

Comparison of Long-term Variability for Standard and Short-wavelength Automated Perimetry in Stable Glaucoma Patients

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• **PURPOSE:** To quantify and compare, on a point-by-point basis, the long-term variability of standard and short-wavelength automated perimetry in a group of stable glaucoma patients.

• **METHODS:** From a group of 53 glaucoma patients experienced in visual field testing, we identified one eye, randomly chosen, from each of 25 glaucoma patients whose condition was found to be stable, based on both standard and short-wavelength automated perimetry visual field criteria. On each of three visits during a period of up to 3 months, each patient performed one standard and one short-wavelength automated perimetry 24-2 visual field in a random order on a Humphrey visual field analyzer. The long-term variability (also referred to as test-retest variability) was defined as the SD of the three threshold decibel values at each test location. The long-term variability for each test point (mean \pm SD) was determined separately for both standard visual fields and short-wavelength automated perimetry.

• **RESULTS:** With all 52 test locations of the 24-2 field averaged, the global long-term variability, mean (\pm SD) for standard visual fields and short-wavelength automated perimetry was 2.37 ± 2.03 dB (95% confidence interval, 2.26–2.48 dB) and 2.92 ± 2.03 dB (95% confidence interval, 2.81–3.03 dB), respectively ($P < .0001$). In 16 of the 52 visual field locations, long-term variability on short-wavelength automated perimetry was significantly higher than long-term variability on standard visual fields. In addition, the long-term variability

increased with greater distance from the point of fixation for both standard visual fields and short-wavelength automated perimetry. The long-term variability decreased closer to fixation, more for standard visual fields than for short-wavelength automated perimetry.

• **CONCLUSIONS:** In a group of stable glaucoma patients, mean long-term variability was 0.55 dB higher for short-wavelength automated perimetry than for standard visual fields. This needs to be taken into consideration when serial visual fields are evaluated for change. (Am J Ophthalmol 2000;129:309–313. © 2000 by Elsevier Science Inc. All rights reserved.)

STANDARD AUTOMATED PERIMETRY IS A GENERALLY accepted method for monitoring visual field damage in glaucoma patients and glaucoma suspects. However, short-wavelength automated perimetry has generated considerable interest because of its potential for earlier detection of glaucomatous visual field defects and more sensitive assessment of visual field progression.^{1–4} One obstacle to the interpretation of short-wavelength automated perimetry fields is the presence of greater long-term variability (also termed test-retest variability) in normal subjects,⁵ which makes differentiation between random variations and true progression more difficult.

Short-term fluctuation is computed from the variability of threshold values found on repeated measurements performed during the same examination. Kwon and associates⁵ and Wild and associates⁶ both showed that short-term fluctuation was significantly higher for short-wavelength automated perimetry than for standard visual fields in normal subjects. Others have shown this difference in short-term fluctuation between standard visual fields and short-wavelength automated perimetry in normal subjects, glaucoma suspects, and glaucoma patients to be much smaller.⁷

As opposed to short-term fluctuation, long-term fluctuation is defined as the variability in threshold values among examinations performed over time, corrected for short-term fluctuation, in the absence of clinically detect-

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able pathologic changes. To describe a change in serial visual fields as true progression, it is necessary to differentiate a true change from the long-term fluctuation. In general, visual field changes attributed to progression should be repeatable and in excess of the long-term fluctuation. It has been previously established in normal subjects⁵ that the long-term fluctuation for short-wavelength automated perimetry is greater than that for standard visual fields. As opposed to long-term fluctuation, long-term variability is a measure of both long-term fluctuation and short-term fluctuation and thus is better suited to describe the total test-retest variability of each individual location. Because long-term fluctuation varies by eccentricity,⁸ we set out to analyze long-term variability separately in each visual field location. The purpose of this study was to quantify and compare the long-term variability in a group of stable glaucoma patients in both standard visual fields and short-wavelength automated perimetry.

METHODS

INCLUSION CRITERIA WERE AGE 39–80 YEARS WITH EVIDENCE of primary open-angle glaucoma in the study eye and intraocular pressure without medication of 18 to 32 mm Hg recorded on two separate visits in the study eye. Primary open-angle glaucoma was defined as glaucomatous optic nerve damage as documented by stereoscopic photographs, and repeatable visual field loss on the 24-2 Humphrey visual field analyzer standard, full-threshold (white-on-white) visual field program. Visual field data were provided by Alcon Laboratories, Fort Worth, Texas, obtained from 14 study centers that observed study patients receiving commonly used pressure-lowering medications.

Optic nerve head damage was defined by the presence of excavation or undermining of the cup, documented cupping, nerve fiber layer defects characteristic of glaucoma, notching, or cup-disk asymmetry of greater than 0.2.

Exclusion criteria on baseline examination included: field loss threatening fixation in either eye; history of acute angle closure, congenital glaucoma, secondary glaucoma, or ocular trauma; history of ocular infection or inflammatory disease within the past 6 months; narrow angles or other angle abnormalities; previous intraocular surgery; use of systemic medications that may affect intraocular pressure; history of severe retinal disease; best-corrected distance visual acuity worse than 20/30; strabismus; refractive error greater than ± 5.00 diopters spherical equivalent or greater than ± 2.50 diopters cylinder; lens opacity exceeding Lens Opacity Classification System III standard photographs⁹ nuclear color 4, nuclear opalescence 4, cortical cataract 3, or posterior subcapsular cataract 2 in either eye; or congenital color vision defects.

Visual field loss on the 24-2 standard visual fields was defined as a glaucoma hemifield test outside normal limits

or corrected pattern standard deviation outside the 95% normal limits. Patients with advanced loss (defined as a mean deviation worse than -10 dB) were excluded.

One eye per patient was randomly selected. Before enrollment in this study, all patients performed eligibility visual fields (one standard and one short-wavelength automated perimetry visual field in each eye), which reduced the likelihood of a residual learning curve effect on the long-term variability. These eligibility visual fields were used only to select patients for the study and were not used for the study itself. All visual fields were performed on Humphrey Field Analyzer I or II (Humphrey-Zeiss, Dublin, California). Reliability criteria included fixation losses of 25% or less, false-positive responses of 25% or less, and false-negative responses of 25% or less. Whenever any given field did not meet the above reliability criteria, it was repeated within 2 weeks and was included only if it then met the reliability criteria. Both the background and the stimulus intensities of all Humphrey units used in this study were checked and recalibrated when necessary before the initiation of the study. Both standard and short-wavelength automated perimetry visual fields were performed on the same visit day, and the order in which they were performed was randomized between patients and visits. A short break separated the two visual field examinations. Two baseline visual fields, at 1 and 2 months with follow-up visual field testing at approximately 3, 6, and 12 months, were evaluated for progression. The 6-month and 12-month fields were used to eliminate those who demonstrated progression of glaucomatous visual fields loss, but were not incorporated into the long-term variability calculations.

Specifically, patients who showed progression against the baseline on two consecutive visual field examinations (the 3-month and 6-month visits) were excluded. Patients who showed progression only on the 6-month visit were rechecked on the 12-month visit and excluded if the 12-month field also showed progression. In summary, patients had to have two consecutive progressive fields (both judged independently against the baseline) among the 3-, 6-, and 12-month visits to be excluded.

On the basis of the following criteria for progression, 25 stable glaucoma patients were identified and included in this study. Of the 53 patients who met the above inclusion criteria, 28 (53%) were subsequently excluded from the analysis because of an incomplete dataset or evidence of progressive visual field loss on two consecutive visits, based on at least one of the following criteria: (1) development of a new scotoma, defined as two adjacent points in a previously normal area, at the .01 probability level on the pattern deviation plot, or one point within the central 10 degrees that declined by 10 dB or more; or (2) expansion of existing scotoma, defined as two contiguous points adjacent to an existing scotoma that declined by 10 dB or more; or (3) deepening of an existing scotoma, defined as

two points in an existing scotoma that declined by 10 dB or more.

These criteria were used separately for standard visual fields and for short-wavelength automated perimetry. The baseline was created on the basis of a point-by-point threshold average of the first two visual fields taken 1 week apart.

For each of the 52 visual field locations (not including the two points immediately above and below the blind spot), we calculated the long-term variability for the standard visual fields and short-wavelength automated perimetry for each patient. Long-term variability was calculated as the SD of three threshold dB values taken from the first three visual fields performed. Then, for each point (location), the long-term variability of all 25 patients was averaged (\pm SD) separately for standard visual fields and for short-wavelength automated perimetry. Locations demonstrating an absolute (" < 0 ") defect (maximal Humphrey Field Analyzer intensity not seen) were assigned a threshold value of -2 . Standard visual fields contained a total of 90/3,900 (2.3%) such " < 0 " values, while short-wavelength automated perimetry visual fields contained a total of 173/3,900 (4.4%). Whenever any specific point was retested during a visual field testing session, the average of the two thresholds was used in the analysis.

The global long-term fluctuation is often defined as the difference between the total variability in threshold sensitivity over time and the variability resulting from short-term fluctuation.⁷ In this study, we chose to calculate the long-term variability, the total fluctuation over time (which contains the short-term fluctuation), because long-term variability is a direct measure of change over time and short-term fluctuation is not collected routinely on a point-by-point basis. In fact, with the use of Humphrey program 24-2, short-term fluctuation is routinely determined at only 10 predetermined locations within the entire visual field, and even in these locations its estimation is based on only two repetitions. Hence, a reliable point-by-point short-term fluctuation value is not routinely acquired. Attempting to substitute the global field short-term fluctuation value as each individual point's short-term fluctuation would not prove reasonable, since short-term fluctuation is location dependent.¹⁰

For each point (location) in the 24-2 visual field, the magnitude of long-term variability was summarized by a mean value (\pm SD) for standard visual fields and short-wavelength automated perimetry and compared by the t test. In addition, point-by-point long-term variability for standard visual fields and short-wavelength automated perimetry separately was correlated with the amount of eccentricity (in degrees) from fixation by linear regression techniques. Eccentricity was calculated as the distance from fixation, in degrees, for each test location. All visual field data are presented in right-eye form. The data were initially arranged in an EXCEL spreadsheet (Microsoft

Corporation, Redmond, Washington), and statistical analysis was performed with JMP statistical software (SAS Institute Inc, Cary, North Carolina).

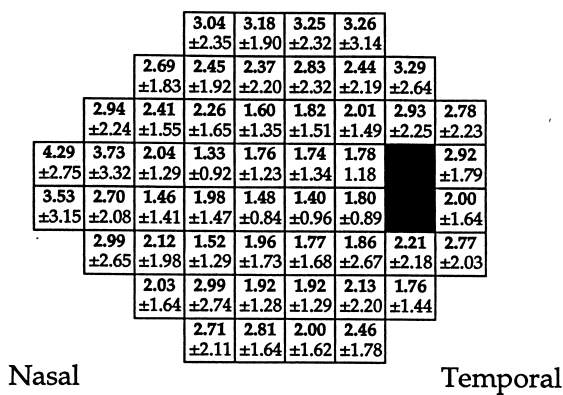
RESULTS

SUBJECTS' AGES RANGED FROM 39 TO 79 YEARS, WITH A mean of 61.0 ± 12.3 and a median of 64.7 years. Thirteen right and 12 left eyes were studied. All visual fields tests were performed between December 1995 and February 1998. The mean interval (\pm SD) between the first and second visual field visits was 6.7 ± 2.9 days (range, 2–16 days), and the mean interval between the first and third visual field visits was 104.4 ± 9.7 days (range, 91–132 days). The average mean deviation (\pm SD) for the entire group was -3.69 ± 2.32 dB for standard visual fields and -4.69 ± 4.49 dB for short-wavelength automated perimetry.

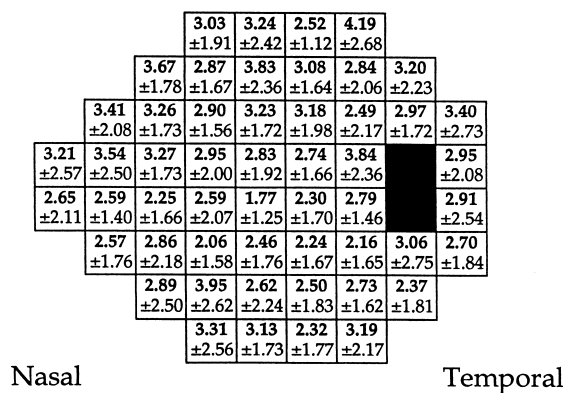
Although all patients enrolled in this study had visual field experience of at least four automated field tests each (one standard and one short-wavelength automated perimetry visual field in each eye), to verify whether a residual learning effect remained, the mean deviation was averaged for each visit separately. The mean deviation for the first, second, and third standard fields was -3.61 ± 2.51 dB, -3.92 ± 2.23 dB, and -3.53 ± 2.29 dB, respectively. The mean deviation for the short-wavelength automated perimetry fields was -5.13 ± 4.68 dB, -5.09 ± 4.87 dB, and -3.85 ± 3.92 dB. A significant learning effect was not demonstrated in this sample (analysis of variance, $P = .83$ for standard visual fields and $P = .52$ for short-wavelength automated perimetry).

The mean long-term variability averaged for the entire 24-2 field (excluding the two blind-spot points) was 2.37 ± 2.03 dB for standard visual fields and 2.92 ± 2.03 dB for short-wavelength automated perimetry (paired, two-tailed t test, $P < .0001$). Figure 1 shows the individual point-by-point values of long-term variability (\pm SD) for standard visual fields and short-wavelength automated perimetry. In 16 of the 52 visual field locations, long-term variability for short-wavelength automated perimetry was significantly higher than that for standard visual fields. These 16 locations did not cluster in any meaningful pattern, but were on the whole located closer to fixation.

The relationship between long-term variability and eccentricity was evaluated separately for standard visual fields and short-wavelength automated perimetry, by plotting each test location for each patient (Figure 2). Although long-term variability for short-wavelength automated perimetry was larger than that for standard visual fields close to fixation, long-term variability for short-wavelength automated perimetry was less dependent on eccentricity than the long-term variability for standard visual fields ($P = .0014$). In addition, these data support that the farther away from fixation a tested point lies, the



Standard VF LTV



SWAP LTV

FIGURE 1. (Top) Mean \pm SD long-term variability (LTV) of the 25 eyes of 25 patients tested for standard visual fields (VFs) at each visual field location. (Bottom) Mean \pm SD long-term variability of the 25 eyes of 25 patients tested for short-wavelength automated perimetry (SWAP) at each visual field location.

larger the long-term variability in both standard visual fields ($P < .0001$) and short-wavelength automated perimetry ($P = .003$) (Figure 2).

DISCUSSION

IN THIS STUDY WE ATTEMPTED TO ISOLATE THE LONG-term variability component of intervisit fluctuations from possible confounders, namely a learning effect, poor (or fluctuating) reliability, and true glaucomatous progression. In contrast, we chose to include the short-term fluctuation (intravisit) component of variability and hence used long-term variability as opposed to long-term fluctuation. We

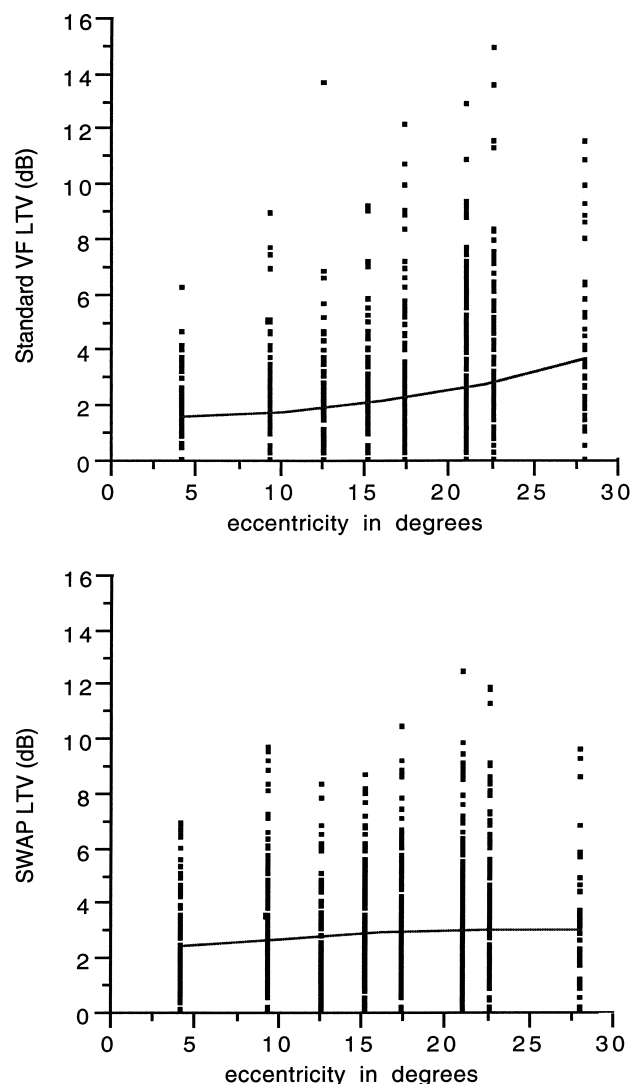


FIGURE 2. The relationship between eccentricity of visual field (VF) points (x-axis) and the amount of long-term variability (LTV) (y-axis) determined separately for standard visual fields (top) and for short-wavelength automated perimetry (SWAP) (bottom). The graphs represent the long-term variability for each of the 52 locations, for each of the 25 eyes of the 25 patients. Long-term variability increased with greater distance from the point of fixation for both standard visual fields ($P < .0001$) and short-wavelength automated perimetry ($P = .003$). Long-term variability decreased closer to fixation, more for standard visual fields than for short-wavelength automated perimetry.

felt that long-term variability is the most readily available parameter to address intervisit variability on a point-by-point basis.

Using visual fields to identify stable patients in a study aimed at quantifying long-term variability is a limitation of the study design. We addressed this potential confounder in three ways. First, all visual fields used for the analysis were obtained within a short period of 3 months. Second,

patients had to be stable on the basis of both standard and short-wavelength automated perimetry visual fields. Had we used only standard visual fields for defining stability, the study design would have been biased against short-wavelength automated perimetry, undermining our goal to compare the variability of these techniques. Third, to allow for large amounts of variability before flagging a change as progression, our criterion for progression was not merely a predetermined amount of change but the necessity of two consecutive visual fields to show clear worsening on both.

For this group of 25 stable glaucoma patients, whole-field long-term variability for short-wavelength automated perimetry was greater than for standard visual fields by an average of 0.55 dB ($P < .0001$). This finding is consistent with a previous study that found a 0.61-dB difference in normal subjects.⁵ While long-term variability differences of less than 1 dB between standard visual fields and short-wavelength automated perimetry may not be of clinical significance for following up individual patients, progression algorithms should incorporate this finding.

Our study confirmed previous findings of an association between variability and eccentricity in normal subjects. Heijl and associates⁸ found a positive correlation, for normal subjects, between intertest threshold variation and eccentricity for standard visual fields. Kwon and associates⁵ demonstrated, for normal subjects, a positive correlation between eccentricity and long-term fluctuation for both standard visual fields and short-wavelength automated perimetry. This correlation was more evident on the Humphrey than on the Octopus perimeter. Our results quantify the amount of long-term variability expected in stable glaucoma patients. Mean long-term variability was 0.55 dB higher for short-wavelength automated perimetry than for standard visual fields. The point-by-point analysis indicates that a global summary of the long-term variability for an entire visual field may not suffice when serial visual fields are evaluated for change, because the magnitude of long-term variability varies considerably by location. A reference group of stable glaucoma patients for both standard visual fields and short-wavelength auto-

mated perimetry should be useful for developing analytical tools for identifying progression in glaucoma patients.

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