

A Fresh Take on Optical Coherence Tomography

Advances in optical technology helped Optovue realize the potential of Fourier-domain OCT for diagnosing glaucoma.

BY JULIA T. LEWANDOWSKI, SENIOR ASSOCIATE EDITOR

Glaucoma Today's "Innovators" column profiles promising technological developments in glaucoma and the companies bringing them to fruition.

Ophthalmologists have long recognized an association between the progressive loss of retinal ganglion cells and glaucomatous changes in the optic disc. Although the standard techniques for evaluating the optic disc—ophthalmoscopy and stereoscopic fundus photography—were useful for identifying thinning of the neuroretinal rim and cupping of the optic nerve, these subjective approaches provided only indirect information about the retinal nerve fiber layer (RNFL).

The advent of optical coherence tomography (OCT) in the 1990s enabled ophthalmologists to measure the thickness of the RNFL objectively. Because this new diagnostic test also provided insight into how changes in the retina affected the appearance of the optic disc, this technology quickly became part of clinical studies and practitioners' standard glaucoma workup.

The original OCT technology introduced by investigators at the Massachusetts Institute of Technology (Cambridge, MA) in 1991 used time-domain techniques to capture images of the retina. In the past few years, researchers have recognized Fourier-domain OCT as an alternative measuring

technique that facilitates significantly higher scanning speeds.

Several companies have since brought Fourier-domain OCT systems to the market, including Optovue, Inc. (Fremont, CA), which in October 2006 launched the RTVue, the first Fourier-domain OCT system approved by the FDA.

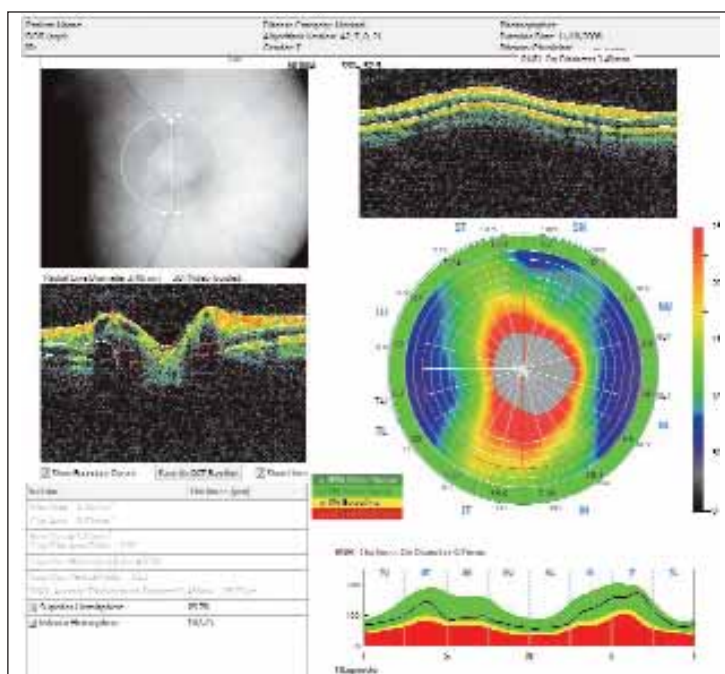
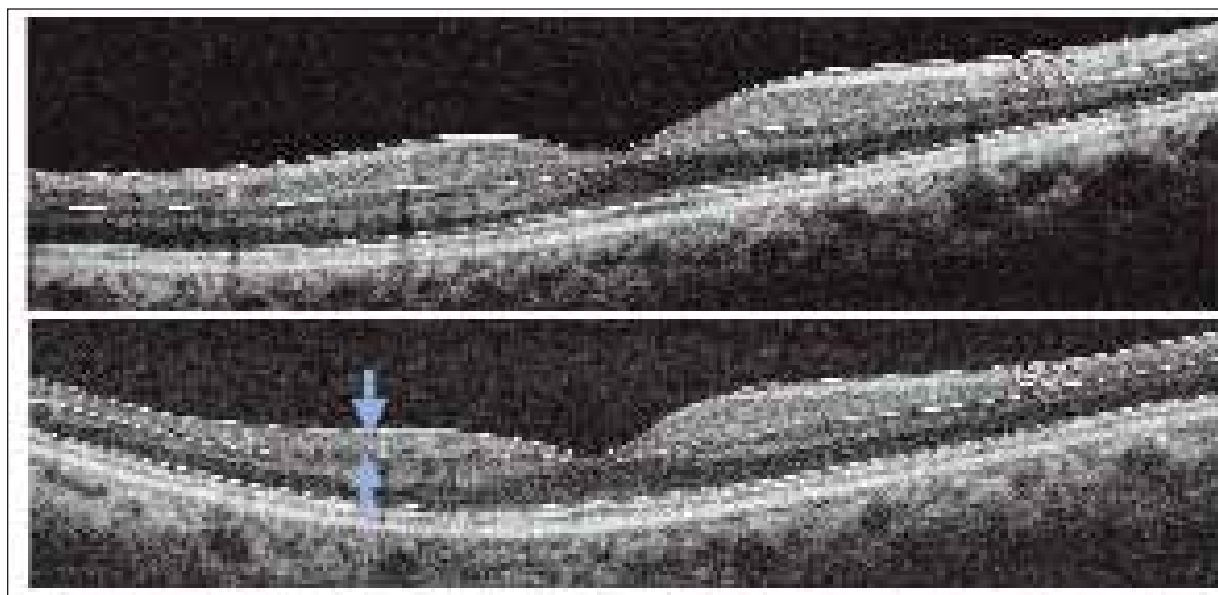


Figure 1. The RTVue's nerve head map (NHM4) provides quantitative information about the peripapillary RNFL, the neuroretinal rim, and the optic disc.

(Courtesy of Optovue, Inc.)



(Courtesy of Vikas Chopra, MD)

Figure 2. The RTVue's ganglion cell complex (GCC) scan provides quantitative information about the retinal layers preferentially affected by glaucoma. This image shows the automated segmentation analysis of a normal (top) and a glaucomatous (bottom) eye. Note the thinner GCC (arrows) in the glaucomatous eye.

This article describes how Fourier-domain OCT is helping clinicians and researchers detect early pathological changes in glaucomatous eyes.

THE FUNDAMENTALS OF FOURIER-DOMAIN OCT

Two parameters differentiate time-domain and Fourier-domain OCT: speed and resolution. Because commercially available time-domain OCT systems depend on the mechanical movement of a reference mirror to measure the reflectance from various layers of the retina, they can only perform 400 A-scans per second. In contrast, Fourier-domain OCT uses a stationary reference mirror and a spectrometer to capture information from all layers of the retina simultaneously, thus performing the equivalent of 26,000 A-scans per second.

David Huang, MD, PhD, is a co-inventor of OCT, Associate Professor of Ophthalmology and Biomedical Engineering at the University of Southern California, Los Angeles, the principal investigator of the NIH-funded Advanced Imaging for Glaucoma (AIG) study consortium, and a consultant to Optovue, Inc. During an interview with *Glaucoma Today*, he stated that the technological breakthrough that made Fourier-domain OCT a clinically viable diagnostic test for glaucoma was the availability of affordable, high-speed line cameras. "I described a Fourier-domain OCT device in my doctoral thesis in 1993," he said. "Although line-scan cameras were available then, they were not advanced enough to

work in Fourier-domain OCT systems. The technology has caught up with the theory, however, and as line-scan cameras become faster, we can expect the performance of Fourier-domain OCT to improve even more."

The second parameter that sets the RTVue apart from conventional time-domain OCT retinal scanners is the resolution of the images they create. Both systems use a superluminescent diode lighting source, but the RTVue's wider spectral bandwidth produces images that are twice as detailed ($5\ \mu\text{m}$) as those obtained by time-domain OCT devices ($10\ \mu\text{m}$).

The RTVue's faster scanning speed and ability to capture higher-resolution images overcome several limitations of commercially available time-domain OCT systems, said Michael J. Sinai, PhD, Optovue's Senior Director of Clinical Affairs, in an interview with *GToday*. "In addition to allowing us to obtain a lot of data quickly, the RTVue's higher scanning speed eliminates much of the motion artifact that can distort images obtained by time-domain OCT systems," he commented.

Rohit Varma, MD, MPH, is the chief of the Glaucoma Service at the Doheny Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, and a principal site investigator of the AIG study. In an interview with *GToday*, he stated that Fourier-domain OCT is valuable because it provides more information about how changes in the inner retinal layer affect the appearance of the optic nerve. "The loss of retinal ganglion cells causes thinning of the

RNFL, which then translates into greater cupping of the optic disc," he said. "By the time we are able to detect damage in a patient's optic disc or thinning of the RNFL, the patient may have lost a significant number of ganglion cells to glaucomatous progression."

According to Dr. Sinai, the RTVue has several scanning patterns specifically designed to detect glaucomatous damage. "The nerve head (NHM4) [Figure 1] and ganglion cell complex (GCC) [Figure 2] maps provide comprehensive information that is invaluable to the clinician for detecting and managing glaucoma," he said.

GLAUCOMA AND THE MACULA

Vikas Chopra, MD, Assistant Professor of Ophthalmology at the University of Southern California Keck School of Medicine is investigating the RTVue's utility for detecting early glaucomatous changes in the macula as part of the AIG study.

"Structurally, the macula is a logical place to look at changes in the RNFL and GCC, because the highest concentration of ganglion cells occurs in this area of the retina," he told *GToday*. "Unfortunately, measuring the total thickness of the macula with time-domain OCT technology does not provide sensitive enough information about glaucomatous change, because the disease preferentially affects the inner retinal layer."

During the 2006 AAO Annual Meeting in Las Vegas, Dr. Chopra and his colleagues presented the results of a study that compared the sensitivity of the Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, CA) and the RTVue for detecting the focal loss of retinal ganglion cells in the eyes of patients with glaucoma.¹

"We found that peripapillary RNFL thickness scans obtained with both OCT systems successfully differentiated between normal and glaucomatous eyes in a sub-

set of eyes from the AIG study," said Dr. Chopra. "The RTVue's novel macular grid scan pattern, however, captured data from a larger area of the macula and provided a more detailed map that allowed us to measure the thickness of the inner retinal layers. We were also able to detect the focal loss of ganglion cells with the high-resolution images obtained by the RTVue's proprietary macular thickness scan."

In addition to using the data from macular scans to create quantitative thickness maps of individual patients' maculae, the RTVue compares this information against a large age-adjusted normative database to create deviation and significance maps that alert the clinician to areas with likely damage (Figure 3).

"This information allows us to determine the percentage of ganglion cells a patient has lost relative to maculae of normal thickness [deviation] and the likelihood that the patient is developing glaucoma [significance]," said Dr. Chopra. "These reports have helped us detect characteristic patterns of focal ganglion cell loss in the superior and inferior poles of the optic nerves of patients with preperimetric glaucoma. When this information is analyzed by the RTVue's GCC Progressional Analysis function, we can detect progressive changes in macular thickness over time."

Dr. Sinai also believes that the RTVue can provide valuable information about the progression of glaucoma. "Because the RTVue is based on Fourier-domain OCT technology, we can quantify the thickness of the macula in microns," he said. "This degree of precision allows us to detect small, consistent changes in the RNFL that cannot be visualized with even the best quality stereophotographic fundus photographs."

In addition to working with Optovue to implement advanced diagnostic scanning patterns, Dr. Huang is

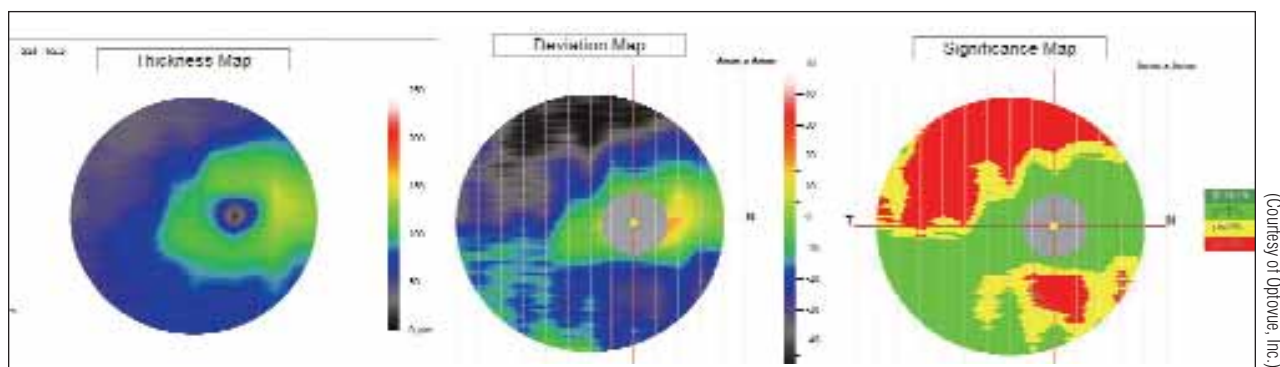


Figure 3. Thickness (left), deviation (center), and significance (right) maps derived from a GCC scan of a glaucomatous eye show a focal loss of ganglion cells superior and temporal to the fovea. The large black area in the deviation map indicates that the GCC is more than 50% thinner than in the corresponding region of a healthy eye. The same area in the significance map is color-coded red to show that the thickness of the GCC in this region is outside normal limits compared with the RTVue's age-adjusted normative database.

collaborating with other investigators from the AIG study to develop image processing software that will improve the RTVue's diagnostic accuracy. According to Dr. Huang, the diagnostic software algorithms developed by the AIG team have been licensed to Optovue through the University of Southern California.

"The RTVue FD-OCT may help us identify patients at risk and intervene before significant vision loss occurs."

—Vikas Chopra, MD

"The most recent results of my research show that the RTVue's GCC and RNFL scans provide diagnostic parameters that are significantly better than those produced by standard time-domain OCT systems,"^{2,3} said Dr. Huang. "I believe this is just the beginning of a long learning curve, however, and that we will benefit even more from Fourier-domain OCT as the technology matures."

Dr. Chopra cites the RTVue's ability to objectively measure early glaucomatous changes in the ganglion cell complex as one of its greatest strengths. "The key to managing glaucoma is early detection," he said. "The RTVue FD-OCT may help us identify patients at risk and intervene before significant vision loss occurs."

FOURIER-DOMAIN OCT FINDS A CLINICAL NICHE

Since Optovue introduced the RTVue in October 2006, several other companies have brought Fourier-domain OCT devices to market. Physicians who are interested in incorporating this imaging modality into their practice can choose from several FDA-approved devices: the Spectralis HRA + OCT (Heidelberg Engineering GmbH, Heidelberg, Germany); the Spectral OCT/SLO (Ophthalmic Technological Industries, Inc., Toronto, Ontario, Canada); the Cirrus HD-OCT (Carl Zeiss Meditec, Inc.); and the 3D-OCT 1000 (Topcon Medical Systems, Inc., Paramus, NJ). The SOCT Copernicus (Reichert, Inc., Depew, NY), is currently awaiting 510(k) clearance.

Dr. Huang acknowledged that Fourier-domain OCT devices have similar performance parameters, and he suggested that the best way for potential buyers to differentiate among systems is to consider the reliability of the device's engineering and software.

"Several factors influence the clinical utility of a particular Fourier-domain OCT system, including the device's scan patterns, its ability to analyze images, and how efficiently it extracts diagnostic parameters from raw data," he said.

Dr. Varma, Joel Schuman, MD, Chairman of the Department of Ophthalmology at the University of Pittsburgh School of Medicine and Director of the UPMC Eye Center, and other glaucoma specialists are helping Dr. Sinai and his colleagues at Optovue refine the RTVue's graphic user interface so that clinicians can quickly and efficiently access critical diagnostic parameters.

Dr. Varma is excited about the RTVue's clinical utility overall, but he thinks the unit's user interface could be improved. "Compared with devices that use time-domain OCT technology, the RTVue gives us a more comprehensive view of how the glaucomatous process damages the retina and the optic nerve," he said. "I would, however, like to see the indicators that describe the reliability and variability of the scans displayed more prominently and clearly on the RTVue's printouts." Increasing the visibility of these indicators, he added, would remind physicians to check the quality of the scan before analyzing the data.

"The RTVue came out of the gate with full retinal and glaucoma capabilities, because we envisioned it as a tool that could give generalists and specialists the information they need to manage ocular disease," said Dr. Sinai. "Our latest update, which includes a large age-adjusted normative database as well as new printouts and progression analysis, provides the flexibility that clinicians need to perform complex analyses or to gather basic clinical information." □

The AIG study is sponsored by National Eye Institute Grant R01EY013516.

Dr. Chopra has received honoraria from Optovue, Inc., but acknowledged no additional financial interest in the products or companies mentioned herein. He may be reached at (323) 442-6428; vchopra@usc.edu

Dr. Huang receives stock options, research support, and patent royalties from Optovue, Inc. He also receives royalty payments from an OCT patent licensed to Carl Zeiss Meditec, Inc. Dr. Huang may be reached at (323) 442-6710; dhuang@usc.edu.

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Dr. Varma has received research support from Optovue, Inc. He may be reached at (323) 442-6411; rvarma@usc.edu.

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