Point-Counterpoint

Section Editors:

Janet Ongkeko-Perez, MD Edgar U. Leuenberger, MD

If there is only one device to monitor glaucoma progression, it would be the

Grace D. Grozman^{1,2}, MD, Celeste Guzman^{1,3}, MD, Patricia M. Khu^{1,4,5}, MD

¹Philippine Glaucoma Society

²Asian Hospital and Medical Center, Muntinlupa

³University of Sto. Tomas Hospital, Manila

⁴Philippine Eye Research Institute, University of the Philippines, Manila

⁵Cardinal Santos Medical Center, San Juan

Disclaimer: The topic was presented during the Philippine Academy of Ophthalmology (PAO) – sponsored Lifelong Educational Access Program (LEAP) last August 4, 2018. The speaker's stance on the controversial issue was randomly assigned and may not necessarily reflect his/her own views and actual practice. The authors report no conflict of interest.

Optical Coherence Tomography Grace D. Grozman, MD

Glaucoma is an optic nerve pathology in which there is progressive loss of retinal ganglion cells. The ultimate goal is to control intraocular eye pressure to slow down disease progression and preserve visual function. Because of this, the early identification of disease progression is vital. 2

Glaucoma progression cannot be identified in the clinics, so ophthalmologists use machines such as the standard automated perimetry, short-wavelength automated perimetry, and frequency-doubling technology.³ Unfortunately, with these tests, it is not easy to differentiate between changes due to glaucoma and age, and there is often lack of consistency in the measurements.² Glaucomatous optic nerve changes also appear years before there are any identifiable visual field changes.⁴

The optical coherence tomography (OCT) objectively records the configuration of the optic nerve head and measures the thickness of the retinal nerve fiber layer (RNFL).⁵ Measurements are very reproducible, especially when a spectral-domain OCT is used.⁶

In a 5-year prospective study by Yu et al. in

2016, the group aimed to find out if progressive RNFL thinning can predict worsening visual field loss in glaucoma.⁷ The study population included 139 open angle glaucoma patients (or a total of 240 eyes). Results showed that continuous RNFL thinning identified by Guided Progression Analysis (GPA) and Trend-Based Progression Analysis (TPA) related to worsening of visual fields.

The Advanced Imaging Glaucoma Study Group compared the detection of long-term glaucoma progression using the OCT and visual field tests. The study included 536 glaucoma suspects (or those with preperimetric glaucoma) and 153 perimetric glaucoma eyes followed for 54.1+16.2 and 56.7+16.0 months, respectively. The study concluded that the OCT can detect progression in early glaucoma better than visual field tests. The value of RNFL decreases in advanced glaucoma; but the ganglion cell complex can still detect progression in all stages.⁸

In conclusion, the OCT is helpful in the management of glaucoma, and can be used in combination with other diagnostic tools for early cases. Because it can take objective measurements, it is highly useful in monitoring for disease progression. Lastly, it is an excellent means to assist ophthalmologists in deciding when to treat and intensify treatment.⁹

Philipp J Ophthalmol 2019;44:25-28

REFERENCES

- American Academy of Ophthalmology. Preferred Practice Pattern: Primary Open-Angle Glaucoma. San Francisco: AAO; 2003. p. 1-40.
- Kotowski J, Wollstein G, Folio LS, et al. Clinical Use of OCT in Assessing Glaucoma Progression. Ophthalmic Surg Lasers Imaging. 2011;42 Suppl:S6-S14.
- Johnson CA, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest* Ophthalmol Vis Sci. 1997;38:413–425.
- 4. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve atrophy precedes the onset of glaucomatous field loss. *Arch Ophthalmol.* 1991;109(1):77-83.
- Leung, CK. Ophthalmology Management. Glaucoma Physician. 2017;21:16-18.
- Wolf-Schnurrbusch UE, Ceklic L, Brinkmann CK, et al. Macular thickness measurements in healthy eyes using six different optical coherence tomography instruments. *Invest* Ophthalmol Vis Sci. 2009;50(7):3432-7.
- Yu M, Lin C, Weinreb RN, et al. Risk of visual field progression in glaucoma patients with progressive retinal nerve fiber layer thinning: a 5-year prospective study. Ophthalmology. 2016;123:1201-1210.
- 8. Vazquez LE, Huang LY. RNFL Analysis in the Diagnosis of Glaucoma. May/June 2016. http://glaucomatoday.com/2016/06/rnfl-analysis-in-the-diagnosis-of-glaucoma/accessed 8 April 2019).
- Zhang X, Dastiridou Á, Francis BA, et al. Comparison of Glaucoma Progression Detection by Optical Coherence Tomography and Visual Field. Am J Ophthalmol. 2017;184:63-74.

Automated Perimeter

Celeste Guzman, MD

If there is only one device to monitor glaucoma progression, it would be an automated perimeter. These are my 5 reasons. First, visual field test is still the most common method for detecting functional glaucoma progression in clinical trials and clinical practice, and currently remains to be the gold standard.¹ Second, a number of strategies incorporated in most perimeters have been developed to assist the clinician in identifying visual field changes suggestive of progression. They simplify the analysis of complex visual field variability and provide a degree of objectivity with excellent sensitivity and specificity.^{2,3} Third, studies have proposed that structural changes measured by optical coherence tomography (OCT) appear to be more useful in detection of progression in early glaucoma, while monitoring functional changes using visual field test is more informative during the later stages of the disease. Correlation between the two tests is ideal, but what if you were to have only 1 device?⁴⁻⁶ Despite the fact that authors have concluded that OCT is more sensitive than perimetry in detection of early glaucoma progression, they still do not advocate reliance on OCT alone in monitoring glaucoma. OCT cannot be used singly to monitor glaucoma progression even in the early stage. Thus, visual field test still has a role in detection of progression in this stage. For detection of progression to occur at the earliest possible time point, frequency of visual field testing must be adequate. Other strategies to increase sensitivity of visual field tests have also been introduced.^{7,8} Fourth, in moderate to advanced glaucoma, the more important stages of the disease, visual field tests have been shown to be more reliable than structural test in the detection of progression. This is due to the "floor effect" from the presence of nonneuronal tissues and retinal blood vessels which may affect measurement of structural changes. Nonstandard functional testing strategies employing a bigger stimulus size or the central 10-degree program may be used in advanced disease.^{2,9} Fifth, visual field loss is clearly associated with decreased quality of life. Visual field tests to demonstrate areas of visual field loss may help to explain a patient's poor quality of life. Only visual field exam can truly reflect the patient's visual field loss. This is something the patient will most likely understand, as well. 10,11

On the other hand, challenges that are inherent with the use of OCT include the following: (1) OCT may be unreliable 20% of the time and will be affected by artifacts in almost 40%; (2) A 5-micron change in average retinal nerve fiber layer (RNFL) thickness is considered significant; (3) RNFL measurements can be affected by dry eye, presence of a vitreous floater, and release of an epiretinal membrane. In patients with myopia, epiretinal membranes and uveitis, OCT parameters do not accurately reflect glaucoma severity. In active uveitis, RNFL may be normal or thick; then will thin out as the inflammation resolves. But this will not necessarily indicate progressive structural damage.

We have heard about all the advantages of OCT and admittedly, there has been much improvement in technology over the years. However, challenges with its use in detecting glaucoma progression still exist and despite all its advantages, it is just not yet ready to replace perimetry. Thus, I maintain that if there is only one device to monitor progression in glaucoma, it is visual field because it is still the gold standard. It has different progression software that may be useful in every stage of glaucoma, and at the end of the day, only functional tests can predict functional loss.

26

REFERENCES

- Nouri-Mahdavi K, Nassiri N, Giangiacomo A, Caprioli J. Detection of visual field progression in glaucoma with standard achromatic perimetry: a review and practical implications. *Graefes Arch Clin Exp Ophthalmol.* 2011; 249(11):1593-616.
- Aref AA, Budenz DL. Detecting visual field progression. Ophthalmology. 2017; 124(12S):S51-S56.
- Artes PH, O'eary N, Nicolela MT, et al. Visual field progression in glaucoma: what is the specificity of guided progression analysis? Ophthalmology. 2014; 121(10):2023-7.
- Medeiros FA, Zangwill LM, Girkin CA, et al. Combining structural and functional measurements to improve estimates of glaucomatous progression. Am J Ophthalmol. 2012; 153(6):1197-205.
- Seth NG, Kaushik S, Kaur S, et al. 5-year disease progression of patients across spectrum assessed by structural and functional tools. *Br J Ophthalmol*. 2018; 102:802-807.
- Zhang X, Dastiridou A, Francis BA, et al; Advanced Imaging for Glaucoma Study Group. Comparison of glaucoma progression detection by optical coherence tomography and visual field. Am J Ophthalmol. 2017; 184:63-74.
- Malik R, Swanson WH, Garway-Heath DF. The structurefunction relationship in glaucoma – past thinking and current concepts. Clin Exp Ophthalmol. 2012;40(4):369-80.
- Camp AS, Weinreb RN. Will perimetry be performed to monitor glaucoma in 2025? Ophthalmology. 2017;124:S71-S75
- Fujimoto N. Comparison of a five-degree visual field between two program of different testing field range. Am J Ophthalmol. 2007;143(5):866-7.
- Medeiros FA, Gracitelli CP, Boer ER, et al. Longitudinal changes in the quality of life and rates of progressive visual field loss in glaucoma patients. *Ophthalmology*. 2015;122(2):293-301.
- Black AA, Wood JM, Lovie-Kitchin JE. Inferior visual field reductions are associated with poorer functional status among older adults with glaucoma. *Ophthalmic Physiol Opt.* 2011;31(3):283-91.
- Hardin JS, Tabbi G, Nelson SC, et al. Factors Affecting Cirrus-HD OCT Optic Disc Scan Quality: A Review with Case Examples. J Ophthalmol. 2015;2015:724150.
- Leung CK, Cheung CY, Weinreb RN, et al. Retinal nerve fiber layer imaging with spectral-domain optical coherence tomography: a variability and diagnostic performance study. Ophthalmology. 2009;116(7):1257-1263.

Consolidating the Evidence Patricia M. Khu, MD

Glaucoma is a chronic disease causing irreversible blindness.¹ Its progression is insidious and the rate variable and unpredictable. Hence, integral to its management is the need for periodic monitoring.

Monitoring of the status of glaucoma can be achieved through assessment of the structural and functional components of the disease—2 different aspects wherein glaucoma damage can be evaluated. Structural damage as manifested by thinning of the retinal nerve fiber layer (RNFL) and thinning of the

ganglion cell complex (GCC) is measured by optical coherence tomography (OCT) and functional damage as manifested by scotomas is quantified by perimetry/visual field (VF).²⁻⁵

Studies have shown that the relationship between structural and functional damage is complex.⁶⁻⁸ This can be attributed to individual variation and disease severity. In glaucoma management, it is believed that structural tests can better identify progression in the early stages of the disease and functional tests can better quantify damage in the later stages of glaucoma.9-12 The Advanced Imaging for Glaucoma Study Group illustrated several methods to evaluate progression in glaucoma suspects and preperimetric glaucoma (GS/PPG) and in perimetric glaucoma (PG).¹³ Progression was detected in 62.1% of PG eyes and 59.8% of GS/PPG eyes by OCT versus 41.8% and 27.3%, respectively by VF.14 When PG eyes were stratified according to severity, OCT had significantly higher detection rate than VF in mild PG but not in moderate and advanced PG.14 The rate of RNFL thinning slowed dramatically in advanced PG but GCC thinning rate remained steady even in advanced disease. This difference has been attributed to the "floor effect" of current OCT machines to measure RNFL thinning in advanced glaucoma. 14-17 Future improvements in software, as well as scanning techniques, will surely improve the sensitivity and specificity of OCT in monitoring progression in advanced disease.

Another reason why OCT has been shown to detect progression higher than VF is its more objective nature, with less variability between scans from different visits compared to VF that is more subjective requiring reliable responses from patients. 18-20 Moreover, the effects of short- and long-term fluctuations in VF testing can confound the monitoring of progression. Several studies have also highlighted the predictive role of OCT RNFL and GCC thinning in functional decline of glaucoma suspects and patients as measured by VF.12,21-22 And others have demonstrated that some patients progress by either functional or structural alone, or both, in all glaucoma stages. 14,16,21 And that if the different methods of measuring progression in OCT and VF were compared, there was only moderate overlap among the different parameters measured.¹⁴ Thus, using OCT and VF together for disease monitoring is a better option than either one alone to better track disease progression more frequently and more thoroughly.

January - June 2019

In summary, clinicians should be knowledgeable of the different structural and functional tests available and the factors that can affect accuracy and reliability of the measurements. Evaluation of the status of glaucoma by both methods can better monitor the disease progression.

REFERENCES

- Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006;90(3):262-267.
- Chauhan BC, Garway-Heath DF, Goñi FJ, et al. Practical recommendations for measuring rates of visual field change in glaucoma. Br J Ophthalmol. 2008;92(4):569-573.
- 3. Bussel II, Wollstein G, Schuman JS. OCT for glaucoma diagnosis, screening and detection of glaucoma progression. Br J Ophthalmol. 2014;98(Suppl 2):ii15-ii19.
- Mwanza JC, Kim HY, Budenz DL, et al. Residual and dynamic range of retinal nerve fiber layer thickness in glaucoma: comparison of three OCT platforms. *Invest* Ophthalmol Vis Sci. 2015;56(11):6344-6351.
- Hood DC, Kardon RH. A framework for comparing structural and functional measures of glaucomatous damage. Prog Retin Eye Res. 2007;26(6):688-710.
- Banegas SA, Anton A, Morilla A, et al. Evaluation of the retinal nerve fiber layer thickness, the mean deviation, and the visual field index in progressive glaucoma. *J Glaucoma*. 2016;25(3):e229-e235.
- Bowd C, Zangwill LM, Berry CC, et al. Detecting early glaucoma by assessment of retinal nerve fiber layer thickness and visual function. *Invest Ophthalmol Vis Sci.* 2001;42(9):1993-2003.
- Medeiros FA, Zangwill LM, Bowd C, et al. The structure and function relationship in glaucoma: implications for detection of progression and measurement of rates of change. *Invest Ophthalmol Vis Sci.* 2012;53(11):6939-6946.
- Zhang KX, Loewen N, Tan O, et al. Predicting development of glaucomatous visual field conversion using baseline Fourier-domain optical coherence tomography. Am J Ophthalmol. 2016;163:29-37.
- Mwanza JC, Oakley JD, Budenz DL, Anderson DR. Ability of cirrus HD-OCT optic nerve head parameters to discriminate normal from glaucomatous eyes. *Ophthalmology*. 2011;118(2):241-248.
- Sehi M, Bhardwaj N, Chung YS, Greenfield DS. Evaluation of baseline structural factors for predicting glaucomatous visual-field progression using optical coherence tomography, scanning laser polarimetry and confocal scanning laser ophthalmoscopy. Eye. 2012;26(12):1527-1535.
- Kuang TM, Zhang C, Zangwill LM, et al. Estimating lead time gained by optical coherence tomography in detecting glaucoma before development of visual field defects. Ophthalmology. 2015;122(10):2002-2009.
- Le PV, Zhang X, Francis BA, et al. Advanced imaging for glaucoma study: design, baseline characteristics, and inter-site comparison. Am J Ophthalmol. 2015;159(2):393-403.
- Zhang X, Dastiridou A, Francis BA, et al. Comparison of glaucoma progression detection by optical coherence tomography and visual field. Am J Ophthalmol. 2017;184:63-74
- Zhang X, Dastiridou A, Francis BA, et al. Baseline Fourierdomain optical coherence tomography structural risk factors for visual field progression in the Advanced Imaging for Glaucoma Study. Am J Ophthalmol. 2016;172:94-103.
- 16. Abe RY, Diniz-Filho A, Zangwill LM, et al. The relative odds

- of progressing by structural and functional tests in glaucoma. *Invest Ophthalmol Vis Sci.* 2016;57(9):421-428.
- Invest Ophthalmol Vis Sci. 2016;57(9):421-428.
 17. Mwanza JC, Budenz DL, Warren JL, et al. Retinal nerve fiber layer thickness floor and corresponding functional loss in glaucoma. Br J Ophthalmol. 2015;99(6):732-737.
- Wollstein G, Schuman JS, Price LL, et al. Optical coherence tomography longitudinal evaluation of retinal nerve fiber layer thickness in glaucoma. Arch Ophthalmol. 2005;123(4):464-470
- Chang RT, Knight OJ, Feuer WJ, Budenz DL. Sensitivity and specificity of time-domain versus spectral-domain optical coherence tomography in diagnosing early to moderate glaucoma. Ophthalmology. 2009;116(12):2294-2299.
- Anton A, Pazos M, Martin B, et al. Glaucoma progression detection: agreement, sensitivity, and specificity of expert visual field evaluation, event analysis, and trend analysis. *Eur J Ophthalmol*. 2013;23(2):187-195.
- Yu M, Lin C, Weinreb RN, et al. Risk of visual field progression in glaucoma patients with progressive retinal nerve fiber layer thinning: a 5-year prospective study. *Ophthalmology*. 2016;123(6):1201-1210.
- Miki A, Medeiros FA, Weinreb, RN, et al. Rates of retinal nerve fiber layer thinning in glaucoma suspect eyes. Ophthalmology. 2014;121(7):1350-1358.

Philippine Academy of Ophthalmology

28