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Guest Editors: Stanislao Rizzo, Francesco Faraldi and Andrea Giorni

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## **Guest Editors**

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### F-01

#### RISK FACTORS FOR UNINTENTIONAL RETINAL DISPLACEMENT AFTER PARS PLANA VITRECTOMY FOR RHEGMATOGENOUS RETINAL DETACHMENT

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**Introduction and objectives:** Unintentional retinal displacement has been recently reported after rhegmatogenous retinal detachment (RRD) surgery and its pathogenesis is still unclear. The purpose of this prospective clinical study was to investigate the potential risk factors for retinal displacement after pars plana vitrectomy (PPV) for RRD.

**Materials and methods:** Sixty-two eyes of 62 patients with primary macula-off RRDs were enrolled. Features of RRDs including extension of detachment, location and number of retinal breaks and fovea status were recorded before and after surgery. Patients underwent tamponade with 20% sulfur hexafluoride (SF6) gas or 1000 centistokes polydimethylsiloxane (PDMS) at surgeon's discretion. Blue-Fundus autofluorescence was performed preoperatively and at 1, 3, 6 and 12 months after surgery to analyze the rate and the direction of retinal displacement in relation to the type of tamponade used and features of RRDs.

**Results:** Forty-eight eyes were tamponated with SF6 and 14 with PDMS. After RRD repair, displacement was detected in 22 out of 62 (35.4%) eyes (20 tamponated with SF6 and 2 with PDMS, respectively). The type of tamponade used was the only significantly risk factor for retinal displacement ( $p = 0.008$ ). The displacement was located downwards in 19 cases (18 tamponated with SF6 and 1 with PDMS) and upwards in 3 (2 tamponated with SF6 and 1 with PDMS) cases. The direction of displacement was not found to be correlated with the location of detachment ( $p = 0.06$ ) or the location of retinal breaks ( $p = 0.29$ ).

**Conclusions:** Displacement of the retina can be observed after PPV for macula-off RRD using either SF6 or PDMS. Although downward and upward displacements may occur with both tamponades, displacement is more frequently dislocated downward. The type of tamponade used seems to be the only significant risk factor potentially related to the onset of postoperative retinal displacement.

### F-02

#### ENDOGENOUS ENDOPHTHALMITIS IN THE DEVELOPING WORLD

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**Introduction and objectives:** The profile of the patient at highest risk of endogenous endophthalmitis would be a diabetic patient with hepatobiliary infection, especially among patients of East Asian ethnicity. In the Caucasian patient, endogenous bacterial endophthalmitis is seen more commonly in the context of gram positive bacteremia, arising from infection of the skin, joint, or endocarditis in predisposed individuals. Infection with virulent organisms usually denotes grave visual prognosis.

**Materials and methods:** Literature review.

**Results:** Current recommendations for empirically treating suspected bacterial endophthalmitis involve combination therapy targeting both gram-positive and gram-negative organisms. Therapeutic combinations of antibiotics should be tailored to the clinical scenario in which endophthalmitis develops and should target the most common causative organisms. Fungal therapy is considered when clinical history and ocular features justify this approach.

Due to the low permeability of pigmented epithelium to systemically administered drugs, intravitreal antibiotics or antifungals are used in cases in which systemic treatment is ineffective or following procedures such as vitrectomy and vitreous tap. Regarding optimized therapy in such patients further studies are required.

**Conclusions:** The outcome of endogenous endophthalmitis (compared with that of exogenous endophthalmitis) is disappointing. The three main factors that result in a poor prognosis include more virulent organisms, compromised host conditions and delay in diagnosis. Even with aggressive treatment, in only about 40% of patients is useful vision preserved.

### F-03

#### OCT PROGNOSTIC SIGNS IN VITREOMACULAR INTERFACE PATHOLOGIES

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**Introduction and objectives:** Over the past two decades, there has been growing interest in investigating the post-operative outcome in eyes with vitreo-macular interface pathologies, such as vitreomacular traction syndrome, epiretinal membrane, and macular hole. Optical coherence tomography (OCT) has evolved into a resourceful imaging technology and has provided the capability to identify signs influencing the final outcome after vitreo-macular interface disease's surgery.

**Materials and methods:** Systematic review of electronic databases was performed. Search queries included: "membrane", "pucker", "vitreomacular traction", "epiretinal", "macular hole", "myopic foveoschisis", "diabetic macular edema", "prognosis", "prognostic", and "optical coherence tomography".

**Results:** Several studies have shown the presence of OCT signs predicting a worse prognosis after surgery, as follows: (i) foveal thickening, (ii) inner nuclear layer thickening, (iii) intraretinal cystic spaces, (iv) discontinuity of the outer retinal layers, (v) detachment of the neuroepithelium, and (vi) presence of neovascularization. Recently, the use of the en face OCT has allowed investigating the macula at various depth-resolved levels. Studies with en face OCT have demonstrated that both inner and outer macular changes are correlated to the post-surgical outcome.

**Conclusions:** The potential role of the OCT in predicting the prognosis in the vitreo-macular interface disease has been fully demonstrated. For this reason, OCT placed itself as the standard imaging modality for macular imaging in either baseline and follow-up visit in eyes affected by vitreo-macular interface diseases.

### F-04

#### LAMELLAR MACULAR HOLE: UPDATED CLASSIFICATION AND SURGICAL INDICATIONS

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The current LMH definition is subject to two major shortcomings. First, progress of retinal imaging has demonstrated a great variability of 'intraretinal splitting' or 'intraretinal cleavage' in LMHs being confused with incomplete separation by intraretinal cyst formation due to vitreomacular traction. Second, OCT studies and histopathology have demonstrated the presence of epiretinal tissue in the majority of eyes with LMHs. Thus, presence of epiretinal membranes is no longer a prerequisite for macular

autofluorescence in the periphery with retained signal at the central macula. NGS identified 2 novel null mutations within the MAK gene: 1) MAK c.297-2A>G, predicted to cause aberrant splicing, and 2) MAK c.1195\_1196delAC p.(Thr399fs), predicted to result in a frame shift resulting in premature termination of translation.

**Conclusions:** The natural history of this individual's RP is consistent with previously described MAK mutations, being significantly milder than that associated with other photoreceptor ciliopathies. We suggest inclusion of MAK as part of wider genetic testing in all individuals presenting with rod-cone dystrophy.

#### OM1-17

##### AN IMPROVED MODEL OF ACHROMATOPSIA FOR PRE-CLINICAL DEVELOPMENT OF GENE AND CELL THERAPIES

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**Introduction and objectives:** We identified a colony of inbred mice with complete achromatopsia and hypothesised that a novel genetic mutation was responsible. Test crossing, electrophysiological testing and candidate gene sequencing were used to investigate the inheritance pattern and genetic cause of the phenotype. A recessive missense mutation was identified in *Cnbg3* causing complete loss of cone function.

**Materials and methods:** We performed dark- and light-adapted electroretinography (ERG) to assess retinal function. Genomic DNA was extracted from tail tissue of mice and genotyped using commercial fluorescent dideoxynucleotide sequencing. Chi-squared test with Yates's continuity correction was used for statistical analysis of phenotypic and genotypic outcomes.

**Results:** Affected mice had absent light-adapted ERG response. DNA sequencing of genes important for cone phototransduction and function revealed a missense mutation in exon 6 of the *Cnbg3* gene, which causes an amino acid substitution at a highly conserved residue. 100% of affected mice ( $n = 16$ ) were homozygous for the mutation ( $X^2 = 28.15$ ,  $p < 0.0001$ ). Mice that were heterozygous for the mutation did not exhibit achromatopsia. Ocular imaging (cSLO and OCT) showed no obvious retinal degeneration or other anatomical problems. Histological sectioning and IHC for Cone Arrestin showed normal retinal architecture and cone cell morphology.

**Conclusions:** The only existing mouse model of *Cnbg3* achromatopsia is a knock-out with partial cone function. Our model demonstrates a novel missense mutation and complete achromatopsia. This absolute absence of cone function makes this mouse an optimal model for future pre-clinical development of therapies.

#### OM1-18

##### WIDEFIELD OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY OF IDIOPATHIC RETINAL VASCULITIS, ANEURYSMS, AND NEURORETINITIS (IRVAN)

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**Introduction:** The purpose of this study was to describe the use of widefield optical coherence tomography angiography (WF-OCTA) in idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) and to present a previously unreported complication.

**Materials and methods:** Case series of two patients with IRVAN disease who underwent swept-source WF-OCTA (PLEX Elite 9000, Carl Zeiss Meditec, Inc., Dublin, USA) and full multimodal imaging, including dye angiography (Spectralis HRA + OCT; Heidelberg Engineering, Heidelberg, Germany and/or California ultra-widefield fundus camera, Optos PLC, Dunfermline, Scotland, UK).

**Results:** Four eyes of 2 consecutive patients (1 female/1 male; mean age  $34 \pm 6$  years) were included in the analysis. WF-OCTA clearly showed areas of peripheral capillary non perfusion and aneurysmal dilations, demonstrating high agreement with fluorescein angiography. Traditional dye angiography better identified superficial retinal neovascularizations. Leaking vessels and late staining of the optic disc were only noted with fluorescein angiography. One of our cases presented with central retinal artery occlusion as first symptom of a previously undiagnosed IRVAN.

**Conclusions:** WF-OCTA reliably showed areas of peripheral capillary nonperfusion and aneurysmal dilations, with an optimal agreement with fluorescein

angiography. The use of WF-OCTA, a non-invasive technique, could be a useful tool for the identification and follow up of severe vascular abnormalities, including atypical presentation and retinal vascular occlusion in patients with IRVAN disease.

#### OM1-19

##### CLINICAL CASE REPORT OF CYTOMEGALOVIRUS RETINITIS ASSOCIATED WITH APLASTIC ANEMIA

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**Introduction and objectives:** Immunosuppression determines manifestation of CMV infection clinical signs and serious complications in specific cases. The high-risk group for CMV infection includes patients after hematopoietic stem cell transplantation (HSCT). CMV retinitis manifests as acute retinal necrosis and can lead to blindness by itself or due to complications such as tractional retinal detachment.

**Materials and methods:** Patient 19 y.o. Early period after HSCT was complicated by CMV viremia and bilateral CMV retinitis that regressed after systemic ganciclovir treatment. In the left eye we observed formation of vitreoretinal traction. 8.5 months after HSCT was performed, tractional retinal detachment occurred. Patient underwent vitrectomy with successful reattachment of the retina. Due to bone marrow transplant hypofunction and absence of immune reconstitution, two weeks after the surgery on the left eye, reactivation of CMV retinitis was observed in the right eye with no viremia. Within 24 hours visual acuity of the right eye decreased from 20/20 to light perception.

**Results:** Ophthalmoscopy revealed significant perivascular inflammation that extended along all four retinal veins. We also observed signs of acute retinal veins obstruction. Angiography could not be performed due to patient's hypersensitivity to fluorescein sodium. Treatment included eight intravitreal injections of ganciclovir 2,0 in 0,1 ml, while performing systemic ganciclovir and donor lymphocyte infusion. The frequency of the injections were once a week and after eighth manipulations we observed complete regression of the inflammatory process with formation of scar tissue at the site of primary lesion. Visual acuity increased to (20/25).

**Conclusions:** The most significant findings of the above stated clinical case are: absence of signs of inflammation after vitrectomy in the left eye during all follow-up period (excluding the specific one which is due to the post-operative period), and throughout all treatment period patient underwent weekly CMV testing (PCR) but viremia was not registered.

#### OM1-21

##### THE IMPORTANCE OF FUNDUS AUTOFLUORESCENCE (FAF) IMAGING TO ESTABLISH PATIENT ELIGIBILITY FOR THE ARGUS® II RETINAL PROSTHESIS SYSTEM

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**Introduction and objectives:** Fundus autofluorescence (FAF) imaging may have an important role in the evaluation of retinitis pigmentosa patients that are suitable for Argus® II retinal prosthesis.

**Materials and methods:** The Argus II Retinal Prosthesis System is now a standard treatment to patients blind from retinitis pigmentosa (RP). The standard procedure for identifying the suitable candidates includes eye examination, Goldmann visual field test, optical coherence tomography, fundus photography, fluorescein angiography, ultrasonic A-scan, and photographic flash test. Although the protocol consists of various preoperative screening, FAF is not one of the required examinations in the preoperative screening protocol. This study is intended to indicate the clinical importance of the FAF measurement in a special RP case.

**Results:** The 68 years old male patient was diagnosed with severe RP. Following the standard screening procedure, the patient was identified to be a suitable candidate to receive the Argus II Retinal Prosthesis System. During

the discussion with the patient the clinician observed that the patient was still able to read information on his smartphone monitor. FAF as an imaging technology, which reveals a biomarker of retinal disease progression (lipofuscin), was performed in addition to the standard eligibility procedure screening. It was observed that foveal area was preserved even the visual acuity of patient was worse than hand motion.

**Conclusions:** Advanced RP patients could have very small central island visual field. FAF should be included as a complimentary tool to the standard screening procedure for identifying suitable candidates to receive the Argus II Retinal Prosthesis System.

#### OM2-01 OPTIMIZATION OF PRL WITH FONDA FAR PRISMS AND MICROPERIMETRY

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**Introduction and objectives:** The PRL (preferred retinal locus) training is based on theoretical concepts and subjective patient feedback. To investigate a validated system to select the PRL and to increase fixation stability using FONDA FAR prisms and microperimetry.

**Materials and methods:** A total of 19 eyes of 14 patients with macular degeneration were enrolled in the study; 8 patients (10 eyes) underwent 6 months training with microperimeter (Maia - Centervue, Padova - Italy): first evaluation showed BCEA@ 95% area >50°. The others (6 patients, 9 eyes) didn't need of the training session (BCEA@ 95% area <50°). All patients had a glasses prescription with FONDA FAR prisms (Fonda Custom Vision Technology, Genova - Italy) order to shift the central macular scotoma. BCEA@ 63% and BCEA@ 95% were measured using the standard grid (37 points), after 1 month glasses prescription. Patients used prisms during the second threshold test: test n. 1 (valuation with prescribed prism); test n. 2 and 3 (same prism; axis positioning  $\pm 10^\circ$  shift).

**Results:** Test n. 1 shows a significant increase of fixation stability (BCEA@63% area =  $3.0^\circ \pm 1.30^\circ$ ; BCEA@95% area =  $6.8^\circ \pm 3.85^\circ$ ). Fixation is not comparable with the average threshold in patients with remarkable saccadic pursuit (BCEA@95%>20°). Test n. 2 and 3 underline a decrease of fixation performances: mean BCEA@63% area =  $4.9^\circ \pm 4.10^\circ$ , BCEA@95% area =  $14.7^\circ \pm 12.35^\circ$ .

**Conclusions:** There is an objective way to select the PRL, combining prisms and microperimetry. Microperimeter sensibility is under investigation for axis variations between  $\pm 5^\circ$ . Fixation and visus score are not always correlated: data are under investigation.

#### OM2-04 DIABETIC MACULAR ISCHEMIA FEATURES USING OCT ANGIOGRAPHY

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**Introduction and objectives:** To evaluate morphological details of diabetic macular ischemia (DMI) in patients with diabetic retinopathy (DR) using optical coherence tomography angiography (OCT-A).

**Materials and methods:** A total of 20 DMI eyes (mean age  $60.8 \pm 12.41$ ) and 20 normal age-matched control eyes (mean age  $49.53 \pm 4.12$ ) were evaluated by ultra-high speed wide-field enface, High Resolution (70.000 A-scan/second) 840-nm wavelength OCT (Optovue, XR-Avanti, Freemont; California) based on split-spectrum amplitude-decorrelation Algorithm (SSADA) in this observational, cross-sectional study. The macular angiography scan protocol covered a  $3 \times 3$  mm area. Motion artifacts were automatically removed by a default software. The angiography was analyzed in correspondence of 2 intraretinal layers: superficial vascular network and deep vascular network. The morphological vascular details, i.e. silhouette, identified as the dilation or flow interruption around the FAZ and thickness, referred as the flow segmentation into the vessels in the acquired images, were compared across groups. Image analyses were performed by two masked observers.

**Results:** Inter-observer agreement of image analyses was 0.90 (K = 0.225,  $p < 0.01$ ). In all normal eyes, both superficial and deep vascular networks showed a regular, uniform distribution around the foveal avascular zone

(FAZ). In DMI eyes, the superficial and deep networks were easily observable, although the features of both networks largely differed from those of normal eyes. There was an enlargement of FAZ ( $p < 0.001$ ) comparing DMI with control eyes. The ischemia area involved both networks. The flow silhouette and/or thickness abnormalities were found in DMI but not in control eyes (15/15 versus 0/15,  $p < 0.01$ ).

**Conclusions:** Optical coherence tomography angiography using SSADA technology is of potential clinical value for DMI diagnosis, providing details that cannot be easily derived by standard angiography. The superficial and deep networks are both involved in diabetic disease. Further studies are needed to quantitatively assess the OCT-A images in the natural history of macular ischemia.

#### OM2-05 SUBTHRESHOLD YELLOW MICROPULSED LASER IN CHRONIC MACULAR DISEASES WITHOUT THERAPEUTIC INDICATIONS

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**Introduction and objectives:** This study evaluates safety and efficacy of the Subthreshold Yellow-577nm Micropulse (SYM) diode laser photostimulation of the Retinal Pigment Epithelium (RPE) to treat two patients affected by chronic macular disease without therapeutic indications.

**Materials and methods:** One eye of a male patient with a 10 years chronic subfoveal Central Serous Chorioretinopathy (CSC) and one eye of a female patient with chronic macular edema, after laser closure of congenital optic nerve pit, were included in this study and treated with SYM laser photostimulation. Best Corrected Visual Acuity (BCVA) examination, Amsler Test (AT) and Optical Coherence Tomography (OCT) were performed before and after laser treatment. The SYM photostimulation treatment was performed by the IQ577 Iridex-MicroPulse® laser with micropulsed confluent-spots laser.

**Results:** After SYM laser photostimulation, BCVA and AT were improved. OCT examination had shown an improvement of macular profile with a great reduction of thickness and also the absence of laser-induced lesions.

**Conclusions:** Photostimulation with SYM laser proved effective and safe. The possibility to reduce macular edema by laser micropulse stimulation of the RPE, even subfoveal, without retina damages, opens new prospects for medical treatment of macular disease actually without therapeutic indications.

#### OM2-06 PASCAL GRID MODIFIED LASER (GML) TREATMENT INCLUDING SUBTHRESHOLD STRATEGY (SS) IN THE TREATMENT OF SEVERE DIFFUSE CYSTOID MACULAR EDEMA (SDCME) IN NON PROLIFERANT DIABETIC RETINOPATHY (NPDR)

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**Introduction and objectives:** Long-term study assessing the efficacy of Pascal GML associated with SS in reducing central macular thickness (CMT) improving visual function in SDCME (CMT>400 microns) in NPDR without intravitreal injection. Assessing utility of angioOCT in retreating decisions.

**Materials and methods:** 23 eyes of 18 patients affected by SDCME. Mean FU: 25 months. GML was performed with Pascal Photocoagulator: focal laser of micro-aneurysms and a mild GML (mean spot 60  $\mu$ m; mean power 130 mw; 20 ms). SS was performed during follow up in 13 out of 23 eyes (100 micron spot and a mean power of 275 mw, 10 ms; SLS: 30% of the tirtrate power value). Re-treatments criteria guided by OCT, Fluorescein angiography (FA) and angioOCT. To assess the influence of metabolic control, patients entered 2 groups (cut-off HbA1c: 7,50%). Group 1 (G1) >7,5%: 10 eyes; group 2 (G2) <7,5%: 13 eyes. Each patient was evaluated with best corrected visual acuity (BCVA), SD-OCT, FA and angio-OCT.

**Results:** BCVA improved in 88% of patients. Mean percentual improvement of BCVA: 59% (G1 41%; G2 54%). Mean BCVA (logmar): Initial 0,45; final: 0,26. CMT improved in almost all patients (mean basal CMT: 537  $\mu$ m; final CMT: 319  $\mu$ m). Observing BCVA and CMT, we stress the importance of glyco-metabolic control.