

12 Optical Coherence Tomography in the Diagnosis of Retinal Vascular Disease

A. Walsh, S. Sadda

Core Messages
- OCT provides both cross-sectional visualization and clinically relevant quantitative measurements of ocular tissues
- OCT is an objective and quantitative method of standardizing disease monitoring both in clinical trials and in clinical practice
- Fluorescein angiography and OCT provide unique yet complementary information that may necessitate the use of both in the evaluation of patients with retinal vascular diseases
- OCT has greatly improved the evaluation and description of the vitreomacular interface
- OCT is useful in monitoring response to retinal vascular disease therapies and in guiding retreatment decisions
- Conventional OCT has substantial limitations both in hardware and in software
- Future OCT systems should be faster and provide more clinically relevant measurements

12.1 Overview

Retinal vascular diseases, in particular diabetic retinopathy and retinal venous occlusive disorders, are important causes of visual loss and blindness. Other important retinal vascular diseases which can affect visual function include arterial occlusive disease, parafoveal telangiectasis, Coat’s disease, vasculitides, macroaneurysms, and hypertensive retinopathy. Despite the various etiologies and underlying pathogenic processes, the mechanisms of visual loss are frequently similar among these diseases. One such common final pathway is the development of occlusions of the microcirculation (capillaries) with attendant retinal ischemia. The most frequent sequela, however, is a compromise in retinal vascular permeability leading to leakage and exudation with accumulation of fluid, lipid, and proteins within the retina [40] or in the subretinal space. Structural alterations are also a frequent outcome of retinal vascular disease. These changes include the development of cystoid spaces in the retina and vitreomacular traction.

The discovery and development of optical coherence tomography (OCT) has had a significant impact on the diagnosis and management of retinal vascular diseases, particularly in the identification of subtle structural alterations of the retina and in the detection and quantification of macular edema.

Although it was first described only 15 years ago, OCT is now positioned to play a major role in clinical trials and clinical practice for the foreseeable future. The application of OCT for the diagnosis and management of retinal vascular diseases is discussed in this chapter.

12.2 Evaluation

The diagnostic armamentarium available to retinal specialists in the early 1990s closely resembled technologies available to practitioners nearly 2 decades prior. This stagnant situation changed rapidly in the mid-1990s, however, with the near-simultaneous explosion of computer and digital imaging technologies. Digital imaging simplified fundus photography and fluorescein angiography by reducing patient wait times and the infrastructure that was needed to develop film negatives. Intranet- and internet-based integration of imaging devices located at different sites and made by different manufacturers enabled ophthalmologists to access data quickly and efficiently. At the same time, knowledge and understanding of computer technology became widespread, enabling a rapid sharing of technical clinical data.

Yet, during this explosion of computer and imaging technology, one thing remained almost unchanged – the means of interpreting and evaluating

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diagnostic imaging data. Time-consuming evaluations of color images for retinal diseases such as diabetic retinopathy were still based on subjective analyses by human graders. Angiographic assessments still required training and expertise, and were plagued by inconsistencies and intergrader variability [32, 38]. Few investigators took advantage of the newly available digital information from these images to perform advanced quantitative analyses.

During that time, Carl Zeiss Meditec, Inc. (Dublin, CA) was quietly developing a fledgling technology that would soon revolutionize the field – OCT. Introduction of this disruptive technology required the development of novel hardware and software as well as a new market in which to sell the instrument. Most importantly, Zeiss chose to make a radical departure from industry standards. Instead of simply providing a fundus image to be viewed and interpreted by the clinician, Zeiss chose to automate the extraction of quantitative information from OCT images. This was a dramatic departure from the industry norm, which only required that fundus images be provided for subjective evaluations, without measurements or automated assessments.

With slit-lamp biomicroscopy firmly established as the gold-standard clinical evaluation and angiography as the principal tool for further disease clarification, many clinicians in the mid 1990s were skeptical of this new technology. Soon, however, unique benefits of noninvasive cross-sectional imaging became apparent. For example, vitreomacular traction syndrome (VMT), which was previously clinically unapparent in many patients, was able to be visualized and diagnosed with confidence using OCT. Macular holes and cysts could also be visualized and monitored. Furthermore as intravitreal therapies for retinal diseases were introduced, OCT’s value in the quantification of retinal thickening and subretinal exudation became certain. The optimal integration of OCT data with other clinical findings to synthesize a clinical care plan is still an evolving subject.

### 12.2.1 Optical Coherence Tomography

**Essentials**
- Provides both cross-sectional visualization and clinically relevant quantitative measurements
- Based on low-coherence interferometry
- Measures reflectivity of tissue interfaces with axial resolution less than 10 μm
- Good reproducibility in patients with diabetes

A complete discussion of OCT is beyond the scope and purpose of this chapter. The reader is referred to several excellent texts on this topic [27, 30, 33, 34]. Briefly, OCT is based on the principle of low-coherence interferometry. Akin to B-scan ultrasonography, OCT uses differences in the reflection of light, instead of sound echoes, to render two-dimensional images (tomograms) of the retina. Various light sources, typically superluminescent diodes or lasers with very short pulses (i.e., femtosecond lasers), are used to generate broad bandwidth light. The depth or axial resolution of OCT is based on the bandwidth of these sources, and the lateral resolution is determined by the diameter of the focused probe beam.

The light is split into two different paths: a reference beam projected inside the instrument and a sample beam focused on the tissue of interest. In time domain OCT, differences in the time of flight for these two light paths are measured using a Michelson-type interferometer. In Fourier domain OCT, these differences are characterized with a spectrometer and Fourier-based mathematical calculations. Differences in the optical characteristics of ocular tissues result in the different reflectivity intensities that are measured by OCT.

A single point of light reflected off the retina forms an A-scan, which contains information about the axial location of these tissue interfaces. These single points of light can be laterally aligned to form B-scan images, which often use a false-color display to depict interface intensities: highly reflective interfaces are rendered in white and red, medium level reflections are shown as yellow and green, and features with low reflectivity are depicted in blue. OCT data can be viewed en face as a C-scan or in dense three-dimensional cubes (3D OCT) by capturing B-scans or C-scans in rapid succession. Whereas the axial resolution of clinical ophthalmic echography is limited to greater than 100 μm, differences less than 10 μm can be discerned with conventional OCT instruments. Newer instruments, potentially coupled with adaptive optics devices, can resolve structures that are separated by less than 2 μm in the axial direction [109].

Scan acquisition is painless for the subject, but requires cooperation and steady fixation. Due to inherent speed limitations in conventional time-domain OCT technology, a radial pattern of scan line capture is often used as a compromise between acquisition time and imaging density. Even with this compromise, time-domain OCT instruments require the subject to maintain steady fixation for many seconds at a time, which may be difficult for patients with macular diseases [15, 38]. Therefore, use of an external fixation light for the fellow eye has been