New Progression Software for the Visual Field and Optic Disc

Guidelines for the clinical management of patients with glaucoma.

BY CHRIS A. JOHNSON, PhD

Two important factors in the clinical management of glaucoma patients are determining that progression is occurring and calculating the rate of glaucomatous progression. The functional (visual fields) and structural (optic disc and retinal nerve fiber layer [RNFL]) assessment of eyes with glaucoma and those with risk factors for the development of the disease is critical. These evaluations help the practitioner to determine whether treatment is appropriate or if more aggressive procedures should be initiated. Currently, every multicenter clinical trial in glaucoma has used different criteria for defining visual field progression[1,2]; the situation is similar for structural properties, and methods to determine the rate of progression are just now emerging.[3,4]

To date, the methods that have been used to determine progression have been clinical judgment,[5] classification or glaucoma disease staging systems,[1,6] event analysis,[1] and trend analysis.[1] Each has its advantages and disadvantages. These procedures demonstrate large differences in sensitivity, specificity, and time to detect progression, and they only agree with each other about 50% to 60% of the time.[2] Developing a standardized method of determining glaucomatous progression and the rate of progression remains a challenge, and achieving a consensus among glaucoma practitioners on such a procedure remains hopeful. This article briefly reviews the commercially available methods currently used for determining progression and its rate for the structural and functional evaluation of glaucoma.

VISUAL FIELD PROGRESSION SOFTWARE

At present, two primary analysis procedures are used for the determination of visual field progression: event analysis and trend analysis. The Glaucoma Change

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Probability program for the Humphrey Field Analyzer (Carl Zeiss Meditec, Inc., Dublin, CA) compares follow-up visual fields to the average sensitivity values for two baseline visual fields. It then determines if pointwise changes in visual field sensitivity are within or outside the 95% confidence limits of variability for glaucoma patients (based on four tests performed within a 1-month period in a group of glaucoma patients).[7] In this manner, the user can determine whether individual test locations have a sensitivity that has remained stable or undergone progression.

Because more than 50 locations are tested during a visual field examination, several locations (5%) are likely to show differences in sensitivity that are outside of the expected variability from one examination to another. The Glaucoma Progression Analysis software, based on results obtained from the Early Manifest Glaucoma Trial (EMGT), required the confirmation of three or more locations outside of the 95% confidence limits that were confirmed on two (possible progression) or three (likely progression) successive follow-up visual field examinations.[8] The system also employs the pattern deviation probability plots rather than total deviation plots to minimize the influence of cataract and other nonglaucomatous conditions that can produce a wide-

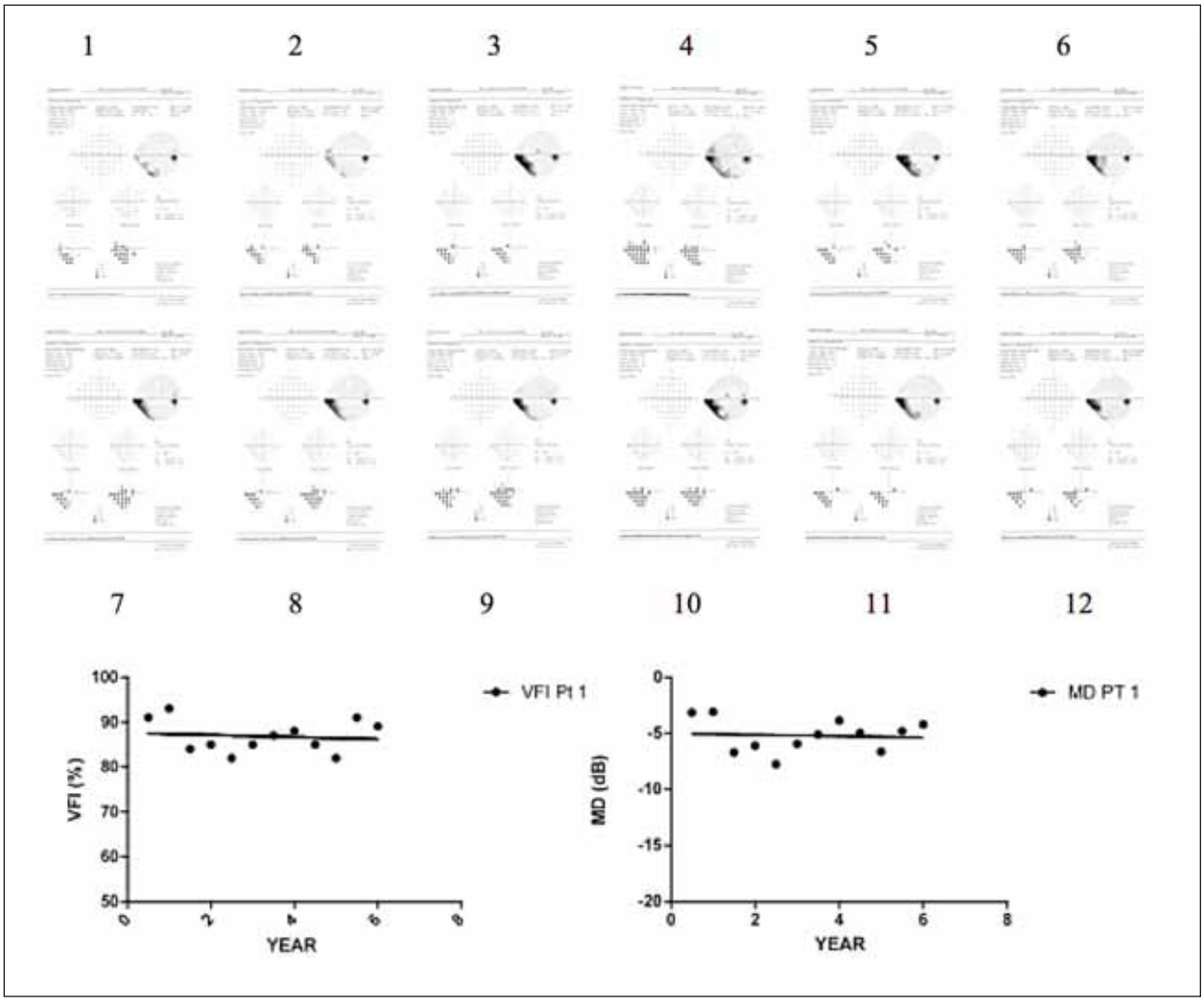

Figure 1. The VFI and mean deviation of the right eye of a glaucoma patient determined over 12 different testing procedures display no indication of visual field progression.

spread or diffuse loss of sensitivity. These modifications improved the performance of this analysis, but it only indicated a change of sensitivity from baseline for one to three follow-up visual fields and did not take into account information from other interim tests that had been performed. Thus, change could be determined, but the magnitude and rate of change were not directly evident from this analysis.

Two procedures that provide this information are the Progressor analysis program[9] and the visual field index (VFI).[4] By performing a least squares linear regression of visual field sensitivity for individual visual field test locations over time (successive perimetric examinations), Progressor determines the intercept (baseline sensitivity estimate) and slope (rate of change in sensitivity). A color-coded graphical display indicates for each visit and visual field location whether the sensitivity has remained stable (slope not statistically significantly different from zero) or has a low-to-moderate suspicion of progression or improvement (slope that is statistically significantly different from zero at $P < .05$) or a high suspicion of progression or improvement (slope that is statistically significantly different from zero at $P < .01$). A test location is considered to have undergone significant progression if the rate of change is greater than -1.0 dB per year and the slope of sensitivity over time is negative and statistically significant at $P < .01$. The implementation of additional analytical techniques and spatial filtering procedures has also improved the performance of this analytical method.[10-12] Progressor is most useful for determining localized glaucomatous visual field changes over time.

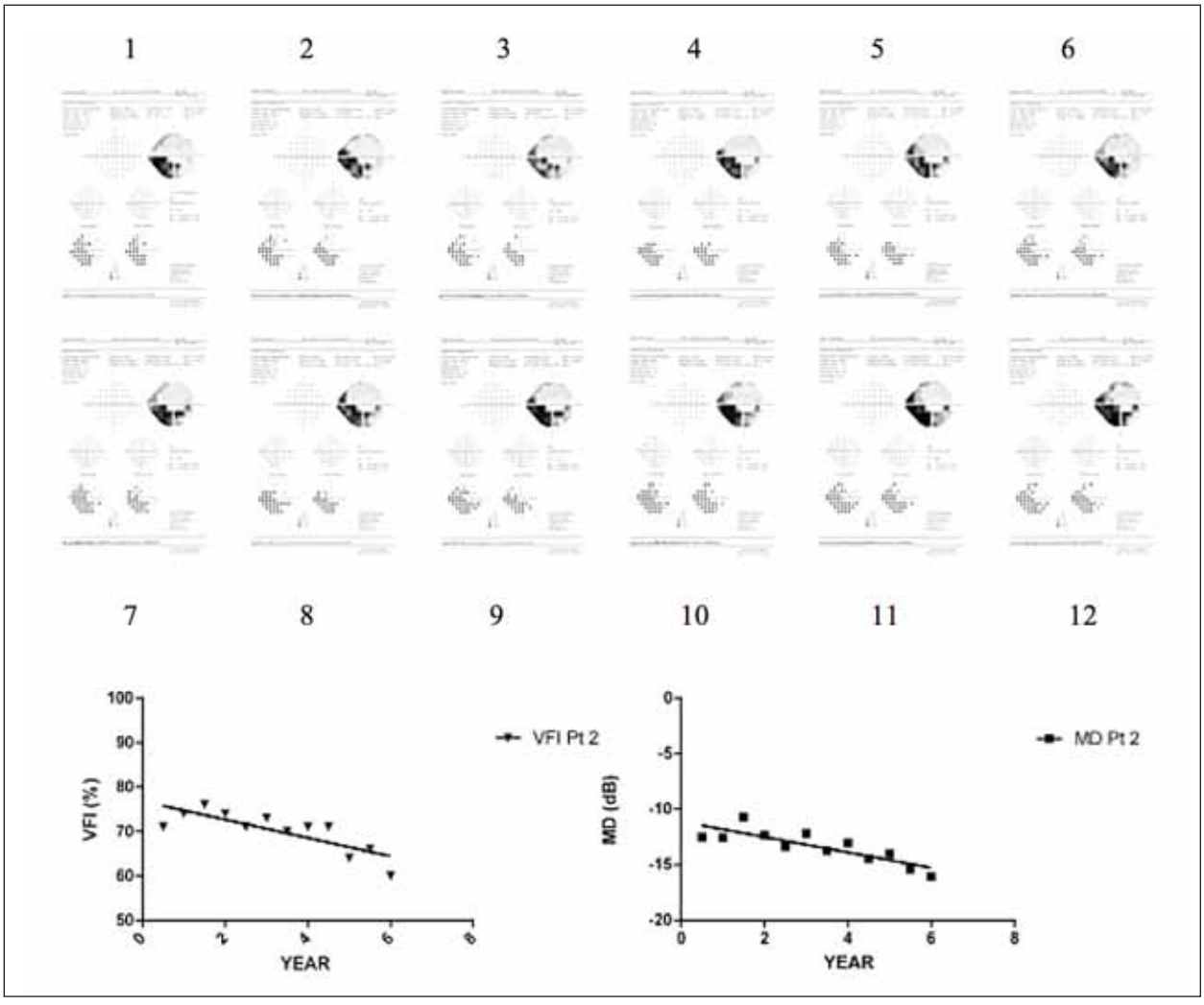

Figure 2. The VFI and mean deviation of the right eye of a glaucoma patient determined over 12 different testing procedures clearly indicate visual field progression.

The VFI evaluates the rate of visual field progression over time.[4] Unlike Progressor, the VFI is designed to indicate the overall general status of the glaucomatous visual field, ranging from normal (100%) to end-stage glaucoma (0%). The procedure requires a minimum of five follow-up visual fields, and it conducts a linear regression of the glaucoma progression index that is based on pattern deviation values (to minimize the influence of cataract progression). The VFI provides greater weight for central points than peripheral test locations, and it predicts visual field status over the next 5 years. Figures 1 and 2 demonstrate the value of this approach.

Figure 1 shows early glaucomatous visual field damage in a patient's right eye. Visual fields were obtained every 6 months for 6 years. There is a suggestion of progression when comparing two successive visual fields (eg, from visual field No. 2 to visual field No. 3), but the lower graphs indicate that the VFI remains essentially unchanged over the 6-year follow-up. Figure 2 presents the right eye of a patient with more advanced glaucomatous visual field loss over a 6-year period (testing every 6 months). When comparing two successive visual field examinations, it is difficult to determine whether the visual field loss has progressed, but the lower graphs indicate a steady loss of visual field sensitivity over time. Thus, the VFI can be a useful clinical tool for the management of glaucoma patients and for following the visual field over time.

OPTIC DISC PROGRESSION SOFTWARE

Similar to progression techniques for glaucomatous visual field loss, the use of imaging devices to measure the topography of the optic nerve and RNFL provide

greater standardization, reliability, and consistency than subjective clinical assessments of ophthalmoscopic viewing or evaluation of optic disc and RNFL photographs. Additionally, event analysis and trend analysis are the techniques that are most commonly used for evaluating the optic disc and RNFL.

Scanning Laser Tomography

The Heidelberg Retina Tomograph (Heidelberg Engineering GmbH, Heildelberg, Germany) is a commonly used confocal scanning laser tomography system that provides a three-dimensional reconstruction of the optic disc and RNFL. The Topographic Change Analysis uses superpixels (4 X 4 arrays of 16 pixels) to compare follow-up images with baseline measures to determine whether they are within the normal 95% confidence limits of variability or if they are statistically significantly better (green color-coding) or worse (red color-coding).[13-15] The system also performs a trend analysis (linear regression) of changes in key parameters (rim area, rim volume, cup volume, cup shape, mean RNFL thickness, mean height of contour, mean contour elevation, contour line modulation temporal, mean cup depth, mean height inside contour line, and a combination of these parameters).[13-15]

Scanning Laser Polarimetry

This technique presents a scanning polarized laser beam to the optic nerve and RNFL to measure the retardation of reflected light produced by the birefringent properties of the retinal nerve fibers. The primary analytical procedure is Guided Progression Analysis, which is an event analysis technique that compares the retardation patterns of follow-up images to a baseline image. Locations that are outside normal limits of variability due to RNFL thinning are indicated as possible progression ($P < .05$) and likely progression ($P < .01$). This is done not only for the entire RNFL region but also for the temporal, superior, nasal, inferior, and temporal (TSNIT) nerve fiber bundle regions.[16]

Optical Coherence Tomography

Optical coherence tomography uses low-coherence interferometry to produce reflective images that provide differential signals from structures in the retina and optic nerve. The use of image segmentation procedures and feature analysis techniques permits optical coherence tomography to identify different layers of the retina, fluid, and other structural elements. Linear regression techniques and event analysis (Guided Progression Analysis) are used to measure changes in the RNFL and optic disc over time.[17]

CONCLUSION

The procedures described in this article offer glaucoma practitioners methods that are standardized, consistent, easy to interpret, and less variable than individual clinical judgments. These tools are of great value in the clinical management of patients with glaucoma and glaucoma suspects. Future research is needed to determine the best method of following glaucomatous progression and to achieve a consensus among glaucoma practitioners. ❑

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1. Spry PGD, Johnson CA. Identification of progressive glaucomatous visual field loss. *Surv Ophthalmol*. 2002;47:158-173.
2. Vesti E, Johnson CA, Chauhan BC. Comparison of different methods for detecting glaucomatous visual field progression. *Invest Ophthalmol Vis Sci*. 2003;44:3873-3879.
3. Smith SD, Katz J, Quigley HA. Analysis of progressive change in automated visual fields in glaucoma. *Invest Ophthalmol Vis Sci*. 1996;37:1419-1428.
4. Bengtsson B, Heijl A. A visual field index for calculation of glaucomatous rate of progression. *Am J Ophthalmol*. 2008;145:343-353.
5. Viswanathan, Crabb, McNaught, et al. Interobserver agreement on visual field progression in glaucoma: a comparison of methods. *Br J Ophthalmol*. 2003;87:726-730.
6. Brusini P, Johnson CA. Staging functional damage in glaucoma: review of different classification methods. *Surv Ophthalmol*. 2007;52:156-179.
7. Morgan RK, Feuer WJ, Anderson DR. Statpac 2 glaucoma change probability. *Arch Ophthalmol*. 1991;109:1690-1692.
8. Heijl A, Leske MC, Bengtsson B, et al; Early Manifest Glaucoma Trial Group. Measuring visual field progression in the Early Manifest Glaucoma Trial. *Acta Ophthalmol Scand*. 2003;81(3):286-293.
9. Viswanathan AC, Ftizke FW, Hitchings RA. Early detection of visual field progression in glaucoma: a comparison of PROGRESSOR and STATPAC 2. *Br J Ophthalmol*. 1997;81:1037-1042.
10. Gardiner SK, Crabb DP. Examination of different pointwise linear regression methods for determining visual field progression. *Invest Ophthalmol Vis Sci*. 2002;43:1400-1407.
11. Gardiner SK, Crabb DP, Fitzke FW, Hitchings RA. Reducing noise in suspected glaucomatous visual fields by using a new spatial filter. *Vis Res*. 2004;44:839-848.
12. Strouthidis NG, Scott A, Viswanathan AC, et al. Monitoring glaucomatous visual field progression: the effect of a novel spatial filter. *Invest Ophthalmol Vis Sci*. 2007;48:251-257.
13. Chauhan BC. Detection of glaucomatous changes in the optic disc. In: Fingeret M, Flanagan J, Liebmann J, eds. *HRT Primer*. San Ramon, CA: Jocoto Advertising; 2005:53-65.
14. Chauhan BC, Blanchard JW, Hamilton DC, LeBlanc RP. Technique for detecting serial topographic changes in the optic disc and peripapillary retina using scanning laser tomography. *Invest Ophthalmol Vis Sci*. 2000;41:775-782.
15. Chauhan BC, McCormick TA, Nicolela MT, LeBlanc RP. Optic disc and visual field changes in a prospective longitudinal study of patients with glaucoma: comparison of scanning laser tomography with conventional perimetry and optic disc photography. *Arch Ophthalmol*. 2001;119:1492-1499.
16. Alencar LM, Zangwill LM, Weinreb RN, et al. Agreement for detecting glaucoma progression with the GDX guided progression analysis, automated perimetry, and optic disc photography. *Ophthalmology*. 2010;117:462-470.
17. Leung CK, Cheung CY, Weinreb RN, et al. Evaluation of retinal nerve fiber layer progression in glaucoma: a study on optical coherence tomography guided progression analysis. *Invest Ophthalmol Vis Sci*. 2010;51:217-222.