and 33 healthy eyes. All patients underwent complete examination, including blood pressure and intraocular pressure (IOP) measurement, had at least 2 reliable Standard Automated Perimetry and 2 Optical Coherence Tomography (OCT) scans in the last 6 months. Optic disc structure was evaluated using swept source OCT. Lamina cribrosa depth (LCD), lamina cribrosa curve depth (LCCD) and lamina cribrosa curvature index (LCCI) were measured manually twice and the mean value considered for analysis. Peripapillary microvasculature was studied using the SS-OCT Angiography (OCTA), with automatic segmentation of the superficial vascular plexus and a 0.75 mm circle beyond the optic disc isolated for quantitative analysis. Vessel density (Vd), fractal dimension (FD) and lacunarity (Lac) were computed using an MATLAB algorithm

## Results

There were no significant differences in terms of age and IOP between the groups. RNFL ( $p<0.001$ ), MD ( $p=0.001$ ), PSD ( $p=0.023$ ) and vertical C/D ( $p=0.008$ ) were statistically different as expected. On lamina cribrosa parameters, only on LCCI was significant different ( $p=0.035$ ). All the OCTA parameters (FD, VD and LAC) were statistically different ( $p<0.01$ ) between glaucomatous and healthy eyes. The ROC curve analysis attained the best performance considering LAC and FD as assessment criteria, with area under curve (AUC) for LAC (AUC=0.821; CI95% 0.625-0.961) and for FD (AUC= 0.800; CI95% 0.658-0.986).

## Conclusions

Regarding diagnostic performance, OCTA quantitative parameters reveal advantage over lamina cribrosa analyse. Microvascular based scores may enhance the predictive power of functional exams in glaucoma diagnosis.

## S004

### Characterization of corneas following different time and storage methods for use as a source of stem-like limbal epithelial cells

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## Purpose

To analyze if the method and time of conservation of corneas (hypothermic storage for 2 to 9 days or maintenance in culture) limits the survival of stem-like limbal epithelial cells.

## Methods

We have analyzed protein expression patterns of limbal stem cell markers (K15,  $\Delta$ Np63 $\alpha$ , ABCG2, vimentin) as well as cell differentiation (K3, K12), proliferation (Ki67) and stromal-epithelial adhesion (type VII collagen) markers using immunofluorescent staining in frozen histological sections of the corneal rims.

## Results

Normal organization of the corneal epithelium is affected after long periods of hypothermic storage or culture of the corneas. In addition, staining with type VII collagen marker shows discontinuities in stromal-epithelial adhesion at long conservation times. All putative markers of stem-like epithelial cells are mostly expressed in the limbal area, as well as in the basal layer of the conjunctival epithelium in all corneas, regardless of their conservation time. Notably, vimentin positive labeling of cells in the limbal epithelium disappears as the days of conservation of the corneas increase. Proliferating Ki67 positive cells can be found in all corneas.

## Conclusions

Stem-like epithelial cells are present in the corneal limbus even in corneas that have been maintained for long periods of time in hypothermic conditions or in organ culture, although their distribution slightly varies in comparison with corneas maintained for shorter periods of time.

## F061

### Optical coherence tomography outcomes in patients with Friedreich ataxia: a longitudinal study

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### **Purpose**

To compare optic coherence tomography (OCT) changes in patients with Friedreich ataxia (FRDA) with healthy controls (HC) and to correlate with neurological disability measured by scale for the assessment and rating of ataxia (SARA).

### **Methods**

Nine FRDA patients and 19 HC were prospectively selected. All participants underwent a complete neurological and ophthalmological evaluation with OCT in order to analyze macular thickness (MT), ganglion cell complex (GCC) and the peripapillary retinal nerve fiber layer (RNFL). All measurements were taken in a basal exploration and after 6 months.

OCT parameters were compared between groups with a linear regression analysis and an adjustment for multiplicity. A  $p < 0.05$  was considered significant. Rho Spearman was used to correlate OCT parameters and SARA.

### **Results**

In FRDA patients with respect to HC there was: I) a GCC significant decrease in all of the patients analyzed, II) a significant involvement of the papillo-macular bundle associated with a decrease of BCVA of 26.59%. All macular parameters decrease after 6 months, except the inferior outer ring, but the BCVA only decreases 5%. III) The average RNFL thickness, all quadrants and sectors, except the 8th one, significantly decreased. In 6 months, there was a statistically significant decrease in the temporal quadrant and sectors 3 and 8. The strongest negative correlations between SARA with OCT were found in the temporal quadrant of the RNFL with a coefficient of -0.801 and a sector 7 with -0.866 ( $p < 0.05$ ).

### **Conclusions**

OCT can detect changes in MT, GCC and RNFL thicknesses in FRDA patients. Thus, the retina, being part of the central nervous system and offering easy accessibility, encourages its use as a potential biomarker in FRDA. The longitudinal study allows us to assess that, over time, these changes remain and progress.

## **F073**

### **Changes in the Vision, Visual Field and Retina by OCT in Early ALS Patients: a longitudinal study**

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### **Purpose**

To compare early visual changes in mild amyotrophic lateral sclerosis (mALS) with healthy controls.

### **Methods**

Prospective and longitudinal study. Twenty eyes from 10 mALS (patients with spinal features in the first 18 months after diagnosis) were selected and compared with 38 eyes from 19 healthy controls. All patients underwent a comprehensive neurological and ophthalmic examination, including the ALS Functional Rating Scale-revised (ALSF-RS-R), best-corrected visual acuity (BCVA) and Humphrey visual field (VF) testing. Additionally, macular thickness (MT), ganglion cell complex (GCC) and retinal nerve-fibre layer (RNFL) thickness were measured by optical coherence

tomography (OCT). All measurements were taken in a basal exploration after 6 months. The OCT parameters were compared between groups with a linear regression analysis and an adjustment for multiplicity. A  $p < 0.05$  was considered significant.

## Results

BCVA and VF parameters did not statistically differ between the study groups. Temporal and inferior inner macular ring sectors were significantly thicker in mALS compared to controls. In mALS no OCT measurement correlated with the ALSFRS-R score. In the longitudinal study, only half of the patients were able to follow-up. No significant statistical changes were observed in OCT although a thinning of 20% in RNFL vertical sectors 5, 6 and 12 hours.

## Conclusions

OCT can detect subtle early changes in macular thickness in mALS and could be helpful as a complementary tool. The longitudinal study not only allows us to notice that there are changes in the MT and RNFL of mALS patients, but also to assess them over time. These changes remain and progress. The use of the retina, being part of the central nervous system and offering easy accessibility, is encouraged as a potential biomarker in non-motor areas for ALS.

## F074

### Vision involvement in optic neuritis and non-optic neuritis eyes in patients with multiple sclerosis or neuromyelitis optica spectrum disorder

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## Purpose

To identify different patterns of retinal and optic nerve damage between multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) and comparing them with aged-matched healthy controls (HC), using optical coherence tomography (OCT) and field visual (VF) in optic neuritis (ON) and non-optic neuritis (NON) eyes.

## Methods

Cross-sectional retrospective study. 96 eyes of 48 patients with MS, 18 eyes of 9 patients with NMOSD and 58 eyes of 29 HC were included. All patients underwent a complete ophthalmologic examination including best corrected visual acuity (BCVA), macular thickness (MT), ganglion cell complex (GCC), retinal nerve fibre layer (RNFL) and visual field (VF) patterns. The OCT parameters were compared between groups with a linear regression analysis proved that this correlation was independent of age and an adjustment for multiplicity. A  $p < 0.05$  was considered significant.

## Results

Changes between HC, MS and NMOSD by OCT were: I) ON compared to NON, both MS and NMOSD showed SS differences in BCVA, MT, GCC and RNFL. II) ON compared to HC, similar affectionation patterns were observed in both diseases but thinner in NMOSD. BCVA was also worse in NMOSD. III) NON compared to HC, GCC of MS showed an SS thinning with respect to HC, which was not observed in NMOSD. RNFL in MS showed changes compared to NMOSD.

In the VF, SS differences only were observed in the group of ON-MS compared to HC. Mean deviation, pattern standard deviation and false negatives were SS superior in ON eyes. When comparing ON-MS and ON-NMOSD, a false negative percentage is also an SS increase in NMOSD.

## Conclusions

In ON eyes BCVA could be a helpful measure to distinguish between MS and NMOSD. The different patterns of affection are better seen in the contralateral eye. The greatest differences were shown in GCC and RNFL.

**S031**

**Cyclosporine pharmacokinetics in healthy volunteers after ocular administration of OTX-101, a novel nanomicellar cyclosporine formulation**

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**Purpose**

This phase 1, open-label, single-arm, single-center study evaluated the pharmacokinetic (PK) profile of OTX-101—a novel, nanomicellar solution of cyclosporine A (CsA) under development for the treatment of keratoconjunctivitis sicca (KCS).

**Methods**

Healthy volunteers  $\geq 18$  years of age received 1 drop OTX-101 0.09% in each eye every 12 hours for 7 days, and once on day 8. Blood was collected predose and 0.25, 0.5, 1, 2, 4, 8, and 12 hours post-first dose on day 1 and day 8. CsA maximum whole blood concentration ( $C_{max}$ , ng/mL) and area under the concentration-time curve from 0 to last measurement ( $AUC(0-t)$ , hr·ng/mL) were assessed using noncompartmental analysis. CsA concentration values  $\geq 0.1$  ng/mL (lower limit of quantification, LLOQ) were used in PK calculations.

**Results**

A total of 15 subjects—aged 22 to 61 years old (9 men, 6 women)—were administered OTX-101, completed the phase 1 study, and provided data for analysis. Systemic exposure to CsA after topical administration of OTX-101 was low; 3 subjects had a CsA concentration  $\geq$  LLOQ on day 1; only 4 subjects had 3 consecutive concentration measurements  $\geq$  LLOQ on day 8. Among these, the mean  $\pm$  standard deviation CsA  $C_{max}$  was  $0.173 \pm 0.020$ ;  $AUC(0-t)$  was  $0.526 \pm 0.059$ .

**Conclusions**

The nanomicellar components of OTX-101 are approved by the FDA for topical ocular use. Systemic exposure to CsA was negligible after twice-daily ocular administration, supporting the systemic safety of OTX-101 in healthy volunteers. Taken together with preclinical and clinical results of OTX-101 studies, these findings further support an acceptable safety profile for OTX-101.

**015**

**What's new in TFOS DEWS II?**

**3533**

**Differential diagnosis of intraocular tumors**

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## **Summary**

Differential diagnosis of intraocular tumors

Intraocular tumors may be benign or malignant, congenital or acquired, progressive or dormant.

The symptoms described by patients with intraocular tumor (blurred vision, visual-field abnormalities flashes, floaters) depend mostly on tumor location. In many cases tumors are asymptomatic. Slit lamp biomicroscopy, gonioscopy and indirect ophthalmoscopy can be used for tumors detection in the eye with clear optical media. Neoplastic infiltration (haziness) of the vitreous body can cause diagnostic problems. The clinical features are helpful in differentiating the most common iris, ciliary body choroidal and retinal tumors. However, many of small retinal and choroidal lesions look similar. Correct clinical identification of simulating lesions and differential diagnosis may be performed with additional examinations (US, OCT, FA, ICGA, FAF, MRI, biopsy). Swept source Optical Coherence Tomography enables visualization of all retinal and choroidal structures and their pathology, which is very useful in differential diagnosis of small choroidal lesions.

The aim of the presentation is to determine characteristic features of intraocular tumors based mainly on US and SS-OCT examination.

**1833**

**Keeping your trial on track - when to start recruiting, how to keep things moving and when to stop**

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## **Summary**

One of the most common sources of problems when performing a clinical trial or study is recruitment. This course will address ways to minimize recruitment issues at different stages of clinical research. At the protocol-writing phase, we will discuss the importance of sample size calculation, the expected time for completing the recruitment and of keeping the protocol as simple as possible. At this phase, the research team should analyze the likely sources of patients for the study. Indeed, investigators greatly overestimate the pool of available patients who meet the inclusion criteria. At the study conduct phase, we will address recruitment strategies, the top reasons for patient non-entry, for investigators not entering eligible patients and ways to reduce the dropout rate. Specifically, the most important factor associated with recruitment is an enthusiastic lead investigator and a friendly study coordinator, having a thorough understanding of the study. At the follow up phase, it is crucial to keep patients motivated, to schedule follow-up visits to coincide with routine visits and minimize the time patients spend in the clinic. We will discuss potential problems arising in each of these phases and ways to overcome them.

**2917**

**Infrared autofluorescence in adaptive optics ophthalmoscopy for imaging retinal pigment epithelial cells in health and disease**

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## Summary

The *in vivo* cellular morphology of the retinal pigment epithelium (RPE) may be useful for evaluating RPE health in diseases such as age-related macular degeneration (AMD). Individual RPE cells have been imaged with several modalities in adaptive optics ophthalmoscopy (AOO). However, most methods have limitations or complexities that make them difficult to use on patients and data in disease states is sparse. Recently, infrared autofluorescence (IRAF), likely arising from melanin, was shown to visualize RPE cells similarly to short wavelength autofluorescence (SWAF) in AOO but with reduced complexity in implementation and improved safety. Here we show that IRAF can be extended to shorter wavelengths, still within the safety profile afforded by infrared light, but with improved detection efficiency. This new implementation successfully imaged RPE cells in several normal eyes and in patients. Like SWAF, NIRAF varied substantially within and between eyes. IRAF in AOO at shorter wavelengths may be an optimal choice for imaging RPE cells in diseased eyes due to its better safety profile and ease of implementation, but more work is needed to understand its limitations.

## S117

### Tunisian retinoblastoma clinical and genetic profile

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## Purpose

To report the relative frequency of presentation's signs in Tunisian children with retinoblastoma. In addition, we proposed to carry out a genetic study in families whose retinoblastoma appears in at least four successive generations.

## Methods

We followed 200 children with retinoblastoma examined between January 2000 and June 20015.

## Results

There were 123 boys and 77 girls. For all cases, mean age at diagnosis was 29.8 month (range, one month to nine years). There were 138 (69%) unilateral cases and 62 (31%) bilateral cases. 19 children (9.5%) have a family history of retinoblastoma. The most common signs were leukocoria (80%) and strabismus (28%) followed by proptosis. Orbital cellulitis and hyphemia are rare presenting findings in retinoblastoma. 26 children (13%) have extra ocular retinoblastoma. Leukocoria and proptosis were associated to worse prognosis. The genetic analysis revealed the existence of several healthy carriers of the mutant allele in the proximal part of the pedigree, and this number could be higher if the analysis was broader and involved more distant relatives, thus illustrating low penetrance.

## Conclusions

The ability to recognize retinoblastoma's symptoms can lead to early diagnosis and good prognosis. The appearance of an attenuated phenotype could be linked to compensation for the loss of RB1 by overexpression of the wild-type allele under parental control or to the existence of genetic modifying factors independent of the RB1 locus.

## S119

### Tunisian experience with antimitotic agents in ocular surface squamous neoplasia



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### **Purpose**

To analyze and discuss the efficiency of antimitotics in the management of squamous neoplasia of the ocular surface in tunisian patients

### **Methods**

We followed 61 patients treated by topical chemotherapy ( mitomycin c with two concentrations: 0.02% or 0.04%) or surgical excision

### **Results**

40 patients received topical chemotherapy. Recurrence was observed in 9 cases after in average time of 9.5 months.

### **Conclusions**

surgical excision was more effective than topical chemotherapy alone in the treatment of ocular surface squamous cell carcinoma. Topical mitomycin can then be indicated in the treatment of small intraepithelial neoplasia or as an adjuvant treatment in cases of incomplete surgical excision.

## **S118**

### **Tunisian uveal melanoma's epidemiological study**

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### **Purpose**

we aimed to evaluate epidemiological factors with possible influence on uveal melanoma's prognosis.

### **Methods**

We followed 80 patients with uveal melanoma . For each patient, we specified the age, sex, laterality,geographical origin, lifestyle, phenotype,habits and profession.

### **Results**

The average age was 58.5 years with extremes of 12 to 80 years. The sex ratio was 1.3. The iris was clear in 17.5% of the cases, eye's melanocytosis was present in 6.25% of cases, 2.5% of patients had choroidal nevus. UV exposure was noted in 18% of cases. Factors significantly associated with poor prognosis were: age greater than 60 years ( $p = 0.001$ ), male sex ( $p = 0.001$ ), ocular melanocytosis ( $p = 0.015$ ) and diagnostic delay ( $p = 0.001$ ).

### **Conclusions**

In tunisian people, ocular and oculopalpebral melanocytosis is the most common predisposing factor for uveal melanomas.

## **T114**

### **Aciclovir-resistant HSV1 keratitis : a clinical and virological study**

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## **Purpose**

Aciclovir resistant (ACVR) herpes keratitis (HK) represents an emerging challenge. Our studies aims at describing the virological and clinical profiles of patients with HK caused by ACVR strains of HSV1.

## **Methods**

In this multicentric retrospective study, we included patients with recurrent HK caused by ACVR HSV1 isolates. HSV1 resistance to ACV was evidenced using a genotypic method with the sequencing of genes encoding thymidine kinase (TK) and DNA polymerase (DNA pol). Collected data included number of episodes before and after the diagnosis of resistance, immune status of patients, ophtalmological features and HSV1 genotypes.

## **Results**

Eighteen patients (13 male, 5 females) aged 67±10years, were included. Duration of disease was 29.8±20.4 years with a number of recurrences > 10 in 15 patients (83%). Genotypic testing for resistance was elicited by recurrences despite well conducted antiviral prophylaxis in 13 cases (72%) and by resistance to curative treatment in 5 cases (28%). Resistance to ACV was caused by mutations in the TK gene in 15 cases (83%) and in the DNApol gene in 3 cases (17%). In immunocompetent patients (N=12, 67%), the number of recurrences preceding the diagnosis of resistance was significantly higher than in immunocompromised patients (16±3.5 versus 11±6 versus p=0.05). After the diagnosis of resistance, patients were followed 31.5±30 months and had 2.8±2.7 recurrences.

## **Conclusions**

ACVR HK must be suspected in case of recurrences despite antiviral prophylaxis and/or resistance to antiviral treatment. ACV resistance occurs in patients with a long duration of disease and multiple recurrences, and may appear more rapidly in immunocompromised patients. There is currently no available efficient antiviral prophylaxis for ACVR HSV1. New therapeutic strategies are warranted to face this emerging problem.

**1261**

### **Effect of topical medication on the ocular surface**

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## Summary

It is now widely admitted that long-term use of glaucoma medication may trigger or worsen ocular surface disease. Recent experimental and clinical research have further elucidated the respective role of both preservatives and active compounds and pathophysiologic mechanisms underlying these alterations that can be either of an allergic or a toxic nature. All components of the ocular surface may be affected, including the tear film, the conjunctival and corneal epithelia, the meibomian glands, and even the corneal innervation.

Most importantly, ocular surface toxicity and inflammation caused by long term glaucoma medications can be responsible for symptoms that may alter patient's quality of life, compliance to treatment and even the prognosis of further filtering surgery.

For all these reasons, ocular surface should be assessed in every glaucoma patient at diagnosis and during follow up and efforts should be made to reduce the impact of glaucoma medications on ocular surface. Available strategies include reduction of toxicity using preservative free eyedrops, selected fixed combinations or therapeutic alternatives such as laser treatments.

## S012

### Modeling of aniridia-related keratopathy by CRISPR/Cas9 genome editing of human limbal epithelial cells and rescue by recombinant PAX6 protein

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## Purpose

Heterozygous PAX6 gene mutations leading to haploinsufficiency are the main cause of congenital aniridia, a rare and progressive panocular disease characterized by reduced visual acuity. Up to 90% of patients suffer from aniridia-related keratopathy (ARK), caused by a combination of factors including limbal epithelial stem cell (LSC) deficiency, impaired healing response and abnormal differentiation of the corneal epithelium. It usually begins in the first decade of life, resulting in recurrent corneal erosions, sub-epithelial fibrosis and corneal opacification. Unfortunately, there are currently no efficient treatments available for these patients and no *in vitro* model for this pathology.

## Methods

We used CRISPR/Cas9 technology to introduce into the PAX6 gene of LSCs a heterozygous nonsense mutation found in ARK patients. Nine clones carrying a p.E109X mutation on one allele were obtained with no off-target mutations.

## Results

Compared to the parental LSCs, heterozygous mutant LSCs displayed reduced expression of PAX6 and marked slow-down of cell proliferation, migration and detachment. Moreover, addition to the culture medium of recombinant PAX6 protein fused to a cell penetrating peptide was able to activate the endogenous PAX6 gene and to rescue phenotypic defects of mutant LSCs, suggesting that administration of such recombinant PAX6 protein could be a promising therapeutic approach for aniridia-related keratopathy.

## Conclusions

More generally, our results demonstrate that introduction of disease mutations into LSCs by CRISPR/Cas9 genome editing allows the creation of relevant cellular models of ocular disease that should greatly facilitate screening of novel therapeutic approaches.

**3364**

**Modeling of aniridia-related keratopathy by CRISPR/Cas9 of human limbal epithelial cells and rescue by recombinant PAX6 protein**

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**Summary**

Haploinsufficiency of PAX6 in humans is the main cause of congenital aniridia, a rare eye disease characterized by iris hypoplasia and reduced visual acuity. Aniridia-related keratopathy (ARK), caused by a combination of factors including limbal stem-cell deficiency, impaired healing response, abnormal differentiation affects up to 95% of patients. Unfortunately, current treatment options for aniridia patients are currently limited. There is no *in vitro* cellular model of AKT needed for therapeutic tools screening and validation. We used genome editing to introduce a nonsense mutation into one allele of the *PAX6* gene in TERT-limbal cells, which remain identical to primary limbal cells able to differentiate into corneal cells. Resulting mutated clones, expressing half of the amount of PAX6 protein and thus representative of haploinsufficiency, was further characterized. The mutated cells displayed reduced cell proliferation and cell migration but enhanced cell adhesion. Known PAX6 targets expression was also altered. Remarkably, addition of recombinant PAX6 protein was able to activate endogenous *PAX6* gene and rescue the phenotype. Our *in vitro* model will be powerful to identify drugs that could rescue the corneal defect.

**1862**

**Animal Case**

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**Summary**

Climbers exposed to high altitudes frequently present local retinal hemorrhages, that can remain symptomless if they don't affect the central part of the retina. In an initial set of experiments aimed at validating a mouse model of hypoxia-induced pulmonary arterial hypertension, we have similarly observed small, no longer active, zones of hemorrhage in mouse retinas after three weeks of exposure to 10% oxygen, mimicking an altitude of 6000 m. We are now exploring earlier phases of the exposure to these low oxygen conditions, combining fundus imaging, angiography and optical coherence tomography, as well as immunohistochemistry.

We will also present recent retinal phenotypes picked up at the Institut Clinique de la Souris, as part of the International Mouse Phenotyping Consortium screen.

**2352**

**Clinical and research applications of modelling ocular biometry**

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## Summary

Although the basic ocular structure relatively simple, only consisting of two refractive elements, a pupil and a screen, there are many shape and alignment imperfections that complicate accurate calculations. This lead to the introduction of simplified schematic eyes, which come in many varieties, e.g. with a gradient index crystalline lens, the possibility of accommodation, or supporting wide-angle analysis. Moreover further simplifications were possible by removing the posterior cornea (simplified eye models) and the crystalline lens (reduced eye models). However, such 'fixed' models suffer from the disadvantage that they are generic and do not incorporate the wide variety in ocular biometry of the general population. As this would reduce applicability various solutions were proposed, such as myopic models, *customized model*, or statistical eye models.

This work discusses all these models and highlights how they may be useful research tools for those without access to real data.

**3425**

## Factors influencing retinal straylight

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## Summary

Nearly everyone has experienced being blinded by the Sun when it is close to the horizon, or by the headlights of an oncoming car. This everyday visual problem is called disability glare and is caused by light scattering of the optical structures of the eye itself. Ideally, light entering the eye should pass undisturbed through all the ocular structures to form a perfect image on the retina. The ocular media are not optically ideal, however, containing a large number of scattering particles instead causing a fraction of the light to scatter and form a veil of light over the retinal image. This straylight leads to a loss in contrast of the retinal image, haloes around bright lights, difficulties recognizing people against the light, difficulties adjusting when going from a light to a dark room, etc., all amounting to a reduced quality of vision. In small amounts straylight is mostly annoying, but large amounts of it can be disabling or even dangerous. Straylight is known to increase with age, eye colour, skin pigmentation and cataract, but is only weakly associated with visual acuity.

This work highlights the factors known to affect straylight and the possible remedies to reduce straylight discomfort.

**F002**

## Transconjunctival bleb sutures for post-trabeculectomy hypotony

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## Purpose

Hypotony due to an over filtering bleb is a recognised complication of trabeculectomy with Mitomycin C and has been reported to occur in up to 18% of patients. Transconjunctival 10.0 Nylon sutures can be applied to the bleb under local anaesthetic and offer a fast and minimally invasive way of managing hypotony due to bleb overfiltration. We describe the procedure and report on a consecutive case series of 11 patients treated with the technique at the Queen Alexandra Hospital Eye Unit, Portsmouth, England.

## Methods

We identified patients who received transconjunctival sutures between August 2016 and December 2017 by searching electronic and written theatre records. Primary outcomes were mean BCVA and IOP change. Secondary outcomes included resolution of hypotony, incidence of complications and requirement for additional procedures. Data were collected from the last pre-operative visit; then at 1 week, 1 month and 6 months after the suture placement.

## Results

The mean number of sutures used was 2.6 and the average time between trabeculectomy and suture placement was 15 months. Mean IOP improved from 3 mmHg to 9.6 mmHg after 6 months. Signs of ocular hypotony resolved in all patients. Mean visual acuity improved from 0.43 logMAR pre-operatively to 0.27 logMAR at 6 months. Two patients required further flap sutures, one patient with uveitic glaucoma had a persistently low IOP despite flap sutures. There were no cases of endophthalmitis or blebitis.

## Conclusions

Our results compare favourably with those reported by Eha et al. (2013) and show that transconjunctival flap sutures are safe and can be effective in treating hypotony due to overfiltration following trabeculectomy.

## T081

### Localized versus 360-degree laser photocoagulation with pars plana vitrectomy in the management of primary rhegmatogenous retinal detachment

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## Purpose

To compare the efficacy of intraoperative localized and 360-degree laser photocoagulation in 23-gauge pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD).

## Methods

This retrospective, comparative, consecutive, interventional study included 155 eyes of 155 patients who underwent primary repair of RRD utilizing 23-gauge PPV at Seoul National University Bundang Hospital from Jan 2012 through Dec.2015. Medical records were retrospectively reviewed, and the corresponding demographic data, preoperative ophthalmic features, surgical management, and postoperative course were recorded. Main outcome measures included single surgery anatomical success, pre- and post-operative visual acuity, and complications.

## Results

Eighty-three patients (group A) received localized laser photocoagulation in PPV, while the remaining 72 patients (group B) underwent 360-degree laser photocoagulation in PPV by two skilled-surgeons. No significant difference was identified in baseline characteristics. The single surgery anatomical success rate was 96.4 % in group A, and 95.8 % in group B, showing no significant difference ( $p=1.00$ ). Single surgery anatomical failure was caused by re-detachment due to break in 2 eyes in each group (no new break 1 eye, new break 1 eye in group A, 2 eyes with no new break in group B), and proliferative vitreoretinopathy in 1 eyes in each group. Other complications were epiretinal membrane in 7 eyes (3 in group A, 4 in group B), and macular hole in 1 eye in group B. There were no differences in pre- and postoperative best-corrected visual acuity(BCVA) as well as BCVA improvement ( $p=0.144$ ,  $p=0.866$  and  $p=0.263$ , respectively).

## Conclusions

Localized laser photocoagulation showed no difference in anatomic and visual outcome in RRD patients, when compared with 360-degree laser photocoagulation in PPV.

## S062

### Effect of intracorneal ring segment implantation on tear film properties in patients with keratoconus

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#### Purpose

Implantation of intracorneal ring segments (ICRS) is an effective and safe therapeutic option for visual improvement in patients with keratoconus. The aim of this study was to investigate the effect of ICRS implantation on tear film properties in patients with keratoconus.

#### Methods

This was a prospective interventional cohort study including 20 patients with stable keratoconus who underwent unilateral Keraring implantation using the Z6 femtosecond laser (Ziemer Ophthalmic Systems, Port, Switzerland). All patients had keratoconus stage 2 or 3 according to the Amsler-Krumeich classification. A complete ophthalmic examination was performed preoperatively and 4 weeks postoperatively, including tear osmolarity (nm/L) with the aid of TearLab device (TearLab Corp, CA, USA), Schirmer test 1 and 2 (mm), Tear Break-up Time (seconds), keratometry (K) readings (in diopters, D), as well as thinnest corneal pachymetry (in microns,  $\mu\text{m}$ ) with the aid of Scheimpflug camera (Pentacam, Oculus Optikgeräte, Wetzlar, Germany). Statistical analysis was performed with MedCalc software programme (MedCalc Software, Ostend, Belgium) using T-test. P values below 0.05 were considered statistically significant.

#### Results

Preoperative mean values of tear osmolarity (304 nm/L), Schirmer test 1 (12.9 mm) & 2 (11.8 mm) and tear break-up time (9.9 seconds) did not change significantly 4 weeks after ICRS implantation (300 nm/L, 12.5 mm, 12 mm and 9.2 seconds, respectively) (all  $p > 0.05$ ). Kmax and Kmean improved significantly postoperatively ( $p = 0.01$  and  $p = 0.02$ , respectively). Thinnest corneal pachymetry did not differ significantly post-ICRS implantation ( $p = 0.1$ ). No complications occurred postoperatively.

#### Conclusions

Our data show that ICRS implantation does not seem to have any negative impact on tear film properties in patients with keratoconus.

## F037

### Bilateral activation of retinal microglia: quantitative analysis of the area the retina occupied by IBA-1 + cells in the nerve fiber layer-ganglion cell layer at different time points after laser-induced ocular hypertension in mice

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#### Purpose

To quantify the area of retina occupied by Iba-1 + cells (Iba-1 RA) in the nerve fiber layer- ganglion cell layer (NFL-GCL) at different time points (1, 3, 5, 8 and 15 days) after unilateral laser-induced ocular hypertension (ULOHT) in OHT-eyes and their contralateral eyes.

### Methods

Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=30, six mice by each time-point analyzed). Retinal whole-mounts were immunolabeled with anti Iba-1 to quantify the Iba-1 RA in the NFL-GCL.

### Results

With respect to naïve-eyes: i) there was a significant increase in the Iba-1 RA both in OHT-eyes (1d, 3d, 5d, 8d and 15d after ULOHT) and in contralateral-eyes (1d, 5d, 8d and 15d after ULOHT), being higher in OHT eyes. The comparison of Iba-1 RA between the different time-points analyzed after ULOHT showed: i) in OHT-eyes there was a progressive increase of Iba-1 RA from 1d to 5d, being statistically significant. From this time-point, the Iba-1 RA decrease significantly until to 15d. ii) In contralateral-eyes there was a significant Iba-1 RA increase at 1d, and then, Iba-1 RA significantly decreased from 5d to 15d.

### Conclusions

ULOHT produces a significant early increase of Iba-1 RA both in OHT-eyes and in contralateral untreated eyes in the NFL-GCL. This microglial activation could be associated with the damaged of the ganglion cells located in this layer. Whether this activation is harmful or beneficial for the retinal ganglion cells needs to be elucidated.

2653

### Population of Pituitary Adenylate Cyclase-Activating Polypeptide and Melanopsin-Expressing Retinal Ganglion Cells in the Albino Adult Rat Retina

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### Summary

**Purpose:** To quantify and characterize topographically the whole population of RGCs expressing Pituitary adenylate cyclase-Activating polypeptide (PACAP) and Melanopsin (ML) in naïve adult albino Sprague Dawley (SD) rat retinas.

**Methods:** Adult female SD retinas were dissected as whole mounts and doubly labelled with antibodies against PACAP and ML. Retinas were examined and photographed under an epifluorescence microscope. The whole population and spatial distribution were quantified and analyzed automatically.

**Results:** The total number of ML<sup>+</sup>RGCs and PACAP<sup>+</sup>RGCs in albino rat retinas was  $2,326 \pm 291$  and  $1,415 \pm 186$  (mean  $\pm$ SD; n=4) respectively. Approximately 30 % and 50 % of the ML<sup>+</sup>RGCs and PACAP<sup>+</sup>RGCs population respectively, co-expressed both proteins. Both populations were distributed as an arciform-like area in the superior retina with the highest densities in the temporal quadrant, where the both protein co-expression level was greater.

**Conclusions:** SD Albino rat showed an arciform area in the superior retina, above the visual streak, that contains the highest ML<sup>+</sup>RGCs and PACAP<sup>+</sup>RGC densities. A subset of these populations co-expressed both proteins.

T090

### Changes in the retina in the evolution of Alzheimer's disease



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## **Purpose**

Alzheimer's Disease (AD) is characterized for the  $\beta$ -amyloid and tau accumulation in central nervous system, even in visual brain areas and in the retina. The aim of this study it was to investigate the use of optical coherence tomography (OCT) as a tool for the AD stage diagnosis and follow-up.

## **Methods**

Eighty-seven patients were included in the study who followed the inclusion criteria. 32 mild AD patients, 20 moderate AD and 35 age-matched controls. All subjects underwent macular and peripapillary OCT.

## **Results**

Foveal OCT thickness in mild AD patients presents a significant thinning in the fovea and in the inner macular ring (with the exception on nasal area) with respect to both the control ( $p < 0.01$ ) and the moderate AD patients ( $p < 0.05$ ). On the other hand, thickness in the fovea and inner macular ring in moderate AD showed a significant increase in comparison with mild AD ( $p < 0.05$ ) but no differences were found with respect to control group ( $p > 0.05$ ) being the mean values in moderate AD and control very much alike. In outer macular ring, there was a significant thickening in the superior, nasal and temporal area in moderate AD patients with respect to the mild AD ( $p < 0.05$ ). The peripapillary thickness in moderate AD patients was significantly thinner in the inferior quadrant with respect to mild AD and control group ( $p < 0.05$ ) but the reduction had no significance between mild AD and control group.

## **Conclusions**

In the macula, in comparison with control, mild AD had a thinning but when the disease progresses we found a significantly thickening in the retina that can be due active gliosis processes. On the other hand, changes in the peripapillary region are only evident when the disease progressed and the cognitive decline is obvious.

**1742**

## **The role of microglia in glaucoma**

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## **Summary**

Microglial cells respond to stress by adopting an activated state. This activation can be triggered in response to autoimmune mechanisms or neuronal injury and ischemia, all associated with progressive neurodegeneration as occurs in glaucoma. These are modulated by their relationship to the nerve cells of their environment and by immune-cell infiltration after injury. The morphology of activated microglia includes enlargement of the soma, retraction and shortening of processes, and increased expression of myeloid-cell markers. Reactive microglia cells can adopt different morphologies: hyper-ramified, stellate with thick processes, and rod-like microglia. In the state of high reactivity, cells acquire an amoeboid morphology. Activated microglia can adopt a variety of distinct functional phenotypes in response to injuries. These phenotypes are similar to the peripheral macrophages, and have been classified based on the expression of cell-surface markers, intracellular enzymes, and secreted

molecules in M1 and M2. In conclusion, microglial cells, may play an important role in retinal homeostasis. However, under inflammatory conditions, they may interact with the adaptive immune system, contributing to glaucoma.

**S096**

#### **Optic nerve remodeling event due to a retinal ganglion cell degeneration in patients with Parkinson disease**

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#### **Purpose**

The visual dysfunctions that Parkinson disease (PD) patients suffer are some of the first signs of the pathology. The aim of this study was to evaluate if there are histological changes in the retina and optic nerve in PD.

#### **Methods**

Fixed control and PD human eyes and optic nerves were used. Optic nerve cryosections were stained with hematoxylin and a morphometric analysis was performed in order to analyze its size, the bundles number, area and distribution. Immunohistochemistry and confocal microscopy were employed to assess ganglion cell density in whole-mount retinas and morphology and distribution of Iba1+ cells in optic nerve cryosections and retinal whole-mounts.

#### **Results**

The total nerve area and the number of bundles are increased in PD optic nerves when compared to controls. Iba1+ cell density is maintained but there is a change in their morphology and their location. In PD, Iba1+ cells present an amoeboid morphology instead of their typical ramified morphology. Besides, in control optic nerves they are only disposed around the bundles, but in PD there is an infiltration and they occupy all the bundle area. Finally, there is a decrease of the number of ganglion cells in Parkinson retinas compared with controls, what can trigger the optic nerve transformations.

#### **Conclusions**

Here we describe a ganglion cell degeneration and an optic nerve remodeling event. This correlates with the ganglion cell layer thinning described in OCT and could explain the visual impairment reported in PD patients.

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**2723**

#### **Assessment of memantine-loaded PEGylated biodegradable nanoparticles in a rodent glaucoma model**

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## Summary

Glutamate-induced excitotoxicity is implicated in glaucoma and NMDA receptor antagonism has been advocated as a potential treatment strategy. Memantine (MEM), an NMDA antagonist approved for the treatment of Alzheimer's disease, could also serve as glaucoma treatment. To increase MEM availability after topical administration, a novel MEM loaded PLGA-PEG nanoparticle (MEM-NP) formulation was optimised using a Quality by Design (QBD) approach and drug release characteristics investigated. Finally, the pharmacokinetics efficacy was then investigated using a well-established rodent glaucoma model.

MEM-NP were characterized by several techniques confirming their suitable size (< 200nm), round shape and stability at different temperatures. Drug release was studied *in vitro* and *ex vivo* demonstrating that incorporation into a nanoparticle enhanced MEM delivery. In addition, MEM-NP were not cytotoxic in human retinoblastoma cells. These systems confirmed to be not irritant *in vivo* and MEM-NP eye drops applied daily for three weeks to a rodent model of ocular hypertension were found to significantly reduce RGC loss.

These results confirm that topical MEM-NP are safe, well-tolerated and neuroprotective in an experimental glaucoma model.

## F069

**The ability of Spectral domain Optical coherence tomography to detect retinal changes in patients with essential tremor: is neurodegeneration an underlying cause?**

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## Purpose

To evaluate retinal changes in patients with essential tremor (ET) using Spectral domain Optic coherence tomography (SD-OCT).

## Methods

twenty-eight eyes of 28 patients with ET and 58 eyes of 58 healthy controls were included in the study. All subjects underwent evaluation of full macular thickness and peripapillary retinal nerve fiber layer thickness (pRNFL) with Spectralis SD-OCT. The pRNFL was assessed with 2 different protocols, RNFL-glaucoma, and RNFL-N Axonal Analytics for neurodegenerative diseases.

## Results

No differences were observed in macular thickness between ET patients and healthy controls. Patients with ET presented reduced pRNFL thickness in the temporal quadrant as measured with the glaucoma protocol (p=0.043) and the Axonal Analytics protocol (p=0.021) compared to healthy subjects.

## Conclusions

Patients with ET present reduced RNFL thickness in the temporal quadrant compared to healthy subjects. These results might reflect neurodegeneration as an underlying cause of this disease, which is detectable with SD-OCT.

## F070

### Evaluation of visual function and retinal changes caused by Multiple sclerosis after a 10-year follow-up

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#### Purpose

To evaluate progression of visual function and retinal changes during 10-year follow-up in patients with multiple sclerosis (MS) and healthy controls.

#### Methods

Fifty eyes of 50 patients with MS and 50 eyes of 50 healthy controls were selected for the study. All subjects underwent a complete ophthalmologic examination that included visual acuity (VA), refractive defects, color vision (using the Ishihara test), perimetry (Humphrey perimeter), and Spectralis optical coherence tomography (SD-OCT). Quality of life was assessed using the MSQOL-54 scale. Patients and controls were re-evaluated after 10 years. The correlation between structural changes and quality of life was analyzed.

#### Results

After 10 years of follow-up, all subjects presented similar results in the functional tests (VA, Ishihara test and perimetry). Patients with MS presented greater thinning of the RNFL in all retinal areas compared to controls, excluding the upper nasal field. This loss was especially remarkable at the lower temporal level, with a decrease in thickness of  $-1,796 \mu\text{m}/\text{year}$  in MS patients compared to  $-0.547 \mu\text{m}/\text{year}$  in healthy controls ( $p < 0.001$ ). There was a significant correlation between quality of life and the RNFL reduction ( $p < 0.05$ ).

#### Conclusions

MS causes progressive RNFL thinning that can be quantified using OCT and, particularly, Spectralis OCT and its NSITE Axonal protocol. This RNFL thickness decrease is greater than that caused physiologically by aging, being especially remarkable in the temporal sectors. Moreover, this reduction is related to patients' quality of life loss.

## S071

### The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): Assessment of corneal biomechanics

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#### Purpose

Our university lab BiiGC patented 2 versions of an ophthalmic bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentation, called OBSERV, supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to compare the corneal biomechanics of whole pig eyeballs versus isolated corneas mounted in the BR.

## Methods

By restoring intra ocular pressure (IOP) and medium renewal, the BR maintained corneal viability over a prolonged period. Nevertheless the compression of the scleral ring in the BR could modify corneal biomechanics. Whole fresh eyeballs were perfused intravitreally by a needle implanted in the optic nerve. The same corneas were then excised and placed in the BR. In both cases, IOP was set to 15, 20, 25, 35 and 45mmHg. For each IOP, measurements were done with the ORA (Reichert): Corneal Hysteresis (CH), corneal compensated IOP (ccIOP) and goldman IOP (gIOP); and with the Corvis (Oculus): peak distance, deformation amplitude, curvature radius and highest concavity.

## Results

For ORA (n=5): whatever the IOP, CH, ccIOP and gIOP did not differ between groups except for CH and ccIOP at 35mmHg. Only gIOP and ccIOP increased with IOP in both groups. For CORVIS (n=8): whatever the IOP, peak distance and highest concavity did not differ between groups. Deformation amplitude was significantly lower and curvature radius was higher in the BR. In both groups, when IOP increased, curvature radii tended to increase and peak distance, amplitude of deformation and maximum concavity tended to decrease, suggesting an increase in corneal stiffness with IOP.

## Conclusions

The OBSERV platform is an original efficient tool to study corneal biomechanics. It complements or replaces animal experimentation for academic or industrial research.

## S034

### The impact of long term glaucoma medications on structure and function of meibomian glands

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## Purpose

Based on clinical and IVCN studies, it has been shown that meibomian gland disease could be included in the spectrum of glaucoma medications-induced OSDs. We combined clinical assessment of MGD and infrared imaging of meibomian glands and the tear film to further assess the impact of long term glaucoma medications on both structure and function of meibomian glands

## Methods

Long term treated glaucoma patients and age-matched controls were included in this prospective cross-sectional study. Clinical ocular surface evaluation included ocular surface fluorescein staining, tear break-up time, Schirmer I test, clinical meibomian gland disease score. Ocular surface related quality of life was assessed using OSDI and OSD QoL questionnaires. Lipid layer thickness was measured using interferometry. Meibomian glands structure was studied using non contact infrared meibography and scored by 2 masked readers for dropout, shortening and distortion. Results were the mean of superior and inferior tarsal conjunctival.

## Results

We included 18 eyes of 18 long term treated glaucoma patients and 14 eyes of 14 controls. Patients received a mean of  $1.8 \pm 0.7$  eyedrops with a mean treatment duration of 35 months. Ocular surface staining and clinical MGD score were significantly higher in patients than in controls. Structural study of MG using meibography revealed that shortening and atrophy of meibomian gland duct was significantly higher in patients as compared to controls. TBUT tended to be significantly shorter in patients ( $p=0.07$ )

## Conclusions

These results suggest that glaucoma treatments induce morphological changes of MG including drop out and and shortening of MG. Integrated / automated analysis of infrared meibography pictures may provide more practical routine analysis of MG structural alterations.

**3122**

### **Wide Field OCT angiography in glaucoma**

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#### **Summary**

Optical coherence tomography angiography (OCTA) is a relatively recent functional extension of OCT. Based on correlation analysis of adjacent B-scans it is possible to visualize the ocular vasculature in a non-invasive and label-free manner. With currently available spectrometer-based OCT technology it is possible to visualize fields of 3x3 or 6x6 mm. Using these fields it is possible to either scan the macular area or the optic nerve area. For both areas it has been shown that glaucoma is associated with a progressive loss of vessel density. With fast OCT engines it has recently become possible to scan even wider fields. Nowadays 9x9, 12x12 or 15x9 mm areas can be imaged. This makes it possible to cover the macular and optic disc area in one scan. The present talk will discuss the potential of this wide-field imaging in glaucoma and will also look into the opportunities to obtain localized vascular defects.

**T097**

### **Effect of flicker stimulation on retinal and optic nerve head blood flow as measured by Laser Speckle Flowgraphy**

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#### **Purpose**

Flicker-induced hyperemia is a physiological key principle of ocular blood flow regulation and might have the potential to serve as a biomarker for ocular diseases. Since the measurement of blood flow is still challenging, the use of this approach is currently limited. The present study set out to evaluate whether Laser speckle flowgraphy (LSFG), a commercially available technique for measuring blood flow, is capable to assess neuro-vascular coupling in the retinal and optic nerve head (ONH) circulation.

#### **Methods**

Twenty healthy male and female subjects participated in this cross sectional study. Before and during stimulation with flickering light, blood flow in the ONH and in retinal vessels was measured using LSFG. For the ONH, mean blur rate (MBR), a measure of relative blood flow velocity, was obtained. For retinal arteries and veins, relative flow volume (RFV), a measure of relative blood flow of the respective retinal vessels, was used.

#### **Results**

Stimulation with flicker light induced a significant increase in optic nerve head MBR by  $+17.5\pm6.6\%$  ( $p<0.01$ ). In retinal arteries, stimulation with diffuse luminance led to an increase of  $+23.8\pm10.0\%$  ( $p<0.05$ ) in total RFV and in retinal veins, an increase of  $+23.1\pm11.0\%$  ( $p<0.05$ ) in total RFV was observed.

#### **Conclusions**

As expected, stimulation with flickering light induced a pronounced increase in retinal and ONH blood flow. These results indicate that LSFG is an appropriate method for the quantification of retinal and ONH blood flow during visual stimulation and may be applied as a non-invasive, easy to use tool to assess neuro-vascular coupling in humans in the future.

Support from the Austrian Science Fund FWF KLI 529 is gratefully acknowledged.

**3543**

#### **Robustness towards position uncertainties – the forgotten factor**

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#### **Summary**

Intraocular lenses (IOLs) are subject to misalignment inside the pseudophakic eye. Especially with IOL designs other than spherical or aberration-free lenses, these position uncertainties may deteriorate the image performance after cataract surgery and reduce or eliminate the benefit of individualized aberration correcting IOL designs. This talk focuses on the effect of IOL-misalignment on the optical performance of individualized aberration correcting IOL designs calculated with custom simulation-model-eyes. Possible ways to improve robustness against misalignment of the IOL will be discussed.

**1762**

#### **Pharmacogenetic influences on nutritional supplementation in prevention of AMD**

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#### **Summary**

The Age-Related Eye Disease Study (AREDS) reported that treatment with antioxidants plus zinc in patients with intermediate or advanced age-related macular degeneration (AMD) was associated with a 25% reduction in disease progression at 5 years. Since that time, AREDS nutritional supplementation has become standard treatment throughout the world.

More recently, several investigators have performed genetic association studies on subgroups of participants from the original AREDS. The topic has become controversial, as some investigators have reported no significant genotype-phenotype associations, some investigators have reported significant genotype-phenotype associations but did not recommend any changes in standard clinical practice, and some investigators have reported significant genotype-phenotype associations and recommended genotype-directed nutritional supplementation.

This presentation will review major findings of these genetic association studies and provide a framework that will assist practicing clinicians (who are not experts in genetics, statistics, or clinical trial design) to care for their AMD patients.

**2153**

#### **Myopic CNV – current diagnosis and management**

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## Summary

Myopic choroidal neovascularization (CNV) is an important cause of permanent visual loss, especially in younger patients. Due to the worldwide increase in myopia, the incidence of this diagnosis is expected to increase. This presentation will review:

- \* the current diagnosis of myopic CNV, including fluorescein angiography, spectral domain optical coherence tomography (OCT), and the emerging role of OCT angiography;
- \* the differential diagnosis of myopic CNV, including other entities causing CNV (age-related macular degeneration, angioid streaks, choroidal rupture, histoplasmosis, other inflammatory diseases) and other macular diseases affecting high myopes (non-neovascular changes in pathologic myopia, myopic foveal schisis, macular hole);
- \* the current therapy of myopic CNV, including observation, anti-vascular endothelial growth factor (VEGF) agents, and less commonly used therapies (photodynamic therapy, thermal photocoagulation).

**2924**

## Famous monocular warriors

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## Summary

Many of history's most successful military commanders have been monocular. This presentation will review some of the more prominent and colorful individuals. Their lives are intriguing and may prove inspirational to ophthalmologists and our monocular patients. These military leaders include:

- \* Philip II (382-336 BC), King of Macedon and father of Alexander the Great, who lost one eye to battlefield trauma;
- \* Hannibal Barca (247-ca.183 BC), leader of the Carthaginian invasion of Rome during the Second Punic War, during which one eye was lost to "conjunctivitis";
- \* Federico da Montefeltro (1422-1482), the Duke of Urbino, who is the subject of a famous painting by Piero della Francesca (1416-1492), and who lost one eye to trauma sustained during a joust;
- \* Date Masamune (1567-1636), Japanese daimyo (feudal lord), who lost one eye to smallpox in childhood;
- \* Horatio Nelson (1758-1805), British naval commander, who is generally portrayed as monocular but some historical evidence disputes this theory. He is commonly said to have ignored a signal flag ordering him to discontinue an attack by holding up his telescope to his "blind" eye.

**T117**

## Interleukin-33 regulates mitochondrial function in the retinal pigment epithelium maintaining immune homeostasis

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### Purpose

Retinal pigment epithelium (RPE) is essential in maintaining homeostasis, loss of RPE cells leads to progression of retinal degeneration. While source of energy metabolism is critical for the viability, differentiation and normal physiology of RPE cells, underlying regulation remains elusive. The aim of this study was to investigate how inflammatory “stress” one of the purported drivers of, for example, Age-related Macular Degeneration (AMD), may influence cellular bioenergetics. Whilst additionally investigating the role of a cytokine interleukin-33 (IL-33) in the maintenance of metabolic homeostasis and mitochondrial dynamics.

### Methods

RPE cells from both human (ARPE-19) and murine (primary RPE) were stimulated with TLR agonists and exogenous IL-33. The effect of endogenous IL-33 was assessed both *in vitro* using both siRNA and CRISPRcas9, and *ex vivo* from *Il-33*<sup>-/-</sup> mice. Metabolism was assessed using Seahorse extracellular flux, C13 glucose tracing and immunoblotting/RT-PCR of involved metabolic components.

### Results

Alternate bioenergetic profiles are licensed by the activity of AMP-activated kinase (AMPK), which supports oxidative metabolism within the mitochondria. Stimulation of RPE with IL-33 leads to increased mitochondrial metabolism. This effect was replicated with induced overexpression of the *Il-33* gene. IL-33<sup>-/-</sup> RPE preferentially utilise aerobic glycolysis and exhibit both structural and functional changes to mitochondria.

### Conclusions

These data pinpoint a “plasticity” in RPE metabolism during innate immune activation that likely governs cellular homeostasis. We have identified IL-33 as a critical factor for optimum cellular bioenergetics, with implications for retinal degeneration such as AMD, where the strain on mitochondrial function with age may subvert the ability of the RPE to respond to the metabolic demands of inflammation.

2332

### “Herpetic keratitis” – a chameleon

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### Summary

In Europe, herpes simplex virus type I (HSV) is a common cause of keratitis. The disease may be well treated if the ophthalmologist is aware of the various types of clinical expressions of this typical unilateral chameleon, and treatment is adjusted accordingly. Types of expression include 1. epithelial keratitis (dendritica/geographica), 2. stromal keratitis (necrotizing “ulcer” vs. non-necrotizing = „interstitial keratitis“), 3. endotheliitis (= „disciform keratitis“), 4. so-called „metaherpetic keratitis“ (= neurotrophic keratopathy), 5. (vascularized) corneal scars. In the acute phase, concomitant ocular hypertension should be treated predominantly without surgery (no prostaglandin analogs!). After keratoplasty and in case of severe recurrences of herpetic keratitis, systemic acyclovir application (2x400mg/day) for at least one year is indispensable!

2732

### Laser systems in corneal surgery

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### **Summary**

Excimer lasers / femtosecond lasers were investigated for corneal surgery for more than 30 / 15 years.

Nonmechanical excimer laser trephination for penetrating keratoplasty has been applied successfully in more than 4000 patients since 1989. It results in less astigmatism, higher topographic regularity and better visual performance. In addition, AS-OCT-guided non-contact excimer laser deep anterior lamellar keratoplasty (DALK) may avoid the disadvantages of conventional DALK in case of conversion for young keratoconus patients.

Femtosecond laser application is always performed with a mechanical coupling and induces deformation of the cornea due to suction. Therefore, results of femtosecond laser supported keratoplasty results in more decentration, donor-host disparity and higher amount of astigmatism and topographic irregularity – especially in advanced keratoconus. Nevertheless, it is considered state-of-the-art for LASIK flaps and indispensable for intrastromal ring segments in keratoconus.

Recently, the picosecond infrared laser (PIRL) a new promising technology for applanation-free corneal trephination has been introduced. In the future a “non-contact” femtosecond laser system for corneal trephination might be considered.

**2935**

### **Excimerlaser-guided deep anterior lamellar keratoplasty (DALK) or penetrating keratoplasty (PKP) in advanced keratoconus**

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### **Summary**

In case of contact lens intolerance and/or central corneal scars, corneal transplantation is indicated for advanced keratoconus. This may be performed as DALK (Deep Anterior Lamellar Keratoplasty) or as penetrating keratoplasty (PKP). Up to now, DALK has not been standardized technically, but it can result in a good visual acuity using the Big-Bubble technique if Descemet's membrane is bared intraoperatively. In addition, the almost healthy endothelium can be preserved and endothelial immune reactions are prevented in keratoconus. In order to avoid high and/or irregular astigmatism after suture removal, excimerlaser-guided trephination should be used for DALK or PKP which ensures symmetrical, tension-free fitting of a circular donor disc in a circular recipient bed with congruent and easily waterproof-adapting incision edges. In 10% to 20% a „conversion“ to PKP is required if perforation of Descemet's membrane occurs during intended DALK. In case of conversion to PKP, excimerlaser-guided DALK prevents disadvantages for the typically young keratoconus patient. Superiority of femtosecond laser assisted PKP or DALK could not be demonstrated over the past 10 years.

**3363**

### **Stem cell tracking, loss and recovery in the corneal epithelium**

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### **Summary**

Fundamental feature of SC that regenerate the corneal epithelium were under debate or unknown. For example, SC location, prevalence and self-renewal mechanisms were under debate or elusive. Consequently, the mechanisms that involve SC failure in pathology are not clear. We established multi-color "Confetti" lineage tracing system which proved that the murine limbus is the major site of bona fide SCs. Additionally, we found that K15-GFP transgene labeled the limbal SC/boundary compartment and were located at the margin site of corneal regeneration, as evident by lineage tracing. Surprisingly, however, surgical depletion of the limbal epithelium and K15-GFP+ SC pool was restored by corneal committed cells which underwent dedifferentiation into bona fide SCs. The recovered corneas were transparent for many months, displayed normal marker expression and appropriate dynamic of SC regeneration. By contrast, damage to the limbal stromal niche abolished K15-GFP recovery, and led typical limbal SC deficiency phenotype. Altogether, this study reconciles major inconsistencies in the field and suggests that the while limbus is the major site of SCs, the cornea has an extremely efficient mechanism of self-repair, even from exhaustive SC loss.

#### **F045**

##### **Resveratrol nanoparticles are neuroprotective in vitro suggesting a potential to cure glaucoma and Alzheimer's disease**

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##### **Purpose**

Resveratrol is a natural polyphenol found in red wine and dark chocolate with potential neuroprotective effects, which could treat glaucoma and Alzheimer's disease. However, its hydrophobicity results in a low bioavailability limiting its clinical use. To date, many groups have attempted to formulate resveratrol with limited success.

##### **Methods**

In this study, we describe the development of a new nanoparticle formulation of resveratrol that allows solubility of more than 10 mg/ml of resveratrol and is stable over 90 days when stored at room temperature. The characterisation of these nanoparticles was achieved using spectrophotometry and dynamic light scattering demonstrating no aggregation and a particle diameter lower than 22 nm.

##### **Results**

Resveratrol nanoparticles are well tolerated and protect R28 cells in vitro against cobalt chloride induced hypoxia with an IC<sub>50</sub> (±SEM) of 938.5±127.0 µM versus 284.4 ± 35.6 µM for control group (p<0.001), glutamate induced excitotoxicity with an IC<sub>50</sub> (±SEM) of 29.32±3.00 mM versus 5.94±1.99 mM for control group (p<0.0001) and DL-homocysteine induced toxicity with an IC<sub>50</sub> (±SEM) of 3.10±0.36 mM versus 2.05±0.06 mM for control group (p<0.05) by increasing significantly their viability in a dose-dependent manner.

##### **Conclusions**

These results show that a newly formulated resveratrol nanoparticle formulation is neuroprotective against insults known to mimic cellular stress of glaucoma and Alzheimer's disease suggesting that it could be used to treat them. However, in vivo studies are needed to prove its efficacy further.

#### **3145**

##### **The role of chemotherapy in malignant ocular medulloepithelioma**

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### **Purpose**

Ocular medulloepithelioma (diktyoma) is a rare paediatric tumour of the non-pigmented ciliary epithelium, which can be teratoid and even malignant. Smaller tumours can be treated with brachytherapy but larger ones require enucleation or exenteration as they can invade locally and even metastasise. Adjuvant chemotherapy can be given in advanced cases, but the indications and regimens remain to be defined.

### **Methods**

This was a retrospective case series of advanced ocular medulloepithelioma treated with enucleation, including those needing adjuvant systemic vincristine, etoposide and carboplatin. Parameters evaluated included histopathology characteristics, chemotherapy regimen, recurrence, metastasis and survival.

### **Results**

Between March 2010 and June 2017, four male patients (mean age 31 months) underwent enucleation for suspected ocular medulloepithelioma. Adjuvant chemotherapy was commenced in 3 patients (75%) due to malignant features on histopathology including retinoblastoma-like areas (75%), numerous mitoses (50%) and invasion of the choroid (50%), cornea (50%) or sclera (25%). Two patients (50%) received 4 cycles of chemotherapy and one patient (25%) received 6 cycles. Two patients (50%) on chemotherapy suffered febrile neutropenia with positive blood cultures and recovered after appropriate treatment. With a mean follow-up time of 40 months (median 30 months, range 7-94 months), none of the patients have had recurrence, metastasis or death from the tumour.

### **Conclusions**

This series is unique in reporting the indications and management of advanced malignant ocular medulloepithelioma. The use of systemic vincristine, etoposide and carboplatin as an adjuvant for advanced tumours with malignant features is effective in preventing metastatic spread.

## **T040**

### **The probability of over-treatment using the treat-and-extend regimen for wet-AMD**

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### **Purpose**

To investigate the probability of over-treatment using the treat-and-extend regimen (TER) in patients who were treated with anti-VEGF therapy q month x 3 followed by PRN (PRN).

### **Methods**

We retrospectively reviewed wet-AMD patients who were treated with PRN and were followed up for  $\geq 2$  years. BCVA at baseline, and at 1 and 2 years, and the number of anti-VEGF injections was analyzed.

### **Results**

In total, 101 eyes of 101 patients were included, and the mean patient age was  $66.4 \pm 7.9$  years. The average total number of injections was  $4.68 \pm 2.35$ ; in the first year, the number of injections was  $3.69 \pm 1.36$ , while in the second year it was  $0.99 \pm 1.51$ . The BCVA (logMAR) at baseline, and at 1 and 2 years was  $0.78 \pm 0.58$ ,  $0.65 \pm 0.62$ , and

0.73±0.65, respectively. At the last follow-up, 28(27.7%) eyes with vision that worsened ≥3 lines were treated 5.86±2.27 times, which was statistically significantly higher than 4.23±2.23 times in 73(72.3%) eyes with vision that worsened <3 lines, and 4.06±2.31 times in 31(30.7%) eyes with vision that improved ≥3 lines (P=0.022). Finally, 45 eyes of maintained group were treated less than 3 times over 2 years.

### Conclusions

In the group of patients whose BCVA improved or maintained, the average number of injections was significantly lower than in the group of patients whose BCVA worsened. Therefore, applying TER to patients who maintain their vision with less than 3 treatments is a probability of over-treatment. If applied selectively to “gain but not maintain” groups, anti-VEGF treatments will have the greatest effect.

### S041

#### Effect of a new topical soft steroid hydrocortisone phosphate 0.335% on treatment of dry eye disease

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### Purpose

To evaluate the effect of preservative free (PF) hydrocortisone phosphate 0.335%, a new topical ‘soft’ steroid, in the treatment of dry eye disease with different etiologies.

### Methods

A prospective clinical case series of 20 patients with dry eye disease who were failing to respond to standard PF hyaluronic acid treatment 4 times a day plus lid warming and hygiene regimes. Patients were asked to continue their treatments and add PF hydrocortisone phosphate 0.335% eye drops (SOFTACORT®, Laboratoires Thea) 4 times a day, for 14 days. Tear break-up time (TBUT), corneal and conjunctival staining, conjunctival hyperaemia, Schirmer test, intraocular pressure (IOP) and symptoms (DEQ-5 questionnaire) were evaluated at baseline and day 14, for both eyes.

### Results

After 14 days median DEQ-5 scores decreased significantly from 14 to 8 (p<0.0001). Mean TBUT increased from 4s to 7.5s (p<0.0001); Schirmer test results increased significantly in both eyes (p<0.0005). The percentage of patients with clinically significant conjunctival hyperaemia (≥2 with McMonnies/Chapman-Davies scale) decreased from 90% to 35% (p<0.0001). The percentage of patients with conjunctival staining scores 2 or 3 (Oxford scale) was almost halved in both eyes (p<0.0004). Corneal staining of scores 2 or 3 (Oxford scale) decreased from 60% to 45% for both eyes (p<0.0003). A small, but not significant change in average IOP values was observed: from 14.5mmHg to 17mmHg for left eyes (p=0.1864) and 14.5mmHg to 16.5mmHg (p=0.2052) for right eyes.

### Conclusions

A 14 day treatment of dry eye patients with a new preservative-free topical soft steroid SOFTACORT®, resulted in significant improvements in patient symptoms, tear film volume and stability, ocular surface staining and redness. There were no significant changes in measured IOP values during this period of treatment.

### S014

#### Anti-inflammatory properties of corneal stroma-derived stem cells: Potential as a topical therapy for the ocular surface

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## **Purpose**

Corneal stroma-derived stem cells (CSSC) show potential as a stem cell source for corneal regeneration and wound healing, by acting as bi-directional sensory “factories” that secrete trophic factors in response to an injured microenvironment. Delivering CSSC topically to an injured corneal surface, using a substrate such as amniotic membrane (AM), represents a novel cellular therapy for severe keratitis conditions that can potentially lead to blindness.

## **Methods**

In this study, we optimised an in vitro inflammation model using human corneal epithelial cells (hCEC) treated with combinations of ethanol, lipopolysaccharide, and pro-inflammatory cytokines, interleukin 1- $\beta$  and tumour necrosis factor- $\alpha$ . The effect of this combined injury was assessed for effect on hCEC viability and proliferation, cytotoxicity, cell lysis, and further expression of pro-inflammatory cytokines. To assess the anti-inflammatory potential of the CSSC, a co-culture system was used, with and without cells seeded on AM. Expression of anti-inflammatory trophic factors by CSSC was analysed using protein arrays and ELISAs.

## **Results**

Co-culture of the optimised hCEC injury model with the CSSC cell therapy led to increased hCEC viability and proliferation, decreased cytotoxicity and cell lysis, and decreased levels of proinflammatory cytokines, when compared to injury alone, demonstrating the anti-inflammatory potential of the CSSC. CSSC could be easily cultured on the AM, establishing a promising method of applying the cells topically to the cornea.

## **Conclusions**

CSSC demonstrate an anti-inflammatory effect with potential to be clinically translated into a topical therapy for the injured ocular surface, using a carrier such as amniotic membrane.

## **S001**

### **A novel preservation technique for long-term storage and ambient distribution of transplantable human corneas**

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## **Purpose**

Worldwide, only 100,000 corneal transplants are performed annually, despite the fact that there are 1.5 million cases of corneal blindness diagnosed each year. One of the biggest limitations to corneal transplantation is access to quality donor tissue in developing countries. There is also few long-term storage solutions for effectively preserving spare donor corneas collected in countries with a surplus. Increased access to tissue can be achieved by development of preservation techniques to increase corneal storage times, allow for global shipping at ambient temperature and storage at room temperature on hospital shelves.

## **Methods**

In this study, we used a novel drying technique to preserve human corneas collected in the US and UK. We assessed weight, thickness, transparency, cell viability, cell membrane permeabilisation, ECM content and structure, comparing to non-dried donor corneas. A subcutaneous implantation model was performed in rats to assess biocompatibility and cell integration of the dry corneas. Clinical suitability was assessed through market access research targeting corneal consultants in the UK.

## **Results**

The dried corneas were comparable to non-dried donor corneas in all aspects except cellular viability. When implanted in rats, the dried cornea was well tolerated, with cellular migration into the matrix and no visible

immune rejection. We spoke to 12 corneal consultants, at 7 different hospitals, all gave positive feedback regarding future use and potential clinical indications.

### **Conclusions**

Our preservation technique provides an easy-to-manufacture, non-viable, dehydrated, cornea suitable for a range of clinical indications and tectonic support in emergency situations. It can be stored on the shelf in hospitals for over 2 years and can be shipped at ambient temperatures worldwide, relieving the global shortage of corneal tissue.

### **F086**

#### **Natural history findings from a large cohort of patients with Leber's hereditary optic neuropathy (LHON): New insights into the natural disease-course**

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### **Purpose**

LHON is a mitochondrial disorder resulting in bilateral central vision loss in one eye, followed by a similar loss in the second within days to months. Three primary mitochondrial DNA mutations cause over 90% of cases. Current knowledge of the disease-course, as well as the rate and nature of spontaneous visual recovery is based on a small group of studies, in which visual acuity (VA) outcomes have different definitions. Here, we report natural history data from an international, multicenter LHON case record survey.

### **Methods**

Data was collated from available medical records of patients with a genetically confirmed diagnosis of LHON from 11 worldwide centers. No exclusion criteria were applied. Demographic data, mutation status, date of onset in each eye and visual assessment results were tabulated for 383 patients. 83 patients provided efficacy data (outcomes cohort).

### **Results**

Primary mutations represented 95.8% of the population studied. The male gender was more frequent across all primary mutation carriers compared to non-primary carriers (> 70% vs. 58.8%). Age at onset showed a maximum incidence between 15 and 35 years of age across all mutations, but the incidence by age group (< 12 years, 12 to 15 years, 15 to 35 years and > 35 years) showed some differences amongst mutations. At baseline (BL), 66.3% of patients in the outcomes cohort had a VA < 1.0 logMAR, while at nadir only 4.8% remained in this category, with 63.9% of patients off-chart (> 1.68 logMAR). At last visit, nearly half of all patients were off-chart, a 10-fold increase from BL. 18.1% of patients had a final VA < 1.0 logMAR, 3.7 times fewer than at BL.

### **Conclusions**

This study provides a new insight into LHON's natural course over time. Overall, the spontaneous evolution during the first 5 years after onset is that of a relevant and profound deterioration of VA.

### **1752**

#### **Lysosomes as regulators of protein clearance**

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## Summary

The retinal pigmented epithelial (RPE) is a single layer of cells interposed between the neurosensory retina and Bruch's membrane. RPE cells are not only among the most active phagocytic cells in the body, but also are post-mitotic cells with high metabolic activity, where a high rate of autophagy could be expected. We have previously shown that  $\beta$ A3/A1-Crystallin is a lysosomal luminal protein that plays a pivotal role in lysosomal-mediated clearance process in RPE cells. Our recent proteomics dataset suggests abnormal phosphorylation profile of proteins involved in calcium signaling pathway comparing *Cryba1* knockout mice to age-matched control mice. We find reduction of phosphorylation levels of calcium/calmodulin-dependent protein kinase type II subunit (KCC2D), calcium regulated heat stable protein 1 (CHSP1), nucleobindin-1 (NUCB1), doublecortin like kinase 1 (DCLK1) and spectrin beta (SPTB2).  $\beta$ A3/A1-crystallin maintains calcium homeostasis in RPE cells and thereby regulates mTORC1 signaling pathway to preserve lysosomal function.

## T087

### Structural impact of arrested foveal development in preterms

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## Purpose

To evaluate the impact of structural changes in foveal layers caused by arrested foveal development in adult preterms compared with control subjects through analysis of optical coherence tomography (OCT) B-scan images.

The objective was to estimate the redistribution of retinal layers in the central fovea of preterms with arrested foveal development characterized by reduced foveal depth and incomplete displacement of inner retinal layers (IRL).

## Methods

Layer thickness was measured in straight and tilt-up scans from preterms and controls. Reflectivity profiles of the Outer Plexiform Layer (OPL) and manual segmentation of the Inner Nuclear Layer (INL) and the combined Ganglion Cell Layer and Inner Plexiform Layer (GCL+IPL) were obtained. The displacement of the cumulative area curve of preterms compared to that of controls was used to estimate retardation of cell migration.

## Results

The retarded migration within the inner retina and OPL had a major impact on available space within the central fovea. A retardation of 150-200  $\mu$ m for cell structures in these layers normally present at the foveal slope resulted in a reduction of available space ranging from 25-60 % in preterms with mild developmental arrest and no retinopathy of prematurity (ROP). The surface available for synaptic communication was further reduced and the impact on the GCL+IPL layer more marked in ROP cases with marked developmental arrest.

Reduced space available within the fovea as a consequence of retarded centrifugal migration is probably of visual significance due to the marked reduction of surfaces for synaptic communication.

## Conclusions

We propose a structural model where the space available for inner retinal cells and synaptic structures are markedly reduced based on evidence of retarded displacement of IRL and OPL in the central retina of preterms with arrested foveal development.

## T015

### Macular retinal capillary density and blood flow differences between black and white subjects using optical



## coherence tomography angiography

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### Purpose

Black populations have been shown to have a higher risk of vision loss by diabetic retinopathy (DR) but the underlying factors of this vulnerability are unclear. The purpose of this study is to investigate differences in the retinal microvascular environment between black and white subjects with optical coherence tomography angiography (OCTA).

### Methods

Prospective observational cross-sectional study. Young healthy black and white subjects with no significant medical or ocular history were studied. All subjects underwent OCTA imaging (Optovue RTVue XR Avanti, AngioVue software). Vessel density (VD), % blood flow area (BFA) of superficial and deep capillary plexuses (SCP and DCP, respectively) and choriocapillaris and size of the foveal avascular zone (FAZ) were measured with AngioAnalytics software.

### Results

Ninety three eyes of 23 black and 24 white subjects matched for age, sex, refractive error and image quality were included. In the SCP, black subjects had significantly lower VD in the fovea compared to white subjects ( $p<0.05$ ), but VD was not different in the parafovea. In the DCP, black subjects had significantly lower VD ( $p<0.05$ ) and lower BFA in the parafovea ( $p<0.05$ ). FAZ area was significantly larger in black subjects in both the SCP ( $p<0.05$ ) and the DCP ( $p<0.05$ ). Black subjects also had decreased BFA in the choriocapillaris ( $p<0.001$ ) compared to white subjects.

### Conclusions

In our study, young healthy black subjects have decreased VD and blood flow in DCP and choriocapillaris compared to white subjects. These findings suggest that retinal capillary differences may contribute to higher risk of black populations for DR development.

2763

## The molecular role of the Six6 transcription factor in glaucoma

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### Summary

Glaucoma is recognized as a complex disease in which multiple genetic and environmental factors interact. Recently, using an animal model, we observed that upon experimentally increased IOP, expression of *Six6* transcription factor increases to directly regulate the expression of *p16Ink4a*, leading to enhanced senescence in RGCs and most likely causing RGC death. Our study indicated that SIX6 variant correlating with high risk of developing glaucoma, despite binding the *p16Ink4a* regulatory regions with the same efficiency as SIX6-protective variant, is a more potent activator of *p16Ink4a* expression, raising an intriguing question about the molecular difference between those two SIX6 variants. Using biochemical and molecular approaches we have investigated the difference in transcriptional potential of both variants. We will present results proving that Six6 protein variant correlating with higher risk of developing glaucoma interacts with co-factors that are most likely important for its higher transcriptional potential. We will also present new data focused on understanding the causative role of newly identified Six6 co-factors in the etiology of glaucoma.

## T070

### Case series: Ozurdex® for macular edema in uveitis

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#### Purpose

Report the safety and efficacy of dexamethasone extended-release (700 mcg) intravitreal implant injection in refractory uveitis-related macular edema.

#### Methods

We described a serie of 5 eyes from 4 patients with significant refractory uveitis-related macular edema, who had intravitreal injection of dexamethasone implant. All patients underwent complete and multimodal ophthalmologic evaluation, with fluorescein angiography, autofluorescence and optical coherence tomography. The main outcome was anatomical resolution of cystoid macular edema. Patients were reassessed 4 to 12 weeks after implant introduction.

#### Results

We analised 5 eyes from 4 patients, 3 female, with a mean age of 55 years, 2 caucasians. The uveitis was idiopathic in 3 cases and associated with polyangiitis in 1 case. All patients have been through topical, periocular and systemic steroids, conventional immunomodulation and biotechnological drugs. All eyes were pseudophakic, 2 were vitrectomized; 1 had a filtering surgery due to uveitic glaucoma. The mean pre-implant visual acuity (VA) was 1.0 logMAR, with a significant improvement in all cases after implant introduction, with a mean VA of 0.40 logMAR. Likewise, after the introduction of the implant, anatomical improvement was observed in all cases, with a mean reduction in central foveal thickness of 293.7 µm, which reduced from 531.7 µm to 238.0 µm. Mean intraocular pressure increased from 12 mmHg to 14 mmHg [9 - 17] after implant introduction, with 2 patients already on hypotensive drugs, and other 2 did not need any medication.

#### Conclusions

In these 4 cases, intravitreal dexamethasone implant resulted in a significant improvement both clinically and structurally of macular edema. It was an effective and safe approach in refractory uveitic macular edema.

## F065

### Is the OCT useful in monitoring idiopathic intracranial hypertension?

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#### Purpose

Idiopathic Intracranial Hypertension (IIH) is a rare entity, more frequent in obese and childbearing women. Papilledema is the most common clinical sign and visual dysfunction is its major morbidity. The purpose is to investigate OCT utility in monitoring disease progression status, through the review of a clinical case.

#### Methods

A 31-year-old female, obese, with right hemiparesis, with involvement of hemiface and right VI nerve palsy, in the context of IIH, was referred to neurophthalmology department by papilledema after ventriculoperitoneal (VP) shunt. We performed complete, multimodal and serial examinations.

#### Results

At presentation patient was asymptomatic, without headache or diplopia, visual acuity was 0.0 logMar, intraocular pressure 12 mmHg and fundoscopy revealed bilateral optic disc edema with choroidal folds. Bilateral diffuse loss of retinal sensitivity was shown in PEC 30/2 and overall thickening of RNFL in OCT (OD 162µm, OS 148µm). During the first 3 months, progressive improvement of papilledema was observed, and progressive decrease in RNFL thickness (OD 121µm, OS 125µm). After 3 months, the decrease in RNFL thickness stopped in OD (OD 126µm, OE 117µm) and 4 weeks later patient reported hemicranial headaches. Neurological evaluation and cranial CT scan were normal. OCT revealed bilateral thickening of RNFL (OD 127µm, OE 122µm). Lumbar puncture was performed (350 mmHg) and placement of a new VP shunt was made. In postoperative period there was clinical improvement, papilledema resolution and normalization of RNFL (OD 95µm, OE 95µm).

### Conclusions

The role of OCT in the management of papilledema in IIH remains unclear. Reduction of RNFL thickness (as edema resolves) may not differ from axonal loss, reflecting disease progression rather than improvement. This case demonstrates the role of serial tomographic evaluation, allowing early detection of clinical worsening.

**3141**

### Use of ocular ultrasound for diagnosis of orbital lesions

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### Purpose

Demonstrate the role of ultrasonography (US) as important adjuvant for clinical assessment of various ocular and orbital diseases.

### Methods

Case reports of patients with orbital masses. All subjects underwent full ophthalmic examination and imaging with A and B scan US.

### Results

Case 1: A 72-year-old male with maxillary pain and a known right orbital lesion on computer tomography scan. Ophthalmologic examination was unremarkable. Ophthalmic US identified a solid lesion, intraconic, between the optic nerve and medial rectus muscle, with well-defined margins, characterized in A-mode by mean internal reflectivity and homogeneous structure. The findings were suggestive of cavernous hemangioma of the orbit, and later confirmed by magnetic resonance imaging (MRI). Case 2: A 15-year-old male with history of right upper lip angioma submitted to surgical excision. Biomicroscopy revealed a pigmented and elevated lesion on the bulbar conjunctiva in the upper quadrants of the left eye. Fundoscopic examination showed thinning of the neuroretinal rim, increased cup to disc ratio and peripheral retinal hyperpigmentation with vascular tortuosity. Ophthalmic US revealed multiple cystic lesions in the anterior orbit, suggestive of orbital lymphangioma. Thickening of the choroid was absent. The diagnosis was later confirmed by MRI. Case 3: A 26-year-old woman with hirsutism and pain with ocular movements in the right eye (OD). Ophthalmologic examination disclosed OD proptosis, abduction limitation and diplopia in dextroversion. Biomicroscopy showed conjunctival hyperemia at lateral rectus muscle (LRM) insertion. US revealed a large thickening of LRM and tendon, suggesting myositis.

### Conclusions

Ophthalmic US can be used as a first-line, non-invasive, efficient, instant feedback imaging modality to guide the diagnosis, management and follow-up of patients with orbital pathology.

**S088**

### Oxidative stress and mitochondrial damage overloads mitophagy in dry age-related macular degeneration like

## PGC-1 $\alpha$ /Nrf-2 knockout mice model

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### Purpose

Growing evidence suggests reactive oxygen species (ROS) and damaged mitochondrial organelles are linked to age-related macular degeneration (AMD). Damaged mitochondria and its clearance via mitophagy has been reported to implicate in number of neurodegenerative diseases including Alzheimer's, Parkinson and Huntington diseases.

### Methods

Samples from one-year old PGC-1 $\alpha$ /Nrf-2 knockout and wild type mice were used for immuno-confocal analysis.

### Results

Here we show that the elevated levels of damaged mitochondria and compromised antioxidative stress in AMD like pathogenesis PGC1- $\alpha$ /Nrf-2 knockout mice overloads mitophagy compared to wild type animals. Immunofluorescence based analysis of retinal pigment epithelial cells (RPE) revealed increased levels of both PTEN-induced putative kinase 1 (PINK1) and E3 ubiquitin ligase (PARKIN) and their colocalization, supported by elevated PARKIN phosphorylation. We also observed high level of colocalized microtubule-associated proteins 1A/1B light chain 3B (LC3B) and damaged mitochondria in retinal pigment epithelial cells in confocal and electron microscopy analysis, respectively.

### Conclusions

Our study provides insight to the potential role of mitophagy and its receptors in AMD pathogenesis, and further contributes to develop new novel treatment strategies.

## F022

### Above Tenons Conjunctival dissection – A modification for Trabeculectomy Surgery.

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### Purpose

Trabeculectomy remains the gold standard for glaucoma filtration surgery. Over the last 40 years modifications have improved both safety and efficacy. Traditional surgery usually involves dissection beneath Tenon's to reduce encystation. However, this complication still occurs postoperatively.

To describe a modification in conjunctival Tenon's dissection with the aim of creating improved bleb morphology. We hypothesized that minimally disturbing Tenon's with sharp dissection high, above Tenons layer causes less tissue trauma, less scarring and a subsequent reduction in encystment.

### Methods

We retrospectively selected 100 consecutive cases of fornix based Trabeculectomy performed by one surgical team with at least a 1 year follow up. All cases were performed using a new modified technique of conjunctival dissection. Conjunctiva was opened adjacent to the limbus from the 10 O'clock to the 2 O'clock position superiorly

and a pocket was crafted using sharp dissection high above the Tenons layer. The remainder of the procedure continued in a traditional fashion.

### Results

Cystic bleb formation was seen minimally using the modified technique with a reduced needling rate compared to published literature.

### Conclusions

High conjunctival dissection for fornix flap creation may be of benefit for bleb morphology in the early postoperative period.

2931

### New aspects on the pathophysiology and molecularbiological background of keratoconus

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### Summary

Keratoconus (KC) is characterized by thinning and conical shape of the cornea, its ethiology remains unknown. Genetic alterations have been described in *Col5A1* and *LOX* genes in this disease, but genetic studies suggest a heterogeneity and complex nature of KC. Beside genetic components, previous studies have shown metabolic changes in keratocytes and association of KC with inflammatory mechanisms. Urea concentration in aqueous humor of KC patients is decreased compared to healthy controls. In cell culture experiments using KC-keratocytes, decreased urea and hydroxyproline concentration have been verified. Our experiments showed increased iNOS mRNA expression in KC-keratocytes, compared to normal controls. iNOS is usually expressed as part of an inflammatory response in tissues, although some cell types express iNOS constitutive. Some researchers also found increased IL-4, -5, -6, -8 and TNF- $\alpha$  concentrations in tears of KC-patients, which further support an inflammatory association of KC. The molecular biological background and the possible inflammatory origin of keratoconus development needs further analysis.

F033

### An unusual case of neo-vascular glaucoma in the post-partum period secondary to severe peripheral retinal ischaemia

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### Purpose

Neo-vascular glaucoma is a severe secondary glaucoma usually resulting from retinal ischaemia. Eales disease is characterised by inflammatory venous occlusion of the peripheral retina, neovascularisation and retinal phlebitis and is a rare cause of neo-vascular glaucoma. It is a diagnosis of exclusion. Here we present a very unusual case of aggressive retinal ischaemia and neo-vascular glaucoma in the postpartum period.

### Methods

A 42-year-old South-Asian woman, with recent gestational diabetes mellitus, developed marked subacute retinal ischaemia, neovascularisation and neo-vascular glaucoma with vitreous haemorrhages in the 2 months after giving birth. She was treated with maximum anti-glaucoma medication, pan-retinal photocoagulation and intravitreal avastin. 2 weeks later her visual acuity had significantly deteriorated. An Ahmed shunt was inserted in her right eye. Her visual acuity and intra-ocular pressure improved bilaterally over the next month.

### Results

She was thoroughly investigated for causes of her retinal ischaemia. Findings included a normal PET scan, routine bloods, inflammatory markers and HbA1c, and negative tests for antiphospholipid syndrome, treponema IgG, QuantiFERON and sickle cell disease. There was good perfusion of both internal carotid arteries.

### Conclusions

Here we present an unusual case of profoundly aggressive bilateral ischaemic retinopathy and neo-vascular glaucoma, without any obvious cause. Whilst the exact mechanism remains controversial, diabetic retinopathy worsens during pregnancy and is most likely secondary to changes in the retinal circulation of pregnant women. We hypothesise that this patient had undiagnosed Eales disease and the hyper-dynamic retinal circulation that occurs in pregnancy triggered and accelerated the disease via similar mechanisms that cause a worsening of diabetic retinopathy in pregnancy.

## 2711

### Hand handled OCT in paediatric ocular oncology

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### Summary

Since its development in 2008, hand-held spectral domain optical coherence tomography (HHSD-OCT) has contributed to improve the management of paediatric ocular oncology cases, by allowing a non-invasive evaluation of the retina and optic nerve of the young children during the under anesthesia examination. In this session, emblematic cases will be presented, which illustrates its role in the differential diagnosis of paediatric tumors and its importance in the management (diagnostic and therapeutic) of retinoblastoma cases.

## 2942

### Intravitreal anti-VEGF in pediatric ocular oncology

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### Summary

Intravitreal injections in eyes with pediatric tumors and especially retinoblastoma have been for a long time prohibited by fear of extraocular spread of the tumor. Since 2012 and the description of a safety enhanced technique of injection, intravitreal chemotherapy of melphalan and/or topotecan is now a worldwide adopted procedure for the management of intravitreal seeding.

In this session, we present Lausanne's experience with intravitreal anti-VEGF in retinoblastoma, used for retinal

and/or iris neovascularization occurring after conservative treatment with intravenous and/or intraarterial chemotherapy.

**014**

## **Introduction**

**3152**

## **Non-invasive imaging of retinal oxygen metabolism**

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## **Summary**

Retinal oximetry is non-invasive measurement of oxygen saturation in retinal blood vessels. It provides insight into retinal oxygen metabolism and the metabolic changes in ischemic and atrophic diseases of the retina and brain.

In diabetic retinopathy, venous oxygen saturation increases and arteriovenous difference decreases. Both correlate with severity of diabetic retinopathy.

In CRVO, vein occlusion causes hypoxia, which is measured directly by retinal oximetry to confirm the diagnosis and measure severity. In both CRVO and DR, the change in oxygen levels is a consequence of disturbed blood flow with resulting tissue hypoxia, induction of HIF and VEGF production.

In atrophic diseases, such as retinitis pigmentosa and glaucoma, retinal oxygen consumption is reduced and this is detected by retinal oximetry. Retinal oximetry correlates with visual field damage and retinal atrophy. It is an objective metabolic measure of the degree of retinal atrophy..

Retinal oximetry opens the field of metabolic imaging of the retina. Biomarkers in metabolic, ischemic, and atrophic diseases of the retina and central nervous system have been discovered.

**1851**

## **The utility of proteomics for understanding the pathophysiology of dry eye**

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## **Summary**

Dry eye has been demonstrated to be an immune based inflammation of the Lacrima Functional Unit. While the immunological pathophysiology has been investigated and better understood over the past several years there is still much to learn as to the events that lead to this chronic disease. Which cell components or synthesized secretions are harbingers of disease progression or indicators of therapeutic efficacy have not yet been identified. There is, additionally, still a lack of correlation between disease signs and symptoms in Dry Eye and the identification of disease specific biomarkers would help to correct this "disconnect" and enhance clinical trial design. Using proteomics to identify these markers would also result in the identification of new therapeutic targets.

The advantage of using proteomics is that large numbers of proteins can be evaluated in one experiment. Advanced bioinformatic analysis is applied to the initial data set in order to determine a more causal relationship between the protein. Once completed, a smaller panel of candidate proteins can be evaluated for utility as a biomarker and therapeutic target. Proteomics are a powerful tool in disease related research.

**1715**

#### **Restitution of visual functions in blind retinitis pigments patients with subretinal implant Alpha AMS**

A. STETT<sup>1</sup>

<sup>1</sup>Retina Implant AG, Excutive Board, Reutlingen, Germany

##### **Summary**

Presented are results from clinical trials and daily living experiences with the visual prosthesis Alpha AMS. It is applied in patients with Retinitis pigmentosa, has received CE mark approval and is reimbursed by the public health system in Germany.

Implant-mediated visual perception was observed in 13 out of 15 patients that participated in a clinical multicenter trial. Two patients were able to distinguish Landolt C-rings of 20/1111 and 20/546, respectively. Twelve patients could determine the orientation of gratings between 0.1 cpd and 3.3 cpd. Detection, localization, and counting of objects was significantly better with the implant "ON" than with the implant "OFF" over the whole observation period. On average 4.6 of 6 different grey levels could be distinguished. The visual perception was stable over the observation period of 12 months after surgery.

The predicted lifetime of the implant is about 5 years. The maximum implanted time of a still functioning Alpha AMS device is 4 years.

For patients, the benefit of the implant in individually different everyday situations is more important than the results of the functional tests. The presentation will show how the implant positively affects the patients in their daily life.

**2735**

#### **Electronical subretinal implants - recent developments**

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##### **Summary**

Subretinal inserted electronic implants replaces the function of photoreceptors by converting images incident on the fundus into electrical impulses stimulating the retina of people who are blinded by retinitis pigmentosa.

The initially developed passive microphotodiode arrays proved to be unusable because of insufficient generation of current from the incident light. The CE mark approved RETINA IMPLANT Alpha AMS utilizes an active chip, 3.2 x 4 mm size, with 1600 light detecting and stimulating pixels, which is placed subfoveally. For power supply it is connected to a retroauricular implanted coil. Since the chip is placed under the retina, it follows the natural eye movements and microsaccades are utilized for image refreshing. Based on a clinical validated aging model, we expect a median lifespan of the implanted system of 5 years.

Psychophysical and subjective data obtained in clinical trials and in daily use show that RETINA IMPLANT Alpha AMS is reliable, well tolerated and can restore limited visual functions in blind people. Patients report a significant



emotional benefit of the implant mediated vision in their daily lives. Regular use of the implant is related to outcome improvements.

#### **T122**

##### **Adalimumab in the management of Acute Zonal Occult Outer Retinopathy: a case report**

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#### **Purpose**

To report the efficacy of adalimumab in a case of acute zonal occult outer retinopathy (AZOOR) documented by fundus autofluorescence (FAF) and optical coherence tomography (OCT).

#### **Methods**

Observational report about a case diagnosed as AZOOR based upon fundus photographs, OCT, Goldmann visual field perimetry, FAF and full-field flash electroretinography (ERG).

#### **Results**

A 38-year-old woman presented with a sudden onset of cloudy vision in the right eye. Her best-corrected visual acuity was 10/10 in both eyes (BE). Slit lamp examination, intraocular pressure and ophthalmoscopy were unremarkable in BE. Visual field testing revealed a central scotoma in the right eye (RE). FAF showed a peripapillary area of hyperautofluorescence along with some satellite lesions nasally in the RE. OCT revealed attenuation of the outer retina. ERG showed a reduction of the scotopic amplitudes. All imaging was normal in the left eye (LE). A complete general work-up was normal. The diagnosis of AZOOR was confirmed and the patient received oral prednisone therapy, slowly tapered off. Ten weeks later, FAF showed speckled hyperautofluorescent lesions in the temporal area of the macular region of the LE. The RE showed no progression. Because of high dependence on systemic steroids and the evolution in the LE, adalimumab was added. The patient responded well on adalimumab weekly and achieved a recurrence-free period of 19 months.

#### **Conclusions**

Adalimumab seemed an effective and safe treatment in uveitis of mixed origin refractory to conventional immunosuppressive therapy in our patient. To our knowledge this is the first report of a case of AZOOR successfully treated with adalimumab.

#### **F013**

##### **The effect of the Valsalva maneuver on the retinal veins**

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#### **Purpose**

The major effect of the Valsalva maneuver (VM) in the eye has been observed as an increase in intraocular pressure (IOP). As a consequence, the ocular perfusion pressure decreases, assuming that the intraocular venous pressure equals the IOP. Recent work has shown that this assumption is not valid in all cases. The purpose of the present study was to measure the retinal venous pressure (RVP) under comparable VM conditions compared to those chosen in IOP measurements. Diameters of the retinal vessels were obtained additionally.

#### **Methods**

Left eyes of 40 healthy volunteers (age: 24.4±3.2 [mean±s], m/f: 28/12) were examined. Instruments: IOP: Dynamic contour tonometry. RVP: Contact lens dynamometry (CLD). Airway pressure: Aneroid manometer. Central

retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE): Static vessel analysis (Imedos, Jena, Germany). Sequence of measurements: IOP. IOP after mydriasis, CRAE and CRVE without and then during VM (airway pressure: 40 mmHg), three times RVP in quick succession during VM (airway pressure: 40 mmHg). Statistics for differences (increase or decrease): one-sample t-test, predicted value=0.

## Results

Initial IOP=Initial RVP=15.4±2.1mmHg. RVP increase during VM=23.6±7.0mmHg, ( $p<10^{-6}$ ). IOP increase during VM=3.5±3.0mmHg ( $p<10^{-6}$ ). Two-sided t-test: Increase RVP vs. increase IOP:  $p<10^{-6}$ . Static vessel analysis: before VM: CRAE=197±17µm, CRVE=210±18µm. Decrease CRAE during VM= -3.4±5.8µm ( $p=0.0007$ ). Increase CRVE during VM=4.6±6.5µm ( $p=0.00008$ ).

## Conclusions

The retinal venous pressure increases more than the IOP during VM. Therefore, the retinal and optic nerve head perfusion pressure is much more decreased by the VM than assumed until now. The changes in the vessel diameters are statistically significant but small.

2163

## Cholesterol dependent homeostasis in the lens - a biophysical perspective

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## Summary

Extremely high cholesterol (Chol) content distinguishes fiber cell plasma membranes from other biological membranes. The need for high Chol content in these membranes remains unclear. However, the disturbance of Chol homeostasis in fiber cells may result in damages associated with cataracts. In fiber cell membranes, Chol not only saturates the phospholipid (PL) bilayer but also leads to the formation of Chol bilayer domains (CBDs). The main hypothesis of this review is that high Chol content and the presence of CBDs play a significant function in maintaining the homeostasis of the fiber-cell plasma membrane, the fiber cell itself, and the whole lens, and thus in the maintaining lens transparency. The saturating Chol content keeps the physical properties of the PL bilayer of the lens lipid membranes constant and independent of changes in the PL composition that occur with age, increases the barrier to oxygen permeation into the lens interior, and increases the membrane hydrophobicity and the barrier to permeation of polar molecules. Evidence indicates that high Chol content, the formation of CBDs, and the formation of Chol crystals should not be regarded as major predispositions for the development of age-related cataracts.

F102

## Corneal astigmatism distribution at Indonesia National Eye Center Cicendo Eye Hospital

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## Purpose

To describe the type and power of astigmatism distribution in astigmatism patient at National Eye Center Cicendo Eye Hospital as well as the correlation between age and astigmatism type and power.

## Methods

A cross sectional study of patients aged above seventeen year old with astigmatism with no history of surgery, trauma, corneal abnormality, palpebral abnormality, and pterygium from February to April 2017. Keratometry examination was performed in all subjects.

### Results

There were 400 eyes from 261 patients included in this study range 18-81 year old. With-the-rule astigmatism was found in 68,5% participants. The largest proportion astigmatism power was 1-3 D (58,25%). With-the-rule astigmatism was dominant in 18-59 year old (54,17%-97,73%) then shift towards against-the-rule after 60 year old (67,61%). Correlation between age and astigmatism type was moderate ( $R=-0,401$ ;  $p=0,000$ ), as well as age and astigmatism power ( $R=-0,552$ ;  $p=0,000$ ).

### Conclusions

With-the-rule astigmatism was dominant at 18-59 year old participants then shift towards against-the-rule astigmatism after 60 year old. The largest proportion astigmatism power was 1-3 D. With-the-rule shift towards against-the-rule as increasing in age. Correlation between age and astigmatism type was moderate, as well as age and astigmatism power.

2522

### TFOS DEWS II Epidemiology and Pathophysiology Reports

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### Summary

To increase our understanding of dry eye disease (DED), the Tear Film & Ocular Surface Society (TFOS), a non-profit organization, launched the TFOS Dry Eye Workshop II (TFOS DEWS II) in March 2015. The objective of the TFOS DEWS II, which required more than 2 years to complete, was to: [a] update the definition and classification of DED; [b] evaluate critically the epidemiology, pathophysiology, mechanism, and impact of this disorder; [c] develop recommendations for the diagnosis, management and therapy of this disease; and [d] recommend the design of clinical trials to assess future interventions for DED treatment. The TFOS DEWS II involved the efforts of 150 clinical and basic science research experts from around the world, who used an evidence-based approach and a process of open communication, dialogue and transparency. This presentation will review the conclusions and recommendations of the TFOS DEWS II reports on the Epidemiology and Pathophysiology of DED. The TFOS DEWS II report was published in the July 2017 issue of *The Ocular Surface*. A downloadable version of the report, written in multiple languages, as well as videos of diagnostic and management techniques, are all available on the TFOS website: [www.TearFilm.org](http://www.TearFilm.org).

3323

### Can we individuaize glaucoma surgery?

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### Summary

The advent of new surgical techniques in the past few years has changed the management of glaucoma patients. Non penetrating surgeries and more recently minimally invasive glaucoma surgery (MIGS) are added to the conventional armament and have modified the approach to glaucoma surgery, in particular indications, timing of intervention, post-operative care and quality of life. This plethora of new surgical options opens a new era of

“individualized surgical treatment” but is not without some caveats. This presentation will try to identify which patient will benefit the most by each surgical technique.

#### **F067**

### **Optical Coherence Tomography as a Diagnostic Tool for Detecting Mild Cognitive Impairment in Parkinson's Disease**

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#### **Purpose**

To compare the optical coherence tomography (OCT) measurements of Parkinson's disease (PD) patients and normal control, and evaluate the association between OCT parameters and various symptom scales in PD patients.

#### **Methods**

Seventy four eyes of 74 PD patients and 53 eyes of 53 age-matched normal control without any neurodegenerative disease were included. Macular, peripapillary retinal nerve fiber layer (pRNFL), macular ganglion cell-inner plexiform layer (mGCIPL) thicknesses were measured by Cirrus HD-OCT. For PD patients, information on the duration of disease, motor and non-motor symptom scales such as: Hoehn and Yahr (HY) scale, Unified Parkinson's disease rating scale (UPDRS) part I, II, and III, non-motor symptom assessment scale (NMSS), Montreal cognitive assessment (MoCA), the Korean version of Mini-mental state examination (KMMSE) were recorded. Correlation between the various symptom scales and the OCT parameters were analyzed and receiver operating characteristic (ROC) curves were calculated.

#### **Results**

PD patients showed statistically significant reduced thickness in average and temporal pRNFL and overall mGCIPL compared with normal control. Among the various symptom scales, MoCA and KMMSE were significantly associated with mGCIPL thickness in PD patients. Minimum and average mGCIPL thickness showed positive correlation with MoCA ( $r = 0.350$ ,  $P = 0.003$  and  $r = 0.302$ ,  $P = 0.011$ , respectively) and KMMSE scale ( $r = 0.367$ ,  $P = 0.001$  and  $r = 0.352$ ,  $P = 0.002$ , respectively). The area under the ROC curve of the mGCIPL parameters for diagnosing MCI among PD patients ranged from 0.70 to 0.80.

#### **Conclusions**

mGCIPL thinning is associated with cognitive impairment in PD patients. OCT measurement might have implications for identifying individuals with MCI among PD patients.

#### **F112**

### **Investigating the movement of the centre of the multifocal hexagonal stimulus array using an electroretinogram function**

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#### **Purpose**

Declines in visual sensitivity at arbitrary points on the retina can be measured using a precise perimetry device with a fundus camera function. However, the retinal layer causing this decline cannot be identified. To investigate cryptogenic diseases, such as macular dystrophy, acute zonal occult outer retinopathy and multiple evanescent

white dot syndrome, we studied an electroretinogram function to move the centre of the multifocal hexagonal stimulus array.

## Methods

We combined an electroretinographic optical system and a perimetric optical system into an experimental device with the same optical system as that of a fundus camera. We also deployed an Edmund infrared camera EO-50231, a lens with 25-mm focal length, a 45-degree cold mirror, a halogen lamp and an 8-inch monitor. Then, we deployed a differential amplifier with gain 10, a high-pass filter with a 21.2 Hz cut-off frequency, a 50 Hz notch filter and two non-inverting amplifiers with gains 1001 and 11. In addition, we used National Instruments' I/O device USB-6216, shielded connector block SCB-68A, the Nihon Kohden plate electrode NE-113A and the LabVIEW 2017 software for data retrieval. The software was used to generate the multifocal hexagonal stimulus array on the monitor using C++Builder 10.2 and to move the centre of the array up and down and towards left and right.

## Results

CONE and bright flash ERGs could be observed using the moving ERG function. The a, b and c waves and the photopic negative response were identified in the CONE ERG.

## Conclusions

The moving ERG function allows the identification of the retinal layer causing visual alterations.

1253

### Mitophagy as a research target

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## Summary

The aged retina is characterized by an increased level of reactive oxygen species (ROS) and impaired autophagy and both are linked with AMD pathogenesis. Mitophagy, is a mitochondria-specific 'housekeeping' subcellular autophagy process, which is an essential part of mitochondrial quality control, a collective mechanism responsible for mitochondrial homeostasis. Alterations in *mitophagy* have been increasingly linked to aging and age-related diseases. The abundance of ROS, DNA damage, and the excessive energy consumption in the aging retina contribute to degeneration of RPE cells and their mitochondria. The Nrf-2 & PGC-1 alpha KO dry AMD mouse model, provide a useful tool for AMD based degeneration assessment in retinal pigmented epithelium, and to reveal the occurrence of mitophagy in mouse RPE with these genetic background. Here we show the direct monitoring of key mitophagy regulator proteins by immunohistochemistry combined with fluorescence microscopy and will report the detection of mitochondrial homeostasis in transmission electron microscopy.

S086

### Morphologic and electroretinographic phenotype of NRF-2 and PGC-1 $\alpha$ deficient mice: a novel model for dry age-related macular degeneration

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### Purpose

Age-related macular degeneration (AMD) is the leading cause of blindness during aging and dry AMD involves impaired protein degradation in retinal pigment epithelial cells (RPE). RPE cells are constantly exposed to oxidative stress that may lead to the accumulation of damaged cellular proteins, DNA and lipids and provoke tissue deterioration during the aging process. The ubiquitin-proteasome pathway and the lysosomal/autophagosomal pathway are the two cardinal proteolytic systems in eukaryotic cells. NRF-2 (nuclear factor-erythroid 2-related factor-2) and PGC-1 $\alpha$  (peroxisome proliferator-activated receptor gamma coactivator-1 alpha) are master transcription factors in the regulation of cellular detoxification.

### Methods

We studied the role of NRF-2 and PGC-1 $\alpha$  in the regulation of RPE cell structure and function by using global double knockout (dKO) mice, light/confocal/electron microscopy and electroretinography.

### Results

The *NRF-2/PGC-1 $\alpha$*  dKO mice showed massive age-dependent RPE degeneration, accumulation of the oxidative stress marker, 4-HNE (4-hydroxynonenal), the endoplasmic reticulum stress markers GRP78 (glucose-regulated protein 78) and ATF4 (activating transcription factor 4), and damaged mitochondria. Moreover, levels of protein ubiquitination and autophagy markers p62/SQSTM1 (sequestosome 1), Beclin-1 and LC3B (microtubule associated protein 1 light chain 3 beta) were significantly higher together with the Iba-1 (ionized calcium binding adaptor molecule 1) macrophage marker and an enlargement of RPE size in dKOs. These histopathological changes were accompanied by visual loss as revealed by electroretinography.

### Conclusions

Consequently, these novel findings suggest that the *NRF-2/PGC-1 $\alpha$*  dKO mouse is a valuable model for investigating the role of proteasomal and autophagy clearance in the RPE and in the development of dry AMD.

### T098

**Evaluation of sex differences in flicker light induced vasodilation and central retinal thickness in healthy young subjects.**

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### Purpose

It has been shown that increased neural activity evoked by stimulation with diffuse luminance flicker increases retinal vessel diameter and leads to a concomitant increase of retinal blood flow. The purpose of the current study was to evaluate potential sex differences in the hyperaemic response to light stimulation.

### Methods

In this study, a total of 137 healthy women and men aged between 18 and 45 years were included. Retinal vessel diameters were assessed at baseline and during flicker stimulation using a Dynamic Vessel Analyzer (Imedos, Germany). In addition, central retinal thickness was measured using OCT.

## Results

Of 137 subjects (age 18-44 years, mean age 25±5) included, 73 were female (53.3%, mean age 24±5 years) and 64 male (46.7%, mean age 25±5 years). No significant difference was detected in flicker induced vasodilation (arteries: women 3.3%±3.2% vs. men 3.7%±5.6% increase,  $p=0.65$ ; veins: women 3.5%±3.1% vs. men 3.4%±4.0% increase,  $p=0.83$ ) and central retinal thickness ( $n=134$ , women 256±19 vs. men 263±22µm,  $p=0.06$ ).

## Conclusions

The results of this study did not reveal a sex difference in flicker light induced vasodilation between healthy young women and men. Although a tendency was observed towards increased central retinal thickness in men compared to women, this effect did not reach level of significance. Larger cross-sectional studies are required to confirm these results.

Support from the Austrian Science Fund FWF KLI 529 is gratefully acknowledged.

## 2135

### Analysis and interpretation of specular microscopy measurements of the corneal endothelium

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## Summary

The corneal endothelium plays an important role in active dehydration of the cornea in order to maintain its transparency. This very sensitive layer cannot be recovered after damage, therefore special care should be given to this hexagonal cell layer. Beside confocal microscopy, specular microscopy is widely used for measurement of corneal endothelium. The results of specular microscopy give a detailed insight into corneal pathologies and evaluation of endothelial measurement is not only restricted to cell density. This talk addresses the task of corneal endothelial measurement and especially the interpretation of the results. Clinical/therapeutic consequences of corneal endothelial cell pathologies will be discussed.

## 2334

### Acanthamoeba keratitis – when to use conservative and surgical treatment?

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## Summary

The typical clinical appearance of acanthamoeba keratitis includes pseudodendritic epitheliopathy, perineuritis, ring infiltrates or multifocal stromal infiltrates and in some cases limbitis with infiltration of the conjunctiva and/or sterile anterior uveitis. Acanthamoeba keratitis is diagnosed by polymerase chain reaction (PCR), confocal biomicroscopy, in vitro cultivation and histopathological examination. Information on reliability and efficacy of conservative and surgical therapy of acanthamoeba keratitis has only been published in case series but not yet

verified through randomized controlled clinical studies. After early diagnosis, acanthamoeba keratitis can often be successfully treated using triple topical therapy with polyhexamide, propamidine isethionate and neomycin. Topical therapy should be continued for up to 1 year. In therapy-resistant cases cryotherapy, amniotic membrane transplantation, crosslinking therapy and early therapeutic keratoplasty can be performed.

**2116**

### **Ischemic optic neuropathies: does the origin of ischemia matter?**

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#### **Summary**

Ischemic optic neuropathies represent a frequent cause of visual loss and visual morbidity. We can classify them in anterior and posterior neuropathy. It will lead to optic disc edema and optic atrophy. The exact pathophysiological processes are incompletely understood.

Anterior ischemic optic neuropathy is the second cause of optic neuropathy after glaucoma. We distinguish arteritic (A-AION) and non-arteritic (NAION). Cortisone is still the gold treatment of A-AION but new therapies are emerging as Tocilizumab.

The postulated hypothesis of non-arteritic neuropathy (NAION) is a perturbation of translaminal perfusion. Age, sleep apnea, hypertension, diabetes, dyslipidemia and crowded disc are some risk factors.

New AngioOCT will maybe help to understand the pathophysiology. The retinal ganglion cells analysis permits a good clinical correlation with visual field deficits. The loss of RGCL is present in all neuropathies but the loss speed is variable.

A better knowledge of vascular mechanism is essential to evaluate the risk profile for vascular optic neuropathy. New therapeutic strategies are now emerging but need further investigations.

**F056**

### **Vascular Complications of Optic Nerve Head Drusen**

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#### **Purpose**

To describe the clinical features of vascular complications secondary to optic nerve head drusen (ONHD).

#### **Methods**

Retrospective observational study of patients with multimodal imaging of ONHD evaluated in our department from 2008 to 2017. All subjects were submitted to B scan ultrasonography, fundus photography, fundus auto-fluorescence (FAF), optical coherence tomography (OCT) of the retinal nerve fibre layer (RNFL), and volumetric OCT scans through the optic nerve head with standard spectral-domain (SD-OCT) and enhanced depth imaging (EDI OCT). Additionally, patients with vascular complications secondary to ONHD underwent visual field test and angiography.

#### **Results**

Eighty-seven eyes of 45 patients with ONHD were evaluated. Vascular complications secondary to ONHD were found in 6 eyes (6,90%), including: choroidal neovascularization (1); anterior ischemic optic neuropathy (1); central retinal vein occlusion (1) and peripapillary retinal haemorrhage (3). Five of the six patients (83,33%) complained of recent onset visual symptoms and one was asymptomatic. The eyes affected by the retinal complication had lower



mean best corrected visual acuity (BCVA) compared to the fellow eye ( $0.55 \pm 0.37$  vs.  $1.00 \pm 0.10$ ,  $p = 0.04$ ). Visual field defects in the eyes with complications were enlarged compared to the fellow eye (mean defect  $-5.90 \pm 5.10$  vs.  $-11.64 \pm 2.35$  dB,  $p = 0.03$ ). Mean global RNFL thickness was inferior in the eyes with complications compared to the fellow eye ( $83.83 \pm 21.33$  vs.  $85.00 \pm 20.19$   $\mu$ m,  $p = 0.39$ ).

## Conclusions

OHND should not be overlooked as a harmless finding in the ophthalmic examination as around 7% disclose complications. Vascular complications of ONHD can lead to an inferior BCVA and larger visual field defects compared to eyes with only ONHD.

## S036

### Gender Differences in Symptoms and Signs of Dry Eye Disease in a Norwegian Cohort of Patients

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## Purpose

To investigate the gender disparities in dry eye symptoms and clinical signs in a Norwegian cohort of patients with dry eye disease (DED).

## Methods

One thousand and twenty-seven patients (283 male, age  $48.3 \pm 18.0$  years; 744 female, age  $54.5 \pm 15.7$  years) diagnosed with DED of different etiologies were recruited. The patients were further divided into subgroups based on age: under 20 years, 20 to 39 years, 40 to 59 years, 60 to 79 years, and over 80 years. Gender differences in Ocular Surface Disease Index (OSDI) questionnaire score, tear osmolarity, tear break-up time (TBUT), ocular surface and corneal staining, Schirmer I test, meibomian gland expressibility and meibum quality were analyzed. General linear model was used to adjust factor of age in inter-group comparisons.

## Results

Female patients presented higher OSDI scores ( $37.9 \pm 22.2$  vs.  $30.9 \pm 19.3$ ,  $p < 0.001$ ), elevated osmolarity ( $314.2 \pm 14.7$  vs.  $309.5 \pm 12.5$  mOsm/L,  $p = 0.005$ ), shorter TBUT ( $4.6 \pm 3.8$  vs.  $6.4 \pm 4.8$  seconds,  $p < 0.001$ ), more ocular surface staining ( $1.6 \pm 2.0$  vs.  $1.3 \pm 1.8$ ,  $p = 0.022$ ) and corneal staining ( $0.6 \pm 1.0$  vs.  $0.4 \pm 0.9$ ,  $p = 0.006$ ), and higher DESL ( $2.1 \pm 0.5$  vs.  $1.9 \pm 0.5$ ). No statistically significant difference was found in Schirmer I test, meibomian gland expressibility, or meibum quality. Among different age subgroups, the same pattern was found in the subgroups of 40 to 59 years and 60 to 79 years, whereas no statistically significant differences in the aforementioned parameters were found in other subgroups.

## Conclusions

In aging patients with DED, female presented with worse signs and symptoms of DED compared to males, which do not seem to be attributed to either differences in tear production or meibomian gland functionality. Interestingly, there were no significant differences before age 40. We speculate that hormonal changes in aging women may be accountable for our findings.

## T108

### Refinement for mouse EAE-model

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## Purpose

Experimentica Ltd. has been focusing on refinement in *in vivo* mouse EAE (experimental autoimmune encephalomyelitis) -model. EAE-model has been developed to study MS (multiple sclerosis) -disease, which is chronic neuroinflammatory demyelinating disorder of the central nervous system.

## Methods

Female C57BL/6J-mice were housed in IVC-cages with constant temperature ( $22 \pm 1^\circ\text{C}$ ) and controlled 12h/12h light cycle in groups of 3-6 animals. Clinical scoring (scale 0-5) was done daily to follow the progress of the disease. Follow up time was total of 28 days. Induction of EAE was done using commercial kit of MOG and PTX (Hooke Laboratories). Because EAE is severe condition, environmental disturbances causing stress were minimized, and perioperative care was provided. Several refinement methods were evaluated in order to decrease the distress suffered by the mice. Mice from two different origins were evaluated, with both lines reaching similar severity scores. In case animals were losing weight, or body temperature dropped, they were kept on heating pad for 1-3 h, where water and supportive food were provided. Supportive food and softened pellets were also given to the animals in their home cages throughout the study, starting several days before the EAE induction, so that the animals were in their best physical condition at the beginning of the study. Stress levels of animals were minimized by having small amount of people handling the animals, using cup method. Anti-skid mattresses were kept on the bottom of the cages to make it easier for the mice to move.

## Results

Mouse was placed on the heating pad with soft food, if its body mass was less than 80% of the baseline, or near the limit. In 85 % of these cases, the animals started eating and the weight increased.

## Conclusions

The refinements led to smaller number of animals euthanized due to humane endpoint.

## S030

### Novel Polymeric Inserts Comprising Nanomicelles for Topical Ocular Delivery of Cyclosporine-A

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### **Purpose**

Preparation of nanomicelles containing Cyclosporine-A (NanoCyA) to increase the drug water solubility and their loading into solid inserts to improve CyA ocular residence time and bioavailability for treatment of the Dry Eye Syndrome.

### **Methods**

NanoCyA were prepared by mixing two non-ionic surfactants (Vitamin E-TPGS and Octoxynol-40) with CyA (0.1%w/v) in water to obtain a clear dispersion suitable for eye application. Size, drug entrapment and loading capacity were assessed. FTIR analysis was also performed. Then, Nano-CyA was incorporated into a solid disc. Five different inserts were prepared by casting of aqueous dispersions containing Nano-CyA and mucoadhesive polymers (PVA, CMC, XG, ALG, CAR). The solid formulations, characterized in terms of weight, thickness and diameter, were subjected to SEM analysis, HPLC analysis of CyA content, and dissolution test. Then, the inserts were solubilized in water and subjected to DLS analysis to verify the presence of nanostructured system.

### **Results**

NanoCyA had a mean size of  $10.80 \pm 0.30$  nm, a good drug entrapment and loading capacity ( $88.9\% \pm 1.45$  and  $9.85\% \pm 0.20$ , respectively). FTIR spectra confirmed the NanoCyA nanomicelles formation. The inserts had a round shape (7 mm in diameter), weight and thickness of about 10 mg and 120  $\mu$ m, respectively, and a CyA content of 60  $\mu$ g. The insert, containing more CMC (F3), showed the smoothest uniform surface (SEM analysis) and maintained a slower CyA release (about 60%) compared to the other formulations after 6h. The aqueous dispersion, obtained by dissolution of F3 insert contained nanomicelles with a mean size of  $10.78 \pm 0.33$  nm.

### **Conclusions**

The selected formulation will be subjected to further *in vivo* animal testing to evaluate their ocular tolerability and precorneal pharmacokinetic behavior.

## **S008**

### **A synthetic metalloporphyrin SOD mimetic protects corneal epithelial cells from oxidative stress-induced damage in vitro and in vivo**

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### **Purpose**

Keratoconjunctivitis sicca (KCS) is a multifactorial disease of the tear glands and ocular surface. Increased tissue levels of reactive oxygen species and the ensuing oxidative stress are common hallmarks KCS and thought to contribute to the associated ocular surface damage. We hypothesized that metalloporphyrin superoxide dismutase (SOD) mimetics can protect corneal epithelial cells from oxidative-stress induced damage *in vitro* and *in vivo*.

## Methods

*In vitro*, human corneal epithelial cells (HCE-T) were exposed to increasing doses of tert-butylhydroperoxide (tBHP) to induce oxidative stress or sodium chloride to increase osmolarity. Cells were treated with the SOD mimetic, manganese(III)-5,10,15,20-tetrakis(N-methylpyridinium-2-yl) porphyrin pentachloride (MnTM-2-PyP) or vehicle. *In vivo*, MnTM-2-PyP (0.1% w/v in saline) was delivered topically in the SiccaSystem™ desiccating stress/scopolamine model.

## Results

MnTM-2-PyP protected HCE-T cells in a dose-dependent manner against tBHP-induced oxidative stress as assessed by resazurin cell viability assay by shifting the IC<sub>50</sub> for tBHP from 317 μM to 595 μM (0.001% w/v), 2.5 mM (0.005% w/v) and 3.4 mM (0.05% w/v). In contrast, MnTM-2-PyP did not protect HCE-T cells from hyperosmolar insult. MnTM-2-PyP permeability across HCE-T cells was assayed using a transwell system. Permeability (P<sub>app</sub>) was  $1.1 \pm 0.1 \times 10^{-6}$  cm/s and the mass balance was  $62 \pm 1\%$ , suggesting low permeability but significant cellular uptake of MnTM-2-PyP. *In vivo*, MnTM-2-PyP resulted in a statistically significant reduction of corneal fluorescein staining ( $n = 10$ ,  $P < 0.05$ ) without any signs of ocular toxicity.

## Conclusions

Our data suggest that MnTM-2-PyP, a prototypic synthetic metalloporphyrin compound with potent catalytic antioxidant activity can improve signs of KCS *in vivo* by reducing oxidative stress in corneal epithelial cells.

2632

### Novel biomaterials for ocular surface surgery

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## Summary

Biomaterials play a pivotal role in surgical therapies of ocular pathologies. They obtain relevance thanks to their unlimited availability and tunable qualities like drug delivery. Established materials like donor tissue are used in ophthalmological surgery and therefore well-established, specifically with respect to suture strength and rupture strength. Electro-spun nanofibers of polymer origin were produced and benchmarked via physico-mechanical characterization against human donor tissues. We therefore established a novel library containing suture and rupture parameter of both manufactured and tissue materials. These biomaterials were then analyzed for their possible use in cell culture and tissue engineering. Our studies show that electro-spun nanofibers are able to mimic macro- and microstructures found in human corneal tissue. They are non-toxic and support the growth of human corneal epithelial cells and corneal keratocytes. Additionally, their physico-mechanical properties position them as conceptual alternatives for use in in ophthalmology-surgery.

T086

### Augmented field of view for ocular endoscopy using deep learning

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## Purpose

In recent years, ocular endoscopy has been increasingly used for posterior segment surgery. However, ocular endoscopy suffers from several limitations, including reduced field of views and limited resolution. This study

purpose is to use a method based on deep learning to increase the field of view during the surgery by creating a dynamic map of the retina.

## Methods

The algorithm estimates the motion between two consecutive frames and start making mosaicking. In order to train it, several dataset have been used. Before the main training, the algorithm have been initialized on the public dataset "Flying chairs", containing 23 000 pairs of images. The training of the network have used 23 000 retinophotographies. Two smaller images of 384x512 pixels have been extracted from each retinophotography with their associated motion maps. This motion correspond to the movement as seen through an endoscope.

## Results

After training FlowNet Simple on the Flying Chairs, an endpoint error (EPE) of 6.25 pixels was obtained. By fintetuning on our artifiical retinal dataset, this error have been reduced to 0.69 pixels. A database of twenty four videos from ocular endoscopic surgeries (mean duration was 35 minutes, min=7minutes, max=64 minutes) have been used to validate the qualitative results.

The training needed 10 "epochs" and 20 hours of calculating on a computer equipped with a NVIDIA Geforce GTX 1080 graphic card.

## Conclusions

This study shows a new approach to build fundus dynamic map using deep learning. Initial experiments show that, unlike any other optical flow estimation method, this model can successfully capture motion be-tween ocular endoscopy image pairs. In order to make ocular endoscopy surgeries more comfortable for surgeons, our next step is to exploit the proposed strategy to start mosaicking the retina over extended time periods.

## S070

### The OBSERV platform (Ophthalmic Bioreactor Specialized in Experimental Research & Valorisation): overview of possible applications

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## Purpose

Our university lab patented 2 versions of a bioreactor (BR): one for long-term eyebanking (in the process of industrialization), the other for preclinical experimentations, called OBSERV and supported by the French Agence Nationale de Sécurité du Médicament et des produits de Santé (ANSM). Aim: to present a first series of applications developed with this platform.

## Methods

By restoring intraocular pressure (IOP) and medium renewal, the BR maintained the viability of cornea (human/animal) over a prolonged period. Its transparency allowed characterizing the tissue with existing or customized devices without compromising its sterility. IOP and medium flow rate could be adjusted. We first characterized stromal deswelling and swelling rates in different conditions in order to determine the respective roles of IOP and of the endothelial pump in hydration's control. We then performed: 1/ a series of DMEK in order to study short-term graft survival and function; 2/ endothelial cell injection therapy; 3/ implantation of a prototype artificial endothelium to study corneal deswelling; 4/ re-epithelialization of organ-cultured corneas in order to

provide high quality research grade corneas; 5/ implantation of new lyophilized amniotic membranes; 6-7/ development of models of HSV and bacterial keratitis; 8/ intra stromal pockets for implantation of innovative inlays; 9/ study of corneal biomechanics using ORA and CORVIS.

## Results

The 9 different experimentations provided reproducible results that were useful during the development of each of the projects. For each, details will be each presented in separate oral communications or posters.

## Conclusions

The OBSERV platform allows studying a wide range of corneal disease and assessing new treatments, using human or animal corneas. It complements or replaces animal experimentation for academic and industrial research.

## S052

### First case of immunohistochemical study of a corneal button after treatment by recombinant Neuronal Growth Factor (cenegermin).

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## Purpose

To provide immunofluorescence images of corneal nerves and epithelial cells in a failed penetrating keratoplasty in a patient who received recombinant Neuronal Growth Factor (NGF) for a refractory corneal ulcer.

## Methods

A 55-year-old man with a history of a major contusive trauma to his single eye had had a first penetrating keratoplasty for irreversible corneal edema. This edema was caused by contact with intraocular silicone tamponade in this aphakic aniridic eye. During surgery, an intraocular lens was sutured to the sclera and the silicone left only in the posterior pole. A refractory persistent ulcer with stromal melting developed a few months after the graft and was assimilated to a neurotrophic ulcer (trauma+360° laser photocoagulation+trephination). After failure of all conventional treatments, stable epithelial healing was achieved only by combining recombinant NGF (Cenegermin, Dompe, Italy) for 8 weeks with a bandage contact lens (continuous wear). Nevertheless, the central corneal thickness was only of 100 µm and central opacity persisted. A regraft was performed 3 months after the NGF was stopped (9 months after the first graft). The 8mm diameter corneal button was analysed by immunolabeling for  $\beta$ III-Tubulin and Neurofilaments, 2 markers of neuronal cytoskeleton.

## Results

The graft contained almost no nerves. Only very short NF+ structures were identified at the graft periphery. No  $\beta$ III-Tubulin structure was visible. No subbasal nerve was visible.

## Conclusions

In this very particular case of neurotrophic ulcer on a penetrating keratoplasty, cenegermin most certainly participated in stimulating epithelial healing. However its action on accelerating the regeneration of corneal nerves remains more hypothetic.

## F012

### Potential metabolic markers in glaucoma and their regulation in response to hypoxia

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### **Purpose**

To assess novel differences in serum levels of glucose, lactate and amino acids in patients with low-tension glaucoma (LTG) compared to age-matched controls; at baseline and in response to universal hypoxia.

### **Methods**

Twelve patients diagnosed with LTG and eleven control subjects underwent normobaric hypoxia for two hours. Peripheral venous blood samples were taken at baseline, during hypoxia and in the recovery phase. Serum glucose and lactate levels were measured by a blood-gas analyzer. Amino acids were analyzed by high-performance liquid chromatography.

### **Results**

Baseline levels of lactate and total amino acids were significantly lower in patients with LTG compared to healthy controls. No differences were seen in blood glucose levels between the two groups. Lactate levels remained unchanged during hypoxia in the control group, but increased in patients with LTG. In the recovery phase, total amino acid levels were reduced in the control group, whereas no changes were found in patients with LTG.

### **Conclusions**

Reduced serum levels of lactate and total amino acids were identified as potential markers for LTG. Moreover, significant different regulatory patterns of certain amino acids were found in patients with LTG compared to control subjects. Over all, our results suggest a link between systemic energy metabolites and LTG and support a novel understanding of glaucoma as an inner retinal manifestation of a systemic condition.

### **F104**

#### **A new reaction time test (Ocusweep® Reaction Time Test) for assessing visual performance and compliance**

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### **Purpose**

Vision is often measured without a time limit, even though visual performance is time-dependent and slow vision is inefficient in real life situations. Ocusweep Reaction Time Test (OcuRT) is a new measure of visual choice reaction time that can be used to assess cognitive speed, as well as attention and compliance in vision testing.

## Methods

59 cognitively healthy subjects were included. The stimulus in this test is a very large Landolt-C with soft edges to minimize spatial requirements of the visual system and maximize temporal performance. First, OcuRT was repeated three times. These results were compared to each other as well as to results on other measures of attention and reaction time, such as the Trail Making Test (TMT), the Useful Field of View (UFOV) test and Vienna's Simple Reaction Time (SRT) and Choice Reaction Time (CRT). To test attention to the stimulus in OcuRT, a random and variable delay is used before displaying the test symbol. Information from the delay, reaction time and wrong answers was used to compute a reliability measure to detect cheating to be both slower or faster than the person actually is. In line with this, OcuRT was done under cognitive load and with instructions to cheat the test.

## Results

The learning effect in OcuRT is small. OcuRT reaction times are significantly correlated with Vienna Simple Reaction Time and Trail Making Test B. Cheating and cognitive load significantly slows reaction time in OcuRT and decreases reliability. OcuRT is approximately five times faster to complete than Vienna's simple or choice reaction time tests.

## Conclusions

OcuRT's reaction time can be used as a basis for a more functional measure of vision, as well as reliable and quick measurements of choice reaction time. Using OcuRT together with other vision tests may be valuable in detecting inattention and cheating.

## T037

### Early changes in retinal thickness when using intravitreal Ranibizumab for age-related macular degeneration

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## Purpose

Treatment regimens for Neovascular Age Related Macular Degeneration (nAMD) have evolved over recent years. Previous real-world data in which Ranibizumab is given on a regular basis until the macula is 'dry' then a decision is made to treat as needed (PRN) have shown a significant decline in vision during the PRN phase. More recently there is increasing use of a 'treat and extend' (TAE) strategy. This more proactive approach aims to improve outcomes and offer service and capacity benefits, however little long-term data is available. We aim to provide real world visual outcome data for patients treated using the TEA strategy

## Methods

Data was analysed from electronic medical records of 126 eyes of patients who were treated according to the TEA strategy using Ranibizumab. We measured change in retinal thickness, visit frequency, injection frequency and visual acuity (VA) over time since first injection for a 36-month period.

## Results

The greatest decrease in central retinal thickness occurred within the first 12 months of treatment. A rapid gain in VA occurred during the first 3 months of treatment, improving to +8 ETDRS letters at month 12. A longer term gradual decline occurred but mean vision remained above baseline. When patients were separated into 4 groups those with lower baseline VA showed greatest benefit, with a mean VA gain of 12 letters by month 4 in the baseline VA <35 group and eyes with good baseline vision (>70 letters) maintained good functional vision. The percentage of eyes achieving 70+ letters (driving standards) nearly doubled from baseline (23%) to month 12 (40%). The mean number of injections was 7.9 in year one, 5.0 in year two and 3.9 in year three.

## Conclusions

A TAE strategy is showing favourable outcomes in routine clinical practise and may be a preferable approach to PRN.



**T053**

**Evaluation of an Artificial Intelligence clinical decision support suite for Diabetic Retinopathy and Age related macular degeneration screening**

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**Purpose**

The objective of this study was to develop robust diagnostic technology to automate Diabetic macular edema (DME), and age related macular degeneration (AMD) screening.

**Methods**

Using computer vision networks, a platform of Artificial Intelligence (AI) was developed aiming to identify DME, dry AMD and wet AMD and detect anomaly on OCT images. The data-driven deep learning system (DLS) was evaluated with a trial of 300 anonymized images in order to compare software performance vs 2 non retina specialists who individually reviewed the scans and were masked from the truth labels.

**Results**

Results of AI OCT classifications were compared to Ground Truth binary labels and also to classifications made by General Ophthalmologists. Accuracy, sensitivity and specificity were compared to Ground Truth and were found to be 0.94, 0.87 and 0.96 respectively for DME, 0.90, 0.83 and 0.92 respectively for dry AMD and 0.82, 0.96 and 0.77 respectively for wet AMD

**Conclusions**

The AI OCT Clinical Decision Support system is able to detect anomalous OCT cubes with accuracies comparable to that of General Ophthalmologists. In addition, AI performs comparably in the detection of the specific pathologies of DME, Wet AMD and Dry AMD.

**2612**

**ERM management**

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**Summary**

Epiretinal membrane (ERM) is a relatively common macular disorder causing decreased and/or distorted central vision. Since the introduction of vitrectomy for the management of ERM, increasingly successful visual outcomes have been reported in numerous studies. However, some cases show poor visual recovery even after complete ERM removal and several factors (including preoperative duration of symptoms, cystoid macular oedema and preoperative visual acuity) have been suggested as prognostic characteristics affecting the postoperative visual acuity.

With the introduction of spectral domain optical coherence tomography (SD-OCT), several features of the preretinal and intraretinal microanatomy have been correlated with the postoperative visual recovery following ERM peeling. Further, OCT has facilitated detailed visualization of the membranes and their relationship to the retinal surface. The type of ERM-macula adhesion has been shown to play a role in different aspects of ERM surgery including surgical difficulty.

The technological advances in vitreoretinal surgery simplified the procedure of ERM removal however, several controversial issues including peeling of the internal limiting membrane require further evaluation.

## **S026**

### **Use of ultra high-frequency ultrasound VevoMD (70 MHz) in ophthalmology**

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#### **Purpose**

Current ophthalmology ultrasound platforms use 10, 15 and 20MHz B-scan probes and 25 to 50MHz ultrabiomicroscopy (UBM) probes. Resolution increases with frequency whereas image depth decreases. An ultra high-frequency (UHF at 70 Mhz) ultrasound system has been commercialized in 2016 to visualize nerves, skin layers, tendons or small vessels and is used in dermatology, neonatology, rheumatology or vascular medicine. Aim: to report the very first use in ophthalmology.

#### **Methods**

The VevoMDhigh-frequency ultrasoundsystem (Fujifilm) was used with the UHF70 transducers. With a frequency ranging from 29 to 71 MHz, it announced 30µm of axial resolution, 65µm of lateral resolution, and maximal image width of 9.7mm and maximal image depth of 10.0mm. We recruited patients with different diseases requiring ultrasound examination. The probe was applied on the eye with carbomer gel as ultrasound coupling gel. When possible, the diseased eye was compared to the healthy eye.

#### **Results**

We obtained images and videos of: a spontaneous scleral fistula, iris cysts, cataracts, corneal dystrophies, anterior retinal detachments and the vitreous basis. Images were compared to the different anatomical structures of the contralateral healthy eyes. No adverse event occurred. Thanks to the small sized probe, tolerance was excellent, similar to the current ophthalmology ultrasound examination.

#### **Conclusions**

This UHF ultrasoundsystem provides high-resolution images of the anterior half of the eyeball. It can advantageously be mutualized between different medical disciplines. This first successful feasibility study prompts us to organize a comparative study with the 50MHz UBM.

## **S027**

### **Management of Salzmann's nodular degeneration by scleral contact lenses**

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#### **Purpose**

Salzmann's nodular degeneration is a rare, slowly progressive degenerative disease that is characterized by elevated bluish grey nodules that may be responsible for irregular astigmatism, decreased visual acuity and discomfort related to tear film disturbances. Usual management combines lubricants, excimer laser phototherapeutic keratectomy (with a risk of recurrence) and exceptionally lamellar keratoplasty. Aim: to present a pilot study on a non-invasive therapeutic approach by scleral contact lenses.

### Methods

Consecutive cases of symptomatic patients with Salzmann's nodular degeneration were fitted with SPOT scleral lenses (Sclerale Permeable à l'Oxygène de Thonon, Laboratoire d'Appareillage Oculaire, France). Best-corrected visual acuity (Snellen) and corneal topography (CASIA1 SS-1000) were measured before and after lens fitting. Lenses tolerance was assessed at regular intervals.

### Results

Nine patients were diagnosed between December 2015 and May 2018. Before treatment: BCVA was 6/10 (median, from 3/10 to 8/10) and irregular astigmatism in all patients. All were equipped with lenses renewal every 2 years. All presented an improvement in BCVA of 2 lines (median from 1 to 6 lines) and ocular comfort with follow-up duration of 18 months (median from 8 to 29). No surgical treatment was necessary and no adverse event occurred.

### Conclusions

Scleral lens fitting is an effective non-invasive approach to reducing symptoms in patients with Salzmann's nodular degeneration. Both vision loss related to irregular astigmatism and ocular discomfort were improved. Scleral lenses are a very interesting alternative to surgery.

### S028

#### Evaluation of the impact of tear layer thickness in scleral lenses on the optical quality of the eye by means of Optical Quality Analysis System (OQAS)

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### Purpose

To evaluate the impact of tear layer thickness in scleral lenses on the optical quality of the eye by means of the double-pass system of the Optical Quality Analysis System (OQAS, Visiometrics).

### Methods

Twenty-four eyes of 12 healthy patients with regular corneas and a best-corrected visual acuity equal or superior to 20/20 were adapted in SPOT scleral lenses (Sclerale Permeable à l'Oxygène de Thonon, Laboratoire d'Appareillage Oculaire, France). Two standardized diameters (Medium and Small) and two standardized sagittal height (3 and 2) were chosen: M3 on the right eye and S3 on the left eye. Tear layer thickness was measured by anterior segment OCT and optical quality was evaluated by HD Analyzer (OQAS). Then, they were adapted in shallower scleral lenses: SPOT M2 for the right eye and S2 for the left eye with the same examinations.

### Results

There was a statistically significant difference between optical scattering index (OSI) without scleral lens: 0.5 (from 0.26 to 0.74) and that with scleral lenses: 0.95 (from 0.38 to 1.51),  $P=0.004$ . Other statistical analyses on MTF cut off, Strehl ratio and between different lenses sizes were not significant, probably due to the small number of patients.

### Conclusions

To the best of our knowledge, no data have ever been reported on this subject. Tear layer of scleral lenses has an impact on the optical quality of the eye, in particular on OSI. This is due to the difference in index between tears and air. This can be measured easily by the OQAS. This double-pass system allows an objective measurement of the optical quality of the eye by quantifying the combined effects of optical aberrations and intraocular scattering.

## **F051**

### **Management of congenital dacryocystocele, complicated by early post-natal dacryocystitis**

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#### **Purpose**

The optimal surgical management of congenital dacryocystocele complicated by early infective dacryocystitis is still debated among experts. Treatment options, after systemic antimicrobials, are nasolacrimal probing or dacryocystorhinostomy. Our purpose is to present our experience of two cases that attended between 2003 and 2017 and their outcome.

#### **Methods**

Both cases presented in the first 4 weeks of life to our hospital, serving a population of 460,000 in Exeter, Devon, UK. The first case, in 2003, was a 20 day old boy with left dacryocystitis and localised cellulitis which required intravenous antibiotics. At 2 months old he underwent surgical management with probing with no use of silicone stenting. Abnormal cranial features were also noted and after further investigations Sæthre-Chotzen syndrome was diagnosed and positive family history was revealed. He is still followed up by our clinic. The second one was a week old girl that presented with preceptal cellulitis and was similarly treated with systemic antibiotics. Once inflammation regressed surgical management ensued with probing, using a Ritleng tube, combined with incision of the lacrimal mucosa. The tube was removed in an outpatient visit using local anaesthetic two months later.

#### **Results**

In both cases symptoms resolved permanently with no recurrence. While the first patient has an underlying syndrome that is accompanied by several other findings such as craniosynostosis and syndactyly, the second patient was completely healthy otherwise.

#### **Conclusions**

It seems that even though canalicular stenting is not mandatory, according to our experience and recent publications the optimal management of these cases is achieved with the insertion of a nasolacrimal tube (where possible) and incision of the nasal mucosa. In both cases the condition resolved. Tube removal can usually take place in an outpatient setting.

## **3462**

### **Having it all?**

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*<sup>1</sup>*

I was determined that having children would not change anything, but I chose to give up full-time employment in 1997 due to the lack of flexible options after the birth of my second child. Returning to the workplace after 3 years

I worked harder than ever to rebuild my career path. It was exhausting then and it still seems to be exhausting for many young working women today.

\r

With a well-educated daughter now at medical school I am reflecting on what expectations I have placed on her and whether “having it all” really worked out for my generation.

\r•\tIs it cool to be a feminist in 2018?

\r•\tWhat has really been achieved to improve the lives and choices for women at work?

\r•\tWhere should we go from here?

\r•\tHow can women of influence give a helping hand to those who come behind?

\r•\tWho really wants to “have it all” anyway?

### **T036**

#### **Three unusual cases of choroidal neovascular membrane (CNV) formation after pars plana vitrectomy for macular pathology**

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#### **Purpose**

To report a rare complication of choroidal neovascular membrane (CNV) after pars plana vitrectomy for macular pathology.

#### **Methods**

Retrospective case series. All cases underwent routine vitreoretinal surgery with membrane blue assisted epiretinal (ERM) and internal limiting membrane (ILM) peel at a teaching hospital in UK. We report detailed demographic details and ophthalmic findings including vision, slit lamp examination, fundus fluorescein angiography (FFA), optical coherence tomography (OCT) and treatment outcome.

#### **Results**

A total of 3 patients (1 male, 2 females) were identified. Mean age was 72.3 years and mean duration of symptoms was 5 months. 2 patients underwent surgery for ERM and 1 for macular hole. Mean pre-op visual acuity was LogMAR 0.6. All patients underwent routine surgery with standard operating time and no intraoperative complications. All cases developed CNV at approximately 3 months post-operatively, which responded poorly to 3 monthly intravitreal injections of antivascular endothelial growth factors (anti-VEGF). Because of the poor response to anti-VEGF therapy, treatment was stopped. At 9 months post-operatively, mean follow-up final visual acuity was LogMAR 1.03.

#### **Conclusions**

Most cases in literature report CNV due to iatrogenic retinal trauma. The exact cause in our series remains unknown. Plausible explanation includes post-operative inflammation and surgical stress that may have contributed to the rapid decline of protective barrier function offered by the retinal pigment epithelium or pre-existing low grade occult CNV. These cases identify the need for careful pre-surgical screening by newer imaging tools such as fundus autofluorescence and OCT angiography to detect any underlying occult disease as we operate on more and more elderly population.

### **F031**

#### **Long term follow-up of patients with plateau iris syndrome after treatment with argon laser peripheral iridoplasty**

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### **Purpose**

To assess safety and efficacy of argon laser peripheral iridoplasty (ALPI) in controlling the intraocular pressure (IOP) in patients with plateau iris syndrome (PIS) in NHS Lanarkshire over a period of 7 years.

### **Methods**

Retrospective case series. We report detailed demographic details and ophthalmic findings including visual acuities, refraction, presenting IOP, Central Corneal Thickness (CCT), Cup-to-Disc Ratio (CDR) and ocular comorbidities. Key areas of focus post-ALPI were the IOP control, the need for topical antiglaucoma medication, the need for cataract or filtration surgery, the progression of optic neuropathy and the complications post-procedure.

### **Results**

9 patients (17 eyes) were identified to have received ALPI for confirmed PIS on gonioscopy performed by a single consultant. All patients presented with repeat angle closure attack despite patent iridotomy. Most common complication was prolonged iritis (2 out of 17 eyes). Pre-ALPI IOP ranged between 10-60 mmHg with a mean of 30.6 mmHg. The mean follow-up was 29.5 months, ranging from 2 weeks to 7 years. 1 eye required trabeculectomy, 4 eyes required repeat ALPI and 1 showed progression of optic neuropathy. Post-ALPI IOP ranged between 12-32 mmHg with a mean of 19.4 mmHg at last follow-up. Pre and post-ALPI IOP difference was statistically significant ( $p=0.0175$ ). At last follow up, 6 eyes were off topical drops, 5 required monotherapy, 2 required dual therapy and 3 required triple therapy.

### **Conclusions**

This study shows ALPI to be an effective and safe means of managing acute IOP rise in patients who presented with repeat angle closure attack despite patent iridotomy. These patients need close monitoring as they may require other intervention like ocular hypotensives, cataract and glaucoma surgery. A larger sample size and longer follow up will improve the validity and quality of the study.

## **S020**

### **Keratoendotheliitis Fugax Hereditaria is Caused by a Mutation in the NLRP3 Gene**

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### **Purpose**

To describe the clinical features and the pathogenic variant in keratoendotheliitis fugax hereditaria, an autosomal dominant keratitis that periodically affects the corneal endothelium and stroma, giving in some patients raise to opacities and decreased vision.

### **Methods**

Forty-two affected and 7 unaffected subjects from 9 families, and 4 sporadic patients from Finland. Ophthalmic examination and photography, corneal topography, specular microscopy and optical coherence tomography, whole exome sequencing in 10 patients and Sanger sequencing in 34 patients.

### **Results**

Unilateral attacks of keratoendotheliitis typically occurred 1-6 times a year, starting at a median age of 11 years, and lasted for 1-2 days. The attacks were characterized by cornea pseudoguttata and haze in the corneal stroma, sometimes with a mild anterior chamber reaction. 17 patients had bilateral stromal opacities. A pathogenic variant c.61G>C in the NLRP3 gene, encoding cryopyrin, was detected in all 34 tested patients and segregated with the disease. This variant is present in both Finnish and non-Finnish European populations at a minor allele frequency of about 0.02% and 0.01%, respectively.

### Conclusions

Keratoendotheliitis fugax hereditaria is an autoinflammatory cryopyrin-associated periodic syndrome caused by a missense mutation in exon 1 of NLRP3 in Finnish patients. It is also expected to occur in other populations of European decent.

3632

### Analysing the function of BAP1 in uveal melanoma

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### Summary

Mutations in the BRCA1 associated protein 1 (*BAP1*) gene cause the BAP1 tumour predisposition syndrome (BAP1-TPDS) with an increased risk of cancers, especially uveal melanoma (UM), mesothelioma, cutaneous melanoma and renal cell carcinoma. UM is a cancer most commonly reported in patients with BAP1-TPDS (31%). The BAP1 is localized on chromosome 3p21.1, and loss of this chromosome (monosomy 3) in UM is associated with risk of metastasis. Loss of nuclear localization of BAP1 in tumour tissue also is associated with adverse outcome. BAP1 is a nuclear-localized deubiquitinating hydrolase. While BAP1 has been categorized as a tumour suppressor, it is not known if a single function of BAP1, or multiple mechanisms, are responsible for this action. BAP1 has multiple proposed functions, including involvement in DNA damage responses, transcriptional activation, chromatin remodelling, and cell cycle regulation. It seems that both nuclear localization and deubiquitinating activity are necessary for BAP1 to act as a tumour suppressor, but BAP1 protein also appears to have functions in the cytoplasm. Currently, it is not known how a loss of BAP1 leads to tumorigenesis of UM, but active research is ongoing to elucidate this.

S038

### Comparison of Ocular Surface Index Score and Clinical Dry Eye Disease Parameters in the Young (aged 0-19) and the Elderly (aged 80-99)

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### **Purpose**

To investigate differences in clinical parameters between two age groups in a Norwegian cohort of dry eye patients.

### **Methods**

Among 2016 patients undergoing treatment at The Norwegian Dry Eye Clinic between 2013 and 2018, patients younger than 20 years (n=26) and 80 years and older (n=80) were compared with regard to ocular surface disease index (OSDI) score and clinical features at their first consultation. All the patients received the same extensive dry eye examination. Independent t-test was performed for the analysis. Results are presented as mean and standard deviation. P-values of less than 0.05 were considered significant.

### **Results**

Mean age was 13.6±6.6 for the young and 83.6±3.7 for the elderly patient group. Sex distribution varied between the two groups, with 17 males and 9 females in the young age group and 14 males and 66 females in the elderly age group. In the young age group, tear film break-up time (5.87±4.83) and Schirmer 1 test (23.6±11.0) was higher compared to the age group of 80 years and more, with tear film break-up time (3.43±3.33, p=0.0064) and Schirmer 1 test (13.9±8.6, p<0.0001). Corneal sensitivity was 57.7±3.4 in the young age group and 51.6±9.5 in the elderly age group (p=0.075). Mean values of ocular surface staining were not different between the two age groups (2.3±1.99 for young versus 2.5±2.34 for elderly, p-value 0.75). Likewise, OSDI score was not significantly different between the two groups (25 ±5.8 for the young versus 29.42±2.5 for the elderly).

### **Conclusions**

Patients in the high age group had signs of more aqueous deficient dry eye disease compared to the very young age group. Interestingly, vital staining and symptom scores in terms of OSDI was similar between the two groups.

1452

### **Design of clinical efficacy and safety studies based on proteomic analysis**

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### **Summary**

Ocular surfaces are delicate structures of the anterior segment of the eye protected, nourished and lubricated by tear fluid and having they own regulatory mechanisms. Ocular surfaces are exposed environmental factors, topical ophthalmic drugs and affected by various ocular and systemic diseases. Inflammation and wound healing are vital processes involved in the defense mechanisms of the human body and pathogenesis of many eye diseases. It is also one of the most important factors in many ocular surgeries e.g. corneal, refractive and glaucoma surgery. It consists of many overlapping processes like inflammation, fibroblast activation, ECM production and remodeling of the ECM and there are many mechanisms and mediators involved in it. For clinical studies dealing with ocular surface either as a therapeutic target or possible site of adverse reactions selection of relevant biomarkers is of great importance. The presentation is focusing on detection of clinically meaningful biomarkers and their use when designing clinical study protocols. The main focus is in using tear fluid proteomics and mass spectrometry for the improvement of the cost-efficacy of the clinical studies in development of new therapeutic options for eye diseases.

1855

### **Ocular surface and proteomic safety biomarkers in topical medication**



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### Summary

Ocular surfaces are delicate structures of the anterior segment of the eye protected, nourished and lubricated by tear fluid. The system has its own regulatory mechanisms. Ocular surfaces are exposed to environmental factors, topical ophthalmic drugs and affected by various ocular and systemic diseases. Chronic topical glaucoma medication is an important risk for the ocular surface disease. It is also a risk for the failure in glaucoma surgery. The mechanism of failing glaucoma surgery is related to the presence of inflammatory cells, accumulation of extracellular matrix proteins in the conjunctiva and the site of surgery, activation of matrix metalloproteinases and their tissue inhibitors and accumulation of oxidized lipids in the conjunctiva and around the site of operation and glaucoma shunts. Tear fluid proteome is a novel technique to get detailed information about the processes of the anterior surfaces of the eye and could easily be performed. It is a powerful tool when developing new, more efficient and safer therapeutic options for eye diseases. It has also proven to be a promising technique for detecting biomarkers for ocular surface disease, ocular inflammation and predicting thus the success of glaucoma surgery.

**2161**

### Cholesterol oxidation and cataract

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### Summary

The plasma membranes of lens fiber cells (LFCs) are the most cholesterol-rich in the human body. The presence of cholesterol concentrated clusters and cholesterol bilayers assists the formation of lipid rafts in LFC plasma membranes. The high levels of cholesterol in the older LFCs is surpassed by dihydrosphingomyelin, the most abundant lipid. These features mean LFC membranes are highly ordered and so even with ageing, there is little turnover of these lipids. Rather the lipid membranes become more ordered as the levels of sphingolipids increase with age. Another consequence of long-lived lipids in LFCs is that peroxidation increases with age and some, such as 7-keto cholesterol, correlate with age-related cataractogenesis. Besides the ageing process, ionising radiation (IR) is another cause of both lipid peroxidation and cataracts. We therefore hypothesize that IR leads to cholesterol oxidation and thus facilitates cataractogenesis by disrupting plasma membrane structure and function. Exposure to X-rays (0.1-4 Gy) confirmed IR-induced oxysterol formation in bovine and mouse lenses both in a time- and dose-dependent manner.

**3636**

### Ethical issues of prognostication in uveal melanoma

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### Summary

Objectives :

Uveal melanoma (UM) is the most common primary eye tumor. Up to 50 % of patients with UM will develop metastases. Prognostication is based on clinical, morphological and genetic cancer features. Chromosome 3 loss and chromosome 8 gain in uveal melanoma are associated to metastatic death.

High-risk patients can be monitored more closely for metastatic disease, so that intervention can be initiated earlier. Such patients may be eligible to clinical trials to evaluate prophylactic systemic therapies. However, no adjuvant treatment has so far extended survival in these patients.

Prognosis is an issue that most doctors describe as difficult to discuss but there is a lack of guidance for clinicians on the best way of approaching prognostic discussions.

Methods:

There is two steps in our study.

We propose a two'step study with (i) semi-structured interviews conducted with six practitioners specialised in UM and two researchers then (ii) a questionnaire to be disseminated in international reference centers in order to compare current practices. Data from the first step will be qualitatively analysed, focusing on physicians' views on communication of prognosis and current practice of delivering prognostic information.

## T009

### **Aflibercept inhibits physiological revascularization and pathological neovascularization in the mouse and rat oxygen-induced retinopathy models**

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#### **Purpose**

The purpose of the study was to quantitatively compare the mouse and rat oxygen-induced retinopathy (OIR) models by determining the effect of aflibercept on retinal revascularization, neovascularization and microgliosis.

#### **Methods**

C57BL/6J mice were exposed to 75% O<sub>2</sub> for five days from postnatal day 7 (P7) to P12. Sprague Dawley rats were exposed to the alternating 50/10% oxygen protocol from P0 to P14. Treatments were administered by intravitreal injection (0.5 µl for mice, 1 µl for rats) on P14. Control groups were sham-injected or left untreated. Retinal vasculature was labelled with Isolectin B4 and avascular areas (AVAs) and neovascularization (NV) were quantified. Microgliosis was visualized with anti-Iba1 antibody staining and quantified using stereology.

#### **Results**

All untreated mice exposed to hyperoxia developed significant vascular abnormalities on P17 (AVA: 16 ± 5.8%; NV 7.7 ± 2.4%). Rats showed a less severe phenotype, where 43% of retinas had AVAs of <5% (mean: 8.4 ± 7.3%) and 71% of retinas had less than 1% of NV (mean: 0.7 ± 0.6%). Aflibercept increased the size of AVAs (47% in mice and 213% in rats) and inhibited NV (98% in mice and 82% in rats), compared to control retinas. PBS injection decreased AVAs by 31% and reduced NV by 42% in mice; a similar effect was not observed with control IgG in the rat OIR

model. Both mouse and rat OIR models resulted in significant microgliosis ( $128 \pm 39$  vs.  $65 \pm 1.2$  cells/mm<sup>2</sup>,  $P=0.01$  in mice and  $406 \pm 171$  vs.  $230 \pm 96$  cells/mm<sup>2</sup>,  $P=0.009$  in rats).

### Conclusions

The mouse OIR model produced more pronounced pathological changes compared to the rat model. Aflibercept blocked physiological revascularization and pathological neovascularization in both species. The robustness of the response makes the mouse OIR model particularly well-suited for efficacy pharmacology studies targeting neovascular processes.

### S092

#### TIM2: a new player in iron homeostasis in the retina

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### Purpose

The retina specifically needs iron, an essential component of the phototransduction cascade. Ferritin, known for its classical role in iron storage and detoxification, and, more recently, as an iron-transporter protein, binds to several cell receptors, such as Scara5 and TIM2. Although Scara5 was recently described in the retina for the first time, the presence of TIM2 remains unknown. This study aimed to unravel the presence of TIM2 in the mouse retina and characterize the retinal localization of TIM2.

### Methods

Immunohistochemistry and western blot analysis were performed to detect and characterize retinal TIM2 expression. Spleen was used as a positive control tissue.

### Results

The presence of TIM2 in the retina was confirmed by western blot analysis. Immunolabeling against TIM2 revealed that TIM2 was expressed throughout the entire retinal parenchyma, predominantly focused in the ganglion cell layer. Furthermore, TIM2 was strongly expressed in Müller cells with higher immunoreactivity in cell processes and endfeet adjacent to the internal limiting membrane, while weakly expressed in the periphery of bipolar, amacrine and horizontal cells nuclei and the inner segments of rods. No expression of TIM2 was found in astrocytes, ganglion cells or cones. Moreover, TIM2 expression was not detected within the vessel nor in endothelial cells.

### Conclusions

Taken together, our results showed that Müller cells, the principal retinal glial cells, are the main cells expressing TIM2 in the retina. Interestingly, Müller cells are responsible for maintaining retinal homeostasis and have been considered as important mediators of iron transport, distribution, and regulation in the retina. TIM2 high and specific expression in Müller cells, together with the involvement of these cells in iron homeostasis, unravels TIM2 as an important player in retinal iron homeostasis.

### T100

#### Retinal ganglion cells loss and caspase 3 activation after ocular hypertension

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### **Purpose**

To analyze the course of retinal ganglion cell (RGC) loss together with the activation of the apoptotic protein caspase 3 at increasing times after ocular hypertension (OHT).

### **Methods**

OHT was induced by laser photocoagulation of limbar and episcleral veins in the left eyes of albino Swiss mice. Intraocular pressure (IOP) was measured with a TonoLab®. Animals were analyzed at 3, 4, 5, 7, 15 or 30 days after OHT. Retinas were dissected as wholemounts and doubly immunodetected against Brn3a and cleaved-caspase 3 (c-casp3) to identify surviving and apoptotic RGCs, respectively. Total numbers of Brn3a+RGCs were automatically quantified and total numbers of c-casp3+RGCs were manually quantified. The distribution of both populations was analyzed by colour isodensity maps.

### **Results**

Laser treatment induced a significant IOP elevation from 24h to 5 days. Afterwards, IOP returned to basal values. RGC loss was first significant at day 3 after OHT, progressing thereafter up to day 30 when 15% of the original population of RGCs survived. This course correlated with the activation of c-casp3, which was significant at day 3, peaked at day 4, and gradually decreased until day 30.

### **Conclusions**

Our data show that OHT in mice results in an early and progressive loss of RGCs that is concomitant with the activation of caspase 3, indicating that OHT triggers RGCs death which is, at least in part, caused by apoptosis caspase 3 dependent.

## **3445**

### **Local tumour control rate and late complications of fractionated stereotactic radiotherapy in uveal melanoma**

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### **Purpose**

Fractionated stereotactic radiotherapy (fSRT) for uveal melanoma (UM) treats the tumour, while retaining visual function. The aim of our study is to evaluate tumour control, late complications and survival of patients treated with fSRT.

### **Methods**

We analysed 187 small to medium-sized uveal melanoma, treated with fSRT from 1999-2014 in Erasmus Medical Center Rotterdam and Rotterdam Eye Hospital, the Netherlands. We included tumours with at least 4 years of follow up. Therefore, tumours treated after April first 2014 were excluded.

### **Results**

The mean tumour thickness decreased from 5.9 mm at baseline to 1.9 mm 4 years after fSRT. Tumour progression was observed in 5% of the melanoma patients after a mean of 33 months. Twenty eight tumours were secondarily enucleated, due to neovascular glaucoma (n=17), tumour progression (n=10) and other reasons (n=1). The most common side effects were radiation retinopathy (to some extent) in 27%, vitreous hemorrhage in 18% and neovascular glaucoma in 14% of the patients. The mean disease free survival was 66 months (SD 48 months).

## Conclusions

The local tumour control rate is 95% in uveal melanoma patients treated with fSRT with 16 years of follow up.

2351

## The physics of light scattering changes with aging

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## Summary

It is well established that disability glare derives from the optical effect of light scattering in the human eye media, causing the visual effect of ocular straylight, and the associated desensitization of the eye. Light scattering removes part of the light from the optical projection on the retina. In light scattering physics this removal of light is called scattering extinction, and adds to the more well-known absorption extinction. In the present study we derived from earlier measurements the extinction values and correlated those with the straylight values as they can be measured clinically as log(s) with the C-Quant from Oculus.

Light scattering was measured for a number of discrete scatter angles and wavelengths for 15 human eye lenses extracted from donor eyes, aging 43 to 82 years. The visually important type of scatter yielded extinctions for a wavelength at the top of the visual spectrum (561 nm) from 2.5% to 20.7% for 14 lenses, and 33.9% for the most cataractous lens. Correlation with the straylight value resulted in  $\text{extinction} = 0.01007 \times 10^{\log(s)}$ . Added to this is non-visually effective Rayleigh type scattering, and the respective extinctions were 1.4% to 25.1% for 14 lenses, and 43.3% for the most cataractous lens.

3422

## Straylight and the slitlamp image: functional effects of scattering versus morphology

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## Summary

The crystalline lens of the human eye scatters part of the light entering the eye, causing the visual phenomenon of light radiation seen around bright lights against a dark background. This is called straylight. It is the basis of much visual disturbance, in particular glare while driving at night, but also problems such as difficulty recognizing faces. The slit lamp image is also based on light scattering, but in the opposite (backward) direction. In the present study both phenomena will be compared.

Forward scatter originates from particles of about wavelength size distributed throughout the lens. Most of the slit lamp image originates from much smaller particles (Rayleigh scatter). For slit lamp observation close to the reflection angles, zones of discontinuity ("Wasserspaltten") at anterior and posterior parts of the lens, show up as rough surface reflections. For retro-illumination imaging it will be argued that the density or opacity seen in areas of cortical or posterior subcapsular cataract show up because of light scattering, not because of light loss. In a

study of 15 lenses extracted from donor eyes, aging 43 to 82 years, backward scattering intensity was around 10x weaker as compared to forward scattering at 10 degrees.

**2343**

### **Uveitis and histopathology in 2018**

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#### **Summary**

Histopathology is only used as all other diagnostic technics are inconclusive. It is far from routine practice and even in specialised uveitis clinics rarely invasive techniques are performed unless the common anterior chamber taps for PCR. Specialised laboratory techniques are necessary because of the small number of cells present in the vitreous in comparison with other cytology specimens. Flow cytometry is an alternative valuable technique but with loss of microscopic images and controls. Histopathology is possible after concentration of the ample cells. In our institute we use a standardised protocol with the Cellient® tissue processor (Hologic). A cell block is automatically prepared and routine stainings, immunohistochemical techniques and genetic analysis can be performed to exclude or diagnose sarcoidosis, malignancies, granulomatous inflammations or more.

**1845**

### **Second cancers in survivors of hereditary retinoblastoma**

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#### **Summary**

Retinoblastoma (Rb) is the most common intraocular malignancy in children. At least 40% of all cases consist of the heritable form of Rb in which patients carry a germline mutation in their RB1 gene and have a 50% chance of passing this mutation on to their offspring. In high resource countries, as a result of better diagnosis and treatments, most Rb patients survive and live into adulthood but they have to deal with the late effects of the disease and its treatment.

Heritable Rb patients are carriers of mutations in the RB1 tumor suppressor gene, which is associated with increased risk of second cancers. Heritable Rb patients have an increased risk of developing (osteo)sarcomas, melanomas and epithelial cancers. The risk of developing sarcomas is increased even more when patients are treated with irradiation therapy. Considering this, systemic chemotherapy and other new therapies have taken a more dominant place in the treatment of Rb although it remains to be seen what the effects of these new therapies are on second cancer development.

Unfortunately for now, because of the excellent survival from Rb itself, second cancers currently are the leading cause of death in patients with heritable Rb.

**F084**

**Optic nerve biopsy in unexplained progressive optic neuropathy**

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**Purpose**

To present two cases of unexplained progressive optic neuropathy in which MRI scanning remained inconclusive, but optic nerve biopsy helped find the diagnosis.

**Methods**

After lack of response to treatment and progressive visual decline, an optic nerve biopsy was performed in both. In one patient cerebral tissue was biopsied as well.

**Results**

Both biopsies demonstrated the presence of pilocytic astrocytoma.

One patient had an associated malignant glioma of the cerebral tissue (multicentric glioma).

**Conclusions**

In cases of unexplained progressive optic neuropathy with the other eye at risk, we propose there is still a place for optic nerve biopsy in rare and well-defined cases.

**T121**

**Epidemiology in paediatric non-infectious uveitis treated with tumor necrosis factor-alpha inhibitors: a retrospective study**

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**Purpose**

To report the epidemiological data of children with non-infectious uveitis in a tertiary center and to evaluate the efficacy of treatment with infliximab and adalimumab.

**Methods**

Retrospective analysis of 88 patients with uveitis diagnosed ≤16 years attending Ghent University Hospital from 2002 to 2017. Epidemiological data of children with non-infectious uveitis receiving anti-TNF-α therapy was collected (n=33; 52 eyes). Efficacy of treatment was evaluated by visual outcome and grading of anterior cells (SUN criteria).

**Results**

The mean age at diagnosis was  $7.48 \pm 4.5$  years. Uveitis was anterior in 69.7%, intermediate in 15.2%, posterior in 0% and panuveitis in 15.2%. The course was mainly chronic (75.8%). Etiology included Juvenile Idiopathic Arthritis (60.7%), Behçet's disease (3%), TINU syndrome (3%) and Sympathetic Ophthalmia (3%). The remaining uveitis cases were idiopathic (30.3%). The cohort included 33 patients (52 eyes) of whom 4 received infliximab, 22 received adalimumab and 7 received both. In the majority of cases (94%) anti-TNF-α therapy was given after failure of non-biological DMARDs (>methotrexate). Significant improvement was observed following anti-TNF-α therapy.

Baseline results versus results at 3 and 6 months from the onset of biologic therapy: cells in the ocular anterior chamber significantly declined ( $p < 0.05$ ) whereas visual acuity improved (19.1% at 3 months and 27.3% at 6 months).

### Conclusions

Anti-TNF- $\alpha$ , primarily infliximab and adalimumab, are used as second line agents in paediatric non-infectious uveitis refractory to non-biological DMARDs, or as first-line treatment in severe complicated disease. Anti-TNF- $\alpha$  therapy is effective in paediatric non-infectious uveitis of mixed origin.

3424

### Comparison between two scatter parameters in a population under age 65 : the C-quant (Oculus) and the HD Analyser (Visiometrics)

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### Summary

We present the results from the selection centre for the Belgian Army and for civil aviation licencing. We use the C-Quant (Oculus) for the evaluation of glare and the HD-Analyser for optical quality.

When comparing the two straylight parameters, Log(s) and OSI, of these instruments, the measurements show a wide range. Log(s) measures glare, while OSI is heavily influenced by optical aberrations.

I will present our data after refractive surgery, and in patients with intra-ocular lenses keratoconus, some types of cataracts as well as our normal data. The problem of a normal value in a young population will be discussed.

Cases with very different values obtained with the two instruments will be shown.

The reasons for these differences are the totally different concept of measuring straylight. The HD-Analyser projects a small laserspot on the retina and deduces all his parameters from the energy distribution in the reflected image. The C-quant stimulates with a peripheral light source and uses a psycho-physical procedure to extract the visual influence on central vision.

T120

### Clinical characteristics and complications in intermediate uveitis: analysis of 15-years experience in a tertiary center for uveitis in Belgium

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### Purpose

To report the clinical characteristics and complications of intermediate uveitis (IU) in 83 patients in a tertiary referral center for uveitis in Belgium.

### Methods

A retrospective cohort study of patients with IU attending Ghent University Hospital from 2002 until 2018.



## Results

83 patients (152 eyes, 55,2% females) were included with mean age at presentation of 27 years. Mean follow-up was 103 months. The most common type was idiopathic (n = 50), followed by pars planitis (n=13), and IU associated with multiple sclerosis (MS) (n=10), sarcoidosis (n=4), Lyme disease (n=3), tuberculosis (n=2) and syphilis (n=1). Epiretinal membrane (61,4%), cystoid macular edema (CME) (49,4%), cataract (30,1%), secondary glaucoma (13,2%) and retinoschisis (12%) were the most prevalent complications. Most sight-threatening complications were CME and glaucoma. Late complications affected mainly the posterior segment and included epiretinal membrane formation, retinoschisis and vitreous haemorrhage. Treatment included local and systemic steroids, immunosuppressive agents and biologics apart from antibiotics in infectious uveitis. Systemic treatment was indicated in case of a drop of visual acuity  $\geq 2$  lines and/or CME. More than half of the patients (n=55) received systemic treatment according to the Belgian Guidelines for the treatment of non-infectious uveitis.

## Conclusions

In our Belgian tertiary center IU was mostly idiopathic, followed by pars planitis and MS-associated. Systemic treatment was indicated in more than half of the patients proving that IU needs a strict follow-up and rarely achieves prolonged remission.

2114

### Choroidal and retinal occlusive vasculitis

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## Summary

Choroidal and retinal occlusive vasculitides are potentially sight-threatening conditions. They may be isolated or associated with inflammatory or infectious retinal and choroidal diseases, including Behçet's disease, sarcoidosis, acute retinal necrosis syndrome or tuberculosis. In addition to thorough clinical workup, ancillary testing such as conventional fluorescein and ICG angiography, combined with more recent diagnostic tools including OCT angiography may help the clinician in identifying those cases at high risk of developing or presenting with retinal or choroidal neovascularization. Therapy is targeted at stopping the progression of ischemia, reducing or eliminating neovascularization, and controlling associated intraocular inflammation. Tips regarding identification and assessment of acute emergencies as well as chronic uncontrolled cases will be reviewed.

S024

### Clinical Outcomes for the Treatment of Corneal Blindness using an Epidescemetic Keratoprosthesis

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## Purpose

to report the successful outcome of penetrating keratoplasty (PKP) following KeraKlear keratoprosthesis (Kpro) implanted in severely diseased corneas.

## Methods

the KeraKlear Kpro can be used as a temporal device in severely diseased corneas in order to quite the clinical condition. The subsequent explantation of the Kpro allows further recovery and improvement of the condition that permits the practice of PKP as a final successful solution.

## Results

four diseased corneas of 4 patients were implanted with KeraKlear Kpro. Following this surgery, the patients partially restored vision allowing the improvement of corneal comorbidities and decreasing the amount of neovascularization. However, after the explantation of the Kpro, further improvement happened allowing the successful indication of PKP afterwards, with good outcome. The BCVA improved from perception of light to 20/400 before the Kpro implantation to a mean of 20/740 with the Kpro and afterwards to a mean of 20/130 after Kpro explantation and PKP. The mean time between the implantation and the explantation of the KeraKlear Kpro was 2.2 years (SD=1.3). All cases remained stable with no evidence of corneal complications.

### Conclusions

the KeraKlear Kpro can be used as a temporal device in severely diseased corneas in order to quite the clinical condition. The subsequent explantation of the Kpro allows further recovery and improvement of the condition that permits the practice of PKP as a final successful solution.

### S061

#### Testing ANN: a neural network to guide keratoconus treatment with ICRS

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### Purpose

to described and validate a neural network aiming to optimized the treatment of keratoconus with ICRS

### Methods

A neural network created from a large number of cases implanted with the different models available of ICRS. Preoperative and postoperative data: visual and refractive parameters, corneal topography and pachymetry was analyzed. To create a model that correctly maps the input to the output using historical data so that the model can then be used to produce the output when the desired output is unknown. Two groups of patients were compared: a) commercial group (simulation of postoperative results from commercial nomogram) and b) neural network group (simulation of postoperative results from the decision proposed by the neural network).

### Results

Fifteen cases with ages ranging from 26 to 49 years (mean age of  $37.00 \pm 7.69$  years) comprised this study. In the commercial group was observed a reduction of flattest keratometry (K1) ( $49.24 \pm 4.66D$  to  $46.26 \pm 3.41D$ ), steepest keratometry (K2) ( $52.98 \pm 4.81D$  to  $50.18 \pm 4.78D$ ) and mean keratometry (KM) ( $51.11 \pm 4.66D$  to  $48.22 \pm 4.02D$ ). In the neural network group was observed a reduction of K1 ( $49.24 \pm 4.66D$  to  $48.14 \pm 4.34D$ ) of K2 ( $52.98 \pm 4.81D$  to  $50.76 \pm 4.30D$ ) and KM ( $51.11 \pm 4.66D$  to  $49.45 \pm 4.25D$ ). No significant differences between the study groups were found in K2 and KM values ( $p=0.06$  and  $p=0.18$ , respectively). However, significant differences between groups were found in K1 values ( $p=0.04$ ).

### Conclusions

Neural network analysis correctly proposed an adequate ICRS selection for the treatment of keratoconus. Increasing the input data into a neural network may lead to a more accurate and optimized results.

### S056

#### Corneal posterior surface characterization in normal and keratoconus patients according to the degree of visual limitation

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## **Purpose**

To describe and analyze the main features of the corneal posterior surface in normal and keratoconus patients taking into account the severity of the visual function.

## **Methods**

Retrospective, clinical study evaluating 477 eyes. All patients were classified according to the degree of the visual limitation as follows: normal group: patients with corrected visual acuity (CDVA) of 1,000 in the decimal scale; grade I, CDVA between 0,900 and 0,980; grade II, CDVA between 0,600 and 0,880; grade III, CDVA between 0,400 and 0,580; grade IV, between 0,200 and 0,380 and grade Plus, less than 0,200. All patients were evaluated using rotating Scheimpflug camera and Placido disc topographer device (Sirius system, CSO, Firenze, Italy).

## **Results**

A significant difference were found in all pair of groups, including normal and keratconic patients, when evaluating the mean steepest posterior keratometric reading (K2) at 3 and 5 millimeters ( $p \leq 0,03$ ) and the root mean square per area unit (RMS/A) at 4,5 and 8 mm ( $p \leq 0,01$ ). Additionally, a high and statistically significant difference was observed between normal and grade I keratoconus patients when analyzing K2 at both 3 and 5 mm ( $p < 0,01$ ). No significant differences were found when comparing the most severe grades (IV and Plus) in terms of K2 and RMS/A ( $p > 0.100$ ).

## **Conclusions**

Corneal posterior analysis in normal and keratoconus patients correlated well with the degree of visual limitation. Posterior keratometry and root mean square per area unit allow us to discriminate between normal and keratoconus patients and also to characterize the severity of the disease according to the visual impairment

## **T041**

### **Retinal oximetry in young patients with type 1 diabetes compared to healthy controls**

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## **Purpose**

Diabetic retinopathy (DR) is characterized by retinal vascular changes, which include oxygen saturation (SO<sub>2</sub>) increase in retinal vessels. We examined the SO<sub>2</sub> in retinal arteries and veins in a cohort of young people with type 1 diabetes (T1D).

## **Methods**

The Atherosclerosis and Childhood Diabetes Study is a prospective population-based study on early atherosclerosis in childhood onset T1D. 324 subjects with T1D aged 8-18 y and 118 age-matched healthy controls were included at baseline in 2006, and followed-up every 5th year. During the ongoing 10 y follow-up, eye examination and oximetry (Oxymap, Iceland) was performed. To date, 119 participants have been examined, 85 with T1D and 34 healthy controls. Mean duration of T1D was 16 years.

## **Results**

Twelve subjects with T1D had mild, 6 had moderate, and 2 had severe non-proliferative DR. In the control group the mean artery and vein SO<sub>2</sub> was respectively 91.9 % and 60.6 %. In the T1D group the mean artery and vein SO<sub>2</sub> was respectively 92.0 % and 60,6 %. There was no significant difference in SO<sub>2</sub> in arteries (mean difference: 0.13, 95% CI: -1.20 to 1.47,  $p = 0.84$ ) and veins (mean difference: 0.01, 95% CI: -1.87 to 1.91,  $p=0.99$ ) when comparing the two groups, but arterial SO<sub>2</sub> increased with increasing grade of DR, the mean values being, respectively: 92 % for no DR, 90 % for mild, 95 % for moderate and 96 % for severe DR. No increase in SO<sub>2</sub> was observed in the veins.

## Conclusions

The data show results from one third of the cohort subjects included in the study to date. SO<sub>2</sub> in retinal arteries was found to increase with increasing grade of non-proliferative DR, which was not the case for veins. Prospective observational studies are needed to show whether changes in retinal SO<sub>2</sub> precede or follow the development of DR, and whether changes occur on the arterial side first.

## F015

### CyPass Ultra: Preloaded delivery system for the CyPass Micro-Stent

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## Purpose

Several novel surgical treatment options and devices for glaucoma, collectively referred to as “micro-invasive glaucoma surgery” (MIGS), have recently been developed to safely, effectively, and sustainably reduce intraocular pressure (IOP). The CyPass Micro-Stent is a 6.35 mm-long device placed in the supraciliary space, creating an outflow pathway from the anterior chamber to the suprachoroidal space. The stent is positioned through a clear corneal incision after being inserted on a small guidewire. The new CyPass Ultra System is a pre-loaded device designed to streamline the implantation process.

## Methods

The CyPass Micro-Stent and applier (CyPass 241) is a well-validated design, following a rigorous, risk-based approach, with safety and effectiveness in lowering IOP demonstrated by results of the COMPASS trial. The new pre-loaded system, CyPass Ultra, is an evolution of CyPass 241 that replaces the manual loader with a loader tip affixed to the distal end of the applier housing the stent, and utilizes a similar drive mechanism for stent loading and delivery.

## Results

The design enhancement for CyPass Ultra builds upon the validation of the CyPass 241 design, and data demonstrating that the new pencap loader allows for ease of loading and resetting of the CyPass Ultra system. In addition, interim 3-year results from the COMPASS 5-year extension study are in line with results from the core study, showing similar safety outcomes for CyPass Micro-Stent with cataract surgery as compared to cataract surgery alone, as well as sustained IOP lowering efficacy through 48 months post-surgery. Final 3-year results of the extension are pending.

## Conclusions

The data generated to date demonstrates the CyPass Ultra pencap loader system provides a design enhancement, and builds upon the proven safety and effectiveness of the previous CyPass system design.

## F028

### Evaluation of a 24 Hour Circadian Rhythm Model for Intraocular Pressure after Implant with a Supraciliary Micro-Stent

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## Purpose

To evaluate a model for the daily fluctuation of intraocular pressure (IOP), and evaluate this model in glaucomatous eyes implanted with the supraciliary micro-stent (CyPass®, MS) with cataract surgery (gp1) versus eyes with cataract surgery alone (gp2) from the COMPASS trial

## Methods

The model parameters were mean IOP (M), amplitude (A), and phase (P). The model is  $IOP = M + A \cdot \cos(2\pi \cdot (t - P)/24)$  where t is time (h) on a 24 h clock. The parameters were estimated using Markov chain Monte Carlo (MCMC) Bayesian methods (PROC MCMC SAS v9.4), where the prior parameter distributions were estimated from an earlier 24 h IOP measurement study. This circadian model was then fit to the unmedicated IOP groups of the COMPASS study. IOP was measured at 8 am, 12 pm, and 4 pm.

## Results

In the COMPASS trial, 73% of gp1 patients had a  $\geq 20\%$  decrease in unmedicated diurnal IOP from baseline at month (m) 24 vs 58% in gp2 ( $P=0.002$ ). Mean IOP at m24 was 16.6 mmHg (95% credible interval [CI], 16.3–16.9) in gp1 and 17.7 mmHg (95% CI, 17.4–18.1) in gp2 (difference  $-1.1$  mmHg [ $-1.6, -0.6$ ]) with  $>99\%$  probability that gp1 had a smaller mean. The amplitudes (mean [95% CI]) for gp1 and 2 were 0.36 (0.22, 0.50) and 0.69 (0.33, 1.08) mmHg (difference 0.33 mmHg [ $-0.07, 0.74$ ]) with a 94% probability that gp1 had a smaller amplitude. Mean phase was 6.3 h (5.6, 7.1) for gp1 and 10.7 h (10.1, 11.4) for gp2 (difference  $-4.4$  h [ $-5.5, -3.4$ ]) with a  $>99\%$  probability that gp1 had a smaller mean.

## Conclusions

The MS reduced the mean IOP and diurnal IOP fluctuations. Average IOP was lower in gp1 by 1.1 mmHg, with a peak at 6.3 h in the morning vs 10.7 h for gp2, indicating that the MS provides better IOP control during early morning, and lowers IOP throughout the day. Reduced diurnal IOP fluctuations may have implications for progression of disease.

## F029

### Comparing the predicted efficacy of one versus two supraciliary micro-stents for lowering intraocular pressure in glaucoma patients using an ocular computational fluid dynamic model

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## Purpose

To evaluate the potential benefit of implanting more than one supraciliary micro-stent (MS, CyPass®) with cataract surgery in glaucoma patients, a computational model was developed to simulate MS implantation and to compare the intraocular pressure (IOP)-lowering effect of one or two MS.

## Methods

A computational multi-physics model representing an average human eye, incorporating physiologic mechanical and hydraulic properties, enabled simulation of device implantation and fluid flow/pressure in the entire eye with or without an implanted MS. Ocular geometries were constructed representing eyes with 0, 1, or 2 MS. Aqueous humor was treated as a simple fluid, all other tissues were modeled using porous flow. Hydraulic resistance of the trabecular meshwork and ciliary body were adjusted to reproduce the pressure and outflow characteristics of normal and glaucomatous eyes. The resistance of the suprachoroidal space was held very low, consistent with free movement of fluid in this space.

## Results

Structural simulations reproduced clinical OCT images of the conformation of the device and of a tented fluidspace allowing unobstructed fluid flow between the aqueous humor and supraciliary space. While qualifying the model using pre- and post-treatment IOP measurements from implanting a single device from the COMPASS clinical trial, it was determined that a single MS defeats the pressure gradient across the ciliary muscle, which separates the aqueous humor from the suprachoroidal space.

## Conclusions

Since a single MS is able to allow the pressure in the suprachoroidal space to equilibrate to within 0.2 mm Hg of the pressure in the aqueous humor, there would be no additional benefit provided by implanting a second MS.

**3633**

### BAP1 in iris lesions

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## Summary

The survival of iris melanoma is significantly higher compared with uveal melanoma in general. Loss of chromosome 3 has been described in 15-45% of iris melanomas. Iris melanomas harbor a molecular profile comparable to both choroidal melanoma and cutaneous melanoma. 80% of iris melanomas carry activating mutations in *GNAQ* and *GNA11*. Mutations in *SF3B1*, *EIF1AX* and *BAP1* are detected in 7%, 17% and 43% of cases respectively. *BAP1* mutations in iris melanoma are not correlated to worse prognosis. Mutations in *NRAS*, *BRAF*, *PTEN*, *c-KIT*, and *TP53* have been found in iris melanoma as well. The mutations that were found in the cutaneous melanoma associated genes of iris melanomas could not be correlated to ultraviolet light damage.

Iris nevi harbor mutations in *GNAQ* and *GNA11*. Mutations in *BAP1* have been detected in 3 iris nevi, 2 of which were classified histologically as borderline malignant. Such cases might be designated as iris melanocytic tumors of uncertain malignant potential (IMTUMP). This would be justified by a combination of histologic and molecular findings.

Iris melanoma and iris nevi should be considered a distinct subgroup, on the basis of clinical and histopathologic criteria but also on molecular grounds.

**1242**

### Standards and guidelines for the interpretation of sequence variants

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## Summary

In the past years, sequencing technology has evolved with the advent of next-generation sequencing (NGS). Genetic testing including analysis of single genes, gene panels, exomes, genomes, and transcriptomes lead to an increasing catalogue of sequence variants. This poses new challenges in sequence variant interpretation. The use of a classification system into five categories ("pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign") will be discussed and is based on population data, phenotypic information, computational data, functional data, segregation data, etc. It follows the 2015 American College of Medical Genetics and Genomics–Association for Molecular Pathology (ACMG–AMP) guidelines, and discusses a more recent classification system called Sherloc, supporting a more consistent approach to variant classification.

These standards and guidelines for variant interpretation will be illustrated with examples in ophthalmic genetics.

References: Richards et al. Genetics in Medicine 2015 17(5):405-24. doi: 10.1038/gim.2015.30; Nykamp et al. Genetics in Medicine, 19(10): 1105–1117. doi: 10.1038/gim.2017.37

## **S111**

### **Vivinex® toric lenses refractive results after cataract surgery, preliminary study including 50 eyes**

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#### **Purpose**

To evaluate the refractive results of Vivinex® toric intraocular lenses after a cataract surgery.

#### **Methods**

We performed a prospective study including 50 eyes of 25 patients, who had a cataract surgery, operated by a unique surgeon, using Callisto® Zeiss with automated conjunctival recognition for the alignment of Vivinex® toric lenses (Hoya). Preoperative corneal astigmatism was evaluated using both corneal topography (OPDII, Nidek) and IOL master 700R keratometry (Carl Zeiss Meditec). The lens power calculator was performed by the on line Toric calculator (V4 Hoya). Postoperative criteria were uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), residual subjective astigmatism and lens rotation observed with a photography (Eyesuite®, Luneau).

#### **Results**

Patients mean age was 69,5 years. Lens distribution was: 45,5% of T3 models, 45,5% of T4 models, and 9% of the T5 one. Mean preoperative astigmatism was 1,53D. Mean postoperative UCVA was 7,7/10, including all lenses. Mean BCVA was 9,8/10. A BCVA>8/10 was obtained in more than 1/3 of patients (36%). The medium residual subjective astigmatism was 0,43D. The mean lens rotation was measured at 4,6°. Thanks to premium lenses, we are now able to perform cataract surgery as a refractive surgery. Toric Vivinex® lens recently arrived in France during 2017 summer. This lens is a new preloading monobloc hydrophobic IOL, which permits to correct corneal astigmatism from 0.75D to 4D. Refractive results are comparable to those obtained with other toric lenses as SN6AT (Alcon) and 709MP (Carl Zeiss Meditec), which are already available, and recently reported by the same author.

#### **Conclusions**

This preliminary study shows satisfactory refractive results and lens stability after one month.

## **S013**

### **Aniridia-Related Keratopathy in naïve corneas and after keratolimbal allograft**

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#### **Purpose**

To compare the structural changes of aniridia patients in naïve corneas that were transplanted for the first time with those after keratolimbal allograft (KLAL) with advanced aniridia-related keratopathy (ARK). In the KLAL transplantation procedure, corneoscleral rims are used for limbal stem cell transplantation and 180° crescents are transplanted to the host eye in order to surround the patient's limbus. It is a procedure of choice when there is primary limbal involvement with minor conjunctival changes, such as in ARK.

## Methods

Two naïve corneal buttons from patients with advanced ARK submitted to penetrating keratoplasty for the first time and one corneal button from an ARK patient that had undergone a KLAL were collected at surgery and imbedded in paraffin. Two healthy donor control corneas were included. Serially sections were treated with antibodies against extracellular matrix components in the stroma and in the epithelial basement membrane (collagen I and IV, collagen receptor  $\alpha 11$  integrin and laminin  $\alpha 3$  chain), as well as markers of fibrosis, wound healing and vascularization (fibronectin, tenascin-C, vimentin,  $\alpha$ -SMA and caveolin-1). The samples were collected with approval of the Regional Ethical Committee.

## Results

Both naïve ARK and KLAL ARK corneas had irregular epithelium, disrupted epithelial basal membrane and similar histopathological changes in the stroma. Collagen lamellae showed an irregular pattern and collagen I was absent in all ARK corneas. The ARK corneas displayed a subepithelial pannus with blood vessels demonstrated by the immunostaining with caveolin-1 and collagen IV.

## Conclusions

The stromal changes associated with ARK were also present after keratolimbal allograft. Our data suggest failure of the keratolimbal allograft in establishing a normal corneal epithelium and protecting the stromal transparency.

## T057

### Efficacy and safety of corticosteroid implant (Fluocinolone Acetonide (FAc) 0.2 µg/day, Iluvien®) for management of Diabetic Macular Edema (DME): a real-life study

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## Purpose

To evaluate efficacy and safety outcomes of Fluocinolone Acetonide (FAc) in the management of Diabetic Macular Edema (DME) in a real-life setting. The advent of Anti-VEGF raised a new hope of pharmacological treatments. However, their effects are short, require repeated injections and can help only in a subset of patients. Intraocular injections of glucocorticoids seem to be effective in reducing DME.

## Methods

Retrospective analysis of 25 eyes treated with FAc, (38,9% treated bilaterally) from 18 diabetic retinopathy patients. Efficacy outcomes [visual acuity (VA), central retinal thickness (CRT), macular volume (mv)] and safety outcomes [cataract surgery, intraocular pressure (IOP)] were measured at baseline, month 1, 3 and every 3 months. Mean follow-up was 18.5±7.0 months (mean±standard deviation)

## Results

At baseline 11 eyes were vitrectomized, 21 pseudophakic, 16% treated with anti-glaucoma drugs and 1 with previous trabeculectomy. Mean HbA1c was 7.8% and, except for 1 patient, diabetic control was poor even with endocrinology help. Before Iluvien implantation, 100% of patients performed laser, 4% bevacizumab, 83.3% ranibizumab, 12.5% aflibercept, 45.8% triamcinolone and 62.5% dexamethasone. At last observation, CRT was significantly lower than baseline ( $p=0.001$ ). MV was significantly lower than baseline at 6th month ( $p=0.012$ ). Mean change from baseline to last observation visit of VA and IOP was 3.74 letters and 0.1 mmHg. IOP emergent medications were used in 13.2%. 3-out-of-4 patients were submitted to cataract surgery.

## Conclusions

This cohort shows that one-single intravitreal Iluvien could improve VA and CRT in non-responsive patients to previous therapies. IOP was manageable with no safety concerns. Due to corticosteroids properties in reducing inflammation and in neuroprotection, we suggest an early use of the implant.



S053

### Orbital biomechanical changes in Graves' disease and Thyroid eye disease: application of Corvis ST

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#### Purpose

Thyroid eye disease (TED) is an auto-immune condition linked to Graves' disease, with orbital biomechanical changes. Corvis ST is a non-contact Scheimpflug-based tonometer that perform the *in vivo* study of cornea biomechanics. The aim of this work is to understand the clinical application of Corvis ST in TED and Graves' disease.

#### Methods

For the study, 92 normal eyes, 28 eyes with Graves' disease without ophthalmologic disease and 18 eyes with TED were selected and examined with Corvis ST. Statistic tests with Statistical Package for Social Studies were performed.

#### Results

Mean age of the subjects was  $52.2 \pm 13.1$  years-old and 72.2% were females, without significant differences between groups. Curvature radius highest concavity (CRhc) mean (mm) was  $7.41 \pm 0.823$  in control's group,  $7.25 \pm 0.995$  in Graves' group and  $6.78 \pm 0.724$  in TED's group, with a significant difference ( $F_{2,137}=4.19; p=0.017; \eta^2=0.058$ ) between control's and TED's ( $p=0.014$ ). A1 length and deflection amplitude had differences between groups ( $X^2(2)=7.41, p=0.025$ ;  $X^2(2)=9.95, p=0.007$ ), with significantly higher mean ranks in Graves' than in control's ( $p=0.018$ ;  $p=0.042$ ). Central corneal thickness ( $\mu m$ ) had lower mean in TED's ( $525 \pm 26.9$ ), without significant differences between groups ( $545 \pm 36.2$  in control's,  $539 \pm 30.6$  in Graves').

#### Conclusions

TED's group had a significantly lower CRhc mean, which means a lower orbital compliance that is independent of Graves' disease. For clinical practice, CRhc mean can be a valuable tool for TED screening. One possible future approach is to prospectively follow Graves' patients and perform CRhc repeated measurements to study its value for an earlier TED detection. The statistically significant differences between controls' and Graves' points to previously made associations between extra-ocular thyroid disease and corneal biomechanics alterations.

F071

### Evaluation of retinal thickness asymmetry in patients with multiple sclerosis against healthy controls

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#### Purpose

To evaluate the homogeneity and/or asymmetry of retinal thinning in eyes of patients with multiple sclerosis (MS) compared to healthy controls (HC)

#### Methods

82 eyes from 37 healthy controls and 44 eyes from MS patients (of whom 4 had suffered a previous optic neuritis episode [ON]) were included in the study. Retinal measurements were performed using the Posterior Pole Retinal

Thickness Map [Displays the retinal thickness over the entire posterior pole (30° x 25° OCT volume scan)] of Heidelberg Spectralis optical coherence tomography (OCT) device, and analyzed using the 8x8 grid positioned symmetrically along the fovea to disc axis (mean retinal thickness is given for each cell). We analyzed the mean thickness of full retina at superior, inferior, nasal, and temporal halves of the grid, and also calculated the hemisphere asymmetry (comparing thickness of nasal vs temporal and superior vs inferior).

## Results

patients with MS showed a significant reduction of every single half of the full retina compared with healthy controls (superior  $p=0.001$ , inferior  $p<0.001$ , nasal  $p<0.001$  and temporal  $p=0.003$ ), but there were no significant differences between the superior versus inferior thickness (HC=7,02±4,40 mm vs MS=6,81±4,37 mm,  $p=0.640$ ) and nasal versus temporal thickness (HC=35,36±6,43 mm vs MS=33,39±9,65 mm,  $p=0.169$ ). In eyes of MS patients with a previous ON episode, also there was not a significant asymmetry between the superior and inferior half and between the temporal and nasal half ( $p=0.586$  and  $p=0.359$  respectively).

## Conclusions

patients with MS present a homogeneous reduction of retinal thickness objectivable using the hemisphere asymmetry. This loss is not significantly asymmetrical but it seems to be more pronounced at inferior half ( $p<0.001$ ), indistinctly of previous episodes of optic neuritis.

## F072

### Retinal thinning in patients with multiple sclerosis: evaluation of the pattern of retinal loss during disease progression

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## Purpose

To evaluate progressive changes in the retinal thickness pattern during the course of multiple sclerosis (MS) evolution.

## Methods

37 eyes from healthy controls and 40 eyes from MS patients were included in the study. Retinal measurements were performed using the Posterior Pole Retinal Thickness Map [Displays the retinal thickness over the entire posterior pole (30° x 25° OCT volume scan)] of Heidelberg Spectralis optical coherence tomography (OCT) device, and analyzed using the 8x8 grid positioned symmetrically along the fovea to disc axis (mean retinal thickness is given for each cell). We analysed the mean thickness of the full retina at the 64 obtained cells, dividing MS patients in 5 different groups at intervals of 5 years of disease duration.

## Results

Patients with MS showed a significant reduction ( $p<0.001$ ) of retinal thickness in the 27 cells that surround the fovea (4 central cells), which seems to be preserved during the 10 first years of disease. An emergence of “hot spots” of retinal thinning ( $p$  between 0.001-0.045) was observed surrounding the fovea in group 1, further thinning points were observed towards the periphery of the grid in group 2, but foveal thickness was still preserved. A significant reduction ( $p<0.001$ -0.002) of retinal thickness around the fovea and affecting foveal thickness was

found in groups 4 and 5. The peripheral cells presented progressive thinning along the groups, with significant thinning affecting the whole grid in group 5.

### Conclusions

Perifoveal and slight papillomacular boundle thinning is objectivable in the first stages of multiple sclerosis with preserved central foveal thickness. After 10 years since diagnosis, a completely damaged papillomacular boundle can be observed, with loss of foveal thickness and expanding retinal thinning towards the arcuate fascias.

2521

### TFOS DEWS II Definition and Classification Report

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### Summary

The new definition of dry eye disease (DED) recognizes the multifactorial nature of dry eye as a symptomatic ocular surface disease where loss of homeostasis of the tear film is the central pathophysiological concept.

The key etiologies of tear film instability, hyperosmolarity, and ocular surface inflammation and damage were determined to be important for inclusion in the definition. In the light of new data, neurosensory abnormalities were also included in the definition for the first time.

The classification of DED, moving from a clinical approach based on signs and/or symptoms, introduces the concept of the existence of a continuum between aqueous deficient and evaporative dry eye.

F032

### The promoter polymorphism -308G>A in the gene of Tumor necrosis factor alpha and the risk for open-angle glaucoma in Bulgarians

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### Purpose

Tumor necrosis factor alpha (TNF- $\alpha$ ) has been recognized to play an important role in the pathogenesis of glaucoma, which is characterized with damages in optical nerve. The normal tissues express TNF- $\alpha$  receptor 1 (TNFR1) in the vasculature of the optic nerve, but do not express at high level TNF- $\alpha$ , while in the retina of glaucoma patients it has been observed elevation of both TNF- $\alpha$  and TNFR1. Several genetic polymorphisms have been described in the *TNFA* promoter region, as *TNFA* -308G>A was found to influence TNF- $\alpha$  expression. In the current studies we investigated the possible role of *TNFA* -308G>A SNP (rs1800629) in development of open-angle glaucoma in Bulgarian population.

### Methods

We genotyped 65 patients with glaucoma and 172 control individuals by PCR-RFLP method.

### Results

The rare AA genotype was significantly more frequent in patients with glaucoma (8%) than controls (2%) ( $p=0.038$ ). Thus, the carriers of AA genotypes appeared to have 4.69-fold higher risk for development of glaucoma than the G genotype carriers (GG+GA) (OR=4.69, 95% CI: 1.20-18.32). Although not statistically significant, we observed that patients with AA genotype had more frequently family history of glaucoma (3 out of 5, 60,0% vs. 15 out of 60, 25%). Moreover, carriers of A allele genotypes (GA+AA) had lower thickness of the cornea of both eyes (right:  $519.3 \pm 31.4 \mu\text{m}$  and left:  $519.7 \pm 31.4 \mu\text{m}$ ) compared to those with GG genotype (right:  $539.9 \pm 39.8 \mu\text{m}$ ,  $p=0.090$  and left:  $541.7 \pm 39.0 \mu\text{m}$ ,  $p=0.067$ ).

## Conclusions

The results of our study suggest that the homozygous AA genotype of *TNFA* -308G>A SNP might be predisposing factor for open-angle glaucoma, and even more, the genotypes supposed to enhance the expression of TNF-alpha cytokine (GA+AA) may influence also the progression of glaucoma by decreasing the central cornea thickness

## S095

### Lactate: More than merely a metabolic waste product

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## Purpose

Intact energy metabolism is essential for cellular survival, and the retina is by far the most energy consuming organ in the body. Likewise, retinal lactate concentrations exceed any other organ specific lactate concentration in the body. Thus, we propose that elevated lactate in the retina must play a predominant role in maintaining survival and function of various retinal cells. The aim of this study was therefore to examine the effects of extracellular lactate on Müller cell and retinal ganglion cell (RGC) survival and function.

## Methods

Human Müller cell lines, primary mice Müller cells and RGC were treated +/- L-lactate. Simultaneously, the cells were incubated +/- 6 mM of glucose. Lactate transport was blocked by MCT inhibitors, 4-CIN and D-lactate. The effects of lactate-receptor GPR81 activation were evaluated by the addition of a GPR81 agonist. Cell survival was assessed through MTT viability assays. Cellular bioenergetics was examined and supplemented with total ATP measurements provided by a commercial assay. <sup>13</sup>C labeling studies were performed to evaluate metabolism of lactate and glucose. Finally, Müller cell function was evaluated by measuring the ability to take up glutamate.

## Results

Present study identified lactate metabolism in Müller cells and retinal ganglion cell as a crucial component in sustaining survival and function. Besides being an active metabolite, and not merely a metabolic waste product, lactate was also shown to display signaling abilities through GPR81 activation, which boosted retinal metabolism.

## Conclusions

Present study provides evidence for lactate-mediated neuroprotection of the inner retina, however future investigations of retinal lactate in whole tissue samples are required to unravel potential pharmaceutical targets, ultimately leading to novel therapies in the cure of inner retinal diseases e.g. glaucoma.

**T068**

**A case of total retinal detachment associated with AIDS-related cytomegalovirus retinal necrosis: the role of combined surgery**

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**Purpose**

The aim of the study is to evaluate the role of combined surgery including scleral buckling (SB) and pars plana vitrectomy (PPV) in the management of total retinal detachment associated with acquired immunodeficiency syndrome (AIDS) related cytomegalovirus (CMV) retinal necrosis.

**Methods**

A 42-year-old man, a case of total retinal detachment associated with AIDS-related retinal necrosis after CMV retinitis. The right eye was blinded 2 years ago. For 3 years he has received highly active antiretroviral therapy (HAART) at outpatient department of infectious diseases without regular follow-up. Our patient had progressively lessening vision to light perception in the left eye. He was administered intravenous valganciclovir with HAART (abacavir, lamivudine and aluvia) and he did not receive intravitreal injection. The CD4+T-cells were 160 cells/mm<sup>3</sup> on moment of surgery treatment. Retinal detachment associated with giant ( $\geq 5$  clock hours) zone of retinal necrosis and PVR grade B/C. The management of total retinal detachment on left eye included PPV and local SB. Our patient underwent 23G PPV with membrane peeling, fluid-air exchange, laser endophotocoagulation and silicone oil tamponade. The localization of scleral buckling seized the zone of necrosis of giant retinal necrosis.

**Results**

We achieved retinal attachment with heavy silicone oil tamponade and local scleral buckling. Postoperative best corrected visual acuity (BCVA) was 5/200. In this clinical case we didn't receive complications of surgery.

**Conclusions**

Development of a retinal detachment associated with large zone of CMV retinal necrosis. The localization of SB should match of zone retinal necrosis. Retinal attachment can be achieved with combined surgery including SB and PPV in the management of total retinal detachment associated with AIDS related CMV retinal necrosis.

**T084**

**Our experience two steps surgical treatment of optic disk pit maculopathy**

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**Purpose**

To evaluate the long-term clinical efficacy and safety of combined treatment of optic disk pit maculopathy with two steps: 1) laser photocoagulation for chorioretinal adhesion of the temporal borders of the optic disk; 2) pars plana vitrectomy and SF<sub>6</sub> tamponade.

**Methods**

The two women with unilateral maculopathy associated with optic disc pit. Initial treatment (step 1) of optic disk pit maculopathy in our patients include chorioretinal adhesion by laser photocoagulation of the temporal borders of the optic disk. Step 2 – following pars plana vitrectomy with pneumatic displacement of the retinal elevation with gas SF<sub>6</sub> injection without focal laser photocoagulation. Patients were followed up for 26–48

months after treatment. Main outcomes were determined by optical coherence tomography (OCT) and best-corrected visual acuity (BCVA).

#### Results

The macular pathology of our patients consisted of macular intraretinal schisis and macular detachment. OCT showed cystoid spaces intraretinally within the outer nuclear layer and subretinal fluid underneath the outer photoreceptor elements. The macular edema finally resorbed 9 months after surgical treatment. This fact was documented at clinical examination, fundus photography and OCT. The follow-up of our patient was 26–48 months, final visual acuity 0.1-0.2. No post-operative complications of maculopathy occurred during the follow-up period.

#### Conclusions

Two steps management included: step 1 – laser photocoagulation; step 2 – pars plana vitrectomy with SF6 tamponade is still a simple, effective, minimally invasive, and economic therapy for optic disc pit maculopathy. OCT demonstrated disappearance of intraretinal schisis and subretinal fluid after the treatment. Surgery should be more sparing and improving visual acuity.

1832

#### Mitochondria to money, how to get that funding

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#### Summary

Mitochondria to money, how to get that funding.

No area of research has a monopoly on funding but there is no doubt that rare, or orphan, disease has been an area where attracting funding has been especially difficult. The situation has begun to change and the importance of rare ocular disease has begun to attract attention. This presentation will outline the opportunities and strategies for obtaining funding, give concrete examples and attempt to clarify some useful tips and dispel some myths.

2364

#### Novel strategies to treat autosomal dominant optic atrophy

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#### Summary

Autosomal dominant optic atrophy (ADOA) is the commonest inherited optic neuropathy

(incidence 1:12-15,000) and in over 70% of patients is due to mutations in the nuclear gene,

OPA1. ADOA present in children and young people and is a cause of blindness, which may be slowly progressive in adult life.

OPA1 protein is targeted to the mitochondria and is required for the normal control of mitochondrial fusion and maintenance of mitochondrial DNA, cristae structure and

membrane potential. OPA1 mutations have been linked with impaired cellular bioenergetics, reduced cellular ATP production and increased production of ROS.

Retinal ganglion cells (RGCs) are particularly susceptible to damage caused by loss of mitochondrial function. They first become dysfunctional and then die, by apoptosis, which then leads to blindness. Currently there is no treatment for ADOA, and there thus exists a clear unmet clinical need.

The aim of current research is to develop a treatment to correct the mitochondrial function in patients with ADOA and thereby to prevent blindness. There are a number of potential avenues being investigated, from gene therapies to pharmacological interventions.

**3524**

#### **Genetic biomarkers in ophthalmology**

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#### **Summary**

The role of genetics in ocular disease is well established and recognised as significant across a range of common ocular disease to those that are classified as rare or orphan diseases. Genetic biomarkers have become a subject for considerable interest and research in glaucoma, age-related macular degeneration, amongst other conditions. This talk will examine the range of markers, with concrete examples from across a wide range of ocular diseases, and summarise the evidence for their relevance and potential for their use as a guide to improving diagnosis, prognostic accuracy or therapeutic efficacy.

**F105**

#### **The influence of cataract light scatters on retinal vessel oxygen saturation**

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#### **Purpose**

The aim of our study was to compare metabolic (oxygen saturation; %) and anatomical (retinal vessel diameter;  $\mu\text{m}$ ) retinal vessel oximetry (RO) parameters of patients with cataract formation against those of controls with clear lenses.

#### **Methods**

A total of 96 eyes of 62 subjects were examined: 51 eyes of 33 cataract patients (mean age: 64.8y) were compared to 45 eyes of 29 controls with clear lenses (mean age: 61.5y). RO was performed with the oxygen saturation measurement tool of the RVA (IMEDOS Systems UG). The oxygen saturation in all major peripapillary retinal arterioles (A-SO<sub>2</sub>) and venules (V-SO<sub>2</sub>) were measured and their difference (A-V SO<sub>2</sub>) was calculated. In addition, we evaluated the corresponding diameter in retinal arterioles (D-A) and venules (D-V). Cataract formation was

graded according to the lens opacities classification system III (LOCS III). For statistical evaluation ANOVA-based linear mixed-effects models were calculated (SPSS®, pairwise comparisons: Bonferroni-corrected;  $p < 0.05$ ).

### Results

Cataract eyes showed significantly lower A-SO<sub>2</sub> and A-V SO<sub>2</sub>, when compared to healthy controls ( $p = 0.002$  and  $p = 0.05$ ). Within cataract group, cortical opacities showed significant interactions with the A-SO<sub>2</sub>, V-SO<sub>2</sub> and the A-V SO<sub>2</sub> parameters ( $p = 0.027$ ;  $p = 0.002$ ;  $p = 0.026$ , respectively).

### Conclusions

These data indicate that the cataract induced light scatter influence optical retinal oxygen measurements. Cortical opacities showed the highest influence on RO measurement, when compared to nuclear opacification, nuclear color and posterior cataract formation. Significantly lower A-SO<sub>2</sub> and A-V SO<sub>2</sub> values in all cataract eyes suppose subclinical ischemia in patients with cataract formation.

## F019

### Long-term follow-up of transscleral cyclodiode for rubeotic glaucoma

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### Purpose

To assess the long-term outcome of patients treated with cyclodiode for rubeotic glaucoma over an 18-year period.

### Methods

A consecutive retrospective case series of 15 eyes of 14 patients that underwent cyclodiode laser treatment for rubeotic glaucoma at a single eye unit between 1999 and 2004.

### Results

Ischaemic central retinal vein occlusion was diagnosed as the cause of rubeotic glaucoma in 50% of patients (7 of 14). Five of fourteen patients (36%) had a diagnosis of diabetes. There was a drop in intraocular pressure (IOP) in all patients. The mean reduction in IOP was 31 mmHg.

Hypotony occurred in 40% of eyes (6 of 15). Five patients required re-treatment. The most recent intraocular pressure ranged from 2 to 42 mmHg. Two of the patients had pressures of above 21 mmHg at long-term follow-up. Seven of fourteen patients died over this period. Amongst this group, the mean period they survived after requiring cyclodiode treatment was 10 years.

### Conclusions

We conclude that cyclodiode is an effective treatment for raised intraocular pressure in rubeotic glaucoma but may need repeating. It is noteworthy that 50% of patients died over the 18-year follow-up period.

## F025

### Nutritional oral supplement containing L-arginine, L-citruline, $\alpha$ -lipoic acid, vitamin B2, vitamin B12, folic acid and Gingko biloba in primary open angle glaucoma patients - a prospective, randomized, controlled study.

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### **Purpose**

To evaluate the effect of the new oral dietary supplement Neuxoft® (Ofta), composed of L-arginine, L-citruline, α-lipoic acid, vitamin B2, vitamin B12, folic acid and Gingko biloba extract on disease progression in primary open angle glaucoma (POAG) patients over a 6-months follow-up period.

### **Methods**

In this prospective, open-label, randomized, controlled trial, 78 eyes of 39 patients with mild to advanced POAG and intraocular pressure well controlled with topical antiglaucoma medications were recruited and randomized into two groups, according to supplementation: (1) oral supplementation with Neuxoft® q.d., (n = 20, mean age 60,3±14,5); (2) control group without any oral supplementation (n = 19, mean age 50,6±13,9). All subjects underwent visual field (VF) tests by frequency doubling technology perimetry (FDT 30-2, Humphrey Matrix, Carl Zeiss Meditec) and retinal nerve fiber layer imaging using scanning laser polarimetry (GDx PRO, Carl Zeiss Meditec) at the beginning of the study (baseline) and after 3 and 6 months respectively. Mean deviation (MD), pattern standard deviation (PSD), peripapillary retinal nerve fibre layer thickness (RNFL) divided into superior sector, inferior sector and cumulative as well as global nerve fiber index (NFI) were considered for the analysis.

### **Results**

None of analyzed parameters : visual field indices (MD, PSD) and nerve fiber layer parameters (RNFL, NFI) showed differences between the control and study groups at the beginning and end of the follow-up. Besides, all the comparisons of these parameters among groups during each visit were also statistically non-significant (p>0.05).

### **Conclusions**

Oral supplementation composed of L-arginine, L-citruline, α-lipoic acid, vitamin B2, vitamin B12, folic acid and Gingko biloba showed no influence on glaucoma progression in studied POAG patients in this short term observation.

## **2142**

### **Role of other biologics in adult uveitis patients**

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### **Summary**

Several studies have demonstrated the efficacy of anti-TNF antibodies in the treatment of non-infectious uveitis. Importantly, in most of the cases, anti-TNF were given to patients resistant to classical immunomodulators and despite this selection of resistant patients are considered efficient in 60 to 80% of the cases. There is no doubt that this is a major breakthrough in the field. However a less optimistic view of those data is that many patients will still be resistant to one classical immunomodulator and one anti-TNF antibody. The management of such patients is particularly challenging and we generally offer them to switch to a different anti-TNF antibody or use a different biological agent. In this context, a plethora of other biologics targeting relevant inflammatory pathways have been extensively tested in other immune mediated diseases. However, data regarding their potential efficacy in uveitis are only available for some of them and unfortunately there is no information about the possibility of predicting a clinical response. There is thus paradoxically a wide range of exciting therapeutical options in those difficult uveitis cases that contrast with a lack of guidelines.

2323

### Ageing, neuronal metabolism and mitochondria in glaucoma

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#### Summary

**Background:** Glaucoma is one of the most prevalent neurodegenerations and neuroprotective strategies are of great therapeutic need. Determining the early molecular events that occur in glaucoma may lead to the development of neuroprotective treatments.

**Methods:** In this study we utilized RNA-sequencing, neurobiological, and cell molecular techniques to elucidate the very earliest mechanisms of retinal ganglion cell degeneration in the DBA/2J mouse model of glaucoma.

**Results:** We determine that metabolism and mitochondrial health decline with age and is exacerbated by periods of high IOP. This is coupled with a marked age-related reduction in retinal NAD<sup>+</sup> levels. Restoring NAD<sup>+</sup> (via nicotinamide treatment, *Nmnat1* gene therapy, and/or the addition of WLDS protein) improves mitochondrial health and potentially protects from glaucoma protecting up to 95% of eyes from severe glaucoma. We next identify an IOP-dependent decline in retinal pyruvate levels. Restoring pyruvate levels also prevents glaucoma in mouse and rat models.

**Conclusions:** Targeting neuronal metabolic decline and neuronal mitochondria may offer safe, neuroprotective treatments for glaucoma and other age-related neurodegenerations.

1744

### The role of the microglia in age-related macular degeneration

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#### Summary

Age-related macular degeneration (AMD) is a leading cause of blindness in industrialized countries. The etiology of AMD is not completely understood. However, genetic association studies in large patient cohorts and *in situ* analyses in AMD eyes as well as animal models mimicking some features of AMD have identified an important contribution of dysregulated innate immunity in the eye. Our data revealed local dysregulation of complement factors in ocular fluids of AMD patients and found a correlation of disease progression with hyperreflective foci (HF) as potential imaging markers for retinal immune cells. Furthermore, using a light damage paradigm and laser-triggered CNV in mice we established a comprehensive analysis of microglia and macrophages in the retina. Resident microglia-specific targeting of key immune pathways and immunomodulatory compounds could elucidate a vicious cycle of microglia reactivity, retinal degeneration and neoangiogenesis. These findings together provide evidence for an interaction of reactive microglia with aberrant complement proteins in the pathogenesis of AMD.

1733

### Minimally-invasive surgical treatment of AAK

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## Summary

Aniridia Associated Keratopathy (AAK) is common cornea disorder in patients with congenital aniridia. Stage III and IV require corneal pannus removing due to significant decrease of Visual Acuity (VA). Corneal pannus removing surgery is simple procedure which does not require general anesthesia and is safe to the patients. Corneal pannus removing increase VA and ocular surface condition.

2132

## High resolution anterior segment OCT CASIA 2 for corneal and anterior segment diagnosis

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## Summary

CASIA 2 SS Optical Tomography is a device for non-contact anterior eye segment imaging. CASIA 2 employs Fourier Domain method at a wavelength of 1310nm, which leads to advanced anterior eye segment imaging. With CASIA 2, the light source of coherency functions is improved, and higher sensibility toward depth is realized compared to other OCT devices. It is possible to measure from anterior cornea to posterior lens within one scan. Scanning depth is approximately 13 mm. Axial resolution is 10  $\mu$ m and horizontal one is 30  $\mu$ m. Scanning speed is 50 000 A scans per second. Morphological and morphometric evaluation is possible. The basics of optical coherence tomography will be presented. Clinical examples will include the use of SS-OCT in glaucoma, corneal infections, eye trauma, qualification of patients for corneal transplants, refractive surgery, cataract surgeries and cross-linking will be presented. At the end, a short quiz will follow.

S099

## Aflibercept Treatment Leads to Vascular Abnormalization of the Choroidal Neovascularization

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## Purpose

Recent studies do not support the hypothesis of vascular normalization in eyes receiving various intravitreal anti-vascular endothelial growth factor (VEGF). In this retrospective study using OCT angiography (OCT-A) we measured complexity level of choroidal neovascularization (CNV) during Eylea treatment.

## Methods

This retrospective study considered 57 eyes of 32 patients with vascular age-related macular degeneration (AMD) undergoing aflibercept treatment. In this study, we measured the vessel density, Horton-Strahler (HS) ramification ratio i.e. complexity level, and the length ratio in 14 eyes with choroidal neovascularization treated with 3–5 Eylea injections, 17 eyes receiving 1–2 injections, and 14 treatment-naïve eyes.

Macular 6 × 6 mm scans were acquired using the DRI OCT Triton by a single trained technician. OCT-A images were standardized, binarized, and skeletonized using ImageJ. Then, the HS analysis of the CNV was performed.

## Results

After quality check only 57 images were included. We found that the vascular density significantly decreases after an anti-VEGF injection 36 and 93 versus 41 and 87 in treatment-naïve patients. Moreover, CNV before the treatment and in a group with 3–5 injections was more complex than after receiving 1–2 injections. The branch length was not changed.

## Conclusions

Our data suggests that repeated anti-VEGF can lead to vascular abnormalization, causing the CNV to be more complex. This may be one of the mechanism responsible for tachyphylaxis during the treatment.

## S044

### Blinking during exercise affects tear osmolarity

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## Purpose

Purpose: Physical exertion leads to rise in tear osmolarity (Tosm). However, previous studies were conducted mostly on males and did not consider the possible alteration in blinking during physical exercise.

## Methods

16 women and 18 men aged 25.09±1.70 were divided into equal groups with eyes open and shut. Participants performed 8-min medium-intensity exercise and 5-min intense exercise on cycloergometer. Tosm (in mOsm/L) was tested before T0, between medium T1 and intense and after exercise T2. Blinking rate was assessed in a group with eyes open. Tear break up time (Tbut) was measured in T0 and T1.

## Results

With Tosm measuring 305.72±1.22 and 313.56±1.90 for men and women, respectively, we observed significant differences in T1. During T2, Tosm in men was 303.3±1.28 vs 310.87±1.36 in women. Blinking rate decreased from 14.24±2.54/min before T0 to 9.41±2.83/min in T1. There was a statistical significant change in Tosm in both groups, that is, in the group with eyes shut from 300.53±1.37 in T0 to 308.06±1.55 in T1 to 304.88±1.54 in T2. In the group with open eyes, Tosm increased from 300.29±1.37 in T0 to 310.76±1.55 in T1 and then dropped to 308.88±1.54. Tbut measured in T0 was 14.7±1.43 vs. 13.53±1.48 in open eyes group.

## Conclusions

Due to physical exercise, short-term changes in Tosm are partially caused by altered blinking. Gender differences in Tosm in response to exertion might confirm the relationship between total body water and Tosm.

## T076

### The role of disorganization of inner retinal layers as predictive factor in patients with epiretinal membrane

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## Purpose

The purpose of this retrospective study was to determine if disorganization of the retinal inner layers (DRIL) in spectral domain optical coherence tomography (SD-OCT) is predictive of postoperative visual acuity in patients with epiretinal membrane (ERM).

## Methods

Participants in the study were 28 consecutive patients diagnosed with ERM, who underwent pars plana vitrectomy for ERM. Best corrected visual acuity (BCVA) measurement and SD-OCT were performed at baseline

(preoperatively), and at months 1, 3 and 6 postoperatively. The DRIL extent and additional OCT parameters were assessed at 1-mm wide foveal centered area.

## Results

There was statistically significant difference in BCVA and central retinal thickness between baseline and month 6. DRIL was observed in 22 out of 28 patients of our study sample (78.6%). Greater DRIL extent at baseline was correlated with worse baseline BCVA, while ellipsoid zone disruption and cystoid macular edema were also significantly associated with worse BCVA. Additionally, baseline DRIL and ellipsoid zone condition predicted the final postoperative BCVA at month 6.

## Conclusions

The change of DRIL extent following vitrectomy for ERM treatment was predictive of which eyes present a higher likelihood of BCVA improvement. Therefore, DRIL can be used as a surrogate biomarker of visual outcome in patients with ERM undergoing vitrectomy.

**3114**

### **3D vitrectomy can replace conventional vitrectomy - Against**

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## Summary

The three-dimensional (3D) imaging system is the latest technological success in the field of vitreoretinal surgery. The high dynamic range camera provides an image quality similar to that of the microscope and turns the optical microscope to digital system. The advantage is the greater image magnification that can be displayed in a big screen. Disadvantages are :the resolution of the 3D system is approximately twice lower of the conventional image through the eyepieces and it is necessary to make more frequent adjustments for focusing during surgery. The displayed image may cause disorientation of the surgeon who may see the surgical procedure in no real time (there is a latency of 80 ms) and a learning period would be necessary before he can change practice . Symptoms of asthenopia and myoskeletal problems due to the surgeon's uncomfortable posture for prolonged surgical time may be also a problem in 3D surgery. The space requirement for the new instrumentation may not fit in many theatre rooms. Finally we have to take under consideration that there are not studies showing that the new technology may improve surgical outcomes in vitreoretinal procedures.

**T110**

### **Suclinal signs persistence in Vogt-Koyanagi-Harada disease (VKHD) patients treated with early high-dose corticosteroids and immunosuppressive therapy**

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## Purpose

To evaluate the impact of early immunosuppressive therapy (IMT) over subclinical inflammation in Vogt-Koyanagi-Harada disease (VKHD).

## Methods

Patients diagnosed with VKHD in the acute phase were prospectively included, with a minimum 12-month follow-up. They were treated with methylprednisolone pulse therapy followed by oral prednisone starting at 1mg/Kg/d with a slow tapering and early azathioprine (within 2 months). Changes in treatment were based on the presence of clinical signs and/or  $\geq 30\%$  worsening of full-field electroretinogram (ERG) parameters. Follow-up protocol included every 3-month clinical and imaging exams [indocyanine green and fluorescein angiographies and enhanced depth imaging optical coherence tomography] performed with Spectralis HRA+OCT. ERG was carried out at inclusion, 6 and 12 months. Eyes were categorized as ERG worsening or stable group. Subclinical signs were defined as: optic disc or perivascular leakage; dark dots and/or subfoveal choroidal thickness increase. Clinical signs were determined as: cells in anterior chamber; choroidal neovascularization and/or macular edema.

## Results

Eleven women were included, with median age at diagnosis of 37 years old and median time from symptoms till treatment of 23 days (range, 8-67 days). During follow-up, 4 eyes (18.2%) were defined as ERG worsening group and 18 eyes (81.8%) as ERG stable group. Both groups presented clinical and subclinical signs of inflammation in a similar proportion. Nevertheless, marked pleocytosis ( $p=0.042$ ) and choroidal folds ( $p=0.002$ ) were more frequent on ERG worsening group. There was no choroidal neovascularization during 12-mo follow-up.

## Conclusions

In this limited sample of patients, subclinical inflammation signs persisted, despite optimal early immunosuppression therapy. Worsening ERG group had indicators of a more severe disease from the onset.

## T115

### Association between visual function and quality of life in patients with Vogt-Koyanagi-Harada disease

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## Purpose

To evaluate associations between visual acuity, disease activity, treatment and visual function with self-reported quality of life metrics in patients with Vogt-Koyanagi-Harada disease (VKHD)

## Methods

Patients with VKHD with minimum 12-month follow-up from acute onset were evaluated. Disease activity was detected by clinical and posterior segment imaging examination. Visual function was measured by best corrected visual acuity (BCVA), full-field electroretinogram (ERG) and contrast sensitivity (CS). The self-reported quality of life was assessed by the NEI VFQ-25 and SF-36 questionnaires. The data were analyzed with Mann-Whitney and Spearman's rho tests.

## Results

19 patients were evaluated (17F/2M; mean age  $36.9 \pm 12.7$  y). BCVA was 20/20 in 63.1% and  $\geq 20/60$  in 94.7% of patients. In SF36 questionnaire, immunosuppressive therapy impacted negatively in physical and social functioning, bodily pain and vitality scores ( $p < 0.05$ ), while higher cumulative corticosteroids dose had negative impact in role physical and social function scores ( $p < 0.01$ ). Worsening scotopic ERG parameters had negative effect on role physical, vitality and social functioning scores ( $p < 0.01$ ). In NEI-VFQ-25 questionnaire negative impact on general vision was related with worse BCVA ( $p < 0.01$ ), its fluctuation ( $p < 0.05$ ), choroidal thickness fluctuation ( $p < 0.05$ ) and higher cumulative corticosteroids dose ( $p < 0.01$ ). Lower CS had negative impact on peripheral and distance vision ( $p < 0.01$ ).

## Conclusions

VR-QoL and HR-QoL questionnaires together with psychophysical measurements of visual impairment bring a more extensive understanding of the impact of choroidal inflammation and treatment in patients with VKH disease

**S064**

### **Epidemiologic study of dry eye disease (DED) in pre-surgery refractive patients**

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#### **Purpose**

Study the prevalence and clinical picture of DED in patients before refractive surgery including the etiological background.

Post-surgical DED is a common problem and the pre-surgery state of the ocular surface is acknowledged the reason. Refractive surgery aggravates the severity of DED and makes it chronic with a persistent discomfort. Besides pre-surgery DED is the reason of miscalculation of ablation options leading to unsatisfactory final results.

#### **Methods**

The study included 600 patients with myopia (39% men, 61% women; 20-42 y.o.) who applied for a refractive surgery. The following tests were performed: OSDI score, evaluation of tear film lipid layer and Meibomian glands function test, TBUT and Shirmer tests, tear meniscus height evaluation, tests with lissamine green vital staining, lid wiper epitheliopathy detection. To estimate the strength of the connection between the etiological condition and the DE, the normalized value of the Pearson coefficient (C') was used.

#### **Results**

The DED prevalence was 38.83% (71.76% mild, 28.83% - moderate).

#### **Conclusions**

Increasing the ophthalmologists' awareness and understanding of early DED manifestations prevalence in pre-surgery refractive patients may optimize the timely detection of this pathology. The most significant etiological condition for DED was MGD, especially risky in females, which leads to lipid-deficiency and thus determines the relevant direction of treatment - the eyelid hygiene. Key words: dry eye, refractive surgery, ocular surface. Financial Disclosure: The study was supported by Grant No. 17-16-23048 of the Russian Foundation for Basic Research (RFBR) and the Ministry of Education, Science and Youth Policy of Krasnodar Territory. There is no conflict of interests.

**3521**

### **Biomarkers in glaucoma**

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#### **Summary**

A *biomarker* is a biological characteristic measured in order to quantify a normal or pathological process. These are especially useful in chronic conditions such as glaucoma where patients are commonly asymptomatic, monitored over many years, and display a detectable latent phase during which treatment can be instigated to prevent or delay the onset of functional loss. The acceptance of open-angle glaucoma as a heterogeneous group of neurodegenerative conditions, in combination with rapid advances in ophthalmic imaging and genomics, calls for new insight into the way in which we diagnose and monitor patients. In research, these new advances are providing better understanding of disease subtypes and pathogenesis, as well as enabling treatments to be trialled

with an approach more closely aligned to clinical endpoints and patient outcomes. In this talk we review the latest evidence behind traditional and future biomarkers, accompanied by the pitfalls surrounding surrogate markers in clinical trials. Following this, we present an exciting vision for the future which will invert the diagnostic and treatment development process as we know it, starting from the genes and cells, upwards.

## F127

### Heritability of corneal curvature and Pentacam topometric indices: a population based study

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## Purpose

To investigate the familial aggregation of anterior and posterior corneal curvatures, corneal astigmatism and some corneal topometric indices using Pentacam in a population based study

## Methods

Of the 3851 eligible individuals who resided in the selected areas, 2779 subjects had the conditions for analysis. However, analysis was limited to families whose pentacam measures were available for at least 2 family members, resulting in 1383 individuals in 382 families. All selected subjects had ophthalmic examinations including refraction, uncorrected and corrected visual acuity, slit lamp biomicroscopy and Pentacam imaging. Heritability estimation was used to calculate familial aggregation.

## Results

The results of this study showed fairly high corneal curvature heritability. The heritability of K2 and K1 in the anterior surface was 58.60% and 55.82%, respectively. The heritability of posterior corneal curvature was slightly higher than that of anterior corneal curvature. The heritability of K2 and K1 in the posterior surface was 63.42% and 59.67%, respectively. In investigating the quantitative topographic indices of the cornea, index of surface variance (ISV), central keratoconus index (CKI) and index of vertical asymmetry (IVA) had the highest levels of heritability (81.2%, 74.99% and 66.46%, respectively) while keratometric power deviation (KPD) and index of height asymmetry (IHA) had the lowest heritability levels (7.48% and 18.31% respectively).

## Conclusions

The results of this investigation indicated a relatively high correlation between corneal curvatures, ISV, IVA phenotypes and genetic factors and warrant further investigation of the genetic mechanisms in keratoconus.

## S054

### Longitudinal evaluation of corneal biomechanical parameters in a 7-11 years old Iranian population

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## **Purpose**

To assess the changes of the corneal biomechanical parameters in a 7-11 years old Iranian population after four years.

## **Methods**

In a longitudinal study, 468 children aged 7-11 years, who were examined in the first phase of the study in 2012, were re-assessed in 2016-2017. The sampling method was multi-stage stratified cluster sampling. Corneal biomechanical properties were assessed using ocular response analyzer (ORA). The corneal biomechanical parameters included corneal hysteresis (CH), corneal resistance factor (CRF) and a number of parameters related to the analysis of the recorded waveform (P1 & P2 areas which were related to more than 75% of the height of the first and second peaks, and A & B indices). Data were analyzed by SPSS.22 software and the significance level was considered to be 0.05.

## **Results**

Of the 468 subjects, 251 were boys. All biomechanical parameters decreased in the second phase, except A index. The mean changes in CH and CRF in all subjects was  $0.68 \pm 0.16$  mmHg after 4 years. Comparison of the mean differences of parameters in the two genders showed more changes in boys than girls in all parameters except for A and B indices. The mean changes in CH and CRF in girls were  $0.23 \pm 0.23$  and  $0.24 \pm 0.23$  mmHg and in boys  $1.03 \pm 0.23$  and  $0.96 \pm 0.23$  mmHg, respectively. The highest and the lowest mean differences between the two genders were related to P1 area and B index, respectively. Changes in different age groups based on age in the initial phase of the study indicated different reductions except for the A index, which increased in the second phase. The 10-year-old age group had the lowest changes in CH and CRF and the 11-year-old age group showed the highest disparity in CH and CRF.

## **Conclusions**

Most of the corneal biomechanical parameters, especially CH and CRF decreased after four years.

## **S009**

### **Effect of Biphalin on Corneal Epithelial Wound Healing**

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## **Purpose**

Biphalin is a synthetic dimeric enkephalin peptide which is selective  $\mu$  and  $\Delta$  opioid receptor agonist. Most of analgesic topical eye drops cannot be used because of their negative effects on corneal epithelial wound healing process. Our purpose is to find out the effects of biphalin on corneal epithelial wound healing.

### Methods

Immortalized human corneal epithelial cells (HCECs) were used. The optimum non-toxic dose of biphalin was found by using MTT assay. We used a standard in vitro scratch assay to assess the effect of biphalin on HCECs. After creating a uniform scratch in cell culture dish, we quantified cell migration by live cell imaging and calculating relative wound area(RWA); cell proliferation by Ki67 proliferation index and cell migration by transwell migration assay, respectively. We also used naloxone to inhibit effects of Biphalin in these assays.

### Results

We showed biphalin has no toxic effects on HCECs in lower concentrations than 100  $\mu$ M in various incubation times. When we administered 10  $\mu$ M biphalin at in vitro scratch assay of HCECs, Biphalin increased wound closure process significantly in terms of RWA, Ki67 proliferation index and migration (all  $P < 0.05$ ). Strikingly, naloxone also increased positive effects of biphalin in wound closure at in vitro scratch assay because naloxone exhibits partial antagonism by binding to opioid growth factor receptors as a competitive antagonist.

### Conclusions

We showed that biphalin has positive effects on epithelial wound healing. Biphalin also has not any negative effects on cell proliferation and cell migration. With these findings, biphalin can be a promising topical analgesic agent for post-surgical and post-traumatic care of corneal epithelial wounds. For next steps, animal experiments for biphalin could illuminate its wound healing effect on cornea in vivo.

### T020

#### Correlation between diabetic macular edema and areas of capillary non perfusion detected by optical coherence tomography angiography

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### Purpose

To study the relationship between retinal capillary non perfusion areas and diabetic macular edema (DME).

### Methods

In this prospective study, we included 33 eyes with DME and 37 eyes without DME. The medical records, including fluorescein angiography (FA), swept-source optical coherence tomography (SS-OCT) and 9x9 mm swept-source optical coherence tomography angiography (OCTA) images were reviewed and compared between the groups. Foveal avascular zone (FAZ), areas of capillary non perfusion and vascular density were analyzed in the superficial capillary plexus (SCP) and in the deep capillary plexus (DCP). The FA and SS-OCT images were compared with OCTA findings.

### Results

Eyes with DME had a larger FAZ in the SCP compared with non-DME eyes (0,492mm<sup>2</sup> vs 0,386mm<sup>2</sup> respectively) and in the DCP (0,763mm<sup>2</sup> vs 0,456mm<sup>2</sup> respectively;  $p < 0,01$ ). Areas of capillary non perfusion were more important in the DME group compared to the non-DME group in the SCP (6,77mm<sup>2</sup> vs 1,79mm<sup>2</sup> respectively;  $p = 0,004$ ) and in the DCP (7,92mm<sup>2</sup> vs 2,19mm<sup>2</sup> respectively;  $p = 0,005$ ). There was a significant correlation between the severity of DME and areas of capillary non perfusion in the DCP. No correlation between vascular density and DME was found.

### Conclusions

The DCP is more affected in DME eyes with a larger FAZ and larger capillary non perfusion areas on OCTA compared to non-DME eyes. The severity of this non perfusion seems to be correlated to the severity of DME.

## **T021**

### **OCT Angiography findings in maternally inherited diabetes and deafness syndrome**

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#### **Purpose**

To describe the clinical characteristics and multimodal imaging of a case of macular dystrophy associated to a genetically confirmed «maternally inherited diabetes and deafness» (MIDD) syndrome.

#### **Methods**

The clinical data and multimodal imaging findings, including fundus color photography, fundus autofluorescence, swept-source optical coherence tomography (SS-OCT), fluorescein angiography (FA) and optical coherence tomography angiography (OCTA) of a case of macular dystrophy associated to MIDD syndrome were documented.

#### **Results**

A 40-year-old woman with insulin-dependent diabetes mellitus and renal transplantation for chronic renal failure under immunosuppressive therapy was referred for screening evaluation for diabetic retinopathy (DR). Visual acuity was 20/20 in both eyes. Fundus examination showed bilateral circumferential perifoveal patches of atrophy without evidence of diabetic retinopathy. FA didn't show any sign of DR. SS-OCT showed parafoveal zones of attenuation of the outer retinal layers with outer retinal tubulations. OCTA showed foveal avascular zone enlargement, areas of retinal capillary rarefaction in superficial and deep capillary plexuses. A genetic investigation showed mitochondrial DNA mutations associated to a MIDD syndrome.

#### **Conclusions**

MIDD syndrome is associated to a mitochondrial mutation causing diabetes mellitus, deafness and commonly a retinal dystrophy characterized by heterogeneous presentations. OCTA is an interesting tool to assess infraclinical signs of DR and characteristics of this macular dystrophy.

## **T026**

### **Swept-source OCT and OCT angiography findings in Alport maculopathy.**

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#### **Purpose**

To study the swept-source optical coherence tomography (SS-OCT) and optical coherence tomography angiography (OCTA) findings in Alport maculopathy.

#### **Methods**

A 25-year-old female patient diagnosed with Alport syndrome since the age of 5, with terminal kidney failure and perceptive deafness, was referred to our ophthalmology department for progressive vision loss in both eyes. Clinical examination, fluorescein angiography, SS-OCT and OCTA were performed.

#### **Results**

Best corrected visual acuity was 20/200 in both eyes. The anterior segment examination was unremarkable. Fundus examination revealed central and perimacular fleck retinopathy and loss of the foveal reflex. No peripheral changes were noticed. SS-OCT showed a temporal retinal thinning and small foveal defects hollowed out from the surface of the inner limiting membrane in both eyes. OCTA showed disruption of the foveal avascular zone and areas of retinal capillary rarefaction in both superficial and deep capillary plexuses. At the level of the choriocapillaris, OCTA showed multiple areas of reduced perfusion or «flow void».

### Conclusions

Ocular involvement is a major diagnostic and prognostic criteria in Alport syndrome. OCT and OCTA can be of a precious help to assess Alport maculopathy. OCTA findings needs to be more clarified.

## F095

### Acute Ophthalmoplegia in Herpes Zoster Ophthalmicus: Clinical Features and Radiographic Findings

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### Purpose

To describe the clinical features and radiographic findings of a series of patients with herpes zoster ophthalmicus (HZO) and associated acute ophthalmoplegia.

### Methods

Medical records of 4 cases and existing literature on HZO with acute ophthalmoplegia were reviewed.

### Results

Three males and one female with a median age of 64 years (range 59 -68) presented with HZO. 3 of them were diabetic, and another one of them had systemic lupus erythematosus (SLE). The onset of acute ophthalmoplegia from initial presentation of HZO was 16 days (range 7-35 days). Clinical findings of ophthalmoplegia included oculomotor nerve palsy (75%), abducens nerve palsy (75%) and a mixture of both (50%). All of them have acute iritis. MRI features demonstrated enhancement of the cavernous sinus (100%), orbital apex (75%), superior orbital fissure (50%) or myositis (25%). Interestingly, one of the patients was found to have enhancement along the route of the trigeminal nerve extending from the brainstem. 3 patients had lumbar puncture, which showed pleocytosis with 1 of them having positive polymerase chain reaction (PCR) of varicella zoster virus (VZV). Treatment with intravenous acyclovir was administered in all patients and systemic corticosteroids were also given in 2 cases. Ophthalmoplegia improved in all patients over weeks to months.

### Conclusions

Ophthalmoplegia is not an unusual complication of HZO, with third and sixth nerve palsy being the commonest. Systemic diseases such as diabetes or immunosuppressive status predispose the patients with HZO to central nervous system involvement. Cavernous sinus enhancement is a common radiographic feature of HZO-related ophthalmoplegia. Improvement of symptoms and signs with systemic antiviral therapy can be expected. The role of systemic steroids in treatment of orbital disease is yet to be determined.

## S011

### Novel model for corneal permeability in vitro testing through the combined use of collagen-based hydrogels with stratified corneal epithelial cells

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## Purpose

The cornea is critical for penetration of topically applied drugs onto the eye and the quantification of permeability properties of drug candidates across the cornea is a pillar stone of early drug development for topical ocular drugs. Nonetheless, permeability tests using animal corneas are costly and time consuming, while experiments using cell culture systems often overestimate permeability due to the lack of modeling the corneal stroma. The purpose of this study was to develop an *in vitro* model for reliable permeability testing based on the combined use of collagen-based hydrogels and stratified human epithelial cells (HCE-T).

## Methods

Apparent permeability coefficient (Papp) values for six clinically used ocular drug molecules (brinzolamide, dexamethasone, chloramphenicol, timolol, pilocarpine and betaxolol) and five fluorescent standard marker molecules (Rhodamine B, Rhodamine 123, 6-carboxyfluorescein, FITC-dextran mol. wt 4000 and 70 000) across HCE-T cells on cell culture inserts and hydrogels with stratified HCE-T cells were measured using a vertical diffusion chamber system. *In vitro* – *in vivo* correlation analysis was performed by comparing *in vitro* Papp values with rabbit corneal permeability values.

## Results

Hydrogels with stratified HCE-T cells better modeled *in vivo* corneal permeability compared with HCE-T cultures on cell culture inserts. Prediction of Papp of lipophilic molecules was improved for hydrogels with stratified HCE-T cells, suggesting that the natural barrier properties of the corneal stroma were adequately modeled by the hydrogels.

## Conclusions

The collagen-based hydrogel layer is efficiently mimicking the permeability properties of the corneal stroma. We propose the use of an *in vitro* model comprising both HCE-T cells and a hydrogel to reliably predict *in vivo* corneal permeability of drug molecules.

1813

## OCT-A in radiation induced maculopathy

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## Summary

Irradiation induced maculopathy occurs following the administration of 20Gy or more with Proton beam, or 30Gy or more with Brachytherapy in the macular area. Diabetes and high blood pressure are additional risk factors.

In irradiation induced maculopathy, we observe a disruption of the inner B/R barrier, which is quantified with fluoresceine angiography; a disruption of the outer B/R barrier giving rise to a macular edema, which is measured with b-mode OCT and OCT "en face"; and finally a vaso-occlusive microangiopathy which is studied with OCT-angiography. In a multivariant analysis including 162 cases of irradiation induced maculopathy investigated with fluoresceine angiography, OCT, OCT "en face" and OCT-angiography, the status of the deep capillary plexus appears as the most significant parameter related to the visual acuity. The presence of SSPIM is an additional factor of bad prognosis. Actual therapeutic approaches with anti-VEGFs are based on the evaluation of this

pathology with OCT-angiography and the monitoring of the therapeutic results with repeated OCT-angiography studies.

**2645**

**Management of malignant conjunctival melanoma ( radiotherapy and local chemotherapy)**

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**Summary**

Management of conjunctival melanomas in selected cases may be challenging. To avoid local recurrences, a combined therapeutic approach is used in the majority of the cases. This includes Ruthenium brachytherapy or Proton beam irradiation in order to sterilize the base of the tumor, conjunctival cryotherapy as well as topical chemotherapy in order to eliminate PAM with atypia. The therapeutic strategy is based on the volume, the localization and the extent of the tumor on the bulbar and tarsal conjunctiva as well as the density of the associated PAM.

The aim of the treatment is to sterilize the tumor and avoid local recurrences which may be associated with systemic diffusion of tumor cells.

**2714**

**Evaluation of the retinal pigment epithelium defects with OCT-A**

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**Summary**

The evaluation of the vascular pattern of the intraocular tumors is independent of the degree of pigmentation and it is mainly related on the metabolic status of the retinal pigment epithelium. Both in choroidal hemangiomas or melanocytic tumors, the intratumor vascular network may be observed exclusively if the RPE is hypo- or hyperfluorescent. In addition, in 25% of these cases, there is an optical projection of the vascular network in the deeper retinal layers simulating an occult CMV. In the peripheral retina, the density of the RPE decreases and this allows the visualization with OCT of the whole vascular pattern in tumors located close to the equator. In conclusion, the density and the metabolic status of the RPE are the main parameters involved in the observation of the choroidal vascular pattern with OCT-angiography.

**2944**

**Intravitreal anti-VEGF for the treatment of irradiation induced optic neuropathy and maculopathy**

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**Summary**

A multivariate analysis of 162 cases of irradiation induced maculopathies with OCT-angiography, OCT "en face", b-mode OCT and fluorescein angiography demonstrated that the status of the deep capillary plexus is the most significant parameter for visual loss ( $p = 0.001$ ). In 80% of cases with interrupted deep capillary plexus, the visual acuity was included between 0.16 and 0.6. This specific group of patients is submitted to a protocol of intra-

vitreal anti-VEGFs repeated every 2 months during one year. At the end of the observation period, the visual acuity of 86% of the cases which followed the protocole, increased or remained the same. On the contrary, only 19% of the cases, which didn't follow the protocole, retained the same visual acuity. In addition, a minimal enlargement (26%) of the non flow area was observed in cases treated according the protocole, and an important enlargement (232%) was observed in cases which didn't follow the protocole. In conclusion, intravitreal anti-VEGFs administrated on OCT-angiography criteria appears as a promising therapeutic approach for the irradiation induced maculopathy.

**1433**

#### **Corneal nerves after PRK and CXL treatment**

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#### **Summary**

Photorefractive keratectomy (PRK) and corneal crosslinking therapy (CXL) remodels corneal stroma resulting in the disruption of corneal nerves and a release of several peptides such as cytokines, growth factors, and matrix metalloproteases from the corneal tissue. These factors participate in the process of corneal wound healing and their balance is necessary for normal reepithelization and stromal remodeling. Since maintaining corneal transparency and restoring normal corneal function are essential, understanding wound-healing response is critical for a successful corneal surgery. The measurement of ocular surface sensitivity is a useful indicator of corneal physiology in corneal diseases. The Belmonte gas esthesiometer uses a fine jet of gas as a stimulus and the flow, composition, and temperature of this gas can be altered to apply mechanical, chemical, and thermal stimuli to the ocular surface. We performed a study to investigate and compare changes in corneal sensitivity after CXL and PRK procedures on the long term. Our preliminary results show, that in the first three months in subjects after CXL treatment there is a decreased corneal pain sensitivity compared to subjects underwent PRK treatment.