OCT has become vital in the diagnosis and monitoring of myriad ophthalmic conditions. The value OCT provides in the pre- and postoperative management of ophthalmic surgical conditions, such as epiretinal membranes and macular holes, led investigators to evaluate the possible role of OCT in the OR itself. In 2005, surgeons first used intraoperative OCT (iOCT), with time-domain technology, to visualize anterior segment structures during lamellar keratoplasty and trabeculectomy procedures. The development of various iOCT technologies followed, ranging from handheld OCT devices to microscope-integrated systems.

The clinical utility of iOCT to date spans anterior and posterior segment applications, and prospective studies suggest that this tool may have the potential to be a future cornerstone of ophthalmic surgery.

**iOCT OPTIONS**

**Portable**

The first handheld spectral-domain OCT (SD-OCT) probe was developed by Cynthia Ann Toth, MD, and Joseph A. Izatt, PhD, at Duke University. The device was first described in clinical use during vitreoretinal surgeries in 2009. Using the handheld probe, Toth et al obtained retinal images during macular surgeries involving epiretinal membranes, full thickness macular holes, and vitreomacular traction. The surgeons were able to see operative tissue configurations difficult to detect using traditional en face microscopic views.

Other studies corroborated the advantages of portable SD-OCT, including its use in vitreoretinal indications such as retinal detachment (RD) and proliferative diabetic retinopathy (PDR) surgeries and pediatric retinal examinations.

FDA-cleared portable OCT systems include the EnVisu handheld OCT probe (Leica Microsystems) and the stand-mounted iVue system (Optovue). Limitations of handheld probes include the need to devote operating time to the process of obtaining images, as well as motion artifacts, challenges in image stabilization, a steep learning curve for image acquisition, and lack of real-time imaging.

**Microscope-Mounted**

Mounting a device on the microscope can improve the stability of the scan axis and reproducibility of images and allow foot-pedal control. The first commercially available device offering this function was the Bioptigen EnVisu (Leica Microsystems). Microscope stabilization dramatically improved image acquisition time, image stabilization, usability across surgeons, and overall efficiency. This broad accessibility enabled the first multisurgeon large scale prospective study of iOCT, PIONEER. However, like the handheld...
devices, microscope-mounted devices did not provide real-time imaging of the instrument-tissue interface.³

**Microscope-Integrated**

In this approach, OCT and microscope optical pathways are integrated, allowing real-time visualization of instrument-tissue interactions with a heads-up external viewing display. Susanne Binder, MD, and Dr. Toth both independently developed early prototypes with this approach. Dr. Toth’s team developed an integrated iOCT system using the Bioptigen engine, whereas Dr. Binder’s team used the Carl Zeiss Meditec Cirrus engine.

Multiple commercial microscope-integrated iOCT systems are now FDA-cleared and available in many global markets. The Rescan 700 (Carl Zeiss Meditec) is integrated with that company’s Lumera 700 microscope platform. The device provides Z tracking and focus controls designed to enhance image quality and stability.¹⁰,¹¹ Haag-Streit’s system uses a mounted side port to incorporate the OPMedT OCT system. Finally, the EnFocus system (Leica Microsystems) uses the Leica surgical microscope with extended-range scanning and high-resolution images from the Bioptigen engine.¹¹

**CLINICAL STUDIES**

Two large prospective iOCT trials, PIONEER and DISCOVER, have examined the feasibility, utility, and safety of iOCT across multiple ophthalmic surgeries. PIONEER evaluated the utility of OCT images derived from a microscope-mounted system in anterior and posterior segment surgeries. OCT images were collected from 98% of the 531 enrolled eyes (256 posterior segment indications) using disease- and procedure-specific imaging protocols with surgeon feedback on the value of the images. The study found that iOCT imaging provided valuable additional information in 43% of membrane peel cases.³

DISCOVER evaluated microscope-integrated iOCT using three OCT prototypes, including the Rescan 700, EnFocus, and a research prototype developed at Cleveland Clinic’s Cole Eye Institute. Over a 3-year period, 820 individuals were enrolled for either anterior or posterior segment procedures. The DISCOVER trial further supported the clinical utility of iOCT, with 29.2% of posterior segment surgeries reportedly affected by iOCT information.¹²-¹⁵

Several studies have since corroborated the clinical efficacy of iOCT. Pfau et al demonstrated a benefit of iOCT in 74.1% of 32 posterior segment and combined cases.¹⁰ Moreover, the addition of iOCT images led to changes in surgical approaches in 41.9% of cases, particularly in surgeries involving membrane peeling and tamponade choice.¹⁰

Binder et al found that iOCT confirmed procedure completion, depicted macular retinal changes, and helped to identify subclinical pathology that ultimately affected surgical management.¹⁶ Following the success of their initial study, the same group compared the efficacy of iOCT for crucial vitreoretinal surgical steps, including visualizing membranes with retinal dyes. The authors found that iOCT images allowed membrane peeling without the use of dyes.
and helped surgeons detect iatrogenic macular hole forma-
tion during vitreomacular traction procedures.\textsuperscript{17}
In a recent study led by Drs. Toth and Izatt, the authors
reported that real-time iOCT images during vitrectomy
for complications of PDR improved dissection of surgical
planes and enhanced retinal traction relief by highlighting
the need for additional peeling.\textsuperscript{18}

\section*{VITREORETINAL APPLICATIONS}

\section*{Macular Surgery}

The use of iOCT has been described extensively in macu-
lar disease, particularly in vitreoretinal interface disorders,
in which the technology provides surgeons with excep-
tional visualization of the epiretinal membrane and tissue
planes throughout the procedure. One study reported that
iOCT-guided membrane peeling was possible without the
use of surgical staining agents in 40\% of cases.\textsuperscript{17} Prospective
studies of membrane peeling procedures found that iOCT
identified occult residual membranes in 12\% of cases—and
confirmed complete membrane peeling contrary to sur-
geon impression in 9\% of cases.\textsuperscript{8}

The DISCOVER trial also demonstrated a disconnect
between surgeon impression and surgical anatomy. In 40\% of
cases in which the surgeon felt that residual membranes
were present, iOCT revealed complete membrane removal
(Figure 1).\textsuperscript{15} Additionally, iOCT has allowed surgeons to
characterize subclinical structural changes in procedures
such as macular hole closure, providing insights into reti-
nal anatomic configurations that may ultimately influence
clinical outcomes.\textsuperscript{19,20}

\section*{Retinal Detachment}

iOCT can enhance visualization of surgical steps during
RD repair, including retina or retinal pigment epithelium
apposition after perfluorocarbon tamponade and after
air-fluid exchange. Specifically, iOCT can assist in locating
retinal breaks or occult membranes and differentiating reti-
nal schisis versus detachment. In the DISCOVER study, the
feedback provided by iOCT altered the RD surgical proce-
dure in 18\% of cases.\textsuperscript{15}

\section*{Proliferative Diabetic Retinopathy}

In posterior segment surgery involving PDR, iOCT can
help surgeons identify difficult-to-visualize surgical planes
and facilitate differentiation of RD versus PDR fibrovascular
membranes. Static and continuous feedback from iOCT
can alter PDR surgery by identifying occult retinal breaks
and membrane dissection planes and differentiating between
tractional and rhegmatogenous RD.\textsuperscript{15,18}

\section*{Emerging Therapeutics}

iOCT can act as a surgical guidance system for sub-
retinal injections, gene delivery, and retinal prosthesis
placement.\textsuperscript{21-23} For example, surgeons used iOCT feed-
back regarding the array-tissue interface and prosthetic
retinal tack placement when performing Argus II implants
(Second Sight Medical Products).\textsuperscript{22}

During gene therapy delivery into the subretinal space,
iOCT can help identify the location and volume of viral
vector injection. In an ongoing phase 2 clinical trial of cho-
roderemia gene therapy, iOCT helped to improve the clin-
cal safety through direct monitoring of foveal stretching
and hole formation.\textsuperscript{23}

\section*{ONGOING ADVANCES}

\section*{iOCT-compatible Instruments}

iOCT images of tissue-instrument interactions are hin-
dered by the properties of most standard vitreoretinal

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{With a 3D immersive system with iOCT integration, the iOCT overlay demonstrates\textsuperscript{[INTRAOPERATIVE] OCT IDENTIFIED OCCULT RESIDUAL MEMBRANES IN 12\% OF CASES—AND CONFIRMED COMPLETE MEMBRANE PEELING CONTRARY TO SURGEON IMPRESSION IN 9\% OF CASES.} a flat full-thickness retinal hole.}
\end{figure}
instruments. Metallic surgical instruments with large profiles (eg, forceps and scissors) result in shadowing of the underlying retinal structures, and light scattering limits the visualization of instrument tip maneuvers with iOCT. The development of iOCT-compatible devices may provide better visualisation of instrument tips and surgical manipulation of tissue.24

Software Systems for Tissue Analysis
iOCT devices require improved analytical software to enable surgeons to perceive minute tissue alterations intraoperatively. For example, in a study examining the use of volumetric analysis algorithms during macular hole surgery, OCT devices proffered automated analysis of macular hole structural dimensions that correlated with clinical stages and visual outcomes.25 In addition, iOCT can detail macular hole covariates, which have been shown to be predictive of successful macular hole closure, in ways that are not obtainable preoperatively.26

Volumetric analysis using iOCT may also help to determine accurate subretinal therapeutic drug delivery and prevent retinal toxicity. iOCT-derived algorithms measuring bleb volumes after subretinal therapeutic delivery have shown validity and reproducibility, as well as illuminating a stark contrast between intended and actual subretinal drug volumes.27,28

Volumetric Real-Time iOCT
Research is under way on the development of microscope-integrated intraoperative swept-source OCT. A research prototype at Duke University can produce real-time volumetric 4D imaging with up to 10 volumes per second while maintaining micron-scale resolution. The images are relayed to microscope oculars using a stereoscopic heads-up device. This platform provides surgical guidance, helping surgeons to visualize retinal pathology and iatrogenic tissue damage in ways not readily visible with current 2D images.29,30

CONCLUSIONS
iOCT can provide a better understanding of tissue architectural changes in the OR, thus assisting with surgical maneuvers and guiding the surgeon’s decision-making (Figure 2). Researchers are working to enhance certain aspects of iOCT performance, such as instrument integration, software analysis, clinical utility, and image quality. Additional prospective randomized controlled trials would help elucidate the ultimate benefit of this technology for patient outcomes. ■


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