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The application of optical coherence tomography angiography in retinal diseases

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ABSTRACT

Optical coherence tomography angiography (OCTA) is a new, noninvasive imaging technique that generates real-time volumetric data on chorioretinal vasculature and its flow pattern. With the advent of high-speed optical coherence tomography, established *en face* chorioretinal segmentation, and efficient algorithms, OCTA generates images that resemble an angiogram. The principle of OCTA involves determining the change in backscattering between consecutive B-scans and then attributing the differences to the flow of erythrocytes through retinal blood vessels. OCTA has shown promise in the evaluation of common ophthalmologic diseases such as diabetic retinopathy, age-related macular degeneration, and retinal vascular occlusions. It quantifies vascular compromise reflecting the severity of diabetic retinopathy. OCTA detects the presence of choroidal neovascularization in exudative age-related macular degeneration and maps loss of choriocapillaris in nonexudative age-related macular degeneration. We describe principles of OCTA and findings in common and some uncommon retinal pathologies. Finally, we summarize its potential future applications. Its current limitations include a relatively small field of view, inability to show leakage, and a tendency for image artifacts. Further larger studies will define OCTAs utility in clinical settings and establish if the technology may offer its utility in decreasing morbidity through early detection and guide therapeutic interventions in retinal diseases.

1. OCTA—a novel technology

1.1. *Introduction*

Optical coherence tomography (OCT) is a noninvasive imaging technique, optically equivalent to ultrasound imaging; however, unlike ultrasound (which uses inaudible sound waves), it uses light waves to generate high-resolution cross-sectional images of the retina, that can be qualitatively and quantitatively evaluated.[39]

Recently, several OCT-based angiography methods were developed for 3-dimensional noninvasive vascular mapping

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at the microcirculation level.[121] Optical coherence tomography angiography (OCTA) is a new, noninvasive imaging technique that uses motion contrast imaging of high-resolution volumetric blood flow to generate angiographic images in a matter of seconds. The use of various software algorithms like split-spectrum amplitude decorrelation angiography (SSADA) improves the signal-to-noise ratio of flow detection and facilitates visualization of retinal vasculature.[57,59,60]

1.2. History and evolution of OCT

OCT has emerged as an important imaging modality in the evaluation and management of retinal disease. The noninvasive nature of the test and its ability to image intraocular structures in vivo with resolution approaching that of histological sections has made OCT particularly useful in the detection and quantification of macular and optic nerve head pathologies.[44,47,99,108,111] Since its introduction in the late 1990s for clinical application in the imaging of retinal disorders, OCT has shown major improvements in technology with increasing resolution of the images.

First reported in 1991, OCT is analogous to ultrasonic pulse-echo imaging, but instead of sound waves, it uses near-infrared light to produce cross-sectional or 3-dimensional images of the retina.[5,44,47,99,108,111,123,140] The images are generated through the measurement of magnitude and echo time delay of backscattered light from an optical beam across the retina. Because direct detection of light echoes is not possible owing to the high velocity of light, measurements are done correlating sample reflections from a reference mirror using a Michelson interferometer. One arm of the interferometer directs lights and collects the backscattered signal from the object of interest. This reflectivity profile contains information about the spatial dimensions and location of structures within the item of interest. A cross-sectional tomographic B-scan is achieved by laterally combining a series of A-scans. In time-domain OCT (TD-OCT), the depth information of the retina is collected as a function of time by moving the reference mirror. This physical forward or backward movement of mirror causes a time delay.

Conventional TD-OCT has several limitations. Because there is a time delay involved during the axial translation of the reference mirror, the number of A-scans acquired are limited, resulting in a B-scan with poor resolution. Another problem is the lack of registration, with poor point-to-point correlation between an OCT B-scan and the patient's fundus. A final critical limitation related to the slow speed of TD-OCT is poor sampling density. Large amount of data are interpolated by sampling only a fraction of the mapped area.

Within the past decade, a new generation of OCT technology known as "spectral-domain OCT" or "Fourier-domain OCT" has evolved. In spectral-domain OCT (SD-OCT), the reference mirror, in contrast, is stationary. The light spectrum from the interferometer is detected by a spectrometer. The interference spectrum data are then Fourier transformed to generate axial measurements of the retina.[92] The measurement of light echoes simultaneously allows high-speed scanning with scan rates 50–100 times faster than conventional TD-OCT. This results in a higher sampling of A-scans within B-scan (the axial resolution on SD-OCT is 4–7 microns compared with 10 microns on the TD-OCT).[5,123,140] Spectralis (Heidelberg Engineering, Vista, CA/Germany.), one of the commercially available SD-OCT, also incorporates the TruTrack technology, which significantly reduces image corruption due to motion artifacts and provides the opportunity to correlate quantitatively the same areas of retinal pathology at sequential time points (Fig. 1).

Lately, there have been several attempts to evaluate clinical applicability of swept-source OCT (SS-OCT).[91,143,146] The SS-OCT system uses a light source with a long wavelength-sweeping laser (1050 nm), yielding an 8-μm axial resolution and with an imaging speed of 100,000 A-scans/s, which is much faster than SD-OCT.[78] SS-OCT systems offer superior imaging because of their longer wavelength, deeper penetration, and lower dispersion. OCTA has recently been developed to study retinal and choroidal microvasculature noninvasively and has allowed examination of different retinal capillary plexuses, as well as the choriocapillaris plexus.[13]

1.3. Principles of OCTA

1.3.1. Basic concept

The basic principle of OCTA involves determining the change in backscattering between consecutive B-scans and then attributing the differences entirely to the flow of erythrocytes through retinal blood vessels. This has been accomplished through a number of methods, including Doppler OCT,[72,137,145] dual-beam scanning OCT,[77,151] phase based (e.g., phase-variance OCT),[64,65,109] and amplitude based (e.g., SSADA—see below).[59,79,87] Various algorithms[150] used in OCTA devices are as follows:

1. OCT-based optical microangiography (OMAG)
2. Split-spectrum amplitude decorrelation angiography (SSADA)
3. OCT angiography ratio analysis (OCTARA)
4. Speckle variance
5. Phase variance
6. Correlation mapping

Two ways to detect change in amplitude are as follows: (1) speckle (or intensity) decorrelation, which detects intensity changes in OCT structural images and (2) phase variance, which assesses changes in the phase of a light wave.[150] Furthermore, based on the signals, OCTA can be full spectrum (e.g., OMAG, OCTARA) or split spectrum (e.g., SSADA).[150] Regardless of algorithm used, OCTA calculates the differences between B-scans and rely on the assumption that all differences arise from blood flow and that the backscattering associated with retinal tissue outside of the blood vessels remains static (motion contrast).[86] OCT samples a discrete tissue volume and generates a numerical value based on the reflectivity of the volume. This numerical value corresponds to a voxel (This is a portmanteau of "volume" and "pixel") in the image displayed. Each voxel is an estimation of the reflective properties of a small volume of tissue. OCTA repeatedly scans the same discrete tissue volume and detects changes in the reflectivity signal. If the changes are above a