Motion Automated Perimetry Identifies Early Glaucomatous Field Defects

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Objective: To determine if motion automated perimetry can identify early glaucomatous visual field defects in patients with suspected glaucoma (by disc), those with ocular hypertension, and those with primary open-angle glaucoma.

Methods: Motion automated perimetry, a foveally centered motion test, and standard visual field tests were conducted on one randomly selected eye of normal patients (n = 38), patients with suspected glaucoma (by disc) (n = 28), patients with ocular hypertension (n = 18), and patients with primary open-angle glaucoma (n = 21). Subjects' performance on both motion tests were compared with their performance on standard perimetry.

Results: Perimetric motion thresholds significantly distinguished the groups (P ≤ .001), while the foveally centered motion test was unable to separate them (P > .32). Of the total patients, 90.5% of those with glaucoma, 39.3% of those with suspected glaucoma, 27.8% of those with ocular hypertension, and 5.3% of the normal subjects had abnormal results on motion automated perimetry testing. Perimetric motion thresholds were significantly correlated with standard visual field thresholds (P < .001).

Conclusion: Motion automated perimetry identifies visual field defects in patients who already show standard visual field loss as well as in a moderate percentage of those with suspected glaucoma and ocular hypertension, indicating that the testing of discrete locations might be necessary for increased diagnostic utility.

SUBJECTS AND METHODS

SUBJECTS

Subjects for this study were patients with primary open-angle glaucoma (n = 21), patients with suspected glaucoma (by disc) (n = 28), patients with OHT (n = 18), and normal controls (n = 38). One eye was randomly chosen from each subject. The different subject groups were not significantly different in age (P = .09). Mean (±SD) ages were 66.3 ± 11.8 years for the glaucoma group, 62.2 ± 11.2 years for the suspected glaucoma group, 57.1 ± 12.7 years for the OHT group, and 62.0 ± 10.3 years for the normal control group.

Patients with primary open-angle glaucoma were defined by the following criteria: (1) open angles with abnormal optic discs based on 1 or more of the following: cup-disc ratio asymmetry between the 2 eyes of 0.2 mm or more, localized or diffuse rim defects, excavation, retinal nerve fiber layer defects, or disc hemorrhages as determined by masked review of simultaneous stereophotographs by a glaucoma expert; (2) previously documented standard visual field loss determined by visual field analysis (program 24-2, Humphrey Visual Field Analyzer 640, Humphrey Instruments, San Leandro, Calif), with corrected pattern SDs outside the 95% confidence limits or glaucoma hemifield test results outside the 99% confidence limits.

Patients with suspected glaucoma were identified by the above criteria for abnormal optic discs. However, they had normal standard visual fields, with corrected pattern SDs within the 95% confidence limits and glaucoma hemifield test results within normal limits.

Normal controls met the following inclusion criteria: (1) normal optic discs based on above criteria; (2) intraocular pressures less than 21 mm Hg on all prior examinations; and (3) normal standard visual fields based on above criteria.

Patients with OHT met all of the above criteria for normal controls except they had intraocular pressures greater than 23 mm Hg on 2 separate examinations.

For this study, visual field reliability indices were set at 25% or less for fixation losses, false-positive errors, and false-negative errors. Mean (±SD) defects on standard perimetry were −7.6 ± 5.61 for eyes with glaucoma, −0.69 ± 1.9 for eyes with suspected glaucoma, 0.26 ± 1.12 for eyes with OHT, and 0.42 ± 1.4 for normal control eyes.

This study was approved by the Human Subjects Committee of the University of California, San Diego, and was undertaken with the informed consent of each subject.

RANDOM-DOT MOTION DISPLAY

The stimulus parameters and design of MAP have been previously reported.4,5 The current stimulus was within known ranges for testing the motion system while still allowing glaucoma patients with impaired vision to perceive the display.

The motion stimulus was produced on a computer-controlled imaging display monitor (Barco, Kennesaw, Ga) with 1024×768 lines of resolution and a refresh rate of 75 Hz. Each pixel subtended 0.31 mm (7.35 minutes of arc at the viewing distance of 16.5 cm). The monitor was driven by a Power PC 8100 Macintosh computer (Apple, Cupertino, Calif) using a 24×14 video card (RasterOps, Santa Clara, Calif).

Seven frames were shown in rapid succession to create the apparent motion stimulus, which lasted for 420 milliseconds. Within each of these frames, 20 dots were randomly placed within a circular test region of 3.5° of visual angle. These dots moved at a constant velocity of 8.2° per second in random directions. A new direction of motion was chosen after each spatial displacement. Randomly chosen signal dots were displaced together in 1 of 4 cardinal directions (right, left, up, down) to create the coherent motion signal that the patients were to detect. The signal ranged in strength from 0% to 100% coherence. Signal dots remained the same for all 7 frames of the display and had the same spatial displacement as the noise. This aspect of the stimulus makes it differ slightly from a traditional RDK, which randomly selects the signal dots after each displacement. The implications of this signal rule have been discussed in a previous article,5 where it was shown that a signal of this nature embedded in a surround of vectored motion is not significantly influenced by nonmotion cues.

Thresholds were determined by means of a staircase procedure. Staircases began with a coherence value of 80% and a step size of 20% coherence. Each staircase reversal resulted in a halving of the step size down to the minimum of 3% coherence. The staircase was terminated by 3 reversals at the minimum step size. Threshold was taken as the mean of the last 3 reversal points.

We designed the perimetric motion stimulus to test 14 retinal locations because early glaucoma is often characterized by localized peripheral visual field loss. The test locations were arranged in a pattern that mapped the subject’s motion thresholds across the central 24° of visual field in approximately 15 minutes (Figure 1). The locations of test were chosen to identify peripheral arcuate and nasal step defects and to overlap with visual field testing locations.

This is in contrast to the 14 subjects required for a significant result when the superior field average from the perimetric motion test was used in the power calculations. Because the mean defect for patients with glaucoma on standard perimetry ranged from −0.57 to −20.26, the analysis was redone excluding all mean defects greater than −6.0 dB to give an evaluation of MAP for detection of early glaucoma (n = 9). The patients with early glaucoma remained significantly different from normal controls (Table 1).
The stimulus for the foveally centered motion test was centered on the fovea and subtended a circular region 25.1° in diameter with a dot density identical to that used in the smaller perimetric displays. All other parameters remained the same.

TEST PROCEDURES

The patient sat in a darkened room with a patch placed over the non-test eye. He or she rested in a chin rest while viewing the screen through proper refraction for the test distance of 16.5 cm.

The patient focused on a black fixation “X” in the center of the display and adapted for 2 minutes to the background illumination. Fixation was monitored by the test administrator on a separate video display system. Trials where fixation was lost were aborted and repeated later in the program. The testing procedure was then explained to the subject.

The session began with a foveal practice test, which was identical to the foveally centered single-stimulus test. The patient’s performance on these trials was observed by the test administrator to make sure that the task was properly understood. After completing the foveal practice, the patient either received the larger foveally centered test or the 14-location perimetric motion test. The order of presentation for the 2 types of motion stimuli was randomized.

For all testing, the patient verbally reported the perceived direction (left, right, up, or down) in which the dots were moving in a 4-alternative forced-choice paradigm. The test administrator pressed an arrow key corresponding to the direction indicated by the subject. The patient could respond at any time during or after the stimulus presentation. The program gave a 2-second delay before presenting the next stimulus. Subjects were informed that they could pause and rest at any time during the test. The whole procedure lasted approximately 30 minutes.

STATISTICAL ANALYSES

The perimetric threshold values averaged across the 14 test points (whole field), the perimetric threshold values averaged across the 7 superior field test points (superior field), the perimetric threshold values averaged across the 7 inferior field test points (inferior field), and motion coherence thresholds for the foveally centered motion test were the main dependent measures of this study. Analysis of variance was performed on all dependent measures to indicate if a significant difference existed in motion thresholds among the normal, suspected glaucoma, OHT, and glaucoma subjects. If a significant difference was indicated, a Tukey-Kramer honestly significant difference test was performed to localize the effect.

The Pearson r was computed for the correlation of the mean differences on MAP and standard perimetry. Mean defect on standard perimetry was computed by averaging the patient’s threshold values for standard visual field test points that overlapped with each of the MAP test locations to create 14 values. These values were subtracted from the normal averages for each test point separately. The obtained difference scores for all 14 points were averaged to give an overall mean defect on standard perimetry for each patient. Mean defect on MAP was the average of 14 difference scores from normal.

An abnormal MAP field was defined as having 3 or more motion threshold values at least 2 SDs above normal with at least 2 of the abnormal points adjacent to each other. This is a conservative definition because 3 motion locations would cover at least 8 standard visual field locations.

Receiver operator characteristic (ROC) analysis was performed on the percent coherence variables for the glaucoma patients. Receiver operator characteristic curves were plotted for sensitivity vs 1 – specificity for possible cutoff points from 0% to 100% coherence. Sensitivity is the ability to correctly identify glaucoma. Specificity is the ability to correctly confirm a normal field. To quantify the ability of each measure to separate the normal subjects and those with glaucoma, we calculated the percentage of area under the ROC curve. This was accomplished by fitting a function to the ROC from the point (x = 100, y = 100) in the upper left corner to the first point where x = 0 (Figure 2). A fit to the data points was accepted if more than 95% of the variance between the points could be accounted for by the function. The area under the curve was determined by integrating the function from x = 0 to x = 100 with the x-axis defining the lower bound of the integration area. Because the total area possible is known, the percent area is the area under the curve divided by 100. Using this measure, an area under the ROC curve of 50% represents chance while an area under the ROC curve of 100% represents perfect discrimination.

Optimal general error rates were computed for the different measures. The general error rate is the percentage of subjects misclassified when a specific cutoff value in percent coherence is selected. Therefore, choosing a cutoff that minimized the general error rate represents a balance between sensitivity and specificity such that the lowest percentage of misses and false alarms possible occurs. The sensitivity, specificity, and optimal cutoff for the different measures are reported at the lowest general error rate.

Although MAP did not differentiate the patients with OHT from normal controls, it did identify 5 (27.8%) of the 18 patients with OHT, 19 (90.5%) of the 21 patients with glaucoma, 11 (39.3%) of the 28 patients with suspected glaucoma, and 2 (5.3%) of the 38 normal subjects as abnormal on the examination.

Receiver operator characteristic analysis indicated that the superior field average from MAP gave the largest area under the ROC curve (98.2%). The general error rate for the superior field average was 5.7%, yielding a specificity of 97.4% and a sensitivity of 91.3%. The larger foveally centered stimulus scored the poorest, with 62.4% of the total area under the ROC curve. See Table 2 for a full listing of the ROC results.

A significant correlation between all patients’ standard visual field and MAP mean defects was found ($r^2 = 0.35, P < .001$) (Figure 3).

Individual patient data are shown as illustrations. Glaucoma patients 1 (Figure 4, top) and 3 (Figure 4, bottom) show a good correspondence between stan-
standard visual fields and MAP. Patient 3 was one of the 2 glaucoma patients who were not identified by MAP because 3 test points were not 2 SDs above normal. Patient 2 (Figure 4, center) shows a more extensive defect on MAP than is present on standard automated perimetry. 

Figure 5 shows the results for 3 patients at risk for developing primary open-angle glaucoma. Patients 5 and 7 had suspected glaucoma. Patient 6 had OHT. All 3 patients’ standard visual fields were normal while their MAP results showed clear defects.

It should be noted that in Figure 4 and Figure 5 the pattern deviation plot (STATPAC II analysis, Humphrey Instruments) was used for comparison to motion threshold values. We chose to use pattern deviation because it reduces the effects on the visual field due to general reduction in sensitivity from optical factors, such as blurring, cataract, and pupil size. Because MAP is resilient to the confounding influences of blurring, cataract, and pupil size,11,12 using the pattern deviation makes it more likely that the results are due to glaucomatous damage and thereby more comparable to MAP.

## Comment

Early attempts to measure motion discrimination thresholds with RDKs used large centrally presented fields of dots and produced mixed results. Silverman et al12 found that motion thresholds were elevated in patients with glaucoma and OHT. This finding was later replicated by Trick et al14 but could not be replicated by Bullimore et al7 and Graham et al.10 The lack of sensitivity to glaucoma reported in these studies could have resulted from either their long presentation durations (>1 second) or their large stimulus aperture sizes (>19°). Long display durations could provide even a damaged motion system with enough time to integrate a noisier or weaker motion signal. Large aperture sizes could allow both spared and nonspared regions of the visual field to contribute to a motion percept.

Consistent with the theory that larger aperture sizes might have lower diagnostic power, perimetric motion tests using small localized targets have had considerable success in detecting glaucomatous visual field loss. Using RDKs with variable aperture sizes in a detection paradigm, Wall and colleagues have reported significant elevations in perimetric size thresholds for patients with glaucoma1 and OHT.17 Similar results using RDKs in perimetric direction discrimination tasks rather than detection tasks have been reported in patients with

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<table>
<thead>
<tr>
<th>Subject</th>
<th>Foveal Location</th>
<th>Whole Field</th>
<th>Superior Field</th>
<th>Inferior Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>18.1 ± 11.6</td>
<td>33.3 ± 8.1</td>
<td>34.5 ± 9.4</td>
<td>32.1 ± 8.0</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>21.7 ± 14.8</td>
<td>39.6 ± 14.2</td>
<td>40.5 ± 14.5</td>
<td>38.8 ± 14.6</td>
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<tr>
<td>Suspected glaucoma</td>
<td>24.6 ± 20.4</td>
<td>44.6 ± 19.5*</td>
<td>45.8 ± 19.3*</td>
<td>43.5 ± 20.9*</td>
</tr>
<tr>
<td>Glaucoma, all patients†</td>
<td>23.7 ± 12.5</td>
<td>59.6 ± 15.1†</td>
<td>70.5 ± 16.7†</td>
<td>48.7 ± 21.1†</td>
</tr>
<tr>
<td>Glaucoma, mean defect &lt; −6.0 dB§</td>
<td>22.3 ± 16.6</td>
<td>53 ± 14.7*</td>
<td>59.1 ± 12.5†</td>
<td>47.6 ± 19.9*</td>
</tr>
</tbody>
</table>

*Significantly different from normal controls.
†For all patients P < .001 for foveal location, and P < .002 for inferior field (analysis of variance).
‡Significantly different from normal subjects, those with ocular hypertension, and those with suspected glaucoma (Tukey-Kramer honestly significant difference).
§For patients with a mean defect less than −6.0 dB, P < .001 for whole and superior fields, and P < .008 for inferior field.
In a previous study to determine if glaucoma-related loss of motion sensitivity is localized in retinal locus, we presented a discrete motion target at a location of standard visual field loss and a location of standard visual field sparing in the same eye of a glaucoma patient.4 The 2 test locations mirrored each other across the horizontal midline. The results indicated a significant difference between spared and nonspared retinal locations, suggesting that glaucoma causes localized loss of motion sensitivity.4

The ROC results of the present study further confirm that a foveally presented RDK is less sensitive to glaucomatous visual field loss than MAP, which tests discrete retinal locations. This becomes apparent when comparing the percentage of area under the ROC curves. The greatest area under the ROC curve and therefore the greatest sensitivity was found for the superior half of the MAP field.

Motion automated perimetry can also identify field loss in a percentage of the patients with suspected glaucoma and OHT, suggesting that loss of motion sensitivity may precede standard visual field loss. The percentage of patients with OHT identified as abnormal is consistent with previous work using RDKs in a detection paradigm17 and indicates that MAP visual field abnormality might exist prior to detectable abnormality of the optic nerve.

While the stimulus design used in this study was successful in separating glaucomatous from normal eyes, more work is necessary to evaluate possible limitations of the current test design. A stimulus duration of 420 milliseconds necessitates careful fixation monitoring in the administration of MAP. A second possible limitation is normal variability. The normal variability creates a relatively high SD (between 8.0% and 11.6% coherence) (Table 1). Future work using direction discrimination tasks should assess test-retest variability and ways to reduce it.

Longitudinal follow-up with MAP and conventional automated perimetry is required to determine if the eyes with OHT and suspected glaucoma with MAP defects will eventually develop standard visual field loss.
Figure 5. Pattern deviation plots for standard automated perimetry (left side) showing the match with their results on motion automated perimetry (right side) in 2 patients with suspected glaucoma and 1 patient with ocular hypertension. For motion automated perimetry, the number at the origin is the threshold for the foveally centered motion test, while the remaining 14 numbers are threshold values from motion automated perimetry.

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