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JUNE 2008

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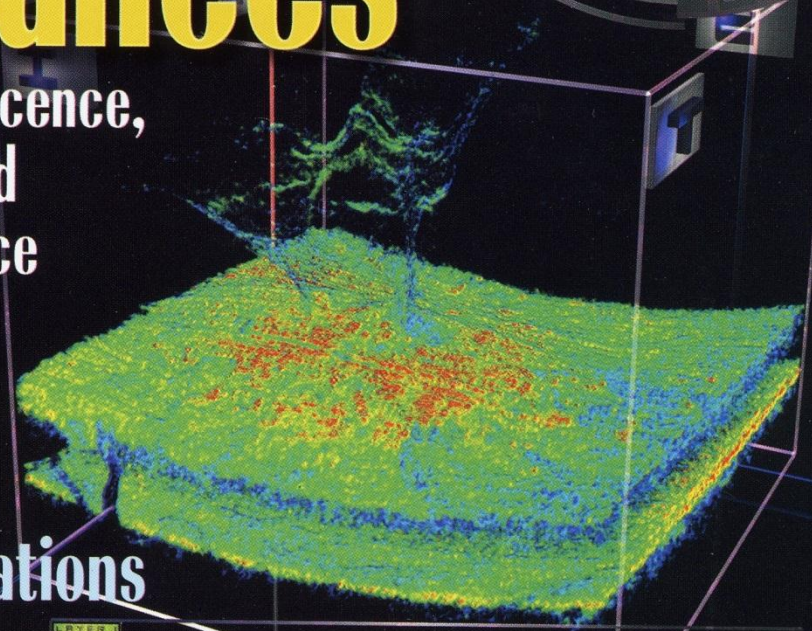
The Eye M.D. Association

Imaging Advances

Autofluorescence, 3-D OCT and Your Practice



...and Tools ...voiding Miscalculations

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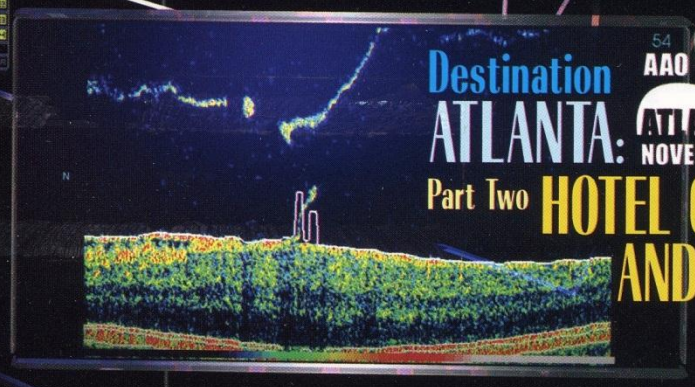
Use It to Solve the Tech Shortage



Destination ATLANTA: Part Two HOTEL GUIDE AND MAP

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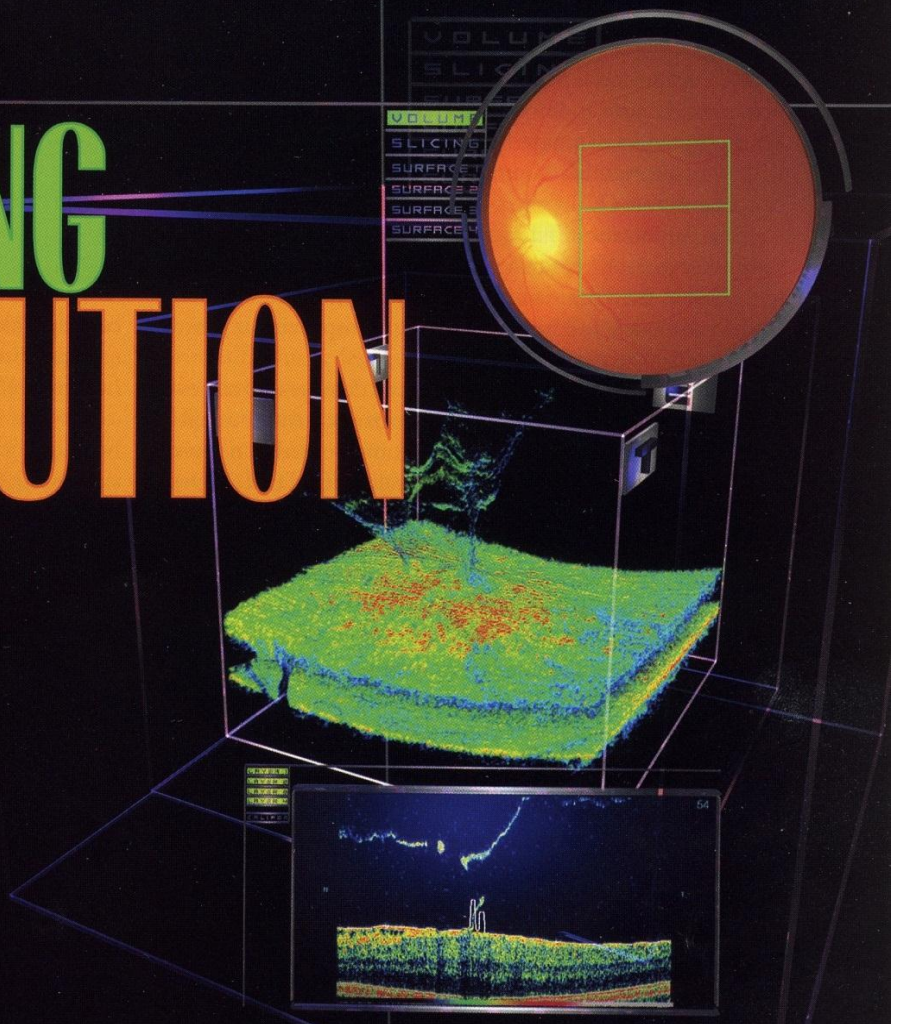
THE IMAGING REVOLUTION

Powerful imaging technology may be transforming the clinical practice of eye medicine, especially in the practices of retina and glaucoma specialists.



BY PAT PHILLIPS, CONTRIBUTING WRITER

Virtually every anatomic structure of the eye is becoming more visually accessible thanks to imaging technologies that didn't exist 10 years ago. New advances in optical coherence tomography (OCT) and autofluorescence (AF) imaging, in particular, are gathering attention both in the United States and internationally. Specialists agree that these technologies are dynamic works in progress and represent different stages of development. The two share a common strength: Both are noninvasive. As is common, however, with emerging technologies, there are issues yet to be resolved.

A NEW GENERATION OF OCT

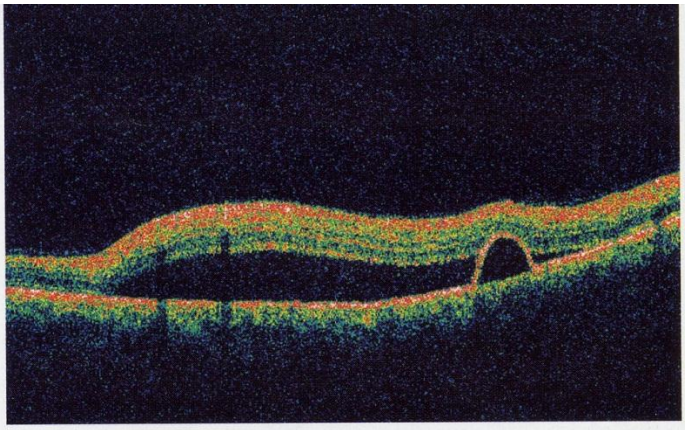
The major applications of conventional OCT have been in retinal disease and glaucoma. "OCT and other emerging technologies have been changing the way we practice medicine," said Joel S. Schuman, MD, professor and chairman of ophthalmology at the University of Pittsburgh. "OCT gives an objective assessment of the ocular structure and standardizes that information at a very high, expert level," he said.

The third dimension. Conventional OCT has been giving way to versions with three-dimensional, high-speed, high-resolution capabilities, also known as 3-D, spectral or Fourier-domain OCT.

When conventional OCT scans a structure the resulting image is a cross section of tissue in two dimensions; 3-D OCT scans faster and more powerfully, producing an enormous amount of rich data that can be rendered virtually in three dimensions on a computer monitor—as in a visual cube. And that cube can be rotated in any direction or cross-sectioned from any angle. It is as though the physician can dissect and scrutinize the anatomy of a patient's eye without ever entering it.

Three-dimensional OCT is now on the market in the United States. The new devices are from 50 to 100 times faster than previous-generation OCT. Seven companies in the United

States, Europe and Japan now manufacture and market these devices compared with only one manufacturer of conventional OCT.



DETACHMENT WOE. A 10-mm line scan image of a serous detachment using 3-D OCT.

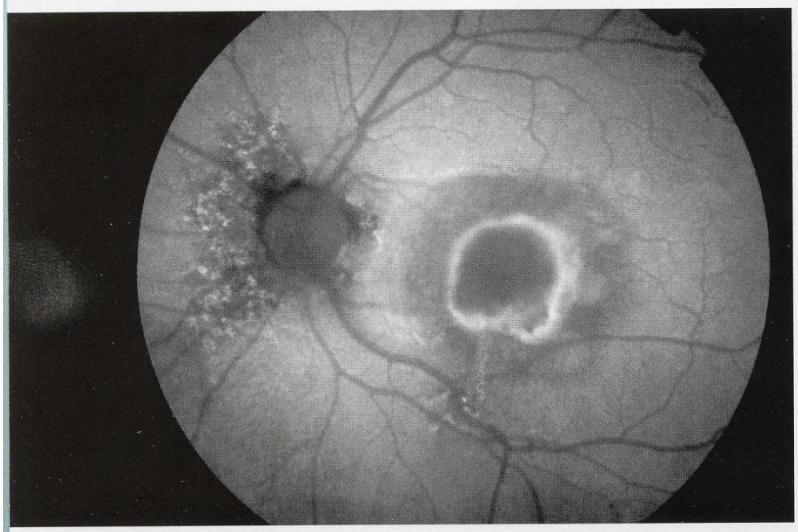
"The important difference is that this technology offers us the ability to get three-dimensional imaging because of its high speed," Dr. Schuman said. "It allows registration of scans from visit to visit and has the promise of improving reproducibility, sensitivity and specificity."

While experts welcome the enhanced data, as well as new possible options for imaging the anterior segment, the challenge lies in the interpretation. Dr. Shuman noted that more studies are needed to prove that the reality of 3-D OCT lives up to the promise.

Retina leads the way. The advent of 3-D OCT is going to change the landscape of ophthalmic practice, according to Dr. Schuman. "OCT had already become the gold standard of imaging for retinal disease. What is exciting is that with 3-D OCT it is now possible to map the retina with a high level of detail, reproducibly, and detect tiny changes in the retina, changes of 5 to 10 microns in the thickness of the tissue. It not only allows us to track the structure of the tissue but also its function. The oxygen content of the tissue can be measured and blood flow can be measured."

Glaucoma is close behind. 3-D OCT has also changed the way that glaucoma is detected and followed, according to Dr. Schuman. "I use imaging to identify abnormalities and then go back to the patient to identify those abnormalities with my own eye. I also see the structure-function correspondence. These devices do as well as an expert observer in discriminating between an eye with glaucoma and a healthy eye," he said.

FUNDUS AUTOFLUORESCENCE. Image of a fibrovascular pigment epithelial detachment in age-related macular degeneration. Image was captured with a fundus camera-based autofluorescence system with excitation wavelength at 580 nm and barrier filter at 695 nm.



Front of the eye brings up the rear. Until recently, OCT had not elicited much interest in the corneal and anterior segment areas, according to Donald Tan, MD, professor of ophthalmology at the National University of Singapore and deputy director of the Singapore National Eye Centre. "Corneal transplantation surgery is changing rapidly, and what OCT has been able to show is extremely useful in diagnosing corneal conditions and what is going on in the different layers of the cornea." Dr. Tan said he has found the imaging useful in planning what type of surgery is needed because the instrument is both qualitative and, to a certain extent, quantitative. "As corneal surgery continues to develop, 3-D OCT will be an invaluable tool both preoperatively and postoperatively. More accurate spatial resolution, better wavelengths, better penetration and measurement through opaque media represent major advances."

Dr. Tan even suggested that 3-D OCT may have a greater impact on surgical practice than medical practice, offering the advantage of imaging the entire cornea, the angles, iris and even the iris-lens interaction. He added that it has been a significant tool for glaucoma, especially for the detection of angle-closure glaucoma, which occurs commonly in Asians.

Picturing a trend. Another advantage of 3-D OCT is the ability to track change over time with the use of precisely registered data, according to Gadi Wollstein, MD, assistant professor of ophthalmology and director of the ophthalmic imaging research laboratories at the University of Pittsburgh. "I can align the data from one visit to another and can extract the data of interest in exactly the same location," he said. "This can substantially reduce the noise and the variability and allow me to identify changes at a much earlier stage, which will help ensure that the treatment is halting the progression of disease. Spectral OCT will be able to identify progression with more certainty than conventional OCT, requiring less progression or destruction of tissue because of the reduced level of variability."

AUTOFLUORESCENCE, THE METABOLIC MODALITY

The contemporary use of autofluorescence is comparable to the earlier days of OCT, according to Howard F. Fine, MD, MHSc, medical director of the Gerstner Clinical Research Center in Vision at Columbia University. "Just as OCT started out as a research tool and has become an indispensable

BOTH IMAGES COURTESY OF TIMOTHY J. BENNETT, CRA, FOPS

clinical tool in most retina practices, autofluorescence is emerging from its research role into clinical applications," Dr. Fine said.

The primary applications of AF imaging are in assessing the health of the retinal pigment epithelium in diseases such as geographic atrophy from AMD, pathologic myopia and central serous chorioretinopathy. Less common disorders that are well-imaged with AF include dystrophies and degenerations, especially those that affect the metabolism of lipofuscin, such as Stargardt's disease, according to Dr. Fine.

Monitoring metabolism. AF imaging, unlike OCT, is a form of metabolic mapping. It visualizes not only morphology but also metabolic changes. "The two imaging modalities serve different purposes," said Frank G. Holz, MD, professor and chairman of ophthalmology at the University of Bonn in Germany. "One imaging technique does not replace the other imaging technique." Dr. Holz pointed out that autofluorescence imaging gives information over and above conventional imaging techniques like fundus photography or fluorescein angiography. He suggested that AF may be more widely used in Europe than in the United States, but recently it has become more popular here. "The novel possibility with simultaneous recordings of scanning laser ophthalmoscope (SLO)-AF images and high-resolution OCT and automated eye tracking now offers the opportunity to study the corresponding microstructural changes in the outer retinal layers," he said.

Benefits for AMD and genetic disease. Dr. Fine also sees potential in managing retinal degeneration. "Autofluorescence is going to be increasingly used, especially as dry macular degeneration becomes more of an issue now that we have better treatments for wet macular degeneration." He added that "tracking geographic atrophy will become crucial once interventions are available in dry AMD as well." He and his colleagues are conducting imaging work to overlay fundus autofluorescence images with various other imaging modalities, including color photography, OCT, angiography, microperimetry and even multifocal electroretinography.

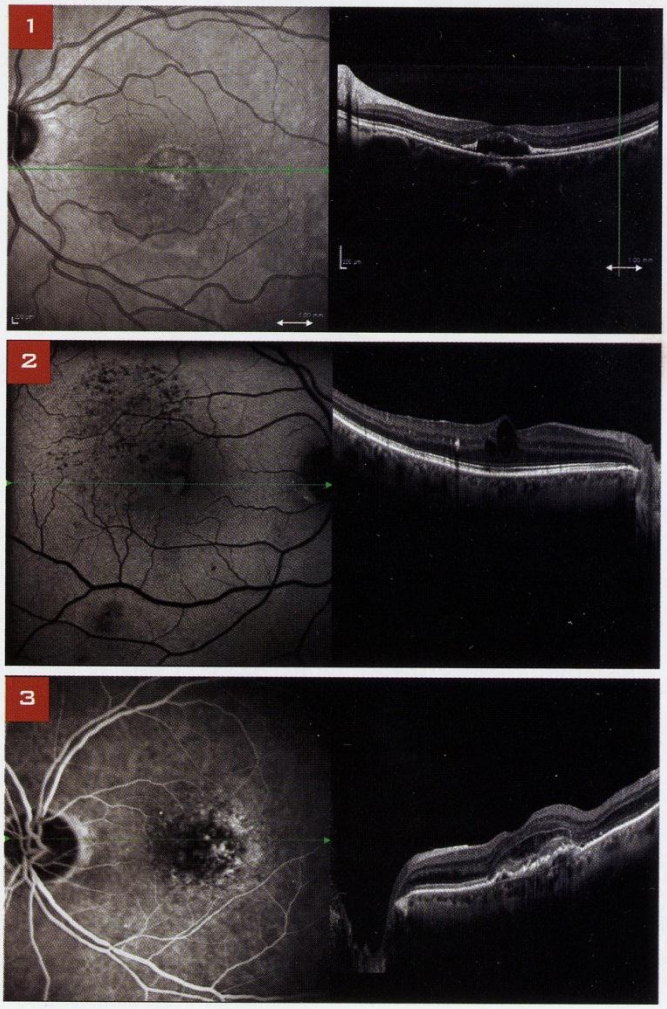
Dr. Fine also has a collaboration with the Allikmets genetics lab, which discovered the complement factor H mutation in AMD. The goal is to correlate AF changes with genotype/phenotype in a variety of inherited conditions. Dr. Fine said. "In the near future, autofluorescence imaging will be used on a day-to-day clinical basis for the diagnosis, classification and management of a number of diseases," he said.

POTENTIAL MISSTEPS IN IMAGE INTERPRETATION

From a general ophthalmologist's point of view, it is important to assess the quality of these imaging technologies and then to interpret the data correctly, Dr. Schuman said.

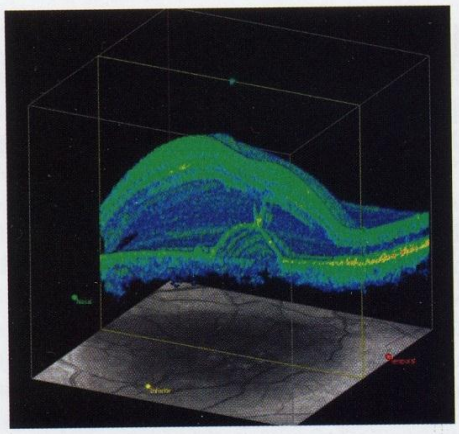
OCT variation. "If the OCT is not a good enough scan, you'll get an analysis that has a high likelihood of false negatives or false positives," Dr. Schuman said. "You need a scan of good quality. With 3-D OCT there are a number of different companies, each with its own data systems, definitions and printouts; this is destined to produce some confusion for clinicians. We need to ensure that the interpretation is correct and use that information to drive us back to the patient for corroboration."

Ophthalmic photographer Timothy J. Bennett, CRA, FOPS, OCT-C, of Penn State University, noted that 3-D OCT is operator-dependent, which may cause inconsistency in results. It is also patient-dependent. "The operator needs to be skilled and knowledgeable in pathology and disease processes and be able to establish some standard imaging protocols," Mr. Bennett said. "There is an extensive menu of scanning protocols, with some easy-to-use fast protocols. The patient needs to be



HEAD-ON AND SIDEWAYS. The latest imaging systems allow simultaneous comparisons between imaging modalities, such as these images of Best's disease (1), taken with infrared and spectral domain OCT, diabetic retinopathy (2) captured with fundus autofluorescence and SD-OCT, and occult choroidal neovascularization (3) with fluorescein angiography and SD-OCT.

HEIDELBERG ENGINEERING



EVERYTHING BUT AN OCEAN VIEW. Faster and richer information processing means that 3-D OCT can render a cube of anatomic volume and rotate it in virtual space or cross-section it on any plane. At left is an example demonstrating serous elevation of the retina and pigment epithelial detachment in a patient with central serous chorioretinopathy, as imaged on a Cirrus OCT.

able to stay still for the few seconds it takes to capture the image and have the visual acuity to see the internal fixation targets."

In a study of OCT and the effect of corneal dryness on the quality of the scan, Dr. Wollstein found the quality significantly deteriorates with dry eyes, perhaps leading to wrong measurements. "In practical terms, we recommend putting artificial tears into everyone who gets an OCT scan," he said. Mr. Bennett added that skilled operators often instill artificial tears when there is not the expected strength of signal during a scan.

In response to the lack of standards in OCT imaging, the Ophthalmic Photographers' Society has developed a rigorous certification program that was launched in November 2007, designed to raise operator skills and improve the consistency and reliability of OCT imaging data. "It has been exciting over the past five years to watch the evolution of diagnostic imaging," Mr. Bennett said. "With continued advancements in technology and automation, it not only will help clinical practice but also is exciting for us as photographers to get our hands on these new instruments."

Autofluorescence incompatibilities. Like OCT, autofluorescence is also vulnerable to artifacts and inconsistencies. "There is a big divide between autofluorescence systems that are based on fundus cameras and those based on SLO systems," said Dr. Fine. "Both systems are hampered by autofluorescence that emanates from the cornea and the lens. As cataracts progress, this artifact increases." The advantages of camera-based systems are that they are quicker, easier for the photographer to use and less expensive than the SLO systems, Dr. Fine said. The advantage of SLO-based systems is their high-quality images, focused directly on the target tissue of interest, according to Dr. Fine. He noted SLO systems have a longer acquisition time, do not yet image highly myopic (more than –9 D) eyes well and typically are more expensive to purchase.

Mr. Bennett pointed out that the SLO imaging technology in autofluorescence is more established than fundus camera–based imaging, but the fundamental problem with both techniques is the very low light levels of fluorescence that need to be captured. The two techniques arrive at autofluorescence images in very different ways using different wavelengths, he said. "There's controversy over whether the images from each technique are comparable, even though they look similar."

One strategy to overcome low light levels is to maximize all the light transmission in the fundus camera and use the lowest gain setting possible to reduce noise, Mr. Bennett said. He noted that SLO systems use image averaging to combat the same problem, with a mean image created from a series of nine to 15 frames to smooth out the noise. Dr. Fine is using image analysis software to assess the veracity of AF images. There is no quantification and no standardization of absolute levels of autofluorescence, meaning that the images can differ from timepoint to timepoint. He noted a lack of standardization between the systems marketed by different companies. In the future, he said, technologies to watch for include quantitative AF as well as wide-angle AF, to better image the peripheral retina.

MEET THE EXPERTS

TIMOTHY J. BENNETT, CRA, FOPS, OCT-C Ophthalmic photographer, Penn State University. *Financial disclosure: None.*

HOWARD F. FINE, MD, MHSC Medical director of the Gerstner Clinical Research Center in Vision at Columbia University. *Financial disclosure: None.*

FRANK G. HOLZ, MD Professor and chairman of ophthalmology at the University of Bonn in Germany. *Financial disclosure: None.*

JOEL S. SCHUMAN, MD Professor and chairman of ophthalmology, University of Pittsburgh. *Financial interests: Has lectured for Carl Zeiss Meditec, Heidelberg Engineering and Optovue; received grant support from Zeiss and Optovue; has patents and/or royalties from Zeiss.*

DONALD TAN, MD Professor of ophthalmology at the National University of Singapore and deputy director of the Singapore National Eye Centre. *Financial disclosure: None.*

GADI WOLLSTEIN, MD Assistant professor of ophthalmology and director, ophthalmic imaging research laboratories at the University of Pittsburgh. *Financial disclosure: Has received research support from Carl Zeiss Meditec and Optovue.*

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