

# Annual Incidence Rate of Visual Field Abnormalities Determined by Frequency Doubling Technology Perimetry

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## ABSTRACT

**Purpose:** To determine an appropriate time interval for conducting mass screening for glaucoma, it is important to gather information on the annual incidence rate. Thus, a retrospective cohort study was conducted to determine the annual incidence rate of visual field abnormalities (VFA) among a workplace cohort.

**Methods:** In an initial visual field test using frequency doubling technology (FDT) perimetry conducted on 3443 employees (mean age  $47.4 \pm 8.9$ , men/women = 2967/476), no abnormalities were observed. Subjects were followed-up with annual perimetric testing for seven years, with VFA being determined using FDT test (FDT-VFA).

**Results:** Using the Kaplan–Meier method (log rank test,  $p < 0.001$ ), cumulative FDT-VFA rates (SE) at seven years for subjects in their 30s, 40s, 50s, and 60s or older were found to be 3.0% (0.6), 4.2 % (0.6), 4.8 (0.8), and 11.3% (0.2), respectively. A linear fit to the Kaplan–Meier results yielded an annual incidence rate of 0.42%, 0.60%, 0.77%, and 1.60% for the 30s, 40s, 50s, and  $\geq 60$ s age groups, respectively.

**Conclusion:** Our data suggest that the annual incidence rate of VFA is  $<0.7\%$  per year in subjects younger than 60 years of age; however, it increases to 1.6% per year in older subjects, thus suggesting that the monitoring frequency of glaucoma patients may need to be adjusted as a function of their age and be performed more frequently after the age of 60 years

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## Introduction

Glaucoma is a relatively common ocular disease characterized by optic neuropathy and is believed to be present only when at least one eye has both typical structural and functional defects (optic disc damage and visual field loss) (1). Within an aging society, glaucoma-induced visual field defects have a particular impact on quality of life (QOL) (2), and their prevention is an important public health concern (3). Characteristics of glaucoma depend on race (4), and in the Japanese population the dominant form of this condition is primary open angle glaucoma (POAG)—particularly normal tension glaucoma (NTG) accounting for more than 90% of POAG (5).

Glaucoma mass screening is an important public health concern, because the number of patients suffering from glaucoma, but not being medically treated, were estimated to be 80% in Japan (5). Previously, we demonstrated the efficacy of screening based on frequency doubling technology (FDT), with a greater than 70% positive predictive value for glaucoma, including “glaucoma suspect” in the workplace (6). Given that the test subjects were relatively young, healthy workers with a lower prevalence of illnesses such as diabetes mellitus or cataracts, these findings indicated that visual field abnormalities (VFAs) identified by the FDT test were mainly related to glaucoma in this study population.

When planning to conduct mass screening, information on the prevalence is required, as the screening performance depends on it. In addition, to determine an appropriate time interval for conducting screening, information on the annual incidence is important. Therefore, the present study was conducted to estimate the annual incidence of new VFA detected by FDT testing.

## Materials and Methods

### Study Subjects

The study subjects underwent a medical health check-up at the workplace. In total, 4143 subjects (mean age  $48.0 \pm 9.2$ , men/women = 3549/594) initially underwent FDT test (Humphrey FDT the first generation, C-20-1 screening mode, Carl Zeiss. Meditec Inc, Dublin, CA). Among these, 292 showed either 165 VFA on FDT testing or 33 no reliable results, or have a present history of 51 glaucoma or 43 other ophthalmic diseases. In this workplace, fundus examination had been performed before starting this study. Of the remaining 3851 subjects, 408 dropped out in the first year, leaving 3443 as subjects for this study (mean age  $47.4 \pm 8.9$ , men/women = 2967/476). Annual FDT testing was conducted over a period of seven years. We analyzed the historical records of the FDT test results. The study was approved by the Ethics Committee of Showa University, Japan.

### VFAs determined by the FDT test (FDT-VFA)

C-20-1 test stimuli are in 17 locations within the central  $20^\circ$  of the visual field, including 1 central fixation point and 4 locations in each of 4 quadrants. The stimuli consist of a sinusoidal spatial waveform composed of alternative white-and-black stripes (0.25 cycle/degree, sinusoidal modulation) that counter-phase flicker at 25 Hz. The target is perceived to have twice its actual spatial frequency (frequency-doubling illusion). The screening protocol uses a suprathreshold strategy and compares the results with a normal database to indicate 4 qualitative loss classifications: within normal limits, mild relative loss, moderate relative loss, and severe loss (7, 8). The FDT-VFA has been described in detail elsewhere (6). Briefly, the protocol consists of two parameters: reproducibility and detection. Reproducibility was determined by immediately conducting a retest on detection of any VFA in the initial FDT test. A positive

result was noted in the reproducibility parameter if a VFA obtained in the retest was the same or in contact with the VFA identified in the initial test. A positive result was noted in the detection parameter, when the FDT results showed one or more VFAs with mild relative loss located within the four central spots on the nasal side of the eye, two or more VFAs in any location, or one or more VFAs with moderate or severe relative loss in any location. The FDT test was shown to detect 83.3% of early stage glaucoma (mean deviation  $>-6$ ) based on the Anderson criteria in the hospital setting, and showed that the positive predictive value was more than 40% in general population (6).

### Information on Myopia

Information on refractive errors was obtained by checking for the presence of refractive errors (use of eyeglasses or contact lenses for myopia) by a nurse on the basis of a self-report.

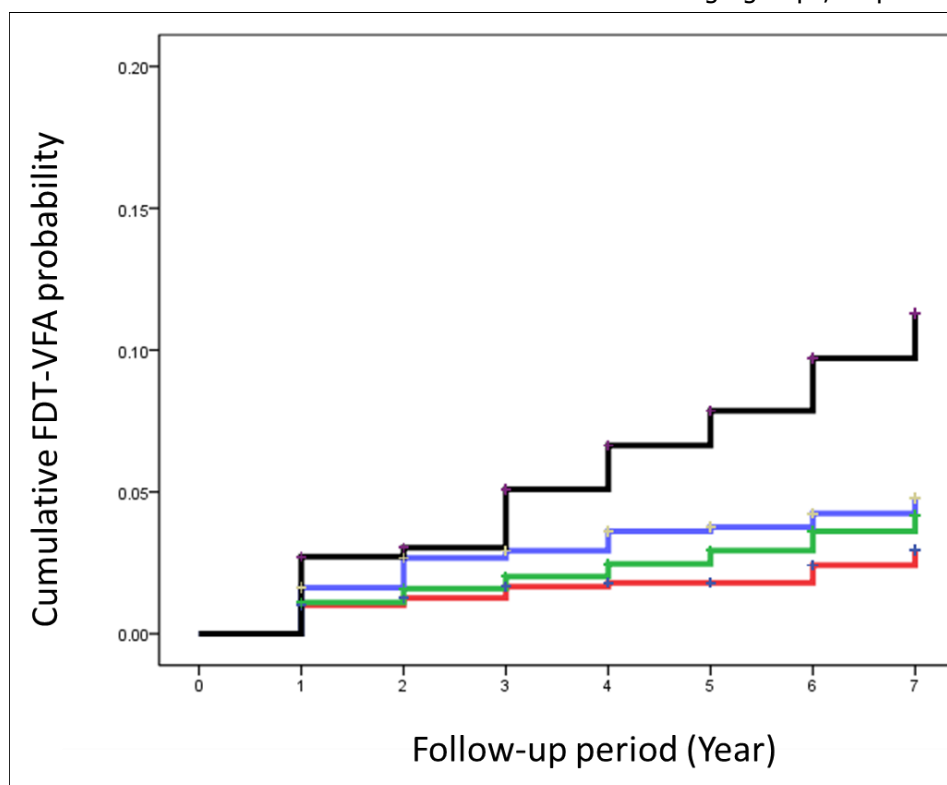
### Statistical analysis

Cumulative FDT-VFA rates were calculated using the Kaplan–Meier method. Significance was determined by the log-rank test. When a subject did not receive an FDT test during a particular year, but the result of the FDT test was normal in the following year, the result was considered to be normal for the previous year as well. All statistical analyses were performed using IBM-SPSS software version 22.0 (IBM SPSS, Tokyo, Japan).  $P < 0.05$  were considered statistically significant.

## RESULTS

### Follow-up Study

The follow-up numbers of subjects in their 30s, 40s, 50s, and 60s and older groups were 795, 1268, 1049, and 331, respectively. Events (FDT-VFA) occurred in 21 (2.6%), 47 (3.7%), 41 (3.9%), and 30 (9.1%) cases, respectively. Cumulative VFA rates for each age group is shown in Fig. 1. Using a linear fit to the Kaplan–Meier results, the annual incidence was calculated to be 0.42%, 0.60%, 0.77%, and 1.60% for the 30s, 40s, 50s and  $>60$ s age groups, respectively (Table 1). There was



**Fig.1** Cumulative FDT-VFA probability according to the Kaplan–Meier method  
Red line = 30s, green line = 40s, blue line = 50s, black line =  $\geq 60$ s

a statistically significant ( $p < 0.001$ ) difference in the cumulative VFA rates between the subjects below and above 60 years of age.

The rate of refractive error (myopia) in this population was 49.9%

## Discussion

To the best of our best knowledge, the present study is the first report to estimate the annual incidence of VFA as determined by annual FDT tests among a large Asian population utilizing a follow-up study design.

correlation with examination frequency. This study examined visual fields with FDT testing a maximum seven times. Second, the other study's glaucoma screening program was based on intraocular pressure (IOP) measurements and fundus photography (9). However, among the Asian population, normal tension glaucoma is dominant (5, 10) and glaucoma mass screening based on IOP is not sufficiently sensitive (5). In addition, FDT test could detect other diseases such as cataracts, diabetic retinopathy, brain tumor and so on. (6). Third, our study population was limited to a workplace cohort. Another previous study showed that

**Table 1.** FD-VFA rate stratified by age group

	FDT-VFA			Cumulative FDT-VFA rate (SE) at 7 years	Annual FDT-VFA rate
	n	case	%		
30's	795	21	0.026	3.0 %(0.6)	0.0042
40's	1268	47	0.037	4.2% (0.6)	0.006
50's	1049	41	0.039	4.8% (0.6)	0.0077
over 60 y	331	30	0.091	11.3% (0.2)	0.016
Total	3443	139	0.04	9.0 (0.5)	0.013

FDT-VFA: visual field abnormalities determined using an FDT-based glaucoma screening protocol

For subjects in their 40s, 50s, and  $\geq 60$ s, our data show a seven-year incidence rate of VFA of 4.2%, 4.8%, and 11.3%, respectively. Based on our previous study, the positive predictive values of the FDT test for glaucoma suspects were 0.67, 0.70, and 0.61 in the corresponding age groups (Tatemichi, unpublished data: supplement table). Thus, the seven-year incidence of glaucoma patients can be roughly estimated to be 2.8%, 3.4%, and 6.9% in the 40s, 50s, and  $\geq 60$ s age groups, respectively. Recently, Kim et al reported the five-year incidence of Primary Open Angle Glaucoma in a cohort study (9). According to their results, the five-year incidence was 0.82%, 1.16%, 1.27%, and 4.31% for individuals in their 40s, 50s, 60s, and  $\geq 70$ s, respectively. Compared with the analysis by Kim et al, we observed a higher incidence in our study. We believe that this discrepancy may have occurred for several reasons. First, the incidence of VFA could be increased in

the major risk factors for glaucoma included myopia (11,12). Our study population was associated with a higher prevalence of myopia; this risk factor applied to our study population, and might have contributed to the higher incidence of VFA observed.

Visual field impairments due to glaucoma progress slowly (1). From the viewpoint of cost-effectiveness, it is important to determine an appropriate screening interval when planning mass screening for glaucoma. Furthermore, such mass screening requires a high performance in the positive predictive value, which depends on the prevalence. Hence, our study provides important data to be considered when planning to screen for glaucoma in the workplace.

It is important to highlight several limitations of the present study. First, major limitation of this study is not to obtain a complete ophthalmic examination on VFA

as determined by FDT. Therefore, further studies are required. However, our study aimed to provide information on the annual rate of VFA, which would enable the planning of a mass screening using the FDT test. Second, our workplace study population included a very few women compared with the general population. Thus, careful interpretation of our results is necessary before they can be applied to the general population; however, no significant difference was observed in the prevalence of glaucoma between Japanese men and women (5).

In conclusion, the annual incidence of VFA is less than 0.7% per year in subjects younger than 60 years old, but increases to 1.6% per year for older subjects, thus suggesting that the monitoring frequency of glaucoma patients may need to be adjusted as a function of their age and should be performed more frequently after the age of 60 years.

**Supplementary Table:**

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Supplement Table. Results of ophthalmic examination on subjects with FDT-VFA

	Normal	Glaucoma-tous	Other disease	total
30's	16 (17.6%)	59 (64.8%)	16 (17.6%)	91 (100%)
40's	20 (12.3%)	109 (66.9%)	34 (20.9)	163 (100%)
50's	14 (9.5%)	104 (70.3%)	30 (20.3%)	148 (100%)
over 60				43

FDT-VFA: visual field abnormalities determined using the FDT-based protocol

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