Ultrahigh speed optical coherence tomography: New developments for ophthalmic imaging

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Optical coherence tomography (OCT) is an imaging technique providing depth-resolved, cross-sectional imaging of biological tissues with micrometer scale resolution. Recent advances in sensitivity and imaging speed have enabled the acquisition of three dimensional (3D) data sets. In ophthalmology, OCT has become an indispensable imaging tool for diagnosis of disease and monitoring therapy. While OCT technology is established in daily ophthalmic clinical use, research groups in the international scientific community are developing new OCT methods and pushing the limits of resolution and imaging speed. In this article, advances in the field of ultrahigh speed OCT and their applications to ophthalmic imaging are presented.

Introduction

Since its invention two decades ago, optical coherence tomography (OCT) has played an increasingly important role in biomedical imaging [1]. Soon after the first demonstration of imaging in vitro tissue, OCT emerged as an effective tool for imaging retinal tissue in the living human eye [2]. While OCT has found numerous applications in fundamental research, ophthalmic medical imaging - in particular retinal imaging - remains the major field of application [3, 4].

OCT is analogous to ultrasound imaging except that it measures the echo time delay and intensity of backscattered or backreflected light rather than sound. OCT can achieve axial image resolutions of 1
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The maximum imaging depth in non-transparent tissue is ~2 to 3 mm because of attenuation from light scattering. Although this depth is shallow when compared to other clinical imaging techniques, OCT can be integrated with catheters and endoscopes to perform internal body imaging and can achieve resolutions 10x to 100x finer than conventional ultrasound, magnetic resonance imaging (MRI), or computer tomography (CT). In ophthalmology, OCT imaging is noncontact and yields high resolution images which cannot be achieved by any other means.

How OCT works

Figure 1 shows a schematic of how OCT imaging works. The internal tissue structure is imaged noninvasively by measuring the echo delay time and intensity of light which is backreflected or backscattered from microstructural features in tissue at different depths. A broadband light source is used with an interferometric setup consisting of a beam splitter, a sample arm and a reference arm (Fig. 1A). At the beam splitter, the light source is split into two beams: One beam of light is directed onto the tissue or specimen to be imaged, and another beam is sent to a mirror to provide a reference reflection with a known time delay. After being backscattered from structures in the tissue and reflected from the reference mirror, the two beams interfere. The interference signal is recorded with a detector and the echo magnitude versus delay or axial depth scan information can be recovered (Fig. 1B). The signal vs. depth information is called an axial scan (A-scan). Two-dimensional imaging is accomplished by performing successive A-scan measurements at different transverse positions on the sample. Three-dimensional (3D) imaging can be performed by recording a stack of two-dimensional images.

OCT image acquisition speed

The first OCT systems were based on time domain detection and recorded only a few hundred axial scans per second, limiting acquisition to a few select cross sections within the few seconds before the patient blinked or moved their eye. Recent technological developments - most importantly, the introduction of Fourier domain detection methods - have dramatically increased sensitivity and image acquisition speed [5, 6, 7]. Most OCT systems today operate with spectral / Fourier domain detection, which uses an interferometer with a broadband light source, spectrometer and line scan camera to measure the interferometer output spectrum. Echo reflections from different depths produce different frequencies in the interference spectrum (similar to MR imaging) and each axial scan is computed using a Fourier transform of the interference spectrum. All echoes of light are detected simultaneously resulting in dramatic improvements in sensitivity (Fig. 2A) compared to time domain detection. State-of-the-art Fourier domain OCT systems in the clinic today operate at 20,000 - 50,000 axial scans per second [8, 9]. These high speeds enable acquisition of 3D data sets within only a few seconds.

Recent advances in light source and data acquisition technology have further increased imaging...
speed. The fastest research spectral / Fourier domain OCT instruments use new high speed CMOS line scan cameras and enable retinal imaging 5 to 10x faster than standard commercial instruments, at up to 300,000 axial scans per second [10]. These research OCT systems can also image the retina with ultrahigh resolution. The axial resolution depends on the bandwidth or wavelength spread of the light source: The broader the spectrum, the finer the axial resolution. Broadband light sources spanning a range of more than 100nm enable ultrahigh axial image resolutions of 2-3 μm in the retina, which can resolve fine retinal features such as capillaries or photoreceptors [11].

Fig. 2A: Methods for high speed OCT using Fourier domain detection. Spectral domain OCT. A broadband light source is used to illuminate the interferometer. The wavelength spectrum of the interference signal is recorded using a spectrometer located at the output of the interferometer. The interference spectrum is acquired, rescaled and Fourier transformed to compute the axial scan information from the interference spectrum.

Fig. 2B: Methods for high speed OCT using Fourier domain detection. Swept source OCT. A wavelength swept laser source is used as the input to the interferometer and a high speed detector measures a beat frequency at the interferometer output. The detector signal is rescaled and Fourier transformed to compute the axial scan information. Each laser sweep generates an axial scan.

Image averaging enhances quality

The high acquisition speeds of OCT systems can be used to improve image quality by image averaging: Multiple cross-sectional images (B-scans) can be rapidly acquired at the same location. After aligning these images to compensate axial shifts due to eye motion, an averaged image can be computed which has reduced noise, higher image contrast and a smoother appearance of tissue structures. It is important to point out that image averaging does not improve the axial resolution of the instrument since the resolution is determined by the light source bandwidth. However, since speckle noise produces discontinuities of fine retinal structures, reducing noise by image averaging improves the continuity of structures, yielding a significant improvement in image quality and generating the perception of improved resolution. Figure 3 shows results of image averaging of ultrahigh, 3 μm resolution OCT images recorded at 70,000 axial scans per second.

Fig. 3: Image averaging improves image quality. (A) Multiple OCT images are recorded at high repetition rate at the same location. Averaging these images enhances signal and reduces noise, improving image contrast and quality. (B) Result of image averaging of ultrahigh resolution OCT B-scan images in a macular hole patient. (C-E) Zoomed portions of image show details of the vitreoretinal interface, macular hole and photoreceptor layer.

Swept lasers set records in imaging speed

Another approach to Fourier domain detection uses a frequency swept light source (Fig. 2B). This method is known as swept-source / Fourier domain OCT [12, 13, 14]. In swept-source / Fourier domain OCT, a narrow bandwidth light source is used and the wavelength or frequency is rapidly swept across a broad spectral range. The interference signal is recorded as a function of time using a detector at the interferometer output. The axial scans are generated by Fourier transforming the detector signal. Each laser sweep generates an axial scan and the image acquisition rates are determined by the repetition rate of the laser sweep. Swept source swept-source OCT systems overcome some of the limitations of spectral / Fourier domain detection and support larger axial depth measurement ranges, because they are not limited by spectrometer resolutions. Thus far, the majority of commercial OCT systems and clinical studies have been performed using spectral / Fourier domain OCT rather than swept source OCT. However, record imaging speeds in the range of
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200,000 to 1,000,000 axial scans per second have been achieved using swept source OCT with special high speed swept lasers [15, 16].

![Image of ultrahigh speed swept source OCT imaging at 1050-nm wavelengths. (A) Fundus photo. (B) 3D rendering of volume showing the optic disk. (C) Averaged cross-section. (D-E) Doppler OCT imaging visualizes the retinal vasculature. (F-H) Wide field imaging of the retina at 200,000 axial scans per second. Fundus image generated from 3D OCT data and extracted B-scan images. (J-L) Anterior segment imaging. (J) 3D rendering. B-scan image of (K) chamber angle and (L) entire anterior chamber.](https://example.com/image)

**Imaging the anterior and posterior eye segment with deep penetration using 1050-nm OCT**

The depth of OCT imaging in scattering tissues, such as the choroid or anterior angle, is limited by attenuation from light scattering. Scattering from cataracts and ocular opacities can also reduce OCT signals. As an alternative to the 840-nm range usually used for retinal OCT imaging, imaging using the wavelength range around 1050 nm has recently been proposed [17]. Longer wavelengths near 1050 nm exist in a window of vitreous (water) absorption. The window only supports ~100 nm bandwidths, so axial image resolutions are limited to ~5 μm. However, studies have shown that long wavelength 1050nm OCT enables visualizing deep structures of the choroid and optic nerve and is less sensitive to scattering from ocular opacities compared with 840 nm wavelengths [17, 18, 19, 20]. Long wavelengths also have better image penetration for imaging structures in the anterior segment of the eye.

Imaging at 1050 nm can be performed using swept-source / Fourier domain OCT and is currently an active topic in OCT research. Examples of ultrahigh speed imaging with a swept source OCT instrument at 1050 nm are shown in Figure 4. Using swept laser sources, a long axial depth range can be achieved, which is necessary for imaging the anterior eye segment. Hence, imaging at 1050 nm wavelengths could enable both long depth range anterior as well as posterior segment imaging using a single, reconfigurable OCT device [21]. Ocular exposures can be higher at 1050 nm than 840 nm, enabling faster imaging speeds. Rather than performing multiple scans using different scan patterns to image the macula and optic disc, it should be possible to use a single scan pattern which captures wide field, three dimensional volumetric OCT data of the retina, which will simplify examination protocols for retinal imaging. Three dimensional OCT data contains comprehensive information on structure and pathology, allowing high definition cross sectional images with any position or orientation to be extracted and retinal layer thicknesses to be measured across a wide field. By extending structural OCT using functional methods such as Doppler OCT, the retinal vasculature can be visualized and blood flow can be measured quantitatively.

**Conclusion**

OCT has become a standard tool for ophthalmic imaging. Recent technological advances enable OCT imaging at ultrahigh speeds of hundreds of thousands of axial scans per second in research instruments. Commercial development of this new generation OCT technology will take time because of the complex engineering and regulatory issues involved, and because clinical studies are needed to assess its ultimate effectiveness. However, the next generation of OCT technology promises to provide the clinician with even further increases in imaging performance and versatility.

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