# (Original Paper)

Long-term fluctuation of glaucomatous visual field defects as measured by frequency doubling perimetry

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#### **SUMMARY**

Purpose: We studied the long-term fluctuation of glaucomatous visual field defects measured by frequency doubling perimetry to compare that by Humphrey field analyzer (HFA) over time.

Methods: The subjects included 35 consecutive patients with primary open angle glaucoma. Visual fields were examined with HFA central 30-2 and frequency doubling technology (FDT) threshold c-20 every 4 months within one year. Mean deviation (MD) and corrected pattern standard deviation (CPSD) measured with HFA were compared among 3 results. MD and PSD with FDT were compared among 3 results. Long-term fluctuation was determined as standard deviation of MD and sensitivity at each point with the 3 results of FDT. Long-term fluctuation of MD was compared between FDT and HFA. Visual field indices were compared between FDT and HFA at every interval.

Results: Long-term fluctuation of MD with FDT was almost the same as that with HFA. Long-term fluctuation of sensitivity at each point with FDT did not vary with eccentricity except at the center. Intraocular pressure and MD and CPSD with HFA did not change within one year, but MD and PSD with FDT deteriorated at the third test results. A significant correlation was found in terms of visual field indices between FDT and HFA at every interval.

Conclusion: The visual field indices with FDT fluctuated in a similar way to those with HFA and correlated with those with HFA over time.

Key words: frequency doubling perimetry, long-term fluctuation, glaucoma

## I. Introduction

Frequency doubling technology (FDT, Humphrey-Zeiss and Welch Allyn, Dublin, CA, USA)

has been developed to screen for glaucoma[1,2]. This perimeter uses black and white sinusoidal flicker stimuli at 25 Hz, inducing frequency doubling illusion. FDT detects the highest

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abnormal rate of glaucomatous visual field defects among 4 perimeters (FDT, blue-on-yellow perimeter, motion perimeter, standard white-on-white perimeter of Humphrey field analyzer, HFA, Humphrey-Zeiss, Dublin CA, USA)[3] and has shown less fluctuation than obtained with HFA[4,5]. These reports covered about one-month follow-up, and the tests were performed every week. They did not actually represent clinical practice. To our knowledge, few reports describing glaucomatous visual field defects with FDT in a long-term study have been performed [6-8].

We studied glaucomatous visual field defects measured with FDT over time to compare those with HFA clinically.

### II. Materials and Methods

The subjects for this study included 35 consecutive patients (25 men and 10 women) with primary open angle glaucoma. None had undergone glaucoma surgery or laser treatment. All patients had glaucomatous cupping, glaucomatous visual field defects, and at least 2 occasions of 21 mmHg or greater intraocular pressure without medication. Glaucomatous visual field defects with HFA were considered to be present by the three criteria described by Anderson and Patella[9]. All had undergone HFA threshold central 30-2 and FDT threshold c-20 testing at least twice. They had 0.5 or better visual acuity. Their ages ranged from 22 to 69 years (mean age, 57.0 years). One eye of each patient was randomly selected for study. All patients continued their own antiglaucoma drops throughout the study. Visual field was examined with HFA central 30-2 and FDT threshold c-20 every 4 months within one year. HFA was performed with appropriate near correction and FDT was performed with far correction. Both tests were performed on different days within one month. Intraocular pressure was measured by applanation tonometry after FDT testing. Long-term fluctuation of MD and sensitivity at each point with FDT was determined as the standard deviation of the 3 values[10]. Long-term fluctuation of MD with HFA was also calculated in the same way. Long-term fluctuation was compared between FDT and HFA. Mean deviation (MD) and corrected pattern standard deviation (CPSD) with HFA were compared among 3 results. MD and PSD with FDT were compared among 3 results. Intraocular pressure at examination was compared among 3 results. MD with HFA at the first test ranged from -26.42 dB to 0.79dB (mean MD, -9.09 dB, Fig. 1). MD with FDT at the first test ranged from -18.86 to 0.59 dB (mean MD, -6.65 dB, Fig. 2). The results in the left eye were converted to those in the right

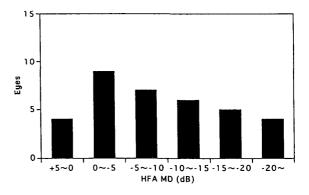


Fig. 1 The first mean deviation (MD) with HFA ranged from early to advanced proportionally.

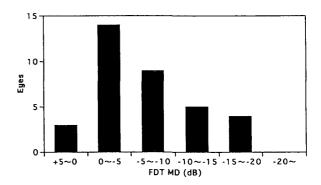


Fig. 2 The first mean deviation (MD) with FDT had many eyes with relatively early stage.

eye.

The results of less than 20% of fixation loss, 20% of false positive, and 33% of false negative with both perimeters were adopted with both perimeters.

Statistical analysis was done with one-way repeated measure ANOVA with posthoc test (Fisher's method) for multiple paired comparison (MD, PSD, and CPSD), one-way ANOVA (Fisher's method) for multiple unpaired comparison (long-term fluctuation of sensitivity at each area), and with Wilcoxon's signed rank test for two paired comparison (long-term fluctuation of MD). The relationship was done with simple regression analysis (visual field indices). P < 0.05 was estimated as significant.

The research followed institutional guidelines and the tenets of the World Medical Association Declaration of Helsinki. We obtained informed consent from each subject studied.

#### III. Results

The average interval between the first and third tests was 8.4 months with FDT and 9.5 months with HFA. Intraocular pressure at

examination with FDT was  $17.2 \pm 0.59$  (mean ± standard errors) mmHg at the first test, 17.3  $\pm$  0.52 mmHg at the second, and 17.3  $\pm$  0.52 mmHg at the third. No significant differences were found among the 3 measurements. Average long-term fluctuation of MD was  $1.06 \pm 0.098$ dB with HFA and  $0.94\pm0.12$  dB with FDT. No significant differences were found between HFA and FDT. Average long-term fluctuation of the entire field (17 areas) with FDT was 2.57  $\pm$ 0.47 dB. Average long-term fluctuation was  $2.68 \pm 0.18$  dB in 4 areas within 10 degrees, 2.67  $\pm$  0.14 dB in 8 areas between 10 and 20 degrees, and  $2.44 \pm 0.11$  dB in 4 areas on the corner of the entire field. No significant differences were found among the three groups. Long-term fluctuation of sensitivity at each area with FDT did not vary with eccentricity except at the center (Fig. 3). MD results and CSPD results with HFA showed no change among the 3 results. MD change between the first and third HFA tests (third results-first results) ranged from -3.46 dB to 3.38 dB (mean change, 0.31dB, Fig. 4). MD change between the first and third FDT tests (third results-first results) ranged -6.06 dB to 2.26 dB (mean change,

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2.42 0.36	2.84 0.52	2.93 0.45	2.69 0.52	2.42 0.36	2.84 0.52	2.93 0.45	2.69 0.52	
2.88 0.49	3.15 0.77	2.48 0.34	2.86 0.29	2.88 0.49	3.15 0.77	2.48 0.34	2.86 0.29	
2.16 0.31	2.73 0.45		2.47 0.23	2.16 0.31	2.73 0.45		2.47 0.23	
2.18 0.28	2.01 0.25	3.17 0.45	2.47 0.35	2.18 0.28	2.01 0.25	3.17 0.45	2.47 0.35	

Fig. 3 Long-term fluctuation of sensitivity in each point with FDT was determined as the standard deviation of 3 values. Long-term fluctuation in each point with FDT did not vary with eccentricity except at the center. Upper figures indicate mean and lower figures indicate SE.

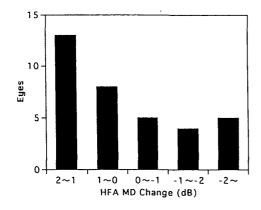


Fig. 4 Frequency distributions of MD change (third results-first results) with HFA are shown.

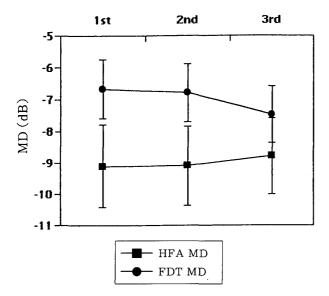


Fig. 6 MD with FDT deteriorated at the third test, but HFA did not. (Mean  $\pm$  SE)

-0.81 dB, Fig. 5). MD results of the first, second, and third FDT test were  $-6.65 \pm 0.92$  dB,  $-6.77 \pm 0.90$  dB, and  $-7.46 \pm 0.89$  dB (Fig. 6) respectively. The differences were significant between the first and third (P= 0.0060), and second and third (P=0.0191). PSD results also deteriorated at the third test (the first and third P=0.0546, the second and third P=0.0482)(Fig. 7). A significant correlation was found in terms of MD between FDT and HFA at every interval (P=0.0448 at the first test, P=0.0386 at the second, and P=0.0088 at the third). The actual value of MD with FDT

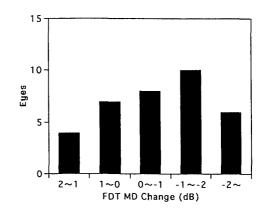


Fig. 5 Frequency distributions of MD change (third results-first results) with FDT are shown.

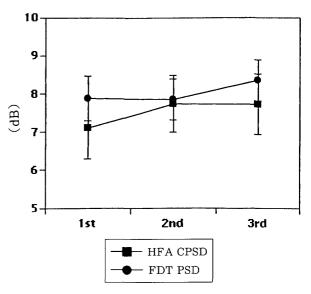


Fig. 7 PSD with FDT deteriorated at the third test, but CPSD with HFA did not. (Mean  $\pm$  SE)

became near that with HFA and the significant level of correlation became higher with time. A significant correlation was found between PSD with FDT and CPSD with HFA at every interval (P=0.0011 at the first test, P<0.0001 at the second, and P=0.0008 at the third).

## IV. Discussion

Automated perimetry has short-term and long-term fluctuation[11-13]. Long-term fluctuation includes learning effects[7,14], psychophysical variation, and progression and

improvement of the pathological process. The first two results before the present study were deleted to remove the learning effects. In fact, no differences between the first and second results after the study were seen. Since the present study covered about one year, the long-term fluctuation included psychophysical variation, progression, and improvement. Long-term fluctuation at each test area in our patients with glaucoma was similar to that in normal subjects[14].

MD with FDT disclosed that visual field deteriorated within one year, but HFA did not show this, although long-term fluctuation of MD with FDT was a little smaller than that with HFA. Diffuse loss (MD) and local loss (PSD) with FDT occurred at the third test. Whether this deterioration was glaucomatous or not will need evidence of change of optic disk topography and thickness of nerve fiber layer defects, or consequent progression of visual field defects determined by HFA[8]. In a longitudinal study by Bayer and Erb[8] it was shown that progression of glaucomatous visual field deficits by FDT was seen before progression of field loss by HFA. Long-term fluctuation of MD with FDT in this study might include progression.

It was difficult to compare visual field indices between HFA and FDT directly. HFA had light sensitivity and FDT had contrast sensitivity at sinusoidal flickering of 25Hz. Because stimulus area, range of testing field, and dynamic range of dB were different between perimeters, it was impossible to compare them under the same value. However, there is a significant correlation between perimeters regarding visual field indices[4,15], and there was a significant correlation in our patients at every interval.

In summary, visual field with FDT fluctuated within one year in patients with glaucoma in the same way as that with HFA. The visual

field indices with FDT correlated with those with HFA over time.

## Acknowledgement

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#### 要旨

【目的】Frequency doubling technology (FDT) は従来の自動視野計とは異なり、比較的大きな網膜 神経節細胞であるM細胞系の機能を評価している。 本来緑内障スクリーナーとして開発されており短時 間での検査が可能である。緑内障において、この視 野計がスクリーニング以上に臨床的な経過観察に有 用であるか、視野の長期変動(long-term fluctuation=LF)について従来の視野計と比較検討した。 【方法】開放隅角緑内障患者35例35眼に対し,HFA (Humphrey field analyzer) 30-2 & FDT threshold c-20を4ヶ月ごとに1年間に3回測定し、視野 全体の感度低下を示す視野指数 MD (mean deviati on), 局所的異常を示す視野指数 PSD (pattern standard deviation), CPSD (corrected pattern standard deviation) について3回の測定結果より 長期変動を求め、その結果を比較した。

【結果】1年間を通して眼圧には有意な変化を認めなかった。FDT における MD の長期変動は0.94dBでHFA の MD の長期変動1.06dBと有意差は無かった。FDT の各測定点の長期変動は中心では1.8dBであるのに対し、周辺では2dBから3dBと大きかった。HFA の MD と CPSD は1年間で有意な変化は認めなかった。FDT の MD と PSD は3回目の測定で有意に悪化した。各測定時期の視野指数 MD と PSD は FDT と HFA で有意の相関を認めた。

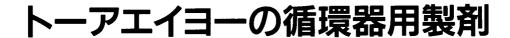
【結論】FDTの視野指数MDとPSDはHFAの視野指数MDとPSDと同様の変動を示し、各時期において有意の相関を示すことがわかった。このことより緑内障性視野異常の経過観察にFDTを用いることが可能であることがわかった。

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フランドルテープS

組成】|枚中、日本薬局方・硝酸イソソルビド40mg含有

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フランドル

【組成】1錠中、日本薬局方・硝酸イソソルビド 20mg含有



狭心症治療用ISMN製剤指》要指

【組成】IOmg錠:一硝酸イソソルビドIOmg含有 20mg錠:一硝酸イソソルビド20mg含有

定量噴霧式・ニトログリセリン舌下スプレー剤

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【組成】Ig中、ニトログリセリン6.5mg(I噴霧中ニトログリセリン0.3mg)含有

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発売 山之の制薬

【薬価基準収載】