Detecting Visual Function Abnormalities Using the Swedish Interactive Threshold Algorithm and Matrix Perimetry in Eyes With Glaucomatous Appearance of the Optic Disc

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Objective: To compare the ability of 24-2 frequency-doubling perimetry (FDP-Matrix) with standard automated perimetry with the Swedish interactive threshold algorithm (SAP-SITA) in detection of visual function abnormalities in patients with glaucomatous-appearing optic discs (GAOD).

Methods: This observational case-control study included 80 patients with GAOD and 54 control subjects diagnosed by masked assessment of optic disc stereoscopic photographs. Abnormal visual function at SAP-SITA and FDP-Matrix testing required consistent abnormalities in 2 visual field examinations, determined using the glaucoma hemifield test outside 99% normal limits, pattern standard deviation outside 95% normal limits, or 3 contiguous points in the pattern deviation probability plot outside 95% normal limits (at least 1 P<1%) within the same hemifield.

Results: The FDP-Matrix and SAP-SITA detected abnormal visual function in 51% and 44%, respectively, of GAOD eyes (P = .26), and both perimetry techniques identified 11% of healthy eyes as abnormal. Agreement between FDP-Matrix and SAP-SITA was moderate (κ = 0.49), as only 35% of GAOD eyes and 2% of healthy eyes had both visual field test results flagged as abnormal.

Conclusions: The FDP-Matrix detected abnormal visual function in more eyes with GAOD than did SAP-SITA, although this difference was not significant. Each visual field test tended to identify different subsets of eyes with GAOD as abnormal. Combination of these perimetry techniques may improve the detection of visual function abnormalities in patients with glaucoma.

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REQUENCY-DOUBLING PERIMETRY (FDP) was designed to emphasize the response characteristics of the parasol ganglion cells. The first-generation instrument used 10° targets to test contrast sensitivity. Recently, a second-generation FDP (the FDP-Matrix) has become available. The FDP-Matrix uses smaller stimuli and more test locations than those of the original FDP device, permitting a stimulus pattern equivalent to the Humphrey field analyzer 24-2 test. This new perimeter can provide greater details of the spatial distribution of visual field (VF) defects.

Several studies have reported that the first-generation FDP had higher levels of discriminatory power for detecting glaucomatous VF loss than did standard automated perimetry (SAP) using the full-threshold (FT) strategy. However, to our knowledge, a comprehensive comparison of the diagnostic performance between SAP using the Swedish interactive threshold algorithm (SITA) and FDP-Matrix in an unbiased population has not been previously studied. The objective of the present study was to compare the ability of FDP-Matrix with that of SAP-SITA, as used in clinical practice, in detection of visual function abnormalities in eyes with glaucomatous-appearing optic discs (GAOD).

METHODS

This was an observational case-control study. All patients have undergone optic disc imaging and visual function testing as part of ongoing longitudinal glaucoma studies conducted at the Glaucoma Service, University of Alabama at Birmingham, between January 2, 2003, and February 28, 2005. Patients with glaucoma were recruited from the university's glaucoma clinics by medical record review, and control sub-
jects were recruited from among university employees and from the general population through advertisement. The protocol included screening, baseline, and regular follow-up visits. Informed consent was obtained from all participants. The institutional review board at the University of Alabama at Birmingham approved all protocols, and all methods adhered to the tenets of the Declaration of Helsinki.

All subjects underwent a comprehensive ophthalmic examination including review of medical history, best-corrected visual acuity, slitlamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, dilated fundus examination using a 78-degree (D) lens, stereoscopic optic disc photography, and automated perimetry. To be included, subjects were required to have an open-angle, best-corrected visual acuity 20/40 or better, spherical refraction within plus or minus 5.0 D and cylinder correction within plus or minus 3.0 D. Patients were excluded if they had a history of intraocular surgery (except for uncomplicated cataract surgery or glaucoma surgery), visually significant cataracts (nuclear sclerotic cataracts with visual acuity worse than 20/40 or posterior subcapsular cataract), problems affecting color vision other than glaucoma, use of medication known to affect visual sensitivity at the time of testing, and other diseases affecting the VF. Some patients with glaucoma were receiving topical intraocular pressure–lowering therapy.

Similar to previous studies designed to compare VF testing in the detection of glaucoma in an unbiased manner, the glaucoma diagnosis was based on the presence of GAOD on stereoscopic photographs taken with a simultaneous stereoscopic fundus camera (Nidek 3Dx fundus camera; Nidek Corporation Ltd, Gamagori, Japan). Visual field test results were not considered for glaucoma diagnosis. Control subjects were required to have intraocular pressure less than 22 mm Hg, no history of increased intraocular pressure, normal findings at bilateral eye examination, and normal-appearing optic discs at stereophotographic evaluation. When both eyes in the same patient were eligible, 1 eye was randomly selected for inclusion in the study.

All stereoscopic photographs were evaluated independently by 3 fellowship-trained glaucoma specialists (J.D.-O., B.E.M., and C.A.G.). Each grader was masked to the subject’s identity and other test results. Stereoscopic photographs with adequate quality were graded dichotomously (GAOD or normal). Criteria for classification were based on observance of typical glaucomatous optic disc characteristics including neuroretinal rim thinning, notching, nerve fiber layer defects, or optic disc hemorrhages. In cases of disagreement (17 eyes), this was resolved by consensus among the 3 graders.

The SAP-SITA-standard perimetry was conducted with the Humphrey field analyzer (Humphrey model 750; Carl Zeiss Meditec, Dublin, Calif), and FDP perimetry with an FDP-Matrix perimeter (Welch-Allyn, Skaneateles Falls, NY; and Carl Zeiss Meditec). The FDP-Matrix uses 5° square spatial frequency-doubling stimuli with exposure for 500 ms. The psycho-physical strategy used by FDP-Matrix is called “zippy estimation by sequential testing.” In brief, this strategy determines the likely distribution of sensitivities according to the patient’s responses to 4 stimuli presentations at each location. When all sensitivities are estimated, its algorithm checks for any points that differ by more than 4 dB from 4 neighboring points, then determines sensitivity again for these points.

The SAP-SITA and FDP-Matrix were conducted using the 24-2 program. The 2 locations nearest the blind spot and the foveal location were excluded from the analysis, leaving a total of 32 test locations for each technique. Each patient underwent both perimetry examinations at the screening and second visits, within 1 to 8 weeks. Patients with eyes with GAOD underwent third SAP and FDP examinations within 12 to 14 months after the second visit. Visual field examinations were performed in random order, with rest periods of at least 15 minutes between tests. Only reliable VF examinations (<33% of fixation losses, or false-positive or false negative results) were considered for analysis.

To compare the performance of these techniques as they are used in clinical practice, SAP-SITA and FDP-Matrix abnormalities were determined by comparing each patient’s results with the manufacturer’s internal normative databases. Abnormal VF results with both examination techniques were defined by any of the following criteria: glaucoma hemifield test results outside of the 99% normal limits; pattern standard deviation outside of the 95% normal limits; or presence of a cluster of 3 contiguous points or more, within the same hemifield, at the pattern deviation probability plot with P < .05 or worse (at least 1 point with P < .01), within the same hemifield in 2 VF examinations.

To ensure that false-positive results on either field test were not due to learning effect or threshold variability, we required consistent results on 2 VF tests with each perimetry technique. Thus, abnormal visual function status required a repeated abnormality at 2 SAP or 2 FDP examinations, and normal visual function required normal findings at 2 SAP or FDP examinations (consistent results). Patients with eyes with GAOD underwent 2 VF tests. Their visual function status with each technique was determined by the results of the first 2 VF tests with consistent results or by results of the third VF test if the first 2 VF tests with any perimetry technique yielded inconsistent results (1 VF test with normal results and the other with abnormal results). However, recruited control subjects performed only 2 VF tests, and their visual function status could only be determined in cases with consistent results for the first 2 VF tests. Control subjects who had inconsistent results in any perimetry technique were excluded from analysis. This should not have biased the results in favor of either test. For analysis purposes, we used the results of the second SAP and the second FDP examinations for control subjects and patients with eyes with GAOD with consistent results, and the results of the third SAP and third FDP examinations for patients with eyes with GAOD who had inconsistent results on the first set of VF examinations with any perimetry technique.

The extension of the VF defect was compared by determining the number of abnormal points (P < .05 or worse) on the pattern deviation and total deviation probability plots for each perimetry technique. Overlapping locations (by quadrants) of VF defects were evaluated in eyes with GAOD that had at least 1 reproducible cluster with any technique. Severity of VF loss was determined using the criteria for SAP of Hodapp et al. Parametric and nonparametric tests were used to compare continuous variables, according to data distribution. The chi-squared test was used to compare categorical data. The McNemar test was used to compare differences in distribution of a categorical variable. The Pearson statistic was used to assess agreement between categorical variables. Pearson correlations were used to correlate global indices between techniques, and correlation coefficients were compared using the method proposed by Glass and Stanley. P < .05 was considered statistically significant. Statistical analyses were performed using JMP5 and SAS statistical software (both by SAS Institute Inc, Cary, NC).

RESULTS

Data for 189 eyes in 189 subjects were obtained from the University of Alabama at Birmingham Optic Nerve Imaging Center database. A total of 94 eyes with GAOD and 95 healthy eyes based on grading of stereoscopic pho-
tographs were initially enrolled. Visual function could be determined in 54 of 95 healthy eyes; 41 healthy eyes with inconsistent results at the first 2 FDP or SAP tests (18 at FDP, 17 at SAP, and 6 at both tests) were excluded. Twenty-four of the 41 healthy eyes with inconsistent results had abnormal results at the first FDP or SAP test (13 at FDP, 9 at SAP, and 2 at both tests) and normal results at the second VF test, suggesting a learning effect. Eighty of 94 eyes with GAOD met our study requirements to determine visual function, and 30 of these required a third VF test to determine visual function because of inconsistent results at the first 2 FDP and SAP tests (14 at FDP, 11 at SAP, and 5 at both tests).

Table 1 gives the demographic data for the study population. Although patients with eyes with GAOD were older than control subjects, only age-corrected parameters from the SAP (StatPac software; StatPac Inc, Bloomington, Minn) and age-normative FDP database (Carl Zeiss Meditec Inc) were considered for VF diagnosis.

Overall, the test time (mean ± SD) for SAP-SITA was shorter than for FDP-Matrix (305 ± 52 seconds vs 315 ± 5 seconds, respectively; \( P = .02 \)). In control subjects, SAP-SITA test time was shorter than for FDP-Matrix (286 ± 31 seconds vs 314 ± 18 seconds, respectively; \( P < .001 \)), but no difference was observed among patients with eyes with GAOD (311 ± 57 seconds vs 318 ± 14 seconds for SAP and FDP-Matrix, respectively; \( P = .21 \)).

Figure 1 shows that test time for both SAP-SITA and FDP-Matrix increased with VF damage (mean deviation); however, the correlation coefficients were significantly different (\( P < .001 \)).

Based on our study criteria, 32 (40%) of 80 eyes with GAOD had normal visual function as assessed with both perimetry techniques. Abnormal visual function was detected in 41 (51%) of 80 eyes with GAOD with FDP-Matrix and in 35 (44%) of 80 eyes with GAOD with SAP-SITA (\( P = .27 \)). Agreement between the 2 examinations was moderate (\( \kappa \pm SE, 0.49 \pm .08 \);

**Table 2** gives the sensitivity and specificity of SAP-SITA and FDP-Matrix for each of the 3 criteria for VF abnormality used in this study. The FDP-Matrix showed a borderline higher sensitivity than the SAP-SITA when using the criteria of a cluster of 3 contiguous abnormal points or more in the pattern deviation plot; however, no differences in sensitivities were observed.
Correlations of global indices (mean deviation and pattern standard deviation) between SAP-SITA and FDP-Matrix were strong ($r=0.75$ for mean deviation and $r=0.83$ for pattern standard deviation, respectively; $P<.001$). The correlations of the numbers of abnormal points in total deviation and pattern deviation probability plots between the 2 techniques were also strong ($r=0.80$ and $r=0.78$, respectively; $P<.001$). Table 3 gives the number of abnormal points on the pattern deviation and total deviation probability plots between the 2 techniques in eyes with GAOD and control eyes; 53% (42/80) of eyes with GAOD had a greater number of abnormal points on the pattern deviation plot at SAP, 36% (29/80) of eyes had a greater number of abnormal points at FDP, and 11% (9/80) of eyes had an equal number of abnormal points on both tests.

In 31 eyes with GAOD, an abnormal quadrant was detected with at least 1 of the perimetry techniques. Of these 31 eyes, 20 (65%) had at least 1 defective quadrant in common at SAP-SITA and FDP-Matrix, 7 (23%) had an overlap of all abnormal quadrants, and 11 (35%) did not have any abnormal quadrant in common.

This study compared SAP-SITA and FDP-Matrix instruments as used in clinical practice to detect visual function abnormalities. While we found no significant difference in visual dysfunction between FDP-Matrix and SAP-SITA examinations, our results indicate that SAP-SITA and FDP-Matrix tended to detect abnormalities in different subsets of eyes with GAOD. Furthermore, disagreement between the techniques occurred in eyes with early and moderate VF loss at SAP-SITA. These results suggest that functional changes in early glaucoma detected at clinical perimetry may differ significantly between individuals.

Sample et al$^5$ compared the results of 4 different VF tests (the first-generation FDP, SAP-FT, short-wave-length automated perimetry, and motion automated perimetry) in the same cohort of patients and observed individual differences in which perimetric tests detected VF losses earliest. Our findings also support that visual function abnormalities in early glaucoma can differ significantly between individuals.

Table 3. Number of Abnormal Points at SAP-SITA and FDP-Matrix Examinations of 80 Eyes With GAOD and 54 Healthy Control Eyes$^*$

<table>
<thead>
<tr>
<th>No. of Abnormal Points</th>
<th>SAP-SITA</th>
<th>FDP-Matrix</th>
<th>$P$ Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes with GAOD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pattern deviation</td>
<td>9.34 ± 9.04</td>
<td>8.07 ± 7.88</td>
<td>0.18</td>
</tr>
<tr>
<td>probability plot</td>
<td>9.67 ± 12.31</td>
<td>10.75 ± 13.07</td>
<td>0.10</td>
</tr>
<tr>
<td>Total deviation</td>
<td>3.18 ± 2.98</td>
<td>2.91 ± 3.60</td>
<td>0.57</td>
</tr>
<tr>
<td>probability plot</td>
<td>1.31 ± 2.27</td>
<td>2.80 ± 5.89</td>
<td>0.07</td>
</tr>
<tr>
<td>Healthy control eyes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pattern deviation</td>
<td>35 47</td>
<td>27 55</td>
<td></td>
</tr>
<tr>
<td>probability plot</td>
<td>89 89</td>
<td>98 87</td>
<td></td>
</tr>
<tr>
<td>Total deviation</td>
<td>44 51</td>
<td>35 60</td>
<td></td>
</tr>
<tr>
<td>probability plot</td>
<td>89 89</td>
<td>98 80</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: FDP, frequency-doubling perimetry; GAOD, glaucomatous-appearing optic disc; SAP, standard automated perimetry; SITA, Swedish interactive threshold algorithm.

$^*$Data are given as mean ± SD.

†Wilcoxon test.
dysfunction in early glaucoma may vary significantly between individuals, and a multimodal functional assessment may be more effective.

Previous reports observed that the first-generation FDP was more sensitive in detecting glaucoma than the SAP using the FT strategy. Boden et al compared the first-generation FDP with the SAP-FT and SAP-SITA in 104 eyes with glucomatous optic neuropathy, and confirmed that the first-generation FDP identified more eyes with glucomatous optic neuropathy than did the SAP-FT. However, when the first-generation FDP was compared with the SAP-SITA, both perimetry techniques detected visual function abnormalities in a similar number of eyes with glucomatous optic neuropathy. Similar to our finding with the FDP-Matrix, the SAP-SITA and the first-generation FDP tended to identify different subsets of eyes as abnormal. Boden et al hypothesized that, although SITA had shown no clinical loss of accuracy for detecting VF defects compared with the FT strategy, the properties of SITA (eg, tighter confidence intervals) may have improved SAP ability in identifying glucomatous VF defects. Moreover, they suggested that a major contribution of the FDP, at least for glaucoma diagnosis, would be to serve as a complement to SAP-SITA for detecting eyes missed by the latter technique. Combining both perimetry techniques in our sample increased the sensitivity (60%), with slight reduction in specificity (80%).

Previous studies have addressed the diagnostic performance of FDP-Matrix. Spry et al observed that FDP-Matrix and SAP using SITA-Fast strategy had a similar diagnostic performance in a population of 48 individuals with suspected glaucoma. However, as mentioned by the authors, a potential source of bias in favor of SAP may have occurred because the ophthalmologist who determined the diagnosis of glaucoma had access to SAP results. Considering SAP results to classify patients as having normal or glucomatous eyes would overestimate SAP diagnosis performance. On the other hand, the requirement of normal SAP findings for diagnosis of suspected glaucoma would prevent SAP deficits from preceding those of the function-specific tests. Brusini et al compared the diagnostic capability of the original FDP with the FDP-Matrix, but the study design did not permit direct comparisons between FDP and SAP-SITA because SAP-SITA results were part of the study inclusion criteria. In addition, it was not mentioned whether the VF defects detected at FDP were required to be repeatable. Medeiros et al observed that FDP-Matrix had a better performance than SAP-SITA for the diagnosis of early glaucoma. However, inasmuch as the main purpose of this study was to describe a statistical approach to evaluate the effect of covariates (disease severity and age) on receiver-operating characteristic curves, only the global index pattern standard deviation was used to determine abnormal visual function. Thus, this previous study did not provide a comprehensive comparison of SAP-SITA and FDP-Matrix as used in clinical practice in early glaucoma detection. We found slightly higher sensitivity with FDP-Matrix using the pattern deviation probability plot criterion, but this was of borderline significance. A larger study population will be required to verify this finding.

In our study, although the mean test time of SAP and FDP-Matrix increased with VF damage (as measured by
mean deviation), FDP-Matrix had a shorter variability in test duration over the mean deviation range and a shorter variability in test duration between subjects with worse mean deviation (Figure 1). The shorter variability in test duration observed in FDP-Matrix examinations may be explained by the properties of its algorithm, presenting a constant number of stimuli per each VF location, and also by the smaller increase in threshold variability with increasing disease severity seen with the FDP.11

There were no significant differences between the number of abnormal points on the pattern deviation and total deviation plots detected at SAP-SITA and FDP-Matrix in eyes with GAOD. In contrast with previous studies,10,14,15 our results suggest that FDP-Matrix may not detect more extensive damage than SAP-SITA.

We observed discrepancies between visual function status as evaluated by FDP and SAP in 10 healthy eyes. Five control subjects had a consistent defect at SAP but normal findings at FDP examination, and 5 had a consistent defect at FDP but normal SAP findings. Figure 4 shows an example of each discrepancy observed in healthy eyes.

Differences between normative databases of SAP-SITA and FDP-Matrix (different populations enrolled for each normative database) might have influenced our results.11 Ideally, a large normative database for both VF tests obtained from the same individuals should be used to provide a more accurate comparison between VF techniques. However, a customized normative database would not be generalizable and would limit the purpose of the study, which was to evaluate how these instruments performed as they are being used in clinical practice. In addition, classification of eyes according to whether they were healthy or had GAOD was based on evaluation of stereoscopic photographs. Because of the wide variability in the optic disc appearance in the nonglaucomatous population, some eyes included in the GAOD group may never develop glaucoma, explaining, in part, the low sensitivity levels observed in the present study. Also, some of the eyes classified as GAOD may be in a stage of the disease process where the detection of functional loss by these instruments is not yet possible. Although these factors might influence the sensitivity and specificity of each technique, it is unlikely they would have affected the comparisons between the 2 instruments. The exclusion of control subjects with inconsistent results on 2 VF tests by any technique may have affected our results. However, consistent results were required in an attempt to minimize the influence of testing artifacts (eg, learning effect), and a similar number of control subjects were excluded because of inconsistent results at SAP and FDP.

In summary, this study shows that FDP-Matrix enabled detection of abnormal visual function in more eyes with GAOD than did SAP-SITA, although this difference was not significant. Each VF test tended to identify a different subset of patients with eyes with GAOD as abnormal. Combination of these perimetry techniques may improve the detection of visual function abnormalities in glaucoma, with slight reduction in specificity.

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REFERENCES