VIEWPOINT

A Promising Future for Optical Coherence Tomography Angiography

Aaron Nagiel, MD, PhD
Retinal Disorders and Ophthalmic Genetics Division, Stein Eye Institute, David Geffen School of Medicine at University of California, Los Angeles.

SriniVas R. Sadda, MD
Doheny Eye Institute, David Geffen School of Medicine at University of California, Los Angeles.

David Sarraf, MD
Retinal Disorders and Ophthalmic Genetics Division, Stein Eye Institute, David Geffen School of Medicine at University of California, Los Angeles; and VA Greater Los Angeles Healthcare System, Los Angeles, California.

Corresponding Author: David Sarraf, MD, Retinal Disorders and Ophthalmic Genetics Division, Stein Eye Institute, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, CA 90095 (dsarraf@ucla.edu).

Fluorescein angiography has been the gold standard imaging modality for the retinal vasculature since its groundbreaking introduction in 1961 by Alvis and Novotny and has revolutionized our ability to diagnose diseases of the retinal vasculature and to identify retinal and choroidal neovascularization.[1] Its greatest advantage may lie in its ability to detect dynamic patterns of dye transit and leakage. Various innovations have broadened the use of angiography, including the application of indocyanine green, wide-field image acquisition, confocal scanning laser ophthalmoscopy, and adaptive optics. However, a major limitation of traditional angiography resides in its inability to image the entire retinal capillary system or to directly visualize nascent vessels, leaving the practitioner to deduce the presence of neovascularization on the basis of other indicators such as fluid, leakage, or edema.

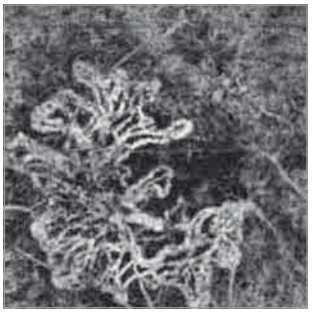
Optical coherence tomography (OCT) angiography applies high-speed OCT scanning to detect blood flow by analyzing signal decorrelation between scans. Compared with stationary areas of the retina, the movement of erythrocytes within a vessel generates a decorrelated signal. The split-spectrum amplitude decorrelation angiography (SSADA) algorithm improves the signal to noise ratio by splitting the source spectrum into 4 parts and averaging the resultant 4 signals. High-density raster scanning of a 2-dimensional area of the retina generates a volumetric rendering of blood flow from the internal limiting membrane to the choroid and allows for direct visualization of normal and abnormal blood vessels. The currently available Optovue AngioVue System uses spectral-domain technology, an 840-nm laser, and the SSADA algorithm (**Figure**). The 70-kHz A-scan rate on this device allows a 3 × 3-mm OCT angiography volume to be acquired in 3 seconds. The lateral and axial resolutions are both 15 µm; the axial resolution is significantly less than that for structural OCT (5 µm) owing to signal averaging. Another device under development by Zeiss will feature a swept-source laser centered at 1040 nm with the potential for augmented signal penetration depth. Future devices may use other approaches for OCT angiography, such as phase contrast or intensity variance.

Unlike traditional angiography, which uses a fluorescent dye and provides limited 3-dimensional information, OCT angiography requires no exogenous contrast and uses dense volumetric scanning to provide depth-resolved visualization of the retinal and choroidal vasculature. The retinal vasculature of the central macula is predominantly a 3-layered capillary bed. Even though one can identify the superficial retinal capillary plexus using fluorescein angiography, this angiographic technique poorly visualizes the intermediate and deep plexuses that are a critical focus of retinal vascular disease.[1,2] Using the SSADA technique, Spaide et al[1] were the first to demonstrate distinct superficial and deep capillary networks, the latter of which includes both the deep and intermediate plexuses. The use of OCT angiography could greatly enrich our understanding of the ischemic processes affecting different layers of the retinal vasculature, such as cotton-wool spots (superficial plexus ischemia), paracentral acute middle maculopathy (deep plexus ischemia),[2] and macular telangiectasia type 2.[3]

Optical coherence tomography angiography may also have the potential to dissect the long-debated origin and microvascular anatomy of neovascularization in age-related macular degeneration, including type 1 (subretinal pigment epithelium), type 2 (subretinal), and type 3 (intraretinal; retinal angiomatous proliferation) neovascularization. In a seminal study, Jia et al[4] generated 3-dimensional reconstructions of choroidal neovascularization and en face OCT renderings to highlight the precise vascular anatomy of choroidal neovascularization. It may be possible to identify distinct morphologies of choroidal neovascularization and then correlate these subtypes with disease course, prognosis, and response to treatment.

In addition to providing enhanced anatomic detail, OCT angiography intrinsically generates data on vascular flow. This powerful feature has enormous implications for understanding tissue perfusion in the absence of obvious morphological changes. A flow index of the optic nerve head can be used to ascertain disc perfusion. For example, glaucomatous optic discs and discs damaged by optic neuritis have significantly diminished flow indices compared with normal discs.[5,6] Remarkably, OCT angiographic measurements are sensitive

Figure. Optical Coherence Tomography Angiography Image of Type 1 Neovascularization



This occult lesion beneath a fibrovascular pigment epithelial detachment is not identifiable using traditional angiography. The larger-caliber vessels appear distinct from the surrounding choriocapillaris.

enough to detect small increases in parafoveal capillary flow elicited by a pattern stimulus projected onto the retina.[7] An enticing possibility is that the anatomic detail and perfusion data provided by OCT angiography may even have predictive value for a wide variety of ophthalmic disorders, including glaucoma, ischemic optic neuropathy, neovascular age-related macular degeneration, and retinal vein occlusion.

Despite the many potential benefits of OCT angiography, our expectations for the technology must be tempered given our limited experience with it. As with any new technique, we must first validate the accuracy and reproducibility of the data. Studies must be performed to define anatomic and physiologic standards before we can assess disease states. Comparative analyses with fluorescein angiography may also be instructive to better understand the significance of vascular patterns observed with OCT angiography and to correlate this to sites of leakage. A major challenge will be to develop automated segmentation algorithms that reliably identify specific retinal vascular layers, even in the diseased eye. At this time, the identification of neovascular tissue must be performed manually, a time-consuming task compared with the review of fluorescein angiography images. Further limitations include suboptimal correction for eye motion artifact and projection artifact from superficial vessels when imaging deeper layers. Distinguishing pathologic vessels from the normal vasculature can therefore be challenging in certain cases. Moreover, the SSADA technique has a relatively poor axial resolution (~15 μm) due to signal averaging, limiting the identification of small-caliber vessels. Finally, it remains unknown how the additional information gleaned from this technique can be used in routine clinical practice.

Traditional angiography will undoubtedly retain a key role in the management of retinal disease because of its ability to identify dynamic dye-transit patterns of occlusion, ischemia, and leakage—especially in the periphery. However, the combination of structural and functional data afforded by OCT angiography may be transformative in its ability to provide 3-dimensional anatomic details and dynamic flow data. The identification of the deep retinal capillary plexus, the direct visualization of neovascular structures, and the analyses of perfusion status are just a few of the ways that OCT angiography could provide significantly greater insight into the mechanisms of retinal and optic nerve disease—a required first step before changing clinical practice and improving treatment outcomes.

ARTICLE INFORMATION

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