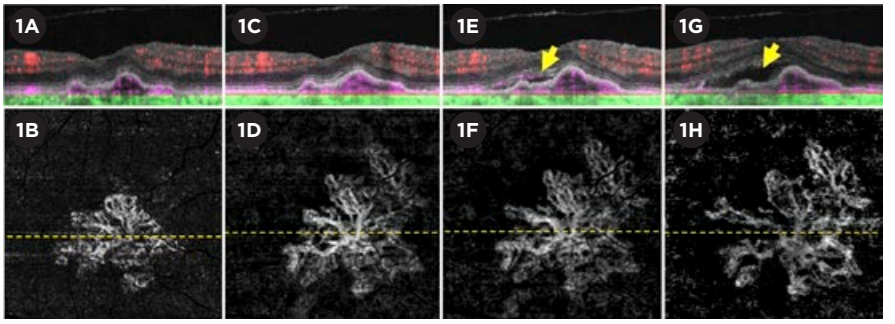
OCT Angiography Finds Exudation Early in Dry AMD



CONVERSION. *This eye had subclinical type 1 MNV at baseline (1A, 1B) and demonstrated exudative disease during 24 months (1G, 1H) of follow-up. (Top images, OCT B-scan; bottom images, SS–OCT-A. Arrow = increase in subretinal fluid.)*

RESEARCHERS HAVE KNOWN SINCE the 1970s that subclinical neovascularization could exist in eyes with dry age-related macular degeneration (AMD).[1,2] Two decades later, indocyanine green angiography (ICG) showed that, in patients with wet AMD in one eye and dry AMD in the other, these subclinical features were a strong predictor for development of exudative disease in the second eye.[3,4] However, monitoring eyes with repeated ICG testing was too invasive and expensive to be practical.

Now, results of a study using swept-source optical coherence tomography angiography (SS–OCT-A) suggest that the technique might enable ophthalmologists to not only identify eyes with these risky subclinical lesions but also quickly begin treatment when symptomatic leakage occurs.[5]

Predicting risk. For this prospective study, researchers used SS–OCT-A to monitor the disease status in 160 eyes with intermediate dry AMD or geographic atrophy (GA). The patients had wet AMD in the fellow eye.

The investigators found that, after 1 year of follow-up, exudative disease developed in 21.1% of the eyes with subclinical macular neovascularization (MNV) at baseline. The risk for exudation was 15.2 times greater (95% confidence interval, 4.2 to 55.4) compared with eyes without subclinical MNV, the scientists reported.

"This has enormous predictive value. It provides us with a tool that allows us to identify those patients who are most at risk, so they don't fall through the cracks," said coauthor Philip J. Rosenfeld, MD, PhD, at the Bascom Palmer Eye Institute in Miami.

"This finding alone—that we can identify these subclinical lesions long before exudation occurs—provides all the rationale we need to justify the use of this noninvasive, safe, and easily performed technology to survey all our patients with intermediate AMD or geographic atrophy," Dr. Rosenfeld said.

Additional findings. The researchers also reported the following results:

- Overall, 14.4% of the 160 study eyes showed subclinical MNV at baseline.
- One year after the first observation of subclinical MNV (either at baseline or during follow-up), 24% of these eyes developed exudation.
- Of the eyes without subclinical MNV on their initial angiogram, 5.4% developed it within 1 year. In these eyes, a druse-like elevation of the retinal pigment epithelium (RPE) was identified at the site. "We believe that these RPE elevations were the first sign of type 1 MNV and can serve as harbingers of impending exudation," the authors wrote.

An essential technology? Dr. Rosenfeld said he views OCT-A as "a requirement for anyone with dry AMD." If subclinical neovascularization is present, he repeats the procedure at least every 2 months. However, he initiates treatment only if the patient becomes symptomatic, he said.

OCT-A can be used to help ophthalmologists avoid unnecessary intravitreal injections, Dr. Rosenfeld said. "Treat as early as possible, but don't treat unless there's exudation. Remember that fluid can come and go in the retina of a patient with dry AMD in the absence of neovascularization, without serious consequences," he said. "And SS–OCT-A can identify those patients who have fluid in the absence of neovascularization."

Dr. Rosenfeld said the barriers to greater use of swept-source OCT to monitor patients with dry AMD are financial: Specifically, the device is double the price of earlier OCT devices.

But the technique's potential to help manage dry AMD patients is enormous, he said. "This strategy will save more vision in the long run than we've been able to accomplish" with intravitreal injections, he said. "We'll be able to treat as soon as symptomatic exudation occurs. Home monitoring will be important as well, but now we can select those patients at highest risk even when they don't have the typical high-risk fundus findings on exam."

—Linda Roach

1 Sarks SH. *Br J Ophthalmol.* 1973;57(12):951-965.
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3 Schneider U et al. *Int Ophthalmol.* 1997;21(2):79-85.
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CATARACT

Barrett II Formula Appears Best For 2 Popular IOLs

FOR 2 WIDELY USED INTRAOCULAR lens (IOL) models, cataract surgeons can attain the lowest levels of refractive prediction error with the Barrett Universal II formula, an analysis of 18,501 cases has found.[1]

"We found that the Barrett was the most accurate across all eyes," said Ronald B. Melles, MD, at Kaiser Permanente in Redwood City, California.

Study specifics. To conduct the study, the researchers used data from 18 months of consecutive procedures performed in the Kaiser Permanente Northern California region. In roughly two-thirds of the cases (n = 13,301), patients received an SN60WF IOL (AcrySof IQ, Alcon) in 1 eye; for the remainder (n = 5,200), an SA60AT IOL (AcrySof Natural, Alcon) was implanted (again, in 1 eye). These 2 IOLs are the most commonly used IOLs at their institution, the researchers noted.

The 145 surgeons involved used standardized preoperative and surgical protocols and a single type of biometer (Lenstar 900, Haag-Streit). They then applied 11 IOL power formulas to the preoperative measurements in each case for the purposes of calculating spherical equivalent formula predictions and comparing the accuracy of the predictions after lens constant optimization.

GLAUCOMA

Eye on Glymphatic System

A TEAM OF GLAUCOMA RESEARCHERS HAS PRO-posed that a paravascular transport system exists in the eye and optic nerve—and that this pathway is likely continuous to a paravascular pathway in the brain known as the glymphatic system.[1]

Brain researchers have proposed that a disturbance of flow of cerebrospinal fluid (CSF) through paravascular pathways may contribute to the development of Alzheimer disease. Now Peter Wostyn, MD, and his colleagues suggest that a paravascular disruption between the eye and optic nerve may explain the pathogenesis of primary open-angle glaucoma (POAG). Their "glymphatic hypothesis of glaucoma" builds on research that acknowledges the collective contribution of vascular, biomechanical, and biochemical factors in the pathophysiology of POAG.

Building the hypothesis. The recently discovered glymphatic system is described as a network of paravascular pathways, or channels surrounding blood vessels, throughout the brain.[2] As CSF circulates through the brain along these pathways, it clears away waste, including amyloid-ß, a hallmark protein in Alzheimer disease. The glymphatic system also distributes other compounds, such as glucose, lipids, growth factors, and amino acids.

"The 'glymphatic hypothesis of glaucoma' suggests that glaucoma might be the result of an imbalance between production and clearance of neurotoxins in the optic nerve due to a dysfunctional ocular glymphatic system," said Dr. Wostyn, at PC Sint-Amandus in Beernem, Belgium.

"Our group has proposed that glaucoma may share a common glymphatic background with Alzheimer disease—and that glaucoma, just like Alzheimer disease, may occur when there is an imbalance between production and clearance of neurotoxins such as amyloid-ß," Dr. Wostyn said.

Finding the pathway. In a postmortem study examining cross-sections of the human optic nerve, Dr. Wostyn's group provided the first histological evidence for a paravascular pathway in the eye.[3] Subsequently, others found evidence for CSF entry into the optic nerve via a glymphatic pathway.[4]

But further evidence is needed to support the existence of a glymphatic system in the optic nerve, Dr. Wostyn acknowledged. He added that, if the presence of this system is confirmed, "emerging imaging technologies may be used to reveal ocular glymphatic abnormalities associated with glaucoma."

—Miriam Karmel

1 Wostyn P et al. *Biomed Res Int.* 2017:5123148.
2 Iliff J et al. *J Clin Invest.* 2013;123(3):1299-1309.
3 Wostyn P et al. *Clin Exp Ophthalmol.* 2017;45(5):539-547.
4 Mathieu E. *Invest Ophthalmol Vis Sci.* 2017; 58(11):4784-4791.

Relevant financial disclosures—Dr. Wostyn: None.

Prediction errors. The analyses revealed that, between axial lengths of 23 to 25 mm, most of the formulas yielded results within 0.1 D of predicted spherical equivalent. However, as axial length, keratometry, anterior chamber depth, and lens thickness varied, most formulas had "notable biases" in their prediction errors, the authors reported. For instance:

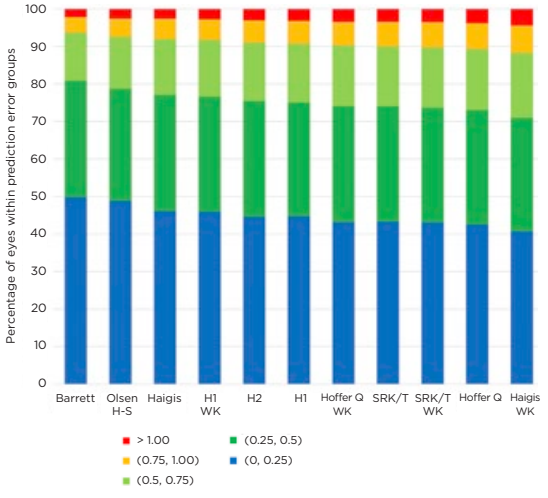
- the SRK/T formula was the most affected in eyes with flat or steep keratometry;
- with the Hoffer Q and Olsen formulas, there was significant bias with varying anterior chamber depth;
- the Haigis formula was most affected by variations in lens thickness; and
- the Wang–Koch modification of axial length for long eyes overcorrected some eyes, leading to myopic errors.

What about other IOLs? The authors cautioned that their findings might not be generalizable to other IOLs, as the lenses used in this study have the same design (anterior asymmetric biconvex) and are from the same manufacturer.

"But as these are 2 of the most commonly used IOLs in the United States, this is definitely relevant to people outside our organization," said coauthor William J. Chang, MD, also at the Redwood City Kaiser Permanente. "If we can guide [our colleagues] by saying the Barrett II does seem to be the best for these 2 lenses, it would simplify their lives as surgeons." —*Linda Roach*

1 Melles RB et al. *Ophthalmology.* Published online Sept. 23, 2017.

Relevant financial disclosures—Drs. Chang and Melles: None.



OUTCOMES. *This stacked histogram compares the percentage of cases within a given diopter range of predicted spherical equivalent refraction outcome for selected formulas and the AcrySof IQ IOL. (H1 = Holladay 1; H2 = Holladay 2; H-S = Haag-Streit; WK = Wang–Koch.)*

WORLD HEALTH

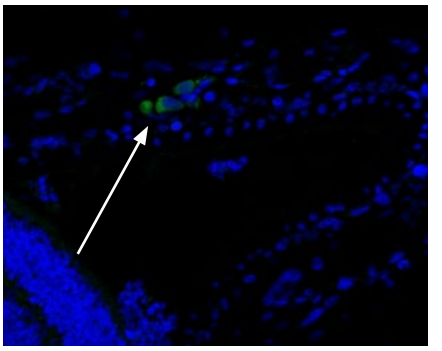
Widespread Impact of Zika on the Eye

RESEARCHERS AT THE BASCOM Palmer Eye Institute in Miami have discovered the extensive reach of the Zika virus (ZIKV) inside the eye, the totality of which suggests possible increased risks for glaucoma, uveitis, and retinal atrophy.[1]

The cellular level. For this observational case series, the researchers evaluated thin samples of ocular issue from 4 deceased fetuses previously diagnosed with congenital Zika syndrome (CZS) at the National Institute of Health in Colombia. Using scanning laser confocal microscopy and immunostaining with a ZIKV protein antibody, the team identified—for the first time—the viral localization within ocular tissue. They found remnants of the virus in the iris, neural retina, choroid, and optic nerve.

In addition, the researchers identified a number of changes, including thinning of the retinal pigment epithelium and choroid, optic atrophy, immature anterior chamber angles, and chronic inflammation.

"Unlike conventional histology with dyes, scanning laser confocal microscopy allowed us to assess—to a much finer degree—exactly what cell types the virus was infecting," said Richard K. Lee, MD, PhD. "Knowing these affected cell types can allow us to put together a pathophysiological explanation for ZIKV infection and how it causes vision and eye problems."



ZIKV. *Positive ZIKV immunofluorescence staining of cells (arrow) within the choroid.*

Informing care. "This more complete understanding of the histology of CZS also suggests that, for infected patients, ophthalmologists should examine specific aspects of the eye for increased risk of ocular disease," said Dr. Lee. They should be especially careful to look for the following.

Retinal disease. Any thinning of the retinal pigment epithelium and choroid along with loss of pigment in the patient could be a precursor to more significant retinal disease in the future, including retinal atrophy.

Glaucoma. The presence of congenital pupillary membranes and immature anterior chamber angles with ZIKV particles present in the optic nerve might suggest a greater risk of developing glaucoma.

Uveitis. Ophthalmologists should also be on the lookout for ZIKV particles in blood vessels. Along with pupillary membranes and inflammatory ocular changes, these findings might serve as a marker for increased risk of virally induced uveitis.

The Bascom Palmer team has plans to continue their research on CZS to aid in future treatment approaches, including vaccine development and pharmacotherapy. —*Mike Mott*

1 Fernandez MP et al. *JAMA Ophthalmol.* Published online Sept. 21, 2017.

Relevant financial disclosures—Dr. Lee: None.

For the financial disclosure key, see page 10. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.