AN UPDATE ON STANDARD AUTOMATED PERIMETRY

A review of progression analysis and testing algorithms and a look ahead at future technologies.

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Perimetry is a valuable diagnostic method for assessing visual function in patients with glaucoma. In addition to identifying and quantifying vision loss at the time of initial diagnosis, perimetry plays a critical role in detecting glaucomatous progression and measuring the rate of change. The subjective nature of this testing modality results in variability and fluctuations between tests, presenting numerous challenges for clinicians seeking to determine the true progression of the disease and tailor therapy appropriately. In this article, Astrid Werner, MD, discusses two main approaches to determining glaucomatous progression—event-based and trend-based analyses—and reviews different analytical tools, including mean deviation plotted against time, guided progression analysis, and visual field index. She also provides an update on newer strategies, such as SITA Faster and 24-2C, which deliver essential data and reduce test duration, and she explores the role of AI in further enhancements of automated progression analysis.

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Figure 1. A trend-based Guided Progression Analysis from the Humphrey Field Analyzer. For this patient, the slope of the line of the visual field index (VFI) plotted over time is determined to be not significant (or, in other words, the VFI results are stable). This rate of progression is also projected forward to predict VFI results at age 80.
METHODS FOR DETECTING PROGRESSION

Clinical judgment is an unreliable method for detecting visual field progression. It should therefore be used in conjunction with trend-based and event-based analyses.

Trend-based analyses use global indices of visual function such as mean deviation (MD), visual field index, and pattern standard deviation plotted over time. Linear regression plots produce an estimated rate of change, and they can be extrapolated forward over a patient’s lifetime—a useful tool when weighing treatment options (Figure 1). These global measures of function are less influenced by intertest variability than are localized measures of visual function, but global indices can be affected by ocular conditions other than glaucoma. Additionally, because they are insensitive to localized loss, these measures can miss meaningful progression, especially early in the disease course.

In contrast, event-based analyses emphasize local visual function, which is inherently more variable than global visual function. Guided Progression Analysis (Carl Zeiss Meditec) is a widely used, automated, event-based analysis tool that emphasizes focal loss by comparing pattern deviation values at each test location to the average values from two baseline plots. Progression is flagged when the same three spots deteriorate beyond the 95% confidence interval threshold for intertest variability on three subsequent tests (Figure 2). Region-wise visual field data provide a compromise between trend-based and event-based analyses. This strategy involves looking at anatomically related clusters of points within the visual field. The EyeSuite software on the Octopus perimeter (Haag-Streit) can perform a trend analysis of 10 visual field sectors. It performs as well as an MD-based trend analysis but is more sensitive to localized loss. The Humphrey Field Analyzer (Carl Zeiss Meditec) offers the Glaucoma Hemifield Test as a region-wise assessment of visual function that is useful in the diagnosis of glaucoma but, to date, is not part of progression analysis algorithms (Figure 3).

OPTIMAL TESTING STRATEGY TO DETECT PROGRESSION

The inherent variability in SAP testing can make it difficult to distinguish true glaucomatous progression from measurement variability. In fact, point-wise variability increases proportionally to field loss, meaning that the timely detection of progression becomes even more challenging as the disease advances. Increasing test frequency is one strategy to decrease the time required to detect progression and minimize the undue influence of
a single test result on the apparent trajectory of the disease. However, real-life constraints limit the feasibility of performing multiple tests.

Several investigators have proposed evidence-based guidance on the optimal frequency of testing. Chauhan et al\textsuperscript{15} recommend six visual field tests in the first 2 years after glaucoma diagnosis to identify patients with rapidly progressing disease (>2 dB of MD loss per year) and decrease the time to detect this progression. Crabb et al\textsuperscript{16} developed a computerized model to determine the influence of testing frequency on the sensitivity and specificity of progression analysis tools, and they found that three tests per year optimized both measures.

More recently, Wu et al\textsuperscript{17} found that the time to detect disease progression decreased significantly when testing increased from once to twice per year. However, they also determined that, beyond this, the gains were smaller and that more frequent testing may not be an efficient use of resources. They recommend obtaining two baseline tests quickly and following with two tests per year as a general strategy that can reliably rule out rapid progression. Although this strategy provides a high negative predictive value for rapid progression, it cannot necessarily detect whether rapid progression is occurring or determine the rate of progression.\textsuperscript{18,19} Thus, individuals with more risk factors for disease progression and patients with higher than average test variability may be better served by more frequent testing.\textsuperscript{20}

**THE FUTURE OF IMPROVED DETECTION OF PROGRESSION**

Recently, AI has been applied to visual field progression analysis and has been shown to detect glaucomatous progression earlier and with more accuracy than currently available analytical tools.\textsuperscript{2} AI has also been shown to improve predictive models of future visual field loss.\textsuperscript{21} Further, AI can incorporate other data sources such as retinal nerve fiber layer OCT analysis into its predictive models to improve the detection of progression.\textsuperscript{22} This is an area of research that holds great promise for the future of automated progression analysis.

Fixation losses are a common source of error that can increase variability and decrease MD values. Fundus-tracking technology presents stimuli to specific areas of the retina under continuous visualization.\textsuperscript{23} This new approach does not require active fixation by the patient and can thus reduce error from fixation losses, thereby decreasing test time and the time required to detect progression.\textsuperscript{19}

**EXAMINING THE CENTRAL VISUAL FIELD**

The 24-2 and 30-2 (or similar) testing strategies are the clinical standard for evaluating glaucoma. However, these protocols emphasize peripheral vision, and they do not sample the macula adequately to enable consistent identification or characterization of central field defects. Recent research has shown that a significant proportion of patients identified as glaucoma suspects or as having preperimetric glaucoma actually have central visual field defects that can be detected on 10-2 tests.\textsuperscript{24-26} Because central vision has a significant impact on vision-related quality of life,\textsuperscript{27} some researchers have asserted that physicians should conduct 10-2 tests on all glaucoma suspects and patients with early glaucoma.\textsuperscript{28} Although this approach seems reasonable, the clinical benefit of this strategy is not yet clear. Incorporating 10-2 fields into routine glaucoma screening would require patients to undergo even more visual field tests as physicians also continue to monitor the peripheral field.

Further, an abnormal macular OCT scan is predictive of an abnormal 10-2 result,\textsuperscript{19,28} and thus the additional 10-2 test may not alter the physician’s clinical decisions.

The 24-2C grid was recently introduced to the Humphrey Field Analyzer 3 (Carl Zeiss Meditec) as a way to increase sampling within the macular region while continuing to monitor the peripheral field. The 24-2C grid adds 10 test points to the traditional 24-2 grid within the central 10° of fixation in locations commonly affected in glaucoma. The 24-2 and the 24-2C protocols perform similarly in terms of global assessments, but the additional 10 points in the latter result in a fourfold improvement in sensitivity for central field loss with a minimal addition of 20 to 30 seconds per test.\textsuperscript{29}

**DECREASING TEST TIME AND IMPROVING USER EXPERIENCE WITH SITA FASTER**

In 2018, Heijl et al\textsuperscript{30} introduced the Swedish Interactive Thresholding Algorithm (SITA) Faster, which significantly reduces test time compared with prior algorithms. Because age-corrected normal SITA threshold values have been identified, SITA Faster can test initial values closer to expected thresholds than prior algorithms, and only one reversal is required at primary test points (compared to two used in earlier SITA tests).\textsuperscript{30} This reduces test time by more than 50% from SITA Standard and 30% from SITA Fast to just under 3 minutes.\textsuperscript{30,31}

SITA Standard, SITA Fast, and SITA Faster perform similarly in terms of MD, visual field index, and Glaucoma Hemifield Test, and all three algorithms show low test-retest variability.\textsuperscript{30,31} False positive rates appear to be higher with SITA Faster compared with SITA Standard, likely because the testing conditions for SITA Faster, in which presentation intensities are initially set very near threshold, are more
difficult than the testing conditions for SITA Standard. Increased seeding point errors—defined as low sensitivity measurements at one or more of the four primary test locations of the 24-2 test grid—in SITA Faster may also reduce reliability and result in a false scotoma. Despite these sources of error, SITA Faster performs well in most clinical scenarios except in the setting of advanced field loss.

CONCLUSION

Although SAP technology has been available for decades, advances continue to improve physicians’ ability to use this technology effectively. Progression analysis tools and appropriate testing frequency can help physicians to detect progression earlier and with greater certainty. Newer technologies, such as AI, may further refine testing capabilities. Moreover, SITA Faster and the 24-2C grid can improve patients’ experiences by obtaining critical visual field data more quickly than with other testing approaches.