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Intraoperative Optical Coherence Tomography

Samet Gulkas and Osman Cekic

Abstract

Recently, surgical instruments and imaging technology in ophthalmology have shown a great improvement. However, advances in the field of the operating microscope technology still remained unchanged with the various limitations for the surgeons. Invention of optical coherence tomography (OCT) led to a revolution in the diagnosis and monitoring of numerous anterior and posterior segment pathologies. Recently, OCT has been introduced into the operating room with an impact on the surgeons. In this chapter, we review the evolution of OCT for intraoperative use with its feasibility, surgical impacts, and limitations.

Keywords: intraoperative optical coherence tomography, microscope-integrated, anterior segment *i*OCT, posterior segment *i*OCT

1. Introduction

Optical coherence tomography (OCT) is a rapid, noninvasive, noncontact, and cross-sectional imaging method that produces images of ocular tissues. OCT uses reflected light to obtain the images from the different layers on the ocular tissues that produce different backscattered lights [1]. After using of spectral-domain OCT (SD-OCT) instead of time-domain OCT (TD-OCT), the images produced by OCT have become with higher resolution; thus, OCT has begun to provide more detailed information on ophthalmologic diagnoses [2]. Recent developments in ocular imaging technology have made the OCT a vital diagnostic tool in patient care. More recently, the availability of OCT during surgery has begun to be discussed. The introduction of OCT into the operating room (OR) called as intraoperative OCT (*i*OCT) has provided new insights into the surgical management during ophthalmic surgeries.

2. Intraoperative OCT

A number of researchers have examined the potential role of *i*OCT in various conditions and procedures, such as macular hole (MH), epiretinal membrane (ERM), retinal detachment surgery, and lamellar keratoplasty [3–6]. However, conventional clinical OCT devices are large and not portable; therefore, it would be difficult and impractical to transfer the conventional OCTs into OR. In addition, the supine position of the patient during a surgery and changes to surgical flow are other potential obstacles for image acquisition with good quality. All these hurdles forced researchers to produce a portable OCT device. Initial attempts with

intraoperative OCT indicated successful results in imaging of excised tumors, postmortem specimens, structural changes after laser surgery, and in vitro human arteries and nerves [7–10]. Early investigations with *i*OCT were based on time-domain technology. Nevertheless, these investigations resulted in suboptimal image quality due to lower sensitivity and speed than novel technologies of SD-OCT and swept-source OCT (SS-OCT). In recent years, to overcome suboptimal imaging during surgeries, researchers have discovered the microscope-integrated OCT devices (MIOCTs). So far, a short overview about the evolution of *i*OCT devices was introduced. The following section will discuss various *i*OCT systems and devices and their technologies.

2.1 Intraoperative OCT systems and devices

*i*OCT devices can be classified into two main categories: portable OCT during surgical pauses and microscope-integrated OCT (MIOCT). Subsequently, portable OCTs have three subgroups: handheld, external-mounted, and microscope-mounted. On the other hand, MIOCTs have two subgroups: live two-dimensional (2D) OCT imaging and live four-dimensional (4D) OCT imaging (**Tables 1 and 2**).

2.1.1 Portable OCT devices

Portable OCT devices were the beginning step for *i*OCT. There are two basic portable systems in the literature: the Bioptigen EnVisu (Bioptigen, Research Triangle Park, NC/Leica, Wetzlar, Germany) and the Optovue *i*Vue (Optovue, Fremont, CA, USA) [6, 11–13]. These devices can be used with the systems, including handheld, external-mounted, and microscope-mounted for image acquisition.

Handheld imaging was the first examples of the portable OCTs [11, 14]. This system has a compact handheld imaging probe connected over flexible optical fiber to a portable device. In spite of restrictions on image reproducibility and optimal aiming with the device, handheld imaging can present a good image quality. Moreover, unlike clinic tabletop OCT devices, handheld OCT has no requirement upright and cooperative patient situation. Nevertheless, the need to protect the sterile surgical field and the occurrence of motion artifacts due to instability are examples of several handicaps of handheld OCT. More importantly, the main disadvantage of handheld OCT is that it is limited to surgical pauses because of the need to remove the microscope from the patient during imaging. Unfortunately, it is impossible to obtain images of the structural changes that ensued from live tissue-instrument interactions during surgery.

System	OCT technology	Speed, resolution, wavelength	Primary visualization modes	Modes of operation	Commercial status
Optovue <i>i</i> Vue	Spectral domain	26k, 5 lm, 840 nm	B-scans, volumes, en face on external monitor	Mounted onto stabilizing arm	FDA approved
Bioptigen Envisu	Spectral domain	17–32k [†] , 3–5 [†] lm, 870 nm	B-scans, en face on external monitor	Handheld, mounted onto microscope	FDA approved

^aSpeed is listed in terms of A-scans/second; resolution refers to axial resolution; wavelength refers to the central wavelength of the source.

[†]Not specified in publications. Range provided by manufacturer.

Table 1.

System specifications and features of commercial HHOCT systems used in human retinal surgery to date.^a With the permission of Carrasco-Zevallos OM et al. under the license of CC licensing [23].

System	OCT technology	Speed, resolution, wavelength	Primary visualization modes	OCT acquisition and features	Commercial status
Haag-Streit surgical iOCT	Spectral domain	10k, 10 lm, 840 nm	Live B-scans on binocular, monoscopic HUD	OCT operator control, surgeon control of OCT display via foot pedal, optical zoom	FDA approved
Zeiss Rescan 700	Spectral domain	27k, 5.5 lm, 840 nm	Live B-scans on monocular, monoscopic HUD	OCT operator control with tracking, surgeon control of OCT scan location via foot pedal	FDA approved
Bioptigen EnFocus	Spectral domain	32k, 4 lm, 860 nm	Live B-scans, static en face on external monitor	OCT operator control, surgeon control via foot pedal	FDA approved

^aSpeed is listed in terms of A-scans/second; resolution refers to axial resolution; wavelength refers to the central wavelength of the source.

Table 2.
 System specifications and features of all commercial MIOCT systems used in human retinal surgery to date.^a
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Mounting systems for the portable OCT systems were developed to address most of the handheld imaging. These external mounts contribute more stability, yet these systems require a supplementary footprint and place in the operating room [4, 6]. The microscope holders allow the surgeon to attach the portable probe directly to the microscope body, thus providing more stability than handheld imaging. Microscope foot pedal controls make it possible to control the probe position with X-Y-Z foot pedals. This foot pedal control makes easier imaging with improved image repeatability [4].

Unfortunately, the main disadvantage of portable OCTs is that it is limited to surgical pauses because of the need to remove the microscope from the patient during imaging. In other words, it is impossible to obtain images of the structural changes that ensued from live tissue-instrument interactions during surgery.

2.1.2 Microscope-integrated OCT devices

A step-by-step initiative in the iOCT has been the integration of OCT into microscope optics called MIOCT. Leica (Leica, Wetzlar, Germany) and Zeiss (Carl Zeiss Meditec, Oberkochen, Germany) were the first examples of these systems. In the Zeiss adaptation, a modified Cirrus (Carl Zeiss Meditec) and a modified Visante (Carl Zeiss Meditec) OCT system integrated into Zeiss microscope optical path for the posterior and anterior segment imaging, respectively, were used [3, 15, 16]. These two systems allow surgeons for real-time imaging by visualizing the instrument-tissue interaction. On the other hand, these two systems bring with it new software requirements, the need for heads-up image acquisition, and the compatibility of OCT with the surgical instrument used during imaging. Additionally, surgical maneuvers during the surgery also require Z-axis stabilization and automated tracking system to improve image quality. After the investigation of first MIOCT systems, three commercial systems were identified. Zeiss Rescan 700 was defined as the first FDA-approved MIOCT system. This system is integrated into the Zeiss Lumera 700

microscope platform. Zeiss Rescan 700 was also integrated into the microscope foot pedal system to provide surgeon targeting, orientation control. More importantly, Zeiss Rescan 700 has the first MIOCT having Z-tracking system [17, 18]. The second FDA-approved MIOCT system was the Haag-Streit MIOCT system (Haag-Streit, Koeniz, Switzerland). This system consists of a side port using OPMedT (OPMedT, Lübeck, Germany) OCT system. This system has not only a microscope-mounted viewing but also a heads-up screen too [19]. Unlike Zeiss Rescan, the Haag-Streit Surgical *i*OCT has no control system with Z-tracking; differently, this system has an optical zoom. The third commercially available and FDA-approved MIOCT system was Bioptigen EnFocus *i*OCT system. This system can be adapted to both Leica and Zeiss microscopes. The system has a 4- μ m resolution and a different static en face on external monitor as a visualization mode. Dissimilarly, Bioptigen EnFocus system has an essential long-fiber that provides more flexibility to insert the OCT device and its computer inside the operating room (**Figure 1**) [20].

With regard to limitations of the MIOCT devices, while a volumetric data could be obtained, acquisition of the volume is slow, and volume analysis as well as visualization has necessitated comprehensive postprocessing. Another important limitation of MIOCT devices is an inefficient display of continuous instrument movement due to intraoperative real-time visualization limited by B-scans. In other words, intraocular instruments used during live surgery generally give rise to shadows on the underlying tissue in B-scan mode. This issue requires alignment of the surgical maneuvers with the B-scan to eliminate instrumental ghosting during surgery. Ehlers et al. [21] described and characterized this shadowing effect with ex vivo porcine eye surgeries. Regarding surgical instrument shading, some authors have suggested the idea of an automated instrument tracking system using a stereo camera pair [22].

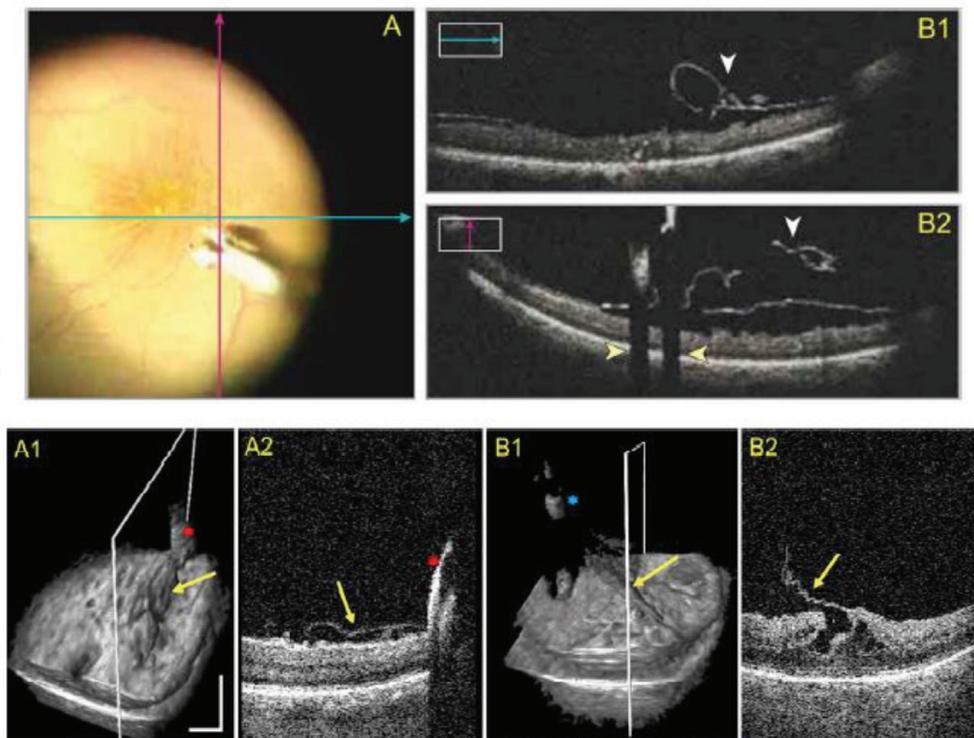


Figure 1. Live 2D MIOCT imaging of human retinal surgery with the commercially available Rescan 700 and a Cirrus HD-OCT system adapted to an operating microscope. (A) Frame captured with the camera that records the surgeon's view through the operating microscope. The orthogonal arrows correspond to the B-scan locations. (B) Horizontal (B1) and vertical (B2) B-scans acquired with the Rescan 700 during inner limiting membrane (ILM) peeling. The membrane edge (white arrowheads) is clearly visible in the B-scans along with "shadowing" (yellow arrowheads) from the intraocular forceps. With the permission of Carrasco-Zevallos OM et al. under the license of CC licensing [23].

All real-time MIOCTs described above were limited to B-scan due to involvement of SD-OCT system having slower A-scan rate. Carrasco-Zevallos et al. [23] were the first authors who described the volumetric *i*OCT imaging of live model eye surgery. They presented a custom ultrafast SS-OCT system operating at 100 kHz of A-scan rate. This speed was three to five times faster than previous MIOCT devices. A software called a special graphics-processing unit was simultaneously used to get, process, and render volumes. Later, the same authors developed a custom microscope-integrated heads-up display (HUD) unit for stereoscopic imaging of MIOCT volumes [24, 25]. SS-MIOCT and stereoscopic HUD together were called as 4D MIOCT. In 2015, 4D MIOCT was first demonstrated by Carrasco-Zevallos et al. [23] for imaging of human retinal surgery. The volumetric frame rate varied 3.3–10 volumes per second during the surgery. Through a special mode “stream saving,” OCT volumes were saved, and thus continuous volumetric recording could be acquired in the surgery. Visualization of the stereoscopic volumes by the HUD was enabled, and the surgeon could control the volume rendering via a foot pedal joystick.

Although 4D MIOCT devices have faster scan rate than 2D MIOCT due to faster A-scan rate, it requires faster A-scan rate as well as human flicker fusion rate (16 Hz) to attain optimal lateral resolution. In addition to that, instrumental shading effect is still one of the major limitations in 4D MIOCT as well in 2D MIOCT devices.

2.2 Clinical applications of intraoperative OCT

In this part of the chapter, we will provide information on the clinical use of *i*OCT. In terms of both anterior and posterior segments, there are numerous of clinical studies related to feasibility and real-time assessment of the surgical feedback during the anterior and posterior surgeries [4–6, 11, 13, 14, 16–18, 20]. The two most important prospective clinical studies are the PIONNER study and the DISCOVER study [4, 20]. In these studies, the portable microscope-mounted *i*OCT in the PIONNER study (n = 531) and the microscope-integrated *i*OCT in the DISCOVER study (n = 227) were evaluated. There are not only large-scale prospective but also numerous smaller clinical studies in the literature. In the section that follows, feasibility and efficacy of *i*OCT for the anterior segment applications will be argued.

2.2.1 Anterior segment

Intraoperative OCT has been used for various anterior segment surgeries involving penetrating and lamellar keratoplasty, cataract surgeries, and excisional biopsy procedures [4, 15, 16, 19, 22].

*i*OCT has been used for full-thickness and lamellar keratoplasty surgeries for decision-making. Particularly, *i*OCT can be very useful to evaluate in cases with extensive synechiae or iridocorneal scars. It may help to protect iris tissue from traumas during initial trephination [26]. Furthermore, the graft-host position can be estimated during surgery; thereby, it can help to construct proper graft-host relationship. In anterior lamellar keratoplasty, the presence of residual corneal opacities following microkeratome-assisted removal of anterior stromal layers can be detected, and their extensions may be easily confirmed by *i*OCT. Again, the thickness of residual stromal bed can be assessed, thus increasing the safety of operation [27]. As is known, it is very important to maintain an intact descemet membrane (DM) during deep anterior lamellar keratoplasty (DALK), and large bubble technique is widely used for this purpose. The *i*OCT helps to confirm the presence of large bubbles, detect subclinical large bubbles, and conduct additional dissections. In addition to these, the presence of any interface fluid can be determined with

the help of the *iOCT*, thus helping to determine the extra maneuvers that need to be done to ensure proper position of tissues to the end of the surgery. However, the instrumental shadowing effect may hinder the visualization of the underlying structures, thereby limiting the effective use of *iOCT* during intrastromal insertion of the needle. Therefore, surgical pause is necessary to evaluate the underlying tissues [17, 28, 29]. *iOCT* is a helpful intraoperative imaging method not only in full-thickness and lamellar but also in endothelial keratoplasty applications, e.g., descemet stripping automated endothelial keratoplasty (DSAEK) and descemet membrane endothelial keratoplasty (DMEK). Especially, in double-pass technique in DSAEK, the residual donor thickness following the first microkeratome passing can be easily determined with guiding *iOCT* to select of ideal blade size for the next microkeratome passing. This will minimize the chance of perforation of donor tissue by obtaining very thin donor lenticules [30]. Additionally, *iOCT* provides an advantage to identify and remove the descemet membrane in case of extreme edematous corneas. Furthermore, *iOCT* allows a continuous monitoring during the graft insertion and unfolding process. In DMEK, *iOCT* is a very convenient tool to provide faster graft orientation and position, especially in cases with edematous cornea [31]. In the DISCOVER study, it was reported that the surgeons required additional surgical maneuvers in 41% of the cases having DSAEK [18]. Similarly, in the PIONNER study, results showed that 19% of the cases in which surgeons believed the graft was completely apposed had still persistent fluid detected in the *iOCT*; hence, it would require more maneuvers and vice versa; in 47% of cases where the surgeon believed the graft to be partially apposed, there was complete apposition in *iOCT* imaging [4]. These two studies have also revealed that *iOCT* aids changes in dissection depth in 38–56% of cases [4, 20]. Briefly, it can be concluded that *iOCT* in keratoplasty procedures can minimize unnecessary manipulations and surgical time.

Recently, *iOCT* has been used in various stages of a cataract surgery. The wound structure, status of posterior capsule, and position of intraocular lens (IOL) can be easily assessed via *iOCT* during a cataract surgery [32]. In a case report, it was reported that MIOCT was a very feasible tool to evaluate the wound architecture, integrity of the posterior capsule, IOL position, and efficacy of stromal hydration. The authors suggested that *iOCT* could be helpful in real-time early detection of various complications of cataract surgery, thus allowing the surgeon to manage the complication immediately [33].

More recently, in taking biopsy and excisional procedures, such as retrocorneal fibrosis and pterygium excision, and evaluating intraoperative changes in corneal structure during excimer laser phototherapeutic keratectomy, feasibility of *iOCT* was assessed, and the results were promising [34, 35].

2.2.2 Posterior segment

Similar to the use of *iOCT* for anterior segment surgery, *iOCT* has a wide range of potentials for posterior segment surgery. Numerous vitreoretinal pathologies were described with *iOCT*, such as retinopathy of premature (ROP), proliferative diabetic retinopathy, macular hole, epiretinal membrane (ERM), retinal detachment, and myopic foveoschisis [4, 5, 20, 36–39]. The *iOCT* has provided new insights into the underlying pathophysiology for some of these conditions. PIONEER and DISCOVER studies provided valuable information about *iOCT* for posterior segment surgeons [4, 20]. We will discuss the results of these studies at the end of this section.

Chavala et al. [11] reported that they identified preretinal structures and retinoschisis with *iOCT* in case of ROP. They suggested that these new findings might

markedly affect the surgeons to make a decision resulting in various alterations during the operation. It is thought that *i*OCT may allow the surgeons to assess the extents of both horizontal and anteroposterior tractional structures in ROP cases; thus, the surgeons could carefully dissect or peel while sparing the other retinal structures. Additionally, *i*OCT is very useful detecting the flat neovascular fronds in ROP cases as well as other vascular retinopathies; thereby, this could prevent iatrogenic hemorrhages by determining the extent and location of the neovascular fronds during the surgery.

The *i*OCT helps the surgeon to determine the firmness of vitreomacular tractions; therefore, in case of foveal cyst, de-roofing risk would diminish, and inadvertent macular hole could be eliminated. Similarly, during an ERM and internal limiting membrane (ILM) peeling, the *i*OCT decreases the risk of inadvertent grasping of the retina while completing ERM/ILM peeling (**Figure 2**).

In a recent study, it was reported that a membrane peeling with the guidance of *i*OCT was enabled without the use of adjuvant dyes to identify of membrane edges [36]. Especially in a macular hole surgery, this advantage of *i*OCT allows visualization of the alterations in the macular hole architecture as well as in the outer retina [37, 40]. In addition, during a macular hole surgery, the surgeon may worry about inadvertent touching or tearing on nerve fiber layer. In such situation, the *i*OCT with real-time feedback can prevent inadvertent damage on nerve fiber layer.

One of the retinopathies in which the *i*OCT is used is myopic foveoschisis. As known, there are multiple layers of schisis in this retinopathy, and this involves vital dye staining to make certain that the whole cortical vitreous has been removed. However, the cases with myopic foveoschisis have a longer axial length, thus giving rise to poor dyeing. The *i*OCT can allow not only to better evaluate the ILM but also to prevent iatrogenic breaks by improving visualization in a myopic retina.

*i*OCT enables to provide more information in retinal detachment cases. In recent various studies, the *i*OCT revealed the presence of subclinical persistent subretinal fluid under perfluorocarbon tamponade in most of the cases undergoing retinal

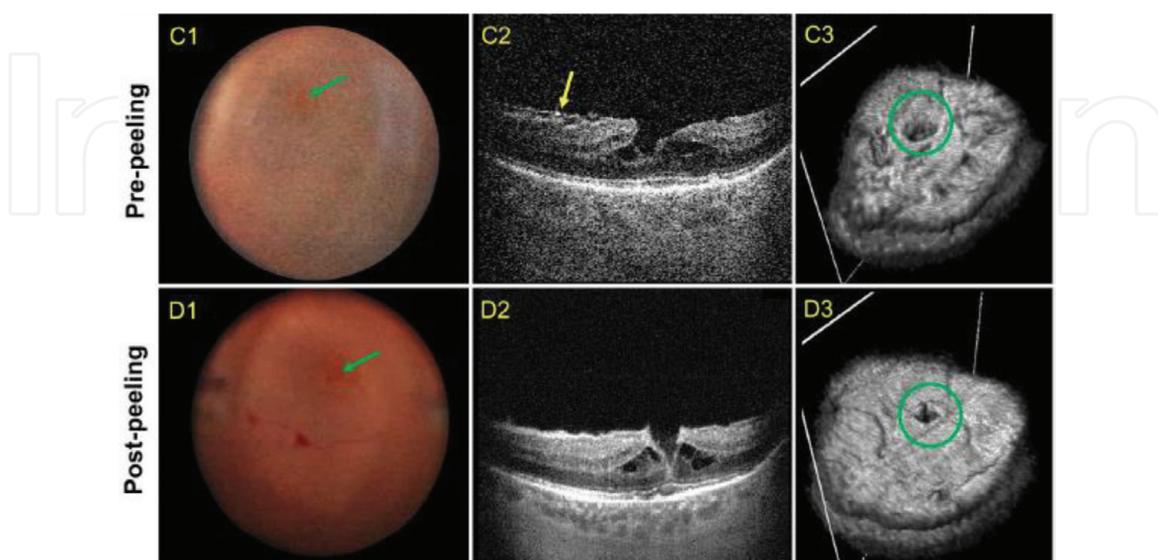


Figure 2. B-scan (C1) and volume (C2) acquired intraoperatively before epiretinal membrane (ERM) peeling with the reconfigured Cirrus HD-OCT system. B-scan (D1) and volume (D2) acquired after ERM peeling. The volumes required intensive postprocessing to render and were visualized postoperatively. The prepeeling volumes depict ERM and puckering of the retina, while the post-peeling volumes show a small residual part of ERM (**Figure 1**). With the permission of Carrasco-Zevallos OM et al. under the license of CC licensing [23].

detachment operation [4, 5, 20]. Furthermore, *i*OCT can help to detect proliferative vitreoretinopathy changes and border architecture of retinal tears.

In proliferative diabetic retinopathy, *i*OCT provides an enhanced imaging during delamination of membranes. For this reason, the *i*OCT facilitates the identification of the surgical plane, which permits membrane peeling in a safe manner. In addition to that, in the cases of dense vitreous hemorrhage, *i*OCT can help to assess intraoperatively the underlying macular pathology, such as intraretinal fluid, macular edema, or presence of a membrane, which may impact the surgeon in changing operation plan [38, 39].

Recently, in the 3-year outcome reports of the DISCOVER study, the use of *i*OCT for image-guided retinal biopsy and placement of Argus II implant was reported. It was demonstrated that *i*OCT facilitates insertion of the biopsy site and enabled confirming placement of the implant in optimal location [41, 42]. More recently, a few studies reported the use of *i*OCT verifying subretinal location of gene therapy and stem cells during the operation [43, 44].

Finally, the outcomes in posterior segment surgery in the PIONNER and DISCOVER studies showed that *i*OCT identified residual membranes in 13–22% of the cases whom the surgeon believed that membrane peeling was completed; conversely, in 15–40% of the cases, the surgeon still thought the presence of residual membrane, yet *i*OCT indicated that complete removal of the membrane had been performed [4, 20]. Additionally, *i*OCT provided addition of useful data concerning surgical anatomic features in 59.4% of the cases, and the information obtaining with *i*OCT impacted the surgery in 29.2% of the cases [20].

3. Conclusion

As known, in a very short time, conventional tabletop OCT has acquired its place in practice; subsequently, real-time intraoperative feedback with the *i*OCT appears to be a revolution in the OCT technology. Up to now, overall study reports related to *i*OCT, especially the PIONNER and DISCOVER study, have enhanced our understanding of *i*OCT technology and its unique advantages in surgical efficiency. *i*OCT may lead to refine and replace conventional surgical procedures with novel procedures, so that, with this technology, improved individual surgical management and patient care can be achieved. However, this technology has still a few limitations. The overall outcomes related to feasibility of *i*OCT need to be validated with additional prospective randomized trials.

Conflict of interest

There are no conflicts of interest.

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