Correlation of Blue-on-Yellow Visual Fields With Scanning Confocal Laser Optic Disc Measurements

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Purpose. Visual field defects and changes in the optic nerve head are signs of glaucoma. It has been shown that blue-on-yellow (B–Y) perimetry can reveal visual field defects earlier and shows them larger than does white-on-white (W–W) perimetry. The Heidelberg retina tomograph (HRT) can produce three-dimensional images of the optic disc. The aim of this study was to find out how B–Y perimetry results correlate with optic disc parameters in comparison with W–W perimetry results.

Methods. One randomly chosen eye was evaluated in each of 40 normal subjects and 37 patients with ocular hypertension and different stages of glaucoma. B–Y and W–W visual fields (program 30-2) were obtained with a Humphrey perimeter. B–Y perimetry results were adjusted for the patient’s age and lens transmission index measured with a lens fluorometer. The B–Y visual field adjusted mean deviation (MD) was calculated as the difference between the measured and expected mean sensitivity values, predicted by the regression model fitted in normal subjects. The HRT with software version 1.11 was used to acquire and evaluate topographic measurements of the optic disc.

Results. The cup shape measure showed strongest correlation with the MD of both the B–Y and W–W visual fields. The multiple correlation coefficients from quadratic regression were 0.65 for both visual fields. Except for peripapillary retinal nerve fiber layer measurements, the statistically significant correlations of the B–Y visual field indexes with other HRT parameters were equal to or better than those of W–W perimetry.

Conclusions. B–Y perimetry MDs are well correlated with optic nerve head parameters measured with the HRT. In early stages of glaucoma, most HRT variables were better correlated with the B–Y MD than with the W–W MD. Invest Ophthalmol Vis Sci. 1997;38:2452–2459.

Visual field defects and changes in the optic nerve head (ONH) are widely regarded as important and definite signs of glaucoma. Because no single test is diagnostic, the consistency of function and structure is crucial in the diagnosis and follow-up of glaucoma. Although clinical assessment of the ONH has been of interest for more than a century, the techniques used have been largely qualitative. The introduction of computerized instruments such as the Heidelberg retina tomograph (HRT; Heidelberg Engineering, Heidelberg, Germany) has made it possible to obtain rapid and reproducible three-dimensional analysis of the optic disc structure by quantitative serial point-by-point comparison of the surface contour.1–9

In recent years, automated static threshold perimetry has become a gold standard in the diagnosis and management of glaucoma. However, detectable retinal nerve fiber layer (RNFL) and optic disc abnormalities usually precede the criteria for typical glaucomatous field loss in conventional white-on-white (W–W) perimetry.10–13 In fact, there is a delay until sufficient damage, on the basis of visual fields, occurs for the definitive diagnosis of glaucoma.

It was reported recently that short-wavelength automated perimetry (SWAP) or blue-on-yellow (B–Y) perimetry can reveal visual field defects earlier and shows them larger than can W–W perimetry.14–23 B–Y perimetry is believed to be more effective because it tests the function of an isolated subset of ganglion...
cells. These isolated cells are selectively more vulnerable to glaucomatous damage or, because of undersampling, have minimal overlap of their receptive fields; therefore, functional loss occurs even if there is proportionately greater loss of other cells.  

Several reports have described a moderate to fairly good correlation between optic disc, RNFL, and W–W visual field parameters. These promising techniques, B–Y perimetry and confocal optic disc tomography, should provide a new method for measuring functional and structural characteristics. In 1995, Tsai et al investigated the relation between W–W and B–Y visual field sensitivity and optic disc parameters using the HRT (software version 1.10). The software has been considerably revised since then. The new standard reference plane has been shown to be better at separating patients with different stages of glaucoma. In addition, several new structural characteristics have been provided for estimation of the optic disc. To our knowledge, the correlation between B–Y visual field indexes and optic disc and RNFL descriptive parameters (e.g., cup shape measure, cup volume, rim volume, mean depth below curved surface, maximal cup depth, height variation along the contour line, mean RNFL thickness, and RNFL cross-sectional area) have not been reported so far.

The purposes of this study were to determine how results of B–Y perimetry correlate with optic disc parameters and to compare the strength of the association of the ONH morphologic variables with the B–Y and W–W visual field mean defect variables.

METHODS

We evaluated 1 randomly chosen eye in 40 nonglaucomatous subjects with a mean age of 57 years (range, 29 to 84 years). Criteria for subject eligibility consisted of normal findings in the ocular examination, a normal W–W visual field, no family history of glaucoma, no history of ocular or neurologic disease, no history of diabetes or other systemic diseases, and no history of use of any medications known to affect the visual system and the technique of lens fluorometry have been previously described. The fluorometry of the lens is based on the assumption that the maximal autofluorescence is approximately the same in the anterior and posterior parts of the lens, and any difference in autofluorescence intensity between the anterior and posterior parts can be attributed to a loss of exciting and fluorescent light in the lens. The autofluorescence of the lens was measured using our fluorometer; its optical system and the technique of lens fluorometry have been previously described. The fluorometry produces a graphic fluorescence profile that consists of anteroposterior juxtacortical peaks and a central plateau. A lens transmission index (LTI) was calculated from the ratio between the heights of the posterior and anterior autofluorescence peaks.

We have shown previously that the reference level for correcting B–Y perimetry results can be determined in nonglaucomatous subjects, W–W visual field MD was obtained using the statistical package provided by Humphrey Instruments. The calculation of B–Y visual field MD was based on results of nonglaucomatous subjects enrolled in this study. Variability of the static perimeter threshold is known to increase with distance from fixation. We therefore decided to use the 24-2 test data to obtain a more precise model of the normal B–Y visual field. In nonglaucomatous subjects, W–W perimetry was carried out during the first visit. To obtain data for the program 24-2 test, we subtracted respective peripheral location values from program 30-2 data.

In conventional W–W perimetry, the deviations of the threshold values are corrected for aging. In B–Y perimetry, however, the lens-induced absorption of the blue light may show large variability in subjects of similar age. We previously presented a procedure to estimate absorption of the blue light in an individual lens by measuring the autofluorescence of the crystalline lens. The fluorometry of the lens was based on the assumption that the maximal autofluorescence is approximately the same in the anterior and posterior parts of the lens, and any difference in autofluorescence intensity between the anterior and posterior parts can be attributed to a loss of exciting and fluorescent light in the lens. The autofluorescence of the lens was measured using our fluorometer; its optical system and the technique of lens fluorometry have been previously described. The fluorometer produces a graphic fluorescence profile that consists of anteroposterior juxtacortical peaks and a central plateau. A lens transmission index (LTI) was calculated from the ratio between the heights of the posterior and anterior autofluorescence peaks.

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We have shown previously that the reference level for correcting B–Y perimetry results can be determined.
were used.41 Therefore, in this study we calculated the age- and LTI-adjusted MD as the difference between the actual and the expected MS values (MD = MS — expected MS) for each subject in all clinical groups.

The HRT (software version 1.11) was used to acquire and evaluate topographic measurements of the optic disc in all the subjects. The HRT is a confocal imaging device that uses a diode laser at 670 nm as a light source. A three-dimensional image was acquired as a series of optical section images at 32 consecutive focal planes. Image acquisition time was approximately 1.6 seconds. The instrument does not require dilatation of the pupil.8 In this study, three 10° images were obtained for each eye, and the mean image of the three scans was used for optic disc structure measurements. The optic disc contour line was manually marked around the disc on the HRT screen with the mouse, the inner edge of the scleral ring (Elschnig’s ring) corresponding to the inner edge of the contour line. The determination of the reference plane for each eye was based on the height of the retinal surface at the papillomacular bundle. The standard reference plane is located 50 μm posterior to the mean contour line height in the segment between —10° and —4°.

The following information was collected. The disc area was defined as the total area within the contour line. The cup area was defined as the total area of parts within the contour line that were located below the reference plane. The rim area was defined as the difference between disc area and cup area. The cup volume was defined as the total volume of parts within the contour line that were located below the reference plane. The rim volume was defined as the total volume of parts within the contour line that were located above the reference plane (the reference plane was used as the lower limit for the measurement). The mean depth below curved surface was defined as the mean cup depth below the curved surface. The maximal cup depth was defined as the mean depth of the 5% of pixels with the highest depth values within the contour line (the depth was determined relative to the curved surface). The cup shape measure, or third moment, was defined as the frequency distribution of depth values relative to the curved surface of parts located inside the contour line. The height variation along contour line was defined as the difference in height between the most elevated and the most depressed points of the corrected contour line. The mean RNFL thickness was defined as reference height minus the mean height of contour. The RNFL cross-sectional area was defined as the mean RNFL thickness multiplied by the length of the contour line.

HRTCALC Utility Version 1.03 (Heidelberg Engineering) was used to calculate the parameter values for the HRT mean images. The data were transported as an ASCII data file to SPSS 6.1.2 for Windows (SPSS, Chicago, IL).

The associations of the ONH morphologic measures with the B—Y and W—W visual field MD were evaluated by quadratic regression models in which each of the ONH structural variables was in turn the outcome variable and the B—Y visual field MD (adjusted for age and LTI) and the W—W visual field...
MD were the regressor variables. The linear and the quadratic terms of the regressors were included in the models to allow for significant departures from linearity in the association. The multiple correlation coefficient from a model including either B-Y or W-W visual field MD (linear and quadratic term) was used to describe the strength of the association between the ONH morphologic variable and the visual field defect measure in question. A forward stepwise procedure was used to find the order of significance of the B-Y and W-W visual field MD variables.

To evaluate the strength of the association of B-Y and W-W visual fields with the HRT parameters in the early stages of glaucoma, we made a further analysis in which the patients with advanced glaucoma were excluded and linear correlation coefficients between the visual field measures and morphologic variables were calculated.

This study was of a descriptive nature, designed to evaluate the strength of the associations between the structural and functional measures and the clinical implications of these associations. Therefore, we considered that it was not meaningful to test statistically null hypotheses of zero correlations. Hence, the estimated correlation coefficients are presented without any probability values.

RESULTS

The fitted regression line for the expected B-Y visual field MS values in normal subjects was $19.31 + 0.123 \times \text{LTI} - 0.122 \times \text{age (in years)}$.

The standard errors of these coefficients were 0.53, 0.030, and 0.058, respectively. The residual standard deviation about the line was 3.09. The multiple coefficient of determination ($R^2$) of the model was 0.72. There was a strong correlation ($R = 0.78$) between the age- and LTI-adjusted B-Y visual field and W-W visual field MD values (Fig. 1). The W-W visual field MD values and the age- and LTI-adjusted MD values of the B-Y visual field showed the highest correlation with the cup shape measure; the $R^2$ values from quadratic regressions were 0.65 and 0.65, respectively (Figs. 2 and 3).

The structural variables under study can be divided into three broad categories with respect to their observed relations to the visual field measures (Table

FIGURE 1. Scatterplot of the association of white-on-white (W-W) visual field mean defect (MD) values with the lens- and age-adjusted blue-on-yellow (B-Y) visual field MD values in the five clinical groups.

FIGURE 2. Scatterplot of the association of the white-on-white (W-W) visual field mean defect (MD) values with the cup shape measure in the five clinical groups.

FIGURE 3. Scatterplot of the association of the lens- and age-adjusted blue-on-yellow (B-Y) visual field mean defect (MD) values with the cup shape measure in the five clinical groups.
TABLE 2. Multiple Correlation Coefficients of B-Y and W-W Visual Field Mean Deviations (MD) With Tomographic Data From Quadratic Regression Models* (n = 77)

<table>
<thead>
<tr>
<th>Tomographic Parameter</th>
<th>MD of B-Y Visual Field</th>
<th>MD of W-W Visual Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Cup shape measure</td>
<td>(-)0.65</td>
<td>(-)0.65</td>
</tr>
<tr>
<td>Mean cup depth below curved surface (mm)</td>
<td>(-)0.35</td>
<td>(-)0.16</td>
</tr>
<tr>
<td>II Cup/disc area ratio</td>
<td>(-)0.59</td>
<td>(-)0.56</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>(+)0.54</td>
<td>(+)0.49</td>
</tr>
<tr>
<td>Rim volume (mm³)</td>
<td>(+)0.54</td>
<td>(+)0.52</td>
</tr>
<tr>
<td>Cup area (mm²)</td>
<td>(-)0.52</td>
<td>(-)0.50</td>
</tr>
<tr>
<td>Cup volume (mm³)</td>
<td>(-)0.34</td>
<td>(-)0.29</td>
</tr>
<tr>
<td>Maximum cup depth</td>
<td>(-)0.30</td>
<td>(-)0.25</td>
</tr>
<tr>
<td>(mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III RNFL cross-sectional area (mm²)</td>
<td>(+)0.48</td>
<td>(+)0.61</td>
</tr>
<tr>
<td>Mean RNFL thickness (mm)</td>
<td>(+)0.49</td>
<td>(+)0.62</td>
</tr>
<tr>
<td>Height variation along contour line (mm)</td>
<td>(+)0.44</td>
<td>(+)0.48</td>
</tr>
</tbody>
</table>

* + or − sign in parentheses indicates the direction of the linear component of the association.
RNFL = retinal nerve fiber layer; B-Y = blue-on-yellow; W-W = white-on-white.

2). In the first class were the cup shape measure and the mean cup depth below curved surface, which were more strongly associated with the B-Y visual field MD than with the W-W visual field MD. However, in these cases, W-W terms also were selected by the stepwise algorithm. Of all structural parameters considered, the linear term of the B-Y visual field MD had the strongest correlation with the cup shape measure (linear R = 0.65). Both the linear and quadratic terms of the W-W visual field MD were significantly associated with the cup shape measure, but the quantitative increment in the value of the multiple correlation coefficient from W-W perimetry results was small (multiple R = 0.70 after including both W-W terms).

The second class consisted of variables that were also more correlated, but not substantially so, with the B-Y visual field than with the W-W visual field MD. However, in these cases, W-W terms also were selected by the stepwise procedure. These parameters were cup:disc area ratio, rim area, rim volume, cup area, cup volume, and maximal cup depth.

In the third category were three structural variables that were more correlated with the W-W visual field MD than with the B-Y visual field MD. The linear term of the W-W visual field MD had the statistically strongest correlation with the RNFL cross-sectional area (linear R = 0.54) (Fig. 4), mean RNFL thickness (linear R = 0.53), and height variation along the contour line (linear R = 0.48). The quadratic term of the W-W visual field MD had some impact, with the RNFL cross-sectional area and mean RNFL thickness, on the linear term (multiple R = 0.61 and R = 0.62, respectively). In all these three variables, addition of the B-Y terms did not improve the fit of the regression.

Scatterplots (Figs. 2, 3, 4, 5) show that the advanced glaucoma group greatly influenced the associations. It was this patient group that made the associations of W-W visual field values with the HRT parameters deviate from a linear pattern. When patients with advanced glaucoma were excluded from the analysis, the associations were linear and the correlation coefficients (ordinary

![FIGURE 4. Scatterplot of the association of the white-on-white (W-W) visual field mean defect (MD) values with the retinal nerve fiber layer (RNFL) cross-sectional area in the five clinical groups.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933420/ on 04/19/2017)

![FIGURE 5. Scatterplot of the association of the lens- and age-adjusted blue-on-yellow (B-Y) visual field mean defect (MD) values with the retinal nerve fiber layer (RNFL) cross-sectional area in the five clinical groups.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933420/ on 04/19/2017)
TABLE 3. Correlation Coefficients (Pearson’s R) of B–Y and W–W Visual Field Mean Deviations (MD) With Tomographic Data (the Eight Subjects With Advanced Glaucoma Excluded; n = 69)

<table>
<thead>
<tr>
<th>Tomographic Parameter</th>
<th>MD of B–Y Visual Field</th>
<th>MD of W–W Visual Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Cup shape measure</td>
<td>-0.46</td>
<td>-0.37</td>
</tr>
<tr>
<td>Mean cup depth below</td>
<td>-0.28</td>
<td>-0.12</td>
</tr>
<tr>
<td>curved surface (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II Cup/disc area ratio</td>
<td>-0.45</td>
<td>-0.30</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>0.57</td>
<td>0.17</td>
</tr>
<tr>
<td>Rim volume (mm³)</td>
<td>0.59</td>
<td>0.27</td>
</tr>
<tr>
<td>Cup area (mm²)</td>
<td>-0.43</td>
<td>-0.33</td>
</tr>
<tr>
<td>Cup volume (mm³)</td>
<td>-0.28</td>
<td>-0.20</td>
</tr>
<tr>
<td>Maximum cup depth</td>
<td>-0.14</td>
<td>-0.02</td>
</tr>
<tr>
<td>(mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III RNFL cross-sectional area (mm²)</td>
<td>0.27</td>
<td>0.37</td>
</tr>
<tr>
<td>Mean RNFL thickness (mm)</td>
<td>0.51</td>
<td>0.40</td>
</tr>
<tr>
<td>Height variation along contour line (mm)</td>
<td>0.14</td>
<td>0.19</td>
</tr>
</tbody>
</table>

RNFL = retinal nerve fiber layer; B–Y = blue-on-yellow; W–W = white-on-white.

Pearson’s R) decreased considerably, more so for the W–W perimetry results (Table 3).

DISCUSSION

In glaucoma, the anatomic loss of neural tissue accompanies deterioration of function. Previous reports have described a correlation between optic disc, RNFL, and achromatic visual field parameters.\textsuperscript{27-37} Compared with other disc parameters, the disc rim area was found to be most highly correlated with visual field MD by several investigators.\textsuperscript{30-33} The correlation coefficient between disc rim area and W–W visual field MD determined in this study was in concordance with previously reported results.

The introduction of confocal optic disc tomography has provided a new range of structural characteristics for estimation of the optic disc. Tsai et al\textsuperscript{37} found that peripapillary retinal height, rim area, and rim:disc area were highly correlated with W–W and B–Y visual field MD when both normal subjects and glaucoma patients were included in the analysis. With only glaucoma patients in the analysis, the peripapillary retinal height was the only parameter significantly correlated with the visual field MD. Weinreb et al\textsuperscript{30} investigated the association between RNFL measurements and W–W visual field loss in 55 patients with primary open-angle glaucoma and found no significant association between RNFL cross-sectional area and global measures of visual field loss. Brigatti and Caprioli\textsuperscript{35} evaluated patients with early to moderate glaucoma using the HRT and W–W perimetry. They found the cup shape measure to be the only parameter correlating statistically significantly with the visual field indexes. No significant correlation was found between mean RNFL height and the visual field indexes. The discrepancies between our results and these studies may be explained by the differences in ONH parameters used and differences in population.

Detectable RNFL and optic disc abnormalities usually precede the criteria considered to be typical glaucomatous field loss in conventional W–W perimetry.\textsuperscript{10-15} The introduction of B–Y perimetry and confocal optic disc tomography seem to provide new techniques for measuring functional and structural characteristics. Tsai et al\textsuperscript{37} reported that rim area, rim:disc area, and peripapillary retinal height measured using the HRT (software version 1.10) were highly correlated with B–Y visual field MD when both normal subjects and glaucoma patients were included in the analysis. Spearman rank-order correlation coefficients for B–Y visual field MD were 0.56, 0.45, and 0.51, respectively. The multiple correlation coefficients determined in our study between B–Y visual field MD and rim area, rim:disc area, and mean RNFL thickness were 0.54, 0.59, and 0.49, respectively. In both studies, the RNFL parameters correlated slightly better with W–W perimetry results, but the optic disc parameters (rim area and rim:disc area ratio) were better correlated with B–Y perimetry results.

In this study, B–Y perimetry results correlated well with ONH parameters measured with a confocal scanning laser tomograph. In view of some previous studies\textsuperscript{14-25} indicating that B–Y perimetry may precede W–W visual field loss, we expected the B–Y visual field MD value to be correlated better with the structural HRT parameters than the W–W visual field index. The results of this study indicate that with all five clinical groups included in the analysis, the superiority of B–Y perimetry over W–W perimetry is not distinct. However, it was obvious from the scatterplots that the advanced glaucoma group greatly influenced the associations. Without the advanced glaucoma patients, the differences of the correlation coefficients of B–Y and W–W visual fields with the HRT parameters increased, suggesting that B–Y perimetry might add information beyond that of W–W perimetry, particularly in early stages of glaucoma.

Moreover, the scatterplots (see Figs. 1, 2, 3, 4, 5) show that 8 of 13 patients (62%) with early glaucoma and 3 of 10 patients (30%) with ocular hypertension, but only 4 of 40 normal subjects (10%), had an age- and LTI-adjusted MD of B–Y visual field of <-5 dB. Although in scatterplots with W–W MD the ocular hypertension and early glaucoma patients, by definition, were clearly separated from the patients with
moderate glaucoma, in the scatterplots with B–Y MD this separation was no longer distinct. In fact, the B–Y MD of some patients with ocular hypertension and early glaucoma approached that of the patients with moderate glaucoma.

Visual field defects and changes in ONH and RNFL are widely regarded as important signs of glaucoma. In this study, the statistically significant correlations between structural and functional characteristics were obtained. However, statistically significant correlations do not necessarily mean that it is possible to predict accurately one value on the basis of another. The highest correlation of $R = 0.65$ yields an $R^2$ value of 0.423, meaning that the one variable can account for only $<43\%$ of the variance observed for the other variable. When the advanced glaucoma patients were eliminated from the data set, correlations were considerably reduced. The highest correlation was $R = 0.46$, which yields an $R^2$ value of approximately 0.21. This means that nearly 80% of the variance of one variable cannot be accounted for on the basis of the other variable. Thus, in early stages of glaucoma, the ability to predict functional properties on the basis of structural measures, or vice versa, is quite poor. This suggests that to provide a full characterization of glaucomatous damage, both structural and functional measures are important.

In conclusion, the results of this study indicate that the structural optic disc parameters as measured with the HRT are well correlated with B–Y visual field test results. Moreover, our results suggest that B–Y perimetry may be more sensitive than W–W visual field testing in reflecting the development and progression of glaucomatous optic neuropathy. Further investigation is needed with more subjects to confirm our results.

**Key Words**

blue-on-yellow perimetry, confocal optic disc tomography, glaucoma, optic nerve head, short-wavelength automated perimetry

**References**


