Optical Coherence Tomography Angiography

A primer on this promising new technology for evaluating retinal vasculature.

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**Optical Coherence Tomography (OCT)** is a commonly used technology that noninvasively generates images of the retina in cross section or in three dimensions.\(^1\)\(^-\)\(^5\) Advances in technology have facilitated additional applications of OCT such as phase-sensitive OCT, polarization-sensitive OCT, and spectroscopic OCT.\(^6\) These methods hold the promise of combining structural information with functional imaging capabilities to assess the metabolic state of the retinal tissue.\(^7\) This article reviews recent developments in the use of OCT technology for noninvasive assessment of the retinal vasculature. We refer to this technology as OCT angiography (OCTA).

**NOMENCLATURE**

The nomenclature of various OCT methods used to visualize retinal vessels can be confusing, so we will take a moment to clarify some terminology. Several OCT–based methods assess retinal blood flow, and almost all of these methods use some aspect of the phase or intensity information from the reflected OCT beam.\(^8\)

Doppler OCT measures the phase shift from moving red blood cells between sequential A-scans performed in the same region. The major limitation of Doppler OCT is that it is useful for measuring blood flow only in the direction parallel to the orientation of the OCT beam and in relatively larger vessels. Because most retinal blood flow is oriented perpendicular to the OCT beam, and the angle between the beam and the vessel of interest is difficult to measure, Doppler OCT has limited practical use. It is ideal for evaluating bulk movement of fluid that occurs in large vessels but cannot resolve the movement of individual erythrocytes, which occurs in capillaries.\(^9\) Because of these limitations, the most robust application of Doppler OCT has been to facilitate 3-D visualization of the retinal vasculature rather than to assess flow rates and direction. This technique is sometimes referred to as optical coherence angiography (OCA)\(^10\) and is analogous to the ultrasound “power Doppler” methodology used by radiologists. Doppler OCT provides information about both velocity and directionality of flow, whereas OCA provides only affirmation of flow without information on directionality or velocity. The main advantage of Doppler OCT and OCA is that no contrast dye injection is needed.

**OCTA IN RETINAL HEALTH AND DISEASE**

OCTA is a method of visualizing blood vessels with OCT technology that also uses phase information but employs a methodology very different from those described above. Another name, which essentially refers to the same method as OCTA, is OCT microangiography (OMAG).\(^11\)\(^12\) Herein, we will collectively use the term OCTA to refer to all methods that use OCT–based intensity or phase variance to assess blood flow. OCTA images blood flow by measuring intrinsic phase and/or intensity variations (not necessarily phase shift) of reflected light from retinal tissue. Therefore, no dye injection is necessary and the procedure (similar to standard OCT) is noninvasive. In general, these systems can be divided into spectral domain–based (SD-OCT) and swept-source (SS-OCT) systems. No systems of these types have been cleared by the US Food and Drug Administration. It is, however, likely they will become commercially available within the next few years.

OCTA discriminates between the scattering signals from stationary and moving tissues to image capillary flow in high resolution.\(^9\) Light scattering from stationary tissues is stable over time, whereas light scattering from moving particles such as red blood cells will vary randomly over time.\(^13\) OCTA assesses phase and intensity changes that result from movement of erythrocytes over multiple B-scans.\(^14\) Sequential OCT cross-sectional scans at one location are used to detect movement of erythrocytes.\(^13\) The intensity and phase changes that result from the moving erythrocytes provide the contrast mechanism for viewing the vessels.\(^15\)

The utility and potential of OCTA to resolve fine vascular detail has been demonstrated in the normal human retina in two recent studies.\(^16\)\(^17\) In these studies, high-resolution images of normal capillary networks were observed in the superficial, inner, and middle retina (Figure 1). OCTA images demonstrated capillary detail that approaches the
resolution of histological studies on human cadaver eyes.\textsuperscript{17} The variation in normal retinal capillary density between the central macula, temporal macula, and peripapillary retina was described in the living human eye for the first time without dye injection using OCTA.\textsuperscript{17} Estimates of retinal vascular density in the inner and middle layers using OCTA are also consistent with human cadaver histology studies, demonstrating the high spatial resolution of OCTA.\textsuperscript{17} A comparison of the radial peripapillary network using OCTA and fluorescein angiography (FA) in normal human patients showed that the peripapillary capillary network was easily visualized in the OCTA images, but not as often or as easily in FA images.\textsuperscript{16} OCTA has also been used to evaluate changes in blood flow upon stimulation of the healthy human retina by flickering light.\textsuperscript{18} This may be useful in assessing functional deficits in patients with diabetes and glaucoma, as these conditions have a known abnormal vascular response to flickering light.\textsuperscript{18}

OCTA has been used to assess perfusion in glaucoma\textsuperscript{19} and multiple sclerosis (MS).\textsuperscript{7} OCTA of glaucomatous optic nerves demonstrated a significant decrease in blood flow compared with controls.\textsuperscript{19} More interestingly, a correlation between blood flow in the disc and visual field pattern standard deviation was observed, implying an association between decreased perfusion of the optic disc and glaucoma severity.\textsuperscript{19} OCTA has also been used to assess the effects of MS on optic disc vasculature.\textsuperscript{7} Patients with a history of optic neuritis and MS demonstrated reduced blood flow in the optic nerve head compared with MS patients without optic neuritis as well as with healthy controls.\textsuperscript{7} Because these are pilot studies, the findings must be confirmed in larger cohorts.

OCTA has been used to visualize choroidal neovascularization (CNV) in patients with age-related macular degeneration (AMD).\textsuperscript{13,20-22} In these studies, OCTA has successfully differentiated type 1 CNV and type 2 CNV as confirmed by corresponding FA and indocyanine green (ICG) images in some patients. In most cases, OCTA defines the size and structure of CNV better than FA or ICG. This is largely due to the depth-resolved sensitivity of OCTA in comparison with either ICG or FA. OCTA also demonstrated changes in the choriocapillaris surrounding CNV lesions.\textsuperscript{13} The ability of OCTA to quantify measurements of CNV area and flow may have major implications for detecting early signs of disease and assessing CNV response to treatment.\textsuperscript{20}

Macular telangiectasia type 2 (MacTel2) provides an excellent disease target for imaging with OCTA.\textsuperscript{12} The retinal vascular changes in MacTel2 are primarily limited to the parafoveal retinal capillaries. Although OCTA does not show leakage, abnormal dilated vessels imaged by OCTA have been correlated with the leakage seen in FA.\textsuperscript{12} This suggests that areas of abnormal vasculature on OCTA may lead to MacTel2 pathology. In addition, because OCTA can extract layer-specific information about capillaries in three dimensions, it may lead to earlier diagnosis and better monitoring of treatment efficacy in this disease. Because the area of the retina involved in MacTel2 is relatively small and the location of the pathology is central, it is an opportune target for OCTA imaging, which currently is limited in field of view.\textsuperscript{12}

Lastly, the diagnosis and management of diseases such as diabetic retinopathy (DR) and retinal vascular occlusions (RVOs; Figure 2) are likely to benefit from OCTA. Ongoing studies in this area are exploring quantitative assessment of areas of impaired capillary perfusion, detection of microaneurysm turnover, and quantification of blood flow.

**CONCLUSION**

OCTA is a promising new technology for evaluating retinal vasculature because it is noninvasive and able to quickly (within 3-4 seconds) capture high-resolution images with capillary-level detail. This suggests that OCTA can be used much more frequently than dye-based methods for visualizing retinal or choroidal vessels. Moreover,
it seems plausible that a single OCTA scan can provide high-resolution images of both the choriocapillaris and retinal vasculature, thereby allowing unprecedented analysis of layer-specific changes in retinal and choroidal vasculature in diseases such as MacTel2 and neovascular AMD.

Applications in DR and RVOs are also likely to be useful and are under investigation in our clinic. The major limitations of OCTA are the relatively small field of view, bulk motion artifacts, and the inability to assess vascular leakage. It is likely that all of these limitations will be overcome as scanning speeds of OCTA systems increase and image tracking software is implemented. The inability of OCTA to assess vascular leakage may also be mitigated by the detailed structural information that is included in corresponding simultaneously obtained OCT images. Therefore, assessment of retinal thickness and cystoid spaces in the structural intensity–based OCT image that accompanies each OCTA may compensate for the lack of information regarding vascular leakage.

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Figure 2. Comparison of FA and OCT angiogram of the macula in a patient with RVO. Late-phase FA of the macula (A) and OCT angiogram of the superficial retina (B) demonstrate capillary abnormalities including microaneurysms, focal areas of impaired perfusion, shunt vessels, and vessel tortuosity.