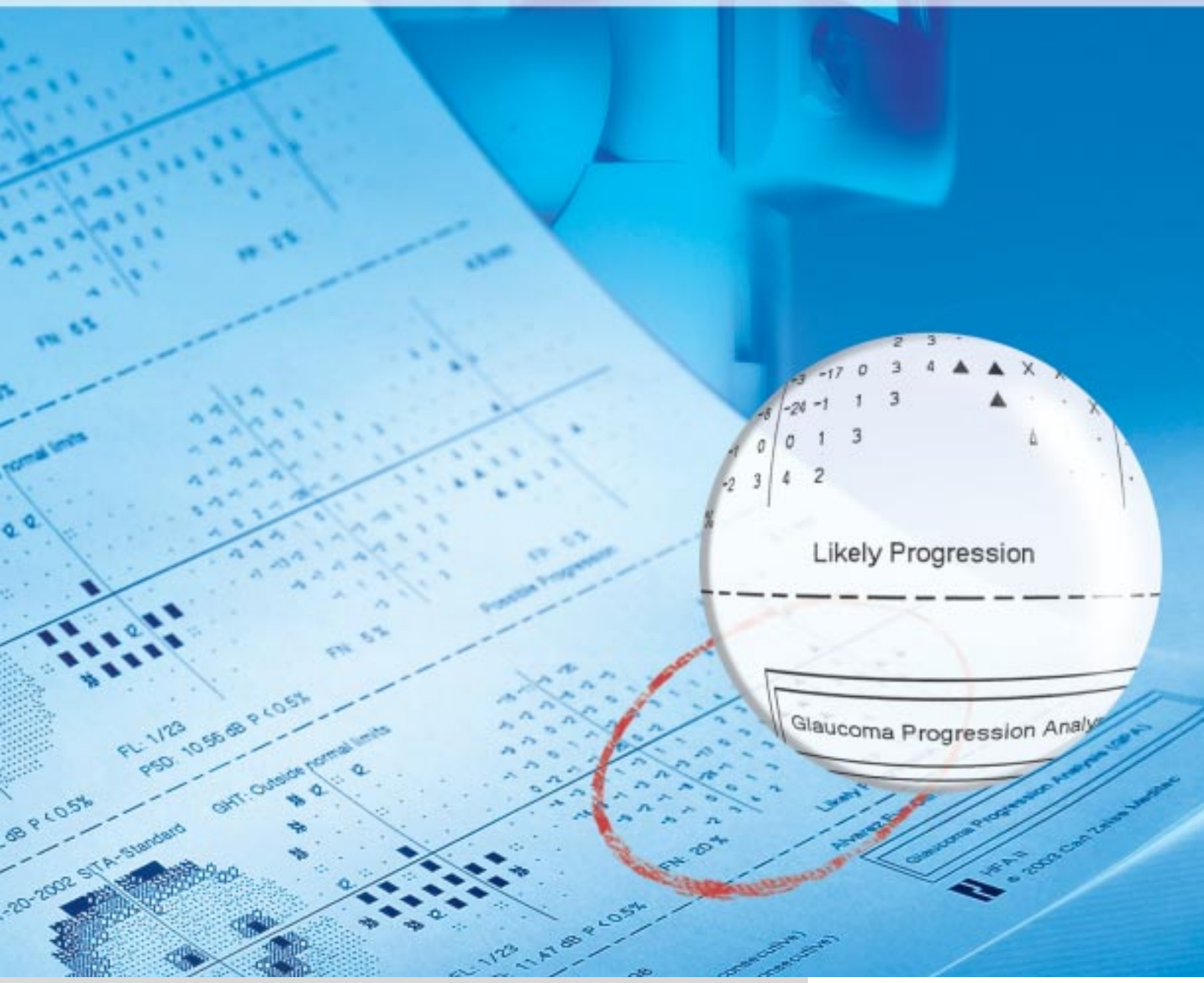
Humphrey® Glaucoma Progression Analysis™ (GPA™) Software

An advanced approach to monitoring disease progression



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ZEISS

Humphrey® Glaucoma Progression Analysis™ (GPA™) Software

Humphrey® Glaucoma Progression Analysis™ (GPA™) Software helps practitioners accurately identify clinically significant progression of visual field loss in glaucoma patients.

The GPA™ highlights any changes from selected baseline exams that are larger than typical clinical variability – as shown in Figure 1, and provides simple plain-language indicators whenever changes show consistent and repeatable patterns of loss. The software analyzes a series of visual field exams (white Size III stimulus) obtained using the Full Threshold, SITA™ Standard and SITA™ Fast testing strategies. The analysis corrects for ocular media effects in order to help the practitioner differentiate between localized loss typical of glaucoma, and overall depression caused, for instance, by progressive cataracts or other media[1].

The analysis is based upon detailed empirical knowledge of the variability found at all stages of glaucomatous visual field loss through knowledge gained in extensive multi-center clinical trials in North America, Europe, and Asia. The plain-language analysis (GPA Alert™) is based upon the criteria used for ten years in the Early Manifest Glaucoma Trial.

Adding Value To Your Practice

- **Simplifies interpretation and improves clinic flow**
- **Accounts for random variability in visual field analysis**
- **Brings the power of the Early Manifest Glaucoma Trial (EMGT[2]) progression criteria into your practice**
- **Compatible with both Full Threshold and SITA™ strategies**
- **Helps identify rapidly-progressing patients**

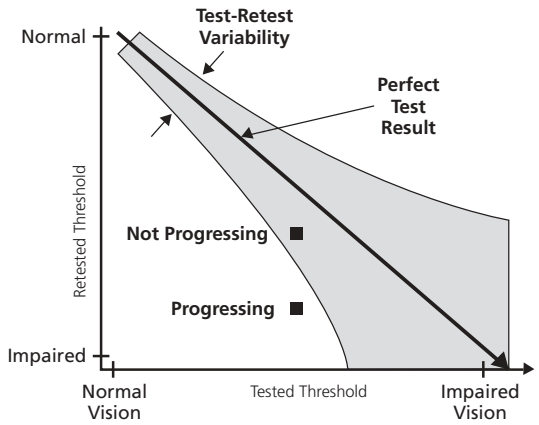


FIGURE 1: Test-Retest Variability in Perimetry

Easy to Use

Designed for Compatibility and Flexibility

GPA™ simplifies the process of incorporating progression analysis into everyday practice. The GPA™ is compatible with the SITA™ Standard and SITA™ Fast testing strategies, and also offers the flexibility of using Full Threshold tests for baseline when necessary. Your new software will be compatible with, and applicable to, your current database of patient test results.

Automated Exam Selection

The GPA™ software is designed for easy use and implementation, and no special staff training or instruction is required. The test selection and set-up procedures are automated to assist your staff in running an accurate analysis. And once GPA™ is set up for a patient, the software retains your choice of baseline tests and automatically adds every new follow-up exam to the analysis.

Verifies Exam Reliability

The GPA™ software assists you in selecting the highest quality exams to produce the best analysis. If the False Positive or Fixation Loss reliability indices exceed acceptable tolerances, the GPA™ software will alert you by generating a **Low Test Reliability** message. Tests showing excessive False Positive response rates are automatically excluded from use in the baseline.

Easy to Understand

Familiar & Simple Printouts

Tests chosen as baseline are presented in the familiar Humphrey® STATPAC™ Overview format. Follow-up tests are then analyzed for the amount of decibel change at each test point (Deviation from Baseline) and whether each change was significant (Progression Analysis Plot).

Points which have changed by more than the expected variability are identified using a simple and intuitive set of symbols:

△ **Open triangle**
Identifies any test point that has worsened by an amount that exceeds the variability expected in all but the most variable five percent (p<0.05) of glaucoma patients having similar visual field status. Thus the symbol is only shown if the change is larger than 95% of the variability seen at that exact test location in fields having a similar Mean Threshold Deviation from normal values.

◭ **Half-filled triangle**
Identifies points changing at the p<0.05 significance level in two consecutive follow-up exams.

▲ **Filled triangle**
Identifies points changing at the p<0.05 significance level in three consecutive follow-up exams.

GPA Alert™ – Plain Language Interpretation

Progression is defined as statistically significant change that is also clinically repeatable and consistent. When significant degradation is seen in the same three or more points on two consecutive follow-up tests, the GPA™ software interprets the patterns for you and automatically alerts you to ***Possible Progression.***

A significant change from baseline in the same three or more points in three consecutive follow-up tests will alert you to ***Likely Progression.***

Using Test Variability as a Tool

GPA™ relies on detailed empirical knowledge of visual field variability typically found in everyday real-world glaucoma patients. Those fields that repeatedly and consistently show changes exceeding what is known to represent typical variability are identified as having "possible" or "likely" progressive visual field loss.

Precisely quantifying the actual range of variability was critical to the development of GPA™. Hundreds of glaucoma patients covering the full disease spectrum, from early to advanced glaucoma, were tested worldwide. Each patient attended the clinic four times in the space of one month, and underwent three visual field tests at each visit – one SITA™ Fast, one SITA™ Standard, and one Full Threshold strategy. Variations seen from visit to visit were used to define the expected and normal test-retest reproducibility for glaucomatous visual fields.

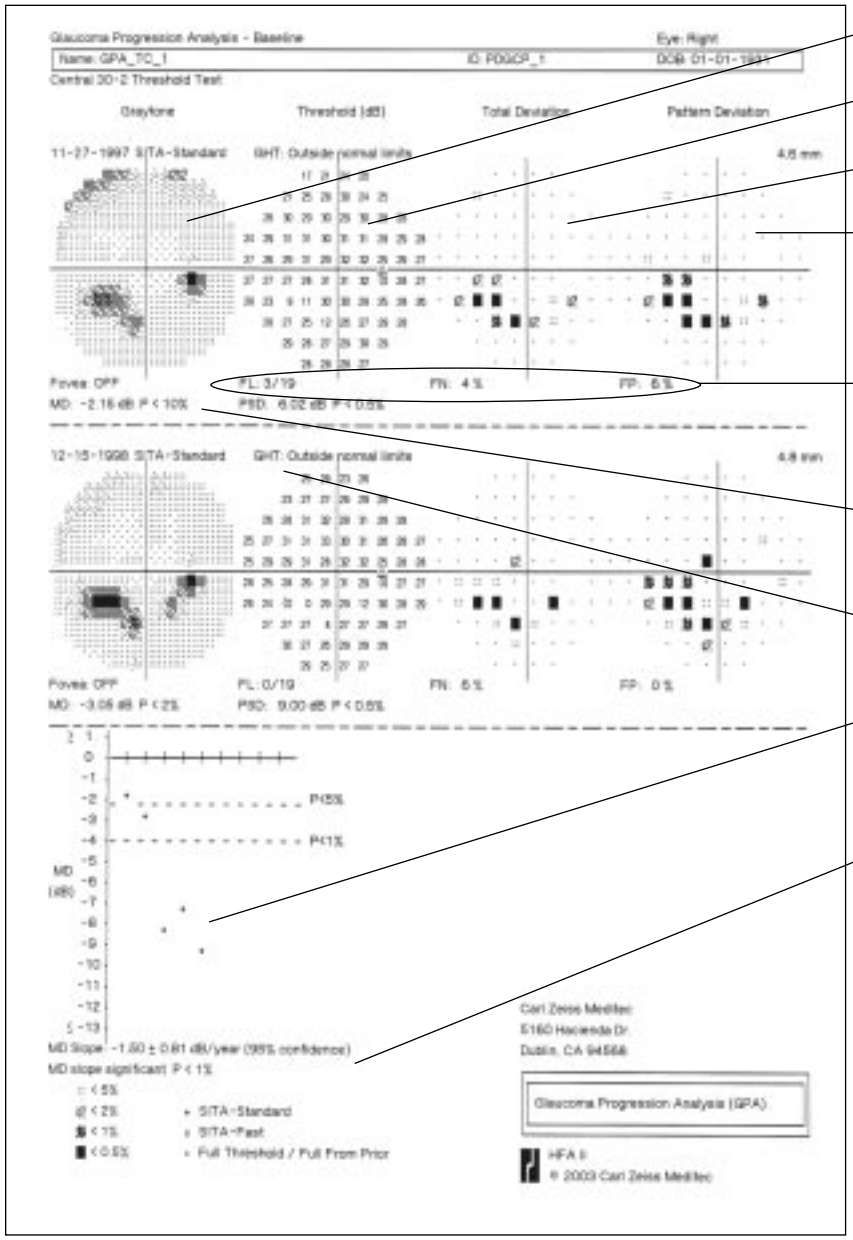
The test-retest variability depends upon a number of factors – as shown in Figure 2. New mathematical methods were developed to calculate the expected variability ranges, and the resulting significance limits have been validated manually using multiple confirmatory methods. Because an understanding of the complex patterns of patient variability are built into the GPA™ analysis, it is no longer necessary to use "rules of thumb" in trying to decide whether a change is significant.

Factors Contributing to Variability[3,4]

- **Eccentricity in the field**
- **Field status as measured by Mean Deviation**
- **Point status – deviation from normal at each individual point**
- **Patient experience in perimetric test-taking**
- **Threshold strategy used**

FIGURE 2

GPA™ Printout (Baseline)



Baseline Test Result

Grayscale Plot

Threshold Values

Total Deviation Probability Plot

Pattern Deviation Probability Plot

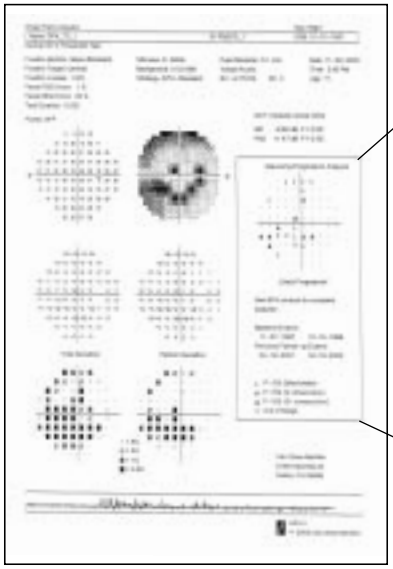
Reliability Indices:
FL: Fixation Losses
FN: False Negative Responses
FP: False Positive Responses

MD: Mean Threshold Deviation from Normal Values

GHT: Results of the Glaucoma Hemified Test

Mean Deviation Plot: All Exams Included in the Analysis

MD Slope: Provides One Method of Tracking Rate of Progression



Single Field Analysis

GPA™ Printout (Follow-up and Single Field Analysis)

Glaucoma Progression Analysis Results

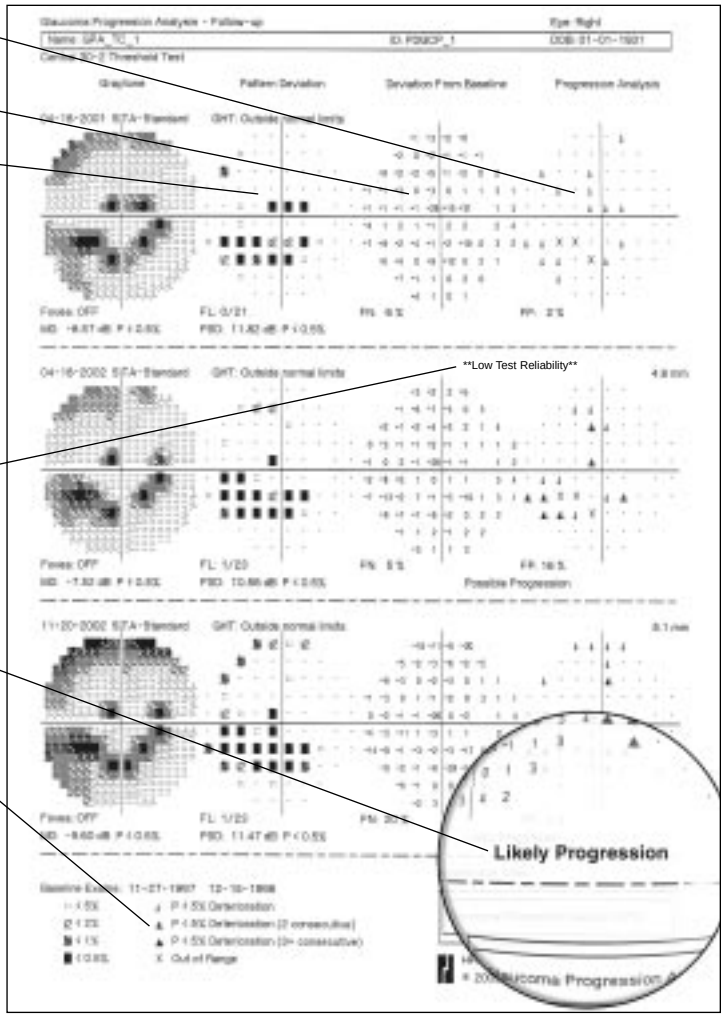
Deviation From the Baseline: (dB)

Pattern Deviation Probability Plot

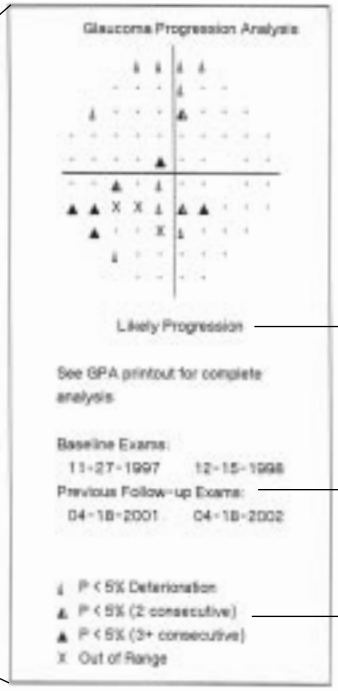
Low Test Reliability: Warning Appears When False Positives or Fixation Losses Exceed Tolerable Levels

GPA Alert™

Key for Understanding GPA™ Symbols



Follow-up Test Result



GPA™ Results

GPA Alert™

Identification of Exams Included in GPA™: Identifies Two Baseline and Most Recent Two Follow-up Exams

Key for Understanding GPA™ Symbols

Integrating GPA™ into your practice

Raising The Standard of Care

Establishing whether glaucoma patients are stable or are experiencing progressive damage has long been one of the most challenging problems faced by eye specialists. One of the missions of the Humphrey® GPA™ is to provide a standard, well-documented tool that can be used by doctors worldwide in measuring progression.

Additionally, determining the rate of progression helps identify high-risk patients. The GPA™ estimates the progression rate using a regression analysis of the Mean Deviation. Other more sophisticated methods of rate analysis which may allow more refined applications of this basic principle are now under development.

Creating an Accurate Glaucoma Progression Analysis

All SITA™ Standard and SITA™ Fast tests resident in your HFA II or HFA II-*i* perimeter database are eligible for inclusion in the analysis. Tests completed using the Full Threshold strategy may be used as Baseline, but not as Follow-up.

GPA™ is easy for your staff to implement. A simplified graphical interface guides the user through each step in the process, from selection of baseline tests to choice of data presentation format. The instrument remembers which tests have been designated as baseline, making it unnecessary to repeat the process at each visit.

Establishing a baseline

While GPA™ is designed to automate the baseline selection process, it is important that the tests chosen for baseline be both reliable and representative of the patient's test-taking ability.

The GPA™ software selects baseline tests by identifying the earliest two tests that are both either Full Threshold or one of the SITA™ strategies. If there are at least three SITA™ tests – either all SITA™ Standard or all SITA™ Fast – the GPA™ software will choose the earliest two SITA™ tests for baseline in order to ensure the most accurate analysis is provided.

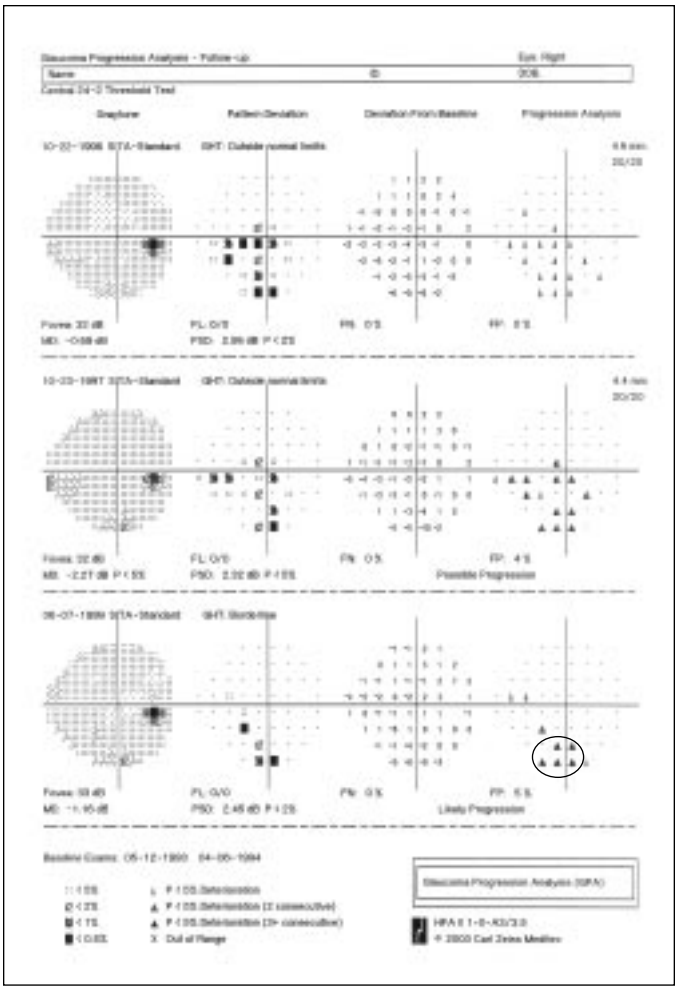
In any case, the operator always has the option of over-ruling the automated choices if necessary. For instance, patients who are taking their first threshold perimetry test frequently produce unreliable fields. If the field appears to be unreliable, or if the first field looks significantly worse than the second, it is recommended that you designate the second and third examinations as baseline. Sometimes, even experienced patients have sessions that produce clearly unreliable results. These examinations should not be included, and can be manually removed from the analysis.

Choosing to re-baseline a patient

From time to time, it is prudent to review the current baseline exam choices, particularly when any of the following events occur during the course of managing a patient's disease:

- If current baseline exams are Full Threshold strategy, you should switch to SITA™ once three exams are available
- After a significant change in course of therapy
- Following ocular surgery or significant trauma to the eye
- As mentioned above, if learning curve effects are suspected or retrospectively identified

CASE STUDY 1



This series of follow-up tests shows a pattern of visual field loss that is typical of developing glaucoma. The five test points (circled) show significant change in all three follow-up tests, resulting in a GPA Alert™ of Likely Progression.

Responding to Confirmed Progression

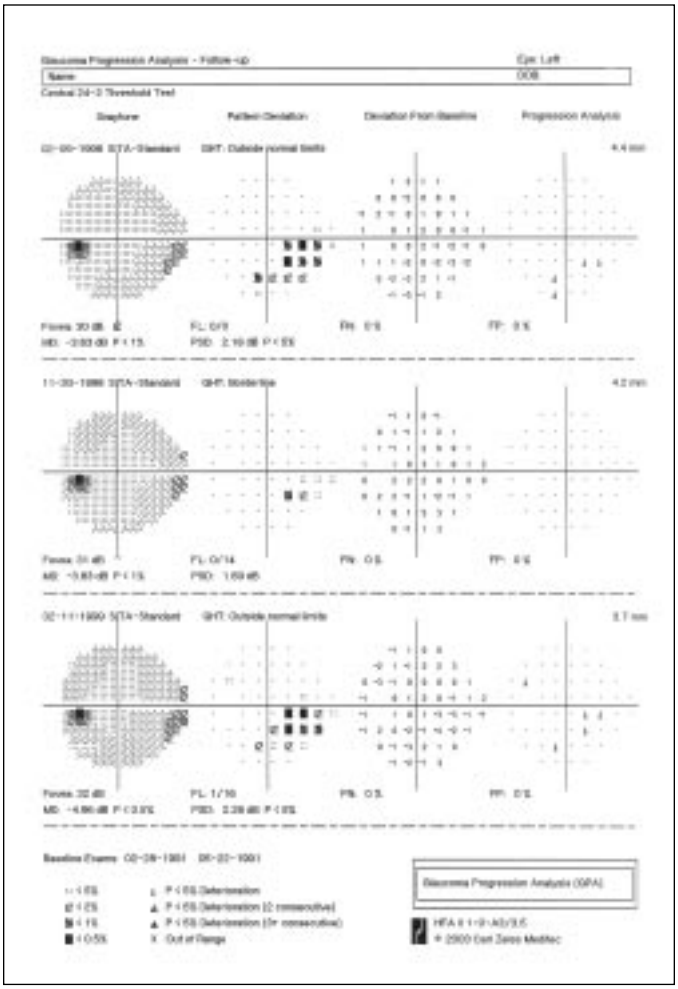
Small triangles on the Progression Analysis plot identify statistically significant change. True glaucoma progression, however, is defined by repeatable, consistent change, as identified by the GPA Alert™ and confirmed by other clinical observations.

Understanding the Symbols

Open Triangles △

An open triangle denotes a point that has progressed at least one time, when compared to the baseline exams. Since we are measuring at the 95% significance level ($p<0.05$), 2 to 3 open triangles (out of the 76 stimuli in a 30-2 exam) can be expected in any given comparison of a follow-up exam to the baseline exams, based upon chance alone. While it is important to follow these points, scattered open triangles are not uncommon in stable patients.

CASE STUDY 2



This series of follow-up tests shows a typical pattern of glaucomatous visual field loss but the location of progressing test points is inconsistent from test to test. The absence of a GPA Alert™ confirms that this is patient variability rather than progression.

Arranging another follow-up exam or confirming progression with other methods of diagnosis is the recommended response. Seeing change for the first time, however, should mark the beginning of the trend analysis that will be used to follow a patient over time.

Half and full triangles ◭ ▲
In general, a minimum of four exams is required to confirm progression – two baseline fields and two follow-up fields. All points showing deterioration in two consecutive follow-up tests are marked with a triangle that is half black and half white. A full triangle denotes a point that has shown significant change in three sequential exams.

GPA Alert™ – Possible and Likely Progression
Years ago, when automated perimetry was first introduced, doctors analyzed visual field results by applying rough "rules of thumb" to the approximate seventy-six threshold sensitivities found on the printout. Even in those early days, doctors looked forward to a time when the confusing threshold data could be replaced by expert, plain-language analyses that could indicate whether or not the visual field was normal and whether the field had changed over time. While a viable solution to the normality question emerged in 1989, with the Glaucoma Hemifield Test, the invention of a reliable, expert progression analysis proved much more difficult.

The GPA Alert™ combines the science of what we now know about clinical test variability with practical clinical requirements – that change be consistent and repeatable. The result is a method we believe to be practical for everyday clinical interpretation of visual fields, from early to advanced stages of the disease.

A diagnosis of significant change in glaucoma status should be based upon the preponderance of clinical evidence. However, if based solely upon perimetric findings, such decisions require that significant change be seen in at least two follow-up tests and that the change be found consistently in the same locations in the visual field. The "Possible Progression" and "Likely Progression" **GPA Alert™** messages automatically identify when these requirements have been met relative to the baseline you have chosen.

Obviously, before ordering a change in therapy, it is prudent to re-confirm that the baseline tests used were appropriate and representative, and that the follow-up tests are reliable. It may also be appropriate to consider and, if possible, rule out causes of perimetric change other than glaucoma.

Establishing Rate of Progression
Once progression is confirmed, it may be helpful to establish the rate at which your patient is progressing. Studies[1] show that rate of progression varies widely from patient to patient and with GPA,™ you can estimate whether a patient is a fast or slow progressor.

The slope of the Mean Deviation from exam to exam is plotted on the baseline exam printout. This slope shows how quickly damage to the field is progressing, however if MD is <-15dB, a patient may appear to be progressing slowly since significant damage was present at the start of the analysis.

Assessing glaucoma progression and determining the rate of progression are critical components of the preferred practice guidelines recommended by both the European Glaucoma Society (EGS) and the American Academy of Ophthalmology (AAO).

It is our sincere hope that the Humphrey® GPA™ software will help you provide enhanced care for the glaucoma patients you manage.

Cataract •
Glaucoma •
Retina •
Refractive •

Technical Specifications

Glaucoma Progression Analysis™ (Test Parameters)

Type of Test:	Threshold
Test Pattern:	Central 30-2 and 24-2
Test Strategy-Baseline:	SITA™ Standard, SITA™ Fast, or Full Threshold
Test Strategy-Follow-up:	SITA™ Standard or SITA™ Fast
Stimulus color:	White
Stimulus size:	III
Fixation target:	Any
Foveal Threshold:	On or Off
Test speed:	Normal or Slow

References

1 Bengtsson B, Lindgren A, Heijl A, Lindgren G, Asman P, Patella M. Perimetric probability maps to separate change caused by glaucoma from that caused by cataract. Acta Opthalmol Scand. 1997 Apr;75(2):184-8

2. Heijl A, Leske MC, Bengtsson B, Bengtsson B, Hussein M, and the Early Manifest Glaucoma Trial Group. Measuring visual field progression in the Early Manifest Glaucoma Trial. Acta Ophthalmol Scand. 2003;81:286–293.

3. Bengtsson B, Heijl A. Inter-subject variability and normal limits of the SITA Standard, SITA Fast, and the Humphrey Full Threshold computerized perimetry strategies, SITA STATPAC. Acta Ophthalmol Scand. 1999;77(2):125–129.

4. Bengtsson B, Heijl A. Evaluation of a new perimetric threshold strategy, SITA™, in patients with manifest and suspect glaucoma. Acta Ophthamol Scand. 1998;76(3):268–272.

Call 800-342-9821 to upgrade your HFA II or HFA II-i

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