Screening for Glaucomatous Visual Field Loss With Frequency-Doubling Perimetry

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Purpose. To conduct a preliminary evaluation of the efficacy of the frequency-doubling contrast test as a means of screening for glaucomatous visual field loss.

Methods. Contrast thresholds for frequency-doubled stimuli were obtained under four test conditions: superior hemifield, inferior hemifield, and central (5° radius) targets using a method of adjustment (MOA); superior hemifield, inferior hemifield, and central targets using a modified binary search (MOBS); four quadrant stimuli and the central target using MOBS; and 16 stimuli (four per quadrant) and the central target using MOBS. One eye each of 36 patients with early (12), moderate (12), and advanced (12) glaucomatous visual field loss was tested, as was one eye each of 36 age-matched normal control subjects.

Results. For hemifield stimuli, the MOBS test procedure had better test-retest reliability, lower individual variation, and greater separation of the normal population and the population with glaucoma than did the MOA procedure. The use of progressively smaller, more localized stimuli produced successively better separation of glaucomatous and age-matched normal control eyes. Area under the Receiver Operating Characteristic curve was 0.81 for hemifield stimuli (sensitivity and specificity, 70% to 75%), 0.91 for quadrant stimuli (sensitivity and specificity, 83% to 85%), and 0.965 for the 16 stimuli (sensitivity 93%, specificity 100%). Test time was approximately 1.3 minutes for hemifields, 1.5 minutes for quadrants, and 5 minutes for the 16 targets.

Conclusions. Preliminary results indicate that the frequency-doubled contrast test provides a quick, efficient means of screening for glaucomatous visual field loss. Test time is relatively short, test-retest reliability is good, and sensitivity and specificity for detection of glaucomatous visual field loss is very good. The use of the MOBS staircase procedure and small, localized stimuli result in the best performance for screening purposes. An expanded normative database and the use of more rapid suprathreshold screening strategies should enhance further the efficacy of this test. Invest Ophthalmol Vis Sci. 1997;38:413-425.

When a low spatial frequency sinusoidal grating (<1 cyc/deg) undergoes high temporal frequency count-erphase flicker at 15 Hz or above (i.e., there is a rapid contrast reversal in which the light bars become dark and vice versa), the grating appears to be twice its actual spatial frequency, as illustrated in Figure 1. This phenomenon, often referred to as the frequency-doubling illusion, was described originally by Kelly1,2 and subsequently was evaluated by many other investigators.3-7 The low spatial frequency and high temporal frequency stimulus characteristics necessary for the percept of the frequency-doubling illusion suggest that it is mediated by mechanisms in the magnocellular (M-cell) pathway. In particular, the frequency-doubling percept is thought to be generated by visual mechanisms with nonlinear response properties,1,2 possibly the result of a full-wave rectification of the stimulus input.4 Maddess and associates8,9 have attributed this phenomenon specifically to the My ganglion cells, a subset of approximately 15% to 25% of magnocellular mechanisms that exhibit nonlinear response properties and that have large-diameter fibers.10,11
The frequency-doubling effect theoretically represents a promising screening procedure for detecting glaucomatous damage. One hypothesis concerning the basis of early glaucomatous damage is that there is a selective loss of large-diameter optic nerve fibers. This is supported by the histopathologic optic nerve studies of Quigley and colleagues\textsuperscript{12-18} in humans and experimental glaucoma in monkeys. Because magnocellular mechanisms with nonlinear response properties tend to have large-diameter fibers, the frequency-doubling effect should be a useful screening procedure for detecting early glaucomatous damage. A related hypothesis, supported by both histopathologic\textsuperscript{19,20} and psychophysical\textsuperscript{21-31} investigations, states that there is a selective loss to optic nerve fibers in the M-cell pathway. Because nonlinear M-cell mechanisms are thought to be responsible for the frequency-doubling effect, this hypothesis also suggests that a screening procedure based on the frequency-doubling percept would be effective in detecting glaucomatous damage.

**FIGURE 1.** Schematic representation of the sinusoidal grating stimulus and its subsequent appearance when it undergoes high temporal frequency counterphase flicker. The spatial frequency-doubled appearance is thought to be mediated by nonlinear visual mechanisms in the magnocellular pathway, as illustrated in Figure 1.

**FIGURE 2.** Mean deviation (MD) plotted as a function of corrected pattern standard deviation (CPSD) for normal control subjects (filled triangles) and patients with glaucoma (open squares).
Recently, an alternative hypothesis concerning early glaucomatous loss, referred to as the reduced redundancy or undersampling hypothesis, has been proposed.\textsuperscript{32,33} This hypothesis states that early glaucomatous losses are detected more readily for visual functions with sparse representation or minimal redundancy and do not necessarily reflect a selective loss to specific fiber types or sizes. In this view, the frequency-doubling effect should be a good screening procedure for glaucomatous damage because only 15\% of the total number of optic nerve fibers is included in the M-cell pathway, and nonlinear properties are found in only 15\% to 25\% of M cells. The mechanisms presumably underlying the frequency-doubling percept thus represent a sparse, minimally redundant system of approximately 3\% to 5\% of all retinal ganglion cells. According to any of these three hypotheses pertaining to early glaucomatous damage, a screening test based on frequency-doubling effects should be able to detect early glaucomatous loss. The frequency-doubling effect has been evaluated by Maddess and associates\textsuperscript{8,9} as a screening procedure for glaucoma. Contrast thresholds were obtained for detection of a 0.25 cyc/deg sinusoidal grating undergoing 25 Hz counterphase flicker by means of a method of adjustment. Using stimuli that were presented to the central 5\° radius, the entire central 17.5\° radius, and the superior and inferior hemifields, their preliminary findings revealed a sensitivity of 82\% and a specificity of 86\%.\textsuperscript{8} In a subsequent follow-up study, Maddess reported sensitivities and specificities above 90\%.\textsuperscript{9} Thus, both the theoretical and the empirical bases of the frequency-doubling contrast test indicate that it should be an effective means of screening for glaucomatous visual field abnormalities.

Unfortunately, the clinical characteristics of the patient population in Maddess' investigations were not well specified, particularly the visual field properties. This makes it difficult to determine the performance characteristics of this test procedure in comparison to methods used for threshold static or suprathreshold static automated perimetry, because it is unclear what degree of glaucomatous damage was present in the patients evaluated in their studies.\textsuperscript{8,9} The primary purpose of the current study was to determine the efficacy of the frequency-doubling contrast test for the rapid detection of early, moderate, and advanced glaucomatous visual field loss. In addition, we examined the performance characteristics and reliability of two different methods of obtaining frequency-doubled contrast thresholds, as well as the use of hemifield, quadrant, and 16 small, localized stimulus patterns. The original procedure introduced by Maddess\textsuperscript{8,9} used a method of adjustment for contrast threshold determinations, a technique that has been reported to have greater variability and higher thresholds than other psychophysical methods for contrast sensitivity measures.\textsuperscript{34,35} We compared the method of adjustment with a modified binary search (MOBS) staircase procedure, a technique that reportedly has been an efficient, accurate threshold estimation procedure.\textsuperscript{36,37} Maddess' original test procedure also used four large stimulus patterns (full 17.5\° radius central field, central 5\° radius, and superior and inferior hemifields).\textsuperscript{8} Because early glaucomatous visual field deficits typically are localized, we examined whether the use of quadrant and smaller stimulus patterns would improve performance of the frequency-doubled contrast test.

**MATERIALS AND METHODS**

Subjects consisted of 36 patients with glaucomatous visual field loss in one or both eyes and 36 age-matched normal control subjects. The average age of the patients with glaucoma was 66.4 years (range, 31 to 86 years), and the average age of the normal control...
subjects was 65.9 years (range, 30 to 85 years). Normal control subjects and patients with glaucoma were paired; the largest difference in age within each pair was less than 3 years. In accordance with the tenets of the Declaration of Helsinki, informed consent was obtained from normal control subjects and from patients with glaucoma by following institutional review board protocol.

Normal control subjects were included if both eyes were normal, as revealed by ophthalmologic examination (including slit lamp biomicroscopy and direct ophthalmoscopy); visual fields had normal mean deviation, normal corrected pattern standard deviation, and normal Glaucoma Hemifield Test indices on the Humphrey Field Analyzer (HFA) program 30-2; best-corrected visual acuity was 20/30 or better; intraocular pressure was <20 mm Hg; and they had no history of ocular disease or surgery. Normal control subjects were excluded if they had diabetes, another systemic disease, or a history of ocular or neurologic disease or surgery.

Subjects with glaucoma were included if they had primary open-angle glaucoma, a history of elevated intraocular pressure >21 mm Hg before treatment,
Frequency-Doubling Perimetry in Glaucoma

PERFORMANCE OF MOA vs MOBS
Hemifield Stimuli
ROC Analysis

MOA: Area under ROC = 0.71
MOBS: Area under ROC = 0.81

HEMIFIELDS vs QUADRANT PATTERNS
MOBS Test Procedure
ROC Analysis

HEMIFIELDS: Area under ROC = 0.81
QUADRANTS: Area under ROC = 0.91

FIGURE 6. (A) Receiver operating characteristic (ROC) curves for the method of adjustment (MOA) procedure (open triangles) and the modified binary search (MOBS) procedure (filled circles) using the whole field, central 10°, and superior and inferior hemifield patterns. Areas under the ROC curve were 0.71 and 0.81, respectively. (B) ROC curves for the MOBS test strategy using the hemifield (filled circles) and the quadrant (open squares) stimulus patterns. Areas under the ROC curve were 0.81 and 0.91, respectively.

Early glaucomatous visual field deficit was defined as a visual field with a characteristic pattern of glaucomatous visual field loss (e.g., a nasal step) with a corrected pattern standard deviation (CPSD) probability worse than the 5% but better than the 1% probability level. Moderate glaucomatous visual field deficit was defined as a characteristic pattern of glaucomatous visual field loss, a CPSD probability worse than 1%, and an mean deviation (MD) better than −10 dB. Advanced glaucomatous visual field deficit was defined as a characteristic pattern of glaucomatous visual field loss and an MD worse than −10 dB but better than −27 dB. Visual field characteristics of the normal control population and the population with glaucoma are presented in Figure 2, which plots MD as a function of CPSD for Humphrey 30-2 test procedures conducted in the study eyes. One eye of each patient with glaucoma who met the requirements for early, moderate, or advanced visual field loss was selected for frequency-doubled contrast testing, whereas the other eye was occluded with an eye patch. Patients with glaucoma were paired with age-matched normal control subjects tested in the same eye. Patients and normal control subjects were familiar with automated perimetry because each had undergone at least one visual field examination in each eye before the study. None of the patients or normal control subjects had undergone frequency-doubling perimetry testing. A brief demonstration was performed to familiarize them with the procedure.

All patients and normal control subjects who met inclusion criteria and who agreed to participate were enrolled in the study, all subjects completed the study, and no patients or normal control subjects were excluded from the data analysis.

Frequency-doubled stimuli were generated on a videomonitor with specialized control circuitry interfaced to a microprocessor. This apparatus was a prototype vision screening device manufactured by Welch Allyn (Skaneateles, NY). The screen subtended a visual angle of 35° horizontally × 30° vertically. An optical system was used to present the stimulus display at optical infinity, with an eyepiece adjustment provided to correct for spherical refraction errors. No other form of optical correction was used because preliminary investigations revealed that refraction errors up to 6 to 7 D produced no change in frequency-doubling contrast thresholds. Preliminary studies revealed that simulated media opacities do affect frequency-doubling contrast thresholds; for this reason, all patients and normal control subjects with visual acuity >20/30 in either eye or with clinical evidence of early cataract development were excluded from the current study. A 0.25 cyc/deg sinusoidal grating undergoing 25 Hz counterphase flicker (contrast reversal of light and dark bars, 50 times/second) was gener-
HUMPHREY FIELD ANALYZER

FREQUENCY DOUBLING ILLUSION

MD = -6.91 dB P< 0.5%
PSD = 11.19 dB P< 0.5%
SF = 2.48 dB P< 5%
CPSD = 10.83 dB
GHT outside normal limits

SUPERIOR NASAL
SUPERIOR TEMPORAL

INFERIOR NASAL
INFERIOR TEMPORAL

FIGURE 7. An example of good correspondence between Humphrey Field Analyzer (HFA) results (grey scale and probability plots shown on the left) and frequency-doubling contrast thresholds (shown on the right). The HFA results show a superior arcuate nerve fiber bundle defect, and the contrast thresholds for the superior nasal quadrant are beyond the normal upper 95% confidence limit (horizontal line).

ated on the monitor for all stimuli, except for the central 10° pattern, which used a 0.5 cyc/deg sinusoidal grating with 25 Hz counterphase flicker. Participants were instructed to fixate a small central spot on the videomonitor and to refrain from looking at eccentric stimuli. Fixation was monitored at all times by means of a videocamera focused on the observer's eye, and a videotape recording of the eye was made for each testing session. If eye movements were made toward an eccentric target, trial results were discarded and the eye was retested. This was necessary in only a couple of instances.

For thresholds measured using the method of adjustment (MOA), subjects were provided a trackball to vary stimulus contrast. At the beginning of a trial, the frequency-doubled pattern appeared at full contrast. At the beginning of a trial, the frequency-doubled pattern appeared at full contrast. Participants were instructed to maintain fixation on a small target located in the center of the screen, to adjust the trackball to make the pattern disappear, and to increase the contrast until the striped pattern was just visible. Three contrast threshold adjustments were made for each stimulus pattern, and the geometric mean of the three trials was used as the final contrast threshold value. For thresholds measured using the MOBS staircase procedure, stimuli were presented for 2-seconds. To avoid temporal transients at the onset and offset of the stimulus, the stimulus was presented within a cosine envelope to provide a gradual stimulus onset and offset. The 2-second presentation time was necessary to assure that the stimulus was presented at maximum contrast for a sufficient amount of time. The interstimulus interval averaged 1 second, and a 25% variation (0.75 to 1.25 second) was introduced to minimize the likelihood that patients would engage in rhythmic responses.

Subjects were instructed to press a response button each time they detected the striped stimulus pattern. Contrast was decreased each time a stimulus was detected, and it was increased each time a stimulus was not detected. Essentially, the MOBS procedure is a staircase test strategy with decision rules that allow it to recover quickly from response errors; it usually provides more robust threshold estimates than conventional staircases. The major differences between the MOBS procedure and conventional staircases are the decision rules governing the step size of stimulus increments and decrements for successive trials and the criteria for exiting the staircase. In addition to a criterion number of staircase reversals, MOBS requires that the upper and lower boundaries of recent presentations be within a specified range. In the current study, the MOBS criteria for staircase completion consisted of at least four staircase reversals as well as upper and lower boundaries that were within 0.3 log units (3 dB) of each other. Details of the MOBS procedure have been published. Threshold was defined as the mean of the last four staircase reversals. Typically, six to seven stimulus presentations were needed to obtain a threshold estimate with the MOBS procedure.
FIGURE 8. Another example of good correspondence between Humphrey Field Analyzer (HFA) results (left) and frequency-doubled contrast thresholds (right). The HFA results show deficits in both the superior and the inferior nasal visual field. The contrast thresholds for frequency-doubled stimuli are elevated beyond normal limits for the superior and inferior quadrants but are within normal limits for the superior and inferior temporal quadrants.

For each presentation, the specific stimulus pattern was selected randomly. Three different groups of stimulus patterns were used. The first group consisted of the original patterns used by Maddess and colleagues: whole central field stimulation (17.5° radius), a central 5° radius stimulus, and the superior and inferior hemifields minus the central 5° radius (Fig. 3a). The second group consisted of the central 5° radius stimulus and four quadrant stimulus patterns minus the central 5° region (Fig. 3b). To examine the efficacy of using smaller, localized targets, a subset of patients and normal control subjects was tested with 16 targets (four per quadrant, 8° squares) compared to quadrant stimuli. In addition, the field of view was expanded to 40° × 40° to provide better capability of detecting peripheral nasal steps. One of the quadrants divided into four smaller targets is presented schematically in Figure 3c.

Data were analyzed according to a stepwise multivariate logistic regression model (STATA [College Station, TX] statistical software) that used the contrast threshold values for each of the stimulus patterns. Results of the logistic regression analyses were used to generate receiver operating characteristic (ROC) curves and sensitivity–specificity values to compare the performance of the two psychophysical methods and the three stimulus pattern arrangements. As a cross-check of the logistic regression results, a CART (Classification and Regression Tree) analysis of the data also was performed. As input variables to the logistic regression and CART procedures, we used specific hemifield and quadrant and 16 localized threshold values. We also computed the maximum of four quadrant values plus the central stimulus value, as well as the maximum average of adjacent pairs for the 16 targets plus the central stimulus value for these two stimulus configurations.

RESULTS

Test–retest (within-subject) variability for the MOA and the MOBS procedures are presented in Figure 4 for age-matched normal control subjects and for patients with glaucoma observing the whole 17.5° radius central field, the central 5° radius target, the superior hemifield, and the inferior hemifield stimulus patterns. For normal control subjects, the test–retest consistency was two to four times better for the MOBS procedure than for the MOA procedure. A similar, but less dramatic, difference in test–retest consistency for MOBS versus MOA procedures appeared for patients with glaucoma. The MOBS procedure demonstrated an average test–retest difference of 2% to 3% (95% confidence interval, 0% to 11%) for contrast thresholds in normal control subjects and an average test–retest difference of 6% to 10% (95% confidence interval, 0% to 20%) for contrast thresholds in patients with glaucoma.
Between-subjects variability is shown in Figure 5 for the MOA and MOBS procedures observed for the whole central field, the central 5° radius, and the superior hemifield and inferior hemifield stimulus patterns. The left graph depicts the results for age-matched normal control subjects, and the right graph depicts the results for patients with glaucoma. The variation in contrast threshold measures among normal control subjects is approximately three to four times smaller for the MOBS test strategy than for the HFA visual field results show an early superior nasal step. Frequency-doubled contrast thresholds are within normal limits for the superior temporal, inferior temporal, and inferior nasal quadrants but are elevated beyond normal limits for the superior nasal quadrant.

FIGURE 9. A third example of good correspondence between Humphrey Field Analyzer (HFA) results (left) and frequency-doubled contrast thresholds (left). The HFA visual field results show an early superior nasal step. Frequency-doubled contrast thresholds are within normal limits for the superior temporal, inferior temporal, and inferior nasal quadrants but are elevated beyond normal limits for the superior nasal quadrant.

FIGURE 10. An example of early glaucomatous visual field loss detected by the Humphrey Field Analyzer (HFA, left) that was not detected with frequency-doubled contrast thresholds (right). The HFA results show a superior nasal step at approximately 25° and subtle inferior arcuate nerve fiber bundle loss. Frequency-doubled contrast thresholds approach the upper 95% confidence limits for the inferior quadrants but are within normal limits.
MOA procedure. Overall, the variability among patients with glaucoma was greater for both procedures. This was to be expected because the patients with glaucoma were selected as a heterogeneous population with early, moderate, and advanced glaucomatous visual field loss. The MOBS strategy appears to demonstrate slightly smaller variability among patients with glaucoma than does the MOA procedure.

Figure 6A presents the ROC curves for the MOA strategy with hemifield targets and the MOBS strategy with hemifield targets. The ROC curves were generated from a stepwise multivariate logistic regression analysis that used the threshold values for each of the stimulus patterns and their squared terms (to examine nonlinear components). The MOBS procedure, in addition to exhibiting lower within- and between-subjects variability than the MOA, also demonstrated better performance in terms of separating the results of eyes with glaucomatous visual field loss from the results of eyes from those of normal control subjects. Areas under the ROC curves were 0.71 for the MOA strategy using hemifield stimuli and 0.81 for the MOBS strategy using hemifield stimuli. At a specificity of 85% on the ROC curve, the corresponding sensitivities are approximately 38% for the MOA strategy with hemifield stimuli and 65% for the MOBS strategy with hemifield stimuli.

Figure 6B presents the ROC curves for the MOBS test strategy using hemifield and quadrant stimuli. Areas under the ROC curve were 0.81 for hemifield and 0.91 for quadrant stimuli. Using 85% specificity as a comparison reference, corresponding sensitivities were 65% for the hemifield stimuli and approximately 83% for the quadrant stimuli. Similar results were obtained using the CART analysis. Both logistic regression and CART analyses produced similar results for individual contrast values and for the maximum of the four quadrants plus the center, reflecting that the differences between patients and age-matched controls were robust to the selection of specific variables to include in the multivariate analysis procedures. Additional cross-validation of the logistic regression model was conducted for the MOBS procedure and quadrant stimuli by using the results of the study eye for the second visit rather than the first visit and by using the results of the second visit for the fellow eye. Areas under the ROC curves were slightly lower than for the original model (0.85 for the study eye during the second visit and 0.83 for the fellow eye during the second visit), but they still demonstrated the validity of the logistic regression model that incorporated contrast thresholds from the four quadrants. With the MOBS strategy and the quadrant stimulus pattern, all incidences of advanced glaucomatous visual field loss and all but one incidence of moderate glaucomatous visual field loss were outside the entire range of normal values for one or more quadrants. Thus, nearly all the false-negative results (glaucoma misclassifications) concerned early visual field loss.

Examples of good correspondence between Humphrey visual field results and frequency-doubling contrast thresholds are presented in Figures 7 to 9. The first example in Figure 7 shows a superior arcuate nerve fiber bundle defect on the HFA gray scale and probability plots (left graphs), with the major deficit residing in the superior nasal quadrant. The right graphs show the contrast thresholds obtained for the frequency-doubled stimuli in each quadrant. Horizontal lines depict the upper 95% confidence limit for contrast thresholds obtained for age-matched normal control subjects. Contrast thresholds are within normal limits for the superior temporal, inferior nasal, and inferior temporal quadrants but are significantly elevated for the superior nasal quadrant.

Figure 8 shows another example of good correspondence between frequency-doubling contrast thresholds and HFA results. In this example, HFA results indicate deficits in the superior and the inferior nasal visual field regions. Frequency-doubled contrast thresholds are elevated in the superior and the inferior nasal quadrants but are within normal limits for the temporal quadrants.

A third example of good correspondence between frequency-doubling contrast thresholds and HFA results is presented in Figure 9. The HFA results show an early superior nasal step. The frequency-doubled contrast threshold is beyond normal limits for the superior nasal quadrant and is within normal limits for the other three quadrants.

Figure 10 presents an example of early glaucoma...
tous visual field loss undetected by the frequency-doubling contrast test. In this example, the HFA results indicate a superior nasal step beyond 25° eccentricity, along with some subtle losses within the inferior arcuate nerve fiber bundle area. Although they approach the normal limits for the inferior quadrants, frequency-doubled contrast thresholds are all within normal limits. The most likely explanation for the failure of the frequency-doubled quadrant stimuli to detect an abnormality is that the targets were too large to detect small, localized deficits.

To determine whether the use of smaller, more localized stimuli and an expanded field of view would provide better performance, 15 normal control subjects and 15 patients with glaucoma were retested with the four quadrant stimuli and with the 16 smaller targets (four per quadrant). Only patients with early or moderate glaucomatous visual field loss were included in this sample. Seven of the 15 patients with glaucoma were selected because their previous results for quadrant stimuli were within or near the limits of the normal population. The other eight patients were selected randomly from the remaining pool of patients with early and moderate glaucomatous visual field loss. Similarly, the seven normal control subjects with the worst results for quadrant stimulus determinations were selected, along with eight other normal subjects selected to provide adequate age matching of the two groups. This was done to provide a challenging sample and a more rigorous test for this screening procedure.

As in the earlier studies, normal control subjects and patients with glaucoma were age matched, and the average age difference was <1 year.

Receiver operating characteristic results that were based on stepwise logistic regression analyses performed for the quadrant stimuli and the 16 targets are presented in Figure 11. The area under the ROC curve for the four quadrant stimuli was 0.85 (sensitivity, 73%; specificity, 93%), which was slightly worse than that obtained earlier for a combination of early, moderate, and advanced glaucomatous visual field loss. The area under the ROC curve was 0.965 for the 16 targets (sensitivity, 93%; specificity, 100%). Only one incidence of early glaucomatous field loss was misclassified. Figure 12 depicts an example of improved detection performance using the 16 stimulus patterns compared to the quadrant patterns. Test-retest measures for the 16-target display were obtained on a limited sample of patients with glaucoma and normal controls, and the results were essentially similar to those reported in Figure 4 for the MOBS procedure.

The average test time for the frequency-doubled contrast test was 2 minutes 42 seconds for the MOA procedure using hemifield test patterns, 1 minute 20 seconds for the MOBS procedure using hemifield patterns, 1 minute 30 seconds for the MOBS procedure using the quadrant stimulus patterns, and 5 minutes 14 seconds for the MOBS procedure using the 16 localized stimulus patterns. There were no meaningful
differences in test times for the normal control subjects and the patients with glaucoma for any of the test procedures. Thus, these test times reflect the average duration for all participants.

DISCUSSION

Numerous methods for rapid, efficient screening for glaucomatous visual field loss have been evaluated in recent years.56–47 With the exception of the Henson visual field screener, which has been reported to be a rapid test with good sensitivity and specificity,46,47 these procedures generally require either large amounts of time for testing or extensive dark adaptation time before testing, or they have poor performance characteristics. In this view, there is still a need for a rapid and effective method of screening for glaucomatous visual field loss. The results of the current investigation suggest that the frequency-doubled contrast threshold test procedure has a theoretical and an empirical basis for providing an effective screening tool for detecting glaucomatous visual field loss. Test times were considerably shorter than those required for conventional automated perimetry. By using suprathreshold static test procedures rather than threshold measures, it should be possible to have a 16-target pattern screening procedure for frequency-doubling testing that requires approximately 1 minute per eye.

Our findings are in agreement with the previous investigations by Maddess and colleagues8,9 to the extent that frequency-doubling contrast thresholds appear to be able to detect glaucomatous visual field loss. However, our results indicate that the method of adjustment for threshold determinations, as originally used by Maddess et al,8,9 produces large test–retest variation, even when the mean of several threshold determinations is used as the threshold measure. In the current study, the MOBS test strategy demonstrated better performance than the MOA procedure in separating patients with glaucoma from normal age-matched control subjects. In addition, the MOBS procedure demonstrated markedly better test–retest reliability within subjects and also had lower between-subjects variability.

In addition, the original patterns used by Maddess et al appear to be too large for effective detection of early, subtle glaucomatous visual field loss. The use of smaller stimuli, which produced more localized target presentation patterns, also improved the performance of the frequency-doubled contrast test. At present, this test procedure with the 16-target pattern, demonstrates sensitivity and specificity properties comparable to the previously reported screening capabilities of quantitative automated perimetry.98 Our findings indicated a sensitivity of 93% and a specificity of 100% for the 16-target pattern. Using the Humphrey visual field indices, similar performance results were obtained for a logistic regression model for MD (area under ROC, 0.985; sensitivity, 97%; specificity, 94%) and CPSD (area under ROC, 0.99; sensitivity, 97%; specificity, 97%). However, it should be kept in mind that this comparison may be inappropriate because MD and CPSD were used as eligibility criteria and as a means of classifying patients with glaucoma. Because subjects were selected on the basis of their Humphrey visual field indices, their performance will necessarily be equal to or better than an analysis based on other measures. Despite this caveat, the frequency-doubling perimetry results for the 16 target display compares favorably with conventional automated perimetry indices as a basis for distinguishing patients with glaucomatous visual field loss from normals.

The use of optimized test strategies and more sophisticated analysis procedures and the development of a large, normative database should improve the usefulness of frequency-doubling perimetry as a screening test for glaucomatous visual field loss.

Key Words

contrast sensitivity, frequency-doubling perimetry, glaucoma, screening, visual fields

Acknowledgments

The authors thank Kimberly Cello, Jacqueline Nelson-Quigg, and Vickie Jaicheun for their assistance in scheduling and testing subjects in this study. They also thank Drs. Daniel Rich and Thomas Kidwell for providing patients and normal control subjects for this investigation and Drs. Richard Nguyen, Jane Galustian, and Jeffrey Caspar for their assistance in performing clinical examinations of the normal control subjects.

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