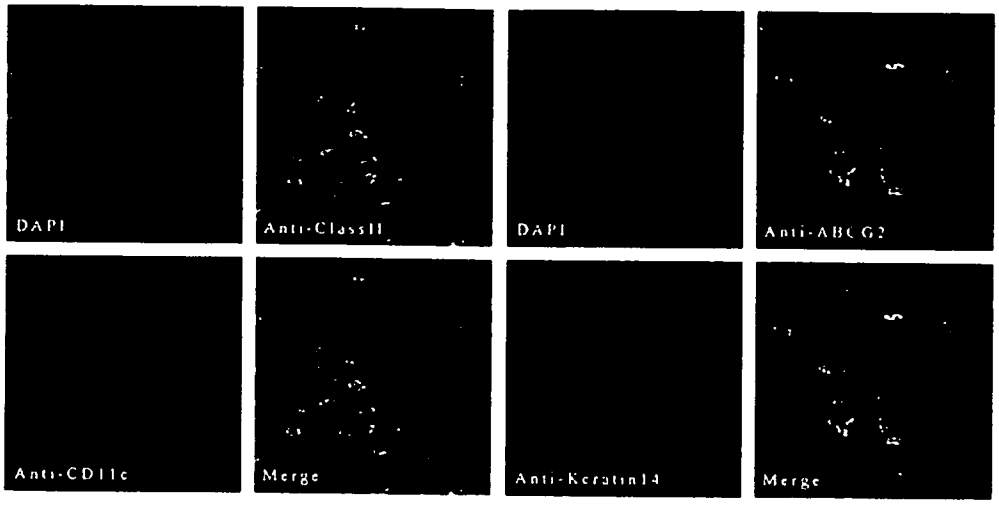

Fig. 4. Expression of MHC class II, CD11c, ABCG2 and keratin 14 in normal limbal basal epithelium. (left) All MHC class II^+ cells in limbal basal epithelium were found to be CD11c positive. (right) Double staining of normal corneal tissues with ABCG2 and K14 showed that some $ABCG2^+$ cells in limbal basal epithelium coexpressed keratin 14 (pink).

33342 dye (Zhou et al., 2001). Limbal $ABCG2^+$ cells, which represent 2.5–3% of the limbal epithelial cells, were found to exhibit greater colony-forming efficiency (CFE) on a 3T3 fibroblast feeder layer than limbal $ABCG2^-$ cells (de Paiva et al., 2005). Furthermore, semiquantitative RT-PCR revealed that the expression of ABCG2 was markedly higher in limbal than in corneal epithelia (Umemoto et al., 2005). These findings, in conjunction with immunohistochemical observation showing ABCG2 transporter is exclusively expressed by a small number of limbal basal cell, have suggested that ABCG2 is a reliable marker for identification of limbal stem cells (Schlötzer-Schrehardt and Kruse, 2005; de Paiva et al., 2005). Using an immunofluorescence double-staining technique applied to confocal microscope, we found that all $ABCG2^+$ cells were located in the limbal basal epithelium and were positive for BrdU label-retaining test. Our study provides direct evidence that in rat $ABCG2^+$ cells in the limbal basal epithelium are slow-cycling cells.

We compared the cell size and N/C ratio of limbal $ABCG2^+$ cells with those of the peripheral and central corneal epithelial cells. It has been suggested that the features that distinguish stem cells from TA cells are correlated with a fundamental difference in the cell size (Gross et al., 1987; Romano et al., 2003). In the epidermis, keratinocytes with high density are found to exhibit larger proliferative capacity (Furstenberger et al., 1986). Similarly, in skin culture the smallest keratinocyte possesses the highest clonogenicity (Barrandon and Green, 1985). In the corneal epithelia, the smallest cells with low granularity and high N/C ratios are found in the limbal basal layer (Romano et al., 2003). Our study extends these findings and confirms that limbal $ABCG2^+$ cells have smaller cell size with larger N/C ratio. Taken altogether, our data show that limbal slow-cycling cells are smaller cells with larger N/C ratio and expression of ABCG2, a limbal stem cell marker. Therefore, we believe that these cells are limbal stem cells.

In the corneal epithelium, we found that the MHC class II^+ cells were exclusively distributed in the limbal and peripheral areas. Further analysis showed that while a few dendrite-shaped MHC class II^+ cells are localized in the surface epithelium of the limbus, a number of round MHC class II^+ cells are present in the basal layer. Given that limbal slow-cycling stem cells are entirely located in the limbal epithelial basal layer, we performed double immunofluorescence staining to investigate whether the round MHC class II^+ cells present in the limbal epithelial basal layer are slow-cycling cells. Immunofluorescence staining on whole mount corneal tissues showed that some MHC class II^+ cells in limbal epithelium could be identified as BrdU LRCs, suggesting that these cells were slow-cycling cells. Cross-sectional studies further confirmed that limbal BrdU LRCs with expression of MHC class II were exclusively located in the limbal basal epithelium. Our data have demonstrated that limbal basal epithelium is indeed endowed with a small number of slow-cycling MHC class II^+ cells. We noted that all MHC class II^+ BrdU LRCs in limbal basal epithelium expressed ABCG2. Moreover, limbal $ABCG2^+$ cells with expression of MHC class II were found to be smaller cells with larger N/C ratio than peripheral and corneal epithelial cells. We also noted that there was no significant difference between limbal $ABCG2^+$ cells with expression of MHC class II and $ABCG2^+$ cells without expression of MHC class II in cellular and nuclear areas, indicating that the cell size and N/C ratio of these cells were similar.

Our results have indicated that nearly four-fifth of limbal $ABCG2^+$ cells are positive for keratin 14, a maker for undifferentiated and less proliferative corneal epithelial cells, but negative for keratin 3, a corneal epithelial differentiation marker. This finding is in agreement with the study reporting that in adult rat cornea keratin 14 positive cells are confined to the limbal and peripheral basal epithelium (Hsueh et al., 2004). In contrast, nearly one-fifth of limbal $ABCG2^+$ cells

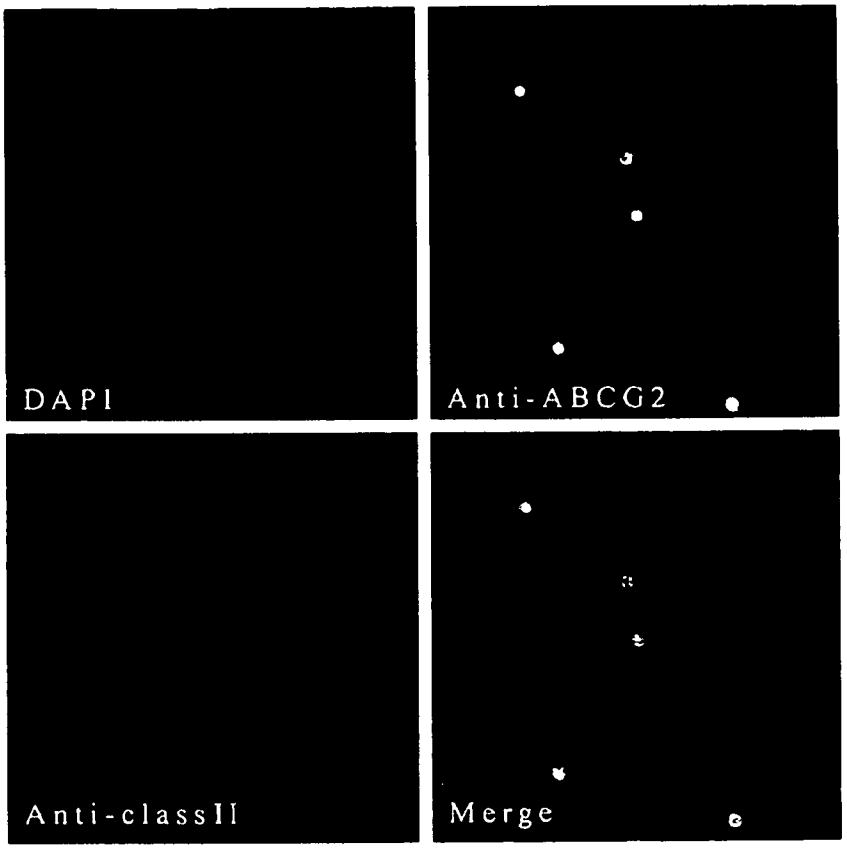

Fig. 5. ABCG2 and MHC class II staining of dissociated limbal epithelium. Representative confocal micrographs of DAPI (A, blue), ABCG2 (B, green) and MHC class II (D, red). An average of 2.6 ± 0.7% cells of limbal cells was found to be $ABCG^+$ cells. Double staining with MHC class II shows that approximately 20% of limbal $ABCG^+$ cells expressed MHC class II antigen.

are negative for keratin 14, exhibiting non-epithelium derivation. It has been demonstrated that the presence of major histocompatibility complex (MHC) class II antigens on the surface of antigen-presenting cells (APCs) has important implications for both the generation and expression of the immune response (Parham and Strominger, 1982; Mellman and Steinman, 2001). Therefore, we speculate that normal limbal basal epithelium contains at least two types of slow-cycling cells: MHC class II^- cells are the progenitor of epithelial cell, which may perform an important role in the replacement of corneal epithelium, while MHC class II^+ cells may serve as the critical sentinel cells of the immune system in the corneal epithelium. To our knowledge, we are the first group to report the existence of slow-cycling MHC class II^+ cells in the limbal basal epithelium of the uninflamed eye.

LCs have been identified as the only cells that constitutively express MHC class II molecules in normal corneal epithelium (Klareskog et al., 1979; Hamrah et al., 2002; Yamagami et al., 2005). They are the professional APCs of the corneal epithelium and serve as the critical sentinel cells

Table 1 Cell sizes measured by confocal microscopy in corneal epithelial cells

	LE $ABCG^+$ cells with expression of class II	LE $ABCG^+$ cells without expression of class II	PCEC	CCEC
Cell area (μm^2)	72.5 ± 14.3*	76.2 ± 12.1*	256.6 ± 98.5	337.5 ± 137.3
N/C ratio	0.89 ± 0.3#	0.87 ± 0.6#	0.32 ± 0.1	0.26 ± 0.1

The cell size was measured in 50 cells of each zones by confocal microscopy and data are expressed as a mean ± SD. LE, limbal epithelial, PCEC, peripheral corneal epithelial cells; CCEC, central corneal epithelial cells.

*$P < 0.005$ compared with PCEC and CCEC.

#$P < 0.001$ compared with PCEC and CCEC.

No significant difference between limbal $ABCG2^+$ with expression of MHC class II and Limbal without expression of MHC class II in cell area and N/C ratio.

of the immune system in the ocular surface (Tamaki and Katz, 1980; Gillette et al., 1982; Dana et al., 2000; Dana, 2004). Like skin LCs, corneal epithelial LCs are bone marrow-derived dendritic cells (DCs) that are capable of taking up, processing, and presenting antigen, and leading to initiation of T-lymphocyte responses (Hamrah et al., 2003). In skin, LCs are found to have a very slow turn over rate of 4 weeks and longer (Czernielewski and Demarchez, 1987; Kanitakis et al., 2004). In the present study, we found that all MHC class II^+ cells in the limbal and peripheral epithelia expressed CD11c, the marker for DC and LC. Taken these facts into account, we consider that limbal slow-cycling MHC class II^+ cells described herein may be LC precursors. Cotsarelis et al. (1989), by transmission electron microscopy, found that limbal basal epithelium is endowed with a small number of LCs. In retrospect, it is not clear whether Cotsarelis et al. were looking at the LCs that were slow-cycling cells and expressed limbal stem cell markers, e.g., ABCG2. It has been proven that inflammatory stimuli and corneal diseases result in the centripetal migration of LCs from the limbus into the central corneal epithelium (Parham and Strominger, 1982; Gillette et al., 1982; Hamrah et al., 2002). In view of the important role of LCs in immune surveillance, further studies are needed to determine the function of limbal slow-cycling MHC class II^+ LCs in corneal immune responses.

In summary, our study demonstrates existence of slow-cycling LCs in limbal basal epithelium. These findings may provide additional information for our understanding of the characteristics of limbal slow-cycling cells.

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Frequency Doubling Technology Perimetry in Open-angle Glaucoma Eyes With Hemifield Visual Field Damage: Comparison of High-tension and Normal-tension Groups

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Purpose: To evaluate the performance of frequency doubling technology (FDT) perimetry in open-angle glaucoma eyes with hemifield visual field damage and to compare it between open-angle glaucoma with high pressure [high-tension glaucoma (HTG)] and those with normal pressure [normal-tension glaucoma (NTG)] groups.

Methods: FDT perimetry with the N-30 full threshold protocol and standard automated perimetry (SAP) using the Humphrey Field Analyzer with the 30-2 full threshold protocol were performed in 20 eyes of 20 HTG patients and 36 eyes of 36 NTG patients with visual field damage confirmed with SAP in only one hemifield.

Results: There was no significant difference in demographics, the Heidelberg Retina Tomography indices, and the Humphrey Field Analyzer indices between HTG and NTG groups. Regarding the FDT perimetry results, mean deviation in the global field ($P = 0.009$) and mean sensitivity in the SAP-spared ($P = 0.001$) and SAP-impaired ($P = 0.011$) hemifields were lower; the numbers of FDT abnormal test points (probability of abnormality $< 5\%$) in the SAP-spared hemifield were significantly greater ($P = 0.005$) in HTG than in NTG groups. Eyes in which FDT results of the SAP-spared hemifield were judged as abnormal was more frequent in HTG groups ($P = 0.007$).

Conclusions: The performance of FDT perimetry to detect early or preperimetric glaucomatous functional changes should be different between HTG and NTG eyes.

Key Words: open-angle glaucoma, hemifield visual filed damage, frequency doubling technology perimetry, intraocular pressure

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Frequency doubling technology (FDT) perimetry is reportedly a useful tool to detect early glaucomatous visual field damage (VFD) compared with such as a standard automated perimetry (SAP),[1] which hardly detects early glaucomatous functional abnormalities until 20% to 40% of the retinal ganglion cells have gone.[2] In glaucomatous eyes with hemifield VFD, functional abnormality even in the SAP-spared hemifield were often found using FDT,[3,4] also suggesting better performance of FDT for detecting early or preperimetric functional damage.

It has been reported that FDT perimetry more sensitively reflects functional abnormalities in magnocellular pathway.[5,6] Axonal transport to the magnocellular layers of the lateral geniculate body was more notably decreased than that to the parvocellular layer in a monkey glaucoma model with chronic elevated intraocular pressure (IOP).[7] Therefore, differences in the performance of FDT perimetry between open-ange glaucoma (OAG) with elevated IOP [high-tension glaucoma (HTG)] and that with normal IOP [normal-tension glaucoma (NTG)] may be suggested. In fact, Kogure et al[8] reported that greater numbers of abnormal points were found with FDT than with SAP in HTG eyes, whereas the numbers were equivalent between FDT and SAP in NTG eyes. Horikoshi et al[9] reported that mean deviation (MD) of FDT was significantly lower in HTG than in NTG, whereas MD of SAP was not different. The subjects in these studies, however, were HTG/NTG eyes with VFD already evident with SAP, and to our knowledge differences in performance of FDT to detect subclinical or very early functional abnormalities between HTG and NTG eyes have never been studied. The aim of this cross-sectional study was to evaluate the differences in the ability of FDT to detect early functional changes in the SAP-spared hemifield between HTG and NTG.

PATIENTS AND METHODS

Patients of OAG were consecutively included from the outpatient clinic of the Department of Ophthalmology of the University of Tokyo Graduate School of Medicine between May 2001 and March 2002. The diagnosis of primary OAG was made according to typical glaucomatous optic disc cupping and VFD in eyes with

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normally open angles and the absence of any contributing ocular or specific systemic disorders. The inclusion criteria were: (1) presence of primary OAG, (2) well-controlled IOP with topical medication or none, (3) no history of intraocular surgeries except laser procedures, (4) corrected visual acuity ≥ 0.7, (5) refractive error $\leq \pm 8$ diopters (D), (6) no media opacities, (7) reliable (fixation loss $< 20\%$ and false positive/negative error $< 33\%$) visual field results with the Humphrey Field Analyzer (HFA, Carl Zeiss Meditec, Dublin, CA) 30-2 full threshold test, and (8) hemifield VFD in the superior or inferior field. Hemifield VFD was determined according to the Caprioli's criteria[10] based on reliable SAP results: impaired hemifield was superior or inferior hemifield with more than 2 adjacent points of which sensitivity loss was 5 dB or more in total deviation or hemifield with more than 1 adjacent point of which sensitively loss was 10 dB or more; spared hemifield had no more than 1 point of which sensitivity loss was more than 5 dB.

SAP testing using the HFA with the 30-2 full threshold test and FDT with the N-30 full threshold protocol were newly obtained for the current study with a 3 or less month interval. All of the patients had experienced the HFA testing twice or more before this study, whereas most of them did not have experience of FDT testing. Unless a patient had experience of FDT testing twice or more, he/she underwent preceding 2 examinations using the C-20 screening protocol and the N-30 full threshold protocol, respectively, to exclude unreliable FDT results during the period with the initial learning curve.[11] On another day following these preceding examinations, the N-30 testing was repeated to obtain a result which was included for this study. If the last result was unreliable (false positive/negative trials $\geq 33\%$ or fixation losses $\geq 20\%$), it could be repeated only once. If the next trial was also unreliable, the patient was excluded. Hemifields of the FDT results were evaluated according to the criteria[4] obtained by modifying those of Quigley[12] and Sponsel et al.[13] A normal hemifield had none or 1 abnormal square with probability of 5%, 2%, or 1% and no abnormal square with probability of 0.5%; and abnormal hemifield had 2 or more abnormal squares with probability of 5%, 2%, or 1%, or one or more abnormal squares with probability of 0.5%.

Data on clinical history including IOP, glaucoma medications, presence or absence of disc hemorrhage during the follow-up periods were retrospectively obtained from the clinical chart. Data of the Heidelberg Retina Tomography II (HRT II, Heidelberg Engineering, GmbH. Heidelberg, Germany) acquired within 1 year before or during this study were also reviewed. The indices included in the current study were disk area, cup area, rim area, height variation contour, cup-shape measure, and mean retinal nerve fiber layer thickness.

The OAG patients included were divided into 2 groups; those with eyes with the highest IOP higher than 21 mm Hg (HTG group) and those with eyes with the highest IOP equal to or lower than 21 mm Hg (NTG group). The highest IOP indicated the uppermost value in IOPs recorded without any glaucoma therapies. Most of the patients in the NTG group had experience of testing the 24-hour diurnal changes in IOP to confirm the diagnosis of NTG, but few of the patients in the HTG group had undergone the test. Corneal thickness was not obtained in the current patients.

Statistical Analyses

The demographic data and the results of SAP and FDT were compared between HTG and NTG groups. Because the present data were not confirmed to show normal distribution and due to the small patient sample, nonparametric statistical tests were applied for the analyses. Means of data were compared between the groups with Mann-Whitney test. Proportions between males and females or between right and left eyes were compared between the groups using χ^2 test or Fisher exact test. A P value less than 0.05 was considered statistically significant. Statistical analyses were performed using a statistical software package, SPSS 13.0J for Windows (SPSS Japan Inc, Tokyo, Japan).

RESULTS

Twenty eyes of 20 patients and 36 eyes of 36 patients were included in the HTG and NTG groups, respectively. There was no significant intergroup difference in the patients' demographics except the highest IOP and the IOP at entry. The highest IOP and the IOP at entry were significantly higher by 5.9 and 2.5 mm Hg in the HTG group compared with the NTG group ($P < 0.001$ and < 0.001, respectively, Mann-Whitney test). There was no significant intergroup difference in the prevalence of disc hemorrhage ($P = 0.16$, Fisher exact test) (Table 1). The indices of HRT II were not significantly different between the groups ($P > 0.14$, Mann-Whitney test, Table 2).

Seven eyes (35%) in the HTG group and 14 (39%) in the NTG group had hemifield defects in the lower side; and 13 (65%) and 22 (61%) had it in the upper side, respectively, in the SAP results. As to the HFA indices, there was no significant difference in MD, pattern

TABLE 1. Comparison of the Demographics Between Patients With HTG and Those With NTG

	HTG	NTG	P
No. eyes	20	36	—
Age (y)	59.4 ± 7.5	57.5 ± 9.3	0.44*
Male/female	12/8	18/18	0.57†
Right/left eyes	13/7	23/13	0.99†
Refraction (D)	−3.7 ± 2.6	−2.8 ± 3.7	0.32*
Highest IOP	23.8 ± 3.2	17.9 ± 2.5	< 0.001*
IOP at entry	16.7 ± 2.6	14.1 ± 2.5	< 0.001*
Presence of disc hemorrhage	6/20	4/36	0.16†

Mean ± standard deviation.
P indicates *P* value in comparison of means or frequency between the HTG and NTG groups (*with Mann-Whitney test, †with χ^2 test or Fisher exact test).

TABLE 2. Comparison of the Indices of the HRT Between Patients With HTG and Those With NTG

	HTG	NTG	P
No. eyes	20	36	—
Disk area (mm^2)	2.22 ± 0.34	2.27 ± 0.66	0.67
Cup area (mm^2)	1.17 ± 0.47	1.11 ± 0.63	0.57
Rim area (mm^2)	1.05 ± 0.33	1.17 ± 0.26	0.14
Height variation contour (mm)	0.39 ± 0.09	0.44 ± 0.17	0.47
Cup-shape measure	−0.09 ± 0.07	−0.11 ± 0.08	0.57
Mean RNFL thickness (mm)	0.21 ± 0.08	0.22 ± 0.10	0.91

Mean ± standard deviation.
Mean RNFL thickness indicates mean retinal nerve fiber layer thickness; *P*, *P* value in comparison of means between the HTG and NTG groups with Mann-Whitney test.

standard deviation, mean sensitivity in the SAP-spared and SAP-impaired hemifields, and mean total deviation in the SAP-spared and SAP-impaired hemifields between the HTG and NTG groups ($P > 0.1$, Mann-Whitney test) (Table 3).

Regarding the results of FDT N-30, MD in the global field ($P = 0.009$, Mann-Whitney test) and mean sensitivity in the SAP-spared ($P = 0.001$) and SAP-impaired ($P = 0.011$) hemifields were significantly lower in HTG group than in NTG group. The numbers of abnormal test points (probability of abnormality < 5%) were significantly smaller in NTG group in the SAP-spared hemifield ($P = 0.005$). Eyes in which FDT results of the SAP-spared hemifield were judged as abnormal according to the modified abnormality criteria[4] was more frequent in HTG group (65%) than in NTG group (33%) ($P = 0.007$, χ^2 test) (Table 4).

DISCUSSION

The current results showed that as to the SAP-spared hemifield the mean sensitivity of FDT perimetry was lower and FDT detected greater numbers of abnormal test points in the HTG group than in the NTG group between which the background data were identical except IOP. This finding contrasts to the fact that the mean of total deviation value in the SAP-spared hemifield tended to be better in the HTG group although the difference was not statistically significant. In OAG eyes with superior or inferior hemifield VFD, functional or morphologic abnormalities were found even in the SAP-spared hemifield using multifocal visual evoked potential technique[14] or scanning laser polarimetry[15,16] and also FDT perimetry.[3,4] In addition to these previous studies, the current study first suggested differences in functional abnormality in the SAP-spared hemifield between HTG and NTG eyes.

Most of the patients had no or little experience of FDT testing prior to this study. As to the learning effects of initial FDT perimetry, Matsuo et al[11] found significant improvement of the FDT perimetry results between the first and second tests but no significant changes between the second and third tests, suggesting the importance of at least 2 preceding tests to obtain reliable FDT perimetry results. Therefore, for the patients who had no experience of FDT perimetry in the current study, 2 sessions of FDT testing with the C-20 screening protocol and the N-30 full threshold protocol, respectively, were performed before obtaining the examination adopted for the analyses.

In the current study, eyes with refractive error less than ± 8 D were included. Because high myopic eyes are relatively common in Japanese population[17] and probably more common among glaucoma patients,[18] if moderate to high myopic eyes were excluded, the studied subjects would become relatively far from the true population of Japanese glaucoma patients. On the other hand, although the refractive error of each patient was corrected according to the manufacturers' recommendation, the influence of myopia on the results of SAP or FDT perimetry could not be ignored. However, if the eyes with myopia < −5 D were excluded from the studied eyes, the means and standard deviations of the FDT and SAP indices would be little changed. For example, the FDT mean sensitivity in the SAP-spared hemifield would be changed from 24.16 ± 3.11 to 23.93 ± 3.74 dB for HTG and from 27.28 ± 3.22 to 27.37 ± 3.14 dB for NTG. This suggests that the influence of high myopic eyes on the current results should not be so large.

TABLE 3. Comparison of the Results of the HFA With the Central 30-2 Full Threshold Test Between Patients With HTG and Those With NTG

	Hemifield	HTG	NTG	P
No. eyes	—	20	36	—
MD (dB)	—	−4.03 ± 3.55	−3.43 ± 2.83	0.72
Pattern standard deviation (dB)	—	8.38 ± 5.03	7.14 ± 4.04	0.54
Mean sensitivity (dB)	Spared	27.91 ± 1.66	27.57 ± 1.70	0.38
	Impaired	18.99 ± 7.06	21.42 ± 5.84	0.36
Mean total deviation (dB)	Spared	0.36 ± 1.46	−0.25 ± 1.53	0.17
	Impaired	−9.04 ± 7.45	−6.55 ± 6.03	0.53

Mean ± standard deviation.
P indicates *P* value in comparison of means between the HTG and NTG groups (Mann-Whitney test); Spared (impaired), spared (impaired) hemifields determined with the HFA results.

TABLE 4. Comparison of the Results of the FDT Perimetry With the N-30 Full Threshold Test Between Patients With HTG and Those With NTG

	Hemifield	HTG	NTG	P
No. eyes	—	20	36	—
MD (dB)	—	−5.59 ± 3.19	−4.13 ± 3.18	0.009*
Mean sensitivity (dB)	Spared	24.16 ± 3.11	27.28 ± 3.22	0.001*
	Impaired	15.33 ± 6.6	19.98 ± 6.2	0.011*
No. abnormal test points	Spared	3.20 ± 2.8	1.14 ± 0.25	0.005*
	Impaired	6.30 ± 2.1	4.89 ± 2.6	0.051*
Rate of eyes with abnormal FDT results in the HFA-spared hemifield	—	13/20	12/36	0.007†

Mean ± standard deviation.
P indicates *P* value in comparison of means or proportions between the HTG and NTG groups (* with Mann-Whitney test and † with χ^2 test); spared (impaired), spared (impaired) hemifields determined with the HFA results.

Between the HTG and NTG groups in the current study, difference in IOP at the entry averaged about 2.5 mm Hg and that in the highest IOP in their clinical charts averaged about 6 mm Hg. Because IOP varied due to medications or other factors, actual differences in mean IOP throughout their clinical history between the HTG and NTG eyes were hardly determined. However, it should be certain that eyes in the HTG group had been exposed to higher IOP for longer period than those in the NTG group. Between the HTG and NTG groups, there was no significant difference in refraction, the morphology of the optic disc evaluated with the HRT II, and prevalence of disc hemorrhage. Although difference in other important factors, including corneal thickness, and unknown factors in the patients' background between the 2 groups can not be excluded, differences in IOP should be one of main causes for discrepancy in the FDT results in the SAP-spared hemifield.

HTG and NTG should be included in the same or continuously spreading clinical entity, which is OAG. IOP is believed to be the most important risk factor for OAG. It can be speculated that IOP plays the more vital role in OAG patients with the higher IOP. On the other hand, risk factors other than IOP may be relatively more involved with the pathogenesis of OAG in patients with lower IOP. Therefore, even small differences in IOP such as 6 mm Hg between HTG and NTG groups in the current study should have possible impact on the clinical findings of OAG, and it should deserve careful investigation. In previous studies,[19,20] the reduction in IOP by approximately 5 mm Hg by medical or surgical therapies showed significant effects to halt or slow the deteriorations in visual field defects or optic disc findings in NTG, suggesting that a 6-mm Hg difference in IOP between HTG and NTG patients in the current study should have clinical implication.

One limitation of this study is the limited number of the patients. However, among the same number of the patients, the results of FDT were significantly different between the HTG and NTG patients with *P* value ranged 0.005 to 0.001 in the SAP-spared hemifield (Table 4), whereas there was no intergroup difference in the HFA indices with *P* value larger than 0.17 (Table 3). A statistical power analysis, with α of 0.05 and the power of 0.8, revealed that if we try to detect the difference in the mean sensitivity of 0.34 dB, which is the intergroup difference in the SAP mean sensitivity in the SAP-spared hemifield (Table 3), the sample size needed is calculated as approximately 760 (380 vs. 380) subjects. Another limitation of the current study is the lack of measurements of corneal thickness which possibly influence the IOP measurements.[21] If corneal thickness were obtained in the current study, some of the patients would be classified into the different group after the correction of IOP using corneal thickness. This should deserve future studies when an appropriate correction method of IOP with corneal thickness will be available.

Although it has recently become the subject of debate, the magnocellular pathway was reportedly more predominantly damaged by chronically elevated IOP in monkey eyes.[7] Magnocellular pathway is thought to play a role in abnormality in FDT perimetry.[5,6] Therefore, it is likely that the current result suggests possible association between elevated IOP and abnormality in FDT results although it should be confirmed by future studies including longitudinal follow-up of greater numbers of the patients. In other words, as to the detection of preperimetric or early functional changes in glaucomatous eyes, FDT perimetry may have higher sensitivity in OAG eyes with higher IOP.

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