The Humphrey Visual Field Analyzer (HFA; Carl Zeiss Meditec, Inc., Dublin, CA) can be equipped with Glaucoma Progression Analysis (GPA) software, which assists clinicians in their evaluation of serial visual fields by identifying areas where progression may be occurring. Currently, this software is available only for standard (white-on-white) visual fields, programs 24-2 or 30-2. It can be used with Swedish Interactive Threshold Algorithm (SITA)-Standard1 and SITA-Fast2 testing strategies (both from Carl Zeiss Meditec, Inc.) for baseline and follow-up examinations. It can also use full-threshold tests as baselines, thereby facilitating a switch from one threshold strategy (full) to another (SITA-Standard) in the same patient. SITA-Fast has not been evaluated in a clinical trial setting for following glaucoma, and this author does not recommend its use for progression analysis.

This article focuses on the clinical application of the GPA software.

THE RATIONALE FOR THE GPA SOFTWARE

GPA is similar to the algorithm employed in the Early Manifest Glaucoma Trial (EMGT),3 a multicenter study that evaluated the effect of treatment versus no treatment on eyes with early glaucoma. GPA differs from a previous HFA algorithm, the Glaucoma Change Probability analysis. The former uses the pattern deviation plot values rather than the total deviation values used by the latter. The rationale is that change in the total deviation values over time may be due to factors other than glaucoma such as advancing cataract or decreased pupillary size.4 By using the pattern deviation values, the GPA software specifically targets the localized change associated with glaucoma. If there were a diffuse component to the glaucomatous change, it would not be reflected in the GPA result, but the more likely localized component due to the formation of new glaucoma-defects or the expansion and deepening of existing defects would be characterized.

HOW DOES THE GPA SOFTWARE WORK?

The GPA software compares a patient’s baseline visual fields (two are needed and are averaged) to each subsequent visual field in a series. Every test location in each follow-up field is evaluated relative to the baseline. Change is flagged if it is greater (at the 95% significance level) than the variability seen in a large group of stable glaucoma patients who were tested over a very short period of time. In addition, the GPA accounts for the known increase in variability found with advancing disease and increased eccentricity.

Data from the EMGT and other clinical studies,3,5,6 using an algorithm similar to GPA, have suggested that change needs to be present in three consecutive visual fields before progression can be confirmed. When change is first noted on a field at a given location, the GPA software will automatically assess the next visual field (and the next) to determine if that change is repeatable.

The EMGT also required change to be repeatable in the same three or more points. Two or three scattered locations with change on a single visual field are not uncommon in stable patients. The GPA software also determines if the same three or more points are flagged on two or three fields.

RUNNING THE GPA SOFTWARE

The GPA software automatically selects the patient’s first two tests (either full-threshold or SITA) as the baseline, and then it evaluates each subsequent test (SITA only) relative to those two baselines. Although the algorithm will automatically deselect baseline tests showing too many false-positive responses, it is important that the clinician evaluate the two tests chosen to rule out excessive losses of fixation or false negatives, inattention, fatigue, or an obvious
learning effect in patients new to visual field testing. Large differences in the pattern and the location of field loss seen in the two baselines may indicate that one of them is not a suitable choice. It is possible to manually override the GPA software in these instances and specify which two tests the clinician would like to set for the baseline. The program will then remember the chosen baselines and automatically add each follow-up examination to the analysis.

There are other instances when new baseline tests should be chosen. If progression has occurred and there is a resultant change in therapy, the clinician should establish a new baseline so that any additional progression can be found. If the patient undergoes ocular surgery or develops another ocular condition, new baseline tests after he stabilizes should be selected for use in evaluating subsequent examinations.

It is important that technicians always enter the patient’s name and/or identification numbers in exactly the same way at each visit so that all of his tests will be available for automatic selection by the GPA software.

**INTERPRETING THE GPA SOFTWARE**

**Overview**

Figures 1 and 2 show the printouts giving the baseline results from two sample patients, one with early and one with advanced field loss. The printouts give much of the same information found on the single field printout and allow clinicians to assess whether the chosen baselines are appropriate.
The grayscale, absolute threshold values, total and pattern deviation probability plots, and mean deviation and pattern standard deviation global indices are provided. Losses of fixation, false negatives, and false positives are also shown so that clinicians can assess the reliability of the two fields.

At the bottom of the printouts appears a mean deviation plot for all of the examinations in the series. This section gives the slope associated with change in the mean deviation. It is important to remember that this change will include anything that affects the subject’s visual sensitivity, including advancing cataract, and that it may not reflect change due to glaucoma.

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Figures 3 and 4 show the GPA printouts for follow-up of the aforementioned sample patients. When change is first noted on a follow-up field at a given location, an open triangle appears at that location on the printout. The GPA software will automatically assess the next visual field (and the next) to determine if that change is repeatable. If it is present on two consecutive tests, a half-filled triangle will appear at the location. For repeatable change on three consecutive tests, a closed triangle will appear.

The GPA software then assesses the repeatability of three or more points and gives a plain-language report of “possible progression” if two consecutive fields show that the same three or more points changed from baseline or “likely progression” if three consecutive fields show change at the same three or more points.
Is It Really Progression?

The GPA software is designed to assist clinicians in looking for progression based on visual field results. Although it goes a long way toward verifying change, physicians should use the system’s findings in conjunction with other clinical information to determine if a report of “likely progression” is reasonable and not due to factors other than glaucoma. Again, it is important that all of the fields in the series be reliable and that the appropriate baselines be chosen.

THE FUTURE

The GPA software provides a type of events analysis of progression. It does not directly provide a rate of change due to glaucoma. Subtle, slow progression that finally exceeds the probability limit for change is not easily differentiated from a larger change reaching the same limit more quickly. An estimate of the rate of progression would be helpful in determining how aggressive treatment should be for a given individual. More sophisticated algorithms are under evaluation in research settings. For example, one such algorithm-using machine that is learning classifiers can assess the progression of specific patterns of glaucomatous defects, provide a verification of change, and estimate the rate of change. These algorithms are not yet available for clinical use.

At present, the GPA software represents a significant improvement over previous HFA progression algorithms. It provides clinicians with information they need to identify and verify change in serial visual fields that is likely due to progressing glaucoma.

Pamela A. Sample, PhD, is Professor and Director of Clinical Vision Research at the Hamilton Glaucoma Center, Department of Ophthalmology, University of California, San Diego. She has received research support in the form of test equipment from Carl Zeiss Meditec, Inc., Welch Allyn Medical Products, and Haag-Streit AG. Dr. Sample may be reached at (858) 534-6629; psample@glaucoma.ucsd.edu.