Optical Coherence Tomography in Glaucoma

An essential imaging modality for diagnosis, monitoring, and management of the disease.

BY NATHAN M. RADCLIFFE, MD, AND SYED AMAL HUSSNAIN, MD

ptical coherence tomography (OCT), a noninvasive imaging modality that uses low-coherence light to obtain a high-resolution cross-section of biological structures, is changing the field of ophthalmology. The technology has evolved dramatically since its first description by Huang et al in 1991.¹ The most significant leap forward occurred when the moving reference mirror used during the collection of time-domain (TD) OCT data was abandoned in favor of Fourier analysis of collected data. As a result, the current spectral-domain (SD) OCT technology collects up to 55,000 A-scans per second with an axial resolution of 5 µm—a 100-fold improvement over the earlier-generation TD-OCT.² Obtaining large data cubes quickly reduces test-retest variability, allows three-dimensional reconstruction and alignment, improves registration, and facilitates test-retest comparisons. Not surprisingly, SD-OCT has been shown to have better diagnostic ability for glaucoma and its progression than TD-OCT.3

CURRENT CHALLENGES IN GLAUCOMA MANAGEMENT

The lack of objective structural or functional tests proven to detect early disease and progression makes glaucoma difficult to manage. As with perimetric findings, structural progression may be focal or diffuse, and it may occur well before any visual deficits are apparent. Structural tests traditionally relied on clinicians' recognizing changes to the optic disc and retinal nerve fiber layer (RNFL) on clinical examination.⁴ Given that the nerve anatomy and topography demonstrate significant interindividual variability, clinicians frequently find it difficult to distinguish physiologic variants such as cupping from those caused by glaucoma (neuroretinal rim loss). Large studies have also demonstrated disagreements between structural and functional tests.⁵⁻⁷ Practitioners rely heavily on clinical experience, and SD-OCT offers objectivity by providing a quantitative assessment of the inner retina.8

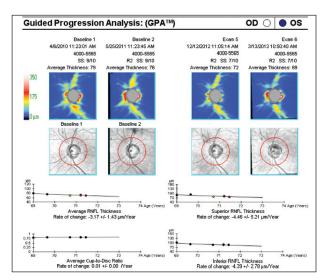


Figure. An example of a patient who experienced progressive RNFL thinning while the visual field and OCT remained normal according to normative databases.

PERIPAPILLARY RNFL EVALUATION

Peripapillary RNFL thickness, as measured by SD-OCT, is the most common method for identifying and monitoring structural damage in glaucoma. This modality detects early, preperimetric disease and progression in glaucoma suspects (Figure). Formulas that approximate the amount of retinal ganglion cell (RGC) loss, a hallmark of glaucomatous damage, from OCT RNFL measurements have also been derived, as have methods of combining both structure and function. 11,12

EVALUATION OF MACULAR THICKNESS

The macula is densely populated by RGCs, containing 30% of the total number of these cells while occupying only 2% of the retina's area. Zeimer et al hypothesized that the loss of RGCs in early glaucoma is more likely to occur in the macula. ¹³ Recent data suggest that the disease affects

the macular thickness early in its course. ¹⁴ Routine evaluations of macular thickness in glaucoma can thus complement other tests, because perimetry using a 6° grid can easily miss central visual defects. Additionally, there is less physiologic variability in the macula compared with the disc and peripapillary region, and peripapillary RNFL measurements mainly identify damage outside the macula.

Although early studies employing TD-OCT showed peripapillary RNFL measurements to have a better diagnostic yield compared with macular thickness, new SD-OCT commercial platforms have the ability to specifically segment the inner retinal layers that are damaged in glaucoma, namely the RNFL, RGC, and inner plexus (IP) layers. Recent studies have shown macular thickness evaluation to be at least comparable to or better than RNFL measurements. 15-17 Current protocols allow macular analysis by segmenting out the RNFL, RGC, and IP layers (RTVue FD-OCT system [Optovue] and 3D OCT 2000 [Topcon Medical Systems]). Other protocols segment out the RGC plus the IP layers (Cirrus HD-OCT [Carl Zeiss Meditec]) or the entire macular thickness (Spectralis [Heidelberg Engineering]).9 Regardless of the prevalence of macular involvement in glaucoma, devices that measure macular changes are valuable because glaucomatous damage within the macula will have a functional impact. Finally, scanning the macula can also detect pathology in elderly patients from age-related macular degeneration or other causes.

A FINAL NOTE ON INTERPRETING OCT DATA

The availability of an objective test like SD-OCT does not absolve clinicians from their responsibility to be hypothesis driven. In conjunction with OCT scans, practitioners must take into account pretest probability based on well-validated risk factors such as age, race, central corneal thickness, and IOP. Continuous likelihood ratios for RNFL and macular measurements instead of an arbitrarily chosen cut-off value can then be used to more precisely assess the posttest probability of disease.

Practitioners must pay attention to the quality of an OCT scan (ie, how the software acquires and analyzes the data) as well as the strength of the signal (ie, quality of the light signal coming into and out of the eye). Factors that decrease signal strength include dry eyes, media opacities such as cataract, and axial length. It is important for clinicians to be aware of artifacts. "Red disease" is a misinterpretation that occurs when a normative database is applied to patients who should not be considered normal (eg, those with high myopia). "Green disease" occurs in patients who have normal global values such as an average RNFL thickness but have small focal defects that are missed. Artifacts caused by pathology occur frequently. For example, epiretinal membranes, edema, and vitreous traction can artifi-

cially elevate RNFL values. Data acquisition problems can occur when microsaccades or an inconsistently tilted head interfere with the registration of the collected data. Finally, segmentation errors can happen when the software tries to outline the RNFL but fails or when a retinal cyst is erroneously included as part of the RNFL measurement.

CONCLUSION

SD-OCT of the macula and optic nerve has greatly enhanced glaucoma care. When combined with a comprehensive ophthalmic examination and careful glaucoma assessment, the technology's use may be even more valuable.

Syed Amal Hussnain, MD, is a resident at Yale School of Medicine, Department of Ophthalmology and Visual Science, in New Haven, Conneticut. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Hussnain may be reached at (203) 785-6345; fax: (203) 785-6123; syed.hussnain@yale.edu.

Nathan M. Radcliffe, MD, is the director of the Glaucoma Service at NYU Langone Ophthalmology Associates in New York, New York. He is a consultant to and speaker for Carl Zeiss Meditec. Dr. Radcliffe may be reached at (212) 263-2573; fax: (212) 263-2574; drradcliffe@gmail.com.

- 1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. Science. 1991;254(5035):1178-1181.
- 2. Kiernan DF, Mieler WF, Hariprasad SM. Spectral-domain optical coherence tomography: a comparison of modern high-resolution retinal imaging systems. *Am J Ophthalmol.* 2010;149(1):18-31.
- Leung CK-S, Chiu V, Weinreb RN, et al. Evaluation of retinal nerve fiber layer progression in glaucoma: a comparison between spectral-domain and time-domain optical coherence tomography. Ophthalmology. 2011:118:1558-1562.
- Medeiros FA, Alencar LM, Zangwill LM, et al. Prediction of functional loss in glaucoma from progressive optic disc damage. Arch Ophthalmol. 2009;127:1250-1256.
- Gaasterland DE, Blackwell B, Dally LG, et al. The Advanced Glaucoma Intervention Study (AGIS): 10. Variability
 among academic glaucoma subspecialists in assessing optic disc notching. Trans Am Ophthalmol Soc. 2001;99:184–
 185.
- Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002;120:701-713.
- Miglior S, Zeyen T, Pfeiffer N, et al. Results of the European Glaucoma Prevention Study. Ophthalmology 2005;112:366-375.
- 8. Smith SD. SD-OCT: what can it offer glaucoma management? Continued evolution may allow for earlier diagnoses. *Ophthamology Management*. February 2012;16:38-40.
- 9. Grewal DS, Tanna AP. Diagnosis of glaucoma and detection of glaucoma progression using spectral domain optical coherence tomography. *Curr Opin Ophthalmol*. 2013;24:150–161.
- 10. Lisboa R, Leite MT, Zangwill LM, et al. Diagnosing preperimetric glaucoma with spectral domain optical coherence tomography. *Ophthalmology*. 2012;119:2261–2269.
- 11. Harwerth RS, Wheat JL, Fredette MJ, et al. Linking structure and function in glaucoma. *Prog Retin Eye Res.* 2010;29:249-271.
- 12. Medeiros FA, Lisboa R, Weinreb RN, et al. A combined index of structure and function for staging glaucomatous damage. *Arch Ophthalmol*. 2012;130:1107-1116.
- 13. Zeimer R, Asrani S, Zou S, et al. Quantitative detection of glaucomatous damage at the posterior pole by retinal thickness mapping: a pilot study. *Ophthalmology*. 1998;105:224-231.
- 14. Hood DC, Raza AS, de Moraes CG, et al. Glaucomatous damage of the macula. *Prog Retin Eye Res*. 2013;32:1–21. 15. Tan O, Chopra V, Lu AT, et al. Detection of macular ganglion cell loss in glaucoma by Fourier-domain optical
- coherence tomography. *Ophthalmology*. 2009;116(12):2305–2314.

 16. Nouri-Mahdavi K, Nowroozizadeh S, Nassiri N, et al. Macular ganglion cell/inner plexiform layer measurements by spectral domain optical coherence tomography for detection of early glaucoma and comparison to retinal nerve fiber layer measurements. *Am J Ophthalmol*. 2013;156(6):1297–1307.
- 17. Nakatani Y, Higashide T, Ohkubo S, et al. Evaluation of macular thickness and peripapillary retinal nerve fiber layer thickness for detection of early glaucoma using spectral domain optical coherence tomography. *J Glaucoma*. 2011;20(4):252-259.