The Promise of Optical Coherence Tomography Angiography in Glaucoma
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Optical coherence tomography angiography (OCTA) studies in primary open-angle glaucoma have consistently demonstrated reduced microcirculation in the superficial optic nerve,1 peripapillary retina,2,3 and the macula4,5 of glaucoma patients. These studies clearly demonstrate the superior resolution of OCTA compared with prior methods that were used to measure ocular blood flow (OBF) or its surrogates. How will OCTA help the glaucoma clinician now and in the future? What else must we learn before achieving more practical usefulness from OCTA for glaucoma?

First, OCTA will supplement current glaucoma diagnostic tools to aid in the early detection of glaucoma. Diagnostic accuracy of OCTA vessel density measurements from small studies to date support its promise in this role, and this surely will be enhanced with ongoing improvements to OCTA hardware and software. Currently, peripapillary retinal nerve fiber layer (RNFL) and inner macula thickness measurements by OCT are routine tools to aid in the detection of glaucoma and its progression, but these are not without limitations. For example, OCT scans of eyes with atypical optic nerve anatomic features such as myopic tilt are fraught with issues that reduce our confidence in the RNFL thickness findings.6 Additionally, OCT RNFL measurements in advanced glaucoma become unhelpful when the RNFL thickness has reached its floor of approximately 50 to 60 μm. It is possible that measuring the microcirculation rather than the nerve tissue itself may improve diagnostic usefulness over a wider range of anatomic features and disease.

Second, OCTA may elucidate the role of vascular pathophysiologic features in glaucoma. We have long known that glaucomatous eyes have reduced OBF,1 but we do not know whether reduced OBF is a cause or the simple result of glaucomatous optic neuropathy (the chicken-or-egg dilemma). Although one explanation is that a reduced number of retinal ganglion cell (RGC) axons leads to lower metabolic demand and thus reduced circulation, the other possibility is that a vascular problem such as unstable OBF or microvascular abnormalities contributes to primary open-angle glaucoma in some, if not all, cases. In fact, there is mounting evidence supporting this idea. Flammer7 and Flammer and Mozaffarieh8 have led significant efforts supporting the idea that unstable OBF resulting from microvascular and autoregulation abnormalities leads to oxidative nerve damage. Longitudinal OCTA studies with structural and functional assessments will help to investigate these hypotheses in a way that was never before possible. If proven true, this will open the door for potential therapeutic targets. What if reduced perfusion on OCTA were a marker for sick dysfunctional RGCs? Chen et al9 found significantly reduced microcirculation in the normal hemisphere of glaucomatous eyes compared with normal eyes, despite no differences in RNFL thickness, suggesting the possibility that perfusion defects may predate visual field abnormalities. The ability to detect salvageable RGCs would be a boon to new therapies that focus on neuroprotection. For example, what if OCTA could show that pharmacotherapy can increase OBF, rescuing sick, poorly perfused RGCs before apoptosis and permanent visual function deficits? We already know that profound intraocular pressure reduction resulting from filtering surgery can reverse visual field defects10; perhaps the mechanism is that of improved microcirculation to the optic nerve. Most of the work to date has focused on the superficial retinal microcirculation in the peripapillary and macular regions, but improved OCTA technology (e.g., swept source with deeper penetration) will improve our understanding of the relationship of glaucoma to the microcirculation of the deeper retinal vasculature.11

How will OCTA help the glaucoma clinician now and in the future?

There are still several unanswered questions that must be addressed as we seek to make sense of and optimize OCTA measurements in glaucoma patients. What ocular, systemic, and physiologic factors affect microvascular perfusion? For example, we know there is reduced perfusion in diabetic retinopathy, but to what extent does well-controlled diabetes affect microvascular perfusion? What about hypertension and antihypertensive medications? Topical β-blockers were shown by Takusagawa et al1 (see http://www.aaojournal.org/article/S0161-6420(16)32385-5/fulltext) in this issue of Ophthalmology to affect vessel density, but do systemic antihypertensive medications also affect OCTA measurements? What are the effects of other topical glaucoma medications on measured microvascular perfusion? The list goes on. In fact, even exercise has been shown to reduce perfusion.11 An improved understanding of these and other factors on OCTA microvascular measurements will increase the usefulness of OCTA. Takusagawa et al demonstrate the usefulness of 2 specific improvements in OCTA algorithms: projection resolution, which aims to remove flow projection artifacts from other layers in the generation of en face images, and reflectance compensation in quantification algorithms, which aims to reduce artifacts caused by media. Ultimately, these efforts will improve accuracy and precision of OCTA measurements, and improvements in hardware, such as the use of swept-source technology, will only serve to enhance these.

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Optical coherence tomography angiography promises to be a tool that will improve early diagnosis of glaucoma, elucidate the vascular mechanisms in glaucoma, and possibly even allow detection of salvageable RGCS for rescue therapies. Through OCTA, there is great potential to advance our understanding of the disease and our ability to detect and treat it.

References


Footnotes and Financial Disclosures

Financial Disclosure(s): The author(s) have made the following disclosure(s): G.M.R.: Equipment support — Carl Zeiss Meditec

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