Comparison of Conventional and High-Pass Resolution Perimetry in a Prospective Study of Patients With Glaucoma and Healthy Controls

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Objective: To determine whether high-pass resolution perimetry detected glaucomatous visual field progression earlier than conventional perimetry.

Methods: In a prospective longitudinal study, we observed 113 patients with open-angle glaucoma and with early to moderate visual field damage and 119 healthy control subjects. Each subject underwent testing at 6-month intervals using conventional and high-pass resolution perimetry (program 30-2 of the Humphrey Field Analyzer [Humphrey Instruments, Inc, San Leandro, Calif] and the Ring program of the Ophthimus perimeter [Hi-Tech Vision, Göteborg, Sweden], respectively). Our predetermined criterion for progression with conventional perimetry was the presence of at least 4 overlapping nonedge locations outside the fifth percentile for test-retest variability of threshold deviations (defined by the Glaucoma Change Probability Analysis of the Statpac 2 program) in 2 of 3 consecutive visual fields. We employed the identical criterion for progression with high-pass resolution perimetry using our own test-retest variability data. We repeated this procedure in the controls to measure the false-positive rate of progression.

Results: Patients were observed for a median of 4.5 years and 11 examinations with each technique. Fifty-seven patients (50.4%) did not show progression with either technique. Twenty-four patients (21.2%) showed progression with high-pass resolution perimetry alone, whereas 6 (5.3%) showed progression with conventional perimetry alone. Of the remaining 26 patients (23.0%) who showed progression with both techniques, 14 (54%) showed progression with high-pass resolution perimetry first (median, 12 months earlier); 5 (19%), with conventional perimetry first (median, 6 months earlier); and 7 (27%), with both techniques at the same time. Controls were observed for a median of 5 years and 11 examinations with each technique. One control (0.8%) showed progression with high-pass resolution perimetry.

Conclusions: Our results suggest that high-pass resolution perimetry detects glaucomatous visual field progression earlier than conventional perimetry in most patients with progression.

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Detecting visual field progression in open-angle glaucoma remains one of the most important and challenging aspects of glaucoma management. Decisions, such as whether to proceed to surgery, may depend critically on evidence of early and reproducible field progression. Whereas static perimetry has benefited greatly from computerization,1,2 standardization of testing algorithms,3 and development of sophisticated data analysis tools,3,5 it may not be capable of detecting the earliest progression in glaucoma.6,7

Glucoma results in the death of retinal ganglion cells. The primate retina primarily contains parvocellular retinal ganglion cells that are responsible mostly for form and color vision and the sparser magnocellular retinal ganglion cells that are responsible mostly for motion and flicker.8 Since conventional perimetry uses a static achromatic stimulus, it is thought to invoke nonselectively both ganglion cell systems. In addition, since there is considerable overlap in the receptive fields of retinal ganglion cells,9,10 a nonselective stimulus may not be sensitive to the earliest, or further, loss of retinal ganglion cells due to the considerable redundancy in the coverage of a given location in the retina.6 There is histopathological evidence to suggest that considerable ganglion cell loss can occur before thresholds measured using conventional perimetry are altered.11,12

Techniques that selectively test the parvocellular or magnocellular systems, or those that are more sensitive to detecting early loss in the physiological redundancy of the retinal ganglion cells, have been developed. These include short-wavelength

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SUBJECTS AND METHODS

SUBJECTS

Our study commenced in July 1991. Patients with glaucoma were recruited on a consecutive basis from the practice of one of us (R.P.L.) and from the Nova Scotia Eye Centre Glaucoma Clinic, Halifax. Controls were recruited from seniors' groups, local church organizations, and employees of a local telephone company. The study was approved by the Camp Hill Medical Centre Research Ethics Committee, Halifax.

Patients were included if all of the following inclusion criteria were met: (1) diagnosis of open-angle glaucoma with characteristic glaucomatous optic disc damage, (2) a visual field with a mean deviation index of −2 to −10 dB, (3) normal open angles determined by gonioscopy, (4) best corrected visual acuity of at least 20/40, and (5) willingness to give informed consent to participate in the study. Patients were excluded if any of the following were found: (1) concomitant ocular disease, (2) systemic disease or systemic medication known to affect the visual field, (3) refractive error exceeding 5 diopters (D) equivalent sphere or 3 D of astigmatism, and (4) contact lens wear.

Controls were included if all of the following inclusion criteria were met: (1) normal ocular examination, (2) best corrected visual acuity of at least 20/40, (3) intraocular pressure of no more than 21 mm Hg, (4) family history negative for glaucoma, and (5) willingness to give informed consent to participate in the study. Controls were excluded if any of the following were found: (1) systemic disease or systemic medication known to affect the visual field, (2) refractive error exceeding 5 D equivalent sphere or 3 D of astigmatism, and (3) contact lens wear.

PERIMETERS

Conventional perimetry was performed using program 30-2 of the Humphrey Field Analyzer (Humphrey Instruments Inc, San Leandro, Calif) using the appropriate refractive correction. High-pass resolution perimetry was performed using the Ring program of the Ophthimus perimeter (Hi-Tech Vision, Göteborg, Sweden). This technique has been detailed elsewhere. In brief, a personal computer is used to generate the ring stimuli on a computer display monitor mounted on an articulated arm. The monitor is placed in front of the seated subject, and special large-aperture lenses are mounted on an arm attached to the monitor to correct for the testing distance of 16.7 cm. Stimulus size is incremented logarithmically, and thresholds are reported in ring units. A total of 50 visual field locations are tested in the central 30° of the visual field (Figure 2). As in conventional perimetry, fixation in high-pass resolution perimetry is monitored using the Heijl-Krakau technique.

TESTING PROTOCOL

Subjects first underwent a full ophthalmic examination. If both eyes were eligible for the study, 1 eye was randomly assigned as the study eye and was the only eye tested for the study. Visual field examinations were then performed using conventional perimetry and high-pass resolution perimetry. The patients with glaucoma underwent retesting with each technique after 1 week to establish a baseline. Follow-up visual field examinations were then performed at 6-month intervals. The order of testing (ie, conventional perimetry or high-pass resolution perimetry first) was randomized at each visit. All patients were experienced with conventional visual field testing, but were not previously exposed to high-pass resolution perimetry. None of the controls had any previous visual field experience. Pupils that were not at least 3 mm were dilated with 0.8% tropicamide and 5% phenylephrine hydrochloride for the visual field examination. All visual field examinations were performed using automated perimetry,\textsuperscript{13,16} motion perimetry,\textsuperscript{15,16} peripheral displacement perimetry,\textsuperscript{17,18} pattern discrimination perimetry,\textsuperscript{19} and high-pass resolution perimetry.\textsuperscript{20}

The stimulus employed in high-pass resolution perimetry is a ring with dark borders and a bright core (Figure 1). The stimulus is high-pass filtered\textsuperscript{21} such that the space-averaged luminance of the borders (15 candelas [cd/m\textsuperscript{2}]) and the core (25 cd/m\textsuperscript{2}) equal that of the background (20 cd/m\textsuperscript{2}). Because thresholds are expressed in size increments with fixed contrast, it is a fundamentally different task compared with conventional perimetry, where thresholds are expressed in contrast increments with fixed stimulus size. High-pass resolution perimetry is thought to test selectively the parvocellular system,\textsuperscript{22} and there is some evidence to suggest a linear relationship between threshold and retinal ganglion cell density.\textsuperscript{23,24}

Other studies indicate that high-pass resolution perimetry has good sensitivity to detect visual field loss in glaucoma\textsuperscript{25,26} and benign intracranial hypertension,\textsuperscript{27} when the diagnostic classification has been made with conventional perimetry. It also has been reported to have good specificity\textsuperscript{20,27}; short-term\textsuperscript{28,29} and long-term\textsuperscript{30} threshold variability that is independent of threshold, visual field eccentricity, and age; and reliability criteria that are at least as good as those of conventional perimetry.\textsuperscript{31} Our purpose was to determine whether high-pass resolution perimetry could detect visual field progression earlier than conventional perimetry in a prospective longitudinal study of patients with early to moderate glaucomatous visual field loss and in healthy control subjects.

RESULTS

There were 113 patients with glaucoma (55 men and 58 women) in the study. The median age at baseline was 64 years (range, 17-89 years). At the time of data analysis (November 1997), the median number of conventional and high-pass resolution visual field examinations per patient was 11 (range, 5-13), with a median follow-up time of 4.5 years (range, 1.5-5.5 years). The mean (±SD) test time with conventional perimetry was 16.77 (±1.90) minutes per test, whereas for high-pass resolution perimetry it was 5.81 (±0.50) minutes.

Fifty-seven patients (50.4%) showed no progression with either technique during follow-up. Of the re-
formed by the same technician (T.A.M.) on the same Humphrey Visual Field Analyzer and Ophthimus perimeter.

DATA ANALYSIS

We analyzed progression of the visual field with conventional perimetry using the Glaucoma Change Probability Analysis described by Heijl et al. This analysis, which is available on the Statpac 2 (Humphrey Instruments) program, establishes a mean visual field from results of 2 individual examinations and then calculates the difference in threshold at all tested locations in each subsequent visual field. Any location at which the difference in the threshold deviation between follow-up and baseline falls outside the 95th or 5th percentiles for test-retest variability in patients with stable glaucoma is indicated as a white triangle (probable improvement) or black triangle (probable deterioration), respectively. This analysis is performed for all follow-up fields. The percentiles are derived from test-retest variability data of patients with varying severity of glaucomatous visual field defects.

In the analysis we first removed all the edge points from the program 30-2 pattern, leaving 50 locations in total. Suspected progression was said to have occurred if there were at least 4 black triangles in a follow-up visual field. Confirmed progression was said to have occurred if there was complete overlap in the location of at least 4 of these black triangles in the next or immediately following visual field. The date of confirmed progression was taken as the progression date. The time to progression (from baseline) was then calculated.

We analyzed progression with high-pass resolution perimetry in the identical manner as that described for conventional perimetry. We derived test-retest confidence intervals stratified by defect depth based on the same data set (second, third, and fourth examinations); however, we used a jackknife technique to remove bias. Thus, when a given patient's data was analyzed for progression, he or she did not contribute toward the data used to derive the percentiles. To reduce the effect of learning with high-pass resolution perimetry (which is usually complete after the first examination), we removed the first visual field from the analysis. Therefore, the mean of the 7-day and 6-month examinations was taken as the baseline (compared with the 0- and 7-day visual fields for conventional perimetry) against which subsequent visual fields were compared. A computer program written by us was used to perform the calculations and print out black circles (analogous to the black triangles in the Glaucoma Change Probability Analysis of the Statpac 2 program) in the follow-up high-pass resolution visual field printouts.

Since there are 50 tested locations in high-pass resolution perimetry and good spatial overlap between the locations analyzed with both techniques (Figure 3), we used the identical criteria for high-pass resolution perimetry as for conventional perimetry, ie, at least 4 black circles for suspected progression and complete overlap in the location of at least 4 of these black circles in the next or immediately following visual field for confirmed progression. The time to progression (from baseline) was then calculated.

We next determined the number of controls who showed confirmed progression with high-pass resolution perimetry (false-positive rate). Because we removed the first visual field from the analysis, the baseline was the mean of the 6- and 12-month examinations. The test-retest variability data were derived from the same normal data set using a jackknifing technique. The criteria for progression were identical to those described for the patients.

The analysis for progression was performed by 2 independent observers who were unaware of the identity of the patient, all clinical information, results from the other technique, and results of the other observer. A third observer arbitrated any discrepancies.

Of the 26 patients who showed progression with both techniques, 14 (54%) showed progression first with high-pass resolution perimetry at a median of 12 months before showing progression with conventional perimetry.
(Figure 4). Five (19%) showed progression first with conventional perimetry at a median of 6 months before showing progression with high-pass resolution perimetry (Figure 5). Seven (27%) showed progression at the same time with both techniques. In all 26 patients, there was complete spatial concordance with respect to the hemifield where the progression occurred.

There were 119 healthy controls (51 men and 68 women) in the study. The median age at study baseline was 47 years (range, 30-84 years). At the time of data analysis, the median number of conventional and high-pass resolution visual field examinations per control was 11 (range, 3-14), with a median follow-up time of 5 years (range, 2-6.5 years). The mean (±SD) test time with conventional perimetry was 14.33 (±1.57) minutes, whereas with high-pass resolution perimetry it was 5.43 (±0.51) minutes. Two controls showed confirmed progression with high-pass resolution perimetry. Glaucoma actually developed in 1 of these subjects. At the time of diagnosis, he had a thin inferior neuroretinal rim with a corresponding superior visual field defect with conventional perimetry (confirmed with the Glaucoma Hemifield Test). His intraocular pressure at diagnosis was 23 mm Hg (compared with 20 mm Hg at enrollment). The false-positive rate of progression with high-pass resolution perimetry was therefore 1 (0.8%) of 119.

To determine whether visual acuity changed during the follow-up for the patients and controls, we analyzed the visual acuity data at baseline and at the last examination. These results showed that 105 patients (92.9%) maintained a visual acuity of 20/30 or better, whereas 118 controls (99.2%) maintained a visual acuity of 20/30 or better. The visual acuity data at baseline and at last visit were converted to logMAR (logarithm of the minimum angle of resolution) to compare the...
Figure 6. Left, Right optic disc of patient 1 (71-year-old man) at baseline (1992) showing inferior notching and a superior temporal peripapillary disc hemorrhage. Right, Five years later (1997), there is thinning of the neuroretinal rim both inferiorly and superiorly adjacent to the site of the previous disc hemorrhage.
change in acuity in the group of patients who did not show progression with either technique with those who showed progression with 1 or both (Figure 5). In the no-progression group, the mean (±SD) logMAR visual acuity at baseline and at last visit were 0.17 (±0.19) and 0.14 (±0.20), respectively, whereas in the progression group the respective figures were 0.12 (±0.18) and 0.16 (±0.25). The change in visual acuity for either group (equivalent to 0.2 Snellen lines) failed to reach statistical significance (P>.10).

REPORT OF CASES

Patient 1 showed optic disc change during follow-up (Figure 6) and visual field progression with high-pass resolution perimetry 2 years before showing progression with conventional perimetry (Figure 7). Patient 2 showed substantial optic disc change during follow-up (Figure 8); however, visual field progression has been detected with high-pass resolution perimetry only (Figure 9).

COMMENT

Our study demonstrated that high-pass resolution perimetry detected progression of glaucomatous visual field loss a median of 12 months earlier than conventional perimetry in 14 (54%) of the 26 patients who showed progression with both techniques. Conventional perimetry showed progression a median of 6 months earlier in 5 (19%) of 26, whereas progression was detected at the same time in the remaining 7 (27%). Our results suggest that high-pass resolution perimetry is more efficacious than conventional perimetry at detecting glaucomatous
Figure 8. Left, Right optic disc of patient 2 (54-year-old woman) at baseline (1992). Right, Four years later (1996), there is a diminution of the neuroretinal rim, particularly inferiorly and temporally.
progression. Considering the short test time of high-pass resolution perimetry (by a factor of 2.5 to 3 compared with conventional perimetry), good reliability indices, and high patient acceptability, the technique also offers some substantial practical advantages.

Defining criteria for the amount of visual field change in studies that require visual field progression as an end point is problematic. Since there usually never is a definitive and external criterion for progression, the criteria for visual field progression are necessarily arbitrary and based mostly on clinical experience. We chose a probabilistic approach based on test-retest variability instead of absolute changes in decibels or ring units for each technique separately. This method allowed a degree of standardization between techniques because, due to the different psychophysical nature of both techniques and the dynamic range of testing, a direct comparison cannot be made between the techniques with respect to the amount of absolute change required for progression. In addition, because the same number of locations in the analysis of each technique was used and the same number of locations to exceed the variability limits (measured for each technique separately) for progression was required, we believed the comparison was valid. Based on the same probabilistic approach, we also determined how many healthy controls showed false progression with high-pass resolution perimetry. In this case, the changes required for significance were determined from variability limits in the controls and not in the population with glaucoma.

High-pass resolution perimetry is fundamentally a peripheral visual acuity test, and therefore, like any task requiring resolution of high-spatial frequency targets, it is sensitive to media opacities and blur. Accordingly, we wanted to rule out the possibility that patients had a

![Follow-up visual fields of the right eye of patient 2 from November 3, 1992, to October 10, 1997 (dates of examination are given in column 5), showing diffuse damage (columns 1 and 2). Glaucoma Change Probability Analysis (column 4) with conventional perimetry does not show visual field progression to date. High-pass resolution perimetry also shows diffuse damage (column 6), and a similar analysis for change (column 7) confirmed superior progression on September 20, 1995 (asterisk).](image-url)
preferential elevation in resolution thresholds compared with differential light thresholds due to the possible development of early and clinically insignificant cataract. Although our study did not formally grade lens clarity, we undertook an analysis of visual acuity and found that most patients retained very good or excellent visual acuity throughout the follow-up. In addition, we were unable to show a statistically significant difference between the visual acuity data at baseline and at last visit in patients who showed visual field progression. Similarly, patients who remained stable also did not show a significant change in visual acuity. House et al. measured lens opacity in a group of healthy subjects aged 20 to 80 years and found that mean resolution thresholds varied by less than 1 ring unit across this age range, and that once age was accounted for, further variation in resolution thresholds were not due to the lens opacity measurements. It is unlikely that aging effects on the lens result in changes in ring thresholds of more than 1 ring unit. In a recent study, Martin showed that in healthy subjects in whom cataracts degraded visual acuity to 20/60, resolution thresholds improved by only 1 ring unit postoperatively after restoration of normal visual acuity.

In our study, the amount of change required from baseline to follow-up to result in significant change at a given location (ie, position of the 5th percentile for retest variability) was typically greater than 2 ring units. Based on these variability limits, the stability of visual acuity in our study, and evidence from other studies, it appears highly unlikely that lens changes can account for the higher number of patients showing progression with high-pass resolution perimetry alone or for high-pass resolution perimetry detecting progression earlier than conventional perimetry.

In the prospective evaluation of new psychophysical tests, it is imperative that there be a parallel healthy control group, since it is difficult to attribute progression detected with the newer technique (and not with conventional perimetry) to greater sensitivity or to false progression. In a parallel group of healthy controls, we determined that a very low percentage (1/119 [0.8%]) of subjects showed false progression. Whereas our control group had a similar age range to that of the patients, we acknowledge that the median age was lower. It may have been useful to conduct a similar analysis for the healthy controls with conventional perimetry; however, the Glaucoma Change Probability Analysis with the Statpac 2 program is valid only for patients with glaucoma, because when matched for threshold deviation, these patients have higher test-retest variability than controls. Furthermore, it was more critical to determine whether high-pass resolution perimetry resulted in falsely high progression rates, given the findings in the patients with glaucoma. Because there was only 1 false-positive case in our control group, it is unlikely that the 24 patients (21.2%) showing progression with high-pass resolution perimetry alone had false-positive results; however, further follow-up will determine whether they will eventually show progression with conventional perimetry.

Compelling evidence suggests that some new psychophysical tests, particularly short-wavelength automated perimetry, detect glaucomatous progression earlier than conventional perimetry. These findings are compatible with the better specificity of the test stimuli used compared with conventional perimetry. Our findings suggest that high-pass resolution perimetry, which has a substantially reduced test time compared with conventional and short-wavelength automated perimetry and better patient acceptance, is also more efficacious than conventional perimetry at detecting progression. The issue of shorter test time is of considerable practical importance, and research should focus on other tests with shorter test times as well as on new time-saving algorithms that are used with conventional perimetry.

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REFERENCES


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A look at the past . . .

WILLIAM MACKENZIE, 1791-1868, ophthalmologist and founder of the Glasgow Eye Infirmary, Glasgow, Scotland, in 1824. His book, Practical Treatise on the Diseases of the Eye, first published in 1830, became the standard work in ophthalmology for his generation. This medal, Figure 1, obverse, and Figure 2, reverse, is an example of the annual MacKenzie Award Medal of the Glasgow Eye Infirmary. It was originally made by the sculptress Kathleen Scott, Birmingham, England, in 1931.

Courtesy of: Jay M. Galst, MD, 30 E 60th St, New York, NY 10022.