Inside this issue:

**Special Focus:** Concept of glaucoma progression, importance of measurement, functional versus structural measurement, evidence from clinical trials

**What's New:** New technologies to measure progression, software, guidance from clinical trial outcomes

**Clinical Issues:** Treatment strategies for prevention, the concept of target pressure

**Practical Tips:** Frequency of visual field measurements and disc imaging

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**LEARNING OBJECTIVES**

- **Special Focus:** A detailed review of the concept of glaucoma progression. It highlights the importance of measurement, discussing options for functional and structural measurement as well as their values, taking into account available evidence from clinical trials.

- **What's New:** A comprehensive summary on new technologies to measure progression, available software as well as guidance from clinical trial outcomes.

- **Clinical Issues:** A summary reviewing treatment strategies to prevent progression in glaucoma, focusing on the concept of individual target pressures for patients.

- **Practical Tips:** An expert discussion on frequency of visual field measurements and disc imaging in clinical practice.

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**Main topic:**

“Glaucoma Concepts – Rate of progression”

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A newsletter is sent out to participants registered to the program.
Special Focus:
Glaucoma Concepts: Rate of progression

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Core Concepts
- Assessment of rates of change is a fundamental aspect of glaucoma management.
- Patients with rapidly progressive disease are at increased risk for developing functional impairment and disability from the disease and, therefore, likely need more aggressive treatment and intensive follow-up. However, other factors need to be taken into account in decision-making, such as life expectancy.
- Sole reliance of standard automated perimetry to measure rates of change in glaucoma may lead to underestimation of actual rates of neural loss in the disease, notably in early stages of damage.
- Analysis of rates of structural change by imaging technologies can provide important information about the velocity of disease deterioration, especially in early to moderate stages of the disease.
- Approaches combining structural and functional tests result in improved estimates of rates of disease deterioration, and allow the best use of different tests according to the stage of the disease.

The importance of measuring rates of change in glaucoma

Glaucoma is a neurodegenerative disease caused by progressive retinal ganglion cell (RGC) loss associated with characteristic structural changes in the optic nerve and retinal nerve fiber layer (RNFL). The neural insult can result in functional losses and decrease in vision-related quality of life. Detection of progression plays a central role in the diagnosis and management of glaucoma. However, although most glaucoma patients will show some evidence of progression if followed long enough, the rate of deterioration can be highly variable among them.\(^1\)\(^-\)\(^3\) While most patients progress relatively slowly, others have aggressive disease with fast deterioration, which can eventually result in blindness or substantial impairment unless appropriate interventions take place.

The ultimate goal of glaucoma treatment is to preserve a patient’s visual function and quality of life. Therefore, management decisions should take into account the risk of development of functional impairment in the patient’s remaining lifetime years. For patients with rapidly progressive disease, such risk will be higher and, therefore, these patients will likely need more aggressive treatment and intensive follow-up. However, several other factors need to be taken into account, such as life expectancy. Figure 1 illustrates this principle. It shows the relationship between disease severity and duration of the disease, from diagnosis until patient’s death. As the disease gets severe enough, there will be a point where it leads to disability and decrease in vision-related quality of life.

Figure 1. The impact of rates of change and life expectancy on the risk of developing disability in glaucoma. If the disease progress to a stage that is severe enough, the patient is likely to develop signs of disability or decrease in quality of life, such as increased risk of falls or driving impairment.

A. A patient with fast progression will have a higher chance of reaching the disability zone before dying, whereas a patient with relatively slower disease progression will remain free of symptoms and will preserve quality of life.

B. For two patients progressing at the same rate, the one that was diagnosed relatively late will have a higher chance of developing disability and decrease in quality of life.
causing, for example, higher incidence of falls, reduced mobility, difficulty reading or driving impairment. The purpose of treatment should be to slow down the rate of progression in order to avoid patients from reaching this “disability zone”. As can be seen from Figure 1A, if a patient has faster progression or longer life expectancy he or she will be at an increased risk for developing disability and, therefore, may need more aggressive treatment than a patient progressing at a relatively slow rate or with a short life expectancy.

Figure 1B illustrates another important aspect. The two patients are progressing at the same rate of change; however, they were diagnosed at different stages of the disease. For the one diagnosed late, the severity of disease is already close to the zone of disability. Therefore, this patient will need a greater reduction in the rate of progression in order to prevent disability. Greater reductions in the rate of progression, however, may require more aggressive interventions, with potentially greater side effects. This underscores the importance of early diagnosis and treatment of the disease.

Rates of functional change
Standard automated perimetry (SAP) is the most commonly used method for assessing rates of visual function loss in glaucoma and estimating risk of impairment from the disease. Rates of change using SAP have traditionally been measured by calculating how fast global visual field indices, such as mean deviation, change over time. This is known as “trend-based” analysis and is usually performed with a statistical technique called linear regression, which obtains an estimate of the slope of change over time, expressed in units of decibels/year (dB/year). More recently, the “Statpac software” of the Humphrey Field Analyzer (HFA II; Carl Zeiss Meditec, Dublin, CA) incorporated an analysis of rate of change using an index called Visual Field Index (VFI) (Figure 1). The VFI, introduced by Bengtsson and Heijl, expresses visual function as a percentage of normal age-corrected sensitivity. Therefore, the VFI of an eye with a completely normal visual field is 100% and the VFI of a perimetrically blind eye is 0%. Change in VFI is also used to estimate the rate of progression as part of the Guided Progression Analysis (GPA), from which the patient’s rate of progression, in percent VFI loss per year, can be determined. The VFI was originally developed to address the shortcomings of MD, and compared to MD, VFI is thought to be less affected by the confounding effects of media opacities, such as cataract.

What is a fast rate of change?
A recent review by Chauhan et al has suggested guidelines for what could be considered a fast rate of visual field progression and how it should be assessed in clinical practice. According to the authors, a patient with early visual field loss (MD = −4 dB) and a rapid rate of progression (−2 dB/y), could be expected to develop total disability (−30 dB) in 13 years. Using the same reasoning, the authors concluded that a rate of change slower than −0.5 dB/y would in general be considered slow and unlikely to lead to blindness in the patient’s lifetime. Such reasoning is fundamentally based on the assumption that rates of MD change over time are linear. However, there is very little evidence in the literature to support this assumption and it may lead to misleading conclusions about the rate of disease progression and risk for impairment from the disease.

Figure 2. Assessment of rate of change by trend analysis using the visual field index (VFI).

Figure 3. The relationship between visual field damage, as assessed by the global index mean deviation (MD) and estimated retinal ganglion cell (RGC) counts. In early disease, large losses of RGCs can occur despite apparently small changes in the visual field, as measured by the MD. In contrast, at relatively late stages of the disease, even small losses of RGCs may translate into large losses of visual function.
patients. An almost identical relationship is seen when VFI is plotted against RGC counts, but it is not shown here. The estimated RGC counts were obtained using previously developed formulas based on experimental studies in monkeys and subsequently validated in histologic studies in human subjects.

There is a clear nonlinear relationship between visual field loss, as measured by the MD, and neural losses. For patients with early disease, large losses of neural tissue can occur despite minimal changes in the MD. On the other hand, for patients with more severe damage, even relatively small losses of RGCs may translate into large visual field losses.

This relationship is essentially the result of the logarithmic scaling of perimetric data. It can explain why a large number of glaucoma patients can develop substantial changes in the optic nerve and RNFL despite visual fields remaining within normal limits. In addition, it has another very important implication from the standpoint of measuring rates of change. It indicates that face value interpretations of linear rates of change in dB/year can be very misleading and lead to underestimation of the rate of neural loss in the early stages of the disease. What appears to be a slow rate of change as measured in dB/year in early disease may actually represent a fast rate of RGC loss.

As Figure 3 demonstrates and as previously published, a change of −0.5 dB in MD in early stages of the disease (with initial MD close to 0 dB) would correspond to a loss of approximately 100,000 RGCs. Such loss would actually be greater than the loss of approximately 35,000 cells that would be associated with a -2 dB change in MD for an eye with severe damage and MD of -15 dB. As another example, consider an eye with initial RGC count of 1,000,000 that is showing a linear rate of loss of 100,000 RGCs per year. This eye would lose all RGCs in 10 years. However, analysis of rates of MD change during the first year of the disease would indicate a rate of only approximately -0.3 dB/year. Sole reliance on linear rates of MD change in this situation could potentially lead to severe underestimation of the risk of functional impairment. In fact, by the time a rate of loss of 100,000 RGCs/year corresponds to -2 dB/year, the eye would have close to 650,000 RGCs, or a loss of 35% of neural tissue.

Although it should be recognized that additional losses of visual function in patients with severe damage would carry a higher risk of producing disability than in those with normal visual fields or early visual field loss, the underestimation of rates of neural damage by SAP in early stages of the disease could potentially lead to underestimation of the risk of functional impairment from the disease. Even if one recognizes the nonlinear relationship between MD and RGC counts as shown in Figure 3 and interprets MD values accordingly, small rates of change in dB/year will be more difficult to detect due to the variability of measurements and, therefore, sole reliance on SAP for measurement of rates of change will still have the potential for underestimating neural losses. It could be argued that treatment could be started later once the eye has shown clear evidence of significant rates of change on SAP. However, as pointed out above, it is important to emphasize that if treatment is initiated late in the course of the disease, a much slower rate of change will have to be achieved in order to prevent development of functional impairment than what would be necessary if treatment had been started earlier. Although it is generally possible to slow down the rate of disease progression and keep patients close to stability even if they have moderate or advanced damage, this usually requires more aggressive interventions compared with what would be necessary if treatment had been started at an earlier stage.

Rates of structural change

Several studies have shown that imaging technologies can provide objective and quantitative estimates of rates of structural change in glaucoma and their use can improve our assessment of rates of disease progression.
4 shows an example of an eye followed with spectral domain optical coherence tomography (SD-OCT) tests over time. The eye developed a progressive loss of RNFL in the inferior temporal region. The quantitative assessment of the RNFL thickness over time allowed a rate of change to be calculated. In this example, the rate of change was 

-1.94 μm/year.

Analysis of rates of structural change can provide important information about the velocity of disease deterioration, especially in early to moderate stages of damage. Figure 5 shows a plot of the relationship between average RNFL thickness obtained from SD-OCT and RGC counts obtained from the same subjects shown in Figure 3. As can be seen in Figure 5, the relationship between RNFL thickness and RGC counts is very different than that between MD and RGC counts. The relationship between RNFL thickness and RGC counts is linear throughout most of the course of the disease, but levels off to reach a plateau in advanced disease. In advanced stages of damage, the relationship between RNFL thickness and RGC counts becomes relatively flat, that is, further decreases in RGC numbers do not result in appreciable changes in RNFL thickness. This seems to be the result of a floor effect of the OCT instrument, which also seems to exist in other imaging technologies. Also, they seem to be related to the remodeling of axonal and non-axonal composition in the RNFL with progressive disease. In addition, there is a residual corresponding to the glia and blood vessels that remains even after total RNFL loss. From Figure 5 it can be seen that the relationship between RNFL thickness and RGC counts becomes flatter as RNFL thickness reaches numbers close to 50 μm, which on average corresponds to MD close to -10 dB. Average OCT RNFL thickness values do not fall much below 50 μm even if the eye progresses to complete loss of neural tissue. The above findings agree with the relatively poor sensitivity reported for OCT in discriminating moderate from advanced disease.11

Figure 5. The relationship between retinal nerve fiber layer thickness measurements obtained by optical coherence tomography and retinal ganglion cell (RGC) counts. The relationship is mostly linear throughout the course of the disease, but reaches a “plateau” in late stages, where the OCT will perform relatively poorly for detection of further neural losses.

Figure 6. E. Graph illustrating the combined relationship between a functional test (standard automated perimetry [SAP] mean deviation [MD]), a structural test (retinal nerve fiber layer thickness [RNFL] measured by optical coherence tomography [OCT]) and estimated retinal ganglion cell (RGC) number in glaucoma. In early stages of the disease, substantial losses in RGCs will generally cause larger changes in RNFL than in SAP MD. In contrast, at moderate and late stages of the disease, SAP MD will show comparatively larger losses than OCT RNFL thickness, as OCT loses its ability to detect further neural losses.

Combined structure-function approaches for measuring rates of change

The limited utility of visual fields for estimating rates of progression in early glaucoma associated with the limited utility of structural assessment by imaging for estimating rates in more severe stages of the disease implies a strong need for combined approaches using structure and function to monitor glaucoma. Recent studies using Bayesian methodology have indicated that a combined approach integrating structural measurements from imaging devices and SAP data can be used to improve inferences obtained from analysis of rates of structural and functional change in glaucoma.15,17 Incorporation of structural information allows more accurate and precise estimates of rates of visual function change and vice-versa, potentially decreasing the need to collect additional data and resulting in more confident decision making to be made earlier with
regard to the statistical and clinical significance of the calculated slopes. However, it should be noted that even though estimation of rates of visual field loss can be improved by incorporating structural data, limitations would still persist from the use of linear trends for assessing change over time if visual function data is expressed in decibels. Also, as sensitivity thresholds are originally acquired in decibels, simple linearization of visual field data and calculation of linear trends will not completely solve the problem.

To overcome these limitations, a recent algorithm has been proposed which combines estimates of RGC loss derived from SAP and optical coherence tomography data in order to obtain a single index of structure and function. 7,10-20

The index can estimate the amount of RGC loss and is obtained by a weighted average of RGC counts obtained from SAP and OCT and measure rates of disease progression throughout the whole spectrum of the disease. The index has successfully been used for staging and detecting glaucoma progression in cross-sectional and longitudinal studies.

Conclusion

In conclusion, assessment of rates of change is at the core of glaucoma management. Decisions about initiating or intensifying therapy should take into account how fast the patient is progressing, along with risk factors and other considerations such as life expectancy. There is a strong need for integrated approaches using structural and functional data for measuring rates of disease progression. Such combined approaches need to take into account the limitations of the tests for detecting change at different stages of the disease. Combined approaches may improve the estimates of rates of disease deterioration and allow the best use of different tests according to the stage of the disease, which will likely result in better assessment of rates of deterioration in glaucomatous patients.

References

What's New
Rate of Progression

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Core Concepts
• Assessment of both optic nerve structure and function are integral components of the glaucoma examination.
• Clinical examination of the optic nerve complex (optic disc, parapapillary area, and retinal nerve fiber layer) can be supplemented by imaging devices such as optical coherence tomography or confocal scanning laser ophthalmoscopy.
• Testing of the visual field using achromatic automated perimetry remains the reference standard for assessment of optic nerve function.
• Glaucoma progression can be assessed by event-based analysis, which compares the most recent test(s) to a pre-determined set of baseline examinations, or trend-based analysis, which can be used to determine the rate of change over time.
• Interpretation of imaging and visual field tests should utilize the change detection algorithms of the specific instruments.
• In addition to risk factor assessment, the clinician should try to determine if the current rate of change will lead to visual disability during the expected lifetime of the patient and then adjust the target intraocular pressure accordingly.

Background
Glaucoma is characterized by progressive optic nerve damage that results in irreversible visual impairment or blindness if not properly treated. This gradual progression of vision loss has both personal and societal costs given its serious impact on quality of life.

Preservation of visual function in glaucoma and prevention of vision-related disability is the goal of glaucoma treatment. Conceptually, all glaucoma patients progress, albeit at different rates, and their rate of change is the most objective measure to guide treatment decisions and interventions. In clinical practice and research, a variety of models have been developed to improve our ability to detect and measure progression.

Glaucomatic progression can be clinically detected either by structural or functional tests. There are currently two different approaches to detect change using either modality of testing: event-based or trend-based analysis. The former has been widely applied in clinical practice and clinical trials. Briefly, event-based analysis evaluates a set of tests by comparing one or a series of tests with a set of baseline examinations, often disregarding interim data. A binary outcome is then defined; progression: yes or no. In trend-based analysis, on the other hand, the entire series of eligible tests is used and plotted as change over time, in a regression line, in which the slope of the regression line corresponds to the rate of change (e.g. decibels of loss per year for visual field testing or microns of loss per year for structural measurements). The following is a brief review on what is new with regard to methods currently employed to detect and measure rates of progression using functional or structural tests in glaucoma.

Does Glaucoma Visual Field Progression Follow a Linear or Non-Linear Pattern?
There is an ongoing discussion in the glaucoma literature on whether visual field progression occurs in a linear versus non-linear fashion over time. Given the fact that sensitivity is measured in log scale (dB) in standard achromatic perimetry, we should be cautious when interpreting time versus sensitivity graphical displays. The implication is crucial: a patient whose baseline mean deviation (MD) is -5.0 dB and progresses at -1.0 dB/yr, loses more sensitivity (measured in linear scale) but with a baseline MD of -10.0 dB. As proposed by the Hood and Kardon structure versus function model1, retinal nerve fiber layer loss and visual field sensitivity (measured in linear scale) are linearly correlated. This means that, in the example above, the loss of nerve fibers is greater at a -1.0 dB/yr rate when the baseline MD is -5.0 dB then when the baseline MD is -10.0 dB in the same patient. In fact, Medeiros et al.2 have reported that one should be cautious when measuring rate of progression as it is dependent on the level of baseline damage. This implies that if a patient progresses at -1.0 dB/yr and the clinician enhances therapy, progression at a similar rate after intervention could actually represent a smaller number of nerve fibers being lost than before intervention. Should the clinician then assume that no change in rate of progression in dB after surgery means successful treatment? Not really: a smaller absolute number of nerve fibers is being lost but the proportion of remaining ‘healthy’ fibers is continuing to decline. Recent studies have suggested that measuring rates of loss of estimated ganglion cell counts could then be helpful to better estimate the efficacy of glaucoma therapy in preserving retinal ganglion cells.3,4

Limitations of standard achromatic perimetry should also be taken into consideration before changing therapy. Once very low sensitivities are reached, a ‘floor effect’ influences the measurement of rates of visual field progression. Gardiner et al.5 have recently shown that at pointwise absolute sensitivities of approximately 15 dB and lower, estimates of the true sensitivity become random and hence unreliable. This means that a decrease in absolute threshold sensitivity from 15 to 10 dB is not as reliable as a change, earlier in the disease, from 20 to 15 dB. Given this observation, and as shown in a further publication,6 novel perimetry algorithms should perhaps spend more time testing the sensitivity of adjacent, less severe points than those that reached a severe point of loss, in
which the test result is less reliable and more random. Understanding this limit of perimetry reduces the likelihood of misinterpretation.

**Should We Measure Progression with Structural Tests?**

The first consensus meeting of the World Glaucoma Association recommended that patients with or suspected glaucoma be assessed and followed with a combination of structural and functional tests.

Certain structural tests are objective and can sometimes detect change earlier than functional tests. Our limited consensus of what represents a ‘clinically significant’ structural change limits our ability to fully answer the question above. Loss of nerve fibers is a surrogate measure of loss of retinal ganglion cells, the preservation of which is one of the goals of glaucoma treatment. However, there is considerable individual variability in the relationship between nerve fiber (and retinal ganglion cell) loss and loss of visual function. In other words, the impact of losing a similar amount of ganglion cells in two patients has different implications on visual functioning for each of them. Therefore, clinicians should consider the use of structural tests as fundamental ancillary methods to improve certainty of the detection and measurement of functional progression, where it is present, and as an indicator of progression when it is not. Along those lines, different research groups have highlighted the role of Bayesian methods – which combine structural and functional data – to improve the accuracy of detection of significant glaucoma progression. In brief, these methods employ new imaging technologies – which are inherently more objective than functional tests – to improve the accuracy of defining functional progression – which despite being less objective, have a strong relationship with vision-related quality of life.

Despite the recent use of this Bayesian approach in research, no commercially available device to date incorporates structure and function to improve the accuracy to measure rates of glaucoma progression.

**Conclusion**

Since our last update on rates of glaucoma progression [published in Glaucoma Now Issue 2/2010] no commercially available device combining simultaneously structural and functional tests to improve accuracy of detection of progression is yet available to help clinicians bridge this gap. Despite important publications in the field, this remains an unmet need for enhanced glaucoma care.

This limitation notwithstanding, clinicians are encouraged to use currently available methods to measure rates of progression – either functional (Humphrey GPA, Octopus PeriTrend, Progressor) and structural (HRT, GDx, OCT), preferably combined with their judgment – to tailor treatment to the individual patient.

**References**


Clinical Issues:
New Insights in Regard to “Target Pressures”

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Core Concepts
• Clinical Trial Data provide clear guidance for IOP treatment goals as therapy begins.
• Even advanced damage patients can generally be stabilized at low normal IOPs.
• Mild-moderately damaged patients can generally be stabilized at mid-teen IOPs.
• New data from CIGTS reveal that nearly as many fields “improved” as “worsened”.
• Genuine improvement correlated with low normal IOPs—now the new optimal goal.
• Up to 80% of apparent visual field changes may be false positives—some confirmation (focal loss, structural change, at least a high IOP) is advisable before making more than minimal risk interventions in mildly damaged patients.

The “Target Pressure” concept emerged from the observations of Paul Chandler1,2 and Morton Grant3, who advised:
“Eyes with advanced cupping…require pressures below the average of the population…”
“Eyes with limited cupping, confined to one pole of the disc, appear to withstand tension better…”
“Eyes with a normal disc appear to withstand pressure well…over many years…”
“The appearance of the disc may serve as an important guide to the management of glaucoma.”

However, the data upon which that advice was based was meager; it took another 40 years and several clinical trials to provide solid evidence to confirm their observations.

In Advanced Damage:
The Advanced Glaucoma Intervention Study publication4 regarding the relationship between IOP during follow up and visual field outcome confirmed that eyes with advanced damage indeed did quite well in 8 years of follow up at consistently reduced pressures, at a group average of 12 mm Hg, while less consistently reduced IOPs and a group average IOP in the mid-teens allowed a mean 2.5 dB MD progression and a group IOP averaging 20 mm Hg was associated with a mean 3.5 dB MD progression. At 12 mm Hg the risk of apparent visual field progression occurred 13% of the time (and 13% appeared better), while in the mid-teens the risk was about 30% and at 20 mm Hg the risk was about 70%. [Figure 1]. Our study of primary antimetabolite filtering surgery confirmed that visual field stability (no average change) can be maintained in advanced damage cases at an IOP averaging 11 mm Hg.5

In Early Damage:
At diagnosis, the Early Manifest Glaucoma Trial6 demonstrated that 68% of eyes with POAG progressed without treatment over 6 years, while, with the sub-optimal treatment used, the risk was reduced to 45%. In the Collaborative Initial Treatment of Glaucoma Study (CIGTS)7, in similar patients there was no average visual field progression in 7 years due to insistence upon achieving an aggressive target pressure, requiring about a 30% IOP reduction in mild cases and progressively lower targets for more advanced cases. Thus, a reduction from an average of 26 to 17 mm Hg in the medical group and to 14 mm Hg in the surgical arm resulted in no net visual field progression in each group.

New Data:
Now comes the surprise that upsets the neat story just told. In CIGTS, it...
was reported that about 15% of subjects progressed from baseline, despite there being no net visual field progression. The explanation for how that could be, was that an equal percentage of subjects appeared to improve. I thought then that repeated testing was collecting “noise”. However, a reanalysis of the CIGTS database, revealed that there was a positive correlation between those appearing to improve with IOP values, gender (females do better), and cardiovascular disease (less chance of improvement). Also a low peak IOP [Table] correlates with improvement. The correlation with pressure accounted for a minimum of 20% of those appearing to improve. The rest of the cases of “improvement” and an equal percentage of those appearing to have progressed are most likely indeed due to noise.

Implication for Practice: When you see two consecutive fields that are worse than two baseline fields by just 3 dB, the chances are that the progression is not real. One would be wise in cases in which the change is not larger than a 3 dB MD diffuse change, to look for some further confirmation - focal progression, or a corresponding structural change, or at least a high IOP - as otherwise it would be best to get a third visual field. While this suggests that the risk of true progression was less than reported, it also suggests that there was a small benefit of achieving low normal IOPs, which are the only ones that unequivocally correlate with some visual field improvement, though one also must consider the risk of achieving such pressures.

In conclusion: mid-teens IOPs may be sufficient to stabilize mildly damaged fields, but do not appear to be optimal, since even lower IOPs can result in a small net visual field improvement. Patients with more than mild damage generally need even lower target IOP levels to best stabilize their vision and to keep them safe.

### Table: Visual Field Improvement in CIGTS Correlated to IOP, Thus Real

<table>
<thead>
<tr>
<th>IOP Category</th>
<th>% visits 3 dB gain</th>
<th>% visits 3 dB loss</th>
<th>Difference</th>
<th>MD change at 5 years</th>
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<tr>
<td>Max IOP in first 5 years</td>
<td>18.7%</td>
<td>6.3%</td>
<td>12.4%</td>
<td>0.39dB</td>
</tr>
<tr>
<td>≤ 13 mm Hg</td>
<td>18.7%</td>
<td>6.3%</td>
<td>12.4%</td>
<td>0.39dB</td>
</tr>
<tr>
<td>n=24</td>
<td>18.7%</td>
<td>6.3%</td>
<td>12.4%</td>
<td>0.39dB</td>
</tr>
<tr>
<td>14-17 mm Hg</td>
<td>10.6%</td>
<td>11.7%</td>
<td>-1.2%</td>
<td>0.01dB</td>
</tr>
<tr>
<td>n=80</td>
<td>10.6%</td>
<td>11.7%</td>
<td>-1.2%</td>
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</tr>
<tr>
<td>≥ 22 mm Hg</td>
<td>8.0%</td>
<td>10.6%</td>
<td>-2.6%</td>
<td>0.46dB</td>
</tr>
<tr>
<td>n=222</td>
<td>8.0%</td>
<td>10.6%</td>
<td>-2.6%</td>
<td>0.46dB</td>
</tr>
</tbody>
</table>

References

**Table:** The data is from Reference 8. Given are the percentages of semi-annual visits over the first 5 years in which the visual field appeared to have improved, or worsened, respectively, by 3 dB of MD compared to the average of the baseline visual fields, stratified by the peak IOP during those 5 years. If apparent visual field changes of 3 dB or more were due entirely to random fluctuation, then the percentage “better” and “worse” would be equal. However, this was not the case, and the difference gives an estimate of the minimum percentage of field changes that correlate with pressure and thus are real. One sees a dose-response relationship. Also given is the mean change in visual field in each peak IOP category, again correlating with peak pressures.

Practical Tips:
Frequency of visual fields/disc imaging

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Core concepts
• A visual field defect must be confirmed at least on two consecutive exams.
• During the first two years, three visual field examinations per year are recommended.
• Visual fields must be repeated when they do not match the optic nerve.
• Three monthly visual fields are needed to assess patient response to rigorous treatment strategies.
• Three sets of baseline images are necessary for retinal imaging such as CLSO and OCT.
• Retinal imaging technologies usually require three or four examinations per year to allow progression analysis.

Standard Automated Perimetry (SAP) is the standard for the detection and monitoring of functional loss in glaucoma1. In routine clinical glaucoma and monitoring of functional loss in glaucoma, Standard Automated Perimetry (SAP) is the standard for the detection of glaucomatous visual field defects. Although laser ophthalmoscopy (CSLO) and scanning laser polarimetry (SLP) may be evaluated objectively using imaging into clinical management, it is dispensable to highlight differences between nerve fibre layer thickness measured with spectral domain OCT and visual field in patients with different stages of glaucoma, which has been validated to be used solely in diagnosis, there is increasing evidence of their usefulness in early detection of progression and individual monitoring, with changes preceding VF loss. Also there are other newer measures on the horizon.

Below are a few recommendations we use for assessing the frequency of patient investigations:
• In the early follow-up, a number of reliable examinations are necessary to establish a baseline. Before accepting a visual field defect, it must be confirmed at least on two consecutive exams, excluding the first one. Similarly, three sets of baseline images are necessary for CLSO (Heidelberg Retina Topography, HRT).
• During the first two years, three examinations per year are necessary for a total of 6 visual fields during this period - reliability indicators should be considered as short and long term fluctuation.
• Rate of MD change of -2 dB/year or worse highlights fast progression, and 3 monthly VFs are needed to assess patient response to rigorous treatment strategies.
• Visual fields must be repeated when they do not match the optic nerve.
• Similar considerations should be given to structural imaging. In cases where large and rapid changes in the optic disc occur, three or four examinations per year may be sufficient for progression analysis. If variability of the image is high and/or change is small, a larger number of examinations is required. Compared with healthy subjects, glaucomatous eyes exhibit significantly thinner RNFL measurements. In pre-perimetric glaucoma, up to 30% reduction of retinal nerve fibre layer (RNFL) thickness may be detected, which is also supported by histological studies showing up to 35% loss of retinal ganglion cells before visual field abnormalities are confirmed.


References
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.

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