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Test-retest variability in visual field testing using frequency doubling technology

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PURPOSE. *To quantify the magnitude of test-retest variability (TRV) for normal subjects in serial visual fields (VF) using the frequency doubling technology (FDT) instrument.*
METHODS. *Twenty-one healthy adults, aged 23 to 60 years, underwent four serial FDT VF tests, using the full-threshold C-20 program of the Zeiss-Humphrey FDT analyzer, on one randomly chosen eye. The VF tests were spaced 2 to 4 days apart. All subjects performed two preliminary FDT tests in order to minimize any learning effect. Test-retest variability was calculated as the standard deviation of each location's sensitivity value across the four VF tests.*
RESULTS. *Mean TRV (±SD) for the entire field was 2.44±1.32 dB. Mean TRV (±SD) for the superior, inferior, nasal, and temporal hemifields were 2.48±1.3, 2.40±1.4, 2.40±1.3, and 2.48±1.3 dB, respectively. Mean TRV (±SD) for the foveal location, the 4 central, and the 12 peripheral locations were 2.49±1.4, 2.16±1.2, and 2.54±1.4 dB, respectively.*
CONCLUSIONS. *TRV was found to be rather uniform across the visual field of the commercially available FDT device, with only a mild, clinically insignificant, effect of both eccentricity and age on TRV. Variability in the FDT VF, for normal subjects, was found to be more uniform than that of both standard and short wavelength automated perimetry. In addition, a strong inverse correlation was found, in normal subjects, between the mean sensitivity and TRV. (Eur J Ophthalmol 2007; 17: 1)*

KEY WORDS. *Visual field, Frequency doubling technology, Glaucoma diagnosis, Test-retest variability, Human, Healthy subjects*

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INTRODUCTION

Frequency doubling technology (FDT), also referred to as frequency doubling perimetry, holds promise as a technique for testing the visual fields (VF) in glaucoma. It provides a shorter test duration and relatively high sensitivity and specificity (1-3). Little is currently known about its role in following patients with glaucoma over time.

The frequency doubling phenomena, initially described by Kelly (4, 5), is obtained when rapidly alternating black and white bars give an illusion of seeing twice as many bars. It is thought that this illusion may be mediated by a subtype of retinal ganglion cells known as the magnocellular cells (6), which are sensitive to low spatial and high temporal frequency. It is speculated that these magnocellular cells and their axons might be more vulnerable to high intraocular pressure (IOP) and hence preferentially damaged in early glaucoma (7).

Test-retest variability (TRV) is a measure of change of the individual threshold values over time. It contains both a short and a long-term component. TRV is perhaps the biggest obstacle to successfully con-

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firming true progression. Among other factors, TRV reflects a true change in the physiologic state of the visual system, from one day to another (8). Much has been published on the characteristics of TRV in static perimetry (9, 10) and short-wavelength automated perimetry (10, 11). Variability over time has also been assessed for FDT for normal individuals (12) as well as for glaucomatous eyes (13, 14). The purpose of this study is to provide further data on the location by location pattern and magnitude of TRV in normal eyes tested using the FDT.

METHODS

Twenty-one healthy individuals over the age of 20 were recruited for this study. Prior to commencing the study, each subject underwent a full eye examination, including an IOP measurement, and a full slit-lamp examination including dilated biomicroscopy. All volunteers were free of any eye disease, except for ametropia, and none took corticosteroids or any eye medications. Excluded from this study were subjects with increased IOP (highest documented IOP >21 mm Hg in either eye), or any other abnormal findings documented during the entry eye examination. Additional exclusion criteria were refraction errors outside ±7 diopters (15), or best-corrected visual acuity worse then 6/9. Informed consent was obtained from all participants and the Hadassah Hospital Human Subject Committee approved the study methodology.

For each volunteer, one eye was chosen at random. Each subject received an explanation about the device and about VF testing. Each volunteer underwent two practice VF tests during week 1, spaced 2–4 days apart, prior to the four VFs considered for this study, in order to minimize the impact of any learning effect (16, 17). After the two initial practice FDT VF tests, each subject was examined four times, again with tests spread out 2–5 days apart, using the commercially available Welch Allyn Frequency Doubling Perimetry device (Carl Zeiss Meditec, Dublin, CA, USA).

The C-20 full-threshold program was used for all examinations (both practice and study tests). The C-20 grid pattern is made of 16 square test locations, each 10 degrees across, encompassing 20 degrees in each direction, and, in addition, a central (foveal) circular grid location spanning 10 degrees in diameter. Each test area presents a black and white stripped sinusoidal grating (0.25 cycles/deg) flickering at 25 Hz. The contrast between the dark and white bars is varied throughout the test. Threshold values are determined at each location from the log contrast sensitivity, and expressed in dB units.

Test-retest variability was calculated as the standard deviation of each location's sensitivity threshold value across the four VF tests. Data were exported from the FDT device into EXCEL (Microsoft Corporation, Redmond, WA) and analyzed using JMP statistical software (SAS institute, Cary, NC, USA).

RESULTS

Twenty-one normal subjects (13 male and 8 female) were recruited. After performing two practice VF tests, each subject underwent four FDT VF tests during a 2-week period, in one randomly chosen eye. The mean age was 32.8±13.3 years (range 23–60 years); 10 subjects were emmetropic and the remaining 11 had a mean refractive error of –2.1 D (range –0.75 D to –4.5 D). Data for the entire study group were collected within a 4-week period, by a single experienced technician, using one FDT unit.

Average reliability indices were false positive errors 2.4%, false negative errors 0%, and fixation losses 8%. The raw threshold values ranged between 18 and 44 dB (mean 32.64±3.3 dB). Figure 1 presents the average (±SD) TRV for each of the 21 VF grid locations. The calculated mean (±SD) TRV for the entire field was 2.44 dB (±1.3). Comparing the four paracentral VF grid locations to the 12 peripheral VF grid locations, we found a significantly lower TRV in the paracentral VF (p=0.025, *t*-test). In contrast, there was no significant difference in the mean sensitivity between the paracentral and peripheral VF (p=0.17, *t*-test). The superior hemifield showed sensitivity and TRV values similar to the inferior hemifield (p=0.57, p=0.56, respectively, *t*-test). The nasal hemifield showed a slightly higher sensitivity than the temporal hemifield (p=0.15, *t*-test), with similar TRV values (p=0.6) (Tab. I). No statistically significant age effect could be demonstrated for TRV in our group of normal subjects. TRV values ranged between 0 and 6.8 dB (Fig. 2). Mean sensitivity of the entire field ranged between 21.8 and 36.8 dB.

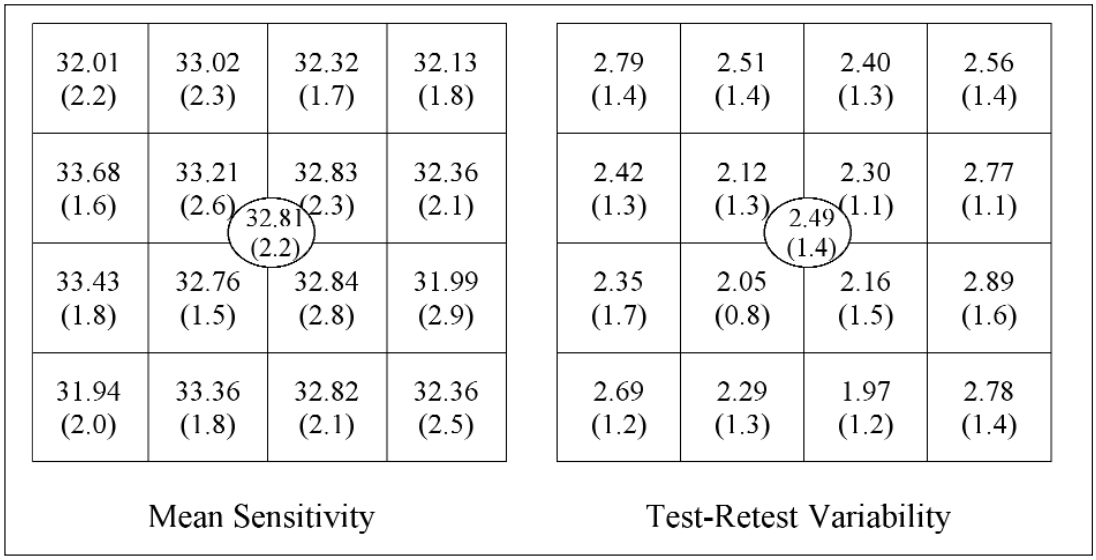

Fig. 1 - *Left: Mean sensitivity in dB (±SD), for each visual field (VF) location. Right: Test-retest variability in dB (±SD), for each VF location.*

Analysis of the data shows that subjects with lower average mean sensitivity tend to have a higher TRV (R-square = 0.17) (Fig. 2). Similarly, subjects with initial lower mean sensitivity on their first test tend to produce higher total TRV.

DISCUSSION

FDT is a relatively new method for quantifying the VF. It is gaining popularity owing to its short test duration, patient acceptance, and initial promising results for diagnosing glaucoma (18, 19). One of the important factors undermining any VF modality is the variability found in any subjective task. A high TRV would undermine any VF test for following disease progression.

TRV has been thoroughly evaluated in white-on-white perimetry (8, 9, 20). Variability was shown to increase with eccentricity of the VF tested location (9). Kwon et al showed an increase in the long-term fluctuation as a function of eccentricity for short wave length automated perimetry ($p<0.001$) (11). It also has been shown that TRV increases as threshold values worsen in glaucomatous eyes (21), up until a floor effect is reached (22).

Iester et al showed an average long-term fluctuation of 3.23±0.5 dB in normal subjects using the FDT device. When omitting the first session from their calculations, a long-term fluctuation of 2.5±0.49 dB was found. They concluded that the FDT shows fluctua-

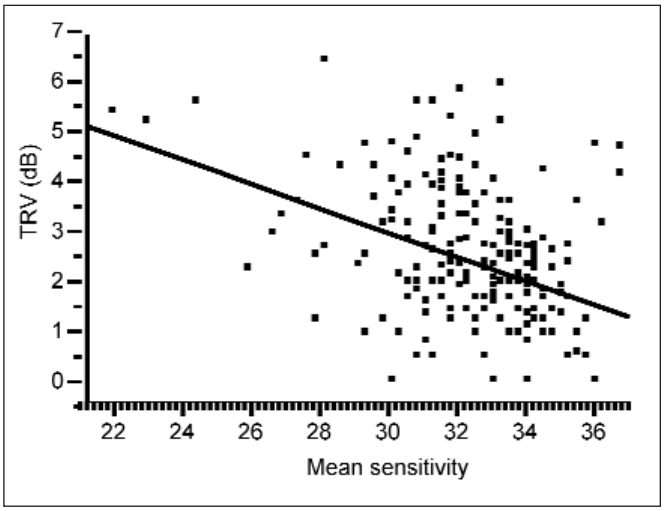

Fig. 2 - *Test-retest variability plotted by mean sensitivity.*

TABLE I - TRV BY LOCATION

VF grid locations	TRV±SD (dB)
Fovea	2.49±1.4
Central ring	2.16±1.2
Peripheral ring	2.54±1.4
Superior hemifield	2.48±1.3
Inferior hemifield	2.40±1.4
Nasal hemifield	2.40±1.3
Temporal hemifield	2.48±1.3

TRV = test-retest variability; VF = visual field.

tion values similar to those of standard perimetry (12). Chauhan et al showed no increase in variability in relation to eccentricity in FDT, when compared to conventional perimetry, suggesting that the use of a large target size in FDT is a major factor responsible for the smaller effect of eccentricity on variability (13). On a small group of normal individuals and patients with glaucoma, Spry et al demonstrated that variability occurring within a single test session contributed more to total variability than between-session variability (23).

The analyzed results of our study show a small, clinically insignificant, increase in TRV with eccentricity (p=0.025), with a rather uniform total TRV of 2.44±1.32 dB across the entire tested C-20 FDT VF grid. These results are in line with data published by Iester et al on the long-term fluctuation found in FDT, after they omitted the first session (12). We found the TRV to be slightly higher for volunteers older than 40 years compared to those younger than 40 years, but this trend did not reach statistical significance (p=0.19).

The effect of eccentricity on TRV as found in our study was not as clinically significant as was found for standard and short wavelength automated perimetry (9, 10). However, it is important to point out that in order to better test for eccentricity, the Matrix FDT with its 24-2-like grid pattern can enable a direct comparison with the 24-2 grids used with both standard and short wavelength automated perimetry.

In conclusion, we found TRV for the commercially available FDT device to be around 2.5 dB range, for normal subjects. TRV across the C-20 grid appears to be rather uniform.

Proprietary interest: None *AA IS IT CORRECT ???.*

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