

Comparison of Frequency Doubling Perimetry With Humphrey Visual Field Analysis in a Glaucoma Practice

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- **PURPOSE:** To determine the sensitivity and specificity of frequency doubling perimetry with Humphrey visual field testing used as the gold standard.
- **METHODS:** Frequency doubling perimetry and Humphrey visual field testing (24-2) were performed on 29 consecutive patients in a glaucoma practice. Data for the right eye were used to calculate sensitivity, specificity, and receiver operating characteristic curves.
- **RESULTS:** For the frequency doubling perimetry in screening mode, and with an abnormal glaucoma hemifield test used as the gold standard, the area under the

See also pp. 314–322, 323–327, and 376–378.

receiver operating characteristic curve was 89.3%, 81.5%, or 75.0% for the presence of mild, moderate, or severe relative defects, respectively. Similar results were found with the use of mean deviation ($P < .05$) to define Humphrey visual field defects. For frequency doubling perimetry in threshold mode, the area under the receiver operating characteristic curve was 93.4% with the presence of any defect ($P < .05$) used as the criterion for an abnormal case, and an abnormal glaucoma hemifield test as the gold standard. In all cases, the threshold mode detected defects better than the screening mode.

- **CONCLUSIONS:** Frequency doubling perimetry showed a high sensitivity and specificity for detecting visual field abnormalities, especially when threshold strategies were used. (Am J Ophthalmol 2000;129:328–333. © 2000 by Elsevier Science Inc. All rights reserved.)

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GLAUCOMA HAS BEEN DEFINED AS “AN OPTIC NEUROPATHY characterized by a specific pattern of optic nerve head and visual field damage.”¹ Humphrey automated visual fields have become an accepted standard of measuring visual field loss in glaucoma.² More recently, frequency doubling perimetry has been used to detect glaucomatous field loss,³ offering the potential advantages of better patient acceptance, portability, and less lengthy testing.

Frequency doubling illusion, the conceptual basis of frequency doubling perimetry, states that a sinusoidal grating of a low spatial frequency presented with a high temporal frequency (>15 Hz) will produce a perceived image that is twice its actual spatial frequency.⁴ The ability to perceive this illusion is a function of the magnocellular pathway, which in glaucoma appears to be damaged early in the disease.⁵ The apparent proclivity of the M cells for early death may represent true selective loss of these large-diameter nerve fibers or apparent selection of under-represented fibers for greater relative destruction. In either case, by testing for early glaucomatous field loss, frequency doubling perimetry theoretically offers the possibility of early detection of glaucoma with a relatively simple screening device.

The purpose of our study was to determine the sensitivity and specificity of frequency doubling perimetry for determining glaucomatous defects compared with Humphrey automated full-threshold 24-2 visual field testing.

METHODS

TWENTY-NINE CONSECUTIVE PATIENTS REFERRED TO OUR glaucoma practice were enrolled in this study. The patients first underwent frequency doubling perimetry (FDT Visual Field Instrument, Zeiss/Humphrey Systems, Dublin, California, and Welch Allyn, Skaneateles Falls, New York) in both the screening and threshold modes. Humphrey full-threshold 24-2 visual fields (Humphrey Field Analyzer,

TABLE 1. Area Under the ROC Curve (%) by Different Criteria for Abnormal Screening Test and Gold Standard

Screening Test (FDP Criteria)	Gold Standard (HVF Criteria)			
	GHT Abnormal or Borderline	GHT Abnormal	MD ($P < .05$)	PSD ($P < .05$)
FDP in screening mode				
Mild, moderate, or severe relative loss	90.6	89.3	81.3	61.9
FDP in threshold mode				
Defect of any severity ($P < .05$)*	89.0	93.7	95.1	80.6
Presence of defect ($P < .02$)*	89.6	94.5	95.8	81.9
Presence of defect ($P < .01$)*	89.6	95.5	94.8	79.4
Presence of defect ($P < .005$)*	88.6	95.0	94.2	74.2

FDP = frequency doubling perimetry; GHT = glaucoma hemifield test; HVF = Humphrey visual field; MD = mean deviation; PSD = pattern standard deviation; ROC = receiver operating characteristic.

* Probability less than the P value that a normal subject of the same age would perform at the threshold level achieved by the patient.

Zeiss/Humphrey Systems, Dublin, California) were also obtained for each eye.

Data for the right eye were used to calculate sensitivity, specificity, and receiver operating characteristic curves. Frequency doubling perimetry in threshold mode provides statistical global indices (mean deviation and pattern standard deviation) and probability levels, similar to the output provided by Humphrey visual field testing. In addition, with frequency doubling perimetry, a plot of the 17 visual field locations tested is produced for each eye separately. The plot has four possible levels of shading for each of the 17 locations. The absence of shading indicates that the person screened attained a threshold level that 95% ($P \geq .05$) of normal subjects of the same age achieved at that test location. The four levels of shading indicate that the probability is less than 5%, 2%, 1%, or 0.5% that a normal subject of the same age would achieve the threshold level attained by the patient. In the screening mode, a plot of 17 visual field locations is also produced for each eye separately. Three levels of shading indicate mild, moderate, and severe relative loss. The absence of shading indicates that the results are within normal limits.

Several definitions for an abnormal frequency doubling perimetry test were evaluated. For frequency doubling perimetry in screening mode, at least one shaded location on the plot was considered abnormal. For the threshold mode, an abnormal case was defined as $P < .05$ for mean deviation or pattern standard deviation, or at least one shaded location on the plot.

We also used several definitions for an abnormal Humphrey visual field. The glaucoma hemifield test included borderline cases as abnormal in one definition and as

normal in the other definition. In addition, $P < .05$ for mean deviation or pattern standard deviation was considered abnormal.

Receiver operating characteristic curves were generated for the number of defects observed with frequency doubling perimetry in screening and threshold modes, with the glaucoma hemifield test, mean deviation, and pattern standard deviation from Humphrey visual field testing used as the gold standard. However, only those receiver operating characteristic curves that used the glaucoma hemifield test as the gold standard are shown. Sensitivity and specificity were calculated for various cutoff points, with the receiver operating characteristic curves plotting sensitivity versus 1 minus specificity. Sensitivity is defined as the proportion of truly diseased persons who are identified as diseased by the screening test. Specificity is defined as the proportion of truly nondiseased persons who are identified as nondiseased by the screening test.

RESULTS

ALL PATIENTS CARRIED A DIAGNOSIS OF GLAUCOMA ($N = 20$) or glaucoma suspect ($n = 9$). Average age was 59 years, with a range of 11 to 85 years. The study sample was 72% African-American and 66% female. The number of glaucoma medications used by the patients studied ranged from zero to four.

For screening frequency doubling perimetry, testing required an average of 73 seconds. The shortest test was 46 seconds; the longest, 133 seconds. Average times were

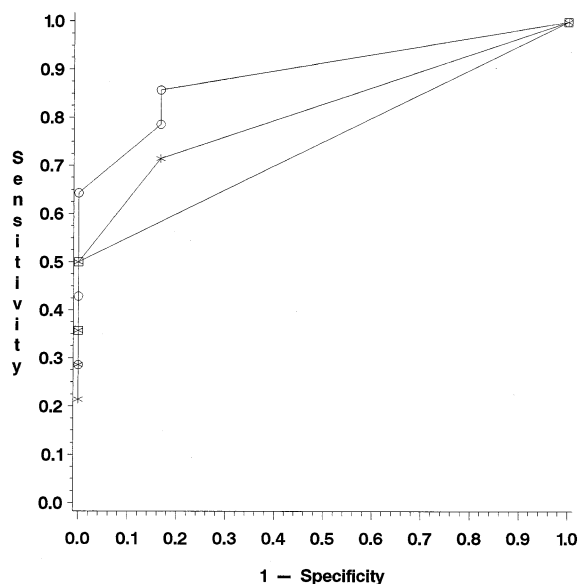


FIGURE 1. Receiver operating characteristic curves comparing mild (circles), moderate (asterisks), and severe (squares) relative defects for frequency doubling perimetry in screening mode with an abnormal glaucoma hemifield test used as the gold standard.

longer for threshold testing, with a mean of 292 seconds (range, 250 to 350 seconds).

Table 1 presents the area under the receiver operating characteristic curve with different criteria for an abnormal screening test (frequency doubling perimetry in screening and threshold mode) and different criteria for the gold standard (different definitions for Humphrey visual field testing). For frequency doubling perimetry in screening mode, and with an abnormal glaucoma hemifield test used as the gold standard, the area under the receiver operating characteristic curves was 89.3%, 81.5%, or 75.0% for the presence of mild, moderate, or severe relative defects, respectively. These receiver operating characteristic curves are shown in Figure 1. As the criterion for an abnormal result of frequency doubling perimetry in screening mode became more stringent, from requiring any defect to requiring severe defects to define an abnormal case, the area under the receiver operating characteristic curve decreased for all definitions of an abnormal Humphrey visual field. Likewise, with the use of an abnormal glaucoma hemifield test as the gold standard, sensitivity decreased from 85.7% to 50.0% and specificity increased from 83.3% to 100.0% when at least one defect of any severity was used as the criterion for abnormal frequency doubling perimetry compared with requiring a severe defect as the criterion (Table 2).

Similar results were found with the use of mean deviation ($P < .05$) to define Humphrey visual field defects. The area under the receiver operating characteristic curve was 81.3% with the presence of any defect used to define an

abnormal case on frequency doubling perimetry screening (Table 1), with sensitivity and specificity of 80% for a cutoff of at least one defect of any severity (Table 2). With the use of severe defects to define an abnormal frequency doubling perimetry screening, the area under the curve was 73.3% (Table 1), with a sensitivity of 46.7% and specificity of 100% for a single defect (Table 2).

For frequency doubling perimetry in threshold mode, the area under the receiver operating characteristic curve was 93.7% with the presence of any defect ($P < .05$) used as the criterion for an abnormal case, and an abnormal glaucoma hemifield test used as the gold standard (Table 1). The area under the receiver operating characteristic curve did not change significantly with more stringent criteria. Sensitivity and specificity for these criteria were 94.7% and 90.0%, respectively, for a cutoff of 10 abnormal locations (Table 2). With an abnormal glaucoma hemifield test used as the gold standard, a sensitivity of 100% and specificity of 90% were achieved with the presence of six defects at $P < .02$ and three defects at $P < .01$ (Table 2). Similar results were found with mean deviation used to define an abnormal Humphrey visual field.

Figures 2 through 4 compare the receiver operating characteristic curves for the frequency doubling perimetry in screening and threshold modes at different levels of defects, using an abnormal glaucoma hemifield test as the gold standard. In all cases, the threshold mode did better than the screening mode in detecting defects.

With the use of mean deviation to define an abnormal examination for both frequency doubling perimetry in threshold mode and Humphrey visual field testing, sensitivity was 95.5% and specificity 85.7%. For pattern standard deviation, sensitivity and specificity were 75.0% and 55.6%, respectively (results not shown).

DISCUSSION

THE RESULTS OF THIS STUDY SHOWED SENSITIVITY AND specificity to be greatest (100%, 90%) when the presence of three or more defects with $P < .01$, or six or more defects with $P < .02$, was used on threshold frequency doubling perimetry, with an abnormal glaucoma hemifield test used as the gold standard. For the screening mode, sensitivity and specificity were not as high (85.7%, 83.3%) for any defect.

When pattern standard deviation ($P < .05$) was used as the criterion for defining an abnormal field for both frequency doubling perimetry and Humphrey visual field testing, sensitivity and specificity (75.0%, 55.6%) were not as high as those obtained with mean deviation ($P < .05$) for defining both abnormal frequency doubling perimetry and Humphrey visual field testing (95.5%, 85.7%).

What accounts for the similarity of frequency doubling perimetry and Humphrey visual field testing for mean deviation, but not for pattern standard deviation? Recall

TABLE 2. Sensitivity and Specificity for Selected Criteria for FDP and HVF

Screening Criterion (FDP)	Gold Standard (HVF)	Sensitivity (%)	Specificity (%)	No. of Defects
FDP in screening mode (relative loss)				
Mild, moderate, or severe	GHT borderline	81.3	100.0	1
	GHT abnormal	85.7	83.3	1
	MD (<i>P</i> < .05)	80.0	80.0	1
	PSD (<i>P</i> < .05)	78.6	66.7	1
Moderate or severe	GHT borderline	68.8	100.0	1
	GHT abnormal	71.4	83.3	1
	MD (<i>P</i> < .05)	66.7	80.0	1
	PSD (<i>P</i> < .05)	64.3	66.7	1
Severe	GHT borderline	43.8	100.0	1
	GHT abnormal	50.0	100.0	1
	MD (<i>P</i> < .05)	46.7	100.0	1
	PSD (<i>P</i> < .05)	21.4	100.0	3
FDP in threshold mode				
Defect of any severity (<i>P</i> < .05)	GHT borderline	95.5	85.7	9
	GHT abnormal	94.7	90.0	10
	MD (<i>P</i> < .05)	95.5	85.7	9
	PSD (<i>P</i> < .05)	100.0	77.8	9
Presence of defect (<i>P</i> < .02)	GHT borderline	95.5	85.7	4
	GHT abnormal	100.0	90.0	6
	MD (<i>P</i> < .05)	81.8	100.0	8
	PSD (<i>P</i> < .05)	100.0	77.7	4
Presence of defect (<i>P</i> < .01)	GHT borderline	86.4	86.4	3
	GHT abnormal	100.0	90.0	3
	MD (<i>P</i> < .05)	81.8	100.0	4
	PSD (<i>P</i> < .05)	90.0	77.8	3
Presence of defect (<i>P</i> < .005)	GHT borderline	68.2	100.0	3
	GHT abnormal	89.5	90.0	2
	MD (<i>P</i> < .05)	81.8	100.0	2
	PSD (<i>P</i> < .05)	80.0	77.8	2

FDP = frequency doubling perimetry; HVF = Humphrey visual field; GHT = glaucoma hemifield test; MD = mean deviation; PSD = pattern standard deviation.

that mean deviation is a statistical expression of the deviation of the threshold stimulus intensity at each point within the visual field compared with age-matched control subjects.⁶ The presence of glaucoma alters the mean deviation, the significance of which is dependent on the extent of depression of retinal sensitivity compared with that in patients without disease. Depression of retinal sensitivity in turn is the functional correlate of the structural changes that occur in glaucoma, namely the loss of retinal ganglion cells at the axonal level evidenced with Humphrey visual field testing⁷ and selective loss of M cells with frequency doubling perimetry.³ Therefore, in the presence of structural damage from glaucoma, one would expect to see a greater mean deviation for both frequency doubling perimetry and Humphrey visual field testing. The deviation would be similar in both tests because the baseline population shows high retinal sensitivity no matter which stimulus is used for testing.

Pattern standard deviation is the relative retinal sensi-

tivity of each point within a visual field of a given eye.⁶ One cannot assume that the “hill of vision” is identical for qualitatively different stimuli because the distribution of different types of cells is not identical within the retina. Patterns of loss in disease may also differ. Accordingly, pattern standard deviation would differ significantly depending on the type of stimulus used for testing, resulting in poorer sensitivity and specificity when two different visual field tests are compared.

Of note, Yamagishi and associates⁸ observed that damaged field zones on short-wave automated perimetry were topographically related to damaged rim sectors on confocal scanning laser ophthalmoscopy in a sample of 14 patients with open-angle glaucoma. Additionally, Weber and associates⁹ noted a topographic relationship between depressed visual field zones on achromatic visual fields and localized loss of rim sectors. These findings suggest that focal loss of neuroretinal rim corresponds to achromatic visual field loss, the functional correlate of a nerve fiber layer defect, as

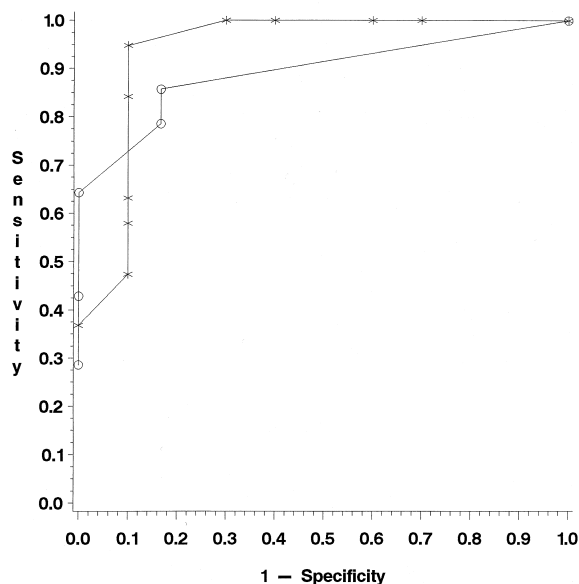


FIGURE 2. Receiver operating characteristic curves comparing mild relative defects in frequency doubling perimetry screening mode (circles) and mild defects ($P < .05$) in frequency doubling perimetry threshold mode (asterisks), with an abnormal glaucoma hemifield test used as the gold standard.

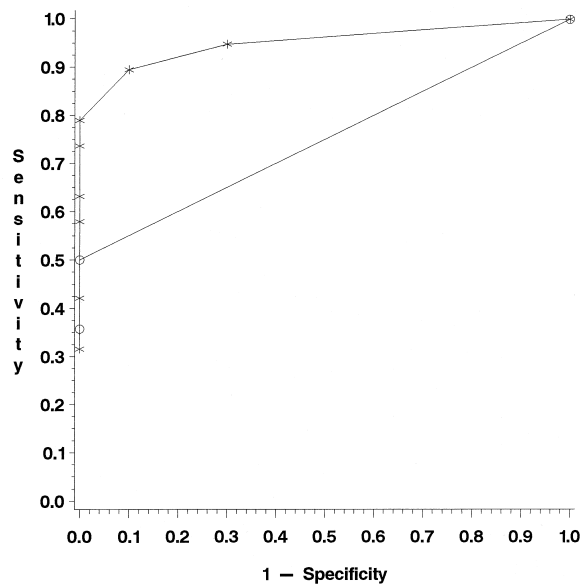


FIGURE 4. Receiver operating characteristic curves comparing severe relative defects in frequency doubling perimetry screening mode (circles) and severe defects ($P < .005$) in frequency doubling perimetry threshold mode (asterisks), with an abnormal glaucoma hemifield test used as the gold standard.

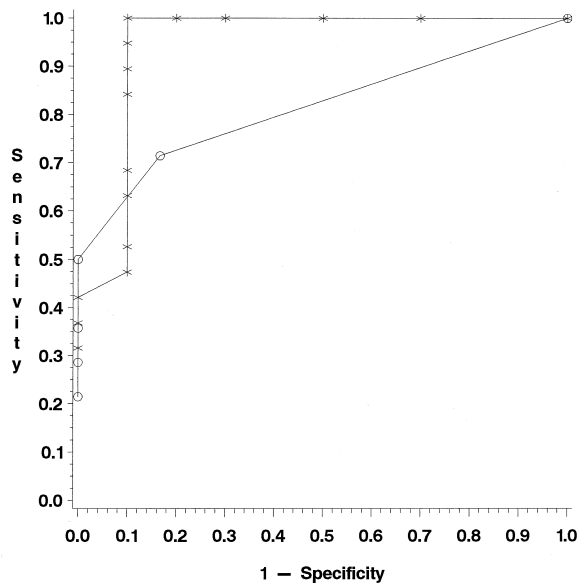


FIGURE 3. Receiver operating characteristic curves comparing moderate relative defects in frequency doubling perimetry screening mode (circles) and moderate defects ($P < .02$) in frequency doubling perimetry threshold mode (asterisks) with an abnormal glaucoma hemifield test used as the gold standard.

well as defects on short-wave automated perimetry, the functional correlate of loss of retinal ganglion cells of the parvocellular pathway.

In a comparison of short-wave automated perimetry and

motion automated perimetry, Sample and associates¹⁰ demonstrated overlap for defective locations in only 21% of 14 eyes that had a diagnosis of glaucoma suspect. Correlation was much stronger (94% overlap) in eyes with a diagnosis of glaucoma. This discrepancy raises the possibility that in the early stages of glaucoma, the location of selective loss of retinal ganglion cells in the magnocellular pathway differs from the location of loss of cells in the parvocellular pathway, which corresponds to achromatic visual field defects in more advanced stages of glaucoma.

Our findings of poorer sensitivity and specificity when we used pattern standard deviation to compare frequency doubling perimetry and Humphrey visual field testing in a population with various degrees of severity of disease are consistent with the relative lack of correlation between tests of diffuse nerve fiber layer loss and damage to the magnocellular pathway in early glaucoma.

Frequency doubling perimetry in the threshold mode performed slightly better than in the screening mode. Frequency doubling perimetry does not provide mean deviation or pattern standard deviation for the screening strategy. Thus, our analysis was limited to the presence and number of defects with suprathreshold testing.

Our findings confirm those of Johnson and Samuels,³ who found high sensitivity (100%) and specificity (96.5%) for frequency doubling perimetry threshold testing compared with severity of visual field defects. In their study, the area under the receiver operating characteristic curve was 93%. In addition, Sponsel and associates¹¹ showed a strong linear correlation of mean deviation and corrected

pattern standard deviation between frequency doubling perimetry threshold and Humphrey visual fields.

In our experience, threshold testing performed better than the screening test. Our findings differed from those of a recent study by Quigley,¹² who showed higher sensitivity and specificity with frequency doubling perimetry screening. In the study by Quigley, all patients had experience in visual field test taking. Such was not the case in our patients, many of whom underwent visual field testing for the first time. It is possible that their inexperience accounts for the relatively lower observed sensitivity and specificity observed in this study. Nevertheless, we have demonstrated that frequency doubling perimetry can be used successfully in detecting visual field defects in a series of patients referred to a glaucoma practice.

Frequency doubling perimetry offers many advantages over standard automated perimetry. It is simple to use, allowing lay personnel to be trained in its operation. The device is portable and the tests require very little time to administer. Because the test is highly sensitive and specific for the detection of glaucomatous visual field defects, it may prove highly valuable as a screening device for the detection of glaucoma.

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