Appearance of the Pattern Deviation Map as a Function of Change in Area of Localized Field Loss

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PURPOSE. To determine the influence of the spatial extent and the depth of localized field loss on the computation of the General Height (GH) method for estimating the diffuse component of visual field loss and, therefore, on the subsequent appearance of the Pattern Deviation (PD) map.

METHODS. Varying shapes and depths of localized glaucomatous field loss were modeled in each of 82 Humphrey Field Analyzer Program 30-2 fields (82 normal eyes) by superimposing, on the fields from the normal eyes, the PD defect depth (P < 0.05) of one visual field from each of 123 patients with glaucoma. The difference in GH between each of the 10,086 modeled fields and the GH in the corresponding measured normal field was derived and the relationship to possible differences in the location-by-location significance levels of each pair of PD maps determined.

RESULTS. For the group mean overestimation in the GH of −0.79 dB, the 50th, 90th, and 95th percentiles of the modeled fields described 23.4%, 37.9%, and 42.6% locations, respectively, exhibiting an underestimation in PD statistical significance. As the size of the superimposed field loss increased, the overestimation of the GH increased, and the underestimation of PD statistical significance became more apparent. This error was independent of defect depth.

CONCLUSIONS. The localized component of field loss in glaucoma produced an overestimation of diffuse loss and a consequent underestimation of the severity of focal loss by PD analysis. This effect increased as the spatial extent of the loss became more extensive and will lead to an underestimation of progressive localized field loss. (Invest Ophtalmol Vis Sci. 2004;45:3099–3106) DOI:10.1167/iovs.03-0617

The measurement of the visual field to document progressive functional damage is important in the management of glaucoma. Glaucomatous visual field loss exhibits both diffuse and localized components1–4; however, the presence of purely diffuse loss in early glaucoma is equivocal.5–15 Cataract causes a diffuse reduction of the visual field,16–18 and the frequent co-existence of cataract and glaucoma confounds the interpretation of the visual field, particularly when one or both disease entities are progressing. Techniques to separate diffuse from localized field loss19,20 and especially to separate progressive diffuse loss from progressive localized loss21,22 are therefore essential for the effective management of glaucoma.

The magnitude of the diffuse component of glaucomatous visual field loss can only be estimated. Any inaccuracy associated with this estimation will, in turn, influence the derivation of the localized component and consequently lead to an erroneous appearance of the measured visual field. Various arbitrary definitions of the diffuse component, and associated methods of estimation, have been used in static perimetry, including the Individual General Sensitivity index,19 the Cumulative Defect Curve,20 and the General Height index (GH).19,23 The Mean Defect24 and Mean Deviation19 (MD) indices are unsuitable for delineating diffuse loss since they average the deviations of all measured values of sensitivity from the corresponding age-corrected normal value across the visual field, both of diffuse and of localized origin, and are therefore also strongly influenced by the presence and magnitude of localized loss.23 The Individual General Sensitivity, the Cumulative Defect Curve, and the GH index are similar in concept to each other but differ from the MD.

The GH index is the measure used to derive the Pattern Deviation (PD) values from the Total Deviation (TD) values obtained with Programs 30-2, 24-2, and 10-2 of the Humphrey Field Analyzer (HFA; Carl Zeiss Meditec Inc, Dublin, CA) and is also used in the Glaucoma Hemifield Test for Programs 30-2 and 24-2.23 In the case of Programs 30-2 and 24-2, the GH index is defined as the 85th percentile (corresponding to the 7th most positive value) of the distribution of the TD values among the 51 stimulus locations corresponding to the stimulus grid of Program 24-2 (the three stimulus locations in the blind spot region are excluded). Such an index, although used as a surrogate for the derivation of diffuse loss, by definition, may contain up to six locations exhibiting thresholds within the normal range.

The extent to which the magnitude of localized field loss influences the GH index is unknown. However, it can be hypothesized that any systematic error in the estimation of the diffuse component resulting from an increase in the spatial extent and/or the depth of the localized field loss will impede the accurate separation of the respective diffuse and localized components. Knowledge of such errors is crucial to the further development of techniques for separating the presence, and progression of, the diffuse and localized components of visual field loss. The purpose of this study, therefore, was to determine the influence of localized field loss, as a function of spatial extent and defect depth, on the outcome of the GH index in glaucoma and, thereby, on a widely used method for estimating the diffuse component of visual field loss.

METHODS

The visual field material was obtained retrospectively from two databases: a cohort of normal individuals and a cohort of patients with primary open angle glaucoma (POAG). All visual field examinations had been undertaken at the Department of Ophthalmology, Malmö University Hospital. The research followed the tenets of the Declaration of Helsinki. informed consent had been obtained both from the normal individuals and from the patients with POAG, after explanation.
of the nature and possible consequences of the study, and was in accordance with the requirements of the Local Ethics Committee of Lund University, Lund, Sweden.

The cohort of normal individuals consisted of 82 subjects who had comprised the Malmö cohort of the normal database used for the derivation of the STATPAC statistical analysis package (Carl Zeiss Meditec) or better in each eye; a distance refractive error of 20.4 diopters mean sphere and ±3.0 diopters cylinder; clinically clear media, an intraocular pressure of ≤22 mm Hg; a normal appearance of the fundus; no systemic medication or disease known to affect the visual field; and no history or family history of glaucoma. All individuals had undergone three visual field examinations derived with Program 30-2 and the Full Threshold strategy of the HFA 640 in each eye over three visits. The results from the initial visit were discarded to minimize the effects of inexperience in visual field examination.

One visual field examination from one randomly designated eye of each subject was randomly selected from the remaining two visits. All visual fields exhibited reliability criteria of ≤33% incorrect responses to the false-negative and ≥20% incorrect responses to the fixation loss catch trials.

The cohort of patients with POAG comprised 123 consecutively presenting patients who fulfilled the eligibility criteria for the study. The exclusion criteria comprised a visual acuity worse than 0.5; a refractive error outside the limits for the normal individuals, described above; history of ocular surgery or severe ocular trauma; poor quality optic nerve head photographs; and concomitant systemic or ocular disease (apart from mild age-related media opacities) known to affect the visual field. The mean age of the sample was 68.4 years (±11.1 SD range, 23.1–85.1 years).

The diagnosis of POAG was based on evaluation of 35 mm color slides of the optic nerve head viewed via a projector. The evaluation was undertaken independently by two experienced observers specializing in glaucoma (PA and AH) who were both masked to the remaining clinical data of the patients including the visual field results. All features of the nerve head were considered in the criteria for the designation of glaucomatous optic neuropathy, but particular attention was paid to the presence of vertical saccuization, focal thinning (notching) and vertical asymmetry of the neuroretinal rim, loss of differential light sensitivity. In this way, 10,086 visual fields from one eye of each of the patients with POAG were graded using a modified Hodapp and associates classification system to emphasize the spatial components in the grading of the field loss. The cohort of 123 patients comprised 50 fields with an Early, 34 fields with a Moderate, and 39 fields with a Severe defect. No patients in the Early group, one in the Moderate group, and 20 of the 59 patients in the Severe group manifested a ratio of incorrect responses to the false-negative catch trials lying outside the standard criteria for reliability of ≤33%.

A model of the visual field was developed which was deemed to contain an addition of a purely localized field defect. The model was produced by superimposing the PD value, if reaching statistical significance of $P < 0.05$, from the measured field of each of the 123 patients with POAG onto the TD value at the corresponding location in each of the 82 measured fields from the normal individuals (Fig. 1). Each modeled field therefore represented a combination of one normal visual field and the abnormal PD values of one visual field from one eye of one patient with POAG. The fields from the cohort of normal individuals were used to ensure a template which represented the normal physiological variability associated with the determination of differential light sensitivity. In this way, 10,086 fields were modeled (82 fields from normal eyes × 125 fields from patients with POAG). Three thousand eight hundred fifty-four modeled fields contained up to 20 superimposed abnormal PD values (resulting from 47 patients with POAG); 2952 modeled fields contained between 21 and 40 abnormal values (36 patients with POAG); 2952 between 41 and 60 values (36 patients with POAG) and 328 fields with >60 abnormal values (4 patients with POAG). Based on the results of the modified Hodapp and associates classification, the visual fields from which the superimposed field loss was taken were representative of the range of visual fields recorded in patients with POAG. The GH value from each modeled field was then compared to the GH value from the corresponding measured normal field.

The effect of the spatial extent of the defect on the GH calculation as a function of defect depth was investigated by separately generating six models of field loss, each again based on the 125 fields in the POAG cohort, which were superimposed on each of the 82 fields from the normal cohort. The superimposed field defect for each of the six models consisted of the same given number, and position, of the stimulus locations exhibiting abnormality by PD probability analysis as the measured defect. In a controlled manner, the defect depth at all those locations exhibiting abnormality was uniformly set, in turn, to one of each of six discrete defect depths of localized loss: −5, −10, −15, −20, −25, and −30 dB. Thus, 125 × 6 × 82 modeled glaucomatous fields were generated which possessed the same shape as the measured defects but which had controlled and uniform defect depths.

RESULTS

The effect of the superimposed field loss on the GH is shown in Figure 2 where the change in GH between each modeled field and the corresponding measured field from the normal group is plotted against the number of stimulus locations (regardless of defect depth) involved in the superimposed defect. The group mean change in GH was −0.17 dB (±0.23 SD; range, −2.34 to 0.00 dB) for up to and including 20 superimposed locations, and −0.59 dB (±0.48 SD; range, −4.82 to 0.00 dB) for 21 to 40 superimposed locations. It then increased more rapidly to −1.61 dB (±0.97 SD; range, −7.58 to 0.00 dB) for between 41 and 60 values and to −2.37 dB (±1.00 SD; range, −9.10 to −0.52 dB) for >60 locations. The group mean change in GH for all superimposed locations was −0.79 dB (±0.91 SD). In clinical terms, the increasing negative difference in GH would indicate an apparent, but falsely induced, increasing diffuse component of visual field loss.

Little difference on the inherent overestimation of diffuse field loss was noted after removal from the analysis of those visual fields in the Moderate and Severe categories of field loss which exhibited incorrect responses to the false-negative catch trials lying beyond the 33% reliability criterion. After removal of the 21 patients who exhibited an abnormally high false-negative catch trial rate, a Moderate criterion, the group mean difference in GH was unchanged for up to 20 superimposed locations (one patient with POAG excluded) and altered by 0.02 dB for 21 to 40 locations (three patients excluded) by 0.13 dB for 41 to 60 (16 patients excluded) and by 0.02 dB for >60 superimposed locations (one patient excluded).

The effect of the spatial extent of the defect as a function of defect depth is shown in Table 1. The increasingly negative...
The change in GH plotted against the PSD of each resulting modeled field (Fig. 3) indicates that, given enough spatial involvement of the localized loss in the modeled field, the GH can change, on average, by 1.0 dB even when the localized loss is associated with a PSD of approximately 7 to 8 dB. A change in GH of 4.0 dB occurred in the modeled fields and resulted from no less than 33 normal individuals combining with the field from one or more of 29 patients with glaucoma.

The number of PD values reducing in statistical significance by one or more levels of probability value within the modeled defect plotted against the number of superimposed abnormal locations is shown in Figure 4A. The number of PD values losing statistical significance (i.e., changing from $P < 0.05$ to nonsignificant) is shown in Figure 4B. The number of PD values exhibiting a reduction in statistical significance increased rapidly from approximately ten superimposed abnormal locations. It can be seen in Figure 4A that, for a defect involving an entire hemifield, approximately 37% of the locations exhibit an underestimation of PD statistical significance in 10% of cases. The reduction in the number of PD values losing statistical significance declined rapidly up to ten superimposed abnormal locations (Fig. 4B).

The more important issue, in any given individual, is not the magnitude of the overestimation of the GH, per se, but rather its interaction with the PD value at each location and with the range within, and between, consecutive significance limits associated with the modified PD value. The overriding clinical implication from the results can be seen in Figures 5 and 6. For
the group mean overestimation in the GH index of $-0.79$ dB, 19.5% of the PD values reduced in statistical significance by one or more levels of probability value in 50% of the modeled fields; 33.1% of the values reduced in statistical significance in 10% of the fields; and 37.4% of the values in 5% of the fields (Fig. 5A). As the overestimation of the GH increased, the number of PD values exhibiting an underestimate of statistical significance became more apparent. With a reduction in GH of $-2.5$ dB, for example, 53.0% of the PD values reduced in statistical significance by one or more levels of probability value in 50% of the modeled fields. For those PD values losing significance, the corresponding data for the group mean overestimation in the GH index of $-0.79$ dB were 1.8% of the values in 50% of the fields, 9.9% of the values in 10% of the fields, and 13.8% of the values in 5% of the fields (Fig. 5B). The clinical consequence of these findings, in terms of PD probability maps, are illustrated in Figure 6.

### Table 1. Effect on GH of Spatial Extent of Defect as Function of Defect Depth

<table>
<thead>
<tr>
<th>Number of Superimposed PD values</th>
<th>Defect Depth</th>
<th>Mean (SD)</th>
<th>Max</th>
<th>Min</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤20</td>
<td>$-5$ dB</td>
<td>$-0.17$ (0.23)</td>
<td>0.0</td>
<td>$-2.0$</td>
</tr>
<tr>
<td></td>
<td>$-10$ dB</td>
<td>$-0.17$ (0.23)</td>
<td>0.0</td>
<td>$-2.0$</td>
</tr>
<tr>
<td>21–60</td>
<td>$-15$ dB</td>
<td>$-0.17$ (0.23)</td>
<td>0.0</td>
<td>$-2.0$</td>
</tr>
<tr>
<td></td>
<td>$-20$ dB</td>
<td>$-0.17$ (0.23)</td>
<td>0.0</td>
<td>$-2.0$</td>
</tr>
<tr>
<td></td>
<td>$-25$ dB</td>
<td>$-0.17$ (0.23)</td>
<td>0.0</td>
<td>$-2.0$</td>
</tr>
<tr>
<td></td>
<td>$-30$ dB</td>
<td>$-0.17$ (0.23)</td>
<td>0.0</td>
<td>$-2.0$</td>
</tr>
</tbody>
</table>

**FIGURE 3.** The change in the GH index of the visual fields from the 82 individuals in the normal group resulting from superimposition of the measured localized loss of the 125 patients with glaucoma against the Pattern Standard Deviation (PSD) of the resulting modeled field. The boxed area denotes the modeled fields with an overestimation of the GH of ≥4.0 dB and which arise from the fields of 33 normal individuals combining with the field from one or more of 29 patients with glaucoma.

**DISCUSSION**

The results indicated that the magnitude of the diffuse component of visual field loss, as determined by the GH index, could be overestimated in the presence of localized field loss. Overestimation of the GH causes an underestimation in the level of significance exhibited by the PD values, including the failure of some to achieve statistical significance, and therefore an under-representation of the extent of localized field loss. The systematic underestimation in the level of significance exhibited by the PD values became more pronounced as the localized field loss increased in spatial extent. The overestimation of the GH is in addition to the increased physiological and pathophysiological variability of the threshold estimate in POAG $^{30,31}$ and will further compound the problems associated with interpretation of field loss.

The reason for the overestimation of diffuse field loss is a necessary selection bias among the stimulus locations used in the calculation of the GH. In clinical terms, as the localized field defect increases in spatial extent, or new areas of localized loss emerge, fewer stimulus locations remain unaffected by the localized field loss. Consequently, the likelihood increases that the field loss will encroach on the location(s) originally used for the designation of the GH. The error associated with the estimation of the GH will be independent of the presence of cataract provided that, as is currently assumed, the field loss due to cataract is uniform across the field.

The number of PD values exhibiting an underestimation in statistical significance varies between individuals. This variation arises from the interaction of three factors: the magnitude of the overestimation of the GH index; the proximity of the measured PD value to that required for a given statistical significance level; and the dB difference between consecutive significance levels. Even small overestimations in the GH index can have profound ramifications since, for example, at least one interval between consecutive significance limits of the PD probability analysis with the Full Threshold algorithm is less than, or equal to, 1.0 dB at 17 stimulus locations within Program 30-2.

Fields with moderately advanced localized glaucomatous loss are especially prone to errors in the GH estimation. Such fields can exhibit large between-location differences in the TD values in the region of the 15th percentile due to the increased physiological variability of the threshold estimate$^{30,31}$ and/or to the increased variability associated with the glaucomatous field loss.

The magnitude of the overestimation of the GH and the associated underestimation of the focal loss becomes increasingly more of a clinical problem as the severity of the superimposed loss increases. The severity of the superimposed loss can be expressed in terms of the PSD. Fields with near normal
values of PSD, which are common in early glaucomatous field loss, were not associated with any clinically significant overestimation of the amount of apparent diffuse field loss. This finding is in accordance with the results of Henson and associates, who found that the estimation of the GH was relatively unaffected in the presence of four or fewer stimulus locations exhibiting PD values of $P < 0.05$. However, the present study indicated that moderately elevated values of PSD were commonly associated with larger, and more clinically significant, errors in GH estimation. Since the effect is independent of defect depth for a given range of superimposed stimulus locations, the influence on the PSD largely emanates from the increase in the number of stimulus locations exhibiting abnormal sensitivity.

**Figure 4.** (A) The percentage of superimposed PD values reducing in statistical significance by one or more levels of probability, due to overestimation of the diffuse component, against the corresponding spatial extent of the superimposed localized loss. The 50th, 90th, and 95th percentiles of the distribution, described in terms of quadratic functions, are illustrated. (B) The corresponding plot for the percentage of superimposed PD values losing statistical significance. The accompanying percentiles are described in terms of inverse functions.

**Figure 5.** (A) The percentage of superimposed PD values reducing in statistical significance by one or more levels of probability, due to overestimation of the diffuse component, against the corresponding overestimation of the GH index. The 50th, 90th, and 95th percentiles of the distribution, described in terms of quadratic functions, are illustrated. The absence of the percentiles for changes in GH of greater than $-5.0$ dB is due to insufficient data. (B) The corresponding plot for the percentage of superimposed PD values losing statistical significance.
the underestimation of the extent of the localized loss should also apply to stimulus grids such as HFA Program 10-2 which features a high resolution grid centered on the fovea and which is used in analysis of macular disease and late stage glaucomatous field loss.

The results described here for the GH index are also applicable to the Individual General Sensitivity index and to the Cumulative Defect curve. In such a curve, primarily increasing the area, but also the depth, of localized field loss increases the likelihood that the entire curve would be reduced in height, thereby overestimating the diffuse component of field loss.

The major clinical consequence arising from the overestimation of the GH will occur in the evaluation of progressive glaucomatous visual field loss within any given patient, but particularly in those with moderate to advanced loss. The full extent to which the underestimation of the severity of the spatial extent of the localized component impedes the early recognition of progressive field loss in glaucoma, at any given severity of defect, unquestionably requires further study. Clearly, such studies need to be considered with respect to Change Probability analysis based on PD. The limitation in

Figure 6. The PD probability map influenced by the overestimation of the GH index (left) by $-0.91 \text{ dB}$ (A), $-1.35 \text{ dB}$ (B), $-2.67 \text{ dB}$ (C), and $-6.77 \text{ dB}$ (D), illustrating an underestimation in the number and/or severity of the statistical significance compared to the true corresponding PD probability map (right). The four maps were generated from four separate normal subjects and four separate patients with glaucoma.

The mean age of the cohort of normal subjects was not matched to that of the patients with glaucoma. However, the difference in age between the two cohorts is unlikely to have materially influenced the results. The significance limits for the TD and PD values are independent of age in that, with the STATPAC analysis, the defect depth for any given patient at any given location is age-corrected and referenced to the normal value from any measured glaucomatous field. The measured PD values from a given glaucomatous field could have been influenced by either a diffuse, a localized, or a combined reduction of differential light sensitivity. Any such diffuse loss could have arisen from media opacities, glaucoma, coexisting media opacities and glaucoma, pilocarpine induced pupillary miosis, or from an artificial contamination such as uncorrected, or poorly corrected, refractive error.

The measured PD values from a given glaucomatous field, which were superimposed on the fields from the normal individuals, may have been taken from a field in which the error associated with the calculation of the GH index would have resulted in an underestimation of the measured PD values, themselves. Such a situation would have had little impact on the given resultant modeled fields and would merely have reduced the depth and area of the glaucomatous localized loss of the superimposed field in proportion to the error associated.
with the estimation of the accompanying GH. The purpose of the modeling was to evaluate the impact of a given superimposed field defect on the GH calculation rather than to study the properties of the measured field itself. Any such underestimation of the superimposed field loss from the measured field would merely have resulted in modeled fields with less severe defects and would not have influenced the conclusions from the study.

The PSD is intended to be a measure of localized field loss and was used as an illustrative measure of the extent of the field loss in the modeled visual fields. However, the PSD is limited by the lack of dynamic range of the perimeter and, as the field loss reaches moderately advanced field levels, the PSD becomes smaller with further field loss. The MD of the given modeled field was not used as an illustrative measure for two reasons. First, it does not describe only the diffuse component of glaucomatous field loss and, second, the modeled field was deemed not to contain diffuse field loss.

The model of glaucomatous localized field loss could have been developed from simulated clusters of typical field loss. However, it was felt that the use of the superimposed PD field loss was more representative of the clinical situation and did not depend on predefined criteria for the shape of localized glaucomatous loss based on arbitrary definitions for the clustering of given locations. 

The influence of the defect depth was modeled in terms of six discrete dB levels independently of the statistical significance associated with the resulting defect. An alternative approach would have been to model the depth in terms of the dB values associated with the fixed P values (5%, 2%, 1%, and 0.5%, respectively) of the PD probability analysis rather than in terms of dB values, per se. Such an approach would have resulted in a model with non-uniform defect depths over the given area of loss but would have accounted for the physiological variability associated with the threshold estimates at each individual location. However, the results of the defect depth modeled in fixed dB steps clearly indicated that the spatial extent, rather than the depth, of the focal loss was the more dominant variable and therefore rendered modeling of the defect depth based on the PD significance levels unnecessary.

The distribution of the severity of the modeled fields, in terms of defect depth and area, was determined by the distribution of the severity of field loss in the cohort of patients with glaucoma. Since the measured field from each of the patients with POAG was applied to each of the fields from the normal individuals, the influence of the most severely damaged measured fields was increased in direct proportion to the number of normal individuals. Such an outcome is of little consequence since the same limitation applies to each of the measured fields regardless of severity.

The overestimation of the GH adjustment and the resultant underestimation of focal loss, which increases with increase in the number of stimulus locations featuring abnormality, will have major consequences for the management of patients with moderate to advanced glaucoma and also those with progressing glaucomatous field loss. Improved methods for the estimation of the diffuse component of the visual field, based on GH and similar techniques, are therefore required.

References


