June 28 (Friday) 11:00-12:30 Room 1 (Auditorium)

2nd International Workshop on Diabetic Retinopathy and Age-Related Macular Degeneration-AMD

Chairs / Moderators: Susumu Ishida *(Japan)*
Timothy Y Y Lai *(Hong Kong)*
Won Ki Lee *(South Korea)*

11:00-11:08	**Thin Pachychoroid** Won Ki Lee *(South Korea)*
11:08-11:16	**Dynamic changes of choroidal conditions in age-related macular degeneration** Yoko Ozawa *(Japan)*
11:16-11:24	**Automated Segmentation of Lesions in AMD** Hyung Chan Kim *(South Korea)*
11:24-11:32	**New therapeutic developments for neovascular AMD: non-VEGF pathways** Timothy Y Y Lai *(Hong Kong)*
11:32-11:40	**Emerging Therapies for Neovascular AMD: Anti-VEGF Pathways** Adrian Koh *(Singapore)*
11:40-11:48	**EVEREST 2 vs. PLANET** Lee-Jen Chen *(Taiwan)*
11:48-11:56	**Molecular Pathogenesis and Therapeutic Challenges in AMD** Rajendra S. Apte *(USA)*
11:56-12:30	**Panel Discussion**

Age-related macular degeneration (AMD) is an eye disease where light-induced oxidative stress triggers inflammation at the retinal pigment epithelium (RPE) level in the macular region. Consequently, two types of AMD develop: wet AMD characterized by choroidal neovascularization and dry AMD also known as geographic atrophy secondary to RPE cell death. Recently, a new concept "pachychoroid disease spectrum" has emerged to better understand the pathogenesis of polypoidal choroidal vasculopathy (PCV). It would be interesting to see how inflammation is associated with these AMD-related diseases. PCV, regarded as an end-stage form of the disease spectrum, is currently treated with photodynamic therapy (PDT) on top of the first-line anti-vascular endothelial factor (VEGF) therapy, and it is also worth noting how PDT affects the thick choroid. In this workshop, we would like to learn from the world's leading experts and share with you the latest information about AMD and related diseases, including the new classification, treatment response, upcoming drugs targeting other molecules than VEGF.

Thin Pachychoroid

Won Ki Lee
Nune Eye Hospital, Seoul, South Korea

Although the term pachychoroid was originally conceived to reflect choroidal thickening, new information has broadened its original description to emphasize additional qualitative features. These features include diffuse choroidal thickening, or focal thickening that is localized within the disease focus and attributable to pathologically dilated Haller veins (pachyvessels). Focal attenuation of choriocapillaris and Sattler layers overlying pachyvessels brings them closer to the Bruch-RPE complex.
The area of maximal choroidal thickness correlated spatially with the distribution of pachyvessels and with the disease focus, even in eyes in which the absolute choroidal thickness was not particularly high. In those eyes, pachyvessels occupied the full thickness of the choroid with loss of overlying Sattler and choriocapillaris layers.

Dynamic changes of choroidal conditions in age-related macular degeneration

Yoko Ozawa
Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan

The dynamic changes of choroidal vascular diameter (CVD) and central choroidal thickness (CCT), and exudative changes during anti-vascular endothelial growth factor (VEGF) therapy in polypoidal choroidal vasculopathy (PCV), a subtype of age-related macular degeneration, were retrospectively analyzed. Medical charts of 100 treatment-naïve eyes of 100 patients with PCV treated with anti-VEGF monotherapy during 24-months were reviewed. The risk for recurrent exudative change was greater in the pachyvessel groups (180 μm ≤ CVD) irrespective of presence or absence of pachychoroid (220 μm ≤ CCT). Mean CVD and CCT decreased when achieving a dry macula, while the values were greater in the patients with initial pachyvessels and pachychoroid than in those without. Mean CVD increased prior to CCT increase and recurrent exudative change. Therefore, both pachyvessels in the choroid and pachychoroid, and dynamic changes in CVD and CCT were related to exudative changes in PCV. Basal levels of CVD and CCT when patients had no exudative changes after anti-VEGF treatment differed between eyes with or without initial pachyvessels and pachychoroid, suggesting involvement of regulatory mechanisms other than VEGF-related in the basal choroidal condition. In contrast, CVD increase preceded CCT increase and recurrent exudative changes and could be treated with anti-VEGF treatments, suggesting that dynamic changes in CVD may regulate CCT and exudative changes most likely in response to VEGF. Dynamic CVD change may be a biomarker of disease activity.

Automated Segmentation of Lesions in AMD

Hyung Chan Kim
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Purpose: To evaluate an automated segmentation algorithm with a convolutional neural network (CNN) to quantify and detect intraretinal fluid (IRF), subretinal fluid (SRF), pigment epithelial detachment (PED), and subretinal hyperreflective material (SHRM) through analyses of spectral domain optical coherence tomography (SD-OCT) images from patients with neovascular age-related macular degeneration (nAMD).
Design: Development of a diagnostic modality.
Methods: We constructed a dataset including 930 B-scans from 93 eyes of 93 patients with nAMD. A CNN-based deep neural network was trained using 11550 augmented images derived from 550 B-scans. The performance of the trained network was evaluated using a validation set including 140 B-scans and a test set of 240 B-scans. The Dice coefficient, positive predictive value (PPV), sensitivity, relative area difference (RAD), and intraclass correlation coefficient (ICC) were used to evaluate segmentation and detection performance.
Results: Good agreement was observed for both segmentation and detection of lesions between the trained network and clinicians. The Dice coefficients for segmentation of IRF, SRF, SHRM, and PED were 0.78, 0.82, 0.75, and 0.80, respectively; the PPVs were 0.79, 0.80, 0.75, and 0.80, respectively; and the sensitivities were 0.77, 0.84, 0.73, and 0.81, respectively. Conclusions: A CNN-based network provides clinicians with quantitative data regarding nAMD through automatic segmentation and detection of pathological lesions, including IRF, SRF, PED, and SHRM.

New therapeutic developments for neovascular AMD: non-VEGF pathways

Timothy Y Y Lai
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Anti-angiogenesis therapy with anti-vascular endothelial growth factor (VEGF) agents such as ranibizumab, aflibercept, conbercept and bevacizumab has revolutionized the treatment of macular diseases. Although VEGF is the major pathway which targets angiogenesis and vascular leakage, it is not the only pathway involved in the pathogenesis of macular disease. Newer molecules are now being developed to target non-VEGF pathways and are being investigated to evaluate their efficacies in treating macular diseases. This presentation will review and discuss recent innovations in anti-angiogenesis therapy based on non-VEGF pathways. In particular, newer agents targeting angiopoietin 2 (ANG2), pigment derived growth factor (PDGF), and tissue factors will be discussed.

Emerging Therapies for Neovascular AMD: Anti-VEGF Pathways

Adrian Koh[1,2]

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Anti-VEGF therapy has been the gold standard for the treatment of neovascular AMD for the past decade and has significantly reduced visual loss. However, there are unmet needs that remain: under-treatment, burden of frequency of injections and monitoring visits and high costs. Newer targets and therapeutic agents might be beneficial in alleviating some of these burdens. The most important of these molecules is Brolucizumab. Results of the phase 2 and pivotal phase 3 studies will be presented. Other potential therapies will also be discussed.

Molecular Pathogenesis and Therapeutic Challenges in AMD

Rajendra S. Apte[1,2]

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AMD is a major cause of blindness. Although therapeutic agents that target vascular endothelial growth factor (VEGF) have revolutionized the treatment of the neovascular form of AMD, challenges including treatment burden, under-responsiveness to chronic VEGF suppression and loss of vision due to neurodegeneration have limited long term visual outcomes. Several attempts at multi-target therapies in combination with anti-VEGF agents have failed clinical trials. In addition, there are no treatments available for the atrophic, neurodegenerative forms of AMD. As such, there is a high, unmet need to identify novel molecular pathways that are important in the pathogenesis of AMD. We will present recent findings on how metabolism and the immune system intersect to regulate drusen biogenesis and AMD progression. These studies might open novel opportunities for therapeutic development.

EVEREST 2 vs. PLANET

Lee-Jen Chen

MacKay Memorial Hospital, Taipei, Taiwan

EVEREST 2 and PLANET studies are two different study design for polypoidal choroidal vasculopathy, EVEREST 2 is PRN, PLANET is fixed dosing then treat & extend, however, both studies still provide some common points for treatment references.
Inactive polyps can exist before and after treatment, following PDT combination treatment, or Ranibizumab or aflibercept, all can have inactive polyps.
Massive subretinal hemorrhage is rare in study period, all three treatment regimens can prevent massive sub retinal hemorrhage from happening, as long as monitor patients regularly and suppress activity when disease reactive again.
PCV is a diverse disease, all treatment still encounter difficult cases in the study, but so far there is no reliable biomarkers to predict treatment outcome.
Polyps exist or not is not related to visual acuity, also leakage is not purely from polyps, so treatment goal should focus on leakage, for ICG angiography or PDT is not available institutes, PCV can be treated like treating AMD.