ARVO 2017 Annual Meeting Abstracts

382 Retinal vascular diseases II (excluding diabetes)
Tuesday, May 09, 2017 3:45 PM–5:30 PM
Program #/Board # Range: 3646–3679/B0271–B0304
Owning Section: Retina

Program Number: 3646 Poster Board Number: B0271
Presentation Time: 3:45 PM–5:30 PM
Quantitative Analysis of Retinal Capillary Density and Foveal Avascular Zone Area Using Optical Coherence Tomography Angiography of Normal Eyes
Sean T. Garrity¹, Nicholas A. Iafe¹, Nopasak Phasukkijwatana¹, Xuejing Chen¹, David Sarraf¹. ¹Ophthalmology, UCLA, Los Angeles, PA; ²Retina, Tufts Medical Center/Ophthalmic Consultants of Boston, Boston, MA.

Purpose: To quantify the retinal vessel density (VD) and foveal avascular zone (FAZ) dimensions in normal subjects according to age using OCT angiography (OCTA).

Methods: 74 healthy subjects (128 eyes) were recruited. All eyes underwent OCTA using AngioVue® with split-spectrum amplitude-decorrelation algorithm (SSADA) and motion correction technology (MCT). The enface images of the retina vasculature were generated using AngioAnalytics research software with 3D projection artifacts removal (PAR) from the OCTA volume data and automatic segmentation of the ILM, IPL, and OPL boundaries. OCTA scans were analyzed and the VD and FAZ area were calculated.

Results: 108 normal eyes were included (mean age 48 ± 20 years). The mean VD was 15.683 ± 1.691 mm² in the superficial capillary plexus (SCP), 15.224 ± 1.435 mm² in the intermediate capillary plexus (ICP), and 16.370 ± 1.919 mm² in the deep capillary plexus (DCP) in 3x3-mm OCTA scans. Mean FAZ area was 0.277 ± 0.090 mm². The annual rate of decrease in VD with increasing age was -0.23% in the SCP, -0.22% in the ICP and -0.29% in the DCP. The rate of increase in FAZ area was 0.25% per year.

Conclusions: This analysis employed novel software to eliminate projection artifact and provides for the first time normative data on the ICP in addition to the SCP and DCP. VD of the macula decreases with increasing age while the FAZ area increases with age.

Commercial Relationships: Sean T. Garrity, None; Nicholas A. Iafe, None; Nopasak Phasukkijwatana, None; Xuejing Chen, None; David Sarraf, Genentech (C), Regeneron (F), Optovue (F), Optovue (C), Genentech (F), Allergan (F)

Program Number: 3647 Poster Board Number: B0272
Presentation Time: 3:45 PM–5:30 PM
Hyperbaric Therapy for Central Retinal Artery Occlusion: Is It Really Worth It? A Cost Benefit Analysis

Purpose: To study the influence of hyperbaric oxygen therapy (HBOT) for central retinal artery occlusion (CRAO), specifically cost-benefit analysis, quality of life improvement and healthcare associated roadblocks.

Methods: Four subjects with CRAO treated with HBOT at Westchester Medical Center between 2012 and 2015 were identified. Variables investigated included time of onset of symptoms to time of arrival, Door-To-Chamber (DTC) time, number of treatments, visual acuity, average cost of treatment and average hospital stay.

Results: 50% of patients who underwent treatment had no improvement in visual acuity while 50% had limited recovery. 100% of patients (4/4) reported no improvement in quality of life. Average time to presentation was 11.85 hours (711 minutes). Average DTC was 8.25 hours (495 minutes). Average total cost including treatment and hospital stay was $17,826/patient.

Conclusions: Poor cost-to-benefit ratio and a strain on hospital resources make HBOT an inadequate treatment modality for CRAO.

Commercial Relationships: Paymohn Mahdavi, None; Brett P. Bielory, None; Robert G. Josephberg, None

Program Number: 3648 Poster Board Number: B0273
Presentation Time: 3:45 PM–5:30 PM
Anti-VEGF treatment of macular edema using a treat-and-extend regimen in retinal vein occlusion in clinical practice: 18 months follow-up
Manar Addou Regnard, Agnes Glacet-Bernard, Rim Sekfali, Alexandra Miere, Eric H SOUIED. ophthalmology, Centre hospitalier intercommunal de créteil, Paris, France.

Purpose: To evaluate long-term visual and anatomical outcomes of a treat-and-extend (T&E) regimen in the treatment by Ranibizumab or Aflibercept of macular edema (ME) secondary to retinal vein occlusion (RVO) in clinical practice.

Methods: Single-center prospective unicentral study of patients with ME secondary to central RVO or its branches treated with intravitreal injections of ranibizumab or aflibercept according to a T&E protocol between 2014 and 2015, and followed for at least 18 months. The data collected were demographic and ophthalmic data before and after treatment (best corrected visual acuity (BCVA), biomicroscopic examination, optical coherence tomography, angiography).

The primary end point was mean change in BCVA and central macular thickness (CMT) at the end of follow-up. Secondary outcomes were number of injections and the interval between injections.

Results: Twelve eyes of 12 patients were included. The mean follow-up was 24 months [18 à 30 mois]. The initial average BCVA and CMT were respectively 56,25 ± 17 ETDRS letters [20 - 75], and 442,1 ± 181 μm [257 - 809]. The mean gain in visual acuity was + 5,5 ± 12,5 letters, p=0,06 [-15, + 30 letters ETDRS] at the end of follow-up. The mean change in CMT was -167,3 ± 196,6 μm, p= 0,013 [-566, +51 μm]. The average number of intravitreal injections was 14,8 ± 5,7 (median = 12) during the follow-up. The average interval between injections was 9,2 weeks [from 4 to 21 weeks]. The median of interval between injections from M0 to M6 was 7,19 weeks, from M6 to M12 was 8 weeks, from M12 to M18 was 9 weeks, and from M18 to M24 was 10 weeks for patients who completed 18 and 24 months of follow-up.

Conclusions: The treat-and-extend regimen was effective in maintaining VA and CMT outcomes during the second year of follow-up in patients with macular edema secondary to RVO, treated by intravitreal injections of Ranibizumab or Aflibercept, with increasing interval between injections and reducing number of visits.

Commercial Relationships: Manar Addou Regnard; Agnes Glacet-Bernard, Rim Sekfali, None; Alexandra Miere, None; Eric H SOUIED, None

Program Number: 3649 Poster Board Number: B0274
Presentation Time: 3:45 PM–5:30 PM
Real life experience of combined fixed-dosing and Treat and Extend protocols for intravitreal Aflibercept injections for Macular Oedema secondary to Central Retinal Vein Occlusion (CRVO)
Caspar Geenen, Karim El-Assal, David Steel, Deepali Varma, Ajay Kotagiri, Jonathan Smith, Maria T. Sandintha, Maged S. Habib. Ophthalmology, City Hospitals Sunderland NHS Foundation Trust, Durham, United Kingdom.

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Purpose: Clinical Trials have demonstrated the efficacy and safety of intravitreal aflibercept for treatment of macular oedema (MO) secondary to CRVO. In clinical practice, several treatment protocols have been adopted for timely delivery of the drug to achieve better outcomes. In this retrospective audit, we evaluated the functional and structural outcomes of intravitreal aflibercept by adopting a modified mixed protocol of fixed dosing (FD) with treat and extend (T&E) following initial loading doses in patients with MO secondary to CRVO.

Methods: Retrospective data was collected for treatment-naïve patients with MO secondary to CRVO initiating treatment with aflibercept between March 2015 and March 2016. All patients received 5 initial monthly loading doses, followed by clinical assessment. Further management was planned based upon their initial response. Stable patients (Best Corrected Visual Acuity BCVA more than 5 letters gain or more than 15% decrease in baseline Central Macular Thickness CMT) received a batch of two 2-monthly injections, then were reassessed. Unstable patients (BCVA less than 5 letters gain from baseline and less than 15% decrease of baseline CMT) received a batch of 3 further injections on 4–6 weekly intervals before reassessment. Resolved patients (BCVA more than 5 letters gain and dry macula) were extended to 3-monthly injections and monitored thereafter.

Demographic and clinical data were recorded, and the number of injections. BCVA was recorded with the ETDRS visual acuity score chart and CMT using Heidelberg Spectralis.

Results: 35 eyes of 33 patients were included. Mean age was 74.6 years (SD 11.8), 57% were males. Baseline BCVA was 37.7 letters (SD 21.4), while baseline CMT was 702.1 (SD 215.9). At month 6, BCVA improved to 50.6 letters (SD 25.1). At 12 months, mean BCVA further improved to 58.1 letters (SD 21.1) with mean CMT of 379 (SD 181.1). Patients received an average of 8 injections in the first year.

Conclusions: Our results demonstrate that in clinical practice, initial BCVA gains can be maintained and improved at one year by adopting a modified mixed FD and T&E approach. Our results are in keeping with published clinical trial results.

The new protocols have the benefit of timely delivery of predetermined scheduled treatments and reducing the burden on clinic capacity.

Commercial Relationships: Caspar Geenen; Karim El-Assal, None; David Steel, None; Deepali Varma, None; Ajay Kotagiri, None; Jonathan Smith, None; Maria T. Sandinha, None; Maged S. Habib, None

Program Number: 3650 Poster Board Number: B0275
Presentation Time: 3:45 PM–5:30 PM
Retinal Artery Occlusion after Intravascular Procedure: Case Series and Literature Review

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Purpose: This study presented clinical characteristics of retinal artery occlusion after intravascular procedure and investigated possible mechanisms.

Methods: This study is a meta-analysis of retrospective case series including 10 new patients with acute RAO following intravascular procedure and previous case reports of 17 cases of RAO associated with intravascular procedures. Demographic and clinical characteristics of patients from current series and previous reports were presented. Total 27 cases of RAO were categorized into two groups according to assumed etiology: group 1 (dislodged embolii): RAO as a result of embolii from dislodged plaque fragments following procedural manipulation, group 2 (new embolii): RAO as a result of embolii from a newly formed thrombus or from the embolic material used, during the procedure.

Results: Of 27 cases, 17 (63.0%) patients had branch retinal artery occlusion and 10 (37.0%) patients central retinal artery occlusion. Proportion of patients with final BCVA ≥ 20/40 was 61.1%. The anatomical regions of the intravascular procedure were carotid artery (48.1%), heart (25.9%), carotid artery or heart (3.7%), brain (11.1%), scalp/glabellar (7.4%), and thyroid (3.7%). 16 cases were categorized as group 1 and 11 cases were categorized as group 2. Cases of group 1 were related with the dislodged plaque from carotid artery (9 cases, 56.3%) heart (6 cases, 37.5%), or carotid artery/heart (1 case, 6.3%; case with transmural cerebral angiography and coronary angiography). Cases of group 2 were related with newly formed thrombi (6 cases, 54.5%) or migrated embolic material via collateral channels between external carotid and ophthalmic arteries (5 cases, 45.5%). 17 (63.0%) patients presented with acute visual disturbance immediately after the procedures, 10 (37.0%) patients showed delayed occurrence (1 day to 3 days after procedure).

Conclusions: In conclusion, retinal artery occlusion can be a complication following intravascular procedures by a dislodged embolic plaque from carotid artery or heart, or by a newly formed thrombus or embolic material via collateral channels. BRAO was presented more often than CRAO after intravascular procedure. RAO with delayed onset can be complicated after intravascular procedure. Therefore, patients should be informed about the possible delayed presentation of RAO, and cautious ophthalmic examination is recommended till a few days after the procedure.

Commercial Relationships: Soo Chang Cho, None; Cheolkyu Jung, None; Joo Yong Lee, None; Sang Jin Kim, None; Kyu Hyung Park, None; Na-Kyung Ryoo, None; Se Joon Woo, None

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Program Number: 3651 Poster Board Number: B0276
Presentation Time: 3:45 PM–5:30 PM
Regulation of neurovascular coupling in proliferative retinopathy through a functional interaction between RORα and semaphorin 3E

Chi-Hsiu Liu, Yi Sun, Zhongxiao Wang, Steven Meng, Samuel Burrim, Jing Chen. Ophthalmology, Boston Children’s Hospital, Boston, MA.

Purpose: Dysregulated crosstalk between the retinal neurons and vasculature contributes to the pathogenesis of proliferative retinopathy, a leading cause of blindness. Class 3 semaphorins (Sema3s) are neuron-secreted axonal and vascular guidance factors protective for suppressing disoriented vascular growth in retinopathy but the upstream regulators in retinas neurons remain unclear. Here we investigated the role of retinoic acid receptor-related orphan receptor alpha (RORα), a lipid-sensing nuclear receptor and transcription factor, in the regulation of Sema3-mediated neurovascular coupling in proliferative retinopathy.

Methods: A mouse model of oxygen-induced retinopathy (OIR) mimicking proliferative retinopathy was used. RORα and Sema3s expressing levels were analyzed in OIR retinas compared with normoxic controls. Potential genes containing RORα-binding DNA elements (ROREs) were analyzed by chromatin immunoprecipitation assay, followed by verification with qPCR. RORα and Sema3E were localized with immunohistochemistry. Sema3E promoter-driven
Deficiency of RORα substantially induced expression of Sema3E (~2-fold upincrease) and decreased NV in Sg/Sg OIR retinas compared with littermate WT controls. Both RORα and Sema3E were localized in retinal ganglion cells. RORα directly recognized and bound to a specific RORE on the promoter of Sema3E in the retinas, showing approximately 2-fold enrichment compared with the positive control. RORα significantly suppressed Sema3E promoter-driven transcriptional activity (>50%) in a dose-dependent manner; conversely, SR1001 enhanced Sema3E promoter-driven luciferase activity. Moreover, suppression of Sema3e in Sg/Sg retinas promoted disoriented pathologic NV in OIR and partially abolished the protective vascular effects of RORα-deficiency.

Conclusions: Our findings suggest that RORα is a novel transcriptional regulator of Sema3E-mediated neurovascular coupling in retinopathy. RORα-Sema3E axis may serve as a potential pathway for treating neovascular eye diseases.

Commercial Relationships: Chi-Hsiu Liu; Ye Sun, None; Zhongxiao Wang, None; Steven Meng, None; Samuel Burnim, None; Jing Chen, None

Support: This work was supported by NIH/NEI (R01 EY024963), Boston Children's Hospital (BCH) Career Development Award, BrightFocus Foundation and BCH Ophthalmology Foundation.

Program Number: 3652 Poster Board Number: B0277
Presentation Time: 3:45 PM–5:30 PM
Central Retinal Vein Occlusion in Younger Patients: Causes, Presentation and Outcomes
Kirin Khan, Akshay Thomas, Adam Rothman, Sharon Fekrat. Duke University, Durham, NC.

Purpose: To evaluate the causes and clinical outcomes in younger patients with central retinal vein occlusion (CRVO).

Methods: In this single center retrospective study, we examined the medical records of all patients presenting with CRVO between January 2009 and July 2016. Risk factors for those presenting with CRVO under the age of 50 years were examined. Presentation, OCT parameters and visual outcomes for those <50 years of age vs. those 50 years of age and greater were assessed with comparative statistics.

Results: 247 eyes of 247 patients were included in this study. 27 of these patients (11%) were younger (<50 years old) at CRVO onset. 14/27 (52%) had traditional risk factors for CRVO such as hypertension, diabetes, smoking, hyperlipidemia or glaucoma. Workup for additional risk factors for CRVO was performed on 21 of these 27 CRVO patients. Additional risk factors for CRVO identified were oral contraceptive use (2 patients), mutations for Factor V Leiden (3 patients), retinal vasculitis (2 patients), elevated homocysteine (1 patient) and pregnancy (1 patient). Two of the 27 patients developed CRVO within 12 hours of intense aerobic exercise. Five younger patients had neither traditional nor additional identified risk factors for CRVO. There was a trend for the younger sub-group to have a higher frequency of non-ischemic CRVO than the older sub-group (67% vs 40%, p=0.058). Younger patients with CRVO had better presenting and final logMAR acuity than the older sub-group (0.43 vs 1.04, p<0.001; 0.58 vs 1.17, p=0.003 respectively). Presenting central macular thickness (CMT) on OCT was lower in those <50 years old (368.3 microns vs. 545.6 microns, p=0.008) but was similar between the groups at final follow-up (299.8 microns vs. 359.5 microns, p=0.672). Additionally, younger CRVO patients were less likely to have cystoid macular edema (CME) at baseline (52% vs 84%, p=0.01).

Conclusions: CRVO can occur in persons less than 50 years old without traditional risk factors. Workup is often unrevealing but may uncover an underlying coagulopathy. CRVO is more often non-ischemic and visual outcomes tend to be better in younger patients with CRVO.

Commercial Relationships: Kirin Khan, None; Akshay Thomas, None; Adam Rothman, None; Sharon Fekrat, None

Program Number: 3653 Poster Board Number: B0278
Presentation Time: 3:45 PM–5:30 PM
Topical bromfenac as an adjunctive treatment with intravitreal ranibizumab for macular edema associated with branch retinal vein occlusion
Yoshitsugu Saishin, Yuka Ito, Masashi Kakinoki, Masahito Ohji. Ophthalmology, Shiga University of Medical Science, Otsu, Japan.

Purpose: Intravitreal injection of ranibizumab (IVR) is an effective treatment for patients with macular edema (ME) secondary to branch retinal vein occlusion (BRVO). Repeated treatments are often required to control ME in many patients and it would be a burden. The purpose of this study is to assess the efficacy of topical bromfenac (0.1%) as an adjunctive therapy for patients with ME secondary to BRVO.

Methods: This is a prospective, double-masked, placebo-controlled study. Forty-five patients with ME due to BRVO were enrolled and randomized to topical bromfenac or saline adjunctive to IVR in a double-masked fashion. Patients received single IVR. Additional IVR injections were administered as needed if the prespecified criteria were met during the study period. Patients were examined at baseline and then monthly from months 1 to 12. The primary endpoint was the number of IVR injections over 12 months. The visual and anatomic responses were also compared.

Results: Four patients did not complete the study because of loss to follow-up and 22 patients in bromfenac group and 19 patients in the control group completed 12-month follow-up. The mean number of IVR injections over 12 months was 2.0 in the topical bromfenac group and 3.1 in the topical saline group. The mean total number of injections was significantly smaller in the topical bromfenac group than in the topical saline group (p=0.032). There was no significant difference in the mean logMAR BCVA at baseline between the two groups (p=0.26). In the topical bromfenac group, the mean logMAR BCVA improved significantly from 0.57 at baseline to 0.16 at month 12 (p<0.05). In the topical saline group, the mean baseline logMAR BCVA improved significantly from 0.56 at baseline to 0.15 at month 12 (p<0.05). The mean logMAR BCVA did not differ significantly at month 12 between the two groups (p=0.51). In the topical bromfenac group, the mean CFT decreased significantly from 563 μm at baseline to 278 μm at month 12 (p<0.05). In the topical saline group, the mean CFT decreased significantly from 618 μm at baseline to 250 μm at month 12 (p<0.05).

Conclusions: Topical bromfenac might reduce the frequency of IVR over 12 months in patients with ME secondary to BRVO, though there was not a significant difference in improvement of visual acuity and retinal thickness between the two groups.

Commercial Relationships: Yoshitsugu Saishin; Yuka Ito, None; Masashi Kakinoki, None; Masahito Ohji, Alcon (R), Senju (R), Santen (R), Carl zeiss (R), Santen (C), Alcon (C), Senju (F), Pfizer (R), Novartis (C), Santen (F), Kowa (R), Bayer (C), Novartis (R), Pfizer (F), Bayer (R), Otsuka (R), Novartis (F), Alcon (F), Otsuka (F), Allergan (C), Bayer (F)

Clinical Trial: UMIN Clinical Trials Registry, UMIN000013410

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Endothelial-specific SIRT1 Deletion Inhibits Retinal Vascular Endothelial Cell Migration
Yong Lin1, Junjie Liu1, Li Li1, Juxiu Ye2, Peter S. Reinach1, Jia Qu1, Dongsheng Yan1
1School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, China; 2State Key Laboratory Cultivation Base and Key Laboratory of Vision Science, Ministry of Health of the People's Republic of China, Zhejiang Provincial Key Laboratory of Ophthalmology and Optometry, Wenzhou, China.

**Purpose:** SIRT1 is a nicotinamide adenine dinucleotide (NAD+)-dependent deacetylase, abundantly expressed in vascular endothelial cells and has an essential role in angiogenesis. However, its contribution to retinal vascular development remains unclear. Here we characterize its involvement in regulating this process during both physiological and pathological retinal vascular development.

**Methods:** Endothelial-specific SIRT1 deletion mice were established using the Cre-loxP system. Vascular endothelial cells (EC) were isolated using magnetic beads coated with anti-CD31 antibody. SIRT1 expression was detected by immunostaining and Western blotting. Retinal whole-mount staining analyzed the retinal vascular pattern and vessel obliteration during development as well as in an oxygen-induced retinopathy (OIR) model. In vitro, SIRT1 was knocked down in cultured retinal ECs using small interfering RNA (siRNA). Transwell and matrigel angiogenesis assays evaluated the role of SIRT1 in modulating cell migration and tube formation, respectively.

**Results:** In EC specific SIRT1 conditional knockout (SIRT1 cKO) mice, their retinal vascularized area size was dramatically smaller than that in control mice (SIRT1 flox/flox) at P5 and P8. In OIR mice model, SIRT1 ablation in ECs suppressed retinal revascularization markedly and consequently increased retinal avascularity compared to that in the control mice. SIRT1 down-regulation in human retinal microvascular endothelial cells inhibited cell migration and tube formation.

**Conclusions:** SIRT1 contributes to both physiological and pathological retinal neovascularization through promoting retinal EC migration. SIRT1 may be a potential drug target to treat retinal diseases in which there is inappropriate vascularization leading to compromise of visual function and even blindness.

**Commercial Relationships:** Yong Lin, Junjie Liu, None; Li Li, None; Juxiu Ye, None; Peter S. Reinach, None; Jia Qu, None; Dongsheng Yan, None

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**Program Number:** 3655 **Poster Board Number:** B0281 **Presentation Time:** 3:45 PM–5:30 PM

**Lack of predictive value of retinal oxygen saturation for visual outcome after anti-VEGF treatment in central retinal vein occlusion**

**Purpose:** Occlusion of the central retinal vein (CRVO) is a frequent cause of visual loss. The severity of ischaemia in CRVO can be studied by fluorescein angiography, but measures of visual function have been shown to be superior for predicting the visual prognosis in CRVO. Previous studies have shown that the oxygen saturation in retinal veins is reduced in patients with CRVO, but the predictive value of retinal oxygen saturation for visual outcome in patients with CRVO has not been studied in detail.

**Methods:** Retinal oximetry was performed in 91 consecutive patients with CRVO (age 70.8, 28-96 years) (mean, range) in one eye referred to the Department of Ophthalmology, Aarhus University Hospital, and the predictive value of the retinal oxygen saturation in larger retinal vessels for the visual prognosis after three monthly intravitreal injections with anti-VEGF medication was studied.

**Results:** At baseline the oxygen saturation in larger retinal vessels was significantly higher for arterioles and significantly lower for venules in the affected (100.7±1.4 % for arterioles and 37.8±2.6 % for venules) than in the unaffected eye (96.3±0.6 for arterioles and 58.2±1.3 for venules), p<0.001 for both comparisons. The best corrected visual acuity (BCVA) showed a significantly negative
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Age threshold for increased risk of RVO among Koreans

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Purpose: RVO is one of most common retinal vascular disorders, leading to visual impairment and subsequent socioeconomic loss among working population. Although prevalence and risk factors of RVO are well known, until now, there is no consensus regarding optimal screening age for persons of high risk. So the purpose of this study was to predict age threshold for increased risk of retinal vein occlusion (RVO) among Koreans.

Methods: This analysis was based on Korean National Health Insurance Database from 2008-2013. Patients who were diagnosed as new RVO from 2008 to 2013 were included. Binary logistic regression analysis was performed to identify the prognostic factors for RVO and odds ratios with 95% confidence intervals. A receiver operating characteristic curve (ROC) for age that optimized the prediction of RVO was constructed.

Results: Among 391,769 individuals, 2,418 (0.62%) developed RVO. The risk factors for RVO were old age, high BMI, high blood pressure, high blood glucose and high blood cholesterol level, presence of diabetic mellitus and hypertension, current or previous smoking history, high alcohol consumption. (p<0.05) The cut-off age for increased risk of RVO for male was 44 years (sensitivity 0.84, specificity 0.62) and 51 years (sensitivity 0.80, specificity 0.62) for females. The area under ROC for age cut off for male was 0.74 (0.73-0.75) and 0.76 (0.75-0.77) for females.

Conclusions: The annual incidence of RVO for less than 40 years of age was 0.06%, which was low. But the incidence of RVO doubled after 40 years of age for both genders. Whether this age threshold could help to define high risk individuals for RVO development among Koreans needs more validation from further studies. Addition to controlling high blood pressure and blood glucose, more attention to modify the unhealthy life style factors like smoking and alcohol consumption after 40 years or older to decrease the risk of RVO should be made.

Commercial Relationships: Shin Koun, None; Han Kyung Do, None; Su Jeong Song, None

Program Number: 3661 Poster Board Number: B0286
Presentation Time: 3:45 PM–5:30 PM

Retinal Vascular Abnormalities in a Large Cohort of Patients Affected by Neurofibromatosis Type-1: a Study Using OCT-angiography

Raffaele Parrozzani1, Elisabetta Pilotto1, Giacomo Miglionico2, Luisa Frizziero1, Francesca Leonardi1, enrica convento1, Sara Trainiti1, Serena Pulze2, Edoardo Midena1,2. Department of Ophthalmology, University of Padova, Padova, Italy; *G.B. Bietti Foundation, IRCCS, Roma, Italy.

Purpose: To evaluate the prevalence, the vascular features and the clinical diagnostic implication of Retinal Vascular Abnormalities (RVAs) associated with neurofibromatosis type-1 (NF1) in a large cohort of patients.

Methods: Three-hundred patients affected by NF1 were consecutively enrolled. The presence of RVAs was detected by means of infrared (IR) confocal scanning laser ophthalmoscopy images. Two masked ophthalmologists evaluated each image. Three hundred age and race matched healthy subjects were enrolled as a healthy control group. Fluorescein (FA), indocyanine green (ICGA) and OCT-angiography (OCT-A) were also performed in patients with RVAs.

Results: RVAs were detected in 18 patients with NF1 (6.0%) and none of the healthy subjects showed it. RVAs appeared in all cases as well defined, small, tortuous retinal vessels with a spiral aspect, originating from small tributaries of retinal veins. RVAs were unilateral in 17 cases (94%) and single in 15 (83.3%) cases, located at the posterior pole in 6 (33.3%) cases or along the temporal vascular arcades in 12 (66.6%) cases. The inter-operator agreement in the detection of RVAs was 1.0 (complete agreement). Presence of RVAs did not correlate with the presence of other specific ocular or systemic NF1 features (p>0.05). Eyes affected by RVAs showed a normal visual acuity. On OCT-A, RVAs appeared as an isolated tortuous vessel of the superficial vascular plexus in all cases, associated with localized anomalous crowded and congested capillary network of the deep vascular plexus in 75% of cases.

Conclusions: RVAs are present in a limited proportion of patients affected by NF1 and can be considered a new specific clinical entity and an additional distinctive sign of NF1.

Commercial Relationships: Raffaele Parrozzani, None; Elisabetta Pilotto, None; Giacomo Miglionico, None; Luisa Frizziero, None; Francesca Leonardi, None; enrica convento, None; Sara Trainiti, None; Serena Pulze, None; Edoardo Midena, None
Program Number: 3662 Poster Board Number: B0287
Presentation Time: 3:45 PM–5:30 PM

Novel mouse model of CRVO induced by intraperitoneal injection of Rose Bengal with laser radiation
Kazutaka Hirabayashi1,2, Yasuhiro Iesato1, Akira Imai1, Yuichi Toriyama1, Sakurai Takayuki1, Kamiyoshi Akiko2, Yuka Ichikawa-Shindo2, Hisaka Kawate2, Megumu Tanaka2, Akihiro Yamauchi1, Toshinori Murata1, Shindo Takayuki2.
1Department of ophthalmology Shinshu Univ., NAGANO, Japan; 2Department of Cardiovascular research, Shinshu Univ., Nagano, Japan; 3Japan Bio Products Co., Fukuoka, Japan.

Purpose: Although anti-VEGF drugs are used for macular edema associated with central retinal vein occlusion (CRVO), it is not a curative therapy. Therefore, a simple animal model is desired for developing novel therapeutical approaches. In this study, we developed a novel CRVO mouse model by using the intraperitoneal injection of Rose Bengal and low-power laser radiation, and examined its pathological features.

Methods: C57BL / 6J 9-12 week-old male mice were injected intraperitoneally with 1 mg of Rose Bengal under anesthesia (N=13). Three minutes later, the central retinal vein was radiated with a low-power laser having a wavelength of 532 nm, an output power of 50 mW, a radiation time of 3 seconds, and a radiation diameter of 50 μm, and it was repeated until vein occlusion. Fluorescence fundus angiography was performed 24 hours later, and the eyes in which with retinal nonperfusion area were enucleated and retinal gene expression was analyzed (N=3). Furthermore, on the 7th day after the operation, Fluorescein Isothiocyanate (FITC) was injected under anesthesia, a retinal flat mount was prepared, and further lectin staining was carried out (N=10).

Results: In retinas of the CRVO group, the expression of VEGF (1.9 folds), inflammatory cytokines IL-6 (64 folds), TNF-α (4.2 folds), IL-1β (3.6 folds), and inflammation and adhesion molecule ICAM-1 (20 folds) was significantly upregulated compared with the untreated group. Furthermore, the expression of adrenomedullin (AM), a peptide that possesses vaso- and neuroprotective functions, increased to 10 folds, while the expression of RAMP2, an AM’s receptor binding protein, decreased to 1/10. Nonperfusion area and CRVO-like findings were obtained in 7 out of 10 eyes subjected to fluorescence fundus angiography examination after 1 week. The non-perfusion site of FITC was coincided with the reduced lectin-staining sites; therefore endothelial cell damage in this CRVO model was confirmed.

Conclusions: The CRVO model using Rose Bengal intraperitoneal injection and low power laser irradiation is simpler than conventional tail vein injection and is useful for therapeutic research.

Commercial Relationships:
Kazutaka Hirabayashi, None; Yasuhiro Iesato, None; Akira Imai, None; Yuichi Toriyama, None; Sakurai Takayuki, None; Kamiyoshi Akiko, None; Yuka Ichikawa-Shindo, None; Hisaka Kawate, None; Megumu Tanaka, None; Akihiro Yamauchi, None; Toshinori Murata, None; Shindo Takayuki, None
Branch retinal vein occlusion with persistent macular edema in 80-year-old patient. (Top left) Optical coherence tomography angiography (OCTA) image in superficial capillary plexus (SCP) shows collateral vessel, vessel telangiectasia and capillary loss in upper right region. (Top middle) OCTA image in deep capillary plexus (DCP) shows vessel telangiectasia and large capillary loss in upper right region. (Top right) Composite image shows capillary loss in DCP but capillary remaining in SCP (blue vessels) in upper right region. (Bottom left) Binarized SCP image and (Bottom middle) binarized DCP image. (Bottom right) Gap vessels were extracted in upper right region.

**Commercial Relationships:** kotaro tsuboi, None; Yuichiro Ishida, None; Motohiro Kamei, None

**Program Number:** 3665 Poster Board Number: B0290

**Presentation Time:** 3:45 PM–5:30 PM

**In Vivo Molecular Imaging of Retinal Hypoxia in a Mouse Model of Laser-induced Retinal Vein Occlusion (RVO)**

Md Imam Uddin1, Ashvath Jayagopal2, Gary W. McCollum1, John S. Penn1. 1Ophthalmology, Vanderbilt University School of Medicine, Nashville, TN; 2Hoffmann-La Roche Ltd, Basel, Switzerland.

**Purpose:** To demonstrate the utility of a new in vivo molecular imaging probe, HYPOX-4, for early detection of retinal hypoxia in a mouse model of retinal vein occlusion (RVO). This method will assist early detection of retinal hypoxia in real time and will facilitate studying the pathogenesis of RVO.

**Methods:** Induction of RVO was achieved in mice using photodynamic retinal vein thrombosis (PRVT) of major retinal vein(s) close to the optic disk. In vivo imaging of the retinal
hypoxia was performed using a new molecular imaging probe, HYPOX-4, that was developed by our laboratory. Pimonidazole-adduct immunostaining was used as an ex vivo method for detecting retinal hypoxia in RVO mice. Retinal vasculature was imaged using fluorescein angiography (FA) and IB4 staining. Retinal tissue morphology was assessed using spectral domain OCT (SD-OCT).

**Results:** Within a few hours of post-PRVT in mice, we observed significant changes in retinal hypoxia as determined by the pimonidazole-adduct immunostaining method. This method also showed that the extent of retinal hypoxia depends on the number of retinal veins occluded. After photocoagulation, the occluded veins reopened within one week as determined by FA, and neovascularization (NV) was observed at 10-14 days post-PRVT. HYPOX-4-dependent in vivo imaging showed retinal hypoxia in RVO mice during this period. This study provides the first qualitative and quantitative evidence of retinal hypoxia in RVO mice at early stages of vein occlusion.

**Conclusions:** This study demonstrated the utility of a new hypoxia sensitive molecular imaging probe, HYPOX-4, in RVO mice at an early stage before the onset of NV. HYPOX-4 could be a powerful predictive biomarker for the retinal NV that occurs in RVO and other vasculopathies. This study showed acute changes in retinal oxygen tension precede and may initiate vascular complications including NV in RVO mice.

**Commercial Relationships:** Md Imam Uddin; Ashwath Jayagopal, None; Gary W. McCollum, None; John S. Penn, None

**Support:** Knights Templar Eye Foundation career starter grant 2016-2017.

**Program Number:** 3666 Poster Board Number: B0291

**Presentation Time:** 3:45 PM–5:30 PM

**Use of the Ischemic Index on Widefield Fluorescein Angiography to Characterize a Central Retinal Vein Occlusion as Ischemic or Non-Ischemic**

Akshay S. Thomas¹, Mridul K. Thomas², Sharon Fekrat¹ ¹, ²

¹Ophthalmology, Duke University, Durham, NC; ²Aquatic Ecology, Eawag: Swiss Federal Institute of Aquatic Science and Technology, Dubendorf, Switzerland; ³Ophthalmology, Durham VA Medical Center, Durham, NC.

**Purpose:** To better define what constitutes an ischemic central retinal vein occlusion (CRVO) based on ischemic index values on ultra-widefield fluorescein angiography (UWFFA).

**Methods:** We performed a retrospective cohort study of all CRVO patients imaged with UWFFA at our institution between January 2009 and July 2016. Ischemic index values were calculated using mid-phase UWFFA images of the involved eye. An ischemic CRVO was defined as those eyes with an afferent pupillary defect (APD), anterior or posterior segment neovascularization, or counting fingers acuity or worse over the course of follow-up. Baseline characteristics, OCT parameters and visual outcomes were compared in eyes with an ischemic index ≥35% and <35%. Logistic regression was performed to characterize the relation between the ischemic index, visual outcomes and development of an ischemic CRVO.

**Results:** 54 eyes of 54 treatment naïve CRVO patients with UWFFA at the initial visit and at least 1 year of follow-up were identified. The mean ischemic index was 22.67% (Range: 0-60.28%; SD: 22.68%); 18 patients (33.3%) had an ischemic index ≥35%. Baseline characteristics such as age, sex, race and CRVO risk factors were similar between the groups. Those with an ischemic index ≥35% were significantly more likely to have an ischemic CRVO during follow-up than those with an ischemic index <35% (83.3% vs 13.9%, OR 24.1, p<0.0001). Baseline and final logMAR acuity was worse in those eyes with an ischemic index ≥35% (1.26 vs 0.50, p<0.001; 1.20 vs 0.55, p=0.005 respectively). Additionally, patients with an ischemic index ≥35% were more likely to have final acuity of 20/200 or worse (66.7% vs 22.2%, OR 5.7, p = 0.005). Baseline and final central macular thickness (CMT) was similar between the groups (p=0.28-0.78).

**Conclusions:** Among patients with treatment naïve CRVO, a baseline ischemic index of ≥35% on UWFFA was strongly associated with classification as an ischemic CRVO over long-term follow-up. Additionally, a baseline ischemic index of ≥35% was associated with poorer presenting and final acuity despite similar baseline and final CMT on OCT.

**Commercial Relationships:** Akshay S. Thomas, None; Mridul K. Thomas, None; Sharon Fekrat, None

**Program Number:** 3667 Poster Board Number: B0292

**Presentation Time:** 3:45 PM–5:30 PM

**Effect of Inspra (Eplerenone) on structural and functional outcome in central serous chorioretinopathy**

Katrin Fasler¹, Jeanne Gunzinger¹, Daniel Barthelmes¹, Malgorzata Roos², Sandrine Zweifel¹, ¹Ophthalmology Department, University Hospital, Zurich, Switzerland; ²Biostatistics, University of Zurich, Zurich, Switzerland.

**Purpose:** There are currently no evidence-based guidelines concerning therapy of central serous chorioretinopathy (CSCR). Eplerenone (Inspra®) has been reported to be beneficial. We report results of Eplerenone treatment on choroidal thickness, central macular thickness (CMT), subretinal fluid and visual acuity (VA) in patients with CSC.

**Methods:** Data of 42 patients with the diagnosis of acute or chronic CSC were retrospectively analyzed. Charts were reviewed for VA, duration and cumulative dosage of Inspra-therapy. Spectral domain enhanced depth imaging optical coherence tomographies (SD EDI-OCTs) and fluorescein-/ICG- angiograms were evaluated for choroidal thickness (CT), maximum subretinal fluid (maxSRF) and central macular thickness (CMT). Results from patients with Eplerenone treatment and patients with observation only were compared.

Data were coded in Excel and analyzed in SPSS version 23. Means, standard deviations, absolute/relative frequencies were computed. Exact test by Fisher was used to investigate association between two discrete variables. Linear mixed models methodology was applied to disclose dependency of maxSRF, CMT, VA (logMAR) and choroidal thickness with respect to Inspra therapy and treatment duration. Results with p value of less than 5% were interpreted as statistically significant.

**Results:** Mean age was 47 years (range 29-74), 98% male (42 pat). Mean choroidal thickness was 413 (SD=105) μm, medians for maxSRF and InVA were 86 (IQR=129) μm and -0.22 (IQR=0.5), respectively. No statistically significant association was found between choroidal thickness or CMT and Inspra therapy. There was a dependency of maxSRF (p=0.001) on Inspra and time (p=0.013). Lower maxSRF values for patients under Inspra and a decrease of maxSRF with time were found. A higher percentage of measurements of zero subretinal fluid under Inspra (24.8%) than without Inspra (13.7%) (p=0.026) was found. There was a tendency of visual acuity improvement (lnVA) with time (p=0.095) but no impact of Inspra therapy (p=0.788).

**Conclusions:** The results suggest that Inspra therapy does not have a statistical significant structural or functional effect in patients with CSC. This finding does not encourage implementation of Inspra as gold standard treatment for CSC. There is a strong need for a...
Commercial Relationships: Katriin Fast, None; Jeanne Guzinger, None; Daniel Barthelmes, None; Malgorzata Roos, None; Sandrine Zweifel, None

Program Number: 3669 Poster Board Number: B0294
Presentation Time: 3:45 PM–5:30 PM
Low dose aldosterone exposure causes increased retinal edema following laser-induced retinal vein occlusion in mice
Michael J. Allingham, Nomingerel Tserentssoodol, Peter Saloupis, Scott W. Cousins. Ophthalmology, Duke University Eye Center, Durham, NC.

Purpose: The pathobiology of retina edema (RE) is incompletely understood. Mechanistic studies are limited by the lack of physiologic animal models. We have developed a model of RE based on laser-induced vein occlusion (RVO) in order to determine the role of the mineralocorticoid receptor in RE pathobiology.

Methods: RVO was induced immediately following intravenous injection of rose Bengal (60mg/kg) using a 532 nm wavelength laser to place 3-7 applications at 80 mW and 50 micron spot size directed at the superior retinal vein one disc diameter away from the nerve. Negative control consisted of placing an equal number of laser spots without targeting the vein. Male and female C57BL/6J mice aged 7-9 months with confirmed absence of Crb1rd8 were used. Aldosterone pellets releasing a daily dose of 1 ug/d were implanted subcutaneously 4 weeks prior to RVO. Retinal imaging by optical coherence tomography (OCT) was performed using a Micron 4 rodent imaging system. Retinas were analyzed by immunohistochemistry using standard techniques. Retinal imaging and tissue analysis were performed 2, 4 and 7 days following RVO. Comparisons were made using Pearson’s Chi Square and Wilcoxon Rank Sum testing.

Results: RE in the form of cystic spaces and retinal thickening was evident both by OCT and by histology. Following standard RVO, RE present on OCT in 88% of eyes at day 2, 38% of eyes at day 4 and 0% of eyes at day 7 (n=8). By comparison, in aldosterone treated eyes, RE was present in 100% of eyes at day 2 and 4 and 50% of eyes at day 7 (n=8). This difference was statistically significant at day 4 (p=0.007) and day 7 (p=0.02). Maximal retinal thickness was higher at day 2 in aldosterone treated mice 1.85 vs 1.27 (p<0.04).

Histologically, areas of edema demonstrate increased macrophage infiltration, Muller cell activation and redistribution of aquaporin 4 and Kir4.1 channels. These findings were more severe in aldosterone treated mice. No RE or changes in Muller cell markers were seen in negative controls.

Conclusions: RVO creates mild to moderate RE which resolves spontaneously. Activation of the MR by systemic low dose aldosterone significantly enhances the severity and duration of RE following RVO and this is associated with macrophage infiltration and Muller cell dysfunction. MR may play a role in pathogenesis of macular edema in RVO and possibly other forms of macular edema.

Commercial Relationships: Michael J. Allingham, None; Nomingerel Tserentssoodol, None; Peter Saloupis, None; Scott W. Cousins, None
Support: NIH K12 grant 5K12EY016333-09; NIH K08 grant 1K08EY026627-01

Program Number: 3670 Poster Board Number: B0295
Presentation Time: 3:45 PM–5:30 PM
Caffeine preferentially protects against oxygen-induced retinopathy
Shuyu Zhang1, Rong Zhou1, Bo Li1, Haiyan Li1, Cun Wang1, Yanyan Wang1, Xuejiao Gu1, Dianjuan Zhong1, Lingyun Tang1, Yuanyuan Ge1, Qiwen Huo1, Jing Lin1, Xiao-Ling Liu1, Jiang-Fan Chen1. School of Optometry and Ophthalmology, Wenzhou Medical University, Wenzhou, China; 2Department of Cellular Biology and Anatomy, Medical College of Georgia, Augusta, ME; 3Icahn School of Medicine at Mount Sinai, New York, NY.

Purpose: Caffeine (CAF) has been shown to be neuroprotective against oxygen-induced retinopathy (OIR). However, the protective mechanisms are still not clear. CAF could be absorbed by retinal vessels by passive diffusion, which results in high concentration of CAF in retinal blood vessels. Therefore, CAF may preferentially exert its protective effects on retinal vascular tissue. The objective of this study was to investigate the preferential protective effects of CAF on retinal vascular tissue in OIR.

Methods: FRG mice were exposed to hypoxia (95% oxygen and 5% nitrogen) from P7 to P14. Systemic infusion of CAF (50 mg/kg) or saline (control) was applied at P5 and continued for 14 days. Following the hypoxic treatment, the retina was harvested at P21 and P28. Cell death in retinal vessels was determined by immunofluorescence staining of cleaved caspase-3 and TUNEL. The expression levels of pro-VEGF and VEGF were measured using western blotting. Results: Our results indicated that CAF significantly reduced cell death in retinal vessels at P21 and P28 (p<0.05). The expression levels of pro-VEGF and VEGF in CAF group were significantly lower than those in control group at both P21 and P28 (p<0.05).

Conclusions: These results suggest that CAF preferentially protects retinal vascular tissue against OIR by reducing pro-VEGF and VEGF expression, which may be involved in the protective mechanisms of CAF against OIR.

Commercial Relationships: None
Purpose: The clinical observation of the reduced severity of retinopathy of prematurity (ROP) in premature infants after caffeine treatment for sleep apnea raises an exciting possibility that caffeine may protect against pathological retinal neovascularization in ROP via adenosine receptor antagonism. Using the oxygen-induced retinopathy (OIR) model of ROP in mice, we evaluated the efficacy, therapeutic window, the receptor and cellular mechanisms for caffeine to confer protection against OIR.

Methods: We treated the mice with caffeine (0.1-1.0 g/L) with four different treatment paradigms (P0-7, P7-12, P12-17 and P0-17 respectively). Retinal vascularization was examined by whole-mounted fluorescence and cross-sectional hematoxylin-eosin staining. Astrocyte activation and tip cell function in retina were determined by isoelectric staining and immunohistochemistry. Retinal apoptosis was determined by TUNEL assay.

Results: Caffeine treatment from P0-P17 dose-dependently and selectively attenuated vaso-oblation and pathological neovascularization in OIR without interfering normal retinal vascularization. The treatment of caffeine at P7-12 was effective in reducing vaso-oblation by attenuating neuronal apoptosis while the treatment of caffeine at P7-12 as well as P12-17 was effective in reducing neovascularization by enhancing tip cell function in OIR. A_{1R}KO was not involved in caffeine's protection against OIR since A_{1R} KO exacerbated OIR and administering caffeine to A_{1R} KO still produced protection against OIR. Caffeine exerted protection against OIR at P12 by acting at the A_{1R}-dependent mechanism since both caffeine and A_{1R} KO produced similar and partial protection against OIR and the combined caffeine A_{1R} KO did not produce further protection. By contrast, caffeine conferred protection at P17 by A_{2R}-dependent as well as A_{1R}-independent mechanisms since the combined treatment of caffeine and A_{2R} R produced additional and nearly full protection against OIR on the top of the partial protection by caffeine or A_{1R} KO alone.

Conclusions: We have demonstrated the preferential protection against OIR, therapeutic window and A_{1R}-dependent and A_{2R}-independent mechanisms of caffeine effects in mouse OIR model. Together with widely use of caffeine in neonate care, our findings provide the proof-of-principle evidence to translate the novel caffeine therapy for prevention and treatment of ROP.

Commercial Relationships: Shuya Zhang, None; Rong Zhou, None; Bo Li, None; Haiyan Li, None; Cun Wang, None; Yanyan Wang, None; Xuejiao Gu, None; Dingjuan Zhong, None; Lingyun Tang, None; Yuanyuan Ge, None; Yuqing Huo, None; Jing Lin, None; Xiao-Ling Liu, None; Jiang-Fan Chen, None

Program Number: 3671 Poster Board Number: B0296
Presentation Time: 3:45 PM–5:30 PM

Extension of peripheral non-perfusion in retinal vein occlusion treated with intravitreal dexamethasone implant

Sandra Rezar, Katharina Eibenberger, Wolf Buehl, Michael Georgopoulos, Guenther Weigert, Ursula Schmidt-Erfurth, Stefan Sacu. Ophthalmology and Optometry, Medical University of Vienna, Vienna, Austria.

Purpose: To investigate differences between eyes with ischemic and non-ischemic retinal vein occlusion (RVO) and evaluate the change of peripheral non-perfusion area (PNP) during intravitreal dexamethasone treatment.

Methods: Forty eyes of 40 consecutive patients with macular edema (ME) due to either branch- or central retinal vein occlusion (25 BRVO; 15 CRVO) were included for analysis. At baseline all patients were treated with an intravitreal dexamethasone implant (Ozurdex®) and re-treated if indicated earliest after 4 months. Ischemic RVO was defined as evidence of >10 disc diameter of PNP at baseline as seen on 200° wide-field fluorescein angiography. Eyes included for follow-up analysis were quantified manually for the total area of PNP by calculating the percentage of the total visible retina (ischemic index).

Results: Eighteen eyes showed evidence of PNP and were graded as ischemic RVO. At baseline and at final follow-up best-corrected visual acuity (BCVA) and central retinal thickness (CRT) did not differ between ischemic/non-ischemic RVO patients (61±14/65±15 letters and 536±172/531±131μm at baseline; 69±15/70±18 letters and 298±107/305±61μm month 6). No difference regarding the time of dexamethasone re-treatment was identified between patients with ischemic/non-ischemic RVO (11/11 received re-treatment at month 4, 3/5 at month 5, 3/4 at month 6). In the ischemic RVO eyes, the mean area of PNP (ischemic index) was calculated to be 14.7% at baseline. One month after initial dexamethasone treatment the mean area of PNP was 13.7% and after three months 16.9% (p=0.8; p=0.4). After re-treatment total PNP area was 16.7% (month 6; p=0.8 in comparison to baseline). In eyes graded as non-ischemic the mean PNP area was 0.3% at baseline, 0.6% after one month, 0.6% after three months and 0.6% after six months, respectively (p=0.05). A significant negative correlation between the total area of PNP and VA was identified (p=0.03).

Conclusions: Using wide-field fluorescein angiography the ischemic index was shown to remain stable under intravitreal Ozurdex® treatment. Functional and anatomical outcomes did not differ between patients with ischemic and non-ischemic RVO.

Commercial Relationships: Sandra Rezar, None; Katharina Eibenberger, None; Wolf Buehl, None; Michael Georgopoulos, None; Guenther Weigert, None; Ursula Schmidt-Erfurth, Boehringer (F), Alcon (F), Allergan (F), Novartis (F), Bayer (F); Stefan Sacu, Pharmaselect (F), Askin (F), Allergan (F), Bayer (F), Novartis (F)

Clinical Trial: 2012-000800-13

Program Number: 3672 Poster Board Number: B0297
Presentation Time: 3:45 PM–5:30 PM

Accelerated Anti-VEGF Dosing for Treatment of Resistant Macular Edema in Patients with Retinal Vein Occlusions

Tara Bryant, Yunwook J. Kim, Archana Seethala Thangappan, Manju Subramanian. Ophthalmology, Boston Medical Center, Boston, MA.

Purpose: Intravitreal therapy has become the gold standard of treatment for cases of macular edema secondary to retinal vein occlusion. There remains a population of patients who show minimal to no improvement in macular edema despite consecutive monthly therapy. For these patients, we have proposed accelerated dosing with alternating anti-vegf injections every two weeks. The primary objective of this study is to examine the clinical outcomes of an accelerated anti-VEGF injection regimen in a select group of patients who have not responded to monthly injections.

Methods: This study was approved by the Boston University Institutional Review Board. We performed a retrospective chart review of patients who received bimonthly intravitreal anti-VEGF injections for diabetic macular edema at Boston Medical Center between January 1, 2015 and September 15, 2016. The subjects were selected using the Current Procedural Terminology (CPT) code 67028 for intravitreal injection. Age, sex, ocular comorbidities, indication for injection, site of injection, injected medication, and dates of injection were recorded for each patient. Outcome measures included central foveal thickness and best corrected visual acuity at the start of bimonthly treatments and at the end of bimonthly treatments.

Results: Total of three eyes in three patients were identified to have received bimonthly intravitreal anti-VEGF injections for macular edema secondary to venous occlusion. The average age...
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of patients was 73 (range: 63 - 82). All patients had previously failed the traditional monthly anti-VEGF injection therapy. Patients received and average of 7.3 (range: 2 - 10) injections of alternating bevacizumab and aflibercept every two weeks. The average central foveal thickness before treatment was 404 microns (range: 309 - 455) and 327 microns (range 240 - 456) after treatment. Two eyes had a decrease in central foveal thickness after treatment with accelerated therapy while one patient showed no improvement. Two eyes showed improvement in best corrected visual acuity while one had no improvement.

**Conclusions:** Patients who show no improvement in macular edema after a series of monthly injections may lose vision permanently if alternate therapies are not attempted. These patients may benefit from alternating antivegf agents, dosed bimonthly with improvement in visual acuity and macular thickness.

**Commercial Relationships:** Tara Bryant, None; Yonwook J. Kim, None; Archana Seethala Thangappan, None; Manju Subramanian, None

**Program Number:** 3673 
**Poster Board Number:** B0298 
**Presentation Time:** 3:45 PM–5:30 PM 
**Characterization of a Laser Induced Branch Retinal Vein Occlusion in a Rat Model**

Konstantinos Nikolakopoulos, Laura Kowalczyk, Tatiana Favez, Catherine Martin, Francine Behar-Cohen, Jean-Antoine Pournaras, Hôpital Ophthalmique Jules-Gonin, Lausanne, Switzerland.

**Purpose:** Anti-VEGF agents are commonly used in the treatment of branch retinal vein occlusion (BRVO). However, the exact mechanism, as well as the reason of possible treatment failure in a number of cases, have not been fully understood yet. Our primary objective is to observe and compare the temporal modifications in the expression of the VEGF family members, and their receptors between normal and BRVO rat retina, in order to establish new targets that will allow improvement of the existing therapies.

**Methods:** By using laser photocoagulation two to three hemi-retinal veins of Long Evans rats (n=35) were occluded. Subsequently, on day 1, 2, 4 and 7 following the occlusion, in vivo and ex vivo analysis were performed in order to characterize the temporal evolution of the morphological and molecular alterations. The in vivo analysis included: eye fundus photography, Optical Coherence Tomography (OCT), and fluo-angiography. Regarding the ex vivo analysis, immunohistochemistry on cryosections and retinal flatmounts, along with Real Time and Quantitative PCR, were performed.

**Results:** Retinal serous detachments occurred in the totality of the eyes at day 1 along with hemorrhages that gradually resolved throughout the follow-up. Reperfusion of the occluded branch retinal veins initiated on day 4 and continued until day 7, where only two veins of two different eyes remained occluded. Despite reperfusion, ischemia and edema were visible and were limited to the areas dependent on the occluded veins. Neovascularization began as soon as day 2, and peaked on day 4 after laser treatment, in accordance to the activation of the VEGF receptors, Flt-1 and Flt-2. On the contrary, no receptor activation was observed in the non-occluded retina. PIGF-1 was expressed on day 1 in the vessels of the treated hemi-retina, and had a maximum expression on day 7, particularly in the impact zone and the neovascular areas. Flatmounts stained for NG2+ pericytes demonstrated a severe pericyte loss, which led to destabilization of the peripheral capillary network.

**Conclusions:** Given the early and sustained expression of PIGF-1 in the occluded hemi-retina, particularly in the neovascular membranes, we believe that this could be a potential therapeutic target against neovascular complications in the BRVO.

Commercial Relationships: Konstantinos Nikolakopoulos, None; Laura Kowalczyk, None; Tatiana Favez, None; Catherine Martin, None; Francine Behar-Cohen, None; Jean-Antoine Pournaras, None

**Program Number:** 3674 
**Poster Board Number:** B0299 
**Presentation Time:** 3:45 PM–5:30 PM 
**Real-life effectiveness of Ranibizumab in RVO patients in a prospective, non-interventional trial over 12 months (OCEAN study)**

Josep Callizo1, Thomas Bertelmann1, Jessica Voegeler2, Steffen Schmitz-Valckenberg3, Georg Spithal1, Nicolas Felten1, Sandra Liakopoulos4, Focke Ziemssen5, •Ophthalmology, Georg-August University, Goettingen, Germany; •Novartis Pharma, Nuernberg, Germany; •Ophthalmology, University of Bonn, Bonn, Germany; •Ophthalmology, St. Franziskus-Hospital, Munster, Germany; •Ophthalmology, University Hospital of Cologne, Cologne, Germany; •Ophthalmology, Eberhard-Karls University of Tuebingen, Tuebingen, Germany.

**Purpose:** The non-interventional OCEAN trial recruited retinal vein occlusion (RVO) patients in order to collect prospective data in a real-life setting. Randomized controlled trials (RCTs) have proven the beneficial effect of vascular endothelial growth factor (VEGF) inhibition with Ranibizumab in several indications including central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). Analysis of this study will allow a better understanding of relevant hurdles and barriers as well as the role of OCT imaging under Ranibizumab treatment.

**Methods:** In the non-interventional, prospective OCEAN study (NCT02194803) 5.779 patients were observed over 24 months. Herein we report the 12-month interim analysis of 744 patients diagnosed with RVO (52% female/ 48% male) with an average age of 70.9 years. The following data were recorded and analyzed: number of visits, visual acuity, number of injections, the use of diagnostic tools (OCT, fluorescein angiography) and adverse events.

**Results:** RVO patients received an average of 4.7 injections during the first year, while undergoing an average of 9.8 BCVA assessments and 4.3 OCT examinations. The average gain in BCVA was 12.3 ETDRS letters at 12 months. Moreover, 148 treatment-naïve BRVO patients even gained on average 15.1 ETDRS letters and 87 treatment-naïve CRVO gained on average 9.1 letters. When more than 6 OCTs were performed within the first year, a higher number of patients gained ≥ 5 letters (63.6%, n=117) in comparison with patients with one or none OCT examination (50.3%, n=102). The mean decrease in central retinal thickness was 166 μm. No new safety signals were identified.

An update of 24-month data will be presented.

**Conclusions:** A 12-month observational period of the OCEAN trial clearly shows beneficial effects of Ranibizumab on BRVO and CRVO patients. The presented results indicate that the underutilization of diagnostic capabilities might accompany a possible undertreatment. Higher rates of OCT examinations were associated with better VA outcomes in RVO patients. This observation underlines the importance of additional measures improving adherence to and persistence of anti-VEGF treatment.

Commercial Relationships: Josep Callizo, Allergan (R), Bayer Healthcare (R), Novartis (R); Thomas Bertelmann, Alcon (R), Bayer Healthcare (R), Novartis (R), Allergan (F), Novartis (F), Alimera Science (F), Bayer Healthcare (F), Alcon (F), Allergan (R), Alimera Science (R); Jessica Voegeler, Novartis (E); Steffen Schmitz-Valckenberg, Bayer Healthcare (R), Allergan (F), Alcon (C), Formycon (F), Optos (F), Allergan (R), Novartis (C), Heidelberg Engineering (F), Genentech/Roche (R), Carl

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Zeis Medi Tec (F), Novartis (F), Bayer Healthcare (F), Alcon (F), Heidelberg Engineering (R), Genentech/Roche (C), Genentech/Roche (F); Georg Spital, Heidelberg Engineering (R), Allergan (R), Pfizer (R), Bayer Healthcare (R), Novartis (R), Novartis (F); Nicolas Feltgen, Roche/Genentech (F), Bayer Healthcare (R), Novartis (R), Pfizer (F), Allergan (F), Novartis (F), Alimera Science (F), Bayer Healthcare (F), Heidelberg Engineering (R), Allergan (R), Alimera Science (C), Alimera Science (R); Sandra Liakopoulos, Novartis (C), Allergan (R), Heidelberg Engineering (R), Bayer Healthcare (R), Novartis (R); Focke Ziemssen, Alcon (R), Novartis (C), Novartis (R), Bayer Healthcare (R), Boehringer-Ingelheim (C), Alimera Science (C), Allergan (R), Biogen (R), Allergan (C), Bayer Healthcare (C)

Clinical Trial: NCT02194803

Program Number: 3675 Poster Board Number: B0300
Presentation Time: 3:45 PM–5:30 PM

Optical coherence tomography angiography and “en-face” optical coherence tomography in retinal vein occlusion
Alexandros Deligiannidis, Daniel Velazquez Villoria, Jose Lorenzo Carrero. POVISA hospital, Vigo, Spain.

Purpose: To evaluate the optical coherence tomography angiography (OCT-A) findings of the superficial and deep capillary plexa in eyes with retinal venous occlusions and compare them with those of “en-face” OCT.

Methods: This is a retrospective, observational case study. Patients presenting with retinal vein occlusions to a tertiary-level hospital underwent a comprehensive ophthalmic examination. Optical coherence tomography angiography was performed with Topcon’s DRI OCT TRITON Swept Source OCT-A system, in 6mm x 6mm regions centered on the fovea. The same system was used to obtain the cross-sectional and “en-face” OCT microstructural data. Image analysis was performed with the IMAGEnet software, that provided automated retinal segmentation data of the superficial and deep capillary plexa. The same software was used for the manual selection and measurements of the areas of impaired retinal perfusion. Further findings as vascular dilation, retinal edema, hard exudates and shunt vessels were assessed.

Results: In this study 39 patients were enrolled, one of them had bilateral retinal vein occlusion (40 eyes). 2 eyes were excluded because of poor-quality images. 10 had central retinal vein occlusion (CRVO) and the remaining 30 had branch retinal vein occlusion. Seventeen patients (44%) were female, 22 (56%) were male and the mean age was of 67 years. Perifoveal capillary arcade was disrupted in 14 eyes (37%). Impaired perfusion areas were more frequent in the deep capillary plexus (34 of 38 eyes, 89%) than in the superficial capillary plexus (24 of 38 eyes, 63%, P<.001) and more extensive (P<.001). Intraretinal cysts were observed in 21 eyes (55%) using the “en-face” OCT and in 11 eyes (29%) using the OCT-A, P<.001. Areas with intraretinal cysts were more extensive when measured with “en-face” OCT than with the OCT-A, P=.037. Shunt vessels were found in 19 eyes (50%), vascular dilation in 33 eyes (87%) and hard exudates in 12 eyes (32%).

Conclusions: In retinal vein occlusion the deep capillary plexus appears to be more frequently and extensively affected compared to superficial plexus. Furthermore, the “en-face” OCT seems to be a better imaging modality to detect intraretinal edema than OCT-A.

Commercial Relationships: Alexandros Deligiannidis, None; Daniel Velazquez Villoria, None; Jose Lorenzo Carrero, None

Program Number: 3676 Poster Board Number: B0301
Presentation Time: 3:45 PM–5:30 PM

5 Pearls of Early Treatment in BRVO
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Purpose: Branch retinal vein occlusion (BRVO) is a retinal vascular disease associated with macular edema (ME) and consequential vision loss. In the past, a ‘watchful waiting’ approach has been advocated in early stage BRVO to allow for possible spontaneous resolution of ME. However, data from the BRAVO study suggest that delaying treatment with anti-vascular endothelial growth factor (VEGF) in BRVO may limit visual acuity (VA) gains. Here we present an exploratory analysis from the 24-month BRIGHTER study on the impact of disease duration and baseline VA in BRVO patients treated with ranibizumab with or without laser, or with laser alone.

Methods: BRIGHTER (NCT01599650) was a 24-month, phase IIIb, open-label, randomized, active-controlled, three-arm multi-center study that enrolled 455 patients with BRVO across 81 sites in Europe, Australia and Canada.

Results: 1) Irrespective of baseline VA and duration, ranibizumab treatment (with or without laser) of all BRVO patients resulted in a significant increase in VA over 24 months (fig.1).
2) Patients with high baseline VA (≥60 letters) achieved significant VA gains (mean best corrected VA change [BCVA] of +12.1 and +11.8 letters, respectively) with ranibizumab treatment (with or without laser) compared with those treated with laser alone (mean BCVA change of +3.3 letters).
3) For patients with low baseline vision (<39 letters), treatment with ranibizumab resulted in a greater letter gain (+23.2 letters) than patients with high baseline vision; however, high baseline vision patients achieved better absolute vision at study end (79.4 vs 56.8 letters for highest vs lowest baseline VA, respectively).
4) For patients with a short disease duration (<12 months), ranibizumab treatment resulted in a mean BCVA gain of 17.3 letters, while patients with a longer disease duration (≥12 months) had a mean BCVA gain of 8.4 letters (fig. 2).
5) For patients with a shorter disease duration (<12 months), ranibizumab monotherapy resulted in a gain of ≥15 letters in a shorter time (85 days) compared with patients treated with ranibizumab plus laser (118 days) or laser alone (266 days).

Conclusions: These results show that ranibizumab intervention earlier, and in those with a higher VA, provides better VA outcomes over 24 months than with laser. Delaying treatment may have a significant negative impact on patient quality of life.

Mean change in VA over 24 months, by baseline VA categories
The data previously suggested that mouse retinal Optical coherence tomography angiography (OCTA) offers a novel method to image retinal vascular diseases including retinal vein occlusions. We performed a retrospective clinical study to identify and compare areas of non-perfusion seen on OCTA to the vasculature visualized on en face spectral domain optical coherence tomography (en face OCT).

**Methods:** This study included a total of 21 eyes, 11 eyes with central retinal vein occlusions and 10 eyes with branch retinal vein occlusions. A masked observer examined the en face OCT, OCTA and fluorescein angiography (FA). We identified areas with vessels seen on en face OCT that were non-perfused on OCTA and correlated these areas with findings at the corresponding location in OCT scans and on FA.

**Results:** Of the eyes studied, 17 had discordance between the vasculature seen on OCTA and en face SD-OCT. Of the eyes with CRVO, 8 had visible vessels on SD-OCT in areas of non-perfusion on OCTA while the remaining 3 cases of CRVO had no visible vessels on en face OCT in areas of non-perfusion on OCTA. Nine of the ten cases of BRVO similarly had persistent vessels on en face OCT in areas which showed non-perfusion on OCTA.

**Conclusions:** Our findings indicate a wide range of variations in the abnormalities on OCTA and en face OCT in non-perfused vessels. Comparison of these discrepancies to FA confirm that non-perfusion on OCTA corresponds to FA non-perfusion. Our findings demonstrate that OCTA precisely delineates areas of non-perfusion. Clinicians should consider multimodality imaging when evaluating BRVO and CRVO.

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subretinal hemorrhages, vitreous hemorrhage, choroidal rupture, retinal tears or detachments, macular detachments, or partial- or full-thickness macular holes. Using the electronic caliper within the OCT, CT was measured from the outer portion of the hyper reflective line corresponding to the retinal pigment epithelium to the inner surface of the sclera. The average of the central horizontal and vertical raster images were used as the final CT reading of each eye. The average of the central 1,500 μm subfoveal CA of the center vertical and horizontal raster lines was used as the final CA reading of each eye. The researchers compared the CT and CA among traumatic eyes to non-traumatic control eyes as well as to best-corrected visual acuity. A paired t-test was used to compare measurements between traumatic eyes and fellow eyes in patients with macular commotio retinae.

**Results:** The subfoveal CT and CA in traumatic eyes with unilateral macular commotio retinae was greater (p=0.0027, p=0.0279) compared to the fellow non-traumatic eye. An increase in CT and CA in the subfoveal area due to commotio retinae was associated with worse logMAR visual acuity (p=0.0180).

**Conclusions:** The choroid was thicker in the subfoveal area in eyes with commotio retinae than in fellow eyes following blunt ocular trauma. Increased CT and CA in macular commotio retinae were associated with vision loss.

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