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Measuring Blood Flow:

So What?

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Ocular blood flow and optic nerve injury have been linked and have remained in a chicken-and-egg quandary since the 19th century. The question of which comes first remains unanswered, and the connection has not been revealed.

The concept of blood flow as it relates to glaucoma damage is clearly sound: less blood flow means more nerve damage, with causality unknown.^{1–3} Imagine a reproducible, quantitative, objective method of assessment of optic nerve or retinal blood flow (global or local), particularly one that does not require an expert technician or observer. Such technology would be a great boon to glaucoma assessment for initial identification, monitoring, and detection of progression.

We have used various devices to assess ocular, optic nerve, and retinal blood flow over the years, with varying degrees of invasiveness, accuracy, and precision. From injectable dyes to ultrasonography to laser, we have been hopeful and subsequently disappointed. Anticipating that a newly introduced method that performed well in the laboratory would be clinically applicable, we have been disappointed when it was poorly reproducible inherently or because of sensitivity to variations in acquisition of data.

Enter optical coherence tomography (OCT) angiography and blood flow measurement. With sophisticated direct and indirect algorithms, OCT can be used to map retinal and superficial optic nerve vasculature and blood flow. The article by Liu et al⁴ in this issue describes a method of extracting angiographic and blood flow information from OCT, as well as its application in discriminating glaucomatous from nonglaucomatous eyes and its association with conventional clinical variables. Liu et al show a correspondence of blood flow and vessel density with visual function as measured by standard achromatic automated perimetry. They demonstrate acceptable reproducibility, better than any other technique to date for measurement of ocular blood flow, which is encouraging. On the other hand, recently acquired OCT angiography images still do not answer the question of which comes

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first: changes in ocular blood flow or optic nerve injury? Such insights will require longitudinal studies of OCT angiography to determine if the changes described by Liu et al precede or follow optic nerve injury.

An objective, quantitative, noninvasive, reproducible method for assessment of vascular density and blood flow that corresponds with ocular function would transport medicine a long way to achieving fully objective glaucoma assessment, at least in the domain of the eye itself. Despite their failings, visual fields offer measurement of the entire visual system, including the eye, optic nerve, and visual brain. All these tissues are influenced by the glaucomatous process because glaucoma affects the visual brain and the eye, even early in the disease. Nevertheless, a quick, noninvasive method such as that described by Liu et al⁴ could bring this assessment into the clinical realm. Measuring the structure and function of the visual brain still requires hefty technology (eg, magnetic resonance imaging), even with the availability of OCT in office-based eye care practices globally.

There are other methods for measuring function of the retinal ganglion cells and the optic nerve, but none have shown the level of correspondence with perimetry demonstrated by Liu et al.⁴ Pattern electroretinography and multifocal visual evoked response each has demonstrated promise, but they have not become useful clinical tools. That may change with time because each also offers the promise of objective, quantitative evaluation of visual function, with visual evoked response involving the visual brain as well.

Several variables could prove problematic for OCT angiography and blood flow measurement. Visualization of small vessels is dependent on OCT acquisition speed. High-speed imaging for angiography shows fewer small vessels than slower-speed imaging, to a point. This is an area that will have to be developed for OCT angiography to become a clinically viable tool.

Another area of potential confounding is the dynamic range. We know that current commercial OCT measurements of retinal nerve fiber layer (RNFL) thickness hit a floor below which they do not decrease. For RNFL thicknesses below that threshold, perimetry is most useful in detection of glaucoma progression, in contrast to structural measurements that prove useful for measurement of RNFL thickness change when the tissue is thicker than the floor measurement (approximately 50–55 μm with Cirrus OCT [Carl Zeiss Meditec, Inc] and approximately 60 μm with RTVue-XR [Optovue, Inc]). The dynamic range of OCT angiography and blood flow assessment as it relates to glaucoma is unknown. Will there be a floor below which or a ceiling above which vessels or flow cannot be reliably measured by OCT? The greater the range over which glaucoma and its progression can be measured, the greater is the ability of the physician to intervene to preserve vision.

What is the correspondence of vascular parameters with perimetric measurements? Liu et al⁴ have shown a correspondence between them, at least when one hemifield is considered relative to the other or in the case of obvious focal defects in vessel density and flow. Will this hold for absolute measurements of vessel density and blood flow? How finely can this association be parsed? Will we be able to achieve the level of detailed functional information that we can obtain from a visual field using OCT angiography and measurements of blood

flow? Perhaps we will be able to achieve a more highly resolved functional measure with OCT, or would even slightly less resolution with less fluctuation be acceptable?

This is an exciting era in glaucoma evaluation. In the past 35 years, we have seen the introduction and widespread adoption of automated perimetry, followed by computer-assisted investigation of the optic nerve head, nerve fiber layer, and macula. Optical coherence tomography is the most powerful of the tools that we now use for structural assessment of glaucoma and could be similarly useful in measuring optic nerve function through evaluation of vascular density and blood flow. If future studies and technology development demonstrate this ability, we will have objective, quantitative, painless, rapid, noninvasive assessment of glaucoma at a level of precision that has previously been unachievable. Glaucoma care will be further advanced to a less artisanal stage and made less variable by the ability to work with definitive, measurable information directly related to the tissues relevant to glaucoma.

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