### RETINA

# Retinal Imaging: Choosing the Right Method

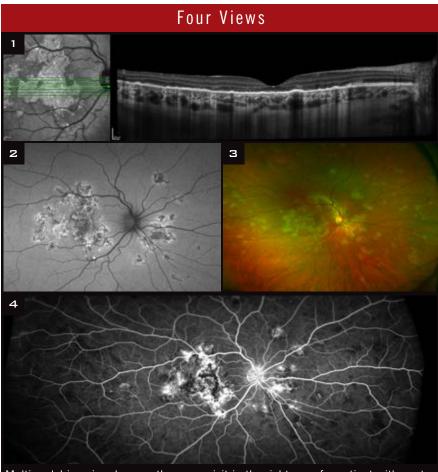
BY MIRIAM KARMEL, CONTRIBUTING WRITER INTERVIEWING JAY S. DUKER, MD, K. BAILEY FREUND, MD, AND DAVID SARRAF, MD

t's just going to keep getting better." That's how K. Bailey Freund, MD, summed up the state of retinal imaging. Perhaps Hermann von Helmholtz said something similar when he introduced the ophthalmoscope in 1851. But he could not have imagined all that his Augenspiegel (eye mirror) has spawned.

Today's devices can reveal all the layers of the retina. Several optical coherence tomography (OCT) devices include color fundus photography capability. And there's a device that takes images and lasers the eye. "All the manufacturers are going in the direction of multiple capabilities in one device," said Dr. Freund, at Vitreous-Retina-Macula Consultants of New York. He called retinal imaging "a hot field, with a lot of advances occurring very quickly."

Though Dr. Freund is not worried yet about being replaced by a machine, he and other retina specialists agree that imaging has changed the way they identify pathology and monitor response to therapy. It has expanded their view, as well as their understanding, of disease mechanisms and manifestations.

"Imaging has revolutionized the management of patients with retinal disease," said Jay S. Duker, MD, at Tufts University. Although OCT may come first to mind, he said, other modalities in the armamentarium keep retina specialists busy debating the relative merits of each.



Multimodal imaging done on the same visit in the right eye of a patient with acute posterior multifocal placoid pigment epitheliopathy. (1) SD-OCT with the Heidelberg Spectralis. (2) Ultra-widefield FAF with Optos 200Tx. (3) Ultra-widefield color (pseudocolor) with Optos 200Tx. (4) FA with Optos 200Tx.

**Optical Coherence Tomography** OCT has changed clinical practice and opened new areas of understanding.

**In practice.** OCT is very good at measuring thickness of the retina, so it's helpful for diseases that cause fluid

buildup, such as retinal vein occlusion (RVO) and diabetic macular edema (DME), said Dr. Duker. "In 2014, you can't treat diabetic macular edema or wet age-related macular degeneration (AMD) without an OCT. It's standard

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of care for treatment of those diseases."

OCT allows evaluation of different levels of macular ischemia not previously seen with prior imaging modalities. "Traditionally, we appreciated only superficial capillary ischemia. But newer OCT and high-resolution systems (resolution down to 3  $\mu$ m from 10  $\mu$ m) have revealed an intermediate and a deeper plexus that can also be ischemic. We never appreciated that clinically," said David Sarraf, MD, at Jules Stein Eye Institute, UCLA.

A new window on disease processes. OCT has revealed previously unknown pathology, said Dr. Freund. For example, "OCT really helped us understand how macular holes occurred. It made us realize that we were not very good at determining whether fluid was in or beneath the retina. It's helped me understand wet macular degeneration by pinpointing the location of the abnormal new vessels." Are they beneath the RPE, in the subretinal space, or proliferating in the retina itself? This delineation of anatomic subtypes of neovascularization, known as types 1, 2, and 3, respectively, has influenced Dr. Freund's treatment choices.

OCT has revealed the following:

• Subretinal fluid (serous retinal detachment) in RVO and DME

• Vitreomacular traction as the cause of primary (formerly called idiopathic) full-thickness macular hole

• Macular schisis as a manifestation of vitreomacular interface disease (epiretinal membrane and vitreomacular traction)

• Macular schisis as a manifestation of optic nerve disease (acquired optic pits)

**Advantages.** OCT is noninvasive, reproducible, and easy to interpret, Dr. Duker said. Dr. Sarraf added that it requires neither dye injection nor the bright lights used for color fundus photography, so it's easy on patients.

**Downside.** OCT doesn't identify blood well, so it won't document or measure a disease with bleeding in the retina, Dr. Duker said.

**On the horizon.** Most U.S. practices use spectral-domain OCT, said Dr. Freund, noting that the next wave will

## Ultra-widefield Cameras Expand the Image

A typical fundus camera delivers a 50-degree field of view, but now ultra-widefield imaging systems can deliver 100 degrees or more. Dr. Freund said two systems are now commercially available in the United States that do ultra-widefield imaging.

**Optos 200Tx.** Using scanning laser ophthalmoscopy, the Optos 200Tx can image the peripheral retina to 200 degrees with single capture. And because it can produce both FA and FAF images, it's becoming more popular among retina specialists, Dr. Freund said. Dr. Sarraf added that it requires no special lenses or dilation.

However, both doctors noted a caveat: The image is created by red and green scanning lasers that produce inaccurate color (pseudocolor), which may limit its interpretation. Further, said Dr. Sarraf, various artifacts may



be present, including those caused by the eyelashes or the nose. He said that it's possible to digitally match peripheral images to create a color montage for greater resolution and a better appreciation of the true nature of the disease.

**Spectralis.** Heidelberg Engineering offers an add-on lens for the Spectralis camera to capture an ultra-widefield view. The add-on is interchangeable with the existing lenses. It has FA and ICGA capability, but not FAF. It is designed to detect and monitor clinically relevant peripheral changes such as microaneurysms, neovascularization, perivascular leakage, or areas of nonperfusion, said Dr. Freund.

include swept source OCT (SS-OCT), which is commercially available outside the United States. SS-OCT allows deeper penetration of tissue and faster acquisition. By capturing enhanced depth images of the choroid, SS-OCT deepens our understanding of central serous chorioretinopathy, which is characterized by a thicker-than-normal choroid, he said. Beyond that, Dr. Freund foresees that adaptive optics will be incorporated into OCT.

In addition, OCT is being studied as a possible tool for large-scale screening of asymptomatic patients for conditions including glaucoma and DME.

#### **Fundus Photography**

Color fundus photography captures 30- to 50-degree views of the retina and optic nerve. "Virtually every ophthalmologist in the country has a fundus camera," Dr. Duker said. "It's widely available, easy to use, and is very good at documenting the appearance of the optic nerve and existence of blood buildup in the eye." But, he added, "We rarely make treatment decisions based on the photos."

**What's new?** Although today's cameras deliver high resolution, color

fundus photography hasn't undergone any major transformations since the 1960s, Dr. Sarraf said. More recent developments include enhanced capabilities for creating color montage photographs of the posterior pole and periphery with automated software.

#### Angiography

**Fluorescein angiography.** FA has been around since the 1960s. It's good at finding focal lesions to laser. But ever since anti-VEGF therapy supplanted focal laser treatment, "focal identification of the lesion is not as important as it once was," Dr. Duker said. "Many of us still use fluorescein when first making the diagnosis of wet AMD."

Dr. Sarraf agreed that standard FA is a good baseline tool for fine-tuning the diagnosis of choroidal disorders and neovascular macular degeneration.

**A wider view.** Ultra-widefield angiography captures 100 to 200 degrees to the periphery and beyond the equator, revealing pathology such as neovascular proliferation or ischemia that can't be identified with standard angiography, Dr. Sarraf said. He uses it to guide laser treatment in diabetic retinopathy and RVO, where lesions extend beyond

the macula to the periphery. Other uses include imaging tumors, choroidal melanoma, and some hereditary diseases.

#### Indocyanine green angiography.

ICGA has a more limited role than FA in the clinic, said Dr. Sarraf, noting some of the differences between the methods: In ICGA, the dye is much more protein bound than fluorescein, so less leakage is visible on the angiogram. In addition, the longer wavelength can better penetrate the RPE and blood. As a result, ICGA complements FA, which captures images of retinal circulation above the level of the RPE.

Uses of ICGA include the following:

• Diagnosing polypoidal choroidal vasculopathy (PCV) and certain choroidal tumors, such as choroidal hemangioma

• Refining diagnoses, such as the finding of choroidal vascular hyperpermeability associated with central serous chorioretinopathy

• Assessing choroidal circulation below the RPE and identifying choroidal neovascular membranes associated with retinal pigment epithelial detachments or obscured by blood

**Fundus autofluorescence.** FAF is not yet in widespread use, although it has gained traction over the last decade and, in some cases, may replace the more invasive fluorescein angiography, said Dr. Sarraf. If you're using FAF, Dr. Freund noted, it's important to know that different systems employ different wavelengths. Heidelberg uses a short blue wavelength; the Optos a longer green wavelength.

Uses include the following:

• Revealing the health of the RPE and buildup of lipofuscin, which is intensely autofluorescent. One such application is in Best disease, which is characterized by lipofuscin deposition and, thus, is easy to diagnose with FAF, Dr. Duker said.

• Seeing where areas of disease have occurred in the back of the eye. "It's useful in hereditary macular diseases because they have specific patterns. It's also good at detecting and monitoring drug toxicities, for example, in patients

## Pearls

**DR. SARRAF.** In a patient who has transitioned from dry to wet macular degeneration, my practice guideline is to obtain a baseline color fundus photo and baseline fluorescein angiogram, along with SD-OCT, to determine if the neovascularization is type 1, 2, or 3, which can influence the prognosis and the aggressiveness of the therapy. Going forward, I use only OCT to judge response to therapy.

**DR. FREUND.** Don't rely exclusively on OCT printouts. Sometimes you've acquired hundreds of scans, but the printout shows maybe two. You need to understand the limitations of the automated algorithms. You may misinterpret the results if you don't look at individual scans on the monitor.

**DR. DUKER.** OCT is going to become increasingly important in the practice of ophthalmology from front to back. Angiography will become increasingly less important because OCT will be able to do some—or perhaps all—of the things that angiography does. Finally, there's a place for autofluorescence in a referral practice.

on hydroxychloroquine (Plaquenil)," Dr. Freund said.

• Monitoring progression of geographic atrophy in clinical trials.

#### **Better and Better**

Regardless of the advances in imaging, the experience of a skilled clinician is still essential in fundus examination, for example, in assessing the health of the disc and identifying peripheral retinal tears and detachments, Dr. Sarraf said. And unlike the exam, no machine can "give a sense of comfort and satisfaction to the patient."

But these sophisticated systems have enhanced clinical practice. "Our understanding of retinal and macular disease is much more clearly defined," Dr. Sarraf said. And there's more to discover. "There's always mystery involved in the retina." Jay S. Duker, MD, is director of New England Eye Center and professor and chairman of ophthalmology at Tufts Medical Center, Tufts University School of Medicine. Financial disclosure: Receives research support from Carl Zeiss Meditec; is a consultant to Alcon/Novartis, Allergan, EMD Serono, Optos, Regeneron, and Thrombogenics; and holds stock in Eye-Netra, Hemera Biosciences, and Ophthotech. K. Bailey Freund, MD, is a member of Vitreous-Retina-Macula Consultants of New York and clinical associate professor of ophthalmology at New York University School of Medicine. Financial disclosure: Consults for Bayer HealthCare, Genentech, Heidelberg Engineering, and Regeneron.

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