CHAPTER 9

INTERPRETATION OF VISUAL FIELD PROGRESSION

INTRODUCTION

Vision-related quality of life is severely diminished both when diffuse deterioration within the central 30-degrees of the visual field (increase of MD) reaches a critical level and when localized progression prevents the performance of normal daily activities (e.g., due to severe progression of a localized inferior paracentral scotoma). In clinical practice, it is essential to detect progression and to measure its speed (i.e., rate of progression expressed as change per year in dB) as early as possible to make decisions about potential interventions before significant visual field loss develops.

Because progression in diseases such as glaucoma is typically slow, the magnitude of fluctuation can be larger than the annual rate of progression. Identifying disease progression from a series of visual fields is therefore a challenging and time-consuming task in clinical practice (FIG 9-1). As a result, expert agreement is moderate at best (45% to 65%). Statistical progression analyses greatly support the assessment of progression that is needed for clinical decision-making. The use of progression software options was shown to improve expert agreement, to also reduce overall visual field analysis time.
CHALLENGES ASSOCIATED WITH ASSESSING VISUAL FIELD PROGRESSION

The EyeSuite Progression Analysis function of the Octopus perimeters has been designed to assess visual field progression in an effective and efficient way. It includes the following three types of progression analysis: Global Trend Analysis (GTA), (Corrected) Cluster Trend Analysis (CTA and CCTA), and Polar Trend Analysis (PTA) are shown in FIG 9-2.

The Global Progression Analysis measures and statistically classifies long-term change in the global indices, namely Mean Defect (MD), Diffuse Defect (DD), Local Defect (LD) and square Root of Loss Variance (sLV). It not only assesses whether a series of visual fields is stable or shows significant change, but also provides information about the rate of change in dB/year and on the local, diffuse or combined nature of progression.

The Cluster Trend Analysis and Polar Trend Analysis have been specifically designed to detect subtle glaucomatous change. The Cluster Trend Analysis assesses cluster-specific progression within ten nerve fiber bundle regions separately, which is particularly useful in glaucoma in which localized (cluster) progression and stability occur at different locations independently from each other in the same eye. Furthermore, the Polar Trend Analysis facilitates the detection of spatially corresponding structural and visual field changes.

The different types of progression analyses make a statement about whether a visual field series is stable or not and also show the location of progression. However, it is also important to know the shape, location and depth of a defect. For example, a deep defect approaching...
the fovea solicits a much more aggressive treatment than a shallow defect in the periphery. To provide this information, the Grayscale of Comparisons representations of all visual field tests are also displayed as a default and may be changed to any other single field representation such as the Cluster Analysis.

**FIGURE 9-2** Octopus perimeters offer 3 types of progression analysis to assess visual field change over time. A Global Trend Analysis based on the four global indices MD, sLV, DD and LD, and, for glaucoma, both Cluster (and Corrected Cluster) Trend Analysis and Polar Trend Analysis. In contrast to simply looking at a series of visual fields, most of these analyses employ statistical methods to determine progression. To provide orientation about both defect location, shape and defect depth, the series of Grayscale representations is also provided.
ASSESSMENT OF GLOBAL VISUAL FIELD CHANGE

CHANGE OF MEAN DEFECT (MD) AS A MEASURE OF GLOBAL CHANGE

To judge whether a current treatment strategy is effective as well as to make a clinical decision about future interventions, it is essential to know whether, overall, a visual field series is stable, worsening or improving. This can be achieved by analyzing the change of the global index Mean Defect (MD) over time.

The global index MD summarizes the sensitivity loss over the area of the visual field that was tested. It is the average of all individual sensitivity losses and is expressed in dB. Consequently, if any visual field location worsens or improves, MD will also change accordingly, even though the change may be small. This makes MD a good index to track overall visual field change. For more information on the definition of the index MD see TABLE 7-1, and for more information on its clinical interpretation see FIG 8-26.

TREND ANALYSIS FOR THE VISUALIZATION OF CHANGE

The simplest way to assess MD change is to plot the MD of each visual field test in a two-dimensional graph. The MD is plotted on the y-axis and test date is plotted on the x-axis. This allows graphical assessment of visual field change over time as shown in FIG 9-3. Because an increasing MD represents visual field worsening, it is most intuitive to use a scale showing the smallest MD at the top and the largest at the bottom.

If there is no fluctuation and the change in MD over time is sufficiently large, it is simple to graphically determine whether a series of visual fields is stable, worsening or improving by drawing a trend line. Intuitively, the trend line corresponds to the line that provides the best linear fit for all the MD points. If this line is flat, then the visual field series is stable, if it is sloping upwards, then the series is improving and if it is sloping downwards, then the series is worsening (FIG 9-4).
**TREND ANALYSIS FOR DISPLAYING OVERALL CHANGE**

<table>
<thead>
<tr>
<th>Test date</th>
<th>MD [dB]</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/2002</td>
<td>0.9</td>
</tr>
<tr>
<td>01/2003</td>
<td>2.2</td>
</tr>
<tr>
<td>06/2003</td>
<td>1.7</td>
</tr>
<tr>
<td>12/2003</td>
<td>4.5</td>
</tr>
<tr>
<td>06/2004</td>
<td>3.3</td>
</tr>
<tr>
<td>01/2005</td>
<td>6.0</td>
</tr>
</tbody>
</table>

**FIGURE 9-3** A simple way to assess visual field change over time is to draw a two-dimensional graph with the test date of each visual field test on the x-axis and the corresponding MD on the y-axis. By drawing a trend line that provides the best linear fit for the individual MD points (red line), it is easy to see that this visual field series is worsening (downward slope).

**GRAPHICAL INTERPRETATION OF A TREND LINE**

**STABLE**

**WORSENING**

**IMPROVING**

**FIGURE 9-4** If visual field change is sufficiently large, just looking at the red trend line allows one to intuitively assess whether a visual field series is stable (flat line, left) worsening (downward sloping line, middle) or improving (upward sloping line, right) over time.
This approach is referred to as trend analysis and is used for all representations that are part of the EyeSuite Progression Analysis. To best fit the trend line to the measured MD values, linear regression analysis with the ordinary least squares fit is used. For more details on this approach as well as key characteristics of trend analysis, refer to BOX 9A.

The steepness of the line is referred to as the slope and is used to assess the rate of change in MD over time. The rate of change is expressed in dB per year and is derived by determining the amount of change in MD (y-axis) that occurs over the selected period of time (x-axis). In FIG 9-5, the rate of change for MD is 1.9 dB/year.

**FIGURE 9-5** To determine the rate of overall visual field change, the best-fit line is drawn through the MD data points in the Global Trend Analysis. Once this trend line is drawn, the actual data points can be discounted and the rate of change can be determined using the slope of the trend line. The rate of change is automatically expressed in dB per year. In this example, the slope or rate of change is 1.9 dB/year.
A key challenge in the assessment of visual field progression is the distinction between a series of visual fields that is truly changing and one that is stable but shows fluctuation. This challenge is greater in cases in which the magnitude of the change is small and the amount of fluctuation is large, which is a common situation when assessing glaucomatous progression.

In clinical practice, the trend line alone is not sufficient to distinguish between stable and changing visual fields. This is because most visual field series will show at least a small trend upwards or downwards. The challenge is to determine whether this trend is significantly different from a flat line (i.e., one with a slope of zero).

To distinguish between a stable and a truly changing series of visual fields, a t-test is used. The t-test is a statistical test of hypothesis that allows the determination of whether two sets of data are significantly different from each other. For trend analysis, the t-test is applied to the observed slope to determine whether it is significantly different from a slope of zero (e.g., flat line showing no change over time, which represents the typical situation of a stable visual field series). The concept of probability is then used to determine the probability (p) that a stable visual field series with an assumed slope of zero would show a given slope (see BOX 9A). Its interpretation is similar to the p values used in the Probabilities plot (see FIG 7-9 and 7-10). If there is a low probability that a stable visual field series would look like the series in question, then that series is unlikely to be stable and consequently it is likely that the visual field series is changing.

To facilitate interpretation, the EyeSuite Progression Analysis uses red downward arrows to show significant worsening and green upward arrows to show significant improvement at two probability levels and also marks floor effects using the following symbols:

- **Worsening at p < 5%**: this visual field series shows overall worsening. There is a smaller than 5% (and larger than 1%) chance that a stable visual field series would look like the series in question, which means there is a high likelihood that the visual field series is worsening.

- **Worsening at p < 1%**: this visual field series shows overall worsening. There is a smaller than 1% chance that a stable visual field series would look like the series in question, which means there is very high likelihood that the visual field series is worsening.

- **Improvement at p < 5%**: this visual field series shows overall improvement. There is a smaller than 5% (and larger than 1%) chance that a stable visual field series would look like the series in question, which means there is a high chance that the visual field series is improving.

- **Improvement at p < 1%**: this visual field series shows overall improvement. There is a smaller than 1% chance that a stable visual field series would look like the series in question, which means there is a very high chance that the visual field series is improving.

Floor effect: There is more than 20 dB sensitivity loss in the visual field series and no significant change, which means that the determination of progression or stability is not possible due to the advancement of the disease.

If there is no symbol, then there is a probability of p > 5% that a stable visual field series would look like the series in question or in other words that the data do not show change at the levels mentioned above. This either means that the visual field is stable, or that the data available are not sufficient to capture change. This is often the case when only a few visual field tests are available and progression is slow or when fluctuation is large as explained in BOX 9A.
**Box 9A**

**General Characteristics of Trend Analysis**

Linear Regression Analysis with Ordinary Least Squares Estimates to Determine the Trend Line

To determine the trend line, EyeSuite Progression Analysis uses linear regression analysis with least squares estimates. Linear regression analysis is a statistical approach for modeling the relationship between two variables using a straight line. An excellent fit for the trend line is obtained using the least squares method, which is a commonly used approach to fit the regression line. The best fit of the trend line is achieved by minimizing the sums of squared residuals (i.e., the vertical distance between each data point and the fitted regression line).

**OcTopus Perimeters Use Least Squares Linear Regression to Best Fit a Trend Line**

The least squares linear regression approach determines a best fitted trend line by minimizing the vertical distance between the individual test points and the trend line. This vertical distance is called the residual and is depicted by the red lines in this example. If the fit were perfect, all individual test points (gray dots) would fall exactly on the trend line (gray line).

**Significance Is Influenced by the Amount of Fluctuation**

The trend line describes the data and allows for the determination of the slope. However, this is not sufficient to distinguish between a stable and changing visual field series because there is typically at least some positive or negative slope (even if it is very small) due to the fluctuation of the variable (e.g., MD) over time.

Therefore, it is necessary to determine whether the observed slope corresponds to a true change, or whether it may be explained by fluctuations in the data. The t-test is used to determine whether the observed slope is significantly different from zero (as would be expected if the series of visual fields was stable) using two levels of significance (p < 5% and p < 1%).

The amount of fluctuation is taken into account by the t-test. This is necessary because the same slope may indicate a significant trend when the fluctuations are small, but may not be significant when fluctuations are large. In other words, a larger slope is needed to detect true change for the same number of tests and the same follow-up length when large fluctuations are present.
ILLUSTRATION OF THE INFLUENCE OF FLUCTUATION ON SIGNIFICANCE

<table>
<thead>
<tr>
<th>MD Mean defect</th>
<th>TREND ANALYSIS</th>
<th>DESCRIPTION</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No symbol indicating change</td>
<td>NO PROGRESSION</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slope 0.9 dB/year</td>
<td>Large slope</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Outliers in 3rd &amp; 4th test</td>
<td>Considerable fluctuation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Significant worsening at p &lt; 5%</td>
<td>WORSENING</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slope 0.6 dB/year</td>
<td>Smaller slope</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Test data close to trend line</td>
<td>Consistent results</td>
</tr>
</tbody>
</table>

In this figure, the visual field series from two different patients are shown over a comparable time period with approximately the same amount of test data. In the example on top, fluctuation is large because the 3rd and 4th test are outliers. As a result, even the relatively large slope (0.9 dB/year) is insufficient to indicate significant change and the series appears to be stable (no symbol). More visual field tests may be needed to identify whether the series is truly stable or progressing. However, when there is less fluctuation in the visual field data (bottom), even a small slope (0.6 dB/year) suffices to detect significant change (red downward arrow) and the series is confirmed as progressing.

SIGNIFICANCE IS INFLUENCED BY THE NUMBER OF VISUAL FIELD TESTS

The number of visual field examinations (n) included in a trend analysis is important because it influences the outcome of the t-test. The EyeSuite Progression Analysis can be performed with a minimum of three visual field tests. However, if there are only three or four visual field tests included in the analysis, the slope must be quite steep to be able to separate true change from fluctuations. On the other hand, if there are many visual field tests included, even a visual field series with a shallow slope can identify significant change. For typical progressing visual fields, trends will not become significant before five or six examinations are included in the analysis. Guidelines on glaucoma treatment typically recommend a minimum of six visual fields in the first two years to reliably detect glaucomatous visual field progression. However, if fluctuation is large and the slope is small, an even larger number of visual field tests are required to detect progression.2,8
MD TREND ANALYSIS

Interpretation of MD Trend Analysis in clinical practice is a fast and straightforward process (if adequate visual fields are selected, which is described in more detail later in this chapter). The decision about whether a visual field series is stable, significantly worsening or significantly improving can be made solely by looking at the red downward (significant worsening) or the green upward (significant improvement) arrows displayed. To assess rate of change, the slope is numerically displayed as change in dB/year at the bottom of the graph (FIG 9-6).
While the detailed graphical presentation of the trend line and the test data is not necessary for deciding about the presence and rate of MD change, it provides valuable information. It allows for a quick assessment of disease severity as well as rate of disease progression. The lower the level of the curve, the more the disease has progressed and the steeper the curve, the more rapid the change.

The graph also allows for a quick determination of the frequency of the visual field tests performed. In addition, it allows one to see at a glance if there is a significant outlier, which calls for more careful evaluation to make sure that this visual field is reliable and whether it should be included in the analysis. For more information, consult the next section in this chapter on adequate selection of visual field tests.

Visual fields included in the analysis are marked in a different color which supports the visual field selection process. Lastly, different symbols are used for each perimeter model to draw attention to a possible perimeter model-related bias. This can for example occur when a patient is tested for the first time on a new perimeter model and shows a strong learning effect. For more information on transitioning from one perimeter model to another, please refer to Chapter 12.

Further orientation is provided by a gray band at the top which indicates the normal range of MD (i.e., the 95% confidence interval) and a red line at 15 dB which represents seriously impaired visual fields. The graph stops at 25 dB because in many countries, an MD of 20 to 25 dB is considered legal blindness.
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INTERPRETATION OF MD TREND ANALYSIS

MD Trend Analysis provides information about the presence and rate of progression as well as the magnitude of the sensitivity loss (i.e., magnitude of MD) of a patient. However, this data is not sufficient to make a clinical decision as these factors have a very different meaning depending on their relation to each other as well as the patient’s age and life expectancy.

For example, an MD of 3 dB in a patient progressing at a rate of 0.4 dB/year has a very different meaning in a 50-year-old patient compared to an 80-year-old patient. Assuming a life expectancy of 90 years for both patients and projecting the current slope linearly into the future, at the end of their respective lifespan, the 80-year-old patient would have an MD of 7 dB whereas the 50-year-old patient would have an MD of 19 dB. However, if this same 80-year-old patient showed a progression rate of 2 dB per year, at age 90 this patient would have an MD of 23 dB, which represents near total visual field loss.

It therefore goes without saying that these factors as well as a patient’s lifestyle, adherence to and persistence with medications, other clinical issues and the practitioner’s overall clinical assessment have to be taken into account to make a clinical decision.

SELECTION OF ADEQUATE VISUAL FIELDS FOR ANALYSIS

IMPORTANCE OF SELECTING ADEQUATE VISUAL FIELD TESTS FOR ANALYSIS

A trend analysis is only clinically meaningful if adequate visual fields are selected for analysis. To facilitate the selection process, the EyeSuite Progression Analysis allows examiners to choose the visual fields to be included in the analysis with a simple click. Visual fields included in the progression analysis should be reliable, be part of a relevant time period, and be tested using the same test parameters. Each of these requirements is described in this section.

EXCLUSION OF UNTRUSTWORTHY VISUAL FIELD TESTS

It is important that only trustworthy visual fields, reliable and free of artifacts, be included in the analysis. Untrustworthy visual fields increase the amount of fluctuation in a visual field series and may change the outcome of visual field trend analysis as illustrated in FIG 9-7.
**Figure 9-7** Visual field tests that are not trustworthy can significantly alter the trend analysis result as the example above illustrates. In this example, the first test is not trustworthy due to a ptosis lid artifact and tests five and six are unreliable due to high false positive rates. If all seven visual field tests are included in the analysis, the series seems to be improving (top), if the lid artifact is excluded (middle), the series appears to be stable and if all three untrustworthy visual fields are excluded from analysis, a significant visual field worsening becomes apparent (bottom).
ADEQUATE TIME PERIOD FOR ANALYSIS

When choosing a time period for visual field progression analysis, it is important to keep in mind that changes in treatment as well as surgical interventions can significantly change both visual field severity and progression rates. For example, a patient with both cataract and glaucoma typically shows a significant improvement of the MD after cataract surgery. This improvement makes it challenging to assess glaucomatous progression rates after surgery, if pre-surgery visual field data are included in the progression analysis. In those cases only post-surgery data should be analyzed.

Another example is the situation in which a switch to more aggressive glaucoma treatment is made. This switch can change the rate of progression. In that situation, it would be much harder to detect the change in rate if pre-treatment data are included. However, it should be noted that the impact of the switch in treatment on rate of progression may only be assessed once a sufficient number of visual field tests become available after the switch. Thus the new rate cannot be assessed immediately following the change in treatment.

COMPARABLE TEST PARAMETERS

All visual fields included in a given progression analysis must have the same test parameters in order to obtain meaningful information about visual field progression. Therefore, the EyeSuite Progression Analysis offers the trend calculations only on visual fields tests that have been done with the same test pattern and stimulus and background characteristics. However, although ideally only one type of test strategy is used, the EyeSuite Progression Analysis allows inclusion of visual field results obtained using different quantitative testing strategies. The rationale for this is that even though the levels of accuracy between the TOP and the other strategies slightly differ, these effects are minimized at the level of the global indices.\(^5,10\)

DISTINCTION BETWEEN LOCAL AND DIFFUSE CHANGE

IMPORTANCE OF DISTINCTION BETWEEN LOCAL AND DIFFUSE CHANGE

When both local and diffuse defects are present, it is not only desirable to know whether there is change but also whether the detected change is local or diffuse. This is important because local and diffuse change can be caused by different clinical situations that may call for different types of intervention (see TABLE 8-1 on the etiology of local and diffuse loss). Because MD is affected by both local and diffuse change, it is impossible to determine the nature of the change by looking at MD alone.

For example, a patient may have both a local defect due to glaucoma and a diffuse defect due to a cataract. If the MD is worsening in this patient, it is essential for a clinician to know whether the cataract, the glaucoma or...
both are worsening. Examples of the presence of both local and diffuse change are presented in **FIG 9-8**.

In addition, the distinction between local and diffuse change is not only helpful in the presence of both a local and diffuse pathology, it is also very useful in all situations in which MD is not sufficiently sensitive to detect subtle local changes. This can for example be the case if there is subtle local glaucomatous change, but the visual field series also shows increased diffuse fluctuation. An example of this is given in **FIG 9-10**.

### USE OF DIFFUSE DEFECT (DD) INDEX TO IDENTIFY DIFFUSE CHANGE

To determine whether there is diffuse visual field change independent from the presence or absence of local change, Octopus perimeters use the global index DD. This index represents the magnitude of the diffuse defect and is calculated from the Defect Curve. For more information on its design and definition see **BOX 7C**.

The DD Trend Analysis uses comparable definitions as the MD Trend Analysis but displays DD values on the y-axis instead of MD values and thus allows assessment of diffuse change. No symbol is displayed if there is no diffuse change, significant diffuse worsening is indicated by red downward arrows and significant diffuse improvement is shown by green upward arrows, similarly to that described for the MD slope.

Four typical situations (stable, local progression, diffuse progression, local and diffuse progression) and the respective behavior of the DD Trend Analysis are shown in **FIG 9-8**.

**FIGURE 9-8** This figure illustrates the typical behavior of the four Global Trend Analyses in potentially worsening visual field series from early to moderate disease. A quick visual inspection of the four global indices provides a straightforward assessment of whether a visual field series is worsening (MD worsening) and of whether the change is caused by diffuse worsening (MD and DD worsening), local worsening (MD, LD, and sLV worsening) or both diffuse and local worsening (MD, DD, LD and sLV worsening). Note that in more advanced disease (e.g., MD > 20 dB), with most visual field locations showing some degree of sensitivity loss, MD and also DD shows worsening while LD and sLV show improvement.
USE OF LOCAL DEFECT (LD) INDEX TO IDENTIFY LOCAL CHANGE

To determine whether there is local visual field change independent from the presence or absence of diffuse change, Octopus perimeters use the global index LD. This index represents the magnitude of the local defect and is calculated from the Defect Curve. For more information on its design and definition see BOX 70.

The LD Trend Analysis uses comparable definitions as the MD Trend Analysis but displays LD values on the y-axis instead of MD values and thus allows assessment of localized change. No symbol is displayed if there is no local change, red downward arrows indicate significant local worsening and significant local improvement is shown by green upward arrows, similarly to that described for the MD slope.

The typical behavior of the LD Trend Analysis in progressing from early to moderate disease (e.g., worsening glaucoma) is shown in FIG 9-8.

USE OF SQUARE ROOT OF LOSS VARIANCE (sLV) TO IDENTIFY LOCAL CHANGE

While the combined evaluation of the DD and LD Trend Analysis is sufficient to distinguish between local and diffuse change, some users are more familiar with the square root of Loss Variance (sLV) index. Octopus perimeters therefore also provide a trend graphic of the index sLV as an alternative to using the DD and LD Trend Analysis. This allows clinicians to choose the analysis they prefer to assess progression.

The sLV global index provides a measure for the inhomogeneity of the visual field. If a visual field is normal, shows a diffuse defect or shows severe pathology (e.g., MD > 20 dB), it is very homogenous and sLV is low. On the other hand, if a visual field shows one or more local defects, it is more inhomogenous and sLV is larger. sLV therefore increases if a local defect is increasing, and it remains stable if a diffuse defect is increasing. While this provides comparable information in a situation in which there is only local or only diffuse change, it becomes challenging to understand the visual field change in case of simultaneous local and diffuse change. For more information on the design and definition of sLV see FIG 7-21 and TABLE 7-1. For more information on its clinical interpretation, see FIG 8-27.

The sLV Trend Analysis uses comparable definitions as the MD Trend Analysis but displays sLV values on the y-axis instead of MD values and thus allows distinction between homogenous and inhomogenous change. No symbol is displayed if there is no change; increasing inhomogeneity is indicated by red downward arrows and increasing homogeneity is shown by green upward arrows, similarly to that described for the MD Trend Analysis.

The typical behavior of the sLV Trend Analysis in progressing from early to moderate disease (e.g., worsening glaucoma) is shown in FIG 9-8.
CLINICAL INTERPRETATION OF GLOBAL TREND ANALYSES

In clinical practice it is helpful to jointly consider the information from the four indices presented in the Global Trend Analysis. It is useful to assess the symbols marking significant change first to get a quick overview of a patient’s series of visual fields. Further analysis of the individual graphs can then be performed given the clinical situation. Two clinical examples are shown in FIG 9-9 and 9-10.

CASE EXAMPLE 1: PATIENT WITH BOTH PROGRESSING CATARACT AND GLAUCOMA

**GLOBAL TREND ANALYSIS**

- **MD**: Stable or overall progression?
  - Fast (1.5 dB/year) worsening of visual field series
- **sLV**: Increasing/decreasing inhomogeneity?
  - Both local and diffuse worsening
- **DD**: Diffuse progression?
  - Progression of cataract and glaucoma
- **LD**: Local progression?
  - Stable
  - Local worsening

**DESCRIPTION**

- MD: Worsening
- DD: Diffuse worsening
- sLV: Stable
- LD: Local worsening

**INTERPRETATION**

**SERIES OF VISUAL FIELDS**

Defect location & depth?

**FIGURE 9-9** This figure illustrates the usefulness of looking at the four global indices in combination. In this example, a patient has both confirmed glaucoma and cataract. While the visual field shows overall significant worsening (MD worsening at p < 0.5%), the MD Trend Analysis does not show which disease is progressing. An analysis of the Diffuse (DD) and Local (LD) Trend Analyses shows both significant local and diffuse progression, suggesting that both glaucoma and the cataract are progressing.
CASE EXAMPLE 2: SUBTLE LOCAL GLAUCOMATOUS CHANGE AND MAINLY DIFFUSE FLUCTUATION

**GLOBAL TREND ANALYSIS**

<table>
<thead>
<tr>
<th>MD</th>
<th>Stable or overall progression?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope: 0.4 dB / Yr</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>sLV</th>
<th>Increasing/decreasing inhomogeneity?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope: 0.5 dB / Yr (p &lt; 0.5%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DD</th>
<th>Diffuse progression?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope: 0.1 dB / Yr</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LD</th>
<th>Local progression?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope: 0.3 dB / Yr (p &lt; 2%)</td>
<td></td>
</tr>
</tbody>
</table>

**DESCRIPTION**

Clinically confirmed pathology: glaucoma

MD Stable

DD Stable

sLV Increasing inhomogeneity

LD Local worsening

**INTERPRETATION**

Slow (0.3 dB/year) local worsening of visual field series

Some fluctuation

Slow local glaucoma progression

**SERIES OF VISUAL FIELDS**

Defect location & depth?

**FIGURE 9-10** This glaucoma patient shows a marked nasal step and some diffuse visual field loss in visual fields 3 and 4 in the series of Grayscale (Comparisons) representation. Looking solely at MD change, the visual field series appears to be stable (no symbol). Nevertheless, the MD Trend Analysis also shows an outlier on the 3rd test, which is also present in the DD Trend Analysis suggesting this is caused by diffuse fluctuation. Assessment of the DD Trend Analysis (no change), sLV Trend Analysis (significant worsening at p < 1%) and LD Trend Analysis (significant worsening at p < 5%) reveals no diffuse change but significant local change. In conclusion, in this situation MD is too affected by diffuse fluctuation to show the significant but local worsening of the nasal step defect. Thus, the additional assessment of local and diffuse change in this situation is more sensitive in detecting subtle local change than the assessment of only the MD Trend Analysis.
CLUSTER TREND AND CORRECTED CLUSTER TREND ANALYSIS

IMPORTANCE OF ASSESSING CLUSTER PROGRESSION IN GLAUCOMA

Typical glaucomatous defects caused by localized retinal nerve fiber damage, as well as some visual field defects caused by optic nerve damage, consist of a cluster of adjacent defective visual field locations (FIG 5-1) that correspond to the path followed by the retinal nerve fiber bundles in the retina (see step 5 in Chapter 8). Localized visual field progression therefore typically occurs in a cluster of visual field locations.

However, if localized glaucomatous progression is small and there is additional fluctuation, the global index MD may not be sensitive enough to detect that subtle cluster change because MD is an average of the sensitivity loss of the whole visual field. While in some instances looking at local change using the LD or sLV indices can lead to the detection of such change, spatial information about where the change occurs is missing.

For example, to determine whether there is a corresponding structural change in glaucoma to confirm a suspected glaucomatous change, it is helpful to know in which area of the visual field the change is happening. In addition, in a constricted glaucomatous visual field with many visual field locations showing absolute defects (i.e., sensitivity thresholds of 0 dB), progression in the remaining central visual field of a patient is of key importance for quality of life but may not be apparent from the MD Trend Analysis, due to its relative insensitivity in detecting localized change.

It is thus helpful to assess Cluster MD progression in addition to the global indices to detect subtle localized visual field change in glaucoma as well as to receive additional spatial information about where the change is happening. This is the purpose of both the Cluster and Corrected Cluster Trend Analysis.

CLUSTER AND CORRECTED CLUSTER TREND ANALYSIS

Cluster Trend Analysis (CTA) is a trend analysis based on the single field Cluster Analysis whose design and definitions have already been explained in FIG 7-12 and 7-13 and BOX 7B and whose clinical interpretation and usefulness have already been shown in FIG 8-20 and 8-21 and BOX 8B. The Corrected Cluster Trend Analysis (CCTA) is very similar to CTA, but is based on the Corrected Cluster Analysis (see FIG 7-20) which eliminates the influence of diffuse defect.

Both types of Cluster Trend Analysis employ the same statistical analysis also used in the global MD Trend Analysis and use comparable symbols to indicate significance of change. However, instead of looking for significant MD change over time, they are looking for significant Cluster or Corrected Cluster Mean Defect (MD) change over time.
CTA and CCTA also use the red downward arrows and green upward arrows to show significant cluster worsening or improvement. However, the graphical display is different from the MD Trend Analysis. The individual Cluster MDs are not shown in a two-dimensional trend graph. Instead, both the Cluster MD change in dB/year and a symbol indicating the significance of this change are displayed in each of the 10 clusters as shown in FIG 9-11.

Similar to the interpretation of Cluster Analysis, some caution is essential in the clinical interpretation of CTA and CCTA. This is because one random cluster showing a p value smaller than 5% is expected to occur even in stable visual fields. Thus, a significant cluster defect is much more clinically meaningful if it is spatially correlated with another meaningful cluster defect or if it correlates with a significant structural change.

Similar to Cluster Analysis (see BOX 8B), CTA has been shown to be highly sensitive in detecting subtle, early glaucomatous change and has been shown to be more sensitive in detecting change than MD Trend Analysis and local event analysis11-13 (not available as a statistical tool in the EyeSuite Progression Analysis).

These findings can be explained with the same rationale used to explain why Cluster Analysis is highly sensitive in detecting early glaucomatous defects. Because glaucomatous change is mostly local, the averaging used to de-
The usefulness of Cluster Trend Analysis (CTA) in a case which shows a considerable amount of fluctuation is visible in the data. This visual field series of a glaucoma patient appears to be stable (no symbol indicating change) on the global index MD, but shows local worsening on the LD index. Using CTA, significant worsening (red downward arrow) is apparent in the superior paracentral, superior and infero-temporal clusters indicating clear local worsening. In this situation, CTA is more sensitive in detecting progression than MD and provides additional information about the location of progression compared to the LD index.
This example presents the visual fields of a glaucoma patient with a severe superior altitudinal defect and no remaining sensitivity in most of the upper visual field (floor effect, no further progression can be detected). All four global indices are stable with no symbol indicating change. However, using the Cluster Trend Analysis, significant localized worsening (red downward arrow) is apparent in the inferior cluster. In such advanced situations, Cluster Trend Analysis can assist in the detection of progression in areas with remaining sensitivity, which is important for the management of the patient.
POLAR TREND ANALYSIS

IMPORTANCE OF ESTABLISHING A RELATIONSHIP BETWEEN STRUCTURAL AND FUNCTIONAL PROGRESSION

In eyes with early glaucomatous damage or only subtle progression, detection of pathological changes is challenging. Therefore, it is often useful to consider both functional and structural change (i.e., neuroretinal rim tissue loss; decrease of retinal nerve fiber layer thickness).

Because visual field damage is often detected in a representation of a retinal location while structural damage is evident at the optic disc, there is a need to use a representation that links the structural to the functional visual field progression. This is the purpose of Polar Trend Analysis.

USE OF POLAR TREND ANALYSIS TO ASSIST IN THE DETECTION OF GLAUCOMATOUS STRUCTURAL PROGRESSION

Polar Trend Analysis is based on Polar Analysis, whose design and definitions have already been shown in FIG 7-14 and 7-15 and whose clinical interpretation and usefulness have been presented in FIG 8-23 and 8-24.

It graphically represents change at each visual field test location where the corresponding retinal nerve fiber bundles arrive at the margin of the disc. It does so by employing the same trend analysis approach also used in the global MD Trend Analysis (see FIG 9-3 and 9-5 and BOX 9A), but applies it to sensitivity loss at each test location (pointwise trend analysis). For more information on the design of Polar Trend Analysis, refer to BOX 9B.

THE DESIGN OF POLAR TREND ANALYSIS

Polar Trend Analysis performs pointwise trend analysis on sensitivity loss data to determine the trend line but not the significance of the slope for each visual field location individually. This is illustrated in the graphic in this box, which uses the example of one superior nasal test location circled in red in the Grayscale representation.

However, the graphical display of Polar Trend Analysis is fundamentally different from the other representations discussed previously. Instead of using the slope to determine a rate of change, the trend line is used to determine a best fitted sensitivity loss for the first (blue point in the graphic in this box) and the last (yellow point) of the visual field tests. It should be noted that these two data points are based on the trend line at the respective test dates, not on the individual visual field test result at a given test date.

These two fitted sensitivity loss values are then marked in the same Polar grid also used for Polar Analysis and connected by a straight line at the position where the corresponding nerve fiber bundles of the test location arrive at the margin of the disc. If there is worsening between that first and last fitted sensitivity loss, then the bar is drawn in red, while it is drawn in green if there is improvement.
Progression (worsening) is represented by a red bar, the length of which corresponds to the best-fitted change in the sensitivity loss in dB. Improvement is similarly represented using a green bar. Though the quantity of change is not given numerically, the approximate change of each defect can be identified on the graph in dB. A gray band in the center indicates approximate normal ranges for those bars (FIG 9-14).
Clinical interpretation of Polar Trend Analysis is straightforward and based solely on the graphical representation. The longer the bar, the more absolute change has occurred during the time period of interest and the further away the bar is located from the center, the more damage was already present at a given test location at the time of the first test.

If there are many red bars indicating worsening clustered at one optic disc location, this indicates a visual field worsening at that position. One can determine whether a corresponding structural change at that same position is present. Defect progression on the Polar Trend Analysis report can be considered as a warning message for localized visual field progression, which may draw the clinicians’ attention to the spatially corresponding potential structural progression. However, it is important to note, no rates of progression or significance of progression are provided by Polar Trend Analysis. For an exact evaluation of these parameters, one can refer to Cluster Trend and Corrected Cluster Trend Analyses. It is important to remember that those representations are oriented as visual fields and not as structural data. This means that related defects will be positioned at the location flipped vertically across the horizontal midline.

Polar Trend Analysis has been shown to correlate well with structural progression data14 and is therefore a very useful and quick tool for assistance with the combined evaluation of both structural and functional progression. A clinical case is illustrated in FIG 9-15.
This glaucoma patient shows significant local visual field worsening (MD, LD and sLV worsening at p < 1%) over a period of 5 years starting from the superior paracentral and superior nasal step areas and expanding to the inferior paracentral area, while deepening at the original defect locations (significant corrected cluster worsening in these areas). Polar Trend Analysis displays strong supero- and infero-temporal worsening. Looking at the change on the OCT retinal nerve fiber layer thickness between 2008 and 2013 (supero- and infero-temporal structural progression), there is a clear spatial relationship between structural and functional change, thus confirming that these changes stem from glaucoma.
REFERENCES


