Published in final edited form as:

Ophthalmic Surg Lasers Imaging Retina. 2017 March 01; 48(3): 216–222. doi: 10.3928/23258160-20170301-04.

Microscope-integrated OCT Feasibility and Utility with the EnFocus System in the DISCOVER Study

Anne Runkle^{1,2}, Sunil K. Srivastava^{1,2}, and Justis P. Ehlers^{1,2}

¹Ophthalmic Imaging Center, Cleveland Clinic, Cleveland, OH

²Cole Eye Institute, Cleveland Clinic, Cleveland, OH

Abstract

Purpose—To evaluate the feasibility and utility of a novel microscope-integrated intraoperative OCT system.

Methods—The DISCOVER study is an investigational device study evaluating microscope-integrated intraoperative OCT systems for ophthalmic surgery. This report focuses on subjects imaged with the Bioptigen EnFocus prototype system. OCT was performed at surgeon-directed milestones. Surgeons completed a questionnaire after each case to evaluate the impact of OCT on intraoperative management.

Results—Fifty eyes underwent imaging with the EnFocus system. Successful imaging was obtained in 46 of 50 eyes (92%). In eight cases (16%), surgical management was changed based on intraoperative OCT findings. In membrane peeling procedures, intraoperative OCT findings were discordant from the surgeon's initial impression in 7 of 20 cases (35%).

Conclusion—This study demonstrates the feasibility of microscope-integrated intraoperative OCT using the Bioptigen EnFocus system. Intraoperative OCT may provide surgeons with additional information that may influence surgical decision-making.

Keywords

intraoperative OCT; iOCT; intraoperative optical coherence tomography; microscope-integrated optical coherence tomography; retinal surgery

Introduction

Optical coherence tomography (OCT) has become invaluable in ophthalmology for both clinical and research purposes because it provides high-speed, high-resolution structural images of tissues that is superior to the *en face* visualization provided by conventional biomicroscopy.¹ Spectral domain OCT (SD-OCT) was initially limited to tabletop systems for use in the clinic, but over the past decade, several research groups have pushed the

Corresponding Author: Justis P. Ehlers, Cole Eye Institute, Cleveland Clinic Foundation, 9500 Euclid Ave/i32, Cleveland, OH 44195. ehlersj@ccf.org.

Financial Disclosures: AR: None; SKS: Bausch and Lomb (C, R); Bioptigen (P); Allergan (R); Synergetics (P); Leica (C), Carl Zeiss Meditec (C); JPE: Bioptigen (C, P), Thrombogenics (C, R), Synergetics (P), Genentech (R), Leica (C), Zeiss (C), Alcon (C);

boundaries of SD-OCT by developing systems for intraoperative use.²⁻¹² Multiple studies have since described the use of intraoperative OCT for imaging of patients undergoing procedures including full-thickness macular hole repair, epiretinal membrane peeling, vitreomacular traction release, lamellar keratoplasty, and phacoemulsification.¹³⁻¹⁵

There have been multiple approaches for adapting SD-OCT for intraoperative use, including hand-held³⁻⁶ and microscope-mounted⁸⁻¹⁰ systems. While these early devices allowed for intraoperative imaging, they require pausing the surgery to move the device into place before obtaining imaging, making real-time visualization of tissue-instrument interaction impossible. More recently, several groups have developed microscope-integrated SD-OCT systems, which adapt OCT systems into the microscope optical pathway, allowing real-time visualization of surgical maneuvers and minimizing delays required for intraoperative OCT imaging.¹⁶⁻²⁰ These early research prototype systems include a Leica microscope-integrated OCT system developed by Dr. Cynthia Toth¹⁶, a Cirrus microscope-integrated OCT system developed by Dr. Suzanne Binder⁷, the Cole Eye Institute prototype developed by our research group.^{9,21} As the field has progressed, three systems have obtained FDA clearance, including the RESCAN 700 (Zeiss, Oberkochen, Germany)^{19,21,22}, the EnFocus (Leica/Bioptigen, Research Triangle Park, NC)^{22,23}, and the Haag-Streit (Haag-Streit, Koeniz, Switzerland).^{13,21}

Both the RESCAN 700 and EnFocus systems were used in the DISCOVER (Determination of Feasibility of Intraoperative Spectral Domain Microscope Combined/Integrated OCT Visualization During En Face Retinal and Ophthalmic Surgery) study, a large-scale prospective study of intraoperative OCT imaging for both anterior and posterior segment ophthalmic surgery.^{22,23} The objective in this report is to provide the 1-year results for the microscope-integrated Leica/Bioptigen EnFocus prototype SD-OCT system.

Methods

The DISCOVER study is a single-site multi-surgeon investigational device study. Patients were recruited from the pool of all adult patients seen at the Cole Eye Institute. The DISCOVER study was approved by the Cleveland Clinic Institutional Review Board and written informed consent was obtained from all participants. For this report, all eyes that underwent surgery with the EnFocus prototype were included in this study.

Two unique Bioptigen EnFocus prototype intraoperative OCT systems were used in the DISCOVER study: a deep-range imaging system and an ultra-high resolution system (Supplemental Digital Content 1). The EnFocus 2300 Ultra-HD is built around the Bioptigen Envisu C2300 OCT engine, and includes a broadband superluminescent light source operating at 860 nm. It provides an imaging depth of 2.5 mm at an optical axial resolution of < 4 μ m. Images are acquired at 32,000 A-scans per second. EnFocus allows continuous visualization in a cross-hair aiming mode or acquisition of volumes of up to 1000 $\times$ 1000 lateral pixels, or an equivalent time series of B-scans. The EnFocus 4400 Ultra-Deep system introduces a new deep imaging spectrometer with an imaging depth of 11 mm in tissue at an optical axial resolution < 9 μ m for full anterior measurements and wide field retina imaging.

EnFocus 4400 images are acquired at 18,000 A-scans per second (Supplemental Digital Content 2 and 3).

Imaging was performed under sterile conditions. The EnFocus and microscope were utilized in both draped and undraped scenarios (Figure 1). The intraoperative imaging protocol directed surgeons to perform intraoperative OCT scanning during key surgical milestones, as determined by the operating surgeon. The obtained OCT images were reviewed by the surgeon intraoperatively on an external display monitor.

For each surgery, a research coordinator assisted with obtaining OCT images. Collected data variables included indication for surgery, procedure, preoperative visual acuity, ocular comorbidities, instrument type and surgical approach, and adverse events. A surgeon feedback data sheet was completed immediately following each surgery, and focused on the effect of the intraoperative OCT on surgical decision-making as well as integration of intraoperative OCT into the surgical workflow.

Results

At the 1-year time point, 50 eyes had undergone imaging with the Bioptigen EnFocus system (Table 1). 25 (50%) of these patients were male and 25 (50%) were female, with a mean patient age of 59 years (range: 22-90 years). The most common indications for surgery were proliferative diabetic retinopathy sequelae (e.g., traction retinal detachment, vitreous hemorrhage; n=10), epiretinal membrane (n=8), retinal detachment (n=7), and full-thickness macular hole (n=6). Twenty-two of the 50 cases (44%) were combined anterior and posterior segment surgeries, while the remaining 28 cases (56%) were posterior segment only.

Intraoperative OCT images were successfully obtained for 46 of 50 eyes (92%). For 15 of 50 patients (30%), surgeons reported that the intraoperative OCT provided valuable feedback. For patients undergoing membrane peeling, intraoperative OCT was able to identify residual membranes and confirm peel completion (Figure 2). During an IOL repositioning procedure with significant corneal edema, intraoperative OCT confirmed optimal placement of the IOL given the limited view through the cornea. In another example, intraoperative OCT confirmed the presence an underlying macular hole following vitreous hemorrhage removal (Figure 3). In 8 of the 50 cases (16%), the surgical management was changed based on intraoperative OCT findings, such as internal limiting membrane peeling/tamponade choice when a macular hole was identified.

Intraoperative OCT Guidance of Surgical Decision Making: Membrane Peeling

Membrane peeling was performed in 20 of 50 eyes (40%). In 14 of these 20 cases, surgeons believed that the membrane peeling was complete prior to intraoperative OCT. In 4 of these 14 cases (29%), intraoperative OCT imaging revealed residual membrane that needed additional peeling. In 3 of the 20 cases, surgeons believed the membrane peeling was incomplete prior to intraoperative OCT imaging. In all 3 of these cases, intraoperative OCT revealed that membrane peeling was complete and no further peeling was required. There were 3 cases where membrane peeling was indeterminate prior to OCT imaging. In total, intraoperative OCT findings were discordant from the surgeon's initial impression in 7 of 20

cases (35%), resulting in alterations to the surgical procedure. Surgeons stated that the intraoperative OCT provided valuable information in 11 of 20 (55%) of membrane peeling cases.

In 5 of 50 cases (10%), surgeons reported that intraoperative OCT interfered with some portion of the procedure. In each of these cases, the length of the surgery was extended or the surgeon was unable to obtain intraoperative OCT images. In two of the five cases, images were initially not obtained due to difficulty centering the aiming beam, but were eventually obtained successfully. In two other cases, software errors led to an inability to capture intraoperative OCT images. In one final case, there was a delay due to software malfunction, but intraoperative OCT images were ultimately successfully obtained.

Adverse Events

No adverse events were reported intraoperatively, and no serious adverse events were reported postoperatively. The most common adverse events at the first postoperative day examination were epithelial defects (16%), increased intraocular pressure (14%), and decreased intraocular pressure (6%). These were attributed to the surgical procedure.

Discussion

In this study, we report the 1-year results of the Bioptigen microscope-integrated SD-OCT unit to obtain pre-incision and intraoperative images of patients undergoing anterior and posterior segment surgery. Intraoperative OCT was feasible in the vast majority (92%) of cases. Surgeons reported that intraoperative OCT was most useful for immediate feedback on tissue anatomy (e.g., membrane peel completion, intraocular lens location). While a wide variety of procedures were included in the study, intraoperative OCT appeared to be most useful for membrane peeling procedures. In membrane peeling procedures, surgeons stated that intraoperative OCT images provided valuable information in 65% of cases and altered the surgeon's decision making in 35% of cases. The most common reason for altering the surgical procedure was discordance between the surgeon's subjective impression of peel completion and the objective intraoperative OCT findings. Given the smaller sample size in this report, these numbers are similar to previously reported studies on the impact of microscope-integrated intraoperative OCT on surgical-decision-making.²³

Overall, surgeons reported that intraoperative OCT provided valuable feedback in 15 cases (30%), and altered surgical decision-making in 8 cases (16%), which is consistent with posterior segment results from the PIONEER study.¹² This number is slightly lower than values reported by Pfau et al., who noted that intraoperative OCT findings altered surgical decision-making in 41.9% of posterior segment and combined surgical procedures.¹⁹ Of note, these changes in surgical decision-making have not been confirmed to translate into differences in outcomes. Additionally, the possibility exists that removal of OCT-identified occult membranes may not require removal.

Interestingly, the two different EnFocus systems were useful for different aspects of surgery. The EnFocus Ultra-Deep was useful for anterior segment procedures that benefitted from a wide-angle view and allowed for simultaneous cornea to posterior capsule visualization

(Figure 4, Supplemental Digital Content 2 and 3). The EnFocus Ultra-HD has a narrower field of view but higher resolution than the Ultra-Deep system, and appeared better-suited for retina visualization.

The main limitations of the DISCOVER study are that it is nonrandomized and nonmasked. In addition, because surgeons knew they were using the intraoperative OCT system, they may have been less aggressive during surgical procedures. It is also important to recognize that there is also potential bias in providing the surgeon with the survey questions following completion of the surgery rather than during surgery. Additionally, this report does not include long-term patient outcomes for patients who have undergone intraoperative OCT imaging as follow-up is still underway. A limitation of the Biotigen EnFocus prototype system is the lack of a heads-up display, which would allow surgeons to view the intraoperative OCT while manipulating the tissue (*e.g.*, while membrane-peeling). In addition, lack of surgeon directed foot-pedal control of the OCT scan beam makes rapid localization challenging without an assistant managing the machine. Lastly, the lack of video overlay of the OCT scanning beam over the surgical area of interest may delay guidance of the OCT to the area of interest. These are all updates that should be feasible in next generation systems.^{16,19,22} New features in the EnFocus FDA-cleared system may also address some of these shortcomings as the system utilized in the DISCOVER study was a prototype.

This report from the DISCOVER study demonstrates the feasibility and value of intraoperative OCT imaging utilizing the Biotigen EnFocus system. The results from the current study add to the growing body of literature supporting the use of intraoperative OCT as a technology, which may facilitate enhanced surgeon knowledge and decision-making. Further research is needed to clarify which surgical procedures show the most benefit from intraoperative OCT use, and to investigate the long-term patient outcomes of PIONEER and DISCOVER study patients. We predict that the results of these ongoing studies will help elucidate the role and clinical impact of intraoperative OCT, and clarify the ideal imaging system for intraoperative OCT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial Support: NIH/NEI K23-EY022947-01A1 (**JPE**); Ohio Department of Development TECH-13-059 (**JPE, SKS**); Research to Prevent Blindness (**Cole Eye Institutional**)

References

1. Sakata LM, Deleon-Ortega J, Sakata V, Girkin CA. Optical coherence tomography of the retina and optic nerve - a review. *Clin Experiment Ophthalmol*. 2009; 37(1):90–99. [PubMed: 19338607]
2. Hahn P, Migacz J, O'Connell R, Maldonado RS, Izatt JA, Toth CA. The use of optical coherence tomography in intraoperative ophthalmic imaging. *Ophthalmic Surg Lasers Imaging*. 2011; 42(Suppl):S85–94. [PubMed: 21790116]

3. Dayani PN, Maldonado R, Farsiu S, Toth CA. Intraoperative use of handheld spectral domain optical coherence tomography imaging in macular surgery. *Retina*. 2009; 29(10):1457–1468. [PubMed: 19823107]
4. Hahn P, Migacz J, O'Donnell R, et al. Preclinical evaluation and intraoperative human retinal imaging with a high-resolution microscope-integrated spectral domain optical coherence tomography device. *Retina*. 2013; 33(7):1328–1337. [PubMed: 23538579]
5. Chavala SH, Farsiu S, Maldonado R, Wallace DK, Freedman SF, Toth CA. Insights into advanced retinopathy of prematurity using handheld spectral domain optical coherence tomography imaging. *Ophthalmology*. 2009; 116(12):2448–2456. [PubMed: 19766317]
6. Scott AW, Farsiu S, Enyedi LB, Wallace DK, Toth CA. Imaging the infant retina with a hand-held spectral-domain optical coherence tomography device. *Am J Ophthalmol*. 2009; 147(2):364–373.e362. [PubMed: 18848317]
7. Binder S, Falkner-Radler CI, Hauger C, Matz H, Glittenberg C. Feasibility of intrasurgical spectral-domain optical coherence tomography. *Retina*. 2011; 31(7):1332–1336. [PubMed: 21273942]
8. Binder S, Falkner-Radler C, Hauger C, Matz H, Glittenberg C. Clinical applications of intrasurgical SD-optical coherence tomography. *Investigative Ophthalmology & Visual Science*. 2010; 51:268.
9. Tao YK, Ehlers JP, Toth CA, Izatt JA. Intraoperative spectral domain optical coherence tomography for vitreoretinal surgery. *Opt Lett*. 2010; 35(20):3315–3317. [PubMed: 20967051]
10. Ehlers JP, Tao YK, Farsiu S, Maldonado R, Izatt JA, Toth CA. Visualization of real-time intraoperative maneuvers with a microscope-mounted spectral domain optical coherence tomography system. *Retina*. 2013; 33(1):232–236. [PubMed: 23190928]
11. Steven P, Le Blanc C, Velten K, et al. Optimizing descemet membrane endothelial keratoplasty using intraoperative optical coherence tomography. *JAMA Ophthalmol*. 2013; 131(9):1135–1142. [PubMed: 23827946]
12. Ehlers JP, Dupps WJ, Kaiser PK, et al. The Prospective Intraoperative and Perioperative Ophthalmic ImagiNg with Optical CoherEncE TomogRaphy (PIONEER) Study: 2-year results. *Am J Ophthalmol*. 2014; 158(5):999–1007. [PubMed: 25077834]
13. Ehlers JP, Tao YK, Srivastava SK. The value of intraoperative optical coherence tomography imaging in vitreoretinal surgery. *Curr Opin Ophthalmol*. 2014; 25(3):221–227. [PubMed: 24614147]
14. Ehlers JP, Tam T, Kaiser PK, Martin DF, Smith GM, Srivastava SK. Utility of intraoperative optical coherence tomography during vitrectomy surgery for vitreomacular traction syndrome. *Retina*. 2014; 34(7):1341–1346. [PubMed: 24667571]
15. Ehlers JP, Kernstine K, Farsiu S, Sarin N, Maldonado R, Toth CA. Analysis of pars plana vitrectomy for optic pit-related maculopathy with intraoperative optical coherence tomography: a possible connection with the vitreous cavity. *Arch Ophthalmol*. 2011; 129(11):1483–1486. [PubMed: 22084218]
16. Ehlers JP, Tao YK, Farsiu S, Maldonado R, Izatt JA, Toth CA. Integration of a spectral domain optical coherence tomography system into a surgical microscope for intraoperative imaging. *Invest Ophthalmol Vis Sci*. 2011; 52(6):3153–3159. [PubMed: 21282565]
17. Vokes DE, Jackson R, Guo S, et al. Optical coherence tomography-enhanced microlaryngoscopy: preliminary report of a noncontact optical coherence tomography system integrated with a surgical microscope. *Ann Otol Rhinol Laryngol*. 2008; 117(7):538–547. [PubMed: 18700431]
18. Hahn P, Migacz J, O'Connell R, Izatt JA, Toth CA. Unprocessed real-time imaging of vitreoretinal surgical maneuvers using a microscope-integrated spectral-domain optical coherence tomography system. *Graefes Arch Clin Exp Ophthalmol*. 2013; 251(1):213–220. [PubMed: 22585009]
19. Pfau M, Michels S, Binder S, Becker MD. Clinical Experience With the First Commercially Available Intraoperative Optical Coherence Tomography System. *Ophthalmic Surg Lasers Imaging Retina*. 2015; 46(10):1001–1008. [PubMed: 26599241]
20. Tao YK, Srivastava SK, Ehlers JP. Microscope-integrated intraoperative OCT with electrically tunable focus and heads-up display for imaging of ophthalmic surgical maneuvers. *Biomed Opt Express*. 2014; 5(6):1877–1885. [PubMed: 24940546]
21. Ehlers JP, Srivastava SK, Feiler D, Noonan AI, Rollins AM, Tao YK. Integrative advances for OCT-guided ophthalmic surgery and intraoperative OCT: microscope integration, surgical

- instrumentation, and heads-up display surgeon feedback. PLoS One. 2014; 9(8):e105224. [PubMed: 25141340]
22. Ehlers JP, Kaiser PK, Srivastava SK. Intraoperative optical coherence tomography using the RESCAN 700: preliminary results from the DISCOVER study. Br J Ophthalmol. 2014; 98(10): 1329–1332. [PubMed: 24782469]
23. Ehlers JP, Goshe J, Dupps WJ, et al. Determination of feasibility and utility of microscope-integrated optical coherence tomography during ophthalmic surgery: the DISCOVER Study RESCAN Results. JAMA Ophthalmol. 2015; 133(10):1124–1132. [PubMed: 26226623]

Figure 1.
Photograph of the operating microscope and Bioptigen EnFocus intraoperative OCT system.
A. Draped system. **B.** Undraped system, showing EnFocus system (red arrow) and connecting cable (yellow arrow).

Figure 2.

Posterior segment intraoperative OCT in an epiretinal membrane case. **A.** Epiretinal membrane peel, thought to be complete, was shown by OCT to be incomplete just outside of the fovea. **B.** After further peeling, OCT demonstrated completion of peel at the fovea.

Figure 3.

Intraoperative OCT identified a full thickness macular hole in a patient with proliferative diabetic retinopathy, vitreous hemorrhage and a dense cataract. Preoperative OCT assessment was not possible due to media opacity.

Figure 4.

Wide-angle images obtained with the EnFocus Ultra-Deep system. **A.** Visualization of both the phaco tip (arrowhead) and the posterior capsule (white arrow) during phacoemulsification, immediately after lens fragment removal. **B.** Normal retina. **C.** Proliferative diabetic retinopathy with traction retinal detachment, with retina attached at the periphery (arrowhead) and central traction retinal detachment (white arrow).

Table 1
Baseline Demographics and Clinical Characteristics

Characteristic	Patients, No. (%)
Age (mean $\pm$ SD), years	59.2 $\pm$ 15.2
Gender, n (%)	
Male	25 (50%)
Female	25 (50%)
Eye	
Right	31 (62%)
Left	19 (38%)
Lens status	
Phakic	33 (66%)
Pseudohakic	16 (32%)
Aphakic	1 (2%)
Preoperative Diagnosis	
Proliferative diabetic retinopathy	10 (20%)
Epiretinal membrane	8 (16%)
Retinal detachment	7 (14%)
Full-thickness macular hole	6 (12%)
Panuveitis	4 (8%)
Vitreous hemorrhage	4 (8%)
Dislocated IOL	3 (6%)
Other	7 (14%)
Procedure	
PPV	43 (86%)
Phacoemulsion and IOL placement	22 (44%)
Membrane peeling	20 (40%)
Endolaser	17 (34%)
Scleral buckle	5 (10%)
Retisert	3 (6%)