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New developments in optical coherence tomography

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Abstract

Purpose of review—Optical coherence tomography (OCT) has become the cornerstone technology for clinical ocular imaging in the past few years. The technology is still rapidly evolving with newly developed applications. This manuscript reviews recent innovative OCT applications for glaucoma diagnosis and management.

Recent findings—The improvements made in the technology have resulted in increased scanning speed, axial and transverse resolution, and more effective use of the OCT technology as a component of multimodal imaging tools. At the same time, the parallel evolution in novel algorithms makes it possible to efficiently analyze the increased volume of acquired data.

Summary—The innovative iterations of OCT technology have the potential to further improve the performance of the technology in evaluating ocular structural and functional characteristics and longitudinal changes in glaucoma.

Keywords

adaptive optics OCT; glaucoma; OCT angiography; polarization-sensitive OCT; swept-source OCT

INTRODUCTION

The progress made in ophthalmic imaging technologies in the past two decades has revolutionized clinical approaches and improved the efficiency of eye care. The ability to visualize ocular structures in vivo and in real time at a micron scale level and automatically quantify these structures provide clinicians important information in the process of clinical decisions. Among the imaging technologies, optical coherence tomography (OCT) has a

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leading role in eye care. This technology has been shown to provide reproducible quantification of ocular structures [1–3], allowing precise detection of structural damage, monitoring of disease progression, and assessment of the effectiveness of treatment in glaucoma and retinal pathologies.

Since the first publication of OCT in the early nineties [4], the technology has evolved substantially with enhancements both in imaging method and image analysis. The developmental path started with time-domain (TD)-OCT, followed by spectral-domain (SD)-OCT and other OCT techniques with higher scan acquisition speed [5,6] and higher axial and transverse resolution [7,8].

Optical coherence tomography provides high-resolution cross-sectional images of areas of interest using the principle of low-coherence interferometry. The current commercially available generation, SD-OCT, projects a near infrared broad-bandwidth light to the eye and the frequency information of the back reflected light is used to generate an image [9]. The image acquisition rate of the device ranges between 25 000 and 75 000 axial scans/second, enabling the acquisition of three-dimensional (3D) data from the area of interest [10,11]. OCT technology is still evolving, and at the time of this writing, OCT has been shown to be capable of scanning speeds of up to 20.8 million axial scans/second in nonophthalmic applications [12].

The purpose of this manuscript is to discuss new developments in OCT technology and its clinical application.

SWEPT-SOURCE OPTICAL COHERENCE TOMOGRAPHY

Swept-source (SS)-OCT is a form of Fourier domain OCT that employs a fast sweeping scan pattern through a broad bandwidth. Instead of a broad-bandwidth light source that is projected at once as in SD-OCT, the SS-OCT uses a single tunable laser that sweeps through different frequencies to rapidly cover the entire broad spectrum. The reflectance of the light from the eye is captured by a photodetector, which is much faster than the charge-coupled device camera used in SD-OCT technology [6,13,14]. This allows a faster scanning speed of up to 400 000 axial scans/second, and eliminates the typical depth dependent signal drop-off observed with the SD-OCT technology [15]. Increased scanning speed results in shorter scanning time and the reduction of image distortions caused by eye movement. This has been shown to improve scan quality and allow better visualization of fine structures [5,16]. In addition, many SS-OCT systems use a light source centered at an approximately 1050 nm wavelength, allowing better tissue penetration than SD-OCT, which typically uses a light source centered at approximately 840 nm. This allows visualization of structures such as the choroid [17,18,19[■]] and lamina cribrosa (Fig. 1) [20[■],21[■]], along with structures at the anterior chamber angle [22[■],23[■]].

Studies that used SS-OCT to examine the lamina cribrosa and the optic nerve head reported that full-thickness and focal lamina cribrosa defects corresponded with neuroretinal rim thinning, concurrent or previous disc hemorrhages, thinning of the circumpapillary retinal nerve fiber layer (RNFL) thickness, and visual field defects. The lamina cribrosa defects

were significantly associated with disc hemorrhages and longer axial lengths. SS-OCT can provide further detailed information on the microstructure of the lamina cribrosa. In a study that used an automated segmentation software for delineating the beams and pores of the lamina cribrosa, the authors evaluated the differences in the lamina cribrosa microstructure between healthy and glaucomatous eyes [24[■]]. The findings demonstrated an increase in beam thickness and a decrease in pore thickness with severe disease [25[■]]. The authors concluded that the changes reflected the remodeling of the eye as part of the glaucomatous process.

The deep signal penetration of SS-OCT has been used to measure the scleral thickness in highly myopic eyes with glaucoma [26[■]]. The authors identified a negative correlation between the scleral thickness and axial length in normal-tension glaucoma (NTG) eyes, and no significant correlation in primary open-angle glaucoma (POAG) eyes. This finding suggests that scleral thickness has a role in NTG, which might explain the difference between NTG and POAG pathogenesis.

The advantages of SS-OCT in anterior segment imaging have been demonstrated in a study that examined the anterior chamber angle topography [27]. The authors demonstrated reproducible identification and quantification of the scleral spur and Schwalbe's line. They reported trabecular meshwork width differences by quadrants, with the inferior trabecular meshwork being the widest compared to other quadrants. Moreover, another study that evaluated the angle in patients with angle closure glaucoma reported that SS-OCT outperforms gonioscopy in measuring the area and the degree of peripheral anterior synechia involvement [28[■]]. Anterior-segment SS-OCT is shown to detect a much higher prevalence of iridotrabecular contact in eyes with a shallow peripheral anterior chamber (AC) compared with ultrasound biomicroscopy [29[■]]. These findings indicate that SS-OCT scanning might be useful for angle closure glaucoma diagnosis and to determine the best surgical approach before laser or surgical procedures at the angle.

The only commercially available anterior-segment SS-OCT at the time of this writing (CASIA SS-1000, Tomey, Nagoya, Japan) provides built-in software that measures the iris–trabecular contact (ITC) index. A study of 108 healthy individuals and 32 patients with angle closure reported good diagnostic performance of the ITC index and moderate agreement on the measured extent of angle closure when compared with gonioscopy [30].

ADAPTIVE OPTICS OPTICAL COHERENCE TOMOGRAPHY

The axial resolution of OCT images depends on the coherence properties of the light source. Currently used light sources provide axial resolution at the range of 5 μm , which is sufficient to resolve the axial dimensions of most retinal cells. Meanwhile, the transverse resolution of an OCT image is limited by the spot size of the light beam when focused on the tissue. The laser beam is prone to optical aberrations when passing through different media in the eye, which limits the transverse resolution to the range of 20 μm . Adaptive optics was introduced to correct the optical aberrations, reduce the projected spot size, and improve the transverse resolution. Adaptive optics systems measure the monochromatic aberrations occurring in the eye and corrects them using a wave-front sensor and deformable mirrors. The improved

resolution provided by the adaptive optics system allows the acquisition of high-quality images, enabling visualization of fine details such as the retinal microvasculature, photoreceptors, lamina cribrosa (Fig. 2), and microstructures within the RNFL and ganglion cell layer.

In a study that examined the photoreceptors in glaucomatous eyes with an adaptive optics OCT (AO-OCT) system, the authors identified evidence of outer retinal changes along with the expected thinning of the inner retina in locations corresponding to the visual field (VF) loss [31]. This was the first in-vivo imaging study to demonstrate the involvement of the outer retina in glaucoma, exhibiting the importance of the highly detailed information provided by this system.

A recent study demonstrated the ability of AO-OCT to detect fine structures inside the lamina cribrosa [32]. An AO-SDOCT system with a 1050 nm wavelength light source was used for healthy, glaucoma suspects, and glaucomatous eyes. Utilizing an automated segmentation software [24[■]], the authors reported good repeatability of lamina cribrosa microstructure measurements. AO-OCT also allowed discerning the RNFL axonal bundles with higher detail than possible with other OCT systems [33].

POLARIZATION-SENSITIVE OPTICAL COHERENCE TOMOGRAPHY

Another modification of the OCT technology is the polarization-sensitive OCT (PS-OCT) that is based on the state of polarized light, which changes through various light–tissue interactions. This allows the differentiation of different tissues and generates images with tissue-specific contrast. The technology can distinguish ocular structures based on properties that alter polarization state, such as birefringence (sclera, RNFL), polarization-preservation (photoreceptors), and depolarization (RPE). Initially introduced in TD-OCT technology, polarization sensitivity can be incorporated into all known OCT systems, such as SD-OCT [34], SS-OCT [35], and AO-OCT [36].

Animal models of experimental glaucoma have shown that changes in the RNFL polarization precede thickness changes [37]. A new normalized RNFL reflectance index was tested in a recent study that used two custom-built PS-OCT systems and a commercial OCT system. The proposed index outperformed RNFL thickness in the ability to distinguish glaucoma suspects from healthy eyes with all utilized OCT devices [38[■]]. This study and others suggest that PS-OCT could be a very attractive candidate for early detection of glaucoma, but at the time of this writing further research is warranted.

A study of eyes that had undergone a trabeculectomy or an Ex-Press tube shunt placement examined bleb morphology using anterior-segment PS-OCT. The registered internal phase retardation was correlated with the functionality of the blebs, which is the most important factor in trabeculectomy success. The study showed that PS-OCT is able to noninvasively estimate bleb fibrosis by measuring birefringence in the filtrating blebs. This information may improve the monitoring of glaucoma-related surgical outcomes [39[■]].

Another recent study demonstrated the ability of PS-OCT to assess the birefringence properties of peripapillary sclera in the rat eye [40]. This in-vivo assessment enables the

detection of collagen orientation in the posterior sclera, which might be useful in the assessment of the biomechanical aspects of glaucoma pathogenesis.

A PS-OCT system with retinal tracking, which operates at up to 60 Hz, has been demonstrated to reduce motion artifacts in healthy and diseased eyes, improving the reliability of acquired images [41].

OPTICAL COHERENCE TOMOGRAPHY BLOOD FLOW

In addition to tissue structure examination, the OCT technique is capable of estimating functional characteristics of scanned tissue such as tissue blood flow using Doppler OCT (Fig. 3) and OCT angiography. The optical frequency of light shifts when it scatters from moving red blood cells. The amount of the shift is related to flow velocity, and this information provides a noncontrast method to visualize and quantify retinal blood flow. The in-vivo estimation of the retinal blood flow can provide insight on the pathogenesis of ocular diseases, such as diabetic retinopathy, macular degeneration, and glaucoma.

A study of retinal blood flow with Doppler OCT in normal and glaucoma patients demonstrated that in glaucomatous eyes with single-hemifield damage, the retinal blood flow was significantly reduced in the hemisphere corresponding with the visual field abnormality [42[■]]. In addition, reduced retinal blood flow was associated with thinner RNFL and ganglion cell complex in the corresponding abnormal hemisphere.

While Doppler OCT provides data on total retinal blood flow, it is not sensitive enough to examine the microcirculation with low-velocity blood flow. A study reported the use of OCT angiography to quantify human optic disc perfusion in glaucoma [43[■]]. The authors utilized a split-spectrum amplitude-decorrelation angiography algorithm to differentiate between static and dynamic tissues. They reported that normal discs had a denser microvascular network compared with the glaucomatous disc. They also introduced a new parameter, the optic disc flow index, which was significantly lower in glaucomatous eyes (wide range of disease severity). Another study that used the same image-processing analysis showed the superiority of this method in comparison with fluorescein angiography in imaging all layers of retinal vasculature without the need of injectable dye [44[■]]. These findings strongly demonstrate the potential of OCT in assessing retinal function by imaging in-vivo blood flow.

EMERGING INNOVATIONS

Optical coherence tomography technology is still rapidly evolving with innovative applications presented frequently. At the time of this writing, two interesting innovations have been recently introduced whose ophthalmic utility is currently under investigation. Photoacoustic ophthalmoscopy technology can detect the ultrasonic waves induced by the tissue when laser light is projected into it. These waves are the results of tissue-specific optical absorption properties. Combining this technology with OCT has been shown in animal models to generate strong signals from the hemoglobin in the blood vessels and the melanin in the RPE while all other retinal layers had very low optical absorption [45]. These

properties can enable in-vivo assessment of retinal blood volume, oxygen saturation, and pigment distribution in the RPE.

Using an innovative light source, a vertical-cavity surface emitting laser (VCSEL) technology that sweeps through the bandwidth, the OCT's properties have been shown to accomplish new imaging levels. This device can reach an ultrahigh imaging rate of up to 580 000 axial scans/second, an axial resolution of 9–12 μm in the tissue, and an imaging depth of up to 38 mm [46]. These exceptional properties allow, for the first time, imaging of the entire eyeball in a single scan. The clinical utility of this device is yet to be determined.

CONCLUSION

In this manuscript, we reviewed recent publications on the main directions of research dedicated to the development and improvement of OCT technology. The ongoing and future trends in the research are promising, and advances in OCT technology are likely to improve detection and monitoring of ocular pathologies.

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KEY POINTS

- Advancement in the OCT technology offers new venues for disease detection and a better understanding of the disease pathophysiology.
- SS-OCT employs a fast sweeping scan pattern through a broad bandwidth, allowing faster scanning speed.
- Adaptive optics coupled with OCT corrects for optical aberrations, thus enabling the acquisition of in-vivo images of the retinal microvasculature, photoreceptors, ganglion cells, and the lamina cribrosa at near the cellular level.
- Polarization-sensitive OCT provides cross-sectional tissue-specific contrast information using the polarization status of the scanned tissue.
- OCT can provide retinal function information by quantifying ocular blood flow.

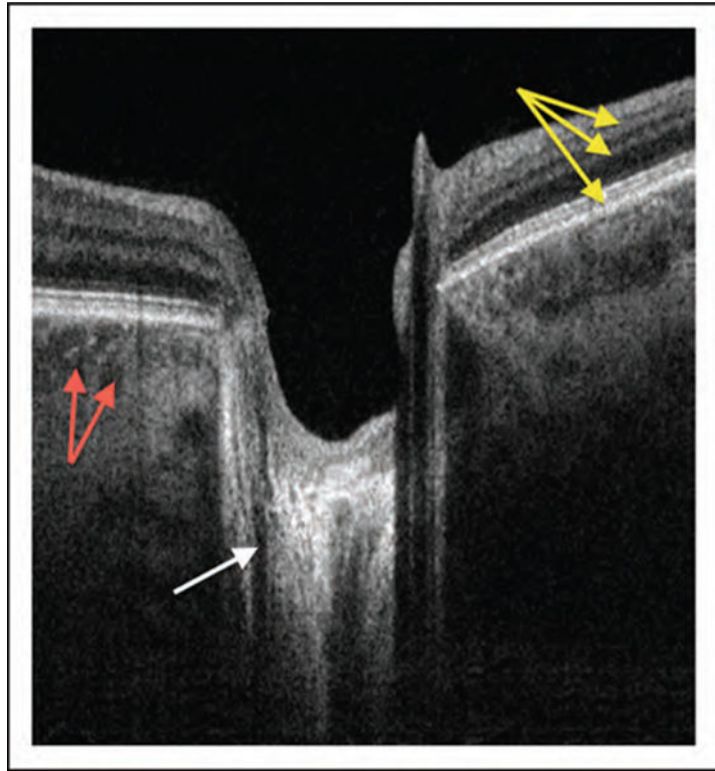


FIGURE 1. Swept-source OCT cross-section. The same scan captures retinal layers (yellow arrows), nerve fiber fascicles passing through lamina cribrosa (white arrow), and choroidal vessels (red arrows) because this technology is less prone to signal drop-off in comparison with other OCT iterations. OCT, optical coherence tomography.

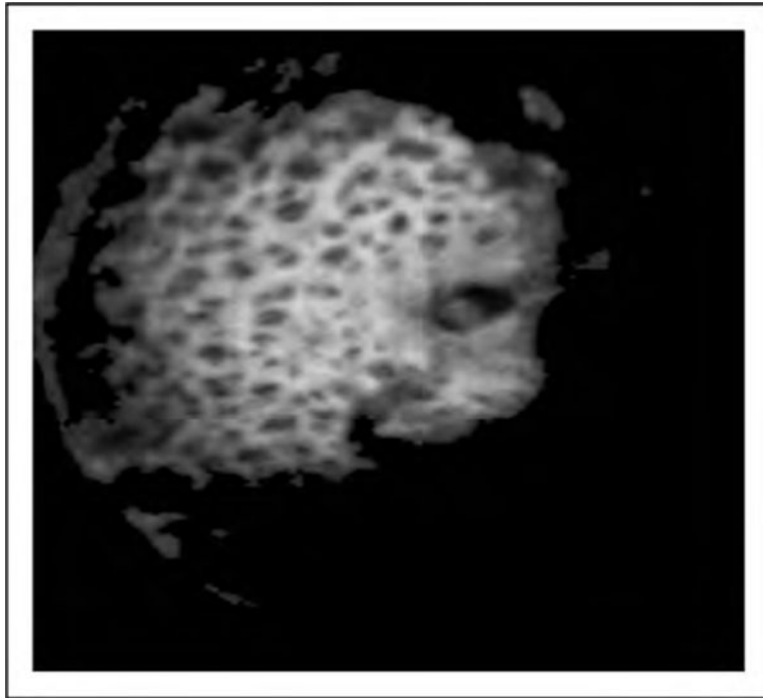


FIGURE 2. Adaptive optics OCT en-face image of lamina cribrosa that clearly demonstrates the mesh-like structure with pores (dark) and beams (white). OCT, optical coherence tomography.

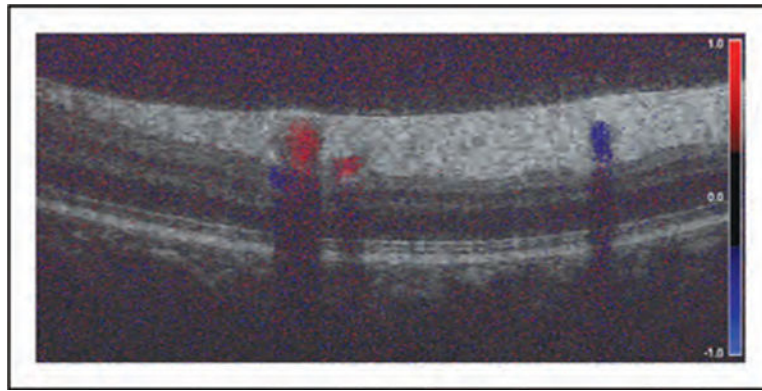


FIGURE 3. Doppler OCT cross-section of the retina. The velocity and direction of retinal blood flow is presented as color-coded filling of the vessels. Vertically elongated shadows are the result of the light beam blockage. OCT, optical coherence tomography.