Intraoperative OCT: An Emerging Technology

Intraoperative optical coherence tomography (iOCT) is a technology that allows ophthalmic surgeons to evaluate the effects of surgical manipulations in real time. Just as OCT now commonly guides decisions in the clinic, iOCT may become a key asset in the surgical setting.[1]

"I was initially skeptical about the value of intraoperative OCT," said Andreas K. Lauer, MD, at Casey Eye Institute at Oregon Health & Science University in Portland. "Now, I see that it is really indispensable, especially for gene therapy, and for other conditions as well."

Evolution of iOCT

The first step, the development of a handheld, portable OCT system, was a huge leap forward in the evolution of intraoperative OCT, said Justis P. Ehlers, MD, at the Cleveland Clinic in Ohio.

Handheld OCT. Before handheld OCT, surgeons who wanted intraoperative OCT would use conventional office-based OCT systems. This, said Dr. Ehlers, "required gymnastics in the OR to turn a system on its side to take images."

Although handheld systems were an improvement over these improvisational techniques, the newer systems weren't perfect, he said. "They came with significant challenges around repeatability of the scan, ability to aim at the area of interest, and delays in taking images during surgery."

Dr. Lauer added that despite the advantage of its high resolution, handheld OCT had the disadvantage of being very operator dependent and increasing the potential for breaking sterile technique.

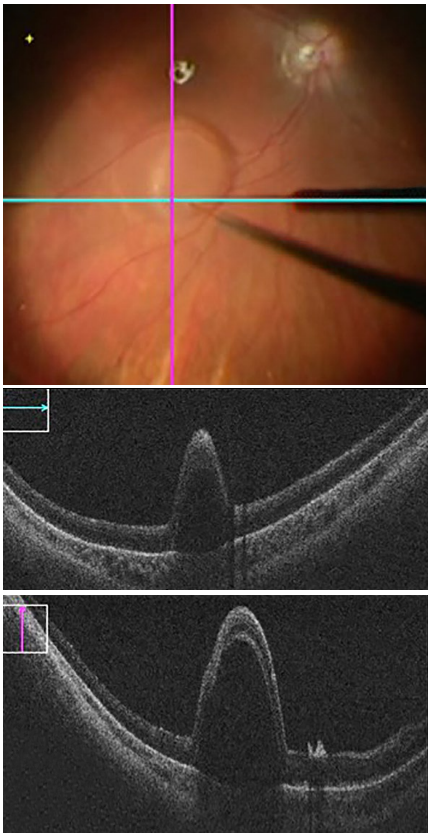
Built into the microscope. As the technology advanced, OCT was built into the microscope, said Dr. Ehlers. This allowed surgeons to more flexibly scan the area of interest and to do real-time OCT while operating, thereby speeding the workflow. "Once OCT was integrated into the microscope," said Dr. Lauer, "surgeons could do surgery while imaging, or pause surgery and image without having to change out devices. You could keep your hands on the instruments in the eye and control the OCT with a foot pedal." Alternatively, an assistant could control the OCT on a microscope panel.

FDA-approved systems. Although iOCT is not yet widely used in the United States, said Dr. Ehlers, 3 FDA-approved systems are available: the Haag-Streit iOCT, Zeiss Rescan 700, and Leica EnFocus. In addition, Leica also makes a handheld OCT system. All of these systems use spectral-domain OCT. He noted that some research systems use swept-source OCT.

iOCT Applications

Although researchers have not yet conducted randomized, controlled trials showing definitive benefits of iOCT, Dr. Ehlers said that it is having an impact in a variety of anterior and posterior segment surgeries.

Anterior segment surgeries. iOCT image acquisition is especially fast for anterior segment procedures, he said, as it typically takes 30 seconds or less



IN SURGERY. *Intraoperative optical coherence tomography during retinal gene therapy surgery using Zeiss Rescan 700. Vertical and horizontal line scans are depicted confirming viral vector delivery into the subretinal space.*

Andreas Lauer, MD, and Huber Vasconcelos, MD.

BY ANNIE STUART, CONTRIBUTING WRITER, INTERVIEWING **JUSTIS P. EHLERS, MD, ANDREAS K. LAUER, MD,** AND **ROBERT E. MACLAREN, MBCHB.**

to procure an image.

Procedures such as lamellar keratoplasty appear to particularly benefit from iOCT, said Dr. Lauer, by allowing the surgeon to image how the transplant is interfacing with the host cornea.

DMEK. One of the challenges of Descemet membrane endothelial keratoplasty (DMEK) is confirming the graft orientation, said Dr. Ehlers. In the United States, it's typically standard to S-stamp the tissue for feedback on graft orientation. "By using iOCT, however, surgeons have been able to eliminate tissue stamping, which may improve endothelial health, reduce cellular loss, and potentially improve graft survival."

DSAEK. Likewise, said Dr. Ehlers, iOCT can provide additional information during Descemet stripping automated endothelial keratoplasty (DSAEK) related to interface fluid and graft-host apposition, which is especially helpful when the cornea is hazy and the view is limited.

Corneal biopsy. "iOCT may also provide key information regarding depth information during anterior lamellar procedures, such as corneal biopsy or deep anterior lamellar keratoplasty," said Dr. Ehlers.

Posterior segment surgeries. "iOCT really comes into its own when you're working underneath the retina," said Robert E. MacLaren, MBChB, at the University of Oxford in the United Kingdom. "The macula is where you get the best images."

iOCT is not ideal for very peripheral retinal exams, but it is possible to get good images in about two-thirds of the retina, said Dr. Lauer. "It is helpful for conditions such as macular hole, epiretinal membrane or macular pucker, traction retinal detachment, and repair in patients with advanced diabetic retinopathy."

For most cases, Dr. Ehlers tends to do the initial part of the procedure and then reevaluate with iOCT to see if he has achieved his objectives. "This may require a 60- to 90-second pause to scan the whole macula or the area of interest," he said. However, the use of iOCT may actually decrease surgical time by confirming completion of surgical objectives earlier in the case.

Membrane peeling procedures. iOCT is helpful in visualizing the contour of the retina when you're peeling membrane, said Prof. MacLaren. Although visualizing agents can highlight these transparent membranes, said Dr. Lauer, there comes a moment of truth during surgery when you must decide "Did I remove enough or do I need to do more?"

"We often use the OCT to guide whether or not we've completed the membrane peeling," said Dr. Ehlers. "Because of the additional information that is provided by iOCT, it is rare that I need to re-stain, eliminating 1 step during surgery."

Choroidal-retinal biopsies. iOCT can be particularly helpful in identifying the optimal location to perform a choroidal-retinal biopsy, said Dr. Ehlers.

Argus implants. "At Cleveland Clinic, we have also found that iOCT can be utilized during Argus retinal implants to confirm and optimize the apposition of the electrode array against the retina," said Dr. Ehlers.

Gene therapy. Prof. MacLaren and Dr. Lauer consistently use iOCT for gene therapy. "For gene therapy to be effective, the material needs to be placed in the subretinal space," said Dr. Lauer, "but the operating microscope alone only provides an axial view of the retina." iOCT can help confirm that the targeted area has been reached. The technology is so useful, he said, that it is mandatory for some gene therapy research protocols.

Tips for Enhanced Use

As with any new technology, said Prof. MacLaren, there's always the chance for things to go wrong. "It's essential to get training so you know how to operate and troubleshoot when things don't work as planned." Other ways to ensure greater success include the following:

Start with simpler cases. "If you're a posterior segment surgeon," said Dr. Ehlers, "start with macular cases, such as epiretinal membranes, macular holes, or proliferative diabetic retinopathy with mild-to-moderate traction detachments."

Learn a step at a time. With different views, types of scan patterns, and image coloration, the instrumentation is powerful and can be overwhelming at first, said Dr. Lauer. As with the multiple features of your smartphone, it's difficult to master everything at once. "Learn 1 thing at a time in a stepwise fashion," he said. "For example, try to get the scan in the area of interest, bringing it into focus with the foot pedal. On a separate day, focus on rotating the image. Next learn how to magnify the image."

Keep at it. There certainly is a learning curve, added Dr. Ehlers. "But we have found that as users continue to apply the technology, their workflow improves and the utilization increases."

Groom an assistant. Having someone in your operating room who is comfortable with manipulating the OCT platform—whether a scrub nurse, circulating nurse, fellow, or resident—can make a big difference in ease of use, especially at first, said Dr. Ehlers.

"Knowledgeable and experienced assistants may even sometimes acquire images faster than the surgeon can," said Dr. Lauer.

Use it as a teaching tool. iOCT not only helps surgeons make more informed decisions, said Dr. Ehlers, "It can also help educate residents and fellows, elevating their clinical judgment by providing immediate feedback to compare with their gut impressions." In addition, said Dr. Lauer, having an OCT record of what was done during surgery can be helpful to study investigators and sponsors.

Barriers to Widespread Use

Prof. MacLaren first started using iOCT for gene therapy. "But once I began using it routinely, I found it quite useful for other cases as well. For example, if you're doing a retinal detachment operation, you can use the OCT to see how much subretinal fluid is in the macula." Still, barriers have prevented widespread use.

Cost. People do see the benefits, said Dr. Ehlers, but cost is keeping many from making the leap. "There is no way to recoup any of the cost because there isn't a code for reimbursement related to the technology, so it's a tough thing

to pull the trigger on." Clinicians need evidence that the modality results in better patient outcomes before they will consider the expense worthwhile, said Dr. Lauer.

"Cost is an issue," agreed Prof. MacLaren, "but it's not exorbitant when compared to other modern-day treatments in ophthalmology, especially if you're in the market for a new microscope. An iOCT microscope system will cost about $150,000-$350,000, depending on whether it is a stand-alone iOCT system or combined within the microscope. If you're doing an injection of Luxturna, that will cost $800,000. If the OCT scan tells you you've got the treatment in the right place, that seems to be a good investment."

Tracking. Tracking software exists in some of these platforms, said Dr. Ehlers, but these systems need improved accuracy and efficiency. Instrument tracking is currently not available but could be an important advancement to enhance surgeon feedback.

Software analysis. Also needed, said Dr. Ehlers, are software platforms that give more rapid, detailed surgeon feedback, for example, mapping out the residual epiretinal membrane or evaluating the amount of residual fluid between a corneal graft and a host cornea. This feedback could also be extremely helpful in the emerging field of subretinal or suprachoroidal drug delivery. "It would be helpful to be able to precisely measure the delivered therapeutic volume," he said.

Imaging quality. Although iOCT imaging quality is quite good, there is still room for improvement, said Dr. Lauer. Given the challenges of imaging in the surgical environment, image quality still lags behind those images obtained in clinical OCT systems, added Dr. Ehlers.

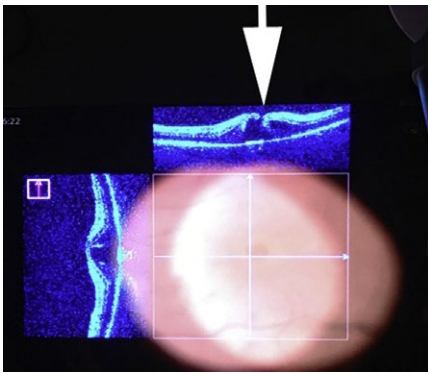
Other desirable enhancements. Prof. MacLaren would also like to see better integration with instruments. "Right now, when you bring an instrument to the retina, it creates a big artifact on the scan," he said. "It would be ideal to have instruments made of transparent material that do not create huge shadows on the retina when it is being scanned by the OCT.

"It would also be good to have the OCT image projected in the view in the assistant's eyepiece during surgery, which could help with training," he said.

Despite these shortcomings, Dr. Ehlers anticipates that iOCT will become a standard feature on microscopes over the next 5 years.

PIONEER and DISCOVER Studies

Whether anterior or posterior segment surgery—what we're finding with iOCT across the board, said Dr. Ehlers, is that it adds information the surgeon wouldn't otherwise have—information that often changes the surgeon's perspective about the status of tissue.[1]



INTRAOP. *Example of iOCT overlay on a flat high-magnification contact lens.*

New or different information. "What we found consistently in PIONEER and DISCOVER—and replicated by other studies—is that a fairly high percentage of surgeons feel the extra information gained is helpful," said Dr. Ehlers. In the DISCOVER study, iOCT membrane peeling findings were discordant from the surgeon's initial impression in 19% of cases.[2]

Changing surgical practices. Studies have suggested that iOCT may change surgical decision-making in about 20% to 35% of cases, Dr. Ehlers said. "You might peel less; you might do a fluid-air exchange without a gas tamponade—things that could change how the patient does postoperatively."

In both the DISCOVER and PIONEER studies, iOCT impacted surgical decision-making and altered the surgical approach in a significant percentage of cases.[2-4]

"Having that extra information is something that has real potential to enhance the value of what we're bringing to patients in terms of precision care and individualized surgical treatments," said Dr. Ehlers.

Clinical trials still needed. "We are working on designing prospective, controlled, multicenter iOCT trials," said Dr. Ehlers. "But it is difficult to control various aspects of surgical procedures that can influence the results of surgical clinical trials." Invariably, there is individual variation in practices, added Prof. MacLaren.

It will take large numbers of patients to confirm the clinical benefits of iOCT, said Dr. Lauer. He suggested that developing a consortium to evaluate iOCT may be one method for gathering more data more quickly.

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1 Ehlers JP. *Eye (Lond).* 2016;30(2):193-201.

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4 Ehlers JP et al. *Ophthalmology*. 2018;125(7):1014-1027.

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