Screening for Glaucoma With Frequency-Doubling Technology and Damato Campimetry

Noriko Yamada, MD; Philip P. Chen, MD; Richard P. Mills, MD; Martha M. Leen, MD; Marc F. Lieberman, MD; Robert L. Stamper, MD; Derek C. Stanford, MS

Objective: To assess frequency-doubling technology (FDT) perimetry (Humphrey Systems, San Leandro, Calif) and Damato campimetry (Precision Vision, Villa Park, Ill) for detecting glaucoma in a public glaucoma screening.

Methods: A 2-day public glaucoma screening was held at 2 different institutions. Each subject underwent 2 visual field screening tests (Damato campimetry and FDT perimetry in screening mode), an ophthalmologic examination, and Humphrey perimetry (24-2 FASTPAC) for each eye. Eyes were divided into 4 categories: normal, ocular hypertensive, glaucoma suspect, and definite glaucoma. The sensitivity and specificity of FDT perimetry and Damato campimetry for detecting glaucoma were estimated with receiver operating characteristic curves.

Results: Among 240 subjects who underwent FDT, the number identified as normal, ocular hypertensive, glaucoma suspect, and definite glaucoma was 151, 28, 35, and 26, respectively; among 175 subjects who underwent Damato campimetry, the numbers for the same groups were 118, 19, 19, and 19, respectively. The areas under the receiver operating characteristic curve for FDT perimetry and Damato campimetry were 0.925 and 0.883, respectively. The optimal sensitivity and specificity for FDT perimetry were 92% and 93%, while those for Damato campimetry were 53% and 90%, respectively. The average test time was 1 minute and 3 minutes per eye for FDT perimetry and Damato campimetry, respectively.

Conclusion: Frequency-doubling technology perimetry was superior to Damato campimetry in this screening for glaucoma.


GLAUCOMA is a leading cause of blindness in the world. By the year 2000, the number of people with primary glaucoma in the world will be nearly 67 million, with 6.7 million of them bilaterally blind. In the United States, an estimated 1.6 million persons aged 40 years or older have primary open angle glaucoma, but half of the glaucoma in the United States is undiagnosed. Since visual field loss from treated glaucoma does not generally progress rapidly, glaucoma screening should reduce blindness due to glaucoma by allowing earlier diagnosis and therapy.

Tonometry alone is inadequate for glaucoma screening. Recent studies have reported the use of perimetric methods in screening for glaucomatous visual field loss. Frequency-doubling technology (FDT) perimetry (Humphrey Systems, Dublin, Calif) and Damato campimetry (Precision Vision, Villa Park, Ill) are approved visual field screening devices for use in glaucoma screening projects sponsored by Prevent Blindness America. Frequency-doubling technology perimetry is intended to isolate a subset of mechanisms usually attributed to retinal ganglion cells in the magnocellular pathway, which may be preferentially affected in glaucoma. Maddess and Henry established that clinical testing based on the frequency-doubling illusion was a potentially useful screening procedure for glaucoma. Damato campimetry is an inexpensive visual field test device that relies on the subject’s eye movements to project a central black stimulus on a specific retinal eccentricity. This study assesses the efficacy and practical use of these 2 portable screening devices to detect visual field loss in a public glaucoma screening.

RESULTS

Of 259 subjects who volunteered for screening, 243 completed the screening ophthalmologic examination, and 240 completed Humphrey visual field testing.
PATIENTS AND METHODS

A publicly advertised glaucoma screening was held on 2 consecutive days at each of 2 different institutions: University of Washington Eye Center, Seattle; and California Pacific Medical Center, San Francisco. Advertisements in print and on the radio emphasized that the screening was free and that the latest technology would be available; the elderly, African Americans, and those with a family history of glaucoma were encouraged to participate. People of all ages were invited to participate, but not all tests were done on children and adolescents. The ophthalmologic history was obtained from each patient, and each eye underwent an ocular examination (best-corrected visual acuity, slitlamp examination, and undilated fundus examination) and Humphrey perimetric program testing (24-2 FASTPAC; Humphrey Systems). We elected to use this specific Humphrey perimetric program to save time, because of the limited number of Humphrey perimeters available. At the time of screening, other testing programs (ie, Swedish Interactive Testing Algorithm; Humphrey Instruments) had only recently been introduced and were clinically untried, and statistical programs to calculate mean deviation and pattern SD were unavailable from the manufacturer. Intraocular pressure (IOP) was measured with a handheld electronic tonometer (Tonopen; Mentor Inc, Norwell, Mass). For a small number of subjects, a dilated fundus examination was performed for adequate disc observation. Written informed consent included a disclaimer that the screening did not substitute for a complete ophthalmologic examination.

Humphrey visual fields were considered glaucomatous if they fulfilled criteria modified from Anderson:

1. at least 3 adjacent points (excluding the outermost rim) on the total deviation plot showing a significance level less than .05, which were also at least 5 dB below normal age-corrected values with at least 1 of those points at the $P<.01$ level; and
2. the qualifying defect was present in the nerve fiber bundle region (paracentral, nasal step, or arcuate defect).

Optic disc changes that were suggestive of glaucoma were defined as a cup-disc ratio of 0.6 or greater, cup-disc ratio asymmetry of 0.2 or greater, or typical glaucomatous disc damage such as a disc notch.

Glaucoma specialists (N.Y., P.P.C., R.P.M., M.F.L., and R.L.S.) who were masked to screening test results allocated each eye of each subject into 4 diagnostic categories, based on ophthalmologic history, examination, and Humphrey visual field results: normal, ocular hypertensive, glaucoma suspect (other than IOP related), and definite glaucoma. Eyes were considered normal if they had an IOP below 22 mm Hg and absence of glaucomatous visual field defects or optic disc changes. Eyes that were considered glaucomatous had evidence of glaucomatous optic nerve and visual field damage independent of the level of IOP. Eyes were considered ocular hypertensive if their IOP was higher than 21 mm Hg but there was no evidence of glaucomatous optic nerve or visual field changes. Eyes were considered glaucoma suspect if they had suspected optic nerve changes without glaucomatous field defects, independent of the IOP level.

Most screening subjects had never previously performed threshold perimetry. In 21 cases, when the visual field demonstrated equivocal defects or an unreliable test, we attempted to recall the subjects for a second threshold test. In 12 subjects, we used the second test as the basis for diagnostic allocation.

For subjects who had the same diagnosis bilaterally, 1 eye of the subject was selected randomly. If a different diagnostic category pertained to the 2 eyes, the worse eye was selected for the analysis. Subjects who had diabetes, a history of ocular or neurologic disease, or a history of eye surgery were excluded from analysis because of the potentially confounding variables.

(3 adolescents did not undergo Humphrey testing). The prevalence of glaucoma in this screening population was 10.7% (26 of 243 eyes). Not every subject underwent every test because of lapses in technician coverage, subject fatigue, or periodic large numbers of screenees.

Frequency-doubling technology perimetry was performed on 243 eyes, while Damato campimetry was performed on 178 of those eyes. The mean ± SD age of those who underwent FDT perimetry and Damato campimetry was 59.6 ± 14.7 and 58.8 ± 15.6 years, respectively. One hundred eight men and 135 women were screened, including 146 white, 70 Asian, 16 Hispanic, and 11 black subjects. Diseases other than glaucoma were diagnosed in 241 subjects, and these subjects were excluded from the data analysis. Of the remaining 240 subjects who underwent FDT perimetry, the number of subjects who were identified as normal, ocular hypertensive, glaucoma suspect, and definite glaucoma was 131, 28, 35, and 26, respectively. Of the 175 subjects who underwent Damato campimetry, the number of subjects who were identified as normal, ocular hypertensive, glaucoma suspect, and definite glaucoma was 118, 19, 19, and 19, respectively. For the determination of ROC curves and sensitivity and specificity, only the normal and definite glaucoma groups were studied.

The area under the ROC curve for the FDT grading method, FDT counting method, and Damato campimetry was 0.925, 0.924, and 0.883, respectively. Figure 1 shows the ROC curves for the FDT grading method and Damato campimetry. We considered the minimum acceptable specificity for a screening test to be 90%; therefore, the optimum sensitivity and specificity for the FDT grading and counting methods using a cutoff of 1 point were 92% and 93%, while those for Damato campimetry with a cutoff of 3 points were 53% and 90% (Table 1). A somewhat higher sensitivity (63%) could be obtained with Damato campimetry at the cost of specificity (83%) with a cutoff of 2 points.

Using the scoring systems previously described, differences between the mean scores of the subject groups were statistically significant between the normal and definite glaucoma, between the ocular hypertensive and definite glaucoma, and between the glaucoma suspect and definite glaucoma groups, using the FDT analysis methods and Damato campimetry (Table 2). In addition, the FDT scoring and FDT counting methods showed statistically significant differences between the normal and glaucoma suspect groups (Table 2).

Frequency-doubling technology perimetry detected at least 1 abnormal point in the visual field in 55 (22.9%)
PERIMETRIC DEVICES

Two visual field screening tests, FDT perimetry in screening mode and Damato campimetry, were performed on both eyes of each subject immediately after the test was explained to the subject. None of the screening subjects had undergone FDT perimetry or Damato campimetry previously. For FDT perimetry, a demonstration was shown to subjects on the monitor before starting the screen test. For Damato campimetry, a verbal explanation was provided.

We performed FDT in the screening mode, in which 25 Hz of counterphase flickering lights are given as supra-threshold stimuli in 17 regions of the central 20° of visual field, including 1 central test stimulus and 4 stimuli in each of 4 quadrants (superior-temporal, superior-nasal, inferior-temporal, and inferior-nasal). Results are printed in each of 17 visual field regions. The screening results are displayed with 4 qualitative loss classifications (“within normal limits,” “mild relative loss,” “moderate relative loss,” and “severe loss”) based on age-related normative references. Testing was performed in a dimly lit room.

We used 2 different methods for analyzing FDT results, grading and counting, to see which one provided better sensitivity and specificity. The grading method gave 0 points for within normal limits, 1 point for mild relative loss, 2 points for moderate relative loss, and 3 points for severe loss. The scores for the 17 visual field locations were summed, giving a possible range for the grading method from 0 to 51. The counting method summed the number of defective field regions without regard to the qualitative loss gradation, with a range of 0 to 17.

Damato campimetry consists of 20 numbers located on a flat white card within the central 30° of visual field. The subject looks from number to number, sequentially reporting whether the central 1.5-mm black spot is visible. There is a 40-cm hinged piece that serves to maintain the appropriate test distance and occludes the nontested eye. Any point missed, other than the physiologic blind spot area, is confirmed once before considering it a true missed point. Damato campimetry was performed in ambient light and scored by summing the total missed points. We scored Damato campimetry results by counting the number of missed points.

ANALYSIS

Receiver operating characteristic (ROC) curves were plotted to describe the ability of a screening test to discriminate eyes with glaucoma from normal eyes. An ROC curve is actually a serial sensitivity and specificity plot using varying cutoff values. The area under the ROC curve is a measure that can quantify the relative performance of the test assuming equal weight is accorded to sensitivity and specificity. A large area under the ROC curve shows good discrimination between the normal and definite glaucoma groups. The ideal test would have an area under the ROC curve of 1.0, whereas a test with no discriminative ability would show an area under the ROC curve of 0.5. We created ROC curves for FDT perimetry and Damato campimetry. Analysis of variance with post hoc comparison using the Tukey honestly significant difference was performed for multiple paired comparisons.

For eyes in the definite glaucoma group, one of us (N.Y.) subjectively compared Humphrey visual field results with FDT perimetry and Damato campimetry results to determine whether defects appeared in the same or different visual field regions: superior or inferior hemifield or the nasal area. Fields were classified into 3 categories: “matched,” in which the field defects were in the same region with both tests; “partially matched,” in which field defects were in overlapping quadrants when both tests were compared; and “not matched,” in which field defects found on the 2 tests did not overlap.

Table 1. Characteristics of the Screening Tests

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Area Under the ROC Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Damato campimetry†</td>
<td>53</td>
<td>90</td>
<td>0.883</td>
</tr>
<tr>
<td>FDT (grading)‡</td>
<td>92</td>
<td>93</td>
<td>0.925</td>
</tr>
<tr>
<td>FDT (counting)‡</td>
<td>92</td>
<td>93</td>
<td>0.924</td>
</tr>
</tbody>
</table>

*ROC indicates receiver operating characteristic; FDT, frequency-doubling technology perimetry. †The cutoff is 1 point. ‡The cutoff is 2 points.

Humphrey visual field test and FDT results in the 26 glaucomatous eyes revealed 18 eyes (69%) considered to have matched defects, 5 eyes (19%) considered partially matched, and 3 eyes (12%) having no match of the abnormal areas. When matched and partially matched grades were combined, FDT and the Humphrey visual field test had an 88% agreement level. This does not match the sensitivity and specificity previously given because other factors were included in the final diagnostic allocation. Of the 3 eyes that did not match, 2 eyes had no defect on FDT testing and 1 eye showed a defect on FDT in a different location from the defect in the Humphrey field.

Figure 1. Receiver operating characteristic curves for the frequency-doubling technology (FDT) perimetry (grading method of scoring) and Damato campimetry.

of 240 eyes, including 11 (7.3%) of 151 normal eyes, 6 (21%) of 28 eyes in the ocular hypertension group, 14 (40%) of 35 eyes in the glaucoma suspect group, and 24 (92%) of 26 eyes with definite glaucoma. Comparison of
The Damato campimeter showed at least 1 abnormality in the visual field in 53 (30.3%) of 175 eyes, including 27 (22.9%) of 118 normal eyes, 4 (21%) of 19 eyes in the ocular hypertension group, 4 (21%) of 19 eyes in the glaucoma suspect group, and 18 (95%) of 19 glaucomatous eyes. Subjective comparisons of the Humphrey visual field test results and Damato campimetry results in the 19 glaucomatous eyes revealed that 12 eyes (63%) were considered to have matched defects, 5 eyes (26%) were considered partially matched, and 2 eyes (11%) had no match between abnormal areas. When matched and partly matched grades were combined, Damato campimetry and Humphrey perimetry had an 89% agreement level. Two eyes with defects on Humphrey perimetry had no defects on Damato campimetry.

Results of screening tests on an eye previously undiagnosed with glaucoma, with abnormal results on Humphrey perimetry, FDT, and Damato campimetry, are shown in Figure 2. The test time for screening-mode FDT was approximately 1 minute per eye, while Damato campimetry took approximately 3 minutes per eye, as recorded by the technicians.

Our results show that FDT perimetry and Damato campimetry have high diagnostic accuracy with large values of area under the ROC curve (0.925 and 0.883, respectively). Both tests are compact devices with a short, simple test procedure that most patients can readily understand. In glaucomatous eyes, we noted good subjective agreement between the location of defects seen on Humphrey visual fields with Damato campimetry and FDT perimetry (89% and 88%, respectively), in agreement with other reports. In this screening, FDT had superior sensitivity and specificity for the detection of glaucoma. Still, we believe that FDT perimetry and Damato campimetry can be viewed as practical, effective devices for glaucoma screening, with different strengths. Damato campimetry is inexpensive and can be performed anywhere there is adequate illumination, while FDT perimetry is more expensive, requires electricity and a semidarkened room, and is faster.

Johnson and Samuels studied the ability of the FDT to separate normal and glaucomatous eyes within a clinic population, but used a threshold staircase strategy rather than the screening mode we used. Their results, using a 16-target pattern in 15 eyes with early or moderate glaucoma compared with age-matched controls, showed an area under the ROC curve of 0.965 with a sensitivity of 93% and a specificity of 100%. Using the screening mode of the FDT, Quigley found a sensitivity and specificity of 91% and 94%, respectively, in a glaucoma clinic-based population of 33 patients with glaucoma who had visual field defects and 33 patients in whom glaucoma was suspected who had normal visual fields. In the present study, using the faster but less exacting screening mode, we also found high discriminative ability with an area under the ROC curve of 0.925, with a sensitivity of 92% and a specificity of 93%. These differences are consistent with the different FDT operating modes used and

### Table 2. Values of Screening Tests in 4 Diagnostic Categories

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Diagnostic Category</th>
<th>Normal</th>
<th>Ocular Hypertension</th>
<th>Glaucoma Suspect</th>
<th>Definite Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Damato campimetry†</td>
<td>0.7 (1.7)</td>
<td>1.3 (2.6)</td>
<td>2.0 (2.9)</td>
<td>3.6 (3.1)</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>118</td>
<td>19</td>
<td>19</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>P‡</td>
<td>.93</td>
<td>.19</td>
<td>.19</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>FDT (grading)§</td>
<td>0.3 (1.2)</td>
<td>2.3 (5.5)</td>
<td>2.7 (4.9)</td>
<td>10.2 (10.1)</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>151</td>
<td>28</td>
<td>35</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>P‡</td>
<td>.11</td>
<td>.02</td>
<td>.01</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>FDT (counting)†</td>
<td>0.2 (0.9)</td>
<td>1.0 (2.2)</td>
<td>1.9 (3.6)</td>
<td>5.4 (4.8)</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>151</td>
<td>28</td>
<td>35</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>P‡</td>
<td>.37</td>
<td>.01</td>
<td>.001</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>15.0 (3.4)</td>
<td>23.7 (2.1)</td>
<td>16.2 (2.6)</td>
<td>17.7 (5.9)</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>139</td>
<td>28</td>
<td>31</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>P‡</td>
<td>.&lt; .001</td>
<td>.34</td>
<td>.003</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Mean deviation, dB</td>
<td>−1.4 (2.3)</td>
<td>−3.5 (2.5)</td>
<td>−3.4 (3.3)</td>
<td>−8.3 (6.8)</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>148</td>
<td>28</td>
<td>35</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>P‡</td>
<td>.02</td>
<td>.01</td>
<td>.003</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Pattern SD, dB</td>
<td>2.6 (1.4)</td>
<td>3.2 (2.5)</td>
<td>3.5 (1.9)</td>
<td>6.0 (3.7)</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>148</td>
<td>28</td>
<td>35</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>P‡</td>
<td>.57</td>
<td>.08</td>
<td>.001</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

Data are given as the mean (SD), unless otherwise indicated. FDT indicates frequency-doubling technology perimetry; IOP, intraocular pressure; and ellipses, data not applicable.

†Scored as number of locations missed.
‡Compared with the normal group; analysis of variance with Tukey post hoc comparison.
§Scored as the sum of 17 visual field locations with 0, 1, 2, and 3 points for normal, mild, moderate, and severe loss, respectively, in each location (range of possible scores, 0-51).
¶P<.001 compared with the glaucoma group.
††P<.001 compared with the ocular hypertension group.
the populations studied (clinic population vs public screening project); the generally lower severity of disease in a largely undiagnosed screening population may have contributed to our slightly lower sensitivity and specificity findings.

Frequency-doubling technology perimetry was developed to target those cells of large-diameter optic nerve fibers in the magnocellular pathway that are selectively lost in eyes with early glaucoma. In the present study, the FDT scoring and counting methods showed statistically significant differences (P < .001) between those in the normal group and those in the glaucoma suspect group. Among those in the glaucoma suspect group, 14 (40%) of 35 eyes had visual field defects only on FDT; such eyes may represent either a high rate of false-positive errors using FDT or truly damaged eyes that were detected earlier by FDT than by Humphrey visual fields. Longitudinal follow-up, especially of patients in the ocular hypertension or glaucoma suspect group, will be necessary to better refine the "true" sensitivity and specificity values.

Using the Damato campimeter, we found a relatively low sensitivity (53%) when a cutoff giving a higher specificity (90%) was used. Other researchers found a sensitivity of 83% to 85% and a specificity of 80% to 88% among clinic-based populations. Some researchers have concluded that Damato campimetry can reliably detect moderate to severe visual field loss when tested on clinic-based populations with normal and glaucomatous eyes, but early visual field loss is less certain to be detected. Indeed, in the glaucoma group of the present study, the 1 eye that had no defect on Damato campimetry was at an early stage of glaucoma. However, Wis- hart found an unacceptably low sensitivity (61%) and specificity (62%) in a study comparing results of oculo-kinetic perimetry and Humphrey visual fields. The Damato campimeter has evolved markedly from its earliest models, and some of the differences between studies may be attributable to these changes, along with population differences and perhaps differences in the training and abilities of technicians administering the test. Perhaps if abnormal test results could be confirmed a second time, a lower number of missed points could be used as a cutoff to improve sensitivity while maintaining reasonable specificity. Unfortunately, time constraints did not allow us to perform additional Damato testing.

The accuracy of diagnostic allocation of screening subjects has a great influence on sensitivity and specificity estimates of screening devices. Our classification was primarily dependent on undilated optic nerve findings and Humphrey FASTPAC visual fields taken by perimetric novices. We tried to recall subjects with equivocal field test results for a second threshold test but were not always successful in doing so, which in turn may have affected the accuracy of our allocation of eyes into diag-
nostic groups. Still, while such misclassification may have affected sensitivity and specificity rates, even glaucoma specialists may disagree on basic clinical observations necessary for diagnostic allocation.\textsuperscript{22}

The Humphrey FASTPAC testing program was chosen to save time when screening a mostly normal population.\textsuperscript{23} Some researchers\textsuperscript{24,25} have found that Humphrey FASTPAC testing underestimates the severity of glaucoma, but we considered the time savings obtained with the Humphrey FASTPAC to be more valuable in our screening situation than determining the true defect depth in eyes with glaucoma damage.

The prevalence of open angle glaucoma in the industrialized world is at least 1.7% in the population older than 40 years.\textsuperscript{26} Shiose et al\textsuperscript{27} performed glaucoma screening in Japan among 8126 residents aged 40 years or older and found an overall prevalence of 3.6%. In the Baltimore Eye Survey, 26% of the subjects had abnormal screening test results, and overall 9.5% of the subjects who completed automated testing were referred for definitive examination due to confirmation of perimetric defects with manual perimetry.\textsuperscript{3} In this study, the prevalence rate of glaucoma was 10.7%. Our screening test was held at a clinic with prior public advertisement. The subjects who joined the screening may have been self-selected as those interested in glaucoma; they may have had a previous borderline IOP reading, a family history of glaucoma, or even curiosity about whether they still had glaucoma in spite of treatment. While these factors may have played a role in the high prevalence of glaucoma in our screening population, the role of possible misclassification as previously discussed should also be considered.

In summary, FDT perimetry and Damato campimetry may be useful for glaucoma screening. Frequency-doubling technology perimetry is faster and has a higher sensitivity, but Damato campimetry is inexpensive and requires little technological support. Each could be considered ideal for different situations, depending on the screening location and population.

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Reprints: Philip P. Chen, MD, Department of Ophthalmology, University of Washington, Box 356485, Seattle, WA 98195-6485.