

# Repeatability of the Glaucoma Hemifield Test in Automated Perimetry

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**Purpose.** To examine the concordance of the Glaucoma Hemifield Test and other global visual field indexes between two consecutive automated visual field tests.

**Methods.** Normal subjects, subjects with ocular hypertension, and subjects with glaucoma had two automated visual field tests on the Humphrey Field Analyzer. The Glaucoma Hemifield Test results, mean deviation, and corrected pattern standard deviation of the two consecutive visual field tests were compared.

**Results.** Forty-one normal subjects were tested within 1 and 2 years of each other. Four hundred seven subjects with ocular hypertension and 95 subjects with glaucoma were tested 1 year apart. The proportion of normal subjects who met a criterion for abnormality on two consecutive tests was 2.4%. The proportion of subjects with glaucoma with normal results of two tests was 10.5%. The specificity of automated visual field testing was improved from 80.8% to 89.9%, with a modest loss of sensitivity if two rather than one abnormal test result was required for entry into a clinical trial enrolling patients with glaucomatous field loss. Similarly, specificity increased from 84.2% to 89.5% if two normal tests were required for entry into an ocular hypertensive clinical trial. Among subjects with more closely spaced tests, the agreement between consecutive tests was similar for tests spaced 4 versus 12 months apart.

**Conclusions.** Although there is concordance of Glaucoma Hemifield Test results on consecutive testing, there is enough disagreement to result in improved specificity from the use of a second test in a clinical trial setting. *Invest Ophthalmol Vis Sci.* 1995;36:1658–1664.

The definition and diagnosis of glaucoma depends on visual field testing as a method of identifying and quantifying optic nerve damage. Several studies have used automated perimetry to estimate the variability of mean sensitivity and sensitivity at individual locations in the field over relatively short periods of time.<sup>1–8</sup>

These studies have found substantial variability, particularly among subjects with glaucoma and those at high risk for glaucoma. The magnitude of variability is important for defining limits beyond which true disease progression is thought to have occurred. However, researchers and clinicians often need to make

decisions about whether one or more visual fields are normal or abnormal to make treatment decisions or for regulating entry into clinical trials of treatments with the potential to slow the progression of field loss. However, the results of two or three tests may differ. This report examines the concordance of the results of two consecutive visual field tests using a commercially available algorithm, the Glaucoma Hemifield Test, that is widely available for classifying individual fields as normal or abnormal.<sup>9–11</sup> We selected the Glaucoma Hemifield Test because it is readily available on the visual field printout and has been shown to have comparable sensitivity and specificity to other algorithms in the classification of visual field tests as normal or glaucomatous.<sup>12</sup> We also examined the differences between the commercially available global visual field indexes of mean deviation (MD) and corrected pattern standard deviation (CPSD) of two consecutive visual field tests to provide information on the magnitude of fluctuations in these indexes from one test to another.

To examine the repeatability of the Glaucoma

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Hemifield Test for visual field classification, we have used data from a longitudinal glaucoma study in which the protocol required automated visual field testing at yearly intervals. The advantages of this data set are that subjects without disease were enrolled and that subjects with glaucoma were classified as such on the basis of a reproducible visual field defect on separately performed detailed static and kinetic perimetry. Hence, the specificity and the sensitivity of repeat automated field testing can be examined against another defined measure of visual field loss. The disadvantage of this data set is that the sensitivity and specificity may be an underestimate of what is attainable by testing closer in time. In a subset of subjects, we also had obtained testing at 4-month intervals with automated perimetry. Hence, these data provide some ability to examine whether sensitivity and specificity are reduced by increasing the time between testing. Most repeated visual field data available in the literature have been used to estimate the variability of threshold values at individual locations or areas of the field.<sup>1-8</sup> Two ongoing clinical trials of glaucoma treatment have reported their experiences with classification algorithms on repeat testing, one for purposes of establishing eligibility for entry into a trial,<sup>13</sup> and the other for identifying whether patients have demonstrated progression of visual field loss.<sup>14,15</sup> Neither study uses commercially available algorithms, and they do not have data on normal subjects or those with ocular hypertension who did not meet eligibility criteria for entry into the clinical trials. In this article, we examine the consistency of the Glaucoma Hemifield Test results in normal subjects, subjects with ocular hypertension, and subjects with glaucoma and estimate changes in sensitivity and specificity associated with the use of two rather than one visual field in the diagnosis of glaucoma or as entry criteria for clinical trials.

## METHODS

The Glaucoma Screening Study was a longitudinal study of early indicators of glaucomatous damage that enrolled and followed subjects from 1981 through 1992.<sup>16,17</sup> Detailed static and kinetic perimetry was performed by all subjects enrolled in the study. The protocol for this perimetry has been described elsewhere; it included testing with at least four test objects with two additional isopters tested in the nasal periphery, and many static presentations within isopter boundaries.<sup>12,16-18</sup> On all observed occasions (minimum of two measurements), normal subjects were shown to have intraocular pressures below 22 mm Hg by applanation tonometry, normal results of ophthalmic examination, and no reproducible visual field loss on detailed manual perimetry. Subjects with ocular hypertension had intraocular pressures above 21 mm Hg

on at least two occasions and no reproducible visual field loss on detailed static and kinetic perimetry. Subjects with glaucoma had intraocular pressures above 21 mm Hg on at least two occasions and reproducible visual field loss on manual static and kinetic perimetry. For glaucoma to be diagnosed, the same defect on manual perimetry had to be present on two fields administered within 3 months of each other. Visual field loss on manual static and kinetic perimetry was defined as one or more of the following: a nasal step at least 10° wide and present in at least two isopters; a paracentral scotoma at least 0.4 log units deep and 5° wide; central or temporal islands of remaining vision.

Subjects were enrolled over several years and underwent annual examination, including manual perimetry. In 1984, automated perimetry using the C-30-2 program of the Humphrey Field Analyzer was introduced into the study. By 1986, all subjects routinely underwent automated testing annually, and a subset in each diagnostic group underwent more frequent testing at 4-month intervals. The protocol for automated testing has been described elsewhere.<sup>18</sup> This included detailed monitoring of the test by technicians and remapping of the blind spot if more than one fixation loss occurred. The final two automated visual fields of all subjects enrolled in the Glaucoma Screening Study were selected for inclusion in this analysis. The protocol specified that all subjects be followed until the end of the study. Although loss to follow-up did occur, only 6.8% refused follow-up, and only a small proportion dropped out because of ocular or medical problems. Most dropouts were subjects who moved out of town, and some subjects died during the course of the 10-year study. Forty-one normal subjects had two fields tested between 1 and 2 years of each other. Of these, 14 were tested every 4 months. Four hundred seven subjects with ocular hypertension and 95 subjects with glaucoma had at least two automated visual field tests spaced 1 year apart, and 54 of the subjects with ocular hypertension and 22 of those with glaucoma were put on the more frequent testing schedule. Subjects who entered the study as subjects with ocular hypertension and were reclassified as having glaucomatous field loss are included as subjects with glaucoma if they had two consecutive automated fields after conversion to glaucoma. Hence, 68 (72%) of the subjects with glaucoma in this analysis represent early but well-documented visual field loss on manual perimetry. The left eye of each subject was selected for analysis. The age of each subject was calculated at the time of the first of the two visits.

The Glaucoma Hemifield Test was used to classify automated visual fields as normal or abnormal.<sup>10-12</sup> The Glaucoma Hemifield Test classifies fields as "within normal limits," "borderline," "outside normal limits," "abnormally high sensitivity," "general-

ized reduction in sensitivity," and "borderline/generalized reduction in sensitivity." Fields with abnormally high sensitivity or borderline fields were classified as normal. Fields with generalized reduction in sensitivity (including those with the borderline designation) were classified as abnormal. This was done because the "borderline" classification indicates a small upper-lower hemifield difference, whereas the "generalized reduction in sensitivity" indicates a diffuse loss of sensitivity across the entire field. We wanted to include "generalized reduction in sensitivity" in the abnormal classification, regardless of whether there was a small upper-lower differential. The percent with abnormally high sensitivity ranged between 0% and 3%, depending on whether it was the first or the second test and on the diagnostic grouping. The percent with generalized reduction in sensitivity was similar. The MD and CPSD also were compared between the two tests. The MD provides a measure of diffuse field loss and CPSD of more localized damage.<sup>19-21</sup> Agreement between fields was estimated using the percent agreement and the kappa statistic, which adjusts the percent agreement for chance concordance.<sup>22</sup>

The tenets of the Declaration of Helsinki were followed with regard to study subjects. The study was approved by the Joint Committee on Clinical Investigations of the Johns Hopkins University School of Medicine, and informed consent was obtained from each subject before enrollment in the study.

## RESULTS

The mean ages of normal subjects, subjects with ocular hypertension, and subjects with glaucoma were  $57.0 \pm 13.6$  years (range, 24 to 86 years),  $59.2 \pm 13.3$  years (range, 21 to 92 years), and  $65.1 \pm 11.9$  years (range, 34 to 86 years), respectively. The subjects with glaucoma were older than the subjects with ocular hypertension or normal subjects, and the difference was statistically significant ( $P < 0.05$ ). Eighty-five percent of normal subjects were given both tests spaced 1 year apart. The remaining subjects were given tests spaced 2 years apart. All subjects had experience with manual perimetry before automated testing. The mean number of automated tests before those used here was 3.5, 3.1, and 3.7 for normal subjects, subjects with ocular hypertension, and subjects with glaucoma, respectively. The percent of subjects who had not performed automated visual field testing previously was 7.3%, 7.3%, and 3.2% for normal subjects, subjects with ocular hypertension, and subjects with glaucoma, respectively.

The patients with glaucoma represented a range of severity of visual field loss, although the majority had mild to moderate loss on the first test. The mean MD was  $-8.40$  (95% confidence interval:  $-9.86$  to

$-6.94$ ), and the mean CPSD was 6.83 (95% confidence interval: 6.14 to 7.52). Twenty-five percent had MD below  $-13.52$ , and 25% had a CPSD greater than 9.24. The mean MD for normal subjects and subjects with ocular hypertension was  $-0.33$  (95% confidence interval:  $-1.07$  to 0.40) and  $-0.84$  (95% confidence interval:  $-1.16$  to  $-0.52$ ), respectively. The mean CPSD for normal subjects and subjects with ocular hypertension was 1.94 (95% confidence interval: 1.35 to 2.53) and 2.17 (95% confidence interval: 1.98 to 2.36), respectively. The MD and CPSD values for normal subjects and subjects with ocular hypertension are well within what are considered normal values.

Among normal subjects, the proportion with two abnormal automated visual fields was 2.4% (Table 1). Based on the clusters of locations used in the cross-meridional method,<sup>23,24</sup> one subject had a defect that was in the same location on both visual field tests. The proportion of subjects with glaucoma who had abnormal results on two Glaucoma Hemifield Tests was 80.0%. Ninety-six percent of these had at least one defect in the same location on both tests. The proportion of subjects with glaucoma with two consecutive normal fields was 10.5%. Tests spaced 1 year apart revealed that among subjects with ocular hypertension, 69.8% had two normal automated fields and 10.1% had two abnormal automated fields. In each of these subjects with ocular hypertension, results of detailed manual testing was normal. The percent agreement was 82.9% for normal subjects, 79.9% for subjects with ocular hypertension, and 90.5% for subjects with glaucoma. Each corresponding kappa statistic was lower than the percent agreement, with subjects with glaucoma having the highest kappa of 0.63, denoting moderate agreement between tests after adjustment for chance agreement.<sup>22</sup>

The average difference in MD between the first and second fields was 0.5 dB ( $P = 0.28$ ) for normal subjects,  $-0.5$  dB ( $P < 0.001$ ) for subjects with ocular hypertension, and  $-1.0$  dB ( $P < 0.01$ ) for subjects with glaucoma. The difference in CPSD between first and second fields was  $-0.1$  for normal subjects, 0.1 for subjects with ocular hypertension, and 0.4 for subjects with glaucoma. None of the differences in CPSD were statistically significant. The 5th percentile for a change in MD among normal subjects was  $-3.68$  dB. Ten percent of subjects with glaucoma and 20% of subjects with ocular hypertension had changes of this magnitude or greater in a 1-year period. The 5th percentile for a change in CPSD among normal subjects was  $-3.38$  dB. The percent of subjects with ocular hypertension and subjects with glaucoma with this magnitude of change was 5.1% and 5.2%, respectively. This is what would be expected if there were no shift in the distribution of CPSD from one test to another. These data suggest that there was some worsening of

TABLE 1. Agreement Between Glaucoma Hemifield Test Results and Global Index Changes Between Two Consecutive Visual Field Tests

First Test	Second Test	Normal (n = 41)		Ocular Hypertension (n = 407)		Glaucoma (n = 95)	
		n	(%)	n	(%)	n	(%)
Normal*	Normal	33	(80.5)	284	(69.8)	10	(10.5)
Normal	Abnormal	3	(7.3)	45	(11.1)	5	(5.3)
Abnormal	Normal	4	(9.8)	37	(9.1)	4	(4.2)
Abnormal	Abnormal	1	(2.4)	41	(10.1)	76	(80.0)
Percent agreement		82.9		79.9		90.5	
Kappa		0.04		0.37		0.63	
95% confidence interval		-0.26, 0.52		0.26, 0.48		0.41, 0.85	
Change in mean deviation		0.5		-0.5		-1.0	
95% confidence interval		-0.2, 1.2		-0.7, -0.2		-1.6, -0.4	
Change in corrected pattern standard deviation		-0.1		0.1		0.4	
95% confidence interval		-0.7, 0.6		-0.1 to 0.3		-0.1, 0.8	

\* Borderline fields are classified as normal.

MD (either through a change in the average MD or a shift in the distribution) but not in CPSD over a 1-year period among subjects with ocular hypertension or glaucoma.

In the subset of subjects who underwent visual field testing at 4-month intervals, there was no evidence to suggest that percent agreement or kappas were larger for tests spaced 4 months apart compared to those spaced 12 months apart (Table 2). A statistically significant decline in MD was observed for subjects with glaucoma over 12 months (1.6 dB decline,  $P = 0.05$ ), but there was no such decline seen with the tests spaced 4 months apart. No other statistically significant differences between test results spaced 4 and 12 months apart were observed in this subset of subjects.

For purposes of assessing the usefulness of a second automated visual field test in the entry criteria for clinical trials, we have identified two types of trials requiring different eligibility criteria. One type of trial might enroll subjects with ocular hypertension but without visual field defects at entry into the study. In this case, the trial outcome is the incidence of field loss. In this trial, only subjects with ocular hypertension with normal results of two successive visual field tests within a specified time window would be enrolled. Another type of trial might enroll subjects with glaucoma in whom one of the defining features of disease is established visual field loss. In such a study, only those with two successive abnormal visual fields would be eligible for enrollment. In this case, progression of established visual field loss would be the outcome of interest. Such strategies increase the specificity of enrollment criteria relative to the use of only one test in the determination of eligibility. Table 3

gives the sensitivity and specificity associated with the use of one versus two tests as criteria for the ocular hypertension and glaucoma trials described above, using confirmed manual field loss as the "gold standard." Our study had a total of 502 subjects with ocular hypertension with and without confirmed visual field loss on manual perimetry (95 with field loss and 407 without loss). If these subjects were potentially eligible for an ocular hypertensive trial, 344 would have had normal results on the first test. Only those with normal results would be retested. Of these, 294 would have had normal results on a second test and would have been included in the trial. The sensitivity of this testing process would be 69.8% because 284 of the 407 subjects with ocular hypertension without manual field loss would have been included in the trial. The specificity would be 89.5% because 85 of 95 subjects with manual field loss would have been excluded from the trial. Hence, using the Glaucoma Hemifield Test, 10% of those with confirmed field loss on manual perimetry would be erroneously included in the trial because they had two normal automated visual fields. This strategy also would reject 30% of those without confirmed field loss on manual perimetry because they did not have two normal Humphrey visual fields.

For trials that enroll subjects with glaucomatous visual field loss on entry into the trial, the sensitivity would have been 80.0% and the specificity 89.9% if two tests were used to determine eligibility. Hence, 10% of subjects without visual field loss on manual perimetry would have been included in the trial because they had two abnormal visual fields, and 20% of subjects with confirmed field loss on manual perimetry would have been rejected from the trial because

TABLE 2. Differences in Agreement Between Visual Fields 4 and 12 Months Apart

First Test	Second Test	Normal (n = 14)		Ocular Hypertensive (n = 54)		Glaucoma (n = 22)	
		n	(%)	n	(%)	n	(%)
4 months apart							
Normal	Normal	11	(78.6)	37	(68.5)	1	(4.5)
Normal	Abnormal	2	(14.3)	0	(0.0)	1	(4.5)
Abnormal	Normal	1	(7.1)	4	(7.4)	2	(9.1)
Abnormal	Abnormal	0	(0.0)	13	(24.1)	18	(81.8)
Percent agreement		78.6		92.6		86.4	
Kappa		-0.11		0.82		0.33	
95% confidence interval		-0.25, 0.04		0.65, 0.99		-0.25, 0.91	
Change in mean deviation		-0.5		0.9		0.3	
95% confidence interval		-2.0, 1.0		0.1, 1.8		-0.7, 1.3	
Change in corrected pattern standard deviation		0.0		-0.1		0.3	
95% confidence interval		-0.6, 0.6		-0.7 to 0.6		-0.4, 1.1	
12 months apart							
Normal	Normal	11	(78.6)	35	(64.8)	2	(9.1)
Normal	Abnormal	1	(7.1)	3	(5.6)	0	(0.0)
Abnormal	Normal	1	(7.1)	6	(11.1)	2	(9.1)
Abnormal	Abnormal	1	(7.1)	10	(18.5)	18	(81.8)
Percent agreement		85.7		83.3		90.9	
Kappa		0.42		0.58		0.62	
95% confidence interval		-0.25, 1.00		0.33, 0.82		0.16, 1.00	
Change in mean deviation		-0.3		-0.1		-1.6	
95% confidence interval		-1.4, 0.8		-0.9, 0.6		-3.1, -0.1	
Change in corrected pattern standard deviation		-0.3		0.2		0.6	
95% confidence interval		-0.7, 0.1		-0.5 to 0.8		-0.4, 1.6	

they did not have two consecutive abnormal visual fields.

Seventeen percent of normal subjects, 16% of subjects with ocular hypertension, and 18% of subjects with glaucoma had two unreliable fields (false-negative or false-positive rate  $\geq 33\%$ , or fixation loss rate  $\geq 20\%$ ). The sensitivity and specificity using one or two tests was improved only marginally by excluding those with two unreliable test results. For example, the specificity for a glaucoma trial was 80.8% using one test and 89.9% using both tests. If those with two unreliable fields were excluded, the specificity was 82.9% using one test and 90.7% using both tests.

## DISCUSSION

To determine that subjects do not have visual field loss at the time of enrollment in a clinical trial, using two visual fields for eligibility would improve specificity at the cost of reduced sensitivity. If both fields were used, 10% of subjects with glaucomatous field loss on manual perimetry would be included, compared with 16% if only one test were used. A similar pattern would

be seen for enrollment of subjects with two abnormal visual fields. In a glaucoma trial, 10% of those without confirmed visual field loss on manual perimetry would be included in the trial because they had two consecutive abnormal Humphrey visual fields. It is important to note that these findings are based on an analysis of data from patients with mild to moderate visual field loss. This makes it most useful for examining the use of the Glaucoma Hemifield Test in the detection of incident field loss. These findings may not be true of trials in which patients should have moderate to severe loss at entry into the trial. These data also do not address the question of progression of visual field loss among patients who already have visual field defects.

Data from the Glaucoma Screening Study have demonstrated that visual field defects on automated perimetry preceded those on manual perimetry in subjects with ocular hypertension.<sup>25</sup> Hence, two abnormal automated fields in some of these subjects with ocular hypertension may be an indicator of early glaucomatous field loss rather than false-positive results, and the 89.9% specificity is likely an underestimate of the true specificity. In both types of trials, the empha-

**TABLE 3.** Sensitivity and Specificity of Single and Repeat Visual Field Testing Using the Glaucoma Hemifield Test to Classify Visual Field Test Results

	One Test		Two Tests					
			OH Trial			Glaucoma Trial		
	GFL	OH	GFL	OH	GFL	OH	GFL	OH
Normal	15	329	10	284	4	37	10	284
Abnormal	80	78	5	45	76	41	76	41
	95	407	15	329	80	78	158	502

  

	OH Trial		Glaucoma Trial	
	One Test	Two Tests	One Test	Two Tests
Sensitivity	80.8	69.8	84.2	80.0
Specificity	84.2	89.5	80.8	89.9

GFL = patients with glaucomatous field loss on manual kinetic perimetry; OH = patients with ocular hypertension with no defects on manual kinetic perimetry.

sis should be placed on maximizing specificity over sensitivity, except when sensitivity is so low that the majority of eligible persons would be rejected from entry into the trial.

Although visual field loss on automated perimetry has been shown to precede that detected on manual perimetry for a majority of patients by at least 1 year,<sup>25</sup> that study did find that 25% of subjects with confirmed defects on manual perimetry had a normal Glaucoma Hemifield Test 1 year before the identification of the defect on manual testing. This is slightly higher than the percent of patients with glaucoma (those with confirmed defects on manual perimetry) in the current analysis, who had one or two abnormal Glaucoma Hemifield Test results. Clearly, there are persons whose manual and automated visual field test results are variable, and confirmation of defects by repeat testing with manual perimetry does not guarantee that the defect is real or that it will be identified by automated testing.

The agreement between test results spaced 4 and 12 months apart was similar, although these data must be interpreted with some caution because of the small numbers of subjects with 4-month fields in the normal group and the group with glaucoma. When all groups are combined (90 subjects), the percent agreement was 89.0% at 4 months and 85.6% at 12 months. Kappas were 0.77 (0.63, 0.90) at 4 months and 0.70 (0.55, 0.85) at 12 months. Hence, the results for fields spaced 12 months apart are likely to be comparable with tests taken closer in time, as is often the case when determining eligibility for clinical trials.

There was no consistent evidence of change in the global indexes provided by the Humphrey Statpac over 1 year, except for a statistically significant decline

of 1 dB in MD among those with glaucoma and 0.5 dB among subjects with ocular hypertension. A decline of 1.6 dB in MD also was seen over a 1-year period in subjects with glaucoma who had more frequent testing, but no decline was evident when tests were taken 4 months apart in this group. Such diffuse changes may be caused by cataract in this older population (average age, 65 years) relative to subjects with ocular hypertension and normal subjects whose average ages were 59 and 57 years, respectively. These diffuse changes also may be caused by age-related loss of retinal neurons, but the relative contributions of these factors cannot be identified using these data. A larger proportion of subjects with ocular hypertension than those with glaucoma had a normal result followed by an abnormal result, though this difference was not statistically significant.

Threshold values at individual locations and global indexes have been found to have high variability on repeat testing, even with fields spaced relatively close in time.<sup>26</sup> The long-term fluctuations of mean deviation or mean threshold sensitivity among normal subjects ranged from 0.4 dB to 1.3 dB depending on the study population, type of field test, and length of time between fields.<sup>3,6,7,27-29</sup> Comparable fluctuations were larger for subjects with glaucoma.<sup>3,27</sup> The Advanced Glaucoma Intervention Study found a slight improvement in visual fields spaced between 1 and 6 weeks apart based on a visual field score that combined reliability criteria with the extent of clusters of depressed locations.<sup>13</sup> However, for purposes of classification into normal and abnormal, we found a high proportion of fields were similarly classified on two tests spaced between 1 and 2 years apart. In addition, for subjects with defects detected on both tests, the

locations of the defects were consistent from the first to the second test in the majority of subjects based on clusters of locations defined by the cross-meridional method of visual field classification.<sup>23,24</sup> Nevertheless, the disagreements between fields did lead to improved specificity, suggesting a benefit to repeat testing in clinical trial settings.

### Key Words

clinical trial, glaucoma, perimetry, sensitivity, specificity

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