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AMD 2023

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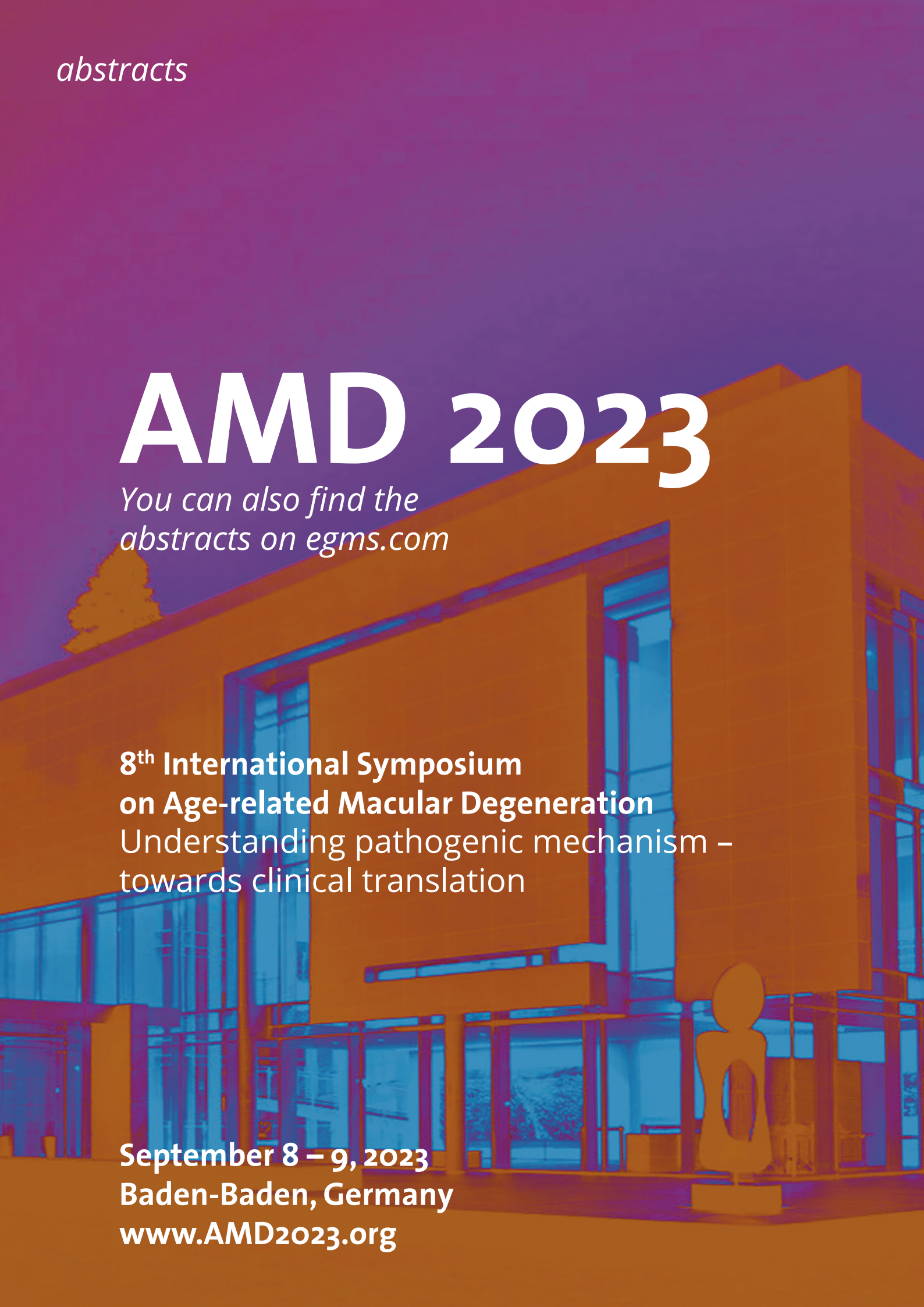

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3. Eichenbaum D et al. ASRS Juli 2022; oral presentation.

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M-DE-00017021

1st session

Genomics, Proteomics, Metabolomics in AMD

01.08 P **Brandi L. Williams**, N.A. Seager, C.M. Pappas, J. Liu, R.A. Anstadt, M.A. Zouache, B.T. Richards, G.S. Hageman (Salt Lake City/USA)

The Chromosome 10q26 locus associated with elevated risk for AMD causes reduced HTRA1 expression specifically in RPE

Genome-wide association studies (GWAS) have shown that one or more single nucleotide polymorphisms (SNPs) and/or an insertion/deletion within the chromosome 10q26 locus (Chr10) significantly increase(s) risk for developing age-related macular degeneration (AMD). Genes within this locus include age-related maculopathy susceptibility 2 (ARMS2) and high temperature requirement A serine peptidase 1 (HTRA1). Using multiple methodologies, we show that HTRA1 mRNA expression is specifically reduced in retinal pigment epithelium (RPE) of human donors with Chr10 risk relative to non-risk donors but is not reduced in the retinas of these same donors, indicating an RPE-specific HTRA1 eQTL effect. Importantly, HTRA1 mRNA in the RPE-choroid from Chr10 risk donors without clinically detectable AMD is low relative to non-risk donors and levels remain low even after disease onset. By comparison, HTRA1 mRNA is higher in non-risk donors both before and after AMD disease onset. Using two independent and validated HtrA1 ELISAs, we demonstrate that levels of HtrA1 protein in human serum, vitreous and retina are unaffected by Chr10 SNPs or AMD status. In contrast, HtrA1 protein levels increase with age in RPE-choroid tissue from Chr10 non-risk donors and this age-dependent increase is absent in donors with homozygous Chr10 risk. Together, these data indicate that altered expression of HtrA1 in RPE tissue from Chr10 risk donors is an early event that precedes disease onset and is a contributing factor to disease initiation and/or progression. It implies that HtrA1 is important for maintaining a healthy RPE-Bruch's membrane interface during the aging process and that decreased HtrA1 protein, specifically in RPE tissue, contributes to increased risk for AMD pathogenesis.

01.09 P **Mahfam Shahabi**[1], A. de Breuk[1], F. Cinque[1], A.I. den Hollander[1], E.T. Thee[2], J.M. Colijn[2], T.J. Heesterbeek[1], C.C.W. Klaver[1,2,3], C.B. Hoyng[1], Y.T.E. Lechanteur[1] ([1]Nijmegen/NL, [2]Rotterdam/NL, [3]Basel/CH)

Disease progression in AMD patients carrying rare variants in complement factor H and complement factor I genes

Background: Complement genes are strongly linked to age-related macular degeneration (AMD). Little is known about disease progression in AMD patients carrying rare variants in these genes. We assessed short-term disease progression in AMD patients with rare variants in the complement factor H (CFH) or factor I (CFI) genes.
Methods: We selected AMD patients carrying a rare (mean allele frequency < 1%), protein-altering or splice-site variant in either the CFH or CFI gene, excluding protective or neutral variants. Patients were followed over time for at least 12 months. The following parameters were obtained at every visit: changes in visual appearance of drusen load compared to baseline (no change/substantial change/regression) on color fundus photography, area (in mm2) of geographic atrophy (GA) on fundus autofluorescence (FAF), mean retinal sensitivity (RS) in decibels (dB) on mesopic microperimetry and visual acuity (VA) in logMAR.
Results: We included 44 patients (88 eyes) with a mean (IQR) age of 61.3 (16.5). There were 29 and 15 patients with a rare variant in the CFH and CFI gene, respectively. The majority of eyes (73/87) showed no substantial change in drusen load after 12 months. The mean area (SD) of GA was 4.5mm2 (5.6) at baseline and 5.5mm2 (6.5) after 12 months in 19 eyes with exclusive signs of GA on FAF (p = 0.499). Mean growth rate (SD) was 1.50mm2 (1.49)/year. VA and mean RS did not change significantly over 12 months, however, subgroup analysis over 20 months showed significant decline in mean RS.
Conclusion: Over this short follow-up period we were not able to detect significant changes in VA, drusen load and GA growth. Mean RS significantly declined over 20 months, and may be a useful biomarker for clinical trials. More data is necessary to compare the progression of these rare variant carriers to regular AMD patients.

2nd session

Pathogenetic mechanism of AMD: Energetic metabolism in the outer retina

02.09 P **Leon von der Emde,** M. Mallwitz, M. Saßmannshausen, F.G. Holz, T. Ach (Bonn/D)

Quantitative autofluorescence of AMD-typical lesions

Background: Fundus autofluorescence imaging allows noninvasive mapping of naturally and pathologically occurring fluorophores of the ocular fundus. A further development, quantitative fundus autofluorescence (QAF), allows for the exact determination of retinal AF intensities. QAF has been shown to be decreased overall in age-related macular degeneration (AMD). The relationship between QAF and various AMD lesions - drusen, subretinal drusenoid deposits (SDD) - is still unclear, but would be relevant for pathophysiological understanding of AMD.

Methods: Multimodal imaging (OCT, QAF) was obtained in 28 eyes of 28 subjects with intermediate AMD. Using modified FIJI plugins, SD-OCT and QAF images were aligned, then AMD lesions (hard/soft drusen, SDD) were labeled in both individual SD-OCT scans and QAF. QAF images from all subjects were averaged to determine the average QAF value for each pixel in the central 30° of the retina (=standard AMD retina). QAF intensities in the lesion area were determined in FIJI, exported, and compared with QAF intensities of the standard AMD retina. The difference in QAF intensity was expressed as a z value (hypothetical parameter measuring the difference in QAF values in number of standard deviations).
Results: Lesions from 17 eyes of 17 patients (9 female; 71.6 ± 7.6 years) with intermediate AMD were annotated to date. Overall, soft and hard drusen showed a very heterogeneous autofluorescence pattern with both increased and decreased autofluorescence. Soft drusen (n=13 patients) had on average decreased autofluorescence with a z-value of -0.091 ± 0.0858. Similarly, hard drusen (n=3 patients) showed locally decreased autofluorescence in the area of the lesion (z-value: -0.003 ± 0.001). SDD (n=3 patients) also had mostly reduced QAF in the area of the lesion (z value: -0.042 ± 0.013).
Discussion: Interestingly, similar to the global QAF at the ocular fundus, the lesion-specific QAF was often reduced, making the AMD typical lesions important in the QAF analysis. While in SDD a reduced QAF could be due to „shadowing" of the RPE by the subretinal lesions, in soft and hard sub-RPE drusen the reduced QAF would be due to redistribution and loss of autofluorescent granules. Lesion-specific QAF values could thus be used in the future for detailed AMD classification, including to characterize AMD lesions more precisely. Autofluorescence of lesions may supplement OCT imaging with information on the health of the RPE and its intracellular composition in the future.

3rd session

Ageing of the outer retina, RPE and choroid: intermediate AMD I

03.02 P

Jost B. Jonas[1], G.M. Kazakbaeva[2], S. Panda-Jonas[2], M.M. Bikbov[2] ([1]Mannheim/D, [2]Ufa/RUS)

Ural Eye and Medical study: prevalence and associated factor in AMD and specifically reticular pseudodrusen

Purpose: To assess the prevalence of age-related macular degeneration (AMD) in a Russian population.
Methods: The population-based Ural Eye and Medical Study conducted in a rural and urban area in Bashkortostan/Russia included 5,899 participants aged 40+ years. AMD defined according to the Beckman Initiative for Macular Research was assessed on fundus photographs and optical coherence tomographic images of 4932 (83.6%) participants.
Results: The prevalence of any AMD, early AMD, intermediate AMD, late AMD, geographic atrophy and neovascular AMD were 18.2% (95% confidence interval (CI):16.8,19.6), 11.6% (95%CI:10.4,12.8), 5.0% (95%CI:4.2,5.8), 1.6% (95%CI:1.1,2.0), 0.7% (95%CI:0.4,1.0) and 0.9% (95%CI:0.6,1.3) respectively, for individuals aged >55 years. Applying an age limit of 40+ years for the AMD definition, prevalence of any AMD, early AMD, intermediate AMD, late AMD, geographic atrophy and neovascular AMD were 14.1% (95%CI:13.1,15.1), 9.4% (95%CI:8.6,10.2), 3.8% (95%CI:3.2,4.3), 1.0% (95%CI:0.7,1.2), 0.4% (95%CI:0.2,0.6) and 0.5% (95%CI:0.3,0.7) respectively, for individuals aged 40+ years. Higher AMD prevalence was correlated with older age (odds ratio (OR):1.15;95%CI:1.13,1.16 ;P<0.001), rural region (OR:1.69;95%CI:1.32,2.17;P<0.001), lower diabetes prevalence (OR:0.56;95%CI:0.38,0.82 ;P=0.003), and shorter axial length (OR:0.89;95%CI:0.79,0.99; P=0.04). AMD prevalence was not significantly (all P≥0.20) correlated with any systemic parameter examined, except for lower prevalence of diabetes.
Conclusions: In this typical, ethnically mixed, urban and rural population from Russia, a higher AMD prevalence was mainly associated with older age, rural region of habitation, shorter axial length and lower prevalence of diabetes mellitus. The AMD prevalence was lower than in Europeans and higher than in East Asians.

03.04 P

Ulrich F. O. Luhmann Ulrich on behalf to the MACUSTAR consortium
(Basel/CH - Roche Pharmaceutical Research and Early Development, Translational Medicine Ophthalmology, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd, Grenzacherstrasse 124, 4070 Basel/CH)

MACUSTAR Study: Results from functional assessments in intermediate AMD

Purpose: Subjects with intermediate AMD (iAMD) have been shown to have difficulty in low luminance and low contrast conditions. To provide further evidence for visual function deficits in iAMD and to evaluate how different aspects of visual function characterized by a wide variety of clinical outcome measures changes longitudinally with disease progression or conversion to late AMD, we here report functional data obtained in the MACUSTAR clinical study during ≥ 3 years.
Method: The MACUSTAR clinical study is a multi-center study at 20 European sites across seven countries funded by the European Innovate Medicine Initiative. The study included a total of 718 individuals, mostly female (66%), 585 with iAMD, 34 early AMD, 43 late AMD and 56 with no AMD. The mean (SD) age at baseline was 71.9±7.0 years. 46 (8%) participants with iAMD had late AMD in the non-study eye. Visual function assessments performed in the

study were: best-corrected visual acuity (BCVA); low luminance visual acuity (LLVA); Moorfields acuity chart (MA); Pelli-Robson contrast sensitivity (CS); International Reading Speed Test (IReST); mesopic and scotopic fundus-controlled perimetry (mAT and sAT; Macular Integrity Assessment, iCare, Finland) and dark adaptometry (AdaptDx, Lumithera, USA). Quality of the visual function data was evaluated centrally every 6 months till the very recent data cut at 3.5 years median follow up. Baseline analyses comparing visual function outcomes across different disease stages were performed by linear regression models adjusted for age, sex, and phakic status with multiple testing correction. To evaluate the proportion of participants with abnormal visual function for each assessment, one sided normal reference limits (95th or 5th percentile) based on the No AMD group were used to establish thresholds and dichotomize the iAMD group.
Results: At baseline all VF measures except IReST were significantly worse in those with iAMD compared to those with no AMD and in general showed more prominent impairment when assessed in subjects with late AMD. However, absolute differences between iAMD and No AMD were smaller than the limits of repeatability and therefore cannot be deemed clinically significant. Using the established thresholds for separating normal from abnormal function, we discovered distinct functionally abnormal iAMD subgroups. Their visual function breaches the normal reference limits for the different assessments with proportion relative to all iAMD participants that range from around 13% for IReST to over 30% for CS and Rod Intercept Time (RIT). Overall, about 71% of iAMD subjects showed at least one functional deficit outside the normal reference limits. The prognostic value of such functional baseline deficiencies for conversion to late stages of AMD will be shared. Preliminary longitudinal analyses relative to baseline for the whole iAMD group revealed changes for functional tests including RIT, LLVA and MP over a period of 3.5 years.
Conclusion: The value of the observed heterogeneous baseline functional deficits in over 70% of iAMD patients as inclusion criteria for enrichment of trial populations and for prognosis of conversion to late AMD as well as the qualification path towards a clinical trial endpoint for functional assessments that describe functional decline within iAMD will be discussed with regulators in the near future.

Conflict of interest statement: UFOL is employee of F. Hoffmann La Roche ltd.

03.08 P **Marlene Saßmannshausen**[1], M. Vaisband[2], S. Döngelci[1], L. von der Emde[1], K. Sloan[3], J. Hasenauer[1], F.G. Holz[1], T. Ach[1] ([1]Bonn/D, [2]Salzburg/A, [3]Birmingham/USA)

Correlation of structural biomarkers to fundus-controlled perimetry in intermediate age-related macular degeneration: asix-year longitudinal study

Background: Age-related macular degeneration (AMD) is a chronic, multifactorial and degenerative retinal disease and still is a main cause for an irreversible vision loss in industrialized countries. Longitudinal structure-function correlations are needed to identify structural and functional biomarkers as early outcome measures for disease progression. Purpose: To correlate presence of age-related macular degeneration (AMD) associated structural biomarkers and changes of retinal morphology to spatially resolved retinal sensitivity assessments by mesopic and scotopic fundus-controlled perimetry (FCP) in patients with intermediate iAMD longitudinally over a follow-up period of 6 years.
Methods: Fifty-nine eyes of 59 patients (mean ± standard deviation (SD): 71.3 ± 8.7 years) with large drusen (>125µm) secondary to iAMD and 27 eyes of 27 age-matched healthy controls were included. Annual follow-up visits were performed over 6 years. Participants underwent multimodal retinal imaging including spectral domain optical coherence tomography (SD-OCT, volume: 30°x25°, 61 B-scans) as well as mesopic and scotopic FCP (56-stimulus grid: MP-1S, Nidek). At each FCP stimuli position and visit, presence of structural biomarkers was computer-assisted manually graded (including sub-retinal pigment epithelium (sub-RPE) drusen, subretinal drusenoid deposits (SDDs), hyperreflective foci (HRF), incomplete/complete retinal pigment epithelium and outer retinal atrophy (i/cRORA)) and spatially resolved retinal layer thicknesses extracted using an ImageJ plugin. Mixed effect models were applied analyzing the association of structural biomarkers and retinal layer thickness changes with mesopic/scotopic sensitivity losses.
Results: Over a 6-year observation period there was a mean change of -0.90 dB ±2.13 dB/year for mesopic and -0.79 dB ± 3.01 dB/year for scotopic testing. Decline was more pronounced for scotopic than mesopic sensitivity in presence of SDDs and sub-RPE drusen (scotopic: estimate: -0.97 dB; p=0.0005, mesopic: -0.53 dB; p=0.016) compared to study eyes with sub-RPE drusen only (scotopic: +0.05 dB; p=0.50 and mesopic: -0.13 dB; p=0.03). Presence of HRF had a stronger correlation to mesopic (-0.37 dB; p<0.001) than scotopic testing (-0.15 dB; p=0.106). A similar correlation was found at FCP positions with atrophy development (mesopic: -0.30 dB; p<0.005 (iRORA) and -0.18 dB; p=0.225 (cRORA) vs. scotopic: -0.16 dB; p=0.136 and -0.26 dB; p=0.149). With decreasing outer photoreceptor layer thicknesses (OS), there was a significant loss of scotopic and mesopic sensitivity testing (-0.02dB; p=0.022 (mesopic) and -0.02dB; p=0.011 (scotopic)).
Conclusions: Presence of SD-OCT based structural biomarkers and retinal layers thickness changes significantly impact longitudinal spatially resolved mesopic and scotopic retinal function in iAMD.

4th session

Ageing of the outer retina, RPE and choroid: intermediate AMD II

04.02 P **Yannick N. Liermann**[1], C. Behning[1], M. Saßmannshausen[1], L. Weinhold[1], B. Isselmann[1], M. Schmid[1], R.P. Finger[1], S. Schmitz-Valckenberg[1,2], F.G. Holz[1], M. Pfau[1,3], C.D. Luu[4], S. Thiele[1]
([1]Bonn/D, [2]Salt Lake City/USA, [3]Basel/CH, [4]Melbourne/AUS)
Functional characterization of the relative ellipsoid zone reflectivity in AMD

Background: First investigations suggest that the relative ellipsoid zone reflectivity (rEZR) on spectral-domain optical coherence tomography (SD-OCT) is an innovative surrogate for outer retinal integrity. Purpose: To better understand the rEZR's potential value as a novel biomarker, this study evaluates the association between the rEZR and retinal function as assessed by fundus-controlled microperimetry (FCP).
Methods: Study participants of the MACUSTAR study with age-related macular degeneration (AMD) and controls underwent SD-OCT Spectralis imaging (241 B-scans, field size 30°x25°). Mesopic and scotopic FCP with a 33-stimulus point grid was performed using the S-MAIA microperimeter (Centervue, Padova, Italy). The rEZR was determined in OCT raw images as the mean per volume scan (global) and spatially-resolved at each aligned FCP test point. Topographical information of the presence of reticular pseudodrusen (RPD) was determined by manual annotation of the RPD area in en-face infrared imaging. Linear mixed-effects models were applied to determine the association between the rEZR [arbitrary units, AU] and retinal sensitivity [dB], with co-variates adjusting for AMD status, age and eccentricity as well as the presence of RPD within the iAMD subgroup.
Results: A total of 281 eyes of 281 patients of (mean±SD) XY±XY years were included. In the global analysis, higher mesopic and scotopic average thresholds (AT) were significantly associated with a higher rEZR (coefficient estimate [95%-confidence interval (min-max)]) of 0.04 (0.01–0.07) AU (p=0.006) and 0.07 (0.04-0.10) AU (p<0.001), respectively. Further, the mesopic (-3.0 [-4.85—1.16] AU) and scotopic (-4.42 [-6.22—2.61] AU) ATs were shown to be more reduced in iAMD eyes with RPD (both: p≤0.002). Topographically, the rEZR was significantly associated with the stimulus threshold (ST) in mesopic (0.16 [0.07–0.26] AU) and scotopic (0.14 [0.03–0.24] AU) FCP (both: p<0.01). The rEZR was more decreased in RPD areas both when considering mesopic (-2.99 [-5.84 – -0.13] AU; p=0.040) and scotopic (-5.56 [-8.55 – -2.56] AU; p<0.001) FCP testing.
Conclusions: The rEZR showed an association with retinal sensitivity both globally and spatially-resolved, highlighting a potential structural-functional relation. Further, the presence of RPD, a known high-risk factor for AMD progression, significantly affects this association.

04.04 P **Jost B. Jonas**[1], T.A. Khalimov[2], S. Panda-Jona[3], M.M. Bikbov[2]
([1]Mannheim/D, [2]Ufa/RUS, [3]Heidelberg/D)
Intravitreal application of epidermal growth factor in non-exudative AMD

Purpose: To assess the safety of intravitreally applied epidermal growth factor (EGF).
Methods: The clinical interventional, prospective, single center, case series study included patients with age-related macular degeneration-related geographic atrophy (GA), in whom the eye with the worse best corrected visual acuity (BCVA) underwent a single, or repeated, intravitreal injection of EGF (0.75µg in 50µL). At baseline and afterwards, the eyes underwent ophthalmological examinations.
Results: The study included 7 patients (mean age:70.0±12.2 years (range:54-86 years), with 5 patients receiving a single injection, and two patients receiving two intravitreal injections in an interval of 4 weeks. Mean duration of follow-up was 97±97 days (median:35 days;range:7-240 days). Mean BCVA was lower at baseline than at study end (1.41±0.44 logMAR versus 0.97±0.12 logMAR;P=0.03). Mean size of the GA lesions did not differ significantly between baseline and study end (29,212±22,887 pixels versus 29,300±22,905 pixels;P=0.59) nor did the mean perimetric mean defect (-10.3±5.9dB versus 12.0±8.8dB;P=0.35) or the electroretinographical b-wave amplitude (44.53±31.7µV versus 64.5±25.5µV;P=0.12). After a second injection 4 weeks after the first injection, one of two patients developed a cystoid macular edema in association with an induced incomplete posterior vitreous detachment. It persisted for three weeks. Visual acuity in this eye improved from 1.0 LogMAR at baseline to 0.80 LogMAR at study end.
Conclusions: Except for one eye with temporary, self-resolving cystoid macular edema, single and repeated intravitreal applications of EGF (0.75 µg) in patients with GA did not lead to intraocular inflammations or any observed intraocular side effect.

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Apellis

04.05 P **Ana Sofia Falcão,** M. Pedro, V. Miguel, R. Coelho, S. Tenreiro, M. Seabra (Lisbon/P)
NRF2 as a therapeutic target in early and intermediate AMD

Age-related macular degeneration (AMD) is the most common blinding disease in the western world and is currently incurable. One of the main pathologic features of AMD is the retinal pigment epithelium (RPE) degeneration as well as the accumulation of autofluorescence (lipofuscin). We have developed a model system that recapitulates some AMD features in vitro where feeding human RPE monolayers in culture with porcine photoreceptor outer segments (POS) leads to accumulation of autofluorescent granules similar to lipofuscin in vivo, mimicking RPE cellular stress and disease. Interestingly, our preliminary results in RPE cells showed that overexpression of the transcriptional regulator NRF2, as well as treatment with dimethyl fumarate (DMF), a known NRF2 activator, can prevent the formation and/or resolve POS derived autofluorescent granules, suggesting that this pathway and the proteins it controls are important for autofluorescent granule formation. Thus, our hypothesis is that induction of an anti-oxidative stress response could represent a therapeutic strategy in early/intermediate AMD. Focusing on repurposing clinically approved drugs that are described to be pharmacological modulators of NRF2, such as Curcumin, Bardoxolone methyl and Sulforaphane, we tested these compounds in our in vitro model, and evaluate their ability to decrease autofluorescent granules formation, as compared with DMF. Our first results point out Curcumin as an emerging pharmacological approach to decrease the accumulation of autofluorescence. Further studies will also include human phenolic metabolites library screening of NRF2 activators. We are also validating protocols for NRF2 activation in RPE cells by using western blot, immunofluorescence and gene expression assays. Overall, this project could represent a major step forward, not only for AMD treatment but also for other age-related diseases, and consequently, will contribute to a healthier ageing. Funding: La Caixa Foundation (HR22-00569 NASCENT); Fundação para a Ciência e Tecnologia (Portugal) through the R&D unit iNOVA4Health (UIDB/04462/2020) and LS4FUTURE Associated Laboratory (LA/P/0087/2020); COST Action BenBedPhar (CA20121).

04.06 P **Erik van kuijk**[1]**,** A.G. Robson[2], D. Pauleikhoff[3], J.D. Moreland[4]
([1]Minneapolis/USA, [2]London/UK, [3]Muenster/D, [4]Keele/UK)
Assessment of macular pigment distribution and stability in healthy subjects, including individuals monitored annually for periods of up to two decades

Background: To assess the foveal and total retinal macular pigment (MP) complement in healthy subjects and to monitor the stability of MP spatial distribution profiles for periods of up to two decades.
Methods: Measurements of MP retinal profiles were made by 51 subjects using the psychophysical technique of minimum motion photometry (test 460nm, comparison 580nm). Two foveal fields (0.9º and 2.2º diameter) and 11 annular segments (eccentricities from 0.8º to 7.5º) were used. The total complement within the central 15 degrees was estimated by numerical integration and compared with foveal values. Four subjects with widely different MP profiles underwent annual testing for periods of 21-25 years.
Results: Detailed examinations characterised a wide range of MP distribution profiles using motion photometry. There was a lack of correlation between peak MP optical density at the fovea and assessments of the total complement of MP within the central 15 or 21 degrees. Serial psychophysical assessments over periods of 21-25 years in 4 cases demonstrated a high degree of stability at all macular locations including the fovea; plots of peak MP optical density against time showed slopes ranging from -0.0026 to +0.0029.
Conclusions: The total amount of macular pigment cannot be accurately estimated from foveal values.Widely different MP distribution profiles in healthy subjects demonstrate a high degree of long-term stability in four subjects. This could be pertinent to studies that aim to monitor MP or fundus autofluorescence in disease, or modify MP through dietary supplementation.

04.07 P **Andrii Serhiienko**[1]**,** N. Dzuba[1], O. Pekaryk[2] ([1]Kyiv/UKR, [2]Winnipeg/CAN)
The influence of photo bio modulation on macular pigment optical density and visual acuity in dry form AMD

Background: Strategies aimed at preventing AMD involve accumulating Xanthophyllic pigments in the macula, which are characterized by changes in Macular Pigment Optical Density (MPOD). The influence of photobiomodulation (PMB) on MPOD had not been studied previously.
Objectives: The goal of this study was to investigate changes in MPOD and BCVA for patients with dry AMD after PMB.
Methods: The main group of 90 patients (152 eyes) underwent two courses of PMB at a 6-month interval, while the control group of 20 patients (36 eyes) did not receive any treatment. All patients did not use drugs containing lutein and zeaxanthin. The observation period was one year, during which MPOD was assessed using the ”Maculux praxis” densitometer and the method of heterochromatic flick photometry.
Results: Before the PMB, MPOD, and BCVA values were equal to 0.25±0.006 units of MPOD and 68±1.14 letters of the ETDRS chart. In the main group, the value of MPOD increased to 0.36±0.008 units after the first course of PMB. After the second course, it increased to the value of 0.43±0.008 units. After the two courses of PMB, BCVA

increased from 68±1.14 to 76±1.16 letters. In the control group, MPOD values remained unchanged (0.25±0.006), and BCVA values decreased from 68±1.13 to 65±1.14 letters. A strong correlation between the dynamics of BCVA and MPOD was noted (0.63).
Conclusion: Two courses of PMB resulted in statistically significant increases in MPOD and BCVA for patients with dry AMD. The maximum MPOD values had been observed one month later after the first and second courses of PMB, respectively.

5th session

Ageing of the outer retina, RPE and choroid: immunity I

05.02 P **Rosa Dolz-Marco,** L. Vidal-Oliver, S. Montolío Marzo, R. Gallego-Pinazo (Valencia/E)
En face high axial resolution optical coherence tomography imaging in atrophic AMD: clinical signs

Purpose: To assess the utility of en face high axial resolution optical coherence tomography (OCT) in the assessment of atrophic lesions in non-neovascular age-related macular degeneration (AMD) using a research OCT prototype (High-Res OCT, Heidelberg Engineering, Germany) with 3 µm optical axial resolution.
Methods: Retrospective review of images of patients with non-neovascular AMD. We analyzed images obtained using a 20x20 ART1 OCT pattern. We collected clinical data including: type of drusen, presence of pigmentary changes and retinal pigment epithelium and outer retinal atrophy (RORA) / hyper-transmission defects (HTD), both in the B-scans and en face images.
Results: 46 eyes of 32 patients with non-neovascular AMD were included. Soft drusen were the most frequent deposit (n=28), followed by subretinal drusenoid deposits (SDD) (n=14), cuticular drusen (n=11), acquired vitelliform lesions (AVL) (n=4), calcified soft drusen (n=4) and drusenoid RPE detachment (n=1). HTD were present in 21 eyes in the en face images, corresponding with areas of RORA in the B-scans. En face images also showed different forms of hyperreflective round areas similar to the HTD. Some of these lesions had an "Halo" appearance (n=35) corresponding to drusen with RPE thinning in the apex of the lesion. Other lesions had a "Inverted Halo" appearance (n=14) corresponding to areas of RORA with central hyperreflective clumps corresponding to pigmentary changes. Other pigmentary changes presented a heterogeneous distribution (n=31) not related to HTD.
Conclusions: Fundus autofluorescence is the gold standard to depict areas of RPE atrophy. However, limitations of this technique include the need of pupil dilatation and the visualization of foveal lesions. En face OCT images using high axial resolution OCT in patients with RORA were able to show areas of HTD, but also demonstrated some confounding factors. Dispersion of pigment limited the visualization of HTD, and the presence of drusen were seen as hyperreflective lesions with a variable halo of hyporeflectivity. Analysis of the B-scans might be necessary to rule out confounding factors.

05.03 P **Scott McPherson,** H. Roehrich, F.J. van Kuijk (Minneapolis/USA)
Detection of sub-retinal epithelial cell layer deposits in mice by zinc staining using ex-vivo and in-vivo methods

Background: The relationship between zinc and age-related macular degeneration (AMD) has only been explored with epidemiological and in-vitro studies. Ex-vivo and in-vitro assays associated with animal models are crucial for understanding zinc's role in AMD. Here we report detection and quantification of sub-retinal epithelial zinc using ex-vivo analysis and in-vivo injection of zinc probes.
Methods: We employed mice deficient in superoxide dismutase-type 1 (CuZn-SOD) or -type 2 (Mn-SOD). Zinc and sub-retinal epithelial deposits were detected using ZPP1 or a novel probe (ZQuinT) that fluoresce upon binding zinc. Retinal flat mounts were stained ex-vivo with zinc probe or examined directly without additional staining following in-vivo injection of probe. Imaging and analysis were done by fluorescence microscopy.
Results: Sub-retinal epithelial cell layer deposits in CuZn-SOD and Mn-SOD deficient mice were detected in flat mounts following in-vivo injection of ZPP1 and ZQuinT. Analysis of probe concentration and incubation time revealed that micromolar concentrations of ZPP1 and millimolar concentrations of ZQuinT allowed to circulate ten minutes were sufficient to detect zinc and sub-retinal epithelial cell layer deposits. Examination of flat mounts showed detection of sub-retinal epithelial cell layer deposits from mice receiving in-vivo zinc probe was similar to detection by ex-vivo staining of retinal flat mounts. We observed increased levels of sub-retinal zinc in normally housed (normal light) CuZn-SOD deficient mice compared to wild type mice suggesting zinc accumulation can be linked to risk factors associated with AMD.
Conclusions: Zinc dysregulation is a crucial initiating factor in AMD. Animal models and in-vivo assays allows for analysis of retinal zinc in response to genetic and environmental factors associated with AMD. Detection of sub retinal epithelial cell layer deposits after in-vivo zinc probe injection is an essential step in developing clinical and research assays that can detect the earliest, sub-clinical cellular changes associated with AMD.

05.06 P **José Hurst,** A.Fietz, S. Schnichels (Tübingen/D)
Inflammatory environment caused dysfunctional autophagy in primary RPE monolayers

Background: Autophagy dysfunction in RPE (retinal pigment epithelium) cells can lead to the accumulation of toxic material, oxidative stress and inflammation, all of which may contribute to the development and progression of age-related macular degeneration (AMD). RPE cells are essential in maintaining retinal health and photoreceptor survival. AMD represents a complex, multifactorial disease, including RPE dysfunction and cell death. The dysfunction of RPE autophagy results in in the accumulation of toxic products, such as drusen, in the subretinal space, which in turn can further damage the surrounding cells. In our inflammatory porcine ex vivo model of AMD, we observed that this inflammatory environment massively disrupts the autophagy-ability of the RPE within a very short time-frame.
Methods: Primary porcine RPE cells were cultured as functional monolayers for 4-5 weeks and then co-cultured with retinal explants for 2 days. TER measurements as well as analysis of inflammatory cytokines and autophagy markers (ELISA, qRT-PCR) and apoptosis level (Caspase 3/7 activity) were performed. Further autophagosome expression, stress fibres (β-Actin) and neutral lipid deposition (Lipidgreen2) were monitored by specific stainings.
Results: A vast increase of TNF-? (3,7-fold%, p<0.01), IL-6 (20-fold%, p<0.05), IL-1? (5,8-fold%, p<0.01), INF-y was observed in the RPE cells as well as in the retinal explant. mRNA expression of the autophagy markers Beclin and Sequestom was reduced, as well as autophagosomes (3-fold, p<0.0001). Apoptosis induction was demonstrated with significantly induced caspase 3/7-activity. Neutral lipids were accumulated, and the number of stress fibres was increased.
Conclusions: RPE cells react very sensitive to an inflammatory environment, resulting in barrier loss, apoptotic cell death and dysfunctional autophagy. Based on this model, the pathogenesis of RPE in inflammatory diseases like AMD can be further explored and therapeutic options investigated.

05.07 P **Yara Lechanteur**[1]**,** M. Shahabi[1], F. Cinque[1], C. Klaver[1,2], B. van den Heuvel[1]
([1]Nijmegen/NL, [2]Rotterdam/NL)
Retrospective evaluation of complement components and activation products measure ments in patients with AMD in a diagnostic setting

Background: Earlier this year the FDA has approved pegcetacoplan injections for the treatment of geographic atrophy (GA) secondary to AMD. Phase III trials have shown a reduction in GA lesion growth in treated subjects. However, given the relatively high prevalence of the disease and risks associated with frequent injections, it would be extremely valuable to know which subgroups of patients would benefit most from this treatment. With this study we hope to gain more insight in the levels of complement components and activation products in AMD patients.
Methods: Complement components and activation products (CFI, CFH, C2, C5, CFB, CFD, Bb, C3a, C3bc, C3bBbP, C4D, C5a, TCC, and properdine) were measured in plasma samples of 43 patients with AMD (18 late AMD and 25 early/intermediate AMD) in a diagnostic setting. We used descriptive analyses to look for patterns and combinations of elevated measurements.
Results: In 40 patients (93%) at least 1 factor was elevated. The most frequently elevated factor was C3bBbP (79%), followed by CFH (45%) and TCC (40%). For C2, C3bc, C4D and Properdine elevated levels were only found in 5% or less. We further noticed that the combination of elevated CFH, C5, CFB and C3bBP levels occurred relatively frequently with 14 patients (33%) having elevated levels of at least 3 of these factors.
Conclusion: We observed specific patterns of elevated levels of complement activation products and components. We are planning future studies, including prospective evaluations of these factors over time with the aim to identify a set of complement components and activation markers that can serve as biomarkers for progression. These would ultimately be ideal candidates for therapy development. In addition, insight in how these levels change during the course of the disease could have implications for patient selection and the window of opportunity for treatment with complement inhibitors.

05.08 P **Sofie ten Brink**[1]**,** L. Koolen[1], G. Gagliardi[1], B. Bakker[1], C.W.W. Klaver[1,2,3], Y.T.E. Lechanteur1, S. Albert[1], R. Bakker[4], A.I. den Hollander[1,5], S. Almedawar[4] ([1]Nijmegen/NL, [2]Rotterdam/NL, 3Basel/CH, [4]Ingelheim/D, 5Cambridge/USA)
Paradoxical complement inhibitor response in highly penetrant CFH variant compared to control iPSC lines

Background: Several CFH variants were previously correlated to age-related macular degeneration (AMD). However, previous in vitro work has mostly focussed on the common p.His402Tyr variant. In this project we characterise an induced pluripotent stem cell derived retinal pigment epithelium (iPSC-RPE) model with CFH variants that are highly penetrant for AMD and treat them with A2E and blue light. We expect a decreased response in AMD lines compared to controls.
Methods: Three iPSC lines were derived from 3 AMD patients with a rare CFH variant (p.Lys204Thrfs*26, p.Ile-

184Leufs*33 or p.Arg175Gln) and 3 controls without AMD (2 wt CFH and 1 with p.His402Tyr), their characterisation was previously described. These lines were differentiated to RPE cells and exposed to A2E for 3 days, followed by blue light exposure. Afterwards, RNA-seq was performed.
Results: In both families of the donors for the lines with truncating variants all family members with the variant had AMD (n = 6 for p.Ile184Leufs*33 and n = 4 for p.Lys204Thrfs*26), those without the variants did not have AMD (n = 4 for the p.Ile184Leufs*33 family and n = 4 for the p.Lys204Thrfs*26 family). In the p.Arg175Gln family all genotyped AMD patients had the variant (n = 6), but healthy . The cell lines displayed RPE morphology and increased expression of RPE differentiation markers RPE65, BEST, MITF, PEDF and VEGF. Treated cells displayed a decreased expression of the complement inhibitors CFH, CFI, CD59 and VTN, as well as CFHR1/2/3/5. However, this effect was reduced in the patient cell lines compared to control.
Conclusion: A paradoxically reduced decrease in CFH, CFI, CD59, VTN, and CFHR1/2/3/5 expression was observed in patient versus control lines after exposure to A2E and blue light. Our data contradict previous observations by Hallam et al. (2017) showing increased CFI and CFH expression in p.His402Tyr lines. These opposing results underline the complexity of complement regulation in AMD.

6th session

Ageing of the outer retina, RPE and choroid: immunity II

06.06 P **Boris Stanzel**[1] **,** C. Burri[2], S. Al-Nawaiseh[1,3], P. Wakili[1], S. J. Gasparini[4], G. Farese[1], C. Krötz[1], B. Greber[5], M. Frenz[2], P. Szurman[1], A. Schulz[1], M. Ader[4] ([1]Sulzbach/D, [2]Bern/CH, [3]Münster/D, [4]Dresden/D, [5]Schorndorf/D)
Large-Area RPE Removal by Laser followed by hiPS-RPE suspension transplantation in rabbits

Purpose: Cell therapeutics for AMD were often implanted regardless of RPE status in the target zone. This may result in RPE multilayering. Here we study a novel laser to remove RPE without collateral damage prior to RPE implantation to encourage better subretinal integration.
Methods: Pigment rabbits (n=26) were triple-immunosuppressed. Using aSLO/ OCT (Heidelberg Engineering) combined with a prototype laser (Meridian Medical), a large area of RPE was selectively removed in 19 rabbits. Animals with laser lesions only, or without laser lesions served as controls (n=7). A 25 gauge vitrectomy (Geuder) with removal of posterior hyaloid membrane was performed thereafter. Human iPS-RPE (1000 cells/µl) were manually injected using a 100 µl syringe (Hamilton) connected to a 38G cannula (MedOne) into the RPE laser lesion, or over healthy RPE in controls, monitored by intraoperative OCT imaging (RESCAN 700, Zeiss). In vivo follow up/ retinal imaging was up to 12 weeks including fluorescein and indocyanine angiography, as well as SD-OCT (Spectralis, Heidelberg Engineering).
Results: Representative RPE laser wounds exhibited mild late phase FA& ICGA leakage, without abnormal outer retinal or choroidal hyperreflectivity on OCT. By contrast, lesions with earlier leakage on FA/ ICGA showed beam-sized outer retinal hyperreflectivity on OCT, suggesting coagulation. The size of the RPE wounds was typically 10-12mm. iOCT demonstrated in an immediate and directed spread of the bleb retinal detachment (bRD) within the lasered zone. By contrast, bRDs performed over non-lasered RPE raised slower with a circu lar spread. Subretinal injection ranged from 5-70?l, with lesser volumes/ larger bRDs areas over lasered regions. At 6 and 12 weeks, none of implanted regions showed FA/ICGA leakage, some lesions had blockage due to hyperpigmentation; on OCT, representative areas showed preserved ellipsoid bands, with some RPE undulations. Lasered/implanted areas with a peripheral hyperpigmentation showed central outer retinal atrophy along with irregular RPE. Control laser and/or implantation sites showed retinal atrophy and a variably thickened RPE band.
Conclusions: Large-area RPE removal with laser disruption is feasible in healthy rabbits and appears to facilitate superior integration of RPE suspension grafts, compared to subretinal injection alone. Future work aims to correlate histology with in vivo imaging.

7th session

Neovascular AMD and Imaging

07.02 P **Oliver Zeitz,** L. Flesch, V. Knecht, D.P. Frentzel, S. Rau, A. Rübsam, S.E. Künzel, S. Wolf, F. Dreher, M. Schuette, B. Lange, M.-L. Yaspo, H. Lehrach, A.M. Joussen (Berlin/D)
The BIOMAC-Study:
Modulation of CNV activity in nAMD and anti-VEGF treatment need through systemic factors

Background: Inflammation and angiogenesis are the key pathophysiological mechanisms of neovascular age-related macular degeneration (nAMD). Both mechanisms are not specific to the eye, yet general mechanisms of the organism. Hence, the BIOMAC study investigated the influence of systemic factors on the course and treatment response in a multi-omics approach.
Methods: BIOMAC is a cohort of 46 nAMD subjects. Twenty-one subjects had well controlled choroidal neova-

scularization (CNV) under anti-VEGF treatment (LF cluster). In the remaining 25 subjects, CNV activity was poorly controlled despite injections every 4-6 weeks (HF cluster). Proteomic profiles in peripheral blood samples were determined by LC-MS/MS mass spectrometry. Extensive in-silico modelling was performed to identify potential proteomic signatures underlying the clinical phenotype.
Results: Both strata were well balanced regarding age (HF 78.4±8.14; LF 79.7±7.00 years), gender (HF 40% LF 61.9% female) and BCVA (HF 61.4±15.7; LF 65.0±12.4). Due to the group definition, central retinal thickness differed between HF and LF (HF 352.2±98.0 vs. LF 274.8±45.7µm. Descriptively, 6 proteins were up- and 3 downregulated in HF vs. LF. Up-regulated proteins: complement c1q subcomponent subunit b (ratio HF/LF=1,84), cytosol aminopeptidase (ratio HF/LF=1.54), and insulin-like growth factor-binding protein 3 (ratio HF/LF=4.1496). Down-regulated proteins: Acidic leucine-rich nuclear phosphoprotein 32 family member A (ratio HF/LF=0.67). Applying advanced statistics, proteome-based clustering results in two distinct clusters of nAMD. One cluster exhibits a strong signature for oxidative stress response. If matched to clinical features, pulmonary dysfunction is identified as underlying health condition in these patients. In contrast, applying a non-linear machine-learning model identifies complex molecular patterns hidden in a high number of proteomic dimensions determining macular disease expression.
Conclusions: So far not considered systemic signals in the peripheral blood proteome contribute to the clinically observed phenotype of nAMD, which should be considered in future translational research on AMD.

07.12 P **Alaa Din Abdin,** O. Hanifa, I. Weinstein, C. Munteanu, B. Seitz (Homburg/Saar/D)
Long-term choroidal thickness changes after anti-VEGF treatment for neovascular AMD depending on the type of macular neovascularisation (5 year follow-up)

Purpose: To evaluate long-term changes in subfoveal choroidal thickness (SFCT) after anti-vascular endothelial growth factor (VEGF) treatment for neovascular age-related macular degeneration (AMD) depending on the type of macular neovascularisation (MNV): MNV type 1 (within the sub-RPE space) and MNV type 2 (within the subretinal space).
Methods: This retrospective study included 101 eyes from 83 patients with MNV type 1 or 2 who received anti-VEGF therapy over a 60-month period. All eyes were treated initially with intravitreal bevacizumab. In case of non-response to bevacizumab, treatment was switched to other agents. SFCT was measured at baseline as well as 6, 12, 24, 36, 48 and 60 months after treatment.
Results: Of the 101 eyes, 62 eyes had MNV-1 (group 1) and 39 eyes had MNV-2 (group 2). There were no significant differences between the study groups regarding patients' age (80±10 vs. 82±9 years, p =0.2) and the number of injections per eye over a period of 60 months (33.5±11 vs. 29±14, p=0.2). In group 1 (MNV-1), SFCT (µm) changed from 198±53 before treatment to 196±56 after 6 months (p=0.31), to 192±59 after 12 months (p=0.06), to 199±60 after 24 months (p=0.82), to 186±58 after 36 months (p=0.01), to 179±55 after 48 months (p=0.001) and to 172±49 after 60 months (p=0.001). In group 2 (MNV-2), SFCT (µm) changed from 191±45 before treatment to 191±54 after 6 months (p=0.88), to 200±61 after 12 months (p=0.11), to 193±60 after 24 months (p=0.71), to 192±59 after 36 months (p=0.72), to 196±68 after 48 months (p=0.80) and to 186±57 after 60 months (p=0.70).
Conclusion: Despite a comparable number of anti-VEGF injections, a significant long-term reduction in subfoveal choroidal thickness was found only in eyes with MNV type 1, as opposed to eyes with MNV type 2. These results might suggest that choroidal thickness changes in eyes with MNV type 1 may be more sensitive to anti-VEGF treatment compared to eyes with MNV type 2.

07.13 P **Wissam Aljundi,** C. Munteanu, B. Seitz, A.D. Abdin (Homburg/Saar/D)
Short-term results of intravitreal faricimab for refractory nMD

Background: To assess short-term functional and anatomical outcomes of intravitreal faricimab (IVF) for previously treated refractory neovascular age-related macular degeneration (nAMD) in real-world setting.
Methods: Retrospective analysis of 15 eyes treated with 4x IVI of faricimab 6 mg/0.05 mL and followed for 4 weeks after last IVI. All patients were switched to IVF after treatment with at least two other anti-vascular endothelial growth factors (VEGF). All eyes received 4x IVI monthly as an upload phase. Main outcome measures: best corrected visual acuity (BCVA), central macular thickness (CMT), and retinal fluid distribution.
Results: 15 eyes of 15 patients with nAMD (67% males) with a mean age of 79±6 years were included. The number of previous anti-VEGF IVIs/eye was 34±20 before switching to IVF. BCVA (logMAR) did not change significantly from 0.7±0.27 to 0.62±0.3 (p=0.48). CMT (µm) decreased significantly from 426±65 to 373±66 (p=0.03). The number of eyes with subretinal fluid (SRF) decreased significantly from 10 (67%) to 4 (16%) (p=0.02). There were no significant changes regarding the distribution of intraretinal fluid or pigment epithelial detachment (p>0.05). A complete retinal and subretinal fluid resolution was achieved in 2 eyes (13%). No adverse events were noticed.
Conclusion: In the short term, IVF resulted in significant decrease in CMT, as well as SRF rate, and thus appears to be an effective treatment alternative for the management of therapy-refractory nAMD. However, a significant increase in visual acuity was not observed.

07.14 P **Jakob Siedlecki,** J.E. Klaas, L.F. Keidel, B. Asani, N. Luft, S.G. Priglinger, B. Schworm (Munich/D)

Progression of type 1 macular neovascularization into aneurysmal polypoidal choroidal vasculopathy within the pachychoroid spectrum

Purpose: To describe the progression of type 1 macular neovascularization (MNV) in pachychoroid neovasculopathy (PNV) into pachychoroid aneurysmal type 1 macular neovascularization (PAT1)/polypoidal choroidal vasculopathy (PCV).
Methods: Patients diagnosed with PNV who had received multimodal imaging for ≥2 years were reviewed for the presence of MNV, aneurysms within the MNV, and subfoveal choroidal thickness (SFCT).
Results: In total, 37 eyes of 32 patients with PNV with a mean follow-up of 3.3 ± 1.1 years (range, 2.0–5.2) were included in the study. At PNV diagnosis, the mean age was 59.7 ± 8.7 years (range, 38.5–78.0 years) and mean SFCT was 357 ± 92 µm (185–589). During the follow-up, 5 (13.5%) eyes developed aneurysms after a mean 3.4 ± 0.8 years (2.3–4.2), defining PAT1/PCV. The risk of PAT1/PCV conversion was 7.4% at year 3, 13.6% at year 4, and 30.7% at year 5. A mean of 5.2 ± 4.0 to 7.9 ± 3.6 intravitreal anti-VEGF injections were given per year, resulting in a significant reduction of SFCT to 317 ± 104 ?m (122–589) (P = 0.0007). The age at diagnosis of PNV was significantly lower in eyes that later went on to develop PAT1/PCV (54.0 ± 5.6 [45.9–60.5] vs. 61.2?±?8.4 [38.5–78.0] years; P = 0.025). At the end of the follow-up, SFCT had on average decreased by 14.0% ± 17.6% (55.9% to 23.1%) in the PNV group, whereas it had increased by mean 6.9% ± 4.4% (0.00%–10.8%) in the PAT1/PCV conversion group (P = 0.0025).
Conclusions: PNV can develop aneurysms within its type 1 MNV, defining the conversion to PAT1/PCV. In this study, Kaplan–Meier estimates of risk for conversion of 7.4% at year 3, 13.6% at year 4, and 30.7% at year 5. A similar process of type 1 MNV to PCV progression should be investigated in age-related macular degeneration.

07.15 P **Francesco Cinque**[1]**,** S. ten Brink[1], M. Shahabi[1], A. de Breuk[1], T. Heesterbeek[1], C. Klaver[1,2,3], C. Hoyng[1], Y. Lechanteur[1] ([1]Nijmegen/NL, [2]Rotterdam/NL, [3]Basel/CH)

Preliminary clinical and progression analysis of a prospective cohort study of unilateral nAMD

Background: Approximately 28.9% of age-related macular degeneration (AMD) patients will experience visual impairment. Neovascular AMD (nAMD) remains a major threat to functional vision. Currently, little is known regarding long-term progression to nAMD nor vision prognoses of fellow-eyes that have not progressed to nAMD.
Method: Unilateral nAMD patients were referred to our tertiary outpatient clinic by collaborating retinal specialists. Patients were then imaged biannually using i.a. SD-OCT, OCT-angiography for at least 1 year. Presenting visual acuity was measured (ETDRS-chart). Ophthalmic history was assessed via questionnaires. Outcomes include the progression rate to nAMD in the fellow eye per 100-person years (PR) and functional vision (best seeing eye >.5 (decimal)). Progression during follow-up was evaluated using fluorescein angiography. Patients lost to follow-up were contacted by telephone. Patients were allotted in groups at the study baseline according to time since nAMD diagnosis ranging from <2 years (group 1), 2 to 5 years (group 2) and 5+ years (group 3). Functional vision and PR group differences were compared via chi-squared tests.
Results: We included n = 133 patients from Jan 2018 to Nov 2022, aged 77 (9) years, (female 87/133). Median (IQR) time since diagnosis was 3 (5) years. PR was 10 per 100 person-years for the total cohort. The PR for groups 1-3 did not differ (14, 10, 10 per 100 person-years resp.) (P >.05). The median (IQR) time since diagnosis in group 3 was 9 (4) years. Only group 3 featured patients without functional vision (87%) whilst group 1 (100%) and 2 (100%) did not (P <.05).
Conclusion: Unilateral nAMD patients remain at a high risk of progression to bilateral nAMD even after a decade. For patients whose fellow-eye does not progress, functional vision is preserved for the majority of patients regardless of time since diagnosis.

Schnell.[1] Stark. Switchen.

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1 Bilgic A et al. J Clin Med. 2021; 10(13): 2758. doi:10.3390/jcm10132758.

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