Determination of Feasibility and Utility of Microscope-Integrated Optical Coherence Tomography During Ophthalmic Surgery
The DISCOVER Study RESCAN Results

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IMPORTRANCE Optical coherence tomography (OCT) has transformed the clinical management of a myriad of ophthalmic conditions. Applying OCT to ophthalmic surgery may have implications for surgical decision making and patient outcomes.

OBJECTIVE To assess the feasibility and effect on surgical decision making of a microscope-integrated intraoperative OCT (iOCT) system.

DESIGN, SETTING, AND PARTICIPANTS Report highlighting the 1-year results (March 2014–February 2015) of the RESCAN 700 portion of the DISCOVER (Determination of Feasibility of Intraoperative Spectral Domain Microscope Combined/Integrated OCT Visualization During En Face Retinal and Ophthalmic Surgery) study, a single-site, multisurgeon, prospective consecutive case series regarding this investigational device. Participants included patients undergoing ophthalmic surgery. Data on clinical characteristics were collected, and iOCT was performed during surgical milestones, as directed by the operating surgeon. A surgeon questionnaire was issued to each surgeon and was completed after each case to evaluate the role of iOCT during surgery and its particular role in select surgical procedures.

MAIN OUTCOMES AND MEASURES Percentage of cases with successful acquisition of iOCT (ie, feasibility). Percentage of cases in which iOCT altered surgical decision making (ie, utility).

RESULTS During year 1 of the DISCOVER study, a total of 227 eyes (91 anterior segment cases and 136 posterior segment cases) underwent imaging with the RESCAN 700 system. Successful imaging (eg, the ability to acquire an OCT image of the tissue of interest) was obtained for 224 of 227 eyes (99% [95% CI, 98%-100%]). During lamellar keratoplasty, the iOCT data provided information that altered the surgeon’s decision making in 38% of the cases (eg, complete graft apposition when the surgeon believed there was interface fluid). In membrane peeling procedures, iOCT information was discordant with the surgeon’s impression of membrane peel completeness in 19% of cases (eg, lack of residual membrane or presence of occult membrane), thus affecting additional surgical maneuvers.

CONCLUSIONS AND RELEVANCE The DISCOVER study demonstrates the feasibility of real-time iOCT with a microscope-integrated iOCT system for ophthalmic surgery. The information gained from iOCT appears to allow surgeons to assess subtle details in a unique perspective from standard en face visualization, which can affect surgical decision making some of the time, although the effect of these changes in decision making on outcomes remains unknown. A prospective randomized masked trial is needed to confirm these results.
Microscope-Integrated OCT During Ophthalmic Surgery

Methods

The DISCOVER study is a single-site, multisurgeon, prospective consecutive case series regarding this investigational device, and it was approved by the institutional review board of the Cleveland Clinic. The study adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients participating in the DISCOVER study.

The study included an intraoperative protocol for imaging during surgical milestones and immediate surgeon feedback. The data variables collected included indication for surgery, type of procedure, visual acuity, ocular comorbidities, details regarding surgical maneuvers/techniques (eg, instrument type and surgical approach), type of OCT images obtained during surgery, and adverse events. Although scheduled study visits were completed following the first postoperative visit, institutional review board approval includes an additional 2-year period of postoperative review of clinical variables, imaging outcomes, and clinical outcomes.

The DISCOVER study includes 3 microscope-integrated OCT prototypes: the RESCAN 700, the Biop igen integrated prototype, and an integrated prototype internally developed at the Cole Eye Institute (Cleveland Clinic). Our report will focus on the RESCAN 700 results during year 1 (ie, March 2014-February 2015). The imaging protocol directed surgeons to obtain imaging during and/or after surgical milestones, as determined by the operating surgeon. The RESCAN 700 system includes a microscope-integrated OCT system, as previously described. Imaging data were reviewed by the surgeon intraoperatively and reviewed independently postoperatively. Surgeons visualized the OCT data stream through the oculars using the heads-up display or an external display monitor, based on their preference. A research coordinator assisted with acquiring OCT images and collecting surgeon feedback and data.

Prespecified surgeon feedback questionnaires were completed for all cases focusing on several specific areas of interest related to the microscope-integrated system and surgical procedure, including the perceived value of iOCT to the procedure (eg, the effect on surgical decision making), the preferred ergonomics of the system (eg, heads-up display or review mode), and issues related to workflow (eg, interference with the case). In addition, in select prespecified procedures (eg, membrane peeling and lamellar keratoplasty), an additional feedback form was completed related to the value of iOCT for that specific procedure.

Results

Clinical Demographics

At 1 year of the DISCOVER study, a total of 227 eyes underwent imaging with the RESCAN 700 system (Table). Of the 227 patients, 121 (53%) were female and 106 (47%) were male. The mean age of the patients in the study was 62 years (range, 19-91 years). Overall, the successful acquisition of iOCT images was obtained for 224 of 227 eyes (99% [95% CI, 98%-100%]). For 2 patients, iOCT images were not obtained owing to the surgeons’ decision not to image, and for 1 patient, iOCT images were not obtained owing to software malfunction.

At a Glance

- We describe the feasibility and effect on surgeon decision making of microscope-integrated intraoperative OCT (iOCT) during 227 ophthalmic surgical procedures from the DISCOVER study.
- During lamellar keratoplasty, iOCT often provided information to the surgeon, altering surgical decision making in 39% of cases.
- During membrane peeling, iOCT information altered surgical decision making in 19% of procedures.
- Advances in OCT-compatible instrumentation, iOCT-specific software, and surgeon guidance systems may facilitate integration into ophthalmic surgery.

Optical coherence tomography (OCT) has evolved from an experimental instrument to a critical clinical diagnostic modality and may have the potential to become a seamless surgical-guidance tool. Recent literature studies examining intraoperative OCT (iOCT) support the potential role for iOCT in ophthalmic surgery. These studies have examined the role for iOCT in multiple procedures and conditions, including epiretinal membranes, a macular hole, vitreomacular traction, retinal detachment repair, lamellar keratoplasty, and cataract surgery. The field of OCT-guided surgery remains a nascent field. Many early reports were retrospective with small sample sizes. The PIONEER (Prospective Intraoperative and Perioperative OCT-guided surgery) study, examining the utility of a microscope attached externally to an OCT device during ophthalmic surgery, provided, to our knowledge, the first large prospective data set to examine the feasibility and utility of iOCT.

However, the vast majority of previous studies focused on systems that were not integrated into the OCT and that did not allow for real-time feedback or heads-up surgeon interfaces. The future of iOCT will likely be founded in integrative technologies. New systems are now emerging that provide the surgeon with microscope-integrated technology and may enable rapid “real-time” feedback on the anatomic changes that occur during surgical manipulations. The key features of these systems with regard to maximizing outcomes and minimizing surgical disruption, as well as the specific procedures that would benefit from microscope-integrated iOCT, remain unclear.

To better understand the feasibility and utility of microscope-integrated iOCT, the DISCOVER (Determination of Feasibility of Intraoperative Spectral Domain Microscope Combined/Integrated OCT Visualization During En Face Retinal and Ophthalmic Surgery) study was initiated. Our report provides the 1-year results for the assessment of feasibility and utility (ie, effect on surgical decision making) of microscope-integrated iOCT for ophthalmic surgery for one of the prototypes in the DISCOVER study, the RESCAN 700 (Carl Zeiss Meditec AG).
Table. Baseline Demographic and Clinical Characteristics of the DISCOVER Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Anterior Segment Surgery (n = 91)</th>
<th>Posterior Segment Surgery (n = 136)</th>
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<tbody>
<tr>
<td>Eye</td>
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<td></td>
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<tr>
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<td>48 (53)</td>
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<tr>
<td>Left</td>
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<tr>
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Abbreviations: CE, cataract extraction; DALK, deep anterior lamellar keratoplasty; DISCOVER, Determination of Feasibility of Intraoperative Spectral Domain Microscope Combined/Integrated OCT Visualization During En Face Retinal and Ophthalmic Surgery; DMEK, Descemet membrane endothelial keratoplasty; DSAEK, Descemet stripping automated endothelial keratoplasty; IOL, intraocular lens; PPV, pars plana vitrectomy.

Anterior Segment iOCT Summary

In the anterior segment arm, 91 eyes were enrolled. The most common procedures included were Descemet stripping automated endothelial keratoplasty (DSAEK), for 43 patients (47%), and deep anterior lamellar keratoplasty, for 8 patients (9%) (Table). During DSAEK (Figure 1 and Video 1) and Descemet membrane endothelial keratoplasty (Figure 2), iOCT provided real-time feedback of trephination depth, allowing for visualization of instrument-tissue interaction and providing immediate information related to the residual stromal bed (Figure 2). Imaging with iOCT confirmed the location of intraocular implants, including glaucoma procedures (eg, relative tube-endothelial location) and corneal inlay procedures (eFigure 1 in the Supplement). During phacoemulsification, multiple steps of the procedure were visualized with iOCT, including capsulorrhexis, hydrosuction, groove depth, and intraocular lens placement (eFigure 2 in the Supplement).

Ergonomics and Value of Microscope-Integrated iOCT During Anterior Segment Surgery

For 82 of 91 patients (90% [95% CI, 84%-96%]), surgeons reported that microscope-integrated iOCT provided valuable feedback. According to surgeons in the study, 40 of 91 patients (44% [95% CI, 34%-54%]) underwent anterior segment surgery that was changed or modified owing to the iOCT findings. For example, during a DSAEK procedure, iOCT revealed subclinical graft detachment in the operating room, and that allowed the surgeon to intervene with rebubbling prior to stopping the procedure. During a corneal inlay procedure, wound depth was increased to optimize implant placement. During glaucoma surgical interventions, iOCT provided valuable data in select cases on optimal tube placement (eg, verifying sulcus placement, or relative tube-cornea location) (eFigure 1 in the Supplement).

For 63 of 91 patients (69% [95% CI, 60%-79%]), surgeons preferred real-time iOCT feedback; however, static feedback was more optimal for 21 of 91 patients (23% [95% CI, 14%-32%]). For 84 of 91 patients (92% [95% CI, 86%-97%]), the heads-up display system was preferred over viewing the OCT information on the video display. There were no reports of the iOCT system interfering with surgery. For 12 of 91 patients (13% [95% CI, 6%-20%]), contamination (eg, contaminated gloves or surgical instruments) occurred during anterior segment surgery. None of these cases of contamination resulted in contamination of the surgical field.

iOCT Guidance of Surgical Decision Making: Lamellar Keratoplasty

For 41 of 43 patients who underwent DSAEK, surgeon feedback was available. For 17 of 41 patients who underwent DSAEK (41% [95% CI, 26%-56%]), additional maneuvers were performed based on iOCT. For 26 of 41 patients who underwent DSAEK (63% [95% CI, 48%-78%]), the surgeons believed that the tissue was completely apposed following tissue placement and prior to iOCT. For the remaining 15 of 41 patients who underwent DSAEK (37% [95% CI, 22%-52%]), the surgeons did not believe the tissue was completely apposed. For 5 of 26 patients who underwent DSAEK (19% [95% CI, 4%-34%]) for whom the surgeon believed that the graft was fully apposed,
**iOCT revealed persistent interface fluid, facilitating additional maneuvers during the procedure.** For 7 of 15 patients (47% [95% CI, 22%-72%]) for whom the surgeon did not believe the tissue to be entirely apposed, iOCT revealed complete adherence of the graft, confirming apposition and minimizing surgical time and unnecessary manipulations.

For 3 of 8 patients who underwent deep anterior lamellar keratoplasty (38% [95% CI, 4%-72%]), the surgeons indicated that the achievement of the big bubble was noted clinically and confirmed on iOCT images. For 2 of the 5 remaining patients (40% [95% CI, 0%-83%]), iOCT revealed subclinical big bubbles, which guided additional maneuvers for dissection. For 3 of 8 patients who underwent deep anterior lamellar keratoplasty (38% [95% CI, 4%-72%]), iOCT affected the stromal resection and helped facilitate the identification of dissection depth.

**Posterior Segment iOCT Summary**

In the posterior segment arm, 136 eyes were enrolled. The most frequent indications for surgery were an epiretinal membrane (34 patients [25%]), a retinal detachment (28 patients [21%]), proliferative diabetic retinopathy (12 patients [9%]), a vitreous hemorrhage (12 patients [9%]), and a macular hole (10 patients [7%]) (Table). For patients with an epiretinal membrane or a macular hole, iOCT revealed residual membranes, allowed for visualization of tissue-instrument interactions, and confirmed completion of surgical objectives (Figure 3). Absolute shadowing was noted with real-time membrane peeling with metallic instruments (Figure 3). In select cases, true OCT-guided membrane peeling was performed when the standard view was poor owing to corneal edema both with real-time visualization of tissue-instrument interactions and with identification of residual membranes that were not otherwise visible. Intraoperative OCT was particularly valuable in complex cases of membrane peeling, such as myopic foveal schisis or vitreouschisis with multilaminar membranes (eFigure 3 in the Supplement and Video 2).

During posterior segment surgery to repair a retinal detachment, iOCT provided visualization of the completeness of...
Figure 2. Intraoperative Optical Coherence Tomography (iOCT) of Lamellar Keratoplasty

A. En face view of DMEK graft placement (left) and B-scan confirming optimal graft orientation (right).

B. En face view of DALK (left) and B-scan revealing striae and trephination depth (right).

C. En face view of DALK (left) and B-scan confirming dissection of Descemet membrane (right).

A. iOCT during Descemet membrane endothelial keratoplasty (DMEK) graft placement (2 arrowheads). B. iOCT during deep anterior lamellar keratoplasty (DALK) revealing corneal striae (arrowhead) and dissection depth (double arrow). C. iOCT during DALK showing bare Descemet membrane (arrowhead) following stromal removal.

The retina/retinal pigment epithelium apposition following perfluorocarbon liquid tamponade, as well as recurrence of subfoveal fluid after air-fluid exchange. Peripheral assessment with iOCT of retinal abnormalities facilitated discrimination between areas of subretinal fluid and areas of white without pressure (Figure 4). For patients with proliferative diabetic retinopathy, iOCT provided visualization of surgical planes and helped surgeons discriminate between retinal tissue and fibrovascular scars, as well as discriminate between traction retinal detachment and focal retinal traction (Figure 4 and Video 3). The visualization of optimal depth during a choroidal biopsy was also possible with iOCT (eFigure 4 in the Supplement and Video 4).

Ergonomics and Value of Microscope-Integrated iOCT During Posterior Segment Surgery

Overall, for 97 of 136 patients (71% [95% CI, 63%-79%]), surgeons reported that microscope-integrated iOCT provided valuable feedback. For 49 of 136 patients (36% [95% CI, 28%-44%]), surgeons preferred real-time iOCT feedback; however, static feedback was more optimal for 39 of 136 patients (29% [95% CI,
For 95 of 136 patients (70% [95% CI, 62%-78%]), the heads-up display system was preferred over viewing the OCT information on the video display. For 7 of 136 patients (5% [95% CI, 1%-9%]), surgeons reported that the iOCT system interfered with surgery, including software malfunctions, microscope failure, and an unresponsive foot pedal. No adverse events occurred secondary to these issues. For 22 of 136 patients (16% [95% CI, 10%-22%]), contamination occurred during surgery (eg, contaminated gloves or surgical instruments). None of these cases of contamination resulted in contamination of the surgical field.

**iOCT Guidance of Surgical Decision Making: Membrane Peeling**

In all cases of membrane peeling, indocyanine green was used prior to initial peeling of the preretinal membranes and the internal limiting membrane. For 41 of 67 patients (61% [95% CI, 49%-73%]), surgeons believed that membrane peeling was complete prior to iOCT. For 9 of those 41 patients (22% [95% CI, 9%-35%]), iOCT revealed residual occult membranes that the surgeon determined needed additional peeling. For 26 of 67 patients (39% [95% CI, 27%-51%]), the surgeons believed that membrane peeling was incomplete prior to iOCT. For 4 of 26 patients (15% [95% CI, 1%-29%]) for whom the surgeon believed that there was additional membrane peeling required, iOCT revealed to the surgeon that membrane peeling was entirely complete and that no further peeling was required. Ultimately, for 13 of 67 patients (19% [95% CI, 10%-28%]) who underwent membrane peeling, the iOCT findings were discordant with the surgeon’s impression and resulted in direct alterations to the surgical procedure.

**iOCT Guidance of Surgical Decision Making: Retinal Detachment**

Surgeons used iOCT for 24 patients who underwent surgery to repair a retinal detachment. For 17 of 24 patients (71% [53%-89%]), iOCT revealed persistent subretinal fluid under perfluorocarbon liquid. The types of iOCT feedback that affected surgical decision making included the identification of a macular hole under perfluorocarbon liquid (n = 1), the identification of residual membranes requiring peeling (n = 2), the identification of optimal placement for drainage based on subretinal fluid (n = 1), and the differentiation between choroidal hemorrhage and subretinal fluid (n = 1). Overall, for 5 of 24 patients (21% [95% CI, 5%-37%]), surgeons indicated that iOCT provided feedback that altered their decision making with regard to surgery.

**Adverse Events**

One serious adverse event (ie, myocardial infarction) occurred postoperatively during the course of the study following a vitrectomy. The most common postoperative day 1 adverse events in both groups included corneal epithelial defects (31 of 227 patients [14%]) and abnormal intraocular pressure values (29 of 227 patients [13%]). All 7 epithelial defects in the anterior segment arm of the study occurred in
eyes undergoing procedures in which epithelial defects would be expected (eg, corneal transplant or dermoid removal). In posterior segment cases, the majority of epithelial defects were in eyes with more complex preoperative diagnoses (15 of 24 eyes [63%]), including proliferative diabetic retinopathy and retinal detachment. Less frequent adverse events included vitreous hemorrhage (4 of 227 eyes [2%]), fibrin (3 of 227 eyes [1%]), and hyphema (2 of 227 eyes [1%]). One partial graft dislocation occurred in a patient who underwent DSAEK during the study.
Discussion

Gateway studies in real-time OCT technology are enabling the transformation in ophthalmic surgical care that could facilitate image-guided surgery in ways not previously feasible. Previous studies1,4-6,11,16,17 have found compelling results from the use of iOCT for many ophthalmic surgical conditions, including both anterior and posterior segment surgical procedures. This report from the DISCOVER study provides a large prospective examination of the feasibility and utility of microscope-integrated iOCT. The rapid advancements transpiring in the field of OCT are pushing the limits of what is achievable in image-guided surgery using real-time surgeon feedback. 2,6,11,14,18 Microscope-integrated iOCT offers immediate image guidance during surgery, allowing the surgeon to gauge procedural progression and completion. This live feedback may facilitate improvements in the surgeon’s judgment, technique, and knowledge during procedural processes.

Although this study represents the largest prospective clinical study to date on microscope-integrated iOCT, there are important limitations that must be acknowledged. This study was noncomparative and nonrandomized and was not masked. All surgeons knew that they would be using the iOCT system, and this may have affected their level of aggressiveness during the surgical procedure. In addition, our report has focused on the intraoperative and early postoperative implications of iOCT on a surgeon’s decision making. Data on long-term patient outcomes are currently being collected, and additional data will be helpful in the future to better understand the role played by iOCT. Our report also focuses on a single integrated iOCT system. One-year enrollment of patients for the other systems in the DISCOVER study is still under way, and the data are expected later this year. Currently, randomized masked controlled studies are also being planned to provide more definitive answers to the overall value of iOCT in patient outcomes.

In our report, iOCT was successfully performed 99% of time. During lamellar keratoplasty, iOCT was reported to alter the surgical procedure in 33% of cases. The most common reason for iOCT changing the approach to the surgical procedure was discordance between the surgeon’s perception of graft adherence and the objective iOCT information. Similarly, during posterior segment membrane peeling, in 19% of cases, iOCT provided new information to the surgeon that was not in agreement with surgeon’s impression. In these cases, the most common reason for altering a surgical procedure was related to the completeness of the peel. These percentages are similar to those in other reported studies. In the PIONEER study,1 surgeons reported that iOCT definitively changed the surgical approach in 9% of cases of lamellar keratoplasty. During retinal membrane peeling, iOCT changed the surgical approach in 13% of cases. 1 Similar to the DISCOVER study, these were cases in which the subjective interpretation of the en face view by the surgeon was discordant with the objective iOCT information.

Generally, surgeons reported that the immediate feedback related to changes in tissue anatomy was the most valuable (eg, completeness of membrane peel or graft adherence). True “real-time” visualization of surgical maneuvers was less commonly reported as critical. Select cases, such as viscodissection and choroidal biopsies, appeared to be particularly helpful with real-time feedback. One current major limitation of real-time visualization is the lack of OCT-compatible instrumentation. 11,13 Metallic instruments result in significant shadowing with suboptimal light scattering properties for OCT visualization. Improvement in OCT-compatible instrumentation may advance the field even further. 11,13 Although the systems in the DISCOVER study represent a significant iterative step forward related to integrative technologies, deficits remain in the technology for true seamless integration. Current deficits include those regarding automated OCT aiming/tracking, optimizing the heads-up display, instrument-depth tracking, and software analysis for iOCT alterations, in addition to OCT-compatible instrumentation. 11,19,20 Optimizing the heads-up display for maximizing surgeon feedback while minimizing distraction will be important. 19 Significant advances have been achieved with iOCT software analysis packages, including the assessment of interface fluid and the analysis of volumetric pathology for features such as a macular hole. 5,19,21

The definitive role for iOCT continues to emerge. Research from the PIONEER study has shown that minimizing interface fluid during DSAEK may reduce the level of postoperative interface haze. 17 In addition, the alterations in the outer retina (ellipsoid zone–retinal pigment epithelium height) may be important for understanding the architectural normalization following repair of a macular hole. 21 An exciting, potentially emerging role for iOCT is in targeted therapeutic delivery with image-guided tissue placement, and objective volumetric measurements may also play a critical role in the future in regenerative medicine and gene therapy.

The 1-year results of the RESCAN portion of the DISCOVER study provide additional evidence for the feasibility and utility of microscope-integrated iOCT. As additional barriers to seamless integration are cleared away, such as software analysis and automated tracking, the role for iOCT in ophthalmic surgery may continue to expand. Ongoing research in long-term patient outcomes related to the PIONEER study, 1 the DISCOVER study, and other ongoing studies will continue to add to our knowledge base and improve our understanding of how iOCT may add value to surgical procedures.

**Author Contributions:** Dr Ehlers had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Ehlers, Dupps, Srivastava. Acquisition, analysis, or interpretation of data: All authors.

**Disclosure:** Dr Ehlers, Dupps, Srivastava, have indicated they have no financial relationships relevant to this article to disclose.

**Drafting of the manuscript:** Ehlers.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Obtained funding:** Ehlers, Dupps, Srivastava.

**Administrative, technical, or material support:** Ehlers, Dupps, Kaiser, Srivastava.

**Study supervision:** Ehlers, Goshe, Srivastava.
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REFERENCES