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CLINICAL INVESTIGATION

# Structural and functional assessment by hemispheric asymmetry testing of the macular region in preperimetric glaucoma

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**Abstract**
*Purpose* To investigate structural measurements of the macular area in preperimetric glaucoma (PG) patients using spectral domain optical coherence tomography with two functional measurements [10-2 Humphrey visual field (HFA) and 10-2 Microperimeter-1 (MP-1)] and by macular symmetry testing.
*Methods* Fifteen eyes of 15 PG subjects with a retinal nerve fiber layer defect in the inferior hemisphere and 15 eyes of 15 normal control subjects were enrolled. Macular symmetry testing was performed between the superior and inferior zones by comparing zone thickness in each hemisphere. Perimetric sensitivity asymmetry was calculated with two functional measurements. Structure–function relationships between macular symmetry testing and the mean retinal sensitivity of the corresponding hemifield or perimetric sensitivity asymmetry were calculated using Spearman's rank correlation and linear regression.
*Results* Macular zone thickness in the abnormal hemispheres was significantly less than that in normal hemispheres in PG eyes and the corresponding hemispheres in control eyes ($P < 0.001$). Macular symmetry testing was significantly lower in PG eyes compared to control eyes ($P < 0.001$). HFA (10-2) and MP-1 (10-2) correlated significantly ($rs = 0.81$, $P < 0.0001$). Macular symmetry testing values were significantly correlated with perimetric sensitivity and perimetric sensitivity asymmetry with two functional measurements ($rs = 0.61$, $P = 0.02$; HFA and $rs = 0.68$, $P = 0.006$; MP-1).
*Conclusions* Our results suggest that macular asymmetry analysis can reveal the structure–functional relationship in PG eyes.

**Keywords** Macular symmetry testing · Spectral domain optical coherence tomography · Central visual field testing

## Introduction

It is widely believed that optic nerve head damage and retinal nerve fiber layer defects (RNFLD) precede perimetric defects as assessed by standard automated perimetry (SAP) in glaucoma [1]. This was explained by the "functional reserve," which asserts that a normal healthy eye has an excess number of retinal ganglion cells so that visual function will remain unchanged until ganglion cell loss has become profound. Garway-Heath demonstrated that the appearance of a functional reserve could be explained as a statistical artifact using log units for perimetric sensitivity and linear units for anatomical measurements [2]. Even now, a structure–function relationship remains controversial in the earliest stages of "preperimetric" glaucoma [3–5].

The 30-2 or 24-2 program for the Humphrey field analyzer (HFA, Carl Zeiss-Meditec Inc, Dublin, CA, USA) has test points 6° apart. The sparse number of test points may be one reason why glaucomatous visual field defects are not detected in eyes with early structural abnormalities. High spatial resolution perimetry allows practical assessment of selected regions of the visual fields at higher resolution than conventional perimetry [6, 7]. Microperimetry,

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also known as fundus controlled perimetry or fundus perimetry, assesses retinal sensitivity while the ocular fundus is directly examined and provides a precise correlation between macular structural pathology and corresponding functional defects. A recent study reveals that microperimetry can detect more subtle glaucoma functional damage than SAP [8]. The commercially available Microperimeter-1 (MP-1, Nidek Instruments Inc, Padova, Italy) has similar stimulus patterns, sizes, durations and testing strategies compared to HFA, but there are differences in background adaptation level and minimum stimulus luminance. Although the dynamic range of MP-1 is narrow compared to HFA, one significant advantage of the MP-1 microperimeter over the HFA is the ability for fixation stability quantification, which leads to lower variability [9, 10]. Accurate measurement of sensitivity in a retinal nerve fiber layer defect enables a better understanding of a precise functional evaluation in very early stage of glaucoma [11]. A paucity of information is available regarding the use of MP-1 to detect visual field defects in preperimetric glaucoma.

Macular thickness evaluation is gaining increasing attention after Zeimer hypothesized that quantitative detection of glaucomatous damage at the posterior pole by retinal thickness mapping may provide a method for detection and monitoring early glaucomatous damage [12]. The introduction of spectral domain optical coherence tomography (SD-OCT) allows us to measure the ganglion cell complex (GCC, the combination of retinal nerve fiber, retinal ganglion cell and inner plexiform layers) covering the central macula. Previous studies demonstrated that GCC thickness was significantly lower in glaucomatous eyes with visual field defects than in healthy eyes [13, 14]. A number of studies report a high correlation between global visual field sensitivity and GCC in glaucomatous subjects using SD-OCT [15, 16].

Meanwhile, horizontal hemifield asymmetry is regarded as very useful in the assessment of early glaucomatous changes as it measures disparity in macular thickness between superior and inferior zone [17, 18]. Glaucomatous damage usually commences in only one horizontal hemifield and is assessed using the glaucoma hemifield test, which measures the disparity in retinal sensitivity between the superior and inferior hemifields [19]. However, few studies used regression analysis to confirm the structure–function relationship between the macula and the central visual field at the very early stages of glaucoma using macular asymmetry analysis.

The aim of this study was to carry out macular scans using SD-OCT in patients with preperimetric glaucoma (PG) and normal participants and to investigate the structure–function relationship between the macula and the central visual field using two different functional measurements (HFA and MP-1) by macular asymmetry analysis.

## Materials and methods

This study met the Helsinki Declaration guidelines and was approved by the Ethical Committee of Kanazawa University Graduate School of Medical Science. Informed consent was obtained from each subject.

Both PG patients and normal subjects were enrolled for examination from May 2008 to October 2008 at the Department of Ophthalmology of Kanazawa University Hospital. One eye of each subject was examined in this study according to the eligibility criteria described below. If both eyes met the eligibility criteria, one eye was randomly selected.

All subjects had complete ophthalmologic examinations including best corrected visual acuity (BCVA), slit lamp examination, intraocular pressure (IOP) measurement using Goldmann applanation tonometry, gonioscopy, dilated fundus biomicroscopy using a 90-diopter lens, stereoscopic optic disc photography and SAP using an HFA with the 30-2 or 24-2 Swedish Interactive Threshold Algorithm (SITA). Inclusion criteria were BCVA $\geq$20/20, open angle and no ocular pathology other than glaucoma. Exclusion criteria included cataract or large refractive errors (outside of the $\pm$6.00 D sphere or 2.00 D cylinder).

Only reliable SAP results, defined as false-negative and false-positive responses <15 % and fixation loss <20 %, were eligible for inclusion in the study. Glaucomatous visual field defects were determined according to Anderson's criteria in which one of the following was present: having a cluster of three or more non-edge points with $P < 5$ % and at least one point with $P < 1$ % in the pattern deviation probability plot; a pattern standard deviation (PSD) of <5 %; or glaucoma hemifield test results outside normal limits [20]. PG eyes underwent SAP at least twice prior to this study. Normal subjects had a normal optic nerve head appearance, IOP <21 mmHg, and normal SAP results. PG eyes had glaucomatous optic disc abnormalities with a localized, wedge-shape RNFLD at areas of rim thinning, but without glaucomatous visual field defects. Wide-angle view fundus images of all PG subjects were obtained using a digital funduscopic camera (VX-10i, KOWA, Tokyo, Japan), which confirmed that an RNFLD was present. Eyes that had no measured or known IOP >21 mmHg were classified as normal tension glaucoma. To compare the upper and lower hemisphere with the corresponding hemisphere between PG and control subjects, we evaluated PG eyes with one localized RNFLD in the inferior hemisphere. Subjects were excluded if they had diabetic retinopathy or other diseases that could cause

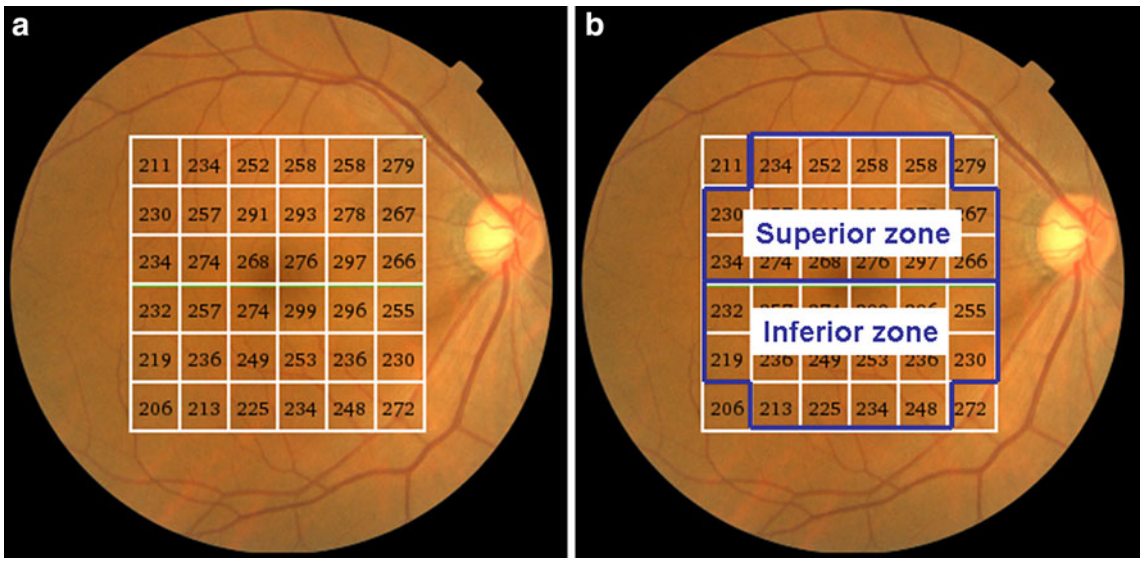


**Fig. 1** Zone thickness map of inferior and superior hemispheres derived from spectral domain optical coherence tomography measurements. **a** Posterior pole retinal thickness map showing the 36 sectors used in spectral domain optical coherence tomography. **b** Superior and inferior zones used for assessment of asymmetry in hemisphere macular thickness

visual field loss or optic disc abnormalities, or if they had undergone a previous intraocular surgery.

### Spectral domain OCT imaging

OCT imaging was performed with the SD-OCT (3D-OCT 1000, Topcon, Tokyo, Japan) after pupil dilation in normal subjects and PG subjects. The instrument uses a superluminescent diode laser with a center wavelength of 840 nm and a bandwidth of 50 nm as a light source. The transverse and axial resolutions were 10 and 6 μm, respectively. The 3D scan protocol was used for macular thickness measurements in this study. This was a raster scan composed of 512 × 128 (vertical × horizontal) axial scans covering a 6 × 6-mm macular region. Built-in software (version 2.10) assessed macular thickness determined between the internal limiting membrane and inner border of the retinal pigment epithelium. Macular thickness measurements were registered according to an overlaid OCT-generated map with 36 sectors (Fig. 1a). All images were obtained with image quality scores >60 as recommended by the manufacturer.

### Macular symmetry analysis

From the macular thickness map, we divided 36 sectors into both superior and inferior zones. Because the visual field test of the central 10° roughly corresponded to a 6 × 6-mm macular region, we arbitrarily selected 32 sectors (excluding 4 sectors at the corners) and divided them into 16 sectors to calculate the average thickness of the superior and inferior zones corresponding to each visual hemifield (Fig. 1b). Macular symmetry testing was performed by comparing the superior and inferior zones (macular thickness in the inferior zone/macular thickness in the superior zone × 100).

### Central visual field testing

Central visual field testing was performed only in PG subjects by using the HFA 10-2 and MP-1 10-2 programs. Two types of testing were performed on a single day, with the order of the tests randomized. Subjects took 15-min rest intervals between the examinations to avoid fatigue. The HFA 10-2 program had 68 locations covering the central 10° with the SITA standard threshold strategy: Goldmann size III white stimuli, 200 ms in duration and white background with a luminance of 10 cd/m$^2$. Visual fields were included when there were <20 % fixation losses, false positives and false negatives. For the MP-1, a 10-2 pattern similar to the HFA 10-2 visual field was used. This pattern also has 68 locations covering the central 10°. White test lights (stimulus size Goldmann III, 200 ms in duration) were presented on a white background with a luminance of 1.27 cd/m$^2$ using a 4-2 threshold staircase strategy. Subjects were asked to fixate on a red cross. Spherical refractive error was corrected by the optics of the instrument. MP-1 allows for automated real-time fundus tracking by infra-red fundus imaging, which compensates for misalignment by pausing the stimulus projection. Visual fields were included when MP-1 classified the fixation stability as

stable or relatively unstable (stable: >75 % of fixation points fell within a 2° diameter circle centered on the gravitational center of all fixation points; relatively unstable: <75 % of fixation points fell within a 2° circle, but >75 % were located within a 4° diameter circle) [21]. Mean sensitivity (MS) at each test location was measured in decibels. MS was also evaluated with unlogged 1/Lambert (1/L) values. The 1/L values were calculated for each test location by dividing the decibel readings by 10 and then unlogging the quotient. In the same way as macular symmetry testing, perimetric sensitivity asymmetry was calculated between inferior and superior hemifields using measurements by the HFA10-2 and MP-1 10-2 programs (perimetric sensitivity in the abnormal hemifield/perimetric sensitivity in the normal hemifield × 100).

### Statistical analyses

Data were presented as the mean ± standard deviation (SD). Differences in the ratios were evaluated using a $\chi^2$ test. Differences in the macular thickness between inferior and superior zones in PG or control eyes were compared using a paired *t* test. Differences between inferior zone thickness of PG and control eyes, or between superior zone thickness of PG and control eyes, were compared using an unpaired *t* test. Macular symmetry testing values of PG and control eyes were also compared using an unpaired *t* test. Correlations between superior and inferior zone macular thickness and visual field parameters of corresponding hemifields were examined by linear regression analysis. Correlations were also examined between macular symmetry testing and visual field parameters in each hemifield as well as between macular symmetry testing and perimetric sensitivity asymmetry. Correlations were expressed as the Spearman's rank coefficient of correlation.

Statistical analyses were performed using SPSS 17.0 software for Windows (SPSS Japan, Inc., Chicago, IL, USA). A *P* value <0.05 was considered statistically significant.

## Results

A total of 45 healthy and 23 PG eyes were enrolled in the present study. Among the 45 healthy eyes, 15 control subjects, who were age- and sex-matched with the PG patients, were selected. In the PG group, one eye with unacceptable OCT scans, one eye with unreliable HFA visual field results and three eyes with multiple RNFLD were excluded. In 18 of the PG eyes, 3 showed a localized RNFLD in the superior hemisphere according to a red-free photograph, leaving 15 eyes with one localized RNFL defect in the inferior hemisphere. All PG eyes were diagnosed as normal tension glaucoma. The mean age was 54.1 ± 10.1 years in the PG group and 56.7 ± 14.7 years in the healthy control group. Refraction and initial IOPs were similar between the two groups. Mean deviation (MD) and PSD of HFA24-2 standard automated perimetry for the PG group and the healthy control group were not different between the groups (MD, 0.1 ± 1.1 and 0.2 ± 1.10 dB, PSD, 1.9 ± 0.4 and 1.4 ± 0.3 dB, respectively) (Table 1).

**Table 1** Clinical characteristics of study population

| | PG eyes ($n = 15$) | Control eyes ($n = 15$) | *P* value |
|---|---|---|---|
| Gender (M/F) | 6/9 | 6/9 | 1.00 |
| Age (years) (range) | 54.1 ± 10.1 (31–66) | 56.7 ± 14.7 (28–71) | 0.11 |
| Spherical equivalent (D) | −1.7 ± 1.9 | −0.54 ± 1.5 | 0.06 |
| IOP (mmHg) | 12.5 ± 3.3 | 13.5 ± 3.5 | 0.87 |
| HFA 30-2 MD (dB) | 0.1 ± 1.1 | 0.2 ± 1.1 | 0.80 |
| HFA 30-2 PSD (dB) | 1.9 ± 0.4 | 1.4 ± 0.3 | 0.40 |

*PG* preperimetric glaucoma, *MD* mean deviation, *PSD* pattern standard deviation, *IOP* intraocular pressure, *HFA* Humphrey visual field analyzer

The difference between each zone thickness is shown in Fig. 2. The inferior zone thickness (abnormal hemisphere) in PG eyes was significantly less than the superior zone thickness (normal hemisphere) in PG eyes (inferior zone: 243.0 ± 21.2 μm, superior zone: 261.1 ± 17.6 μm, paired *t* test, $P < 0.001$) (Fig. 2a). Similarly, inferior zone thickness of control eyes was significantly less than superior zone thickness in control eyes (inferior zone 261.3 ± 7.3 μm, superior zone, 268.7 ± 11.8 μm, paired *t* test, $P < 0.001$) (Fig. 2b). Superior zone thickness (normal hemisphere) of PG eyes was not significantly different compared to superior zone thickness of control eyes (unpaired *t* test, $P = 0.15$). In contrast, inferior zone thickness (abnormal hemisphere) of PG eyes was significantly thinner than inferior zone thickness of control eyes (unpaired *t* test, $P < 0.001$).

All HFA visual field parameters of abnormal hemifields were significantly less than those of normal hemifields in PG eyes. The average MP-1 total deviation (TD) values of abnormal hemifields were significantly less than normal hemifields in PG eyes. MP-1 MS values were small in abnormal fields compared to normal hemifields, but the difference was not significant (Table 2). The correlation in abnormal hemifields between HFA TD and MP-1 TD was significant in PG eyes (rs = 0.81, $P < 0.0001$).

In the PG eyes, the thickness of the inferior or superior zones did not correlate with TD or MS in the corresponding hemifields (Table 3).

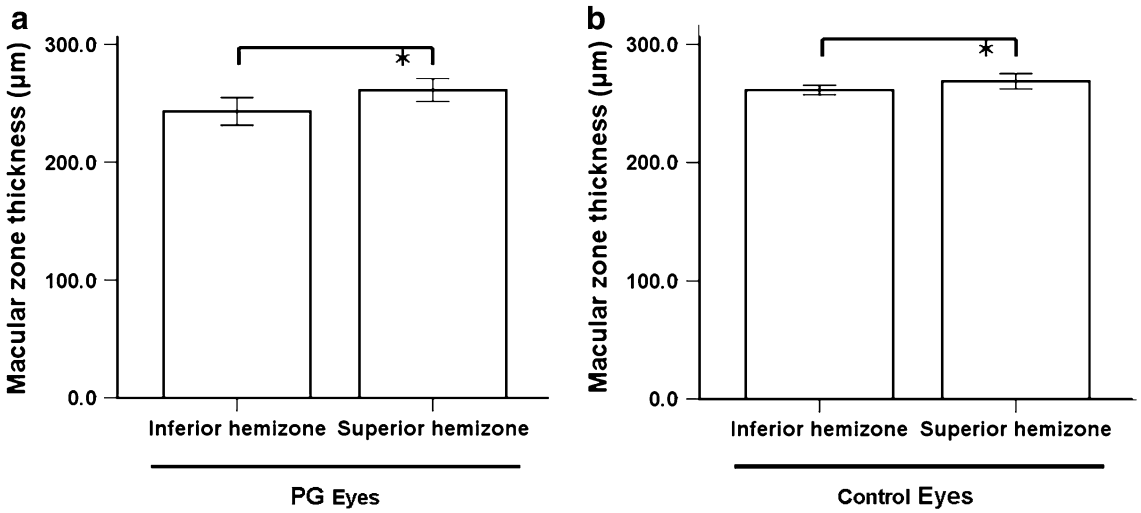


**Fig. 2** Graph showing the distribution of zone thickness of each hemisphere in preperimetric glaucoma (PG) or control eyes. The figure illustrates the distribution of zone thickness measurements of each hemisphere by spectral domain optical coherence tomography in PG and control eyes. **a** The macular zone thickness of inferior and superior hemisphere in PG eyes. **b** The macular zone thickness of inferior and superior hemisphere in control eyes. The *vertical bars* illustrate the upper and lower limits of the 95 % confidence intervals. The inferior zone thickness in PG eyes was significantly less than the superior zone thickness in PG eyes ($P < 0.001$) (**a**). Inferior zone thickness of control eyes was significantly less than superior zone thickness in control eyes ($P < 0.001$) (**b**)

**Table 2** Comparison of central visual field data between each hemifield in PG eyes

| | Abnormal hemifield | Normal hemifield | *P* value |
|---|---|---|---|
| HFA10-2 TD in hemifield (dB) | −1.3 ± 2.6 | 0.3 ± 1.0 | 0.02 |
| HFA10-2 MS in hemifield (dB) | 31.0 ± 2.6 | 33.3 ± 1.1 | 0.03 |
| HFA10-2 MS in hemifield (1/L) | 1725.2 ± 571.2 | 2317.8 ± 600.4 | 0.001 |
| MP-1 10-2 TD in hemifield (dB) | −1.6 ± 1.8 | 0.2 ± 0.8 | 0.001 |
| MP-1 10-2 MS in hemifield (dB) | 18.4 ± 1.9 | 19.2 ± 0.9 | 0.07 |
| MP-1 10-2 MS in hemifield (1/L) | 81.8 ± 17.3 | 84.3 ± 14.4 | 0.54 |

*TD* total deviation, *PG* preperimetric glaucoma, *MS* mean sensitivity, *HFA* Humphrey visual field analyzer, *MP-1* Microperimeter-1, *1/L* 1/Lambert

In the analysis of macular symmetry testing values, the mean value of macular symmetry testing in PG eyes was significantly less than that of control eyes [93.0 ± 4.4 (range 85.0–101.5) in PG eyes and 97.4 ± 2.8 (range 94.5–97.4) in control eyes, unpaired *t* test, $P = 0.003$].

In the PG eyes, macular symmetry testing correlated significantly with TD and MS values in abnormal hemifields of HFA and MP-1 (Table 4). In addition, macular symmetry testing values correlated with perimetric sensitivity asymmetry in PG eyes (rs = 0.61, $P = 0.02$; HFA and rs = 0.68, $P = 0.006$; MP-1) (Fig. 3).

**Table 3** Correlation between OCT parameters and corresponding visual field parameters of each hemifield in PG eyes

| Parameters | Correlation in abnormal hemifield | | Correlation in normal hemifield | |
|---|---|---|---|---|
| | rs | *P* value | rs | *P* value |
| HFA 10-2 TD (dB) | 0.11 | 0.70 | 0.12 | 0.66 |
| HFA 10-2 MS (dB) | 0.20 | 0.49 | −0.17 | 0.54 |
| HFA 10-2 MS (1/L) | 0.26 | 0.34 | −0.13 | 0.64 |
| MP-1 10-2 TD (dB) | 0.24 | 0.39 | −0.05 | 0.85 |
| MP-1 10-2 MS (dB) | 0.25 | 0.37 | 0.01 | 0.98 |
| MP-1 10-2 MS (1/L) | 0.37 | 0.17 | 0.01 | 0.98 |

*OCT* optical coherence tomography, *TD* total deviation, *PG* preperimetric glaucoma, *MS* mean sensitivity, *HFA* Humphrey visual field analyzer, *MP-1* Microperimeter-1, *1/L* 1/Lambert

**Table 4** Correlation between the macular symmetry testing value and central visual field parameters of each hemifield in PG eyes

| Parameters | Correlation in abnormal hemifield | | Correlation in normal hemifield | |
|---|---|---|---|---|
| | rs | *P* value | rs | *P* value |
| HFA 10-2 TD (dB) | 0.65 | 0.008 | 0.21 | 0.44 |
| HFA 10-2 MS (dB) | 0.73 | 0.002 | 0.23 | 0.42 |
| HFA 10-2 MS (1/L) | 0.74 | 0.002 | 0.24 | 0.39 |
| MP-1 10-2 TD (dB) | 0.80 | 0.001 | 0.06 | 0.83 |
| MP-1 10-2 MS (dB) | 0.78 | 0.001 | 0.29 | 0.29 |
| MP-1 10-2 MS (1/L) | 0.73 | 0.002 | 0.29 | 0.29 |

*TD* total deviation, *PG* preperimetric glaucoma, *MS* mean sensitivity, *HFA* Humphrey visual field analyzer, *MP-1* Microperimeter-1, *1/L* 1/Lambert

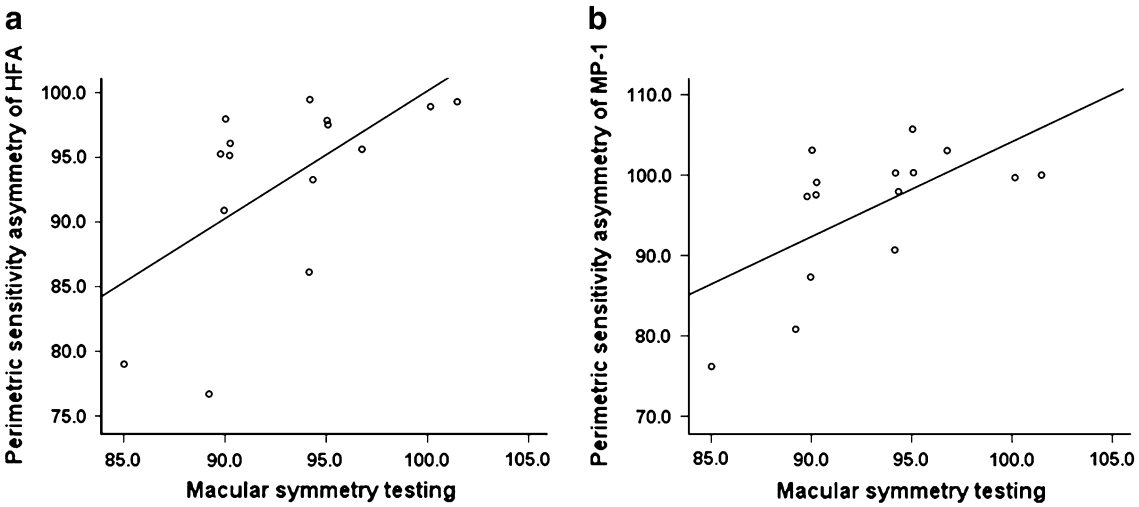


**Fig. 3** Correlation between macular symmetry testing values and perimetric sensitivity asymmetry in preperimetric glaucoma (PG). Scatter plot illustrating the correlation between macular symmetry testing values and perimetric sensitivity asymmetry [Humphrey Field Analyzer (HFA) 10-2 (**a**) or Microperimetry-1 (MP-1) 10-2, (**b**)]. Macular symmetry testing values were significantly correlated with perimetric sensitivity asymmetry in PG eyes (rs = 0.61, $P = 0.02$ for HFA 10-2; rs = 0.68, $P = 0.006$ for MP-1 10-2)

## Discussion

We investigated the regional relationship between the structure (the superior and inferior macular zone thickness measured by SD-OCT) and the function (HFA and MP-1 central visual field testing with 10° in each hemifield) in the PG and control eyes. The present study showed that the inferior zone macular thickness with RNFLD was thinner than the normal superior zone in PG eyes and corresponding inferior zone in control eyes. Furthermore, analysis of macular thickness asymmetry revealed a significant correlation for central visual field damage in PG eyes, suggesting a structure–function relationship in the central region.

Zeimer showed that the Retinal Thickness Analyzer (RTA, Taila Technology Ltd., Neve-Ilan, Israel) mapping of the posterior pole may detect retinal thickness loss in glaucoma patients [12]. Tanito et al. [22] reported that perifoveal average thickness values in PG eyes were significantly less than in normal control eyes using RTA. Bagga et al. [17] evaluated macular thickness in abnormal and normal visual hemifields using time-domain OCT (Stratus OCT, Carl-Zeiss Meditech, Dublin, CA, USA). They reported that a comparison between the macular thickness of perimetrically abnormal and normal hemizones resulted in a significant reduction in corresponding abnormal visual hemifields. Inuzuka et al. [23] report that macular retinal thickness decreased with an apparently normal hemifield in glaucoma patients using SD-OCT, showing that retinal structural changes preceded the loss of visual field. Our study is in agreement with these reports and showed that macular thickness of an abnormal hemisphere with localized RNFLD was thinner than a normal hemisphere without localized RNFLD in the PG subjects and as compared to the corresponding normal hemisphere of control subjects. This indicates that structural changes occurred in the very early stages of glaucoma. Meanwhile, our results showed that the inferior macular hemizone was significantly less than the superior macular hemizone. We arbitrarily selected 32 sectors, excluding 4 sectors at the corners of a 6 × 6-mm macular region. Ooto et al. [24] performed a 3D raster scan to measure the mean regional retinal thickness on an Early Treatment Diabetic Retinopathy Study (ETDRS) layout in normal Japanese patients using a 3D OCT-1000, the same as our device. Their report showed that the superior macular thickness was significantly greater than the inferior macular thickness. The macular hemizone in our study was different from the ETDRS layout, but our results are in agreement with their report.

Moreover, GCC measurements derived from SD-OCT are reported to be advantageous in detecting early glaucomatous damage. Takagi et al. [25] reported that macular GCC thickness decreased in the apparently normal hemisphere in glaucomatous eyes compared to the corresponding hemisphere in normal eyes. However, they also reported that there was no significant difference in macular thickness between apparently normal hemispheres of glaucomatous and normal eyes. Direct comparison was difficult because they tested apparently normal hemispheres of glaucomatous subjects, while our current study examined macular hemizone thickness with RNFLD in PG

eyes. Nevertheless, our results indicate that macular thickness was affected in PG eyes with a definite localized RNFD in one hemisphere.

Macular sensitivity decreased in abnormal hemifields with RNFLD compared to sensitivity corresponding to normal hemifields in PG eyes. This result was in agreement with Orzalesi's report that documented the presence of decreased retinal sensitivity corresponding to a localized RNFLD using a high density of targets in scanning laser ophthalmoscopy [7]. Kanadani et al. [26] evaluated the macular area in glaucoma patients with an HFA 10-2 threshold test and reported that 98.2 % of eyes with glaucoma had perimetric changes. The 24-2 distribution of test locations in the central 10° was limited to 12 locations, each separated by 6°. The 10-2 pattern affords a high-resolution measurement of central vision function as it samples 68 locations separated by 2°. Prior studies of the structure–function relationship in glaucoma correlated the 24-2 pattern of visual field locations with early to moderate glaucomatous stages. Our current study used the 10-2 pattern of locations and concentrated on patients with preperimetric glaucoma in an effort to better understand the structure-function relationship at the very early stages of disease.

In the current study, we used two perimetric devices to evaluate macular sensitivity: HFA and MP-1. Both methods demonstrated the same significant correlation ($rs = 0.81$). Migor et al. [27] reported that microperimetry does not have any advantage over standard perimetry in cases of diffuse nerve atrophy, but they also reported that early loss of retinal sensitivity could be detected in eyes with localized RNFLD but normal standard visual fields. Lima et al. [8] demonstrated that macular sensitivity evaluated by SLO microperimetry had a significant correlation with SAP paracentral visual field defects. Ozturk et al. [28] reported MP-1 correlated with HFA in detecting glaucomatous visual field defects in the macular area. These reports are in agreement with our results. The dynamic range of MP-1 (20 dB) was smaller than that of SAP or SLO microperimetry. However, the MP-1 device has an electronic eye tracking system for automatic correction of stimulus position as a function of eye movement, and it allows precise automatic follow-up examinations irrespective of baseline fixation. This may be one reason why SAP 10-2 and MP-1 10-2 results significantly correlated with macular parameters.

Bagga et al. [17] showed that a macular thickness symmetry test had the potential to detect glaucomatous damage using TD-OCT. Salgarello et al. [18] reported that hemispheric asymmetry in glaucomatous eyes increased compared with the control group using RTA. These results are in agreement with our report where macular symmetry testing values of PG eyes were significantly different from those of control eyes using SD-OCT measurements. Moreover, we demonstrated a significant correlation between macular symmetry testing values and visual field parameters, indicating that macular symmetry analysis could be a sensitive index to reveal structural damage in early stages of glaucoma.

Our study had several limitations. First, our study included a relatively small sample size. However, all of our patients had PG eyes with localized RNFLD in the inferior hemisphere. Therefore, a detailed analysis of the macular thickness and central visual field could enable the detection of a structure-function relationship in PG eyes. Second, macular parameters were assessed by total macular thickness. Recently, a symmetry test of macular thickness, the posterior pole asymmetry analysis, has been installed in the Spectralis (Heidelberg Engineering, Heidelberg, Germany) SD-OCT. This offers the potential of improved diagnostic capability compared to the previously reported symmetry test [29]. Further studies will be needed to study the structure–function relationship using macular GCC symmetry analysis and central visual field sensitivity using the 10-2 program.

In conclusion, we showed that the lower half of macular thickness with RNFLD decreased on SD-OCT testing in PG eyes. In addition, a structure-function relationship was exhibited when we used macular symmetry testing compared to central visual field sensitivity measured by HFA or MP-1 10-2 patterns in PG eyes. Macular symmetry testing is useful for assessing the very early stages of the structural and functional relationship in preperimetric glaucoma.

**Conflicts of interest** C. Kawaguchi, None; Y. Nakatani, None; S. Ohkubo, None; T. Higashide, None; I. Kawaguchi, None; K. Sugiyama, None.

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