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TARGET AUDIENCE
This educational activity is intended for general ophthalmologists, glaucoma specialists, and resident ophthalmologists.

LEARNING OBJECTIVES
- Discuss the importance for glaucoma diagnosis of structural changes to the optic disc and retinal nerve fiber layer
- List four structural changes to the optic disc and retinal nerve fiber layer associated with glaucoma progression
- State the issues that make the correlation of structural changes with functional loss difficult in glaucoma
- Explain why SITA testing is faster than full threshold perimetry
- List five key aspects of the optic nerve/retinal nerve fiber layer examination.
- Describe the process of detecting glaucoma progression using standard software programs that evaluate the results of automated perimetry

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SPECIAL FEATURE

Glaucoma: Diagnosis, Progression and Structure-Function Relationships

Felipe A. Medeiros, MD, Christopher Bowd, PhD, and Robert N. Weinreb, MD

From a clinical perspective, glaucoma is a progressive optic neuropathy with characteristic structural damage that is frequently accompanied by a specific type of visual field defect.[1,2] Although elevated intraocular pressure (IOP) is one of the most consistent risk factors for glaucoma, several population-based studies have documented optic disc and visual field damage characteristic of glaucoma in individuals with statistically normal IOP. Conversely, a large number of people with statistically raised IOP do not develop glaucoma even during lengthy follow-up.

No Consensus on Glaucoma Definition

A clear, widely agree-upon definition of glaucoma has proven elusive. This is illustrated by a review of 182 journal articles published on open-angle glaucoma (OAG) in three major ophthalmic journals. These articles were reviewed to identify the optic nerve, visual field, and IOP criteria used to define glaucoma. Of the 182 articles, 120 (66%) included a definition of OAG. Among these, approximately 36% used both optic disc and visual field criteria, 13% used optic disc or visual field criteria, 26% used only visual field criteria, 20% used only IOP, and 5% used only optic disc criteria.[3]

The absence of a consensus definition of glaucoma prevents accurate estimation of prevalence and the accumulation of valid clinical evidence on the effectiveness of treatment or risk factors for the disease. The effect of applying different commonly used criteria for diagnosis of open angle glaucoma has been examined.[4] Prevalence figures ranging from 0.1% to 1.2% in the same population were identified. The use of study-specific case definitions impairs the interpretation and comparison of research results.

The lack of a detailed case definition for glaucoma that can be applied in clinical practice results in considerable uncertainty about the diagnosis of this condition. This has relevance for clinicians because someone misdiagnosed with glaucoma may suffer a life of unnecessary treatment and follow-up, possibly resulting in a significant negative impact on the patient's

A Paradigm for Glaucoma Diagnosis

Both optic disc/RNFL and visual function evaluation are essential

- Corresponding structural or structural-functional abnormalities
  - Disc abnormality with corresponding RNFL defect
  - Disc (or RNFL) abnormality with corresponding functional defect

OR

- Progressive structural or functional change
  - Progressive change in optic disc, RNFL or visual field

Medeiros FA, Zangwill LM, Bowd C, Sample PA, Weinreb RN. Am J Ophthalmol 2005;139:1010-8

FIGURE 1 A paradigm for glaucoma diagnosis.

GLAUCOMA TOPICS&TRENDS

STATEMENT OF NEED AND PROGRAM DESCRIPTION Recent months and years have seen significant advances in our understanding of glaucoma. Much has been learned, not only about damage mechanisms and pathogenesis, but also about diagnosis and management. Treatment options—both medical and surgical—continue to expand. This program will review this new knowledge with an emphasis on incorporating recent insights into day-to-day practice.

GENERAL INFORMATION In order to receive CME credit, participants should read the report, and then go to our online test engine at: **http://cme.ufl.edu/selfstudy/glau/** After completing the posttest, a score of 70% is required to qualify for CME credit. You will be able to print your certificate at the completion of the posttest. There is no fee to participate in this activity. Estimated time to complete the activity is 60 minutes.

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mental status or physical health (from treatment side effects). On the other side of the coin, lack of knowledge about the clinical features of the disease, including the characteristic signs of glaucomatous damage to the optic nerve, can result in late diagnosis and irreversible loss of visual function.

Optic Disc Examination

With retinal ganglion cell death and nerve fiber loss in glaucoma, particular structural changes in the appearance of the optic nerve head are observed, including neuroretinal rim thinning and excavation. Other characteristic changes include vertical elongation of the cup, notching of the neuroretinal rim, presence of asymmetry in the cup-to-disc ratio measurements between the two eyes, splinter hemorrhage, parapapillary atrophy, and regional pallor. Retinal nerve fiber layer changes, in a localized and/or diffuse pattern, can be observed concomitantly with changes in the optic nerve head.

Progressive Optic Nerve Damage

Identification of progressive glaucomatous damage to the optic disc is one of the most important aspects of glaucoma management, yet it remains largely subjective and imprecise. Progressive change in the appearance of the optic disc or retinal nerve fiber layer (RNFL) often, but not always, precedes the development of visual field defects in glaucoma.[5] Since visual field defects on standard automated perimetry (SAP) may only be detected after a substantial number of nerve fibers ~~has~~ havebeen lost, assessment of the optic disc and RNFL is essential for monitoring the initial stages of the disease. Before the development of visual field defects, structural changes in the optic disc or RNFL may be the only evidence that the glaucoma is progressing and treatment needs to be intensified. Even in the presence of visual field defects, progression of optic disc damage may occur without any detectable evidence of functional deterioration.

Evaluation of Serial Optic Disc Photographs

Due to the wide variability of the optic disc appearance in the normal population, it is frequently not possible to establish the diagnosis of glaucoma based on a single examination of the optic disc, especially in the early stages of the disease. For some patients, a confirmed diagnosis can only be established by demonstrating change during follow-up (Figure 1).

Demonstration of change requires continued monitoring and documentation of the optic disc and RNFL appearance. Optic disc photographs are considered the gold standard for documentation and monitoring of optic disc appearance. Monocular photographs often fail to provide enough information on the contour of the optic disc cup to permit an adequate assessment of progressive changes. Therefore, whenever possible, stereo photographs should be used to document the optic disc appearance.

Signs of glaucoma progression on the optic disc can be very subtle and easily overlooked unless a meticulous examination is performed. Differences in magnification, focus, illumination, color, or stereopsis can influence the comparison between photographs, resulting in either false-positive or false-negative assessments of glaucoma progression. Changes in the color of photographs can produce changes in the rim color giving a false impression of progression. The characteristics of the neuroretinal rim and optic disc cup should be carefully compared between photographs. Progressive changes in the position of blood vessels are useful clues in detecting progressive rim loss. The position and location of deflection of blood vessels should be compared across all available photographs to uncover changes that may indicate neuroretinal rim loss in a specific sector.

When evaluating serial photographs, the examiner should compare the brightness and striations of the RNFL to detect the presence of diffuse or localized loss. The photographs should be compared for development of new wedge-shaped defects or enlargement of previously existing ones (Figure 2). Special attention must be given to the presence of optic disc hemorrhages, as they constitute one of the main risk factors for progression

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of glaucoma.

When evaluating disc photographs for progression, it is also important to observe the changes in the area of parapapillary atrophy, especially in the beta zone. Progression of parapapillary atrophy can indicate progressive glaucomatous damage to the optic nerve. An increase in the beta zone of parapapillary atrophy is associated with progressive neuroretinal rim loss in the corresponding optic disc sector and with progression of visual field defects in glaucoma.

Among the limitations of stereophotography for optic disc monitoring is the lack of consistency in the quality of photographs over time and the subjectivity involved in their interpretation. The quality of the comparison of photographs for detection of progression is often a function of the examiner's skill. To reduce the subjectivity of optic disc evaluation, several objective imaging methods have been developed, including confocal scanning laser ophthalmoscopy, scanning laser polarimetry, and optical coherence tomography. The application of these technologies to diagnosis and evaluation of glaucoma progression has been reviewed elsewhere.[6,7]

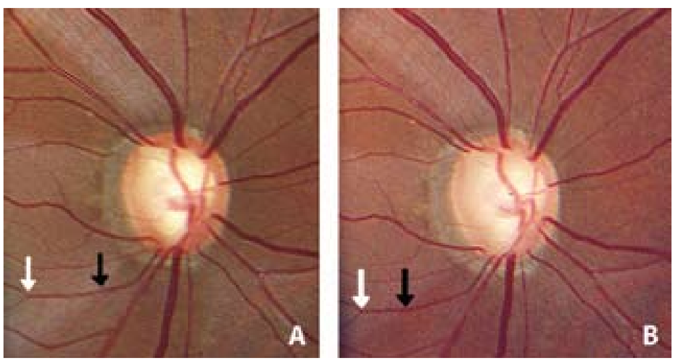

FIGURE 2 Progression of localized retinal nerve fiber layer defect. There is broadening of the wedge-shaped RNFL defect in B compared to A. Note that the border of the RNFL defect (black arrow) in B is closer to the bifurcation of the blood vessel (white arrow).

Progressive Visual Field Loss

Glaucoma affects several aspects of the visual function. The best known functional consequence of glaucoma is the progressive deterioration of visual field, which usually begins in the midperiphery, often in the superior field, and may progress in a centripetal manner to result in a remaining central or temporal island of vision in advanced cases. These characteristic visual field defects correspond topographically to the RNFL loss.

Other functional changes in glaucoma include loss of color sensitivity, especially for short-wavelength (blue) light, as well as loss of spatial resolution, motion detection, and temporal contrast sensitivity. Testing for loss of sensitivity to blue light with short-wavelength automated perimetry (SWAP) has been demonstrated to be more sensitive for diagnosing and monitoring glaucomatous visual field loss than standard automated perimetry.[8]

Frequency doubling technology perimetry also seems to be more sensitive for detecting early changes in visual function in glaucoma.[9] Although many of these changes have been observed to occur years before abnormalities in standard perimetry are noted, these tests have not been widely used in clinical practice.

Conventional white-on-white perimetry remains the cornerstone of clinical visual field testing in glaucoma. However, perimetry is a subjective test with considerable variability in the results. Repeated testing over a period in which measurable change is unlikely will usually not yield identical results. These fluctuations in test results can confound the interpretation of real change and assessment of progression.

Several algorithms have been proposed to systematically evaluate progression in a series of SAP visual field tests. The Advanced Glaucoma Intervention Study (AGIS), the Collaborative Normal Tension Glaucoma Study (CNTGS), the Collaborative Initial Glaucoma Treatment Study (CIGTS) and the Ocular Hypertension Treatment Study (OHTS) all used different criteria to evaluate progressive deterioration of visual fields. However, studies comparing the methods of progression used in these clinical trials have reported a poor to fair agreement among the different objective criteria.[10]

For this reason, subjective assessment of a series of visual fields still remains the most widely used method to evaluate progression. However, there are no well-accepted standards for subjective interpretation, and the criteria for progression will most likely differ among different examiners. When assessing visual fields for progression, it is always necessary to confirm by repeat testing any suspicious progression. In addition, it is important to correlate the visual field findings with the other clinical information, such as the optic disc appearance and IOP measurements.

Core Concepts

- **The lack of a consistent definition of glaucoma hampers interpretation and comparison of research results and creates uncertainty about clinical diagnosis**
- **Identification of progressive glaucomatous damage to the optic disc is one of the most important aspects of glaucoma management, yet it remains largely subjective and imprecise**
- **In glaucoma, significant nerve loss takes place before there is loss of visual function. Therefore, examination of the optic disc and retinal nerve fiber layer are critical for diagnosis, especially in the early phases of the disease.**
- **Functional testing (eg, perimetry) and examination and imaging of the optic disc are surrogate measure for the issues of real interest in glaucoma: the degree of retinal ganglion cell loss and the quality of function of the remaining cells.**

Structure-Function Associations In Glaucoma

Assessing cross-sectional structure-function associations is important in glaucoma because it is assumed that visual loss reflects underlying structural defects attributable to the disease. Clinicians often use a combination of structural and functional information to corroborate diagnoses. Ideally, it would be helpful to know the amount of structural loss that results in a measurable decrease in visual function. However, clinical structure-function relationships are not well understood and the best way to assess them in glaucoma patients is not clear. In most cases, the strength of these associations is assessed using optical imaging techniques to measure optic disc and/or RNFL structure and perimetric testing to measure visual function. Importantly, these techniques are surrogate measurements of the variables of interest, namely ganglion cell count and ganglion cell function.

Using optical imaging and standard (ie, achromatic) automated perimetry in humans, recent studies suggest that the strength of structure-function associations varies as a function of

1. severity of disease in the selected population[11],
2. retinal and corresponding visual field areas in which the association is assessed[12-14],
3. description of the form of the association (eg, linear, quadratic, logarithmic)[11,13-15], and 4. possibly the imaging device with which the association is assessed.[11,16]

Currently, it is accepted that structure-function association is strongest in more advanced disease. This is expected because as disease advances, the ranges of optic disc/RNFL measurements and of visual sensitivity are truncated. Secondly, structure-function associations are stronger inferiorly (including inferotemporally) and superiorly (including superotemporally) compared to temporally and nasally. This also is expected because glaucoma has its measurable effects primarily in these areas.

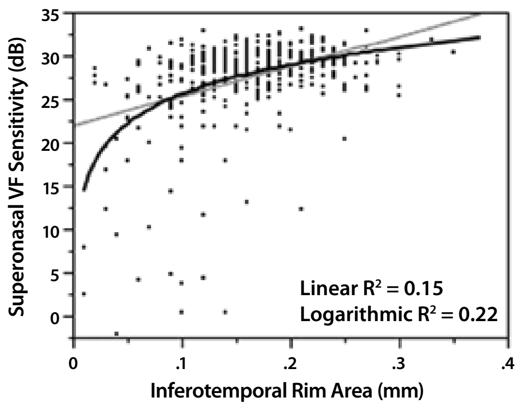

FIGURE 3 Structure-function associations between confocal scanning laser ophthalmoscope (HRT II) measured neuroretinal rim area (inferotemporal region) and standard automated perimetry (HFA II with SITA) measured visual sensitivity (superonasal region) for 358 eyes (normal, suspect, glaucoma patient) expressed linearly (grey curve) and logarithmically (black curve). The strength of association is somewhat stronger using a logarithmic fit but in neither case does the structure-function fit describe more than 25% of the variability in function (although both fits are significant with *P* < .001).

Structure-function associations, when the continuum of disease severity is considered, appear to be curvilinear when structural measures are expressed on a linear scale and functional measures are expressed on a logarithmic scale (as is common). However, curvilinear associations are not always significantly better than linear ones, and if early disease and late disease are assessed independently, resulting relationships have been described as linear with differing slopes.[17] Finally, no matter the fit used, structural measurements generally account for less than 60% of the variability present in functional measurements (Figure 3).[11-14, 16]

A more accurate description of the structure-function relationship could be sought in studies that assess structure or function directly. Unfortunately, direct assessment of visual function (e.g., measuring ganglion cell activity on a large scale) is not currently possible. However, direct assessment of structure can be accomplished by counting retinal ganglion cells or measuring RNFL thickness histologically. Using the former technique, recent studies have investigated the structure-function relationship in primate glaucoma models. In these studies, monkeys are behaviorally trained to perform perimetric testing using positive reinforcement. After serving as psychophysical observers for some time, the animals are sacrificed and histology is performed. Using this method, it has been reported that up to 40% of ganglion cells can be lost before a measurable decrease in SAP-measured sensitivity occurs.[18,19]

This finding suggests that to optimize the strength and accuracy of the structure-function relationship overall, ganglion cell loss likely should be expressed on a logarithmic scale (similar to visual sensitivity measured using SAP).[19] To optimize this relationship for very early defects however, linear scaling of structure and function measurements is recommended.[19] Although the behaving monkey paradigm likely provides a more accurate description of the structure-function relationship than human studies, it is important to consider that 1) experimental glaucoma is not the same as primary open-angle glaucoma and 2) ganglion cell counts are susceptible to variability (eg, effect of tissue preservation methods and strategy for cell counting).

The Structure-Function Relationship Over Time

Another possible complication in the search for a robust cross-sectional structure-function association is the theoretical time lag between structural and functional defects over the time course of progressing glaucoma. It is easy to imagine some early, undetectable, structural insult resulting in misfiring sick and dying cells, subsequently resulting in further structural change. This complication hints at what might be the most important reason for investigation structure-function associations in glaucoma: to determine at what points along the disease continuum structural and functional tests are most useful for diagnosis (or how information from these measurements should be weighed).

To date very few studies assessing the association between structure and function over time have been published, although one study investigating this association showed it to be poor.[20] In addition, although these studies likely will provide important information related to the course of glaucoma and its treatment, they still will be complicated by the use of imperfect surrogate measures.

Even if there is little or no cross-sectional structure-function relationship measured using currently available surrogate techniques, structural testing and perimetry still are both essential for patient treatment. We know that neural loss will necessarily result in functional loss. Moreover, if neural loss is detected early, some future functional loss may be spared with treatment. In addition, we know that psychophysical results represent visual function and worsening visual function usually demands treatment. Currently, however, the amount of structural loss that results in a measurable decrease in visual function is not known definitively.

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Additional references for this article can be found on www.GlaucomaTopics.com

UPDATE

Principles Behind New Technology in Visual Field Testing and Optic Disc Analysis

David P. Crabb, PhD, David F. Garway-Heath, MD FRCOphth

Automated perimetry is the benchmark for testing visual function in glaucoma and remains the outcome of most importance in clinical trial settings. However, visual field testing is very demanding on the patient and yields measurements that are inherently noisy.

Standard automated Perimetry: SITA testing

SITA, the Swedish Interactive Testing Algorithm, has successfully made these tests quicker and, therefore, easier to perform. This is based, in part, on clever mathematics rather than changes to the instrumentation.[1] This article will briefly summarize how this is achieved but also emphasize that the results from SITA testing are no less noisy than those from standard full threshold (FT) methods.

Speeding Up the Process

FT testing uses a simple "staircase" principle for estimating the seeing threshold at different points in the visual field (Figure 1). SITA reduces the number of stimulus exposures required by measuring closer to the patient's true seeing threshold using a principle of Bayesian probability that can be explained by analogy. In a horse race, certain animals have a higher probability of winning than others, and this is reflected in the odds offered by a bookmakers. These probabilities are adjusted just before the race to account for the quality of the jockey and other factors.

Similarly, at the start of SITA testing (before the patient presses the response button) not all thresholds are assumed to have an equal probability of occurring; they are adjusted based on the expected response (using factors like the patient's age, location in the field, and normal reference data). In horse racing, the probability of a horse winning changes throughout the race. Similarly, in SITA testing as the patient responds to seeing different thresholds with yes/no answers, the probability of a particular measured threshold being the final outcome is adjusted. The range of possible outcomes is summarized by likelihood functions, which can be thought of as graphs of all the likely final thresholds with the final position and shape of the graphs giving the estimated threshold (Figure 2).

Significant reduction in test time is also achieved by adapting the interval between stimulus presentations to the characteristics of the patient's reaction time (RT). Furthermore, these RTs can be used to estimate patients false responses (eg, the trigger-happy subject), obviating the need for extra trials where pseudo-stimuli are presented. FT testing doesn't exploit the fact that visual field locations that are close to each other are related and likely to give similar thresholds as compared to locations that are physiologically further apart. SITA accounts for this by using a physiological map of the expected relationship between the sensitivity at points in the field that adjusts the testing sequence at points and quickens the examination.

Core Concepts

- SITA testing reduces examination time
- SITA testing is no more accurate than FT testing
- SITA Fast provides quicker tests but with reduced accuracy.
- Interchanging SITA and FT is not recommended in longitudinal follow-up
- Scanning laser tomography provides reproducible and quantitative measurements of optic disc structure
- Trend analysis of surface height at each pixel is a sensitive means to detect and localize progression
- Trend analysis of structures, such as rim area, allows a rate of progression to be estimated

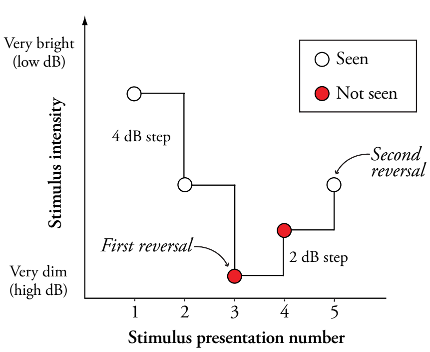

FIGURE 1 The staircase algorithm for standard full threshold (FT) perimetry. The stimulus intensity is varied in 4dB steps until the first reversal occurs and subsequently in steps of 2dB. With the Humphrey Field Analyzer (Zeiss-Humphrey Instruments, Dublin, CA), the stimulus intensity of the last-seen presentation is taken as the final threshold estimate, after a second response reversal has occurred.

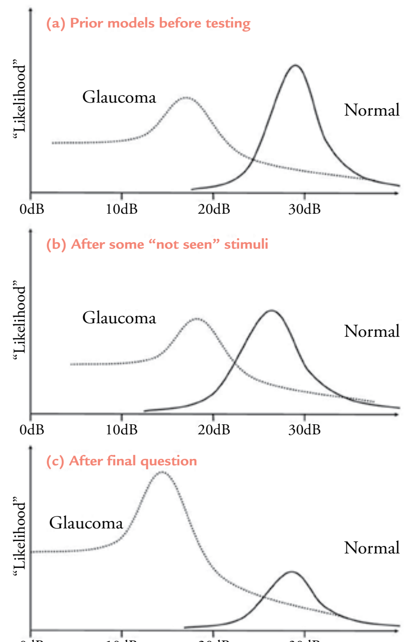

FIGURE 2 Schematic illustrating the use of likelihood functions for efficiently estimating thresholds in SITA. Each point in the visual field has two starting likelihood functions as illustrated in panel a. (In FT testing the curves would simply be rectangles with all responses equally likely). The curve for the normal response has the higher peak to start with, but the shape of both functions alters as a patient responds to the stimulus at different intensities. For example, b illustrates curves after a series of stimuli are not seen, indicating that the patient's response is more likely to fall within the glaucoma curve. After more unseen responses, the glaucoma likelihood function dominates (c), and the threshold is estimated from some location on the curve, normally the peak, but this can be further adjusted when compared to neighboring locations.

SITA Caveats

Technically speaking, SITA is far from simple.[2] There are other caveats: SITA has been designed for glaucoma, and use with other clinical conditions should only be considered with caution. In addition, interchanging SITA and FT is not recommended in longitudinal follow up of patients.[3,4]

SITA Fast, which uses larger step sizes in stimulus presentation and is, therefore, quicker still, may have a role in testing subjects who find longer tests impossible to complete. But SITA Fast is subject to greater measurement noise than either SITA or FT and should not be used in follow-up.[5]

A New Gold Standard

SITA is becoming the new gold standard for threshold perimetry because quicker tests are appealing to patient and clinician. The research evidence suggests that measurements from SITA agree well with those from FT, but there is no evidence to suggest that SITA provides more accurate measurement or better test-retest variability than FT. In fact, the test-retest variability may have a different "profile," which may be important in developing methods for detecting progression.[5] SITA testing does not preclude the need for careful clinical judgement and prudent repeated testing in both diagnosis and follow-up.

Optic Disc Trend Analysis

Optic disc trend analysis was first described for neural rim measurements from stereo photographs (planimetry).[7] However, planimetric measurements are subjective, and it was not until the advent of scanning laser tomography that reproducible quantitative measurement of the optic disc topography came on the scene.[8]

Approaches to identifying trends of change are similar to those in visual field analysis:[9] point-by-point and summary measure analysis. Point-by-point approaches probably have greater sensitivity and localize change, whereas summary measures give a more easily understood quantification of a rate of change.

Patterson and colleagues advocate a point-by-point (or pixel-by-pixel) approach, where the significance of change at each pixel is determined from the rate of surface height change and the measurement variability inherent in each patient's series of images.[10] Significant change is displayed as a color-coded map (Figure 3). An alternative approach was recently introduced in the Heidelberg retina tomograph software on its model HRT3. This modification extends the topographic change analysis and quantifies the area and volume of significant clusters over time (Figure 4).[11]

FIGURE 3 Statistic Image Mapping (SIM): a color-coded map of height change at each pixel over the optic nerve head.[10] Right eye of a 64-year-old subject with ocular hypertension after 7 years of follow-up. Visual field loss developed after 5 years of follow-up. Pixels with a significant rate of change (trend) are color-coded according to the depth of change (at trend) at last follow-up, with red representing greater, and yellow representing lesser, loss in surface height. (Image courtesy of Andrew Patterson).

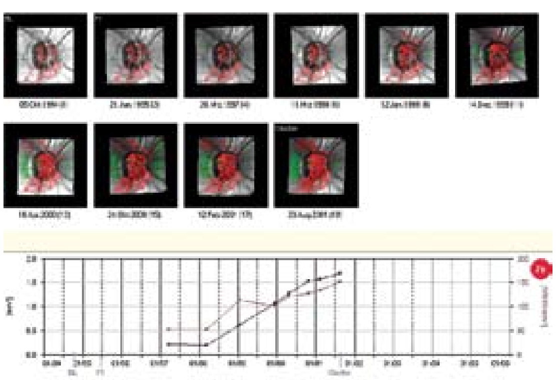

FIGURE 4 Topographic Change Analysis (TCA): pixels with significantly reduced height, compared to baseline, are colored red, with color saturation indicating the extent of height change.[11] Pixels with significant height gain, compared to baseline, are green. The new HRT3 software extends the TCA analysis and plots the area and volume change over time within a cluster of significant pixels. The optic nerve head illustrated is the same as that in Figure 2.

Summary Measures

Summary measures, for example, neural rim area, may also be tracked over time. For the HRT, rim area has been shown to be one of the most reproducible parameters and is a good candidate for identifying clinically meaningful change. The rate of rim loss has been used to identify progression in eyes with ocular hypertension, with significance limits adjusted according to the image quality of the series.[12] In a similar approach, the significance level for a trend for change in rim area has been used to quantify the Evidence of Change in series of HRT images in eyes with glaucoma.[13] Tend-based analyses show great promise for identifying clinically meaningful change.

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Visual Field Progression

Ravi Thomas, MD, Rajul Parikh MS

Core Concepts

- Visual field testing is a vital aspect of determining whether glaucoma progression has taken place
- Determination of progression detected by visual field testing should correlate with optic nerve head examination and other patient data
- The "Overview" program may be suggestive of glaucoma progression, while progression is often confirmed with GPA "likely progression" message (assuming the presence of corroborative physical findings)

There are many strategies for determining visual field progression, but for brevity we will summarize only our own clinical routine (Table 1). Specifically, we rely primarily on the "Overview" and "Glaucoma Progression Analysis" (GPA) programs. Considerations for interpretation of a single field are provided in Table 2.

The "Overview"

The Overview program prints a sequential series of fields obtained from the same patient on a single piece of paper. It contains all the information provided in the single field analysis including total and pattern deviation plots. Eyeballing the "Overview" gives a feel for whether field deterioration is present, and if so, whether it is due to generalized or localized loss of field.

TABLE 1 Judging Visual Field Progression*

Method	Tool
Clinical judgment	"Overview"
Defect classification	AGIS score, CIGTS score
Trend analysis	Box plot, Moorfield`s regression
Event analysis	GCP, GPA

AGIS = Advanced Glaucoma Intervention Study
CIGTS = Collaborative Initial Glaucoma Treatment Study
* Modified from: Spry PG, Johnson CA. Identification of progressive glaucomatous visual field loss. *Surv Ophthalmol* 2002;Mar-Apr;47(2):158-73.

In general, worsening of the total deviation plot by itself is due to anterior segment causes (eg cataract, refractive error, miosis) rather than glaucoma. Persistence of such total deviation plot defects in the pattern deviation plot suggests a localized defect which is more likely in glaucoma. The Overview tells a story and makes for a good first look (Figure 1). It does not, however, provide the statistical help most of us need to initiate changes in management, especially surgical intervention.

The "Glaucoma Change Probability" (GCP) program did provide such statistical help. However, as the GCP was based on the total deviation plot; changes that caused overall loss of vision (eg, cataract) were flagged as progression. Thus, it made clinical sense to develop a program based on the pattern deviation plot instead.

The GPA

Briefly, in the GPA, the threshold value from the pattern deviation plot of each test point location in every follow-up field is compared with an average of the threshold values from the same test point in two selected baseline fields. The GPA summary is incorporated in the single field printout (Figure 2). If three or more points at any location in the field have worsened on two consecutive tests, the GPA states "Possible" progression (Figure 3A). If three or more points at any location deteriorate in three consecutive tests the program labels this as "Likely progression" (Figure 3B).

How are these programs used clinically? First, false Progression must be excluded (Table 3). Choosing the two baseline fields is very important and should not include "learning curve" fields. When an intervention is undertaken, it is necessary to change the baseline for future comparisons. Retesting of visual field abnormalities, significantly improves accuracy in recognizing progression.[1,2]

Randomized controlled clinical trials typically require three or more "confirmatory" fields to report progression. In the clinic, however, the judgment of progression is more "corroborative." There are other factors, including intraocular pressure (IOP), appearance of the disc and nerve fiber layer, presence of hemorrhage, etc. If these suggest progression, eyeballing the overview gives us an idea as to what is taking place and we assess the GPA.

"Possible progression" on the GPA, when it corroborates our clinical findings, or a repeat field with the message "likely progression" is probably enough to base management decisions on, especially if the deteriorating points correlate with our disc findings. It is reported that the GPA may sometimes underestimate visual field progression, even in cases without evidence of increasing media opacity.[3] We feel that consideration of the "Overview" program (total deviation plot) in combination with the GPA analyses addresses this concern.

To summarize, progression is suspected by clinical findings, suggested by the "Overview" program, and confirmed with the use of the GPA "likely progression" message.

TABLE 2
Interpretation of a Single Field Printout

1. Systematically evaluate each zone of the printout including patient, test, and reliability parameters[4].
2. **Do not** rely on grey scale for diagnosis (or progression).
3. Total deviation plot highlights generalized loss of vision, usually due to anterior segment issues, eg cataract.
4. Defects in the total deviation plot that **persist** in the Pattern Deviation plot (if repeatable) confirm the presence of a localized scotoma.
5. The Glaucoma Hemifield Test is a sensitive and specific indicator of glaucoma damage.
6. Always correlate with clinical findings.
7. **Never** make a diagnosis based on the visual field alone.

TABLE 3 Causes of False Progression

- Unreliable field
- Change in pupil diameter (particularly miosis)
- Inattentive or fatigued patient
- Long term fluctuation
- Artifacts
- Media opacity

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Disc Assessment: Five Key Points

Remo Susanna Jr., MD

Core Concepts

1. IOP measurement is a flawed method of glaucoma detection/ diagnosis.
2. Visual examination of the optic nerve and RNFL may be a more valuable method of glaucoma diagnosis.
3. A systematic approach to optic nerve/RNFL evaluation is presented.

The reliance on intraocular pressure (IOP) for glaucoma diagnosis has several limitations: corneal thickness affects accuracy; IOP fluctuates; and IOP damage thresholds vary among individuals. It is therefore critically important that detection of glaucomatous optic neuropathy (GON) rather than elevated IOP become the basis for diagnosing glaucoma. This is entirely reasonable considering that many patients with IOPs in the normal range go blind from glaucoma; but, irrespective of IOP, few if any patients go blind from glaucoma with a normal optic disc.

A Systematic Approach to Diagnosis

The literature describes the characteristic signs of GON, but there is no widely accepted systematic approach to optic disc examination. Several years ago we described a systematic approach to clinical evaluation of the optic disc and retinal nerve fiber layer (RNFL).[1] This method had five cardinal points:

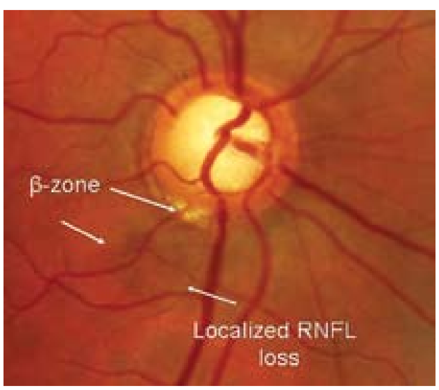

FIGURE 1 **A beta zone in any portion of the rim other than the temporal border of the disc may indicate a rim or RNFL abnormality. Note RNFL loss (between arrows) corresponding to the beta zone.**

1. Observe the rim. The "ISNT" rule—in which the inferior rim of the optic nerve head is thickest followed in descending order by the superior, nasal, and temporal rims—should apply. Deviation from this pattern is often one of the earliest signs of glaucoma. For small discs, the most important parameter is an optic cup too large for the given optic disc size.

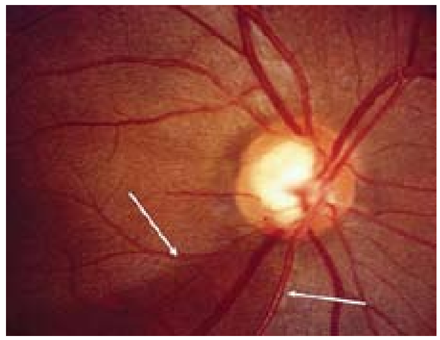

FIGURE 2 **Localized RNFL loss (dark zone between arrows).**

2. Observe the parapapillary region. The presence of a beta zone of parapapillary atrophy is helpful in the detection of glaucoma and for differentiating the various types of primary and secondary glaucomas.[2,3] Although a beta zone may be present in roughly 25% of normal eyes, when the beta zone appears in any other position other than the temporal border of the disc, it may indicate a rim or RNFL abnormality (Figure1).

3. Examine the RNFL. With diffuse loss, there is general reduction of the RNFL brightness. Localized RNFL loss appears as wedge-shaped dark areas emanating from the optic disc (Figure 2).

4. Observe the lamina cribrosa. The presence of an acquired pit of the optic nerve (APON) is almost pathognomonic for glaucoma and may be a risk factor for glaucoma progression. In 70% of cases it is located in the inferotemporal sector of the disc, while in the remaining cases it is located in the superior temporal portion. It represents a deep, localized excavation of the neural rim and loss of the normal architecture of the lamina cribrosa.

5. Look for optic disc hemorrhages. Retinal and optic disc hemorrhages, which are indicative of glaucoma progression, have a very high diagnostic specificity (Figure 3). They are transient, lasting from 2-6 months, but may recur.

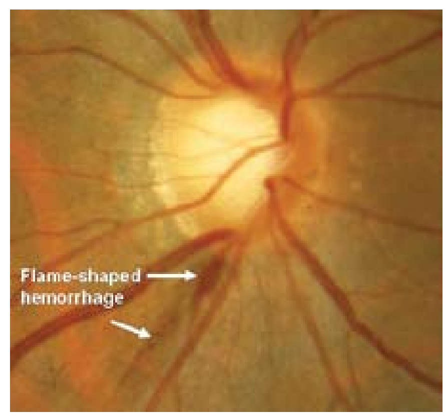

FIGURE 3 **Disc hemorrhage.**

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