Color Perimetry for Assessment of Primary Open-Angle Glaucoma

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The authors report the development of a color perimetry procedure which compares sensitivity of the short-wavelength color-vision mechanism in the peripheral visual field for normal eyes, eyes with ocular hypertension, and eyes with primary open-angle glaucoma. To isolate the short-wavelength cone mechanism, they modified an automatic projection perimeter to blue-on-yellow color perimetry and used a monochromatic 440-nm stimulus and a broad-band bright yellow background. The three groups of subjects were matched for age and lens density. Refraction, pupil size, acuity, and medication were controlled. Under these conditions, most glaucomatous eyes showed reduced sensitivities more than two standard deviations below normal. Normal control eyes were significantly different from eyes with ocular hypertension only in the superior nasal field (P < 0.05), but normal eyes differed from eyes with primary open-angle glaucoma in all areas of the field (P < 0.01). Invest Ophthalmol Vis Sci 31:1869-1875, 1990

Several investigators have assessed the role of color vision for diagnosing glaucoma, and studies indicate that blue-green color-vision deficits are apparent early in the disease. This suggests that the short-wavelength sensitive cones or their neural connections are more susceptible to damage from increased intraocular pressure than are the long-wavelength and mid-wavelength sensitive cone systems. Evidence for blue-green deficits on central color-vision tests such as the Farnsworth-Munsell 100-hue test, the Farnsworth D-15, and the Pickford-Nicholson anomaloscope is often present before peripheral visual field loss is found by standard perimetry. However, color-vision screening tests have not been very useful for predicting the progress of the disease. This failure may be due to several factors. Primary among these is lack of control over variables which may influence test results, such as lens density, pupil size, macular pigment, and other biologic reasons, such as diabetes, which are known to affect color vision. Subjects also should have appropriate refractive correction and be matched for age. We found, however, that when these factors are controlled, significant differences between normal eyes and eyes with primary open-angle glaucoma remain.

Two other factors which may reduce the predictive ability of color-vision tests are the emphasis on visually presented (fixated) stimuli and the use of tests designed originally to assess congenital color-vision deficits. Tests which isolate short-wavelength cone mechanisms and which exploit the known loss of peripheral visual field sensitivity may be more appropriate for assessing eyes with primary open-angle glaucoma.

In this study, we isolated the short-wavelength sensitive mechanisms with a nearly monochromatic 440-nm test stimulus presented on a bright yellow background. Using this combination in color perimetry, we found significant differences between control and patient groups.

Materials and Methods

We modified a Humphrey visual field analyzer, model 620, automated perimeter to provide a bright yellow background of 80.9 cd/m², which would produce a retinal illuminance of approximately 2.8 log photopic trolands. The background was within the range suggested for best isolation of the short-wave-length mechanism. To produce the background, we mounted a carousel projector on the left side of the perimeter cabinet, as seen from the front, and made an additional aperture above the left light source. We used mirrors to channel the light from the projector through this aperture. Two layers of diffusion film (0.5 mm each) covered the opening. We inserted Wratten #12 filters in front of all background light sources to produce a yellow background. The combination of diffusion material and the Wratten filter produced sufficient lack of short-wavelength cone stimulation by the background (Fig. 1). We then iter-
Fig. 1. The relative spectral radiances of the modified automated perimeter’s bright yellow background (— — —), the “blue” filter that is standard in the perimeter ( — — ), and the 440 nm interference filter used in this experiment ( — — ).

atefully adjusted and calibrated the background until it displayed equal luminance across the central 30° of visual field.

We placed a filter holder in the stimulus light path just behind the perimeter’s shutter box and inserted a 440-nm interference filter (half-bandwidth of 4 nm, Fig. 1). Insertion of the 440-nm interference filter used for the test greatly reduced the amount of usable light. To improve the intensity range of the stimulus with this filter in place, we increased the available intensity of the test light source by rewiring the bulb (12 Volts, 50 Watts) to run at 13 Volts instead of its normal operating voltage of 9.5 Volts. The combination of increased intensity and shift in color temperature at 13 Volts provided an additional 0.7-0.8 log units (measured photometrically, and psychophysically on three eyes) for a 3.0-log unit range of usable intensities. These adjustments were made on completion of the unit’s internal calibration routine to avoid unwanted automatic corrections which the unit makes when stimulus or background levels change.

We used the Humphrey program 24-2 which incorporates 54 points within the central 25° of visual field. The experimenter monitored fixation through the telescope to reduce the possibility of errors which may result from relying on the Heijl-Krakau blind spot monitoring technique. This allowed corrections for shift in alignment and reinstruction of subjects as necessary. We used a Goldmann size V (1.8°) stimulus of 200-msec duration to enhance short-wavelength cone isolation.10-13 Test–retest results on 11 glaucomatous eyes yielded well-correlated thresholds for the 52 points in the overall field (r = 0.92; P < 0.001) with mean log thresholds within 0.1 log unit.

To obtain an index of lens density for each subject, we used a procedure and apparatus we reported previously.14,15 This procedure yields results consistent at all ages with those obtained by objective methods,16 and test–retest values are well correlated (r = 0.97; P < 0.001). Briefly, after 30 min of dark adaptation, scotopic thresholds were obtained for 560- and 410-nm stimuli. Test flashes of 100 msec, subtending a 1.8° visual angle, were presented 15° in the periphery to enhance rod participation and to avoid macular pigment. A software gateway through the serial I/O port of the Humphrey allowed the test to be controlled by an external computer.15 A double-staircase procedure with three reversals was used, giving two threshold determinations for each wavelength. The lens density index (LDI) was determined by first equating the two wavelengths for equal radiance and then by taking the difference threshold (560 - 410 nm). We chose a LDI of 0.42 as the standard and corrected the color-perimetry threshold values for each subject on the basis of difference from this standard. For example, if a patient’s eye had a measured index of 0.92, the threshold values would be increased by 0.5 log units (or 5 decibels [dB]). Eyes with cataracts, requiring a correction greater than 0.7 log units were eliminated from the study. Threshold values for those eyes were often unobtainable due to the limited maximum intensity of the light source, filtered by the 440-nm interference filter in combination with higher lens densities. The chance of poor thresholds due to increased absorption by the lens was thereby reduced, leaving the disease process the most likely candidate for any observed differences between the subject groups.

Ten normal control subjects, 14 glaucoma-suspect patients, and 16 primary open-angle glaucoma patients were studied after the nature of the procedures had been fully explained, and informed consent was obtained. Control subjects and patients were matched on the basis of age and lens density. Ages ranged from 54-68 (60.10 ± 5.90) yr for normals, 53-69 (62.64 ± 5.08) yr for glaucoma-suspect, and 54-69 (63.31 ± 4.01) yr for glaucoma patients. Lens densities ranged from 0.37-1.12 (0.68 ± 0.27) for normal eyes, 0.17-0.97 (0.58 ± 0.19) for glaucoma-suspect eyes, and 0.01-1.07 (0.70 ± 0.34) for eyes with glaucoma. These controls were designed to minimize the effects of these two variables. Therefore we did not have a significant correlation between age (r = -0.26) or lens density (r = 0.09) and total scores for the overall field or for any quadrant. The importance of age over and beyond changes in ocular-media absorption can be seen in our preliminary results on normal age-related changes in short-wavelength sensitivity with this color perimetry procedure.
We randomly selected one eye from each subject. All eyes had a complete ophthalmologic examination including best-corrected visual acuity, slit-lamp biomicroscopy, gonioscopy, applanation tonometry, stereoscopic funduscopy, and standard visual fields. Acuities were 20/30 or better. Pupil sizes were in a normal range of 3.0–5.0 mm in the light and 5.0–7.5 mm in the dark. All subjects were properly refracted for both standard and color visual field tests. Only subjects with intraocular pressures less than 21 mm Hg, normal optic discs, normal standard visual field tests defined as thresholds within 4 dB of the perimeter’s internal norms at all test points, known diabetes, no known color-vision loss, and no family history of glaucoma were included in the normal group. Glaucoma suspects all had intraocular pressures exceeding 24 mm Hg on at least two separate occasions. They had normal standard visual fields and normal-appearing optic discs. Glaucomatous eyes had optic disc abnormalities, characteristic mild-to-moderate visual field loss (less than 1.0 log unit on average) with no absolute scotomas, and intraocular pressures of at least 24 mm Hg without treatment.

Results

In addition to choosing the background level, stimulus wavelength, and test size most likely to assure short-wavelength cone isolation, we used three other control procedures. The first was to obtain threshold versus intensity curves for two subjects for the 440-nm test on increasing intensities of the yellow background. The results were compared with predictions based on Stiles’ data for this background wavelength combination. These results showed that detection with the background intensity we used was mediated by pi, (a short-wavelength mechanism). Stiles’ data predict that detection by pi, (the mid-wavelength mechanism) should be approximately 1.7 log units below that for pi, Our results showed a separation of 1.5 log units, which is well within the normal variance found for his subjects.

The second control was to demonstrate the presence of transient tritanopia. In this phenomenon, the threshold for a short-wavelength target is found after the eye is adapted to a bright yellow background. If it is the short-wavelength mechanism that is being measured, the visual system will be less sensitive to the target when the background is extinguished. Transient tritanopia could not be demonstrated using our background with the perimeter’s internal blue filter. The phenomenon was assessed using the 440-nm stimulus in three normal, two glaucoma-suspect, and six glaucomatous eyes. In all cases, transient tritanopia of both the first and second kind was present for several seconds. There were no apparent differences between normal controls and patients for the duration of the effect.

The third control procedure tested a 34-year-old congenital tritanopic patient, diagnosed on the basis of her test results on the Farnsworth-Munsell 100-hue test, the anomaloscope, the Ishihara plates, the Farnsworth F2 tritan plate, and her tritan match on a colorimeter. She had no visual field loss on standard perimetry and a LDI of 0.32. If the short-wavelength mechanism is adequately isolated, her thresholds should fall more than 1 log unit below normal thresholds. At the point where the middle-wavelength system can begin detecting the stimulus. This patient’s mean log threshold for the overall field on color perimetry was 1.2 log units below the mean of five age-matched normal controls.

Figure 2 depicts the mean relative threshold in dB for the three groups at each of the 55 color visual field locations. Table 1 gives means, standard deviations, and coordinates for each location. We chose single-factor analysis of variance to analyze the data comparing normal eyes with those with primary open-angle glaucoma or ocular hypertension. Following one approach used to analyze standard (white-on-white) visual fields, we compared the mean defect for

<table>
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<tr>
<th>Location</th>
<th>Fixation</th>
<th>East</th>
<th>24</th>
<th>22</th>
<th>20</th>
<th>18</th>
<th>16</th>
<th>14</th>
<th>12</th>
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<th>8</th>
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Fig. 2. Mean relative threshold in dB for each of the 55 color visual field locations. The top number in each cluster denotes the mean for normal eyes, the middle is for suspect eyes, and the bottom value is for glaucomatous eyes. Values are relative to 0 dB (0.0 log units), the maximum stimulus intensity. The vertical axis is elongated to accommodate three numbers per location (see Table 1 for coordinates).
the entire field, and for each of the quadrants, with the norms for that perimeter. Comparing normal and glaucomatous eyes, we found that the superior nasal quadrant (P < 0.001), the superior temporal quadrant (P < 0.01), the inferior nasal quadrant (P < 0.001), the inferior temporal quadrant (P < 0.01), and the overall field (P < 0.001) were significantly different.

Normal and glaucoma-suspect eyes differed significantly only in the superior nasal field (P < 0.05). Of interest, the superior nasal field location has been shown to be the most diagnostically significant for detection of early glaucomatous damage on standard visual fields, although individual patient eyes may first show a deficit at some other location. Figure 3 depicts the mean log threshold values and fall-off with eccentricity for the superior nasal field. Means and standard deviations for these values are given in Table 2.

### Table 1. Mean (standard deviation) log threshold for each of the three groups at each of the 55 visual field locations (in degree coordinates) in Program 24-2

<table>
<thead>
<tr>
<th>Location</th>
<th>Eccentricity</th>
<th>Normals</th>
<th>Suspects</th>
<th>Glaucomas</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Eccentricity</td>
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<td>Horiz./vertic</td>
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<tr>
<td>21.20</td>
<td>2.20(2.75)</td>
<td>2.11(2.11)</td>
<td>1.88(6.61)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>2.20</td>
<td>2.20(2.71)</td>
<td>1.74(6.21)</td>
<td>1.62(5.73)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>12.73</td>
<td>2.21(2.60)</td>
<td>1.76(5.08)</td>
<td>1.44(5.78)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>15.30</td>
<td>2.11(2.77)</td>
<td>1.53(4.75)</td>
<td>1.31(5.73)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>17.49</td>
<td>1.94(1.90)</td>
<td>1.59(6.43)</td>
<td>1.17(4.55)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>21.21</td>
<td>1.63(3.77)</td>
<td>1.25(5.77)</td>
<td>1.1(4.89)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>22.85</td>
<td>1.59(4.20)</td>
<td>1.27(5.72)</td>
<td>0.99(3.75)</td>
<td>1.72(4.39)</td>
</tr>
<tr>
<td>27.17</td>
<td>1.39(4.18)</td>
<td>1.11(4.73)</td>
<td>0.97(4.48)</td>
<td>1.72(4.39)</td>
</tr>
</tbody>
</table>

### Table 2. Mean (standard deviation) log threshold by eccentricity for each of the three subject groups for the superior nasal field

<table>
<thead>
<tr>
<th>Eccentricity from fixation</th>
<th>Normal</th>
<th>Suspect</th>
<th>Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>2.42(2.65)</td>
<td>2.21(5.75)</td>
<td>2.16(3.01)</td>
</tr>
<tr>
<td>4.24</td>
<td>2.23(2.11)</td>
<td>1.88(6.61)</td>
<td>1.72(4.39)</td>
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<tr>
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<td>0.97(4.48)</td>
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</table>

![Fig. 3. The mean relative log threshold values and fall-off in sensitivity with eccentricity for the superior nasal quadrant of the visual field for the three subject groups. An average value was used for eccentricities with more than one test point location.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933580/)
The major advantage to the total-score approach is that it allows comparison of the individual patient eyes with the range of normal values. We could identify patient eyes with scores corresponding to one and two standard deviations from the normal threshold values for the overall field and for each quadrant. Nine of the 16 glaucomatous eyes fell more than two standard deviations below the norm in two or more quadrants. Only two eyes were always within one standard deviation of the norm.

Of the 14 glaucoma-suspect eyes, four fell more than two standard deviations below normal in two or more quadrants and two additional eyes did in at least one quadrant. Five eyes were always within one standard deviation of normal.

We also compared results on standard visual fields. We found no significant differences between normal and glaucoma-suspect eyes. Normal eyes and eyes with primary-open angle glaucoma were significantly different in the superior nasal field only \( (P < 0.05) \). Glaucoma-suspect and glaucomatous eyes differed in the superior nasal field only \( (P < 0.025) \).

Using Anderson's criteria to determine visual field loss, we compared standard and color fields for the 16 eyes with primary open-angle glaucoma; 81% (13) had overlapping loss on both tests with more extensive damage on the color visual field. One of the remaining three had a diffuse loss on both. The remaining two had more extensive damage on their standard field. Glaucoma-suspect eyes were all within normal limits on standard visual fields. With color perimetry they commonly showed patterns of field loss primarily located in the superior nasal field and similar to those seen on standard visual fields for eyes in the early stages of glaucoma (Fig. 4).

![Fig. 4. An example of the color visual field results (Program 24-2) for a suspect eye. Numbers indicate defect depth from mean normal threshold. Plusses indicate results within 4 dB of mean normal threshold.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933580/)

**Fig. 4.** An example of the color visual field results (Program 24-2) for a suspect eye. Numbers indicate defect depth from mean normal threshold. Plusses indicate results within 4 dB of mean normal threshold.

**Discussion**

There are several possible advantages to color perimetry over clinical measures of foveal color vision. First, it combines assessment of color vision with assessment of peripheral field sensitivities, an important feature because glaucoma is traditionally associated with peripheral visual field loss. Second, the method is familiar to patients. Third, the equipment is available with minor modifications to existing perimeters. Fourth, the reliability is comparable to standard perimetry as evidenced by the test-retest values reported here. Fifth, the results can be directly related to achromatic sensitivities on the same eye with the same equipment and procedures. Finally, and perhaps most importantly, corrections for sensitivity losses due to lens density can be made.

In addition to knowing the individual's lens density, the importance of age-matched normative data is illustrated in Figure 5, which depicts the fall-off in mean log threshold sensitivity with eccentricity for normal control eyes within one of the following decades, 20–29 (n = 4), 30–39 (n = 5), 40–49 (n = 3), 50–59 (n = 5), 60–69 (n = 5), and 70–79 (n = 4). Figure 6 shows the same information with standard error of the mean for the youngest and oldest groups. Threshold results from each eye were corrected for lens density before analysis for both figures. Although these results are preliminary, they are consistent with other reports of retinal or neural changes in short-wavelength cone sensitivity with age.
Prior attempts (including our own\textsuperscript{26}) to develop a diagnostically useful color visual field test have been disappointing.\textsuperscript{27-30} We hypothesized that the limited success of our previous attempt was related to incomplete isolation of the short-wavelength mechanism. The broad-band blue filter provided with the perimeter may allow mid-wavelength cones to mediate detection in the presence of reduced short-wavelength cone sensitivity (Fig. 1). There is psychophysical evidence to support this hypothesis and our subsequent selection of 440 nm as the stimulus of choice. Mollon and Polden\textsuperscript{8} assessed several stimulus wavelengths and background levels in their attempts to evaluate the role of the blue-yellow opponent pathway in the phenomenon of transient tritanopia. They found that stimuli above 475 nm did not manifest the phenomenon even on very intense backgrounds. Although the lights appeared blue, they were primarily exciting mid-wavelength cones. These authors recommended stimuli in the region of 440 nm for demonstrating transient tritanopia. Marr\textsuperscript{31} succeeded in isolating the short-wavelength mechanism by using a 440-nm stimulus and an adapting background. She used this method to demonstrate foveal and parafoveal deficits in several diseases other than glaucoma.\textsuperscript{32} Finally, Stiles\textsuperscript{33} recommended this wavelength for isolation of the short-wavelength pi mechanisms. Monochromatic stimuli above approximately 480 nm required very intense backgrounds to get good separation between $p_{\text{hi}}$ (short-wavelength mechanisms) and $p_{\text{ia}}$ (mid-wavelength mechanisms).

We propose that a 440-nm stimulus and broad-band yellow background be used in color perimetry. With this combination, we found significant differences in sensitivity for short-wavelength cone mechanisms between normal control eyes and those with ocular hypertension and glaucoma. The procedure lends itself to a program incorporating repeated measures and long-term follow-up, two facets necessary to validate its use as a predictive test. However, one puzzle remains. The normal rate of turnover from glaucoma suspect to glaucoma is approximately only 1% per year,\textsuperscript{34,35} yet estimates of damage based on psychophysical tests range from as low as 20–30% with evoked potentials\textsuperscript{36} to as high as 80% for a study on flicker sensitivity.\textsuperscript{37} This trend to overestimate the number of suspects at risk is apparent in studies using various psychophysical procedures. For example, results of contrast-sensitivity function showed abnormal results in 67% of the eyes with ocular hypertension,\textsuperscript{38} and results on the desaturated D-15 color vision test showed 58% of these eyes failing the test.\textsuperscript{3}

In this study, 43% of the glaucoma-suspect eyes fell greater than two standard deviations below normal in at least one quadrant of the visual field. Even for this older age group, this percentage is high.\textsuperscript{39} Future research efforts should address this discrepancy. The long-term follow-up planned for our patients should help to answer some major questions, such as: What percentage of these eyes will be diagnosed as having glaucoma within the next 5 years? Can substantial deficits in performance on color visual fields persist while standard achromatic visual fields remain normal? Is the criterion use of standard visual field loss for diagnosis of glaucoma sufficient if other measures of visual function indicate significant deficits?

Regardless of the mechanism underlying the effect, some eyes with ocular hypertension exhibit abnormal color vision before standard visual field loss or optic disc changes appear. Color perimetry using a 440-nm stimulus and a broad yellow background showed a significant difference between patient eyes and normal control eyes. We were able to identify individual patients who fell more than two standard deviations below normal who can now be followed to see if they are at greater risk for the development of visual field loss.

**Key words:** glaucoma, ocular hypertension, color vision, color perimetry, psychophysics

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**References**