Glaucamous Visual Field Progression with Frequency-Doubling Technology and Standard Automated Perimetry in a Longitudinal Prospective Study

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PURPOSE. To compare frequency-doubling technology (FDT) perimetry with standard automated perimetry (SAP) for detecting glaucomatous visual field progression in a longitudinal prospective study.

METHODS. One eye of patients with open-angle glaucoma was tested every 6 months with both FDT and SAP. A minimum of 6 examinations with each perimetric technique was required for inclusion. Visual field progression was determined by two methods: glaucoma change probability (GCP) analysis and linear regression analysis (LRA). For GCP, several criteria for progression were used. The number of locations required to classify progression with FDT compared with SAP, respectively, was 1:2 (least conservative), 1:3, 2:3, 2:4, 2:6, 2:7, 3:6, 3:7, and 3:10 (most conservative). The number of consecutive examinations required to confirm progression was 2-of-3, 2-of-2, and 3-of-3. For LRA, the progression criterion was any significant decline in mean threshold sensitivity over time in each of the following three visual field subdivisions: (1) all test locations, (2) locations in the central 10° and the superior and inferior hemifields, and (3) locations in each quadrant. Using these criteria, the proportion of patients classified as showing progression with each perimetric technique was calculated and, in the case of progression with both, the differences in time to progression were determined.

RESULTS. Sixty-five patients were followed for a median of 3.5 years (median number of examinations, 9). For the least conservative GCP criterion, 32 (49%) patients were found to have progressing visual fields with FDT and 32 (49%) patients with SAP. Only 16 (25%) patients showed progression with both methods, and in most of those patients, FDT identified progression before SAP (median, 12 months earlier). The majority of GCP progression criterion (15/27), classified more patients as progressing with FDT than with SAP. Contrary to this, more patients showed progression with SAP than FDT, when analysed with LRA; e.g., using quadrant LRA 20 (31%) patients showed progression with FDT, 23 (35%) with SAP, and only 10 (15%) with both.

CONCLUSIONS. FDT perimetry detected glaucomatous visual field progression. However, the proportion of patients who showed progression with both FDT and SAP was small, possibly indicating that the two techniques identify different subgroups of patients. Using GCP, more patients showed progression with FDT than with SAP, yet the opposite occurred using LRA. As there is no independent qualifier of progression, FDT and SAP progression rates vary depending on the method of analysis and the criterion used. (Invest Ophthalmol Vis Sci. 2005;46: 547–554) DOI:10.1167/iovs.04-0973

The management of glaucoma requires effective techniques for detecting and monitoring the progression of glaucomatous visual field loss. Standard automated perimetry (SAP) has been used for many years; however, it is considered to have certain shortcomings. It has high variability that increases with defect severity and eccentricity. In patients with stable glaucoma, it has been shown that when initially normal test locations are retested, sensitivity may vary by as much as 10 dB, and that this test-retest variability may increase to 21 dB in moderately damaged locations. Thus, in some cases, the test-retest confidence interval can be almost as wide as the entire dynamic range of the instrument, making it difficult to differentiate true progression from variability. Another inadequacy is that SAP is incommensurate with early loss of retinal ganglion cells (RGCs) in glaucoma. These shortcomings have led to the development of new perimetric techniques that may be useful in determining glaucomatous visual field loss earlier and more accurately.

One of the new techniques is frequency-doubling technology (FDT) perimetry, developed to detect glaucomatous visual field loss by targeting a specific class of RGCs. The stimulus used is a low-spatial-frequency sinusoidal grating that is counterphase flickered at a high temporal frequency. Such a stimulus produces a frequency-doubling illusion, in which the grating appears to have twice the actual number of bars. This may be lost before a defect is actually detected with SAP. As for test-retest variability with FDT does not increase with defect severity or eccentricity as much as it does with SAP, probably because of the large stimulus size used. Also, validity of the technique is suggested to some extent by studies that have found a correlation between SAP mean deviation (MD) and FDT MD. For instance, test–retest variability with FDT does not increase with defect severity or eccentricity as much as it does with SAP, probably because of the large stimulus size used. Also, validity of the technique is suggested to some extent by studies that have found a correlation between SAP mean deviation (MD) and FDT MD. Furthermore, several studies have shown that FDT has high sensitivity and specificity for the detection of early glaucoma, when SAP visual field loss is used as the diagnostic criterion. However, little is known about the ability of FDT to detect glaucomatous visual field progression over time.

Longitudinal observations of glaucomatous loss detected with FDT are available from only three studies, each of
which included a different type of subject sample: patients with open-angle glaucoma,\textsuperscript{15} ocular hypertension,\textsuperscript{16} or suspected glaucoma.\textsuperscript{17} Although FDT defects were found to be predictive of future glaucomatous visual field loss, all these studies were somewhat biased, because the development or progression of an SAP defect was assumed to be the appropriate gold standard criterion for glaucomatous loss. Furthermore, a selection bias may have been introduced in two of the studies.\textsuperscript{16,17} The inclusion of only patients with normal baseline SAP, but not necessarily normal baseline FDT, potentially excluded some patients who may have had an SAP-detected defect before an FDT-detected defect. Also, the number of follow-up FDT examinations in these two studies was limited.\textsuperscript{16,17} In all studies, only the development of new FDT defects was investigated.\textsuperscript{15,17} Hitherto, progression of existing FDT defects has not been investigated. The purpose of the current investigation was to compare FDT with SAP for detecting glaucomatous progression in patients with established open-angle glaucoma. Specifically, we wanted to compare the two perimetric techniques in a longitudinal prospective study and to investigate glaucomatous visual field progression in patients with baseline SAP loss and or FDT loss.

**METHODS**

**Subjects**

Data were obtained from a longitudinal prospective study on visual field and optic disc changes in glaucoma, which commenced in 1991 at the Department of Ophthalmology and Visual Sciences, Dalhousie University. Patients with glaucoma were recruited on a consecutive basis from the practice of one of the authors (RPL) and the Glaucoma Clinic of the Eye Care Centre (Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia). The study was approved by the institutional ethics committee and adhered to the tenets of the Declaration of Helsinki. All patients gave informed written consent before participation in the study.

The inclusion criteria for participation were a diagnosis of open-angle glaucoma with glaucomatous optic disc damage (e.g., notching or progressive thinning of the neuroretinal rim), open angles by gonioscopy, a visual field with an SAP MD index between $-2$ and $-10$ dB, a best corrected visual acuity of 20/20 (20/40) or better, and a minimum of 6 examinations with both FDT and SAP. The exclusion criteria were concomitant ocular disease, systemic disease or medication known to affect the visual field, refractive error exceeding 5 D spherical equivalent or 3 D of astigmatism, and contact lens wear.

**Perimetric Techniques**

All patients were examined with FDT perimetry and SAP in this part of the study, which commenced in 1998 after the introduction of the first commercially available FDT perimeter (Welch Allyn Inc., Skaneateles, NY; Carl Zeiss Meditec, Dublin, CA). FDT perimetry was performed with the full-threshold C-20 program during the first 6 months of the study and, thereafter, with the full-threshold N-30 program. FDT is described in detail elsewhere.\textsuperscript{7} Briefly, the FDT perimeter uses a vertical sinusoidal grating stimulus of low spatial frequency that is counterphase flickered at a high temporal frequency (25 Hz) to produce the frequency-doubling illusion. The C-20 program of the FDT perimeter presents 17 of these stimuli in various locations within the central 20° of the visual field: four square stimuli ($10° \times 10°$ with spatial frequency 0.25 cyc/deg) located in each quadrant and one circular stimulus ($10°$ in diameter with spatial frequency 0.50 cyc/deg) located centrally. In addition to these, the N-30 program presents two square stimuli located nasally above and below the horizontal midline between 20° and 30° eccentricity. In full-threshold testing mode, the minimum contrast necessary to detect the stimulus in each location is determined with a modified binary search technique.

SAP was performed with a size III stimulus (0.43° in diameter) using the Humphrey Field Analyzer (HFA; Carl Zeiss Meditec Inc.) full-threshold 30-2 program.

**Testing Procedures**

Patients first underwent a full ophthalmic examination. If both eyes were eligible for the study, one eye was randomly assigned as the study eye. Only the study eye was tested. All patients had experience with SAP as part of the earlier longitudinal study, but not with FDT. Therefore, one SAP examination was performed at the first visit for this part of the study, whereas two baseline FDT examinations were performed in order to minimize learning effects, even though these have been shown to be negligible.\textsuperscript{18} After the first visit, patients were examined with both FDT and SAP once every 6 months. The optimal refractive error correction was used in all examinations.

**Analysis of Progression**

As the FDT C-20 program was used to examine patients in the early phase of the study, we used this pattern of test locations for analysis rather than the subsequently administered N-30 pattern. Thus, the two extra nasal locations of the N-30 pattern were excluded. Furthermore, to balance as closely as possible the area of the visual field examined using the FDT C-20 pattern and SAP, we analyzed only the central 52 test locations with the latter. Thus, 22 of the outermost and the 2 blind-spot test locations of the HFA SAP 30-2 pattern\textsuperscript{19} were excluded. To analyze the progression of these FDT and SAP test locations, we used two methods: glaucoma change probability (GCP) analysis and linear regression analysis (LRA). Within each method, several criteria for progression were applied and compared.

**GCP Analysis.** The GCP analysis described by Heijl et al.\textsuperscript{20} was used. With this method, a mean visual field is established from the results of two baseline examinations. For FDT, this was achieved during the two examinations performed at the first study visit. For SAP, the mean baseline visual field was determined from the one SAP examination performed at the first visit for the current part of the study and from the results of an SAP examination performed 6 months prior, as part of the earlier longitudinal study. Next, the pointwise difference in total deviation between the baseline and a follow-up visual field is calculated. Any locations for which the difference falls outside the 95th or 5th percentiles of test–retest variability are identified on the printout. Results are printed for each follow-up examination, with probable progressing/deteriorating test locations and probable improving test locations represented by different symbols. The GCP analysis of the Statpac program (Carl Zeiss Meditec) was used to perform the analysis for SAP. For FDT perimetry, we used a computer program based on the method described by Heijl et al.,\textsuperscript{20} which incorporated previously published data on FDT test-retest variability.\textsuperscript{21} Visual field progression was determined with GCP using several criteria for the number of test locations required for fields to be identified as progressing, and the number of examinations required for confirmed progression. The criteria for the number of progressing locations were specifically chosen to equalize, as much as possible, the difference in the total number of locations tested with FDT compared with SAP. The following nine criteria were chosen for the number of locations defining visual field progression with FDT compared with SAP: 1:2, 1:3, 2:3, 2:4, 2:6, 2:7, 3:6, 3:7, and 3:10, where 1 test location progressing with FDT to 2 with SAP represents the least conservative or least strict criterion and 3 FDT to 10 SAP locations represents the most conservative criterion. In addition, we chose the following three criteria for the number of consecutive examinations required to confirm that test locations were progressing: 2-of-3, 2-of-2, and 3-of-3, where an increase in the required number of confirmation examinations gives greater confidence that test locations classified as progressing represent true progression. Thus, the total number of GCP progression criteria applied and compared was 27.\textsuperscript{22}

**Linear Regression Analysis.** LRA was also used to determine progression, by evaluating the change in threshold sensitivity over time.\textsuperscript{23,24} Specifically, we chose to apply LRA to (1) the mean sensi-
TABLE 1. Methods of Analysis and Criteria for Determining Progression

<table>
<thead>
<tr>
<th>Method</th>
<th>Criteria for Progression</th>
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| GCP*    | Number of progressing test locations:  
          Number of consecutive examinations required to confirm test location progression:  
          2-of-3; 2-of-2; 3-of-3  
| LRA†   | Test locations analysed over time:  
          (1) Global: mean sensitivity of all test locations  
          (2) Hemifield: mean sensitivity of locations in each of central 10°, superior and inferior hemifields beyond 10°  
          (3) Quadrant: mean sensitivity of locations in each quadrant  
          Slope and significance of the regression line:  
          For each of the above applications (1–3), any negative slope with P ≤ 0.05, in one or more subdivisions |

* Based on total deviation.  
† Based on threshold sensitivity.

activity of all test locations in the visual field (global LRA); (2) the mean sensitivity of test locations within the central visual field to 10° eccentricity, the superior hemifield beyond 10°, and the inferior hemifield beyond 10° (hemifield LRA); and (3) the mean sensitivity of test locations within each quadrant (quadrant LRA). For each of the three LRA methods, the criterion used to classify progression was any statistically significant, negatively sloping regression line in one or more subdivisions (P ≤ 0.05). The approach was identical with both FDT and SAP. All methods of analysis and criteria used to determine glaucomatous visual field progression are summarized in Table 1.

Statistical Analysis

We calculated the number of patients in whom glaucomatous visual field progression was identified with FDT and SAP, for each GCP and LRA criterion. For patients who showed progression with both techniques, the difference in time to progression and the concordance of the region of progression was also analyzed. To determine the concordance between the region of progression with FDT and SAP, a number was assigned, where 1 was progression in the superior hemifield, 2 was progression in the inferior hemifield, and 3 was progression in both regions, and the percentage agreement was calculated. The κ statistic was used to evaluate the significance of agreement. In addition, for patients who were classified as showing progression, we determined the concordance between the GCP and linear regression methods of analysis within each perimetric technique using percent agreement and the κ statistic.

The assumptions underlying each of the statistical tests used were verified, checks were made for outliers, and goodness of fit statistics were evaluated for regression analysis models. All statistical tests (SPSS, ver. 12.0 for Windows; SPSS Inc., Chicago, IL) were two-tailed.

RESULTS

Patient Demographics

There were 65 patients with glaucoma in this study (34 men and 31 women) whose mean age at baseline was 63 ± 11 years. The median follow-up was 3.5 years (range, 2.0–4.5 years), and the median number of examinations was 9 (range, 6–11), with both FDT and SAP. The mean MD for FDT at baseline was −4.28 ± 4.29 dB and for SAP was −5.89 ± 4.62 dB.

Progression with FDT and SAP Determined by GCP Analysis

Predictably, with both FDT and SAP, as the criterion for the required number of deteriorating test locations was increased, progression was shown in fewer patients (Fig. 1). In fact, if three or more deteriorating locations were required with FDT, or seven or more were required with SAP, fewer than four (6%) patients showed progression. Likewise, as more examinations were required for confirmation, progression was identified in fewer patients. For the least conservative location and confirmation criteria used with each perimetric technique (i.e., one progressing location in 2-of-3 examinations with FDT and two progressing locations in 2-of-3 examinations with SAP), progression was shown in 32 (49%) patients with FDT and 32 (49%) with SAP. Of the total 27 progression criteria analyzed, 3 classified an equal proportion of patients as showing progression with FDT and with SAP, and 9 classified a greater proportion of patients as showing progression with FDT than with SAP. For example, using progression criteria of 1 FDT or 2 SAP locations and increasing the required number of deteriorating test locations was increased to 2 FDT or 6 SAP locations and confirmation was required in 2-of-3 examinations, 10 (15%) patients showed progression with FDT, whereas progression was identified in only 10 (15%) with SAP. In a further example, in which the required number of progressing test locations was increased to 2 FDT or 6 SAP locations and confirmation was required in 2-of-3 examinations, 10 (15%) patients showed progression with FDT compared with 5 (8%) with SAP.

For patients in whom both FDT and SAP showed progression, there was a similar pattern of results (Fig. 2). Again, as the number of deteriorating test locations and confirmation examinations was increased, fewer patients were classified as showing progression. At most, 16 (25%) patients had progression shown with both FDT and SAP. The proportion of patients with progression reached its lowest value when a criterion of 2 FDT and 6 SAP test locations was used (FDT:SAP = 2:6, Fig.
The percentage of patients classified as showing progression with FDT before SAP, and SAP before FDT, for various test location criteria where \( n = 4 \) or more, are shown in Figure 3. Results are shown only for confirmed progression in 2-of-3 examinations. This confirmation criterion classified a large enough number of patients as showing progression with both FDT and SAP for meaningful comparisons, and the results are representative of the pattern of findings for the 2-of-2 and 3-of-3 confirmation criteria. For a criterion of 1 FDT and 2 SAP test locations (FDT:SAP = 1:2), 44% of 16 patients showed progression with FDT before SAP and the same proportion with SAP before FDT. For the more conservative criterion of 1 FDT and 3 SAP test locations (FDT:SAP = 1:3), FDT progression occurred before SAP in most of the patients (60% of the 10 who showed progression with both FDT and SAP). Contrary to this, as the required numbers of test locations were further increased (FDT:SAP = 2:3 and 2:4 in Fig. 3), progression occurred with SAP before FDT in the majority of patients (75% of the four in whom both FDT and SAP showed progression).

Regardless of whether progression occurred first with FDT or SAP, the two techniques varied by as little as 6 and as much as 30 months in the time at which they identified progression. Figure 4 shows the difference in time to progression between FDT and SAP for the criterion classifying the greatest number of patients as showing progression with both techniques (i.e., FDT:SAP = 1:2 test locations in 2-of-3 confirmation examinations). When progression was shown with FDT first, it was by a median of 12 months earlier than SAP. When progression was shown with SAP first, it was by a median of 18 months earlier than FDT. A similar pattern of results was found using a criterion of FDT:SAP = 1:3 locations in 2-of-3 confirmation examinations. The time to progression with FDT and SAP for two case examples is compared in Figure 5, which shows the GCP analyses of a patient showing progression with FDT before SAP and a patient showing progression with SAP before FDT, depending on the progression criteria used. For the two location criteria that classified progression in the greatest number of patients with both techniques in 2-of-3 confirmation examinations (i.e., FDT:SAP = 1:2 and 1:3 test locations) the concordance of the region of progression was 56% and 50%, respectively (Table 2). This level of agreement between region of progression with FDT and SAP was not statistically significant \( (P > 0.05); \) Table 2).

Progression with FDT and SAP Determined by LRA

Of the three methods of visual field subdivision used in LRA, progression was classified in more patients using the quadrant method than using the hemifield or global methods (Fig. 6). Furthermore, more patients showed progression with SAP compared with FDT for all LRA methods (Fig. 6). The number of patients showing progression with FDT ranged from 8 (12%) using global LRA, to 20 (31%) using quadrant LRA, and using SAP ranged from 14 (22%) using global LRA, to 23 (35%) using quadrant LRA. The range of patients showing progression with both FDT and SAP ranged from 3 (5%) using global LRA, to 10 (15%) using quadrant LRA. In the 10 patients (15%) identified as having progression with both FDT and SAP using quadrant LRA, the concordance of the region of progression was 60% (Table 2). This level of agreement between region of progression with FDT and with SAP was statistically significant \( (P = 0.02); \) Table 2).

Agreement between GCP and LRA

The agreement between the two methods of analysis within each perimetric technique was determined for criteria of 1 FDT location progressing in 2-of-3 examinations, 2 SAP locations progressing in 2-of-3 examinations, and quadrant LRA, as
these classified sufficient patients with progression for a meaningful comparison (Fig. 7). For those patients classified as showing progression using one or more of these criteria, the concordance between GCP and LRA was 37% for patients showing progression with FDT, 38% with SAP, and 37% with both. The agreement between GCP and LRA was significant for patients in whom progression was identified with FDT and with both FDT and SAP, but just failed to reach statistical significance with SAP (Fig. 7).

**DISCUSSION**

Since its introduction, FDT perimetry has become a more widely used technique for both screening and follow-up of glaucomatous visual field loss. There are various theories on the mechanisms that make it a more logical choice of visual field test in glaucoma. Originally, the response to an FDT-type stimulus was considered to be mediated by spatially nonlinear mechanisms in the magnocellular (MC) pathway—a subset of RGCs in the MC pathway, the My cells, (Maddess T, et al. **IOVS** 1990;31:ARVO Abstract 1134).6-23 However, this theory was based on the cat model of vision, and its applicability to humans is uncertain. In a recent physiological study, White et al.24 found no evidence of a separate subset of nonlinear My cells in the primate retina. In addition, Anderson and Johnson25 found no evidence that the contrast sensitivity to an FDT stimulus differs from a spatially uniform flickering stimulus at high temporal frequencies. This suggests that the mechanisms underlying the two tasks are similar,25 and that the FDT stimulus does not test a specific subset of MC cells, but rather it seems likely to test the contrast sensitivity of MC cells in general.24 Nevertheless, MC cells have large-diameter axons, and some histologic studies have shown that RGCs with large-diameter axons may be preferentially damaged in early glaucoma.4,26 Indeed, this was the premise on which FDT perimetry was developed, that MC RGCs are preferentially damaged in early glaucoma and that the FDT stimulus would selectively test those cells.7 However, this selectivity theory has since been questioned.27,28 Regardless of whether the theory is correct, FDT is likely to be sensitive to glaucomatous visual field losses because it tests a sparse population of RGCs. MC RGCs comprise approximately only 10% of the entire RGC population.29 Stimulating only this population reduces RGC redundancy.27,30 There is reduced ability of the visual system to use other subsets of RGCs to compensate for damaged RGCs of the type being tested.28 Also, damage to one RGC within a sparse subset of RGCs is more likely to have a greater effect on visual function than damage to one of numerous RGCs.27

In this study, we found that FDT identified progression in more patients than did SAP, for the majority of GCP criteria. In addition, the proportion of patients showing progression with both FDT and SAP was small (at most, 25%). These findings may suggest a difference in the sensitivity of each technique; however, the different progression rates obtained may have been in part due to the criteria chosen for the required number of progressing test locations. Although we attempted to equalize the required number of progressing FDT and SAP locations and we investigated several alternatives, it is possible that there was some imbalance that influenced the results. Verification of balanced progression criteria is difficult, and this is a limitation of current methods of progression analysis. One approach would be to study progression rates with each perimetric technique in a control group (i.e., specificity). A large sample size would be necessary to obtain a meaningful indication of whether the chosen progression criteria were of equal specificity and indeed balanced. Another possible interpretation of our findings, given the low percentage of patients in whom both FDT and SAP showed progression, is that the two techniques may have been identifying different subgroups of patients with glaucoma.

Similar to our GCP results, Bayer and Erb15 found that a greater proportion of their total study sample of patients with open-angle glaucoma showed progression with FDT than with SAP (51% and 39% with FDT and SAP, respectively). A relatively small proportion (29%) of the 138 eyes with primary open-angle glaucoma they investigated at 6-month intervals over a period of 30 months, showed progression with both FDT and SAP. Although these findings have a pattern comparable to ours, the progression rates found by Bayer and Erb are greater in magnitude. To some extent this may be due to their study sample comprising patients with more advanced glaucoma (mean SAP baseline MD −9.02 dB and mean baseline cup-to-disc ratio 0.76, at a mean age of 53 years). However, we propose that it is mostly due to the use of different methods and progression criteria. Bayer and Erb used the Collaborative Normal Tension Glaucoma Study Group progression criteria for SAP (which they considered sensitive to minimal progression).31 For FDT, they used a criterion of one abnormal test location (P < 5%) verified in 2-of-3 examinations performed at 1 and 3 months after initial detection.15 Indeed, our present investigation demonstrated that the specific percentage of patients classified as showing progression varied depending on the criteria chosen, even within a single study sample and within a single method of analysis. We found that as more progressing locations and more confirmation examinations were required for GCP analysis, the percentage of patients classified as showing progression decreased, a finding that is supported by other studies that have applied GCP analysis to SAP.32-34 Therefore, it is very likely that specific progression rates will vary between studies using different methods and progression criteria.

Our GCP results also indicated that FDT identified progression before SAP in the majority of patients with glaucoma, when fewer locations were required to classify progression. For these patients, FDT identified progression before SAP by a median of 12 months, which is consistent with the findings of Bayer and Erb,15 despite the different progression criteria. However, our results also indicated that when the progression...
criterion was made more conservative and more locations required, SAP identified progression before FDT in most of the patients, although it should be noted that the absolute number of patients classified by the more conservative criteria used in this study was small. Further investigation with a larger sample size and longer follow-up is necessary to confirm these findings.

LRA also yielded paradoxical findings. More patients showed progression with SAP than with FDT, for all methods of visual field subdivision to which LRA was applied. Using quadrant LRA, 31% of patients showed progression with FDT and 35% with SAP. However, it should be noted that the difference in the percentage with progression identified by each technique was small, and the clinical importance of such
total deviation maps are shown in the first column, and follow-up GCP maps in the second column. Shaded circles: progressing locations for each perimetric technique using various criteria. For the patient in (A), using a criterion of FDT:SAP/H110051:2 deteriorating locations in 2-of-3 consecutive examinations, progression with FDT was confirmed in September 2000, 13 months earlier than with SAP, with which progression was confirmed in October 2001. The difference in time to progression was greater using a criterion of FDT:SAP/H110051:3 locations in 2-of-3 examinations, where progression with FDT was confirmed 26 months earlier than with SAP (September 2000 with FDT compared with November 2002 with SAP). However, using a criterion of FDT:SAP/H110052:4 locations in 2-of-3 examinations, progression was not identified with FDT until 6 months after SAP (May 2003 with FDT compared with November 2002 with SAP). In comparison, for the patient in (B), using a criterion of FDT:SAP/H110051:2 locations in 2-of-3 examinations, progression with SAP was confirmed 30 months earlier than with FDT (November 2000 with SAP compared with May 2003 with FDT). The difference in time to progression was less (12 months), using a criterion of FDT:SAP/H110051:3 locations in 2-of-3 examinations (May 2002 with SAP compared with May 2003 with FDT). These cases show the discordance between the perimetric techniques and the dependence of progression on the criteria used.

**Figure 5.** GCP analysis. Case examples of two patients (A, top two rows; B, bottom two rows), followed with FDT and SAP examinations. Baseline total deviation maps are shown in the first column, and follow-up GCP maps in the second column. Shaded circles: progressing locations for each perimetric technique using various criteria. For the patient in (A), using a criterion of FDT:SAP/H110051:2 deteriorating locations in 2-of-3 consecutive examinations, progression with FDT was confirmed in September 2000, 13 months earlier than with SAP, with which progression was confirmed in October 2001. The difference in time to progression was greater using a criterion of FDT:SAP/H110051:3 locations in 2-of-3 examinations, where progression with FDT was confirmed 26 months earlier than with SAP (September 2000 with FDT compared with November 2002 with SAP). However, using a criterion of FDT:SAP/H110052:4 locations in 2-of-3 examinations, progression was not identified with FDT until 6 months after SAP (May 2003 with FDT compared with November 2002 with SAP). In comparison, for the patient in (B), using a criterion of FDT:SAP/H110051:2 locations in 2-of-3 examinations, progression with SAP was confirmed 30 months earlier than with FDT (November 2000 with SAP compared with May 2003 with FDT). The difference in time to progression was less (12 months), using a criterion of FDT:SAP/H110051:3 locations in 2-of-3 examinations (May 2002 with SAP compared with May 2003 with FDT). These cases show the discordance between the perimetric techniques and the dependence of progression on the criteria used.

**Table 2.** Agreement between Region of Progression with FDT and SAP, Using GCP and LRA

<table>
<thead>
<tr>
<th>Progression Criteria</th>
<th>Patients with Concordance of Region of Progression n (% agreement)*</th>
<th>κ Statistic</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDT:SAP /H11005 1:2 locations in 2-of-3 examinations</td>
<td>9 (56)</td>
<td>0.21</td>
<td>0.23</td>
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<tr>
<td>FDT:SAP /H11005 1:3 locations in 2-of-3 examinations</td>
<td>5 (50)</td>
<td>0.15</td>
<td>0.43</td>
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<tr>
<td>LRA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Quadrant method</td>
<td>6 (60)</td>
<td>0.43</td>
<td>0.02</td>
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</tbody>
</table>

* Number of patients with agreement in region of progression out of the number progressing with both FDT and SAP.
a difference is unknown. As with GCP analysis, we found the percentage of patients showing progression with both FDT and SAP using LRA was small (at most 15%). Unlike the results of GCP, using LRA we found a significant moderate agreement between the region of progression with FDT and SAP (κ = 0.43, P = 0.02).

LRA results in this study also showed that more patients were classified as showing progression when the method was applied to smaller visual field subdivisions. We found that more patients showed progression when LRA was applied to the mean threshold of quadrants in the visual field than when it was applied to hemifields or to the mean threshold of all test locations. This was the case with both FDT and SAP and is consistent with results in several SAP studies investigating LRA, which demonstrate higher progression rates for more specific methods (e.g., pointwise LRA) compared with global methods (e.g., MD LRA). It is likely that global methods, such as MD and mean threshold of all test locations, attenuate and fail to capture important information from the typically localized changes in glaucoma, whereas smaller visual field subdivisions are better able to capture such information.

Directly comparing the two methods of analysis used in this study, we found that for the least conservative progression criteria, GCP classified a higher percentage of patients as showing progression compared with LRA. Furthermore, we found that the concordance between GCP and LRA was low (<40%), which is consistent with the findings of an SAP study using computer simulation. We suggest that there may be several factors influencing these findings. First, the specific progression criteria used for GCP and LRA are likely to influence progression rates, as also demonstrated by McNaught et al. Second, short- and long-term fluctuation may have a different effect on the progression rate determined by GCP and LRA. Also, the assumption underlying the use of LRA is that there is a gradual, linear visual field loss in glaucoma. Although this has been shown in the majority of cases, and linear models of progression seem the most appropriate, episodic patterns have been documented. It has been suggested that GCP may be additionally sensitive to such patterns of progression.

In conclusion, we have shown that FDT perimetry was able to detect glaucomatous visual field progression. However, the proportion of patients showing progression depended on the method of analysis and the criterion used to define progression. Indeed, the progression rate with FDT was greater than with SAP for the majority of progression criteria investigated using GCP analysis, and on the contrary, the progression rate with SAP was greater than FDT using LRA. It is possible that the two perimetric techniques and the two methods of analysis identify different glaucoma subgroups. Irrespective of this possibility, our investigation suggests that studies using different methods to analyze glaucomatous visual field progression, or even different progression criteria within one particular method, are likely to yield inconsistent results. At present, there is no method of analysis or progression criterion that has gained universal acceptance. Until then, comparisons between...
any two perimetric techniques, both within and between studies, will remain a topic of considerable debate.

References