OVERVIEW
Reduced blood flow through the vasculature can drive retinal disease and glaucoma. Using adaptive optics scanning laser ophthalmoscopy or OCT techniques, blood flow through the fundus can be mapped noninvasively, i.e. without the injection of fluorescein. Both drop-out of blood vessels and vascular proliferation can be seen and related to a patient’s prognosis. The oxygen supply to the inner and outer retina is probed with an even wider variety of methods, providing a better understanding of diseases such as diabetic retinopathy and glaucoma.

OBJECTIVES
1. To present a review of existing research and new research on retinal imaging of blood flow.
2. To update attendees on ocular oxygenation and how oxygenation is related to retinal eye diseases.
3. To introduce to attendees new techniques for assessment of ocular health that may be seen in clinical instruments in the near future.

SPEAKERS
Robert A. Linsenmeier, BS, MS, PhD
Professor of Biomedical Engineering, Neurobiology, and Ophthalmology
Northwestern University

Hao F. Zhang, BE, MS, PhD
Associate Professor of Biomedical Engineering
McCormick School of Engineering, Northwestern University
Technological Institute

Mahnaz Shahidi, BS, MS, PhD
Professor of Ophthalmology
Riffenburgh Professor in Glaucoma
Vice Chair for Translational Research
University of Southern California
USC Roski Eye Institute

David Huang, MD, PhD
Peterson Professor of Ophthalmology
Professor of Biomedical Engineering
Center for Ophthalmic Optics & Lasers
Casey Eye Institute
Oregon Health & Science University

Brett J. King, OD, FAAO
Clinical Associate Professor
Chief of Ophthalmic Disease
Indiana University School of Optometry
MODERATORS
Dr. Ann E. Elsner, PhD, FAAO
Professor, Indiana University School of Optometry

Dr. Dean A. VanNasdale, OD, PhD, FAAO
Assistant Professor, Ohio State University

PRESENTATIONS:

Title: Oxygen Supply to the Inner and Outer Retina
Presenter: Robert Linsenmeier, BS, MS, PhD

Abstract
In general terms, the oxygen supply to the outer retina, mainly photoreceptors, comes from the choroidal circulation, and the supply to the inner half of the retina, consisting of second and third order neurons and glia, comes from the retinal circulation. However, even under normal conditions the situation is more complex, with the outer retina relying for up to 20% of its oxygen supply on the deep capillaries in the retinal circulation in darkness. In contrast, in light adaptation, the choroid can supply a small part of the oxygen to the inner retina. During systemic hypoxia, the photoreceptors rely more on the retinal circulation. Under other conditions, such as retinitis pigmentosa, the choroid may take a larger role. Most of these conclusions rely on intraretinal oxygen measurements that have been made in animals, and these measurements and the resulting picture of retinal oxygen supply will be described.

Title: Visible-light OCT: Seeing Retinal Functions Beyond Existing OCT
Presenter: Hao F. Zhang, BE, MS, PhD

Abstract
As the elderly populations of Europe, China, and the U.S. grow, the prevalence of major ophthalmic disorders such as glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy are also expected to increase, fueling new demand for improved diagnostic and surgical systems to help physicians manage and treat these diseases. Optical coherence tomography (OCT) devices currently represent the gold standard for ophthalmic diagnostics, providing high-resolution imaging and proven clinical benefit in improving the patient's quality of life. Despite the success of OCT, however, the full potential of this imaging modality has yet to be realized. While other imaging methods such as MRI and PET have been revolutionized with the development of functional imaging (e.g. fMRI), functional OCT remains an emerging technology. Visible-light OCT (Vis-OCT) represents a cutting-edge functional OCT imaging technique that aims to dramatically improve the diagnostic capabilities and clinical benefit of OCT in ophthalmology. Vis-OCT is currently the only OCT technology capable of combining both high-resolution structural imaging (~ 1 µm) with precise measurements of metabolic activity, such as retinal oxygen saturation and retinal blood flow. Using dual band scanning with visible light and NIR light wavelengths, Vis-OCT represents a next generation functional OCT tool with the potential to fundamentally change how ophthalmologists and optometrists use OCT in the diagnosis, treatment and monitoring of numerous major ocular disorders.
Title: Retinal Oxygen Metabolism in Diabetes
Presenter: Mahnaz Shahidi, BS, MS, PhD

Abstract
Diabetic retinopathy (DR) is a common cause of vision loss in working age adults. Retinal hypoxia has been implicated in advanced stages of DR, as supported by retinal capillary non-perfusion and upregulation of vascular endothelium growth factor. Inadequate oxygen availability can impair retinal oxygen metabolism and damage retinal tissue. Recent studies in human DR have reported reduced retinal blood flow, increased arterial and venous oxygen saturation, and reduced oxygen extraction fraction, implying impaired oxygen metabolism. We directly measured retinal oxygen delivery and metabolism in diabetic mice and showed concurrent reduced oxygen delivery, increased oxygen extraction fraction, and a marginal decrease in oxygen metabolism as compared to non-diabetic mice. The increase in oxygen extraction fraction maintained oxygen metabolism, but limited the oxygen supply reserve, such that the diabetic retina may be more vulnerable to normal fluctuations in tissue oxygenation or to superimposed metabolic stress. Hence, we expect increased neural activity by light flicker would stimulate a lesser increase in oxygen metabolism of the diabetic retina than the healthy retina. We showed diabetic rats had a reduced oxygen extraction fraction response (less increase) to light flicker stimulation as compared to non-diabetic rats. Likewise, we demonstrated that with similar light-flicker induced vasodilation, DR subjects displayed a diminished oxygen extraction fraction response (less decrease) as compared to non-diabetic subjects. Better understanding of alterations in retinal oxygen metabolism due to physiologic and pathologic challenges is helpful for the development of metabolic-mediated preventative and therapeutic strategies for DR.

Title: OCT-A in Glaucoma and Retinal Diseases
Presenter: David Huang, MD, PhD

Abstract
OCT angiography is a rapidly developing technology to non-invasively image and measure retinal, choroidal, and optic nerve blood flow. This presentation discusses technological approaches, disease applications, and clinical interpretation.

OCT angiography uses flow motion as intrinsic contrast, therefore interpretation differs from fluorescein angiography, in which dye transit and leakage provide the primary contrast. The 3-dimensional nature of OCT angiography allows for detailed examination of vascular anatomy in both cross-sectional and en face displays that separate the normal vascular beds and vascular pathologies. Selection of slab boundaries using reference anatomic surfaces is key to proper visualization and recognition of pathologies. Superficial flow is projected onto deeper reflective structures in OCT angiography. This artifact can be recognized and suppressed using a computer algorithm. The course will teach these visualization techniques.

In OCT angiography, choroidal and retinal neovascularization can be classified according to the depth of the pathologies in age-related macular degeneration, diabetic retinopathy, pathologic myopia, central serous chorioretinopathy, and macular telangiectasia. Non-perfusion of the superficial and deep retinal plexuses, and the choriocapillaris can be visualized and quantified. Attenuation of the disc circulation, radial peripapillary capillary plexus, and macular superficial vascular complex can be quantified and localized in glaucoma and other optic neuropathies.

The non-invasive nature of OCT angiography will allow it to be used much more frequently than was ever possible with conventional fluorescein angiography. The new generation of commercial OCT systems has sufficient speed to perform OCT angiography using special software, which is already available internationally.
**Abstract**
Microvascular abnormalities are a hallmark of multiple retinal disorders, such as having been reported to occur more frequently in patients with open angle glaucoma compared to age-similar controls. Current advances in imaging such as adaptive optics scanning laser ophthalmoscopy (AOSLO), ocular coherence tomography angiography (OCTA), and retinal oximetry may further our understanding of progression in disease and effects of current treatments. Additionally, these advanced techniques can be applied to new potential treatments for improved indications in management. A review of these new and investigational techniques will highlight clinical implications now and in the near future.

Investigations with AOSLO have demonstrated early findings in diabetic retinopathy beyond noted with clinical and standard color photography. These early microvascular changes such as capillary loops can highlight the need for therapeutic intervention earlier in management. New standards for risk may arise from these findings going beyond traditional ETDRS recommendations.

High resolution imaging from AOSLO also has the ability to further our understanding of vascular change and autoregulation in patients with glaucoma. The ability to develop precise capillary maps as well improved measurements of autoregulation may help us better manage patients by investigating the therapeutic effects of current and investigational medications.

OCTA has led to new parameters, such as capillary density, for following and managing patients with retinal disease and glaucoma. This new non-invasive clinical tool can have a large impact on following vascular changes in multiple patient populations. Understanding vascular maps will be critical in future care.

Retinal oximetry may go beyond imaging microvascular changes, but indicate areas of concern prior to progression. Again this new tool has the potential to improve our understanding of risk as well as the effects or our therapeutic management of retinal disorders and glaucoma.

**PANEL DISCUSSION**