The Statistical Interpretation of Blue-on-Yellow Visual Field Loss

John M. Wild, Ian D. Moss,* David Whitaker,* and Eamon C. O'Neill†*

Purpose. To evaluate short-wavelength-sensitive perimetry in the detection of glaucomatous field loss.

Methods. The sample consisted of 27 normal subjects, 24 patients with primary open angle glaucoma (POAG), and 27 patients with ocular hypertension (OHT). Blue-on-yellow (B–Y) and standard (W–W) perimetry was undertaken with a modified Humphrey Field Analyzer 640 on one eye of each subject and patient. The B–Y data were corrected for individual ocular media absorption. Results were compared to an age-matched normal database of 50 subjects (age range, 60 to 82 years; mean age, 70.0 years; SD, 6.4 years). Visual field indices and total and pattern deviation probability maps were calculated for both W–W and B–Y fields.

Results. The B–Y normal database exhibited increased between-subject variability compared to the W–W normal database ($P < 0.001$). The greater variability increased with the increase in eccentricity ($P < 0.001$) and with the increase in age ($P = 0.032$). All patients with POAG exhibited B–Y field loss; 11 demonstrated greater B–Y loss than the corresponding W–W field. In advanced POAG, the B–Y and the W–W fields were similar. Twenty-five of the 27 normal subjects exhibited normal B–Y fields. Five of the 27 patients with OHT manifested B–Y focal abnormality and a normal W–W field: in two, W–W focal loss subsequently developed.

Conclusions. Short-wavelength-sensitive perimetry can identify visual field loss before that detected by W–W perimetry. However, the increased between-subject variability necessitates stringent statistical analysis in the definition of abnormality. Invest Ophthalmol Vis Sci. 1995;36:1398–1410.

There is considerable interest in short-wavelength-sensitive (SWS) perimetry for the early detection of visual field loss in primary open angle glaucoma (POAG).[1–14] The technique uses a blue stimulus that preferentially stimulates the blue (SWS) cones and a high-luminance yellow background to adapt the green (MWS) and red (LWS) cones and to saturate rod activity simultaneously. Preliminary reports suggest that SWS visual field defects occur before conventional white-on-white (W–W) field loss in POAG and exhibit progression in advance of that recorded with conventional W–W perimetry.[6,10,12] The SWS loss is thought to have diffuse and focal components,[1–14] with the focal loss corresponding to nerve fiber bundle patterns.[1] It has been suggested that the diffuse reduction of SWS sensitivity may be related to the degree of intraocular pressure (IOP).[9] Nevertheless, SWS deficits have also been recorded in low-tension glaucoma.[14]

The evaluation of conventional W–W visual field abnormality is based on rigid statistical procedures, such as global indices[15,16] and total and pattern probability plots.[17,18] Both techniques compare the patient's visual field with that of the age-corrected normal hill of vision adjusted for the normal between-subject variability.[19] This normal between-subject variability within an examination increases with an increase in eccentricity and age.[19] The global indices describe the overall height and shape of the field, whereas the total and pattern probability plots assign a probability level

*From the *Department of Vision Sciences, Aston University, and the †Glaucoma Department, Birmingham and Midland Eye Hospital, Birmingham, United Kingdom.*
Presented in part at the XIth International Perimetric Society Meeting, Washington DC, July 3–7, 1994.
Supported in part by a Research Studentship from the Royal National Institute for the Blind (IDM).
Submitted for publication August 8, 1994; revised November 14, 1994; accepted January 18, 1995.
Proprietary interest category: N.
Reprint requests: John M. Wild, Department of Vision Sciences, Aston University, Aston Triangle, Birmingham, B4 7ET, United Kingdom.

Investigative Ophthalmology & Visual Science, June 1995, Vol. 36, No. 7

at each stimulus location to the likelihood of the measured deviation in sensitivity lying outside the normal population. In addition, the probability plots separate the general reduction in sensitivity, arising from such factors as media opacities, pupillary miosis, and defocus, from the localized reduction in sensitivity.

To date, the statistical analysis of B–Y visual field loss has not been as robust as that of W–W loss. Blue-on-yellow abnormality has been defined for the field as a whole in terms of mean deviation.[1–14] It has also been specified at each stimulus location in terms of a constant defect depth, regardless of any differences in the normal variability across the visual field[11–14] and with respect to the 95% and 99% confidence limits for normality based on the overall height of the hill of vision.[1,4–7,10] Furthermore, the short-term fluctuation has been found to be greater for B–Y perimetry than for W–W perimetry.[7,20,21] However, little is known about the magnitude of the normal between-subject variability of B–Y perimetry and the extent of any such variations with eccentricity and with increase in age.[4,22] Indeed, the between-subject variability of the normal B–Y response has not been compared to the W–W response in the same sample of subjects. In addition, no attempt has been made to separate the localized SWS loss from the generalized component of sensitivity by adjusting for the height of the B–Y hill of vision in a manner similar to that of the W–W pattern probability plots. As such, the true nature of the focal loss has not been identified. Furthermore, the application of B–Y perimetry as a function of the severity of field loss has not been studied in relation to pattern deviation analysis. The investigation of established POAG thus becomes important for the study of the onset, and progression, of SWS field loss in patients initially admitted for OHT.

The purpose of this study, therefore, was fourfold: to determine the magnitude of the between-subject normal variability of B–Y perimetry with respect to eccentricity and age and to compare the findings with those for W–W perimetry; to evaluate the sensitivity and specificity of B–Y perimetry in the detection of glaucomatous field loss using the total and pattern deviation probability analyses; to investigate the use of B–Y perimetry for the examination of those areas within the glaucomatous visual field exhibiting normal sensitivity to W–W perimetry; to apply the statistical procedures to a sample of patients with OHT.

METHODS

Sample

The material for the study comprised four separate samples: a normal age-matched control group, a separate group of normals, a group with POAG, and a group with OHT.

Normal Age-Matched Control Group. The normal control group was composed of 50 randomly recruited, age-matched normal subjects whose ages spanned two decades (age range, 60 to 82 years). Twenty-five subjects were between 60 and 69 years of age (mean age, 64.9 years; SD, 4.0 years), and 25 subjects were between 70 and 82 years of age (mean age, 75.1 years; SD, 4.0 years). Inclusion criteria were as follows: IOP < 21 mm Hg; normal optic nerve head appearance; a normal HFA W–W Program 24-2 field; refractive error in the examined eye $< \pm 5$ D sphere and < -3 D cylinder; visual acuity of 6/9 or better; minimal lenticular changes not greater than NI, CII, or PI by LOCS II[23]; no history of congenital color vision defect; no systemic medication known to influence the visual field; no ocular surgery or trauma; no history of diabetes mellitus; and no family history of glaucoma or diabetes mellitus. One eye of each age-matched normal subject was selected for the study.

Normal Group. The additional normal sample consisted of 20 subjects with inclusion criteria identical to those of the normal age-matched control group (age range, 60 to 78 years; mean age, 66.5 years; SD, 5.8 years) and included seven more subjects with NIII, PIII, or CIII cataract or worse as classified by LOCS II.[23] The 20 subjects were known to exhibit normal W–W visual fields by both total and pattern deviation plots. The visual acuities in the group with cataract ranged from 6/12 to 6/36. The subjects with cataract were known to exhibit normal W–W pattern deviation plots. Subjects with clinically significant cataract were deliberately included in the sample to test the efficacy of the B–Y total and pattern deviation analysis. One eye of each normal subject was selected at random for examination unless there was marked difference in the severity of cataract between the two eyes, in which case the eye with the more advanced cataract was selected.

Group With Primary Open Angle Glaucoma. The POAG sample consisted of 24 patients consecutively recruited from the Glaucoma Department of the Birmingham and Midland Eye Hospital. The mean age of the sample was 69.2 years (range, 60 to 83 years; SD, 8.7 years). Patients with POAG were treated with topical β-blockers only, and they exhibited characteristic optic nerve head abnormalities, IOP > 22 mm Hg, and characteristic W–W field loss. The sample was deliberately structured to include the widest range of glaucomatous visual field loss, and it incorporated 10 patients with altitudinal loss. The W–W mean deviation ranged from -1.20 dB to -20.35 dB. The mean IOP on admission was 27.78 mm Hg (SD, 4.0).

Group With Ocular Hypertension. The OHT sample consisted of 27 patients also consecutively recruited from the Glaucoma Department of the Birmingham and Midland Eye Hospital. Ocular hypertension was

defined as pressure > 22 mm Hg and normal W–W fields. The mean age of the sample was 68.2 years (age range, 60 to 82 years; SD, 6.4 years) The mean IOP on presentation to the hospital was 24.7 mm Hg (SD, 2.9 mm Hg). Of the 27 patients with OHT, 9 were classified at at low risk (IOP < 28 mm Hg and vertical C/D ratio < 0.6) and 14 at medium risk (IOP < 28 mm Hg and vertical C/D ratio < 0.6, with positive family history; or IOP > 28 mm Hg and/or C/D > 0.6, but not both, and positive family history). The remaining four patients with OHT were classified at high risk (IOP ≥ 28 mm Hg and C/D ≥ 0.6) and were receiving topical β-blockers.

All the patients with OHT and POAG conformed to inclusion criteria identical to the age-matched normal control group except for the criteria for IOP, optic nerve head appearance, visual field, and family history of glaucoma. One eye of each patient was examined. For the group with POAG, the eye with the least field loss was selected, whereas for the group with OHT, the eye with the highest IOP was examined.

The research followed the tenets of the Declaration of Helsinki, informed consent was obtained from all subjects and patients after the nature and possible consequences of the procedure were fully explained, and the study was approved by the Aston University Human Science Ethical Committee.

Perimetry

Perimetry was performed using Program 24-2 of a modified Humphrey Field Analyzer (HFA) 640. The modifications and associated calibration necessary for B–Y perimetry have been described elsewhere.[24–28] The blue stimulus filter was an OCLI (Optical Coatings, Dunfermline, Scotland) blue dichroic filter transmitting wavelengths below 475 nm. The yellow background was provided by a Schott OG530 filter (Schott Glaswerke, Mainz, Germany) transmitting above 500 nm, and the bowl luminance was 330 cdm^{-2}.

Each subject and patient underwent three separate perimetric examinations. The first visit was a training session involving standard W–W perimetry (Goldmann size III; background luminance 10 cdm^{-2}) and B–Y perimetry (Goldmann size V). The purpose of this first session was to minimize the learning effects present in both W–W and B–Y perimetry,[27] and the results were discarded. The same protocol was used at the second visit. The order of perimetric test within a session was randomized between patients to minimize order effects. A size III white stimulus was chosen because it is the clinical standard. A size V blue stimulus was used for compatibility with other studies: The larger stimulus increases the dynamic range of the perimeter and is in accord with the greater SWS isolation reported for a 2° diameter stimulus.[29] The combination of stimulus and background filters, together with the 330 cdm^{-2} bowl luminance, provided approximately 1.4 log units of SWS isolation.

Appropriate refractive correction was used for the viewing distance of the perimeter bowl. Fixation losses were <20%, and false-negative and false-positive responses were <33% for all subjects. The efficiency of fixation was constantly monitored with the video monitor of the HFA because the reduction in the maximum stimulus luminance of the blue stimulus also reduces the efficiency of the Heijl–Krakau blind spot monitoring technique. Similarly, the efficiency of the procedure for testing false-negative responses may be altered because the luminance of the B–Y false-negative stimulus is closer to threshold than that for W–W perimetry. Extensive rest periods were given within and between tests to minimize fatigue effects,[30,31] and no single visit lasted more than 60 minutes.

Ocular Media Characteristics

At the third visit, measurements were undertaken of ocular media absorption using the technique of Sample et al.[32,33] This involved the measurement of two scotopic thresholds of equal sensitivity to rhodopsin (i.e., 410 nm and 560 nm) at approximately 15° eccentricity in each quadrant. The differences in scotopic sensitivity are attributed to wavelength-dependent absorption by the ocular media. The procedure was used because it is the currently accepted psychophysical method with the HFA for correcting the results of B–Y perimetry for ocular media absorption.[1,4–7,9–14,20–22,25–28] Threshold for each wavelength was taken as the grand mean of the three separate determinations for each patient at each of the four stimulus locations. The difference between the thresholds was then scaled according to the crystalline lens of the standard observer of Norren and Vos.[34] When field loss was present at 15° eccentricity in a given quadrant for a specific patient, the thresholds at that location were not included in the calculation of the grand mean. All perimetry and the measurement of ocular media absorption were undertaken by a single experienced perimetrist (IDM).

Analysis

Normal Database. The perimetric sensitivities for the W–W and B–Y stimulus combinations were each calculated in log units relative to the maximum stimulus intensity of the given stimulus. Left eye data were converted to right eye data when necessary. The B–Y sensitivity at each stimulus location for each age-matched normal subject was corrected for the individual measure of ocular media absorption. Stimulus locations at which the B–Y threshold exceeded the maximum available stimulus intensity (i.e., 0.0 log units) were not corrected for absorption.

The group mean and standard deviation of the

sensitivities at each of the 52 stimulus locations of Program 24-2 for each age group of the normal age-matched control group were separately calculated for the W–W and B–Y stimulus combinations. The two stimulus locations above and below the blind spot were omitted from the analysis. The distributions of sensitivity for both the W–W and B–Y stimulus combinations at each stimulus location were tested for normality using a one-tailed Kolmogorov–Smirnov test. The sensitivities at each of the 52 stimulus locations exhibited a Gaussian distribution for both W–W and B–Y stimulus combinations. Pointwise deviations from the normal sensitivity for each age group—corresponding to 95%, 99%, and 99.5% probabilities—were then calculated based on a Gaussian distribution from the group mean at each stimulus location for W–W and B–Y fields.

Normal Subject and Patient Samples. The B–Y sensitivity at each stimulus location for each subject in the second normal sample and for each patient with POAG or OHT was similarly corrected for the individual measure of ocular media absorption. The W–W and B–Y fields of each subject and patient were then compared to the respective age-matched normal groups. The unweighted global indices mean deviation, short-term fluctuation, and corrected pattern standard deviation were calculated for each stimulus combination using the formulae of Heijl et al.[16] The mean deviation expressed the deviation in the height of the measured visual field from that recorded in normal subjects of the same age. The short-term fluctuation was a measure of intratest variability. The corrected pattern standard deviation represented the deviation in shape of the measured field from that of the normal and is corrected for the effect of the short-term fluctuation. Total and pattern probability maps were produced for each W–W and B–Y field of each patient. The total probability map indicated the frequency with which the measured sensitivity at each individual location deviated from that found in the normal age-matched population. The pattern probability analysis indicated the frequency with which the measured sensitivity at each individual location deviated from that found in the normal age-matched population and was adjusted for any overall differences in the height of the measured hill of vision. The height of the field was calculated in an manner identical to that of Heijl et al[17] by ranking the magnitude of the deviation from the normal value of sensitivity at each stimulus location and then subtracting the seventh highest ranked deviation from each of the 52 deviations. The corresponding W–W indices and probability maps derived from the W–W STATPAC printout were also used to compare the sensitivity and specificity of the normal age-matched control W–W database.

The resultant indices and probability plots derived for the W–W and B–Y fields of the normal group and the patient group were then evaluated by one of the authors (JMW) experienced in the interpretation of automated perimetry. The examiner was masked as to the diagnosis and to the remainder of the fields for the given patient or subject. The visual field was considered abnormal if a cluster of three or more stimulus locations exhibited a defect depth of <5% on the pattern probability plots[6] and was further evaluated with respect to the total deviation plot and as to whether the abnormality was typical of that in glaucoma.

Follow-up

The study of the patient group was prospective in nature. The mean duration of follow-up was 11 months (range, 4 to 14 months), and the mean number of examinations per patient was 2.3. The rationale for the frequency of follow-up was governed by a number of factors, including an increase in IOP, the risk category of the patient with OHT, a discrepant field, and an apparently progressing W–W or B–Y field or both.

RESULTS

Group mean ocular media absorption for the normal age-matched control group was 0.98 log units (SD, 0.12 log units) and 1.13 log units (SD, 0.10 log units) for the 60- to 69-year-old group and the 70- to 82-year-old group, respectively. Analysis of covariance with sample type as a between-subjects factor and age as a covariate showed that ocular media absorption increased with an increase in age ($P < 0.001$) but that the magnitude of the absorption was similar across all four samples ($P = 0.52$).

The group mean global mean sensitivity and short-term fluctuation of the normal age-matched control group for each of the two stimulus combinations as a function of the two age groups is given in Table 1. A repeated measures analysis of covariance with stimulus combination as a within-subjects factor and age as a covariate showed that, overall, the B–Y short-term fluctuation was larger than the W–W short-term fluctuation ($P = 0.002$) regardless of patient age ($P = 0.96$).

The standard deviation of the group mean sensitivity at each stimulus location (demonstrating the within-test, between-subject variability) of the normal age-matched control group for each of the two stimulus combinations as a function of the two age groups is given in Figure 1. A repeated measures analysis of variance with age as a between-subjects factor and eccentricity and stimulus combination as within-subjects factors showed that, overall, the standard deviations increased with an increase in age ($P = 0.002$) and across the visual field ($P < 0.001$) for both stimulus

TABLE 1. Group Mean Mean Sensitivity and Short-term Fluctuation for the Two Stimulus Combinations for Each of the Two Age Groups of Normal Subjects

Stimulus–Background Combination	*Visual Field Index*			
	60–69 Year Group		*70–82 Year Group*	
	MS	*SF*	*MS*	*SF*
W–W	2.71 (0.22)	0.13 (0.04)	2.61 (0.27)	0.15 (0.03)
B–Y	1.91 (0.27)	0.17 (0.05)	1.87 (0.37)	0.17 (0.05)

Values are expressed in log units. One log unit is equivalent to 10 dB. One standard deviation is given in parentheses.
MS = mean sensitivity; SF = short-term fluctuation.

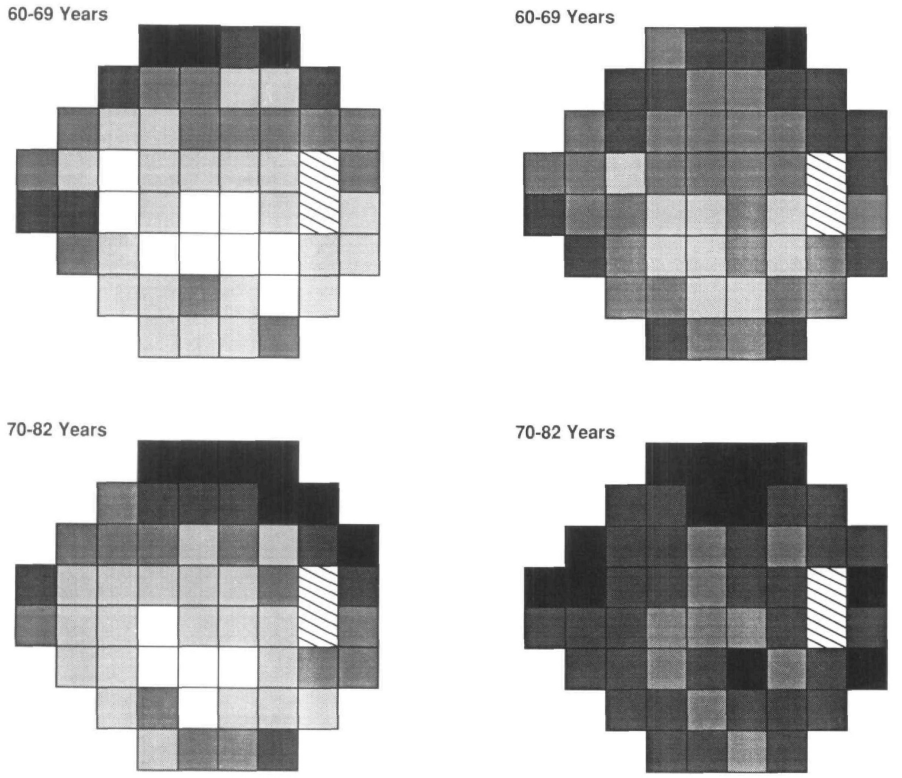

FIGURE 1. Grey-scale representation of the standard deviation of the group mean sensitivity of the normal age-matched control group at each stimulus location of Humphrey Field Analyzer Program 24-2. (*top left*) W–W, 60 to 69 years of age; (*bottom left*) W–W, 70 to 82 years of age; (*top right*) B–Y, 60 to 69 years of age; (*bottom right*) B–Y, 70 to 82 years of age. An increasing standard deviation is represented by an increase in the shade of grey. The grey scale is in log units.

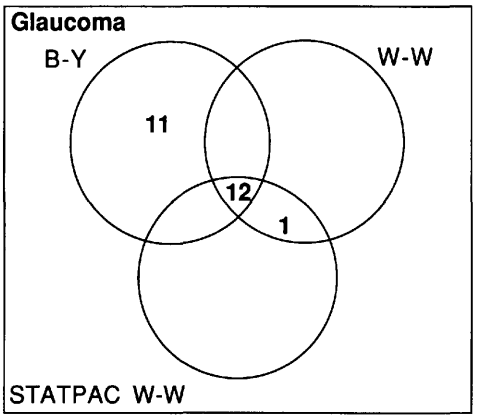

FIGURE 2. Visual field abnormality. Venn diagram illustrating the level of agreement in field loss based on the probability plots alone, between the B–Y and W–W stimulus combinations, for the group with POAG. Of the 24 patients, 12 had a similar level of B–Y field loss compared to each of the two W–W methods of analysis. Six patients, however, exhibited wider focal loss with the B–Y stimulus combination.

combinations. The variability was greater for the B–Y stimulus combination compared to the W–W ($P < 0.001$), particularly across the visual field ($P < 0.001$) and with an increase in age ($P = 0.032$). There was no difference in the magnitude of the variability between the B–Y data corrected for absorption and that not corrected for absorption ($P = 0.24$).

Twenty-five of the 27 normal subjects exhibited a normal B–Y field. The remaining two subjects each exhibited one cluster of three abnormal pattern deviation points at the 5% level: One cluster corresponded to an upper lid artifact, whereas the second was situated in the arcuate area. All seven patients with cataract, exhibited an abnormal B–Y total deviation plot but a normal B–Y pattern deviation plot. All 24 patients with POAG manifested abnormal B–Y fields.

The level of agreement in terms of the severity of the field loss between the B–Y and W–W stimulus combinations for the group with POAG, based on the probability plots alone, is summarized in Figure 2. Of the 24 patients, 12 had a similar level of B–Y field loss compared to each of the two W–W methods of analysis. Six patients, however, exhibited wider focal loss with the B–Y stimulus combination; an example of such loss is illustrated in Figure 3. Five more patients demonstrated substantially greater diffuse loss on the B–Y total deviation plot but exhibited similar W–W and B–Y pattern probability plots. No patients exhibited new scotomata. One patient consistently exhibited a B–Y field different than that of the corresponding W–W field.

The degree of agreement in the number of abnormal fields between the B–Y and W–W stimulus combinations for the group with OHT is summarized in Figure 4. Of the 27 patients with OHT, 20 exhibited normal B–Y fields at the first examination and normal W–W fields compared with the normal control group and the STATPAC analysis. Two patients had borderline fields on B–Y and W–W analyses; the loss, however, was not consistent with that of a glaucomatous field defect. Five patients, all at medium risk, exhibited repeat abnormal B–Y focal defects at the outset and normal W–W fields compared to the normal control group and to the STATPAC analysis, although in one patient, the W–W field relative to that of the normal age-matched control group was borderline. Subsequent follow-up of these five patients revealed a confirmed W–W focal loss in two (Figs. 5, 6). No patients showed evidence of a diffuse type of loss.

A repeated measures analysis of covariance with diagnostic category (i.e., OHT or POAG) as a between-subjects factor, stimulus type as a within-subjects factor, and age as a covariate was separately performed for each of the visual field indices, mean deviation, short-term fluctuation, and corrected pattern standard deviation. As expected, the mean deviation was greater overall for the group with POAG ($P < 0.001$) than the group with OHT, and this difference increased with age ($P = 0.041$). The mean deviation for the B–Y stimulus combination was greater than the mean deviation for the W–W stimulus ($P = 0.002$) irrespective of diagnosis ($P = 0.36$) and age ($P = 0.36$). The short-term fluctuation was greater for the group with POAG ($P = 0.001$) than the group with OHT, but there was no difference in the short-term fluctuation between the W–W and B–Y combinations ($P = 0.59$) regardless of age ($P = 0.32$). Not surprisingly, the corrected pattern standard deviation was greater for the group with POAG than for the group with OHT ($P < 0.001$), but this difference was independent of age ($P = 0.08$) and stimulus combination ($P = 0.85$).

DISCUSSION

The increase in the standard deviation of the group mean normal pointwise B–Y and W–W sensitivities with an increase in eccentricity and an increase in age is in agreement with the findings for W–W perimetry[19,35] and is compatible with those for B–Y perimetry.[4,22] The sensitivities at each location were normally distributed for both the W–W and B–Y combinations. The 5%, 1%, and 0.5% probability levels were obtained from calculations based on this Gaussian distribution rather than from empirical derivations. The normal distribution of the W–W data is in contrast to the W–W data of Heijl et al,[19] who found a non-

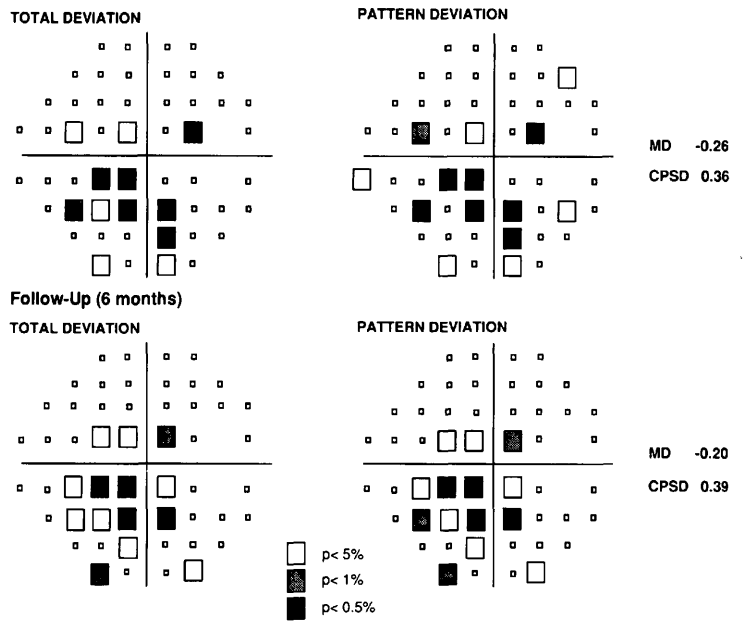

FIGURE 3. Total and pattern deviation plots for W–W (*top*) and B–Y (*bottom*) illustrating a POAG with an abnormal W–W field and greater B–Y loss at the outset and at the 6-month follow-up. The indices are in log units.

Gaussian distribution. The reason for the difference in the type of W–W distribution between the two studies is unclear, particularly because the experimental protocols were similar. However, the Heijl study involved the collection of data from both eyes at the same visit. It is known that the fatigue effect is greater for the second eye,[30,31] and it is possible that this may have influenced the outcome of the distribution. Nevertheless, the standard deviations of the group mean age-matched normal W–W sensitivities were similar to those of Heijl et al[19] at each location.

The finding of an increased within-examination variability in the age-matched normal group for the B–Y perimetry compared to W–W perimetry is in agreement with Sample et al,[20] who found that the short-term fluctuation was higher for B–Y perimetry in normal eyes, although the difference was not statistically significant. The similarity of the short-term fluctuation for the W–W and B–Y stimulus combinations in the group with OHT and the group with POAG is in agreement with Sample et al,[20] who also failed to find a statistically significant difference. Our results and those of Sample et al[20] are compatible with Nelson–Quigg et al,[21] who reported a 25% to 30% greater B–Y short-term fluctuation. The apparent increased variability of the B–Y short-term fluctuation in the age-matched normal group may have been artifactual because of a decreased W–W short-term fluctuation arising from the requirement for a normal W–W field. However, the B–Y short-term fluctuation was also higher (mean, 1.67 dB; SD, 0.43 dB) than the W–W short-term fluctuation (mean, 1.32 dB; SD, 0.38 dB) in the normal group of 20 subjects, and this difference reached statistical significance ($P < 0.007$). Nevertheless, the magnitude of the B–Y short-term fluctuation still lies within the normal range encountered for the W–W short-term fluctuation.

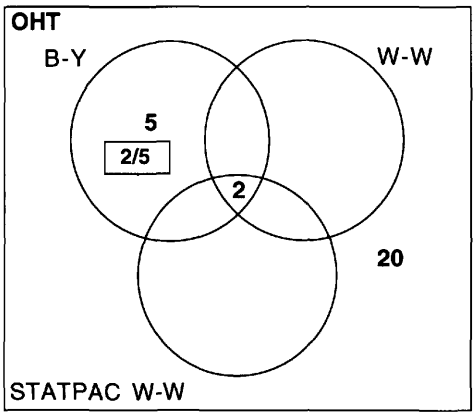

FIGURE 4. Visual field outcome. Venn diagram illustrating the presence of field loss between the B–Y and W–W stimulus combinations for the group with OHT. The value outside the circles indicates the number of patients with normal fields for the B–Y and both W–W analyses. The boxed number within the circle, representing the B–Y stimulus combination, indicates the number of patients subsequently manifesting a repeatable W–W loss.

A consequence of the increased magnitude of the B–Y pointwise standard deviations is that, for a given probability level, the deviation of the measured B–Y sensitivity from that of the normal value is larger than the equivalent W–W deviation. The magnitudes of the within-subject and the between-subject normal variability in B–Y sensitivity for the new, faster testing algorithms developed for W–W perimetry is unknown.[36–38]

As expected, the correction of the B–Y data for ocular media absorption resulted in an increase in the mean sensitivity at each stimulus location. Surprisingly, however, the magnitudes of the standard deviations of the pointwise mean sensitivities remained unchanged compared to those without correction, indicating that the between-subject variability is unaffected by correction for ocular media absorption. Indeed, the magnitude of the between-subject variation in the ocular media absorption correction factor of approximately 0.1 log units is smaller than that of the between-subject difference in B–Y sensitivity at each stimulus location of at least 0.3 log units. This finding is compatible with that of Johnson et al,[22] who found that correction for ocular media absorption did not reduce the between-subject variability of the B–Y mean sensitivity. The similarity of the standard deviations with and without correction for absorption implies that the assessment of ocular media absorption on an individual basis could be avoided when using a broadband blue stimulus because the magnitude of the deviation from normality required for a given probability level would not be affected. Any individual difference from the height of the average age-matched normal uncorrected field because of ocular media absorption could be removed using the pattern deviation approach. Such an approach would ignore any diffuse component from optical factors such as forward light scatter[25,26,39] or from neural damage. The difficulty in separating such components in W–W perimetry[39] would also be present in B–Y perimetry. The general height reduction caused by the magnitude of absorption increases as the wavelength of the stimulus decreases. Nevertheless, the magnitude and trend of the pointwise standard deviations across the field of the broadband filter are in general agreement with the 440-nm narrow band filter used by Sample et al.[11]

Probability maps indicate the frequency with which the given pointwise sensitivity is seen in a normal population. The model and limits assigned in the

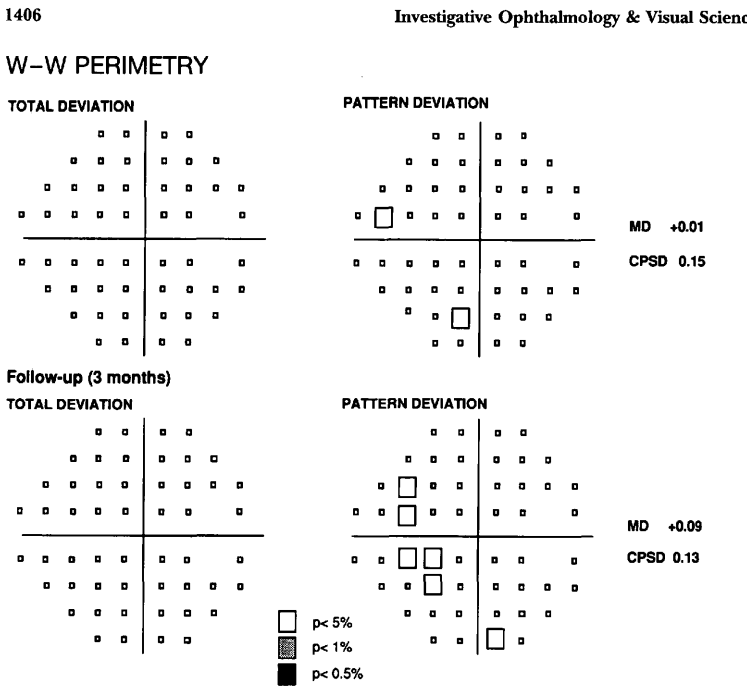

FIGURE 5. Total and pattern deviation plots for W–W (*top*) and B–Y (*bottom*) illustrating an OHT with a normal W–W but an abnormal B–Y field at the outset and the appearances at the 3-month follow-up. The indices are in log units.

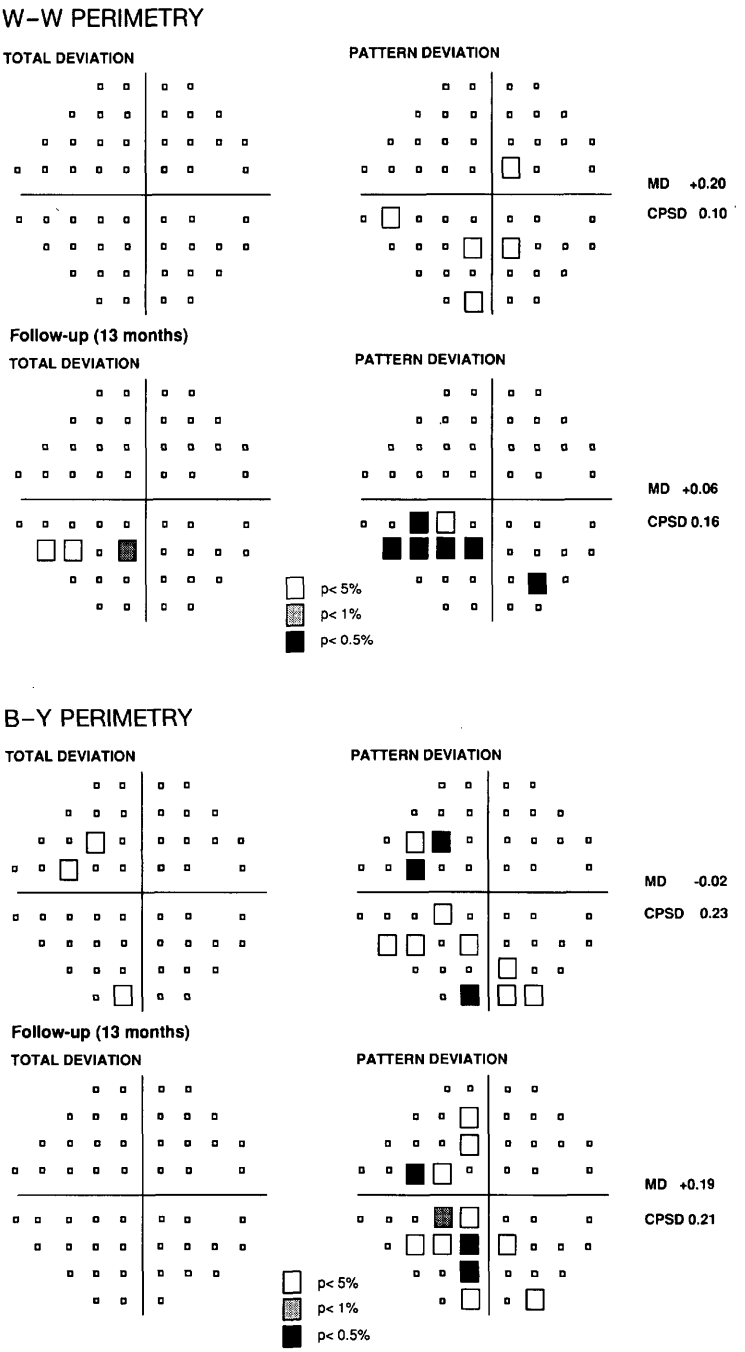

FIGURE 6. Total and pattern deviation plots for W–W (*top*) and B–Y (*bottom*) illustrating an OHT with a suspicious W–W field but an abnormal B–Y field at the outset and the appearances at the 13-month follow-up. The indices are in log units.

B–Y maps gave good specificity for a separate sample of normal individuals, including varying degrees of cataract: 25 out of 27 eyes were normal on the pattern probability map. This finding is in good agreement with the STATPAC specificity of approximately 90%.[17] Furthermore, the finding that all 24 eyes with POAG were abnormal on B–Y pattern probability maps is also in agreement with the sensitivity of STATPAC.[17]

In early to moderate glaucomatous loss, the results of the current study show that compared to W–W perimetry, B–Y perimetry identifies a wider, and to some extent deeper, area of focal loss. The development of new B–Y scotomata was not present. Indeed, based on total deviation plots, such findings are compatible with those of Johnson et al,[6,7,10] who found that B–Y perimetry identified field progression before W–W perimetry.

The results of the pattern probability analysis for the group with OHT is consistent with the concept that B–Y perimetry is capable of detecting glaucomatous visual field loss in ocular hypertension earlier than that identified by W–W perimetry.[1–14] Caution needs to be exercised in distinguishing between variability and progression on the basis of two to three fields obtained within the 1-year study period. Interestingly, none of the four patients with OHT who were at high risk, all of whom were treated with β-blockers, manifested a B–Y field defect. Several unpublished studies discussed patients who manifested abnormal W–W fields and normal B–Y fields (Flanagan JG, personal communication, 1994). No such patients were found in the current study.

Recognition of differences in the depth of focal loss by comparison of pattern deviation probability plots between B–Y and W–W perimetry is limited in that a given probability symbol covers a given range of defect depths. Furthermore, the range of probability levels for W–W and B–Y perimetry is truncated at a probability level of 0.5%. In addition, the depth of B–Y loss required to attain significance is greater because of the increased normal between-subject variability; at a probability level of $P < 0.005$, then, the deviation from B–Y normal sensitivity approaches the magnitude of SWS isolation with the HFA of approximately 1.4 log units.[22] Therefore, once a defect depth corresponding to a probability level of $P < 0.005$ occurs, it is unlikely that progression of the defect can be followed in terms of a pure SWS response. When the defect depth exceeds the value of isolation, the perimetric response is no longer solely mediated by the SWS pathway, and the response is most likely governed by the MWS pathway.[3,9] In such a case, the use of the B–Y stimulus combination would also be limited by the available dynamic range.

The value of B–Y perimetry compared to W–W perimetry at stimulus locations in which SWS isolation is lost warrants further study. Statistical elevation or depression of the hill of vision can markedly alter the apparent depth of focal loss displayed by the pattern deviation plot for W–W and B–Y stimuli. The magnitude of the defect depth in relation to the available SWS isolation should, therefore, be evaluated by inspection of the total deviation plot alone. An additional problem may arise in the calculation of the global short-term fluctuation and the corrected pattern standard deviation whereby, as a result of the local short-term fluctuation, a stimulus location may exhibit an initial threshold apparently mediated by the SWS pathway and a second threshold apparently mediated by the MWS pathway. Until the relationship is known between the W–W sensitivity and the B–Y sensitivity at a location where the B–Y defect depth is beyond the level of isolation, any analytical package for B–Y perimetry should identify those stimulus locations that lie outside the limits of SWS isolation.

W–W visual field loss is considered to be more localized in normal-tension glaucoma[40–47] and to be more diffuse in high-tension glaucoma.[48–54] However, the extent to which W–W diffuse loss is a component of glaucomatous damage has been questioned because the loss resembles that caused by media opacities.[55–58] The reduction of B–Y sensitivity in glaucoma has been shown to exhibit diffuse and focal components.[1–14] In the current study, neither diffuse B–Y or W–W loss on the total deviation maps was evident among the patients with OHT. However, five patients with POAG with advanced glaucoma showed greater B–Y diffuse loss on the total deviation plot compared to that of W–W, despite equivalence of the W–W and B–Y pattern deviation plots. These latter findings were not considered to be caused by cataract or pupil size.

The inherent increase in between-subject variability for B–Y perimetry must be accounted for in the determination of abnormality. Failure to do so will result in a large number of false-positive defects. Nevertheless, the technique gives good specificity and can produce a wider loss compared with W–W perimetry in POAG. The data are also consistent with the concept that B–Y perimetry provides an earlier indication of field loss in OHT compared to W–W perimetry. However, the interaction of the wider confidence limits for B–Y normality, together with the magnitude of SWS isolation, can limit the range over which SWS defects can be detected and monitored.

Key Words

automated perimetry, color, glaucoma, interpretation, focal loss

References

1. Adams AJ, Johnson CA, Lewis RA. S cone pathway sensitivity loss in ocular hypertension and early glau-

coma has nerve fibre bundle pattern. In: Drum B, Moreland JD, Serra A, eds. *Colour Vision Deficiencies X.* Dordrecht: Kluwer; 1991:535–542.
2. Flanagan JG, Trope GE, Popick W, Grover A. Perimetric isolation of the SWS cones in OHT and early POAG. In: Mills RP, Heijl A, eds. *Perimetry Update 1990/91: Proceedings of the IXth International Perimetric Society Meeting.* Amsterdam: Kugler and Ghedini; 1991:331–337.
3. Hart WM, Silverman SE, Trick GJ, et al. Glaucomatous visual field damage: Luminance and color contrast sensitivities. *Invest Ophthalmol Vis Sci.* 1990;31:359–367.
4. Johnson CA, Adams AJ, Lewis RA. Automated perimetry of short-wavelength mechanisms in glaucoma and ocular hypertension. In: Heijl A, ed. *Perimetry Update 1988/89: Proceedings of the IXth International Perimetric Society Meeting.* Amsterdam: Kugler/Ghedini; 1989: 31–37.
5. Johnson CA, Adams AJ, Casson EJ, Brandt JD. Blue-on-yellow perimetry can predict the development of glaucomatous visual field loss. *Arch Ophthalmol.* 1993;111:645–650.
6. Johnson CA, Adams AJ, Casson EJ, Brandt JD. Progression of early glaucomatous visual field loss as detected by blue-on-yellow and standard white-on-white automated perimetry. *Arch Ophthalmol.* 1993;111:651–656.
7. Johnson CA, Adams AJ, Casson EJ. Blue-on-yellow perimetry: A five-year overview. In: Mills R, ed. *Perimetry Update 1992/93: Proceedings of the Xth International Perimetric Society Meeting.* Amsterdam: Kugler; 1993:459–465.
8. de Jong LAMS, Snepvangers CEJ, van den Berg TJTP, Langerhorst CT. Blue-yellow perimetry in the detection of early glaucomatous damage. *Doc Ophthalmol.* 1990;75:303–314.
9. Lewis RA, Johnson CA, Adams AJ. Automated perimetry and short wavelength sensitivity in patients with asymmetric intraocular pressures. *Graefe's Arch Clin Exp Ophthalmol.* 1993;231:274–278.
10. Casson EJ, Johnson CA, Shapiro LR. Longitudinal comparison of temporal-modulation perimetry with white-on-white and blue-on-yellow perimetry in ocular hypertension and early glaucoma. *J Opt Soc Am.* 1993;10:1792–1806.
11. Sample PA, Weinreb RN. Color perimetry for assessment of primary open-angle glaucoma. *Invest Ophthalmol Vis Sci.* 1990;31:1869–1875.
12. Sample PA, Weinreb RN. Progressive visual field loss in glaucoma. *Invest Ophthalmol Vis Sci.* 1992;33:2068–2071.
13. Sample PA, Taylor JDN, Martinez GA, Lusky M, Weinreb RN. Short-wavelength color visual fields in glaucoma suspects at risk. *Am J Ophthalmol.* 1993;115:225–233.
14. Sample PA, Juang PSC, Weinreb RN. Short-wavelength automated perimetry for analysis of secondary and normal tension glaucoma. ARVO Abstracts. *Invest Ophthalmol Vis Sci.* 1994;35:2189.
15. Flammer J. The concept of visual field indices. *Graefe's Arch Clin Exp Ophthalmol.* 1986;224:389–392.
16. Heijl A, Lindgren G, Olsson J. A package for the statistical analysis of computerised fields. *Doc Ophthalmol Proc Ser.* 1987;49:153–168.
17. Heijl A, Asman P. A clinical study of perimetric probability maps. *Arch Ophthalmol.* 1989;107:199–203.
18. Heijl A, Lindgren F, Olsson J, Asman P. Visual field interpretation with empiric probability maps. *Arch Ophthalmol.* 1989;107:204–208.
19. Heijl A, Lindgren G, Olsson J. Normal variability of static perimetric threshold values across the central visual field. *Arch Ophthalmol.* 1987;105:1544–1549.
20. Sample PA, Cook JN, Weinreb RN. Variability and sensitivity of short-wavelength color visual fields in normal and glaucoma eyes. In: *Noninvasive Assessment of the Visual System Tech Digest Ser.* 1993:292–295.
21. Nelson–Quigg JM, Johnson CA, Casson EJ, Adams AJ. Long and short term variability for perimetry of short wavelength sensitive (SWS) mechanisms. ARVO Abstracts. *Invest Ophthalmol Vis Sci.* 1990;31:190.
22. Johnson CA, Adams AJ, Twelker JD, Quigg JM. Age-related changes in the central visual field for short-wavelength sensitive pathways. *J Opt Soc Am.* 1988;5:2131–2138.
23. Chylack LT, Leske C, McCarthy D, Khu P, Kashiwagi T, Sperduto R. Lens opacities classification system II (LOCS II). *Arch Ophthalmol.* 1989;107:991–997.
24. Hudson C, Wild JM, Archer–Hall J. Maximising the dynamic range of the Humphrey Field Analyser for blue-on-yellow perimetry. *Ophthalmic Physiol Opt.* 1993;13:405–408.
25. Moss ID, Wild JM. The effects of forward light scatter on the SWS visual field. *Graefe's Arch Clin Exp Ophthalmol.* 1994;232:409–414.
26. Moss ID, Wild JM, Whitaker D. The influence of age-related cataract on blue-on-yellow perimetry. *Invest Ophthalmol Vis Sci.* 1995;36:764–773.
27. Moss ID, Wild JM. The influence of induced forward light scatter on the normal blue-on-yellow perimetric profile. *Graefe's Arch Clin Exp Ophthalmol.* 1994;232: 409–414.
28. Hudson C, Wild JM. The influence of pre-receptoral absorption on blue/yellow perimetry. In: Mills RP, ed. *Perimetry Update 1992/93: Proceedings of the Xth International Perimetric Society Meeting.* Amsterdam: Kugler; 451–457.
29. King–Smith PE, Carden D. Luminance and opponent-color contributions to visual detection and adaptation and to temporal and spatial integration. *J Opt Soc Am.* 1976;66:709–717.
30. Searle AET, Wild JM, Shaw DE, O'Neill EC. Time-related variation in normal automated static perimetry. *Ophthalmology.* 1991;98:701–707.
31. Hudson C, Wild JM, O'Neill EC. Fatigue effects during a single session of automated static threshold perimetry. *Invest Ophthalmol Vis Sci.* 1994;35:268–280.
32. Sample PA, Esterson FD, Weinreb RN, Boynton RM. The aging lens: In vivo assessment of light absorption in 84 human eyes. *Invest Ophthalmol Vis Sci.* 1988;29:1306–1311.
33. Sample PA, Esterson FD, Weinreb RN. A practical method for obtaining an index of lens density with

an automated perimeter. *Invest Ophthalmol Vis Sci.* 1989;30:786–787.
34. Norren DV, Vos JJ. Spectral transmission of the human ocular media. *Vision Res.* 1974;14:1237–1244.
35. Heijl A, Lindgren G, Olsson J. Perimetric threshold variability and age. *Arch Ophthalmol.* 1988;106:450–451.
36. Weber J. Eine neue Strategie fur die automatische statische Perimetrie. *Fortschr Ophthalmol.* 1990;87:37–40. In German.
37. Olsson J, Bengtsson B, Heijl A, Rootzen H. New thresholding algorithms for automated static perimetry. In: Mills RP, ed. *Perimetry Update 1994/95: Proceedings of the XIth International Perimetric Society Meeting.* Amsterdam: Kugler; 1995:219.
38. Flanagan JG, Moss ID, Wild JM, et al. Evaluation of FASTPAC: A new strategy for threshold estimation with the Humphrey Field Analyser. *Graefe's Arch Clin Exp Ophthalmol.* 1993;231:465–469.
39. Funkhouser AT, Fankhouser F, Weale RA. Problems related to diffuse versus localised loss in the perimetry of glaucomatous visual fields. *Graefe's Arch Clin Exp Ophthalmol.* 1993;230:243–247.
40. Hitchings RA, Anderton SA. A comparative study of visual field defects seen in patients with low-tension glaucoma and chronic simple glaucoma. Br J Ophthalmol. 1983;67:818–821.
41. Caprioli J, Spaeth GL. Comparison of visual field defects in the low-tension glaucomas with those in the high-tension glaucomas. *Am J Ophthalmol.* 1984;97:730–737.
42. Caprioli J, Sears M, Miller JM. Patterns of early visual field loss in glaucoma. *Am J Ophthalmol.* 1987;103:512–517.
43. Zeiter JH, Shin DH, Juzych MS, et al. Visual field defects in patients with normal-tension glaucoma and patients with high-tension glaucoma. *Am J Ophthalmol* 1992;114:758–763.
44. Samuelson TW, Spaeth GL. Focal and diffuse visual field defects: Their relationship to intraocular pressure. *Ophthalmic Surg.* 1993;24:519–525.
45. Araie M, Yamagami J, Suzuki Y. Visual field defects in normal-tension and high-tension glaucoma. *Ophthalmology.* 1993;100:1808–1814.
46. Funkhouser AT. A new diffuse loss index for estimating general glaucomatous visual field depression. *Doc Ophthalmol.* 1991;77:57–72.
47. Flammer J, Drance SM, Augustiny L, Funkhouser AT. Quantification of glaucomatous visual field defects with automated perimetry. *Invest Ophthalmol Vis Sci.* 1985;26:76–81.
48. Drance SM, Douglas GR, Airaksinen PJ, Schulzer M, Hitchings RA. Diffuse visual field loss in chronic open-angle glaucoma and low-tension glaucoma. *Am J Ophthalmol.* 1987;104:577–580.
49. Drance SM. Diffuse visual field loss in open-angle glaucoma. *Ophthalmology.* 1991;98:1533–1538.
50. Feur WJ, Anderson DR. Static threshold asymmetry in early glaucomatous field loss. *Ophthalmology.* 1989;96:1285–1297.
51. Chauhan BC, Drance SM, Douglas GR, Johnson CA. Visual field damage in normal-tension and high-tension glaucoma. *Am J Ophthalmol.* 1989;108:636–642.
52. Glowazki A, Flammer J. Is there a difference between glaucoma patients with rather localised visual field damage and patients with more diffuse visual field damage? In: Greve EL, Heijl A, eds. *Doc Ophthalmol Proc Ser 49.* Dordrecht: Nijhoff/Junk; 317–320.
53. Lachenmayr BJ, Drance SM, Chauhan BC, House PH, Lalani S. Diffuse and localised glaucomatous field loss in light-sense, flicker and resolution perimetry. *Graefe's Arch Clin Exp Ophthalmol.* 1991;229:267–273.
54. Lachenmayr BJ, Drance SM, Airaksinen JP. Diffuse field loss and diffuse retinal nerve-fiber loss in glaucoma. *Ger J Ophthalmol.* 1992;1:22–25.
55. Heijl A. Lack of diffuse loss of differential light sensitivity in early glaucoma. *Acta Ophthalmol.* 1989;67:353–360.
56. Heijl A. Some characteristics of glaucomatous visual field loss. In: Kriegelstein GK, ed. *Glaucoma Update IV.* Berlin: Springer–Verlag; 1991:133–139.
57. Langerhorst CT, Thomas JTP, van den Berg TJTP, Greve E. Is there a general reduction of sensitivity in glaucoma? *Int Ophthalmol.* 1989;3:31–35.
58. Asman P, Heijl A. Diffuse visual field loss and glaucoma. *Acta Ophthalmol.* 1994;72:303–308.