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State-of-the-art retinal optical coherence tomography

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Abstract

OCT functions as a type of optical biopsy, providing information on retinal pathology *in situ* and in real time, with resolutions approaching that of excisional biopsy and histopathology. The development of ultrabroad-bandwidth and tunable light sources, as well as high-speed Fourier detection techniques, has enabled a significant improvement in ophthalmic optical coherence tomography (OCT) imaging performance. Three-dimensional, ultrahigh-resolution OCT (UHR OCT) can provide information on intraretinal morphology that is not available from any other non-invasive diagnostic. High-speed imaging facilitates the acquisition of three-dimensional data sets (3D-OCT), thus enabling volumetric rendering and the generation of OCT fundus images that precisely and reproducibly register OCT images to fundus features. The development of broadband light sources emitting at new wavelengths, e.g., ~1050 nm, has enabled not only 3D-OCT imaging with enhanced choroidal visualization, but also reduced scattering losses and improved OCT performance in cataract patients. Adaptive optics using high-stroke, deformable mirror technology to correct higher order aberrations in the human eye, in combination with specially designed optics to compensate chromatic aberration along with three-dimensional UHR OCT, has recently enabled *in vivo* cellular-resolution retinal imaging. In addition, extensions of OCT have been developed to enhance image contrast and to enable non-invasive *depth-resolved* functional imaging of the retina, thus providing blood flow, spectroscopic, polarization-sensitive and physiological information. Functional OCT promises to enable the differentiation of retinal pathologies via localized, functional retinal response or metabolic properties. These advances promise to have a powerful impact on fundamental as well as clinical studies.

Contents

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1. Introduction

Optical coherence tomography (OCT) generates cross-sectional or three-dimensional images by measuring the echo time delay and magnitude of backscattered or back-reflected light. The earliest measurements of one-dimensional, axial information, which is analogous to ultrasound A-scans, were demonstrated in the mid-1980s (Fercher et al., 1988; Fercher and Roth, 1986; Fujimoto et al., 1986). OCT, the generation of cross-sectional or two-dimensional images, which is analogous to ultrasound B scans, was demonstrated in 1991 (Huang et al., 1991). The first *in vivo* OCT imaging studies of the human retina were performed in 1993 (Fercher et al., 1993; Swanson et al., 1993). Since that time, OCT has rapidly developed as a non-invasive, optical medical diagnostic imaging modality that enables *in vivo* cross-sectional visualization of the internal microstructure in biological systems (Fercher, 1996; Fujimoto, 2003; Fujimoto et al., 1995). OCT provides images of retinal structure that cannot be obtained by any other non-invasive diagnostic technique. Ocular media are essentially transparent; transmitting light with only minimal optical attenuation and scattering, and providing easy optical access to the retina. For these reasons, ophthalmic diagnosis is one of the most clinically developed OCT applications (Bowd et al., 2001, 2002; Brancato, 1999, Chauhan et al., 2000, Gaudric et al., 1999, Hee et al., 1995a–d, 1998; Massin et al., 2000; Muscat et al., 2002; Pons et al., 1999; Puliafito et al., 1995; Sanchez-Galeana et al., 2001; Sanchez-Tocino et al., 2002; Schuman et al., 1995, 1996, 2004, Spaide, 2002; Spaide et al., 2002).

The rapid development of OCT, the growing interest in this field, and its increasing impact in clinical medicine can also be evaluated by the tremendous growth in the number of publications and citations, from ~200 peer-reviewed journal publications in 2000, to more than 800 publications in 2006; thus resulting in a total of ~4000 publications to date. In 2000, OCT publications were cited 1000 times; whereas in 2006, more than 10,000 citations referred to OCT research. Furthermore, it is noteworthy that ~50 percent of all OCT publications (~2000) have been published in ophthalmic journals, thus demonstrating the powerful impact of OCT in this clinical speciality. Another 25 percent of OCT publications (~1000) have been published in optics journals, thus indicating numerous technical advances that have been accomplished since its invention. The clinical impact of OCT in ophthalmology is also demonstrated by the fact that a fourth generation of commercial instruments has recently been introduced and that, worldwide, there are a half-dozen companies commercializing this technology for ophthalmic diagnosis.

The important technological parameters of any (morphological) imaging modality that significantly influence its ultimate clinical and research utility are: axial (depth) image resolution, transverse resolution, measurement (data acquisition) time, detection sensitivity, image penetration depth in tissue and image contrast. Axial image resolution has been a significant parameter for ophthalmic imaging because of the layered organization of the retina. Ultrahigh axial image resolution enables visualization of the detailed architectural morphology of the retina on the level of individual retinal layers. In addition to aging and the pathological changes of intraocular media, which impose limits to any optical imaging modality in clinical practice, transverse image resolution traditionally has been limited by ocular aberrations. However, with the development of adaptive optics (AO), transverse resolutions are approaching levels necessary to resolve individual cells. Measurement or data acquisition time governs the number of transverse pixels in an OCT image, which is the number of OCT images or the size of a three-dimensional data set that can be acquired. Detection sensitivity determines the ease with which good-quality OCT images can be acquired, especially in situations where ocular opacities are present. Since detection sensitivity and imaging speed trade off with each other, improved sensitivity can be traded off with improved speed. This is an especially important issue for retinal imaging because incident light levels are limited by exposure safety considerations. Sufficient image depth penetration is an important issue in optical imaging modalities. Imaging depth is mainly determined by the interaction of light with specific endogenous (or exogenous) chromophores and optical properties of the tissue, and hence it strongly depends on the tissue being imaged and the imaging wavelengths. In addition to structural imaging, functional tissue information plays an increasingly important role as an adjunct diagnostic parameter or source of image contrast. Improved structural visualization of tissue morphology can be accomplished by several new techniques, and it promises to have an increasing impact on clinical applications. However, advances in techniques for functional imaging, and the ability to integrate structural and functional imaging, promise an even broader impact on clinical applications, since many early markers of disease involve functional as well as structural changes.

Since the new millennium, all important technological OCT parameters have been significantly improved, thereby enabling a substantial enhancement in imaging performance. Axial resolutions of only a few micrometers are now achievable due to advances in broad-bandwidth light source technology. Ultrahigh-resolution imaging is possible in a variety of new wavelength regimes with enhanced image contrast and tissue penetration. High-speed imaging with 25,000–50,000 A-scans/s is now routinely possible due to advances in spectral/Fourier domain detection and high-speed, line-scan charge-coupled device (CCD) camera technologies. Volumetric imaging with more than 300,000 A-scans/s was recently demonstrated using ultrahigh-speed, swept light sources and swept source/Fourier domain detection. Interfacing OCT with emerging technologies such as AO, which employ high-stroke deformable mirrors, recently enabled significant improvements in transverse OCT image resolution in the living human eye, and it was an important step toward cellular-resolution OCT retinal imaging. In addition, functional extensions of