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Advances in intraoperative optical coherence tomography for surgical guidance

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Abstract
Translation of optical coherence tomography (OCT) technologies for intraoperative visualization enables *in vivo* micron-resolution imaging of subsurface tissue structures and image-guided clinical decision-making. Over the last decade, intraoperative OCT has evolved from two-dimensional imaging using handheld probes to include biopsy-needles for minimally invasive deep-tissue imaging, surgical instrumentation using optical feedback for tremor dampening and stabilization, and stereomicroscope integrated systems that provide real-time three- and four-dimensional visualization of surgical maneuvers. In addition, several preliminary studies have demonstrated the feasibility and utility of combining intraoperative OCT imaging with novel image-processing and display methods to implement augmented/virtual reality and robotic surgical guidance platforms. While research and commercialization of these innovations have been largely driven by needs in ophthalmology, OCT is finding new clinical applications in surgical oncology and neurosurgery. In this paper, we review recent developments in intraoperative OCT and discuss current trends and future directions of the technology.

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Optical coherence tomography, Optical imaging, Surgical guidance, Ophthalmic imaging, Cancer margin imaging.

Abbreviations
OCT, Optical coherence tomography; FD-OCT, Fourier-domain OCT; PS-OCT, Polarization-sensitive OCT; FF-OCT, Full-field OCT; MEMS, Microelectromechanical systems; HUD, Heads-up display; ROI, Region-of-interest; FOV, Field-of-view; GPU, Graphics processing unit; MH, Macular hole; ERM, Epiretinal membrane; DALK, Deep anterior lamellar keratoplasty.

Introduction

Optical coherence tomography (OCT) enables exogenous contrast-free *in vivo* volumetric imaging of tissue microstructures [1]. When combined with latest-generation broadband light sources and detection schemes, OCT achieves 1–10 μm axial resolution at up to megahertz line-rates [2–11]. The high resolution and detection sensitivity of OCT have benefited clinical imaging in cardiology [12], gastroenterology [13], and oncology [14–16], and OCT imaging has become standard practice in ophthalmic clinical diagnostics [17,18]. Over the last decade, translation of OCT technologies to applications in surgical planning and guidance in ophthalmology [19–29] and other specialties [15,30–43] has been an active area of research and commercialization. Benefits of intraoperative OCT include verification that surgical goals have been achieved; enhanced contrast using optical or computational methods; improved axial resolution and visualization of subsurface features-of-interested as compared to surgical stereomicroscopy; image-guided surgical maneuvers, especially during minimally invasive and microsurgical procedures; and real-time feedback on interactions between surgical instruments and underlying tissue morphology.

Technological innovations, thus far, have primarily focused on addressing critical barriers to translating OCT into the surgical suite. Novel scanner designs for handheld imaging probes [19,21–23,44–47], surgical instrumentation [26,28,29], and microscope-integrated systems [20,24,27,48] have been driven by the need for optimal surgical ergonomics and optical performance, and compliance with electrical, optical, and patient-safety standards [49–52]. Concurrently, advances in parallel detection [17,18,53–56], novel high-speed swept laser sources [4–6], and graphical processing unit (GPU) based image processing [24,57–59] have led to significant increases in imaging speeds, which allow for denser spatiotemporal sampling and reduced motion-induced artifacts when imaging surgical dynamics. To achieve real-time feedback, novel image-processing algorithms and visualization hardware have enabled rendering and display of three- [57] and four-dimensional (several volumes-per-second) [24,58–60] data. Finally, OCT has been integrated with complementary technologies for precision guidance of micro-surgical maneuvers that include augmented reality (AR) overlays of volumetric OCT data onto the surgical microscope view [27] using heads-up display (HUD) [48,61] and commercial virtual reality (VR) headsets [62,63]; image-based instrument tracking [25], depth stabilization [64–66], and active tremor cancelation [67]; and integrated surgical tools for robotic-assisted surgery [68,69].

In this article, we provide a survey of the state-of-the-art and recent developments in intraoperative OCT technology and discuss their clinical potential and impact. Applications in ophthalmic surgery are emphasized because ophthalmology is by far the largest market for intraoperative OCT and drives much of the research and commercialization efforts in the field [70,71] as compared to other specialties, which are in early stages of technology development and clinical adoption (Table 1). In addition, overviews of intraoperative OCT systems and applications in surgical oncology and neurosurgery are also provided. The article concludes with a summary and discussion of the future directions of intraoperative OCT.

Ophthalmology

Perioperative imaging with hand-held and microscope-mounted probes

In 2001, Radhakrishnan et al. described the first handheld probe for intraoperative anterior segment OCT [44]. The system employed time-domain detection with a 1310 nm center wavelength light source, and the imaging optics were packaged into a handheld probe with a miniature single-axis galvanometer scanner that provided a lateral scan range of 5 mm at 8 frames-per-second (fps). *In vivo* imaging results showed visualization of structure and dynamics such as corneal epithelial and stromal layers, angle of the anterior chamber, and pupillary reflex due to a light stimulus. This study demonstrated the potential utility of OCT for guidance in refractive surgery.

Later generation systems employed Fourier-domain OCT (FD-OCT) detection, including both spectrometer and swept-source systems, which allowed for larger field-of-views (FOVs) and higher sampling densities. The speed advantage of FD-OCT has also enabled volumetric imaging [19,21] while use of MEMS scanners has substantially reduced the size of latest-generation handheld probes, which provide improved portability and ergonomics (Figure 1(A)) [45,47]. In a 2009 clinical study using a commercial handheld probe (Bioptigen, Inc.), Dayani et al. showed successful perioperative visualization of macular changes due to surgical intervention in eight patients undergoing vitrectomy [19]. Here, we use the term perioperative to define imaging systems that are not optically combined with conventional surgical microscopy and, thus, require pauses during surgery for intraoperative imaging. In a subsequent study, Ray et al. presented a custom mount that attached the Bioptigen handheld probe to an ophthalmic surgical microscope [21]. This enabled manual alignment of the OCT field using the microscope foot-pedal controls, which reduced motion artifacts as compared to handheld imaging and allowed aiming of the OCT FOV to image regions-of-interest (ROIs). In this study, OCT images from 24 patients undergoing macular hole (MH) or epiretinal membrane (ERM) surgery were analyzed. Quantitative measurement of MH geometry and retinal thickness provided novel insight into the anatomical changes in the retina resulting from macular surgery. These observational studies were the first to demonstrate the utility of OCT for verifying completion of ophthalmic surgical goals and to provide image-based feedback to benefit clinical decision-making during surgical cases. More recently, a two-year prospective clinical trial (PIONEER) reported on the feasibility and safety of OCT in 531 enrolled eyes over a wide range of surgeries including cataract, bullous keratopathy, corneal graft, keratoconus, ERM, MH, retinal detachment, proliferative diabetic retinopathy, and vitreous hemorrhage [23]. The authors used a microscope-mounted handheld OCT probe [21] and concluded that intraoperative imaging enhanced surgeon understanding of the underlying anatomy in more than 40% of the cases during lamellar keratoplasty and

Table 1

Overview of recent intraoperative OCT publications.

	Commercial	Research/Pre-clinical
Cardiology		[12]
Gastroenterology		[13]
Ophthalmology	Handheld probes: Bioptigen Inc. [19,21,23] OptoVue Inc. [22,72] Microscope-integrated: Carl Zeiss Meditec [9,64,76,77] Haag-Streit/OptoMedical Technlogies, GmbH [11,78]	Benchtop: [1,5,6,18,55] Handheld probes: [28,48,49,51] Microscope-integrated: [20,24,25,27,52,59–65,74,75,80–82] Intraocular probes: [26,28,29,66–69,84,85,90]
Breast Cancer		[14–16,31,32,34,36,37,39,41–43]
Neurosurgery		[30,33,35,40,91]