Int Ophthalmol (2019) 39:127–136
https://doi.org/10.1007/s10792-017-0796-8

ORIGINAL PAPER

Circumpapillary microperimetry to detect glaucoma: a pilot study for sector-based comparison to circumpapillary retinal nerve fiber layer measurement

Yoshiyuki Kita · Gábor Holló · Tsunehiro Saito · Akiko Murai · Ritsuko Kita · Akito Hirakata

Received: 2 June 2017 / Accepted: 11 December 2017 / Published online: 16 December 2017

Abstract
Purpose To evaluate and compare the diagnostic performance of circumpapillary microperimetry (MP) sensitivity and circumpapillary retinal nerve fiber layer thickness (cpRNFLT) measured with optical coherence tomography (OCT) for detection of early to moderate open-angle glaucoma.
Methods Eleven eyes (11 patients) with early or moderate open-angle glaucoma and seven normal eyes (7 subjects) underwent MP (MP-3 microperimeter, NIDEK, Japan) and cpRNFLT measurement (RS-3000 Advance OCT, NIDEK, Japan) using an identical circumpapillary circle and similar measurement sectors. The structure–function relationship and the area under the receiver-operating characteristics curve (AUROC) were investigated for each sector, respectively.
Results Significant differences ($P < 0.05$) between glaucoma and normal eyes were found for five of the 12 OCT sectors and seven of the 24 MP sectors. High correlation between cpRNFLT and MP sensitivity was found in the inferotemporal area (OCT sector 5) and superotemporal area (OCT sector 1) ($r = 0.818$, $P < 0.001$, and $r = 0.796$, $P < 0.001$, respectively). The AUROC values in these sectors ranged 0.890–1.000 for cpRNFLT and 0.825–0.981 for MP sensitivity. Overall, the AUROC ranged 0.506–1.000 for sector cpRNFLT and 0.591–0.981 for sector MP sensitivity.
Conclusions In this pilot study, circumpapillary MP sensitivity and cpRNFLT showed similar diagnostic power. The structure–function relationship was strong for the superotemporal and inferotemporal circumpapillary areas. Our results suggest that circumpapillary MP represents a new aspect of microperimetry in glaucoma. Further studies on larger populations are necessary to clarify whether the current results are confirmed in clinical practice.

Keywords Glaucoma · Microperimetry sensitivity · Retinal nerve fiber layer · Spectral-domain optical coherence tomography · Structure–function relationship

Y. Kita (✉) · T. Saito · A. Murai · R. Kita · A. Hirakata
Department of Ophthalmology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo 181-8611, Japan
e-mail: kitakita220@gmail.com

G. Holló
Department of Ophthalmology, Semmelweis University, Budapest, Hungary

Introduction

Microperimetry (MP) or fundus perimetry is a novel functional method, which has been successfully used to analyze central macular sensitivity in various retinal diseases, including age-related macular degeneration (AMD), diabetic macular edema, epiretinal membrane,

and retinitis pigmentosa [1–7]. In MP, the fundus image is viewed using an infrared fundus camera, and it is tracked and adjusted throughout the testing process, whereas visual field data are mapped directly to the fundus image [6]. Retinal sensitivity determined with MP effectively detects functional deficits in the early stages of AMD [1, 7]. The functional deficit in early AMD was found to correspond with macular changes detected using spectral-domain optical coherence tomography (SD-OCT). In another study, long-term follow-up using MP was found useful for the evaluation of functional recovery after an epiretinal membrane surgery [2].

The information on the usefulness of MP in glaucoma is limited. In a recent study, macular ganglion cell and inner plexiform layer (GCIPL) thickness measured using the Cirrus HD-OCT showed statistically significant structure–function relationship with the central visual field sensitivity of MP in glaucoma [8, 9]. Recently, Rao et al. reported that the relationship between macular sensitivity measured with standard automated perimetry (SAP) and MP, respectively, showed a similar relationship with the macular GCIPL thickness in glaucoma [10]. Rao et al. also reported that the GCIPL thickness performed significantly better than the macular sensitivity measurements with MP in glaucoma diagnostics [11].

The currently available information on MP in glaucoma addresses only the sensitivity in and around the macula, which may be influenced by other common concomitant diseases of the elderly, such as diabetic maculopathy and AMD. Circumpapillary MP made along the circumpapillary OCT measuring circle of 3.45 mm diameter around the optic nerve head center, however, is not influenced by macular diseases, and may potentially be useful for the glaucoma investigations.

In order to investigate the potential usefulness of circumpapillary MP measurement in glaucoma in the current pilot study, we investigated circumpapillary MP sensitivity values in healthy eyes and eyes with early or moderate open-angle glaucoma along a 3.45 mm circle around the disc center. We evaluated the sector-based structure–function relationship between the corresponding MP sensitivity and OCT circumpapillary retinal nerve fiber layer thickness (cpRNFLT) values and determined and compared the diagnostic accuracy of the corresponding cpRNFLT and MP values, respectively.

Materials and methods

The study population comprised of 18 Japanese patients (7 healthy subjects and 11 primary open-angle and normal tension glaucoma patients), who were examined between November 2016 and March 2017 at the Kyorin University Hospital (Tokyo, Japan). The participants were retrospectively selected from the clinical research database. The patients were scheduled for a cross-sectional examination visit, and all participants signed the informed consent before entering the study. One eye per participant was randomly selected for inclusion. All study participants underwent a complete ophthalmologic examination that included visual acuity testing, slit-lamp biomicroscopy, gonioscopy, Goldmann applanation tonometry, and a dilated stereoscopic fundus examination. Non-cycloplegic refraction was measured using an auto Refracto/keratometer (ARK-530; NIDEK, Aichi, Japan). Refraction data were converted into the spherical equivalent, defined as the spherical power (in diopters) plus half the cylindrical power. To assess the visual field, the Swedish interactive threshold algorithm (SITA) 30-2 standard test of the Humphrey Field Analyzer (HFA, Humphrey-Zeiss Systems, Dublin, CA) was used. A reliable visual field was defined as a fixation loss ratio less than 20% and false-positive and false-negative rates less than 15%. A glaucomatous visual field result was defined as an abnormal result of the glaucoma hemifield test, a pattern standard deviation (PSD) of $< 5\%$, or 3 non-edge test points with an abnormal sensitivity threshold ($< 5\%$ probability of being normal), with 1 point having a pattern deviation of $< 1\%$.

To be included in the normal group, the healthy control subjects had to have normal intraocular pressure (IOP, < 21 mmHg) and normal optic nerve head (ONH) appearance, open anterior chamber angles, a normal and reliable visual field test result, clear optical media, a best-corrected visual acuity of 20/20 or better, a refractive spherical error between $+ 3.00$ and $- 6.00$ diopters, and a refractive cylindrical error of < 3.0 diopters. An eye was considered to have a normal ONH if the stereoscopic fundus examination revealed a vertical cup-to-disc ratio of ≤ 0.6, a uniform neuroretinal rim, no RNFL defects, and no ONH abnormalities (e.g., diffuse or localized rim thinning, disc hemorrhage), and an interocular difference in vertical cup-to-disc ratio < 0.2). Healthy

subjects with a possible history of elevated IOP (e.g., iridocyclitis, trauma), any eye disease or any other condition that affected the visual field, the cpRNFLT, and the circumpapillary MP measurements (e.g., pituitary lesions, demyelinating diseases, and diabetic retinopathy) were not included.

The glaucoma group comprised eyes with primary open-angle glaucoma and normal-tension glaucoma. Patients had to have a best-corrected visual acuity of 20/20 or better, clear optical media, a refractive spherical error between + 3.00 and − 6.00 diopters, a cylindrical refractive error of < 3.0 diopters, and open anterior chamber angles with gonioscopy (Shaffer grade > 2). All patients had characteristic glaucomatous optic neuropathy defined as neuroretinal rim narrowing at the optic disc margin with notching, excavation, and/or a visible RNFL defect, and reliable, reproducible glaucomatous visual field defect with the SITA 30-2 test (mean deviation (MD) value up to − 12 dB). Glaucoma patients were not included if they had any other retinal pathology, neurological disease, diabetes, or a history of retinal laser or intraocular surgery procedures. The glaucoma eyes were treated with topical intraocular pressure lowering medication.

The MP test and the OCT examination were conducted on the same day in each case. MP testing was always done first. MP and SAP tests were made within a one-month period.

Microperimetry

The MP examination was performed using the MP-3 microperimeter (NIDEK; Aichi, Japan). The protocol selected for the current investigation employs test point locations along a circle centered on the optic disc center. The circle has a diameter of 3.45 mm and contains 24 points evenly distributed along the test circle (test point separation 1.5°) (Fig. 1a). The measurement circle was manually positioned on the center of the optic disc. During MP testing, the eye-tracking function was activated. The test was performed in a dim room after pupil dilation with 0.5% tropicamide and 0.5% phenylephrine hydrochloride combination eye drops. The stimulus size was equal to the Goldmann size III stimulus. Background luminance was set at 31.4 apostilb, with a maximum luminance of 10,000 apostilb, a stimulus dynamic range of 34 dB, and a with red single cross fixation target of 1°. Visual sensitivities were estimated using a 4-2 staircase threshold strategy [6, 8]. Only stable fixation test results (fixation control within 1 degree from the fixation center in ≥ 75%) were included in the analysis. All participants received a 12-point training MP test session. The participants then completed the detailed 24-point MP test, for which the numbers of the test point locations started at the 12 o'clock position (Fig. 1a).

Optical coherence tomography

OCT measurements were made with an RS-3000 Advance OCT (software version 1.4.2.1; NIDEK; Aichi, Japan). The RS-3000 instrument includes a confocal scanning laser ophthalmoscope, allowing fundus images to be monitored and SD-OCT equipment allowing 3D tomographic imaging. RS-3000 collects ocular microstructural images using a scanning laser diode that emits a scan beam with a wavelength of 880 nm. The OCT equipment has a 7-µm tissue depth resolution and a 20-µm transverse resolution [12, 13]. Single 3D data sets are acquired in 1.6 s. After pupil dilation, a well-trained operator obtained good-quality OCT images (signal strength index > 7, no eye movement was not corrected with the software). Internal fixation was achieved in all patients. For cpRNFLT imaging, raster scanning over a 6 × 6 mm^2 area centered on the optic disc center was conducted at a scan density of 512 A-scans (horizontal) × 128 B-scans (vertical). cpRNFLT measurements were performed along a 3.45-mm diameter circle automatically positioned around the optic disc. The numbering of the 12 (30-degree size) cpRNFLT sectors was initiated at the 1 o'clock position (Fig. 1b). The circumpapillary protocol scan circle did not pass over any parapapillary atrophy in any case.

Spatial correspondence of the MP and cpRNFLT sectors

The 360-degree circumpapillary circle was divided into 12 RNFLT sectors and 24 MP test points. Two MP test points correspond to one RNFLT sector. The corresponding test point locations and RNFLT sectors have the same number, but each second MP test point location clockwise is marked with a comma. For

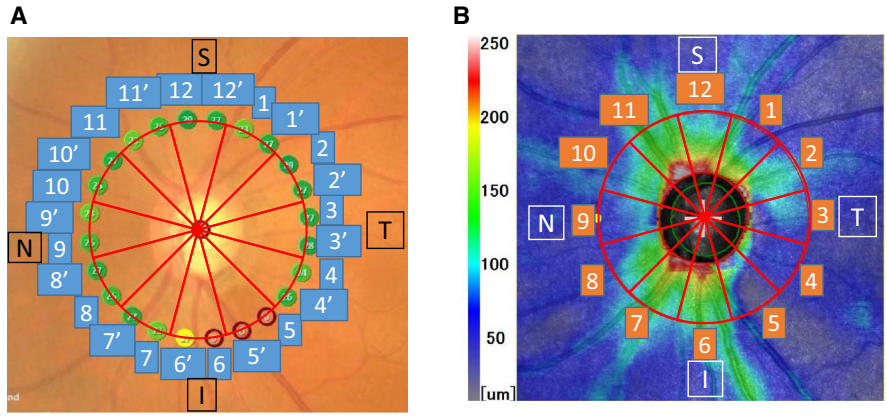

Fig. 1 Positions of the circumpapillary microperimetry retinal sensitivity sectors (**a**) and the circumpapillary retinal nerve fiber layer sectors (**b**) used for analysis in the current investigation. The measurement points are evenly distributed along the same 3.45 mm circle around the disc center. *S* superior, *T* temporal, *I* inferior, *N* nasal

Table 1 Demographics of study subjects

Variable	Normal group ($n = 7$)	Glaucoma group ($n = 11$)	*P* value
Gender, no. of subjects			
Male	5	5	0.367
Female	2	6	
Age (years)	48.9 ± 16.6	62.9 ± 8.67	0.067
IOP (mmHg)	15.3 ± 2.21	17.2 ± 2.09	0.085
Spherical equivalent ± SD (D)	− 1.91 ± 1.81	− 1.56 ± 2.75	0.954
MD in HFA (dB)	0.68 ± 1.21	− 5.53 ± 3.99	0.003**
PSD in HFA (dB)	1.45 ± 0.23	8.44 ± 4.45	0.001**
Glaucoma severity	n.a.	Early 7/moderate 4	

D diopter, *MD* mean deviation, *PSD* pattern standard deviation, *HFA* Humphrey field analyzer, *n.a.* not applicable, *IOP* intraocular pressure

**$P < 0.01$ (two-sample *t*-test)

example, cpRNFLT sector 1 corresponds to MP test point location 1 and 1′.

Statistical analysis

Differences between groups were assessed using a Mann–Whitney U test or Student's *t*-test, as appropriate. The Spearman's rank correlation was used to characterize the correlation between the corresponding MP sensitivity and cpRNFLT values. Receiver-operating characteristic (ROC) curves were used to assess the ability of each of the variables to differentiate the glaucomatous eyes from the normal eyes. The ROC curve shows the trade-off between the sensitivity and 1-specificity. An area under the receiver-operating characteristics curve (AUROC) of 1.0 represents perfect discrimination, whereas an AUROC of 0.5 represents chance discrimination. MedCalc, version 11 (MedCalc Software, Mariakerke, Belgium), was used to draw and compare the ROC curves. The other statistical analyses were performed using SPSS statistical software (Version 23.0, SPSS Inc., Chicago, IL). The normal distribution of the study sample was assessed with the Shapiro–Wilk test. Descriptive statistics are presented as the mean ± standard deviation for normally distributed variables and median and inter-quartile range for non-normally distributed variables. $P < 0.05$ was considered statistically significant.

Results

According to the criteria, of 20 eyes that qualified for initial inclusion, two eyes were excluded due to poor fixation during the MP tests. The final analysis

Table 2 Comparison of the circumpapillary retinal nerve fiber layer thickness between the groups

RNFLT	Normal group Mean ± SD (μm)	Glaucoma group Mean ± SD (μm)	*P* value
Sector 1	138.6 ± 18.16	92.1 ± 37.9	0.008**
Sector 2	81.4 ± 8.02	71.7 ± 20.4	0.252
Sector 3	62.7 ± 1.00	64.0 ± 9.98	0.793
Sector 4	73.3 ± 12.8	58.8 ± 7.29	0.007**
Sector 5	139.0 ± 21.97	62.7 ± 25.9	< 0.001**
Sector 6	126.4 ± 13.79	88.7 ± 23.4	0.001**
Sector 7	88.9 ± 17.5	82.7 ± 22.4	0.549
Sector 8	58.4 ± 14.6	50.4 ± 8.50	0.156
Sector 9	50.3 ± 12.7	45.7 ± 8.06	0.362
Sector 10	76.3 ± 17.2	61.4 ± 16.9	0.089
Sector 11	97.6 ± 13.3	83.0 ± 24.1	0.165
Sector 12	123.1 ± 19.00	78.4 ± 22.7	0.001**

RNFLT circumpapillary retinal nerve fiber layer thickness

**$P < 0.01$ (two-sample *t*-test)

Table 3 Comparison of the circumpapillary retinal sensitivities between the groups

MP-3	Normal eye group Median (IQR) (dB)	Glaucoma group Median (IQR) (dB)	*P* value
Sector 1	27.0 (6.00)	19.0 (6.00)	0.003**
Sector 1′	27.0 (2.00)	25.0 (4.00)	0.020*
Sector 2	27.0 (6.00)	25.0 (9.00)	0.211
Sector 2′	27.0 (4.00)	25.0 (4.00)	0.104
Sector 3	27.0 (6.00)	25.0 (3.00)	0.104
Sector 3′	29.0 (2.00)	27.0 (4.00)	0.126
Sector 4	27.0 (4.00)	27.0 (2.00)	0.246
Sector 4′	27.0 (2.00)	26.0 (6.00)	0.151
Sector 5	27.0 (4.00)	13.0 (23.0)	0.003**
Sector 5′	25.0 (2.00)	5.00 (23.0)	< 0.001**
Sector 6	25.0 (8.00)	19.0 (25.0)	0.020*
Sector 6′	25.0 (4.00)	23.0 (4.00)	0.027*
Sector 7	27.0 (2.00)	25.0 (4.00)	0.104
Sector 7′	27.0 (6.00)	23.0 (6.00)	0.104
Sector 8	27.0 (4.00)	25.0 (4.00)	0.085
Sector 8′	27.0 (6.00)	27.0 (2.00)	0.425
Sector 9	27.0 (4.00)	25.0 (2.00)	0.285
Sector 9′	29.0 (4.00)	25.0 (4.00)	0.151
Sector 10	27.0 (3.00)	25.0 (4.00)	0.151
Sector 10′	27.0 (3.00)	25.0 (4.00)	0.328
Sector 11	27.0 (6.00)	23.0 (8.00)	0.056
Sector 11′	27.0 (3.00)	23.0 (2.00)	0.015*
Sector 12	25.0 (2.00)	25.0 (10.0)	0.536
Sector 12′	25.0 (2.00)	25.0 (4.00)	0.479

Two MP test points correspond to one RNFLT sector. The corresponding test point locations and RNFLT sectors have the same number, but each second MP test point location clockwise is marked with a comma. For example, cpRNFLT sector 1 corresponds to MP test point location 1 and 1′

IQR interquartile range

*$P < 0.05$, **$P < 0.01$ (Mann–Whitney U test)

included 18 eyes. The normal group was comprised of one eye from seven patients ($n = 7$), and the glaucoma group consisted of one eye from 11 patients ($n = 11$). The demographics of the participants are given in Table 1. No significant difference in sex distribution, age, IOP, and refraction was seen between the groups.

Table 4 Correlation between the circumpapillary retinal nerve fiber layer thickness and the corresponding circumpapillary retinal sensitivities

RNFLT	MP-3	*r*	*P* value
Sector 1	Sector 1	0.796	< 0.001**
	Sector 1′	0.480	0.044*
Sector 2	Sector 2	0.216	0.389
	Sector 2′	0.349	0.155
Sector 3	Sector 3	− 0.225	0.370
	Sector 3′	− 0.280	0.260
Sector 4	Sector 4	0.031	0.904
	Sector 4′	0.062	0.807
Sector 5	Sector 5	0.734	0.001**
	Sector 5′	0.818	< 0.001**
Sector 6	Sector 6	0.412	0.090
	Sector 6′	0.414	0.087
Sector 7	Sector 7	− 0.348	0.157
	Sector 7′	− 0.172	0.494
Sector 8	Sector 8	− 0.190	0.451
	Sector 8′	0.437	0.070
Sector 9	Sector 9	0.309	0.212
	Sector 9′	0.290	0.244
Sector 10	Sector 10	0.514	0.029*
	Sector 10′	0.225	0.369
Sector 11	Sector 11	0.383	0.116
	Sector 11′	0.505	0.033*
Sector 12	Sector 12	0.107	0.673
	Sector 12′	− 0.090	0.722

Two MP test points correspond to one RNFLT sector. The corresponding test point locations and RNFLT sectors have the same number, but each second MP test point location clockwise is marked with a comma. For example, cpRNFLT sector 1 corresponds to MP test point location 1 and 1′

r Spearman's rank correlation coefficient

*$P < 0.05$, **$P < 0.01$

The test duration of the HFA SITA test was 434.7 ± 69.7 s. For MP, the test time was 263.9 ± 125.3 s ($P < 0.001$).

Table 2 shows the circumpapillary sector RNFLT results and their comparison between the normal and glaucoma group. Statistically significant differences were found for sectors 1, 4, 5, 6, and 12. (Fig. 1b).

Table 3 shows the MP sensitivities result in the normal and glaucoma groups, respectively. Significant differences were found for sectors 1, 1′, 5, 5′, 6, 6′, and 11′ (Fig. 1a).

Table 4 shows the relationship of sector MP sensitivity and cpRNFLT values for all participants and each sector, respectively. Statistically significant correlations were found between MP sensitivity and cpRNFLT values for six MP sectors (1, 1′, 5, 5′, 10, and 11′). Among these, the highest correlation was seen for sector 5′ (inferotemporal area; $r = 0.818$, $P < 0.001$), whereas the second highest correlation was seen for the sector 1 (superotemporal area; $r = 0.796$, $P < 0.001$).

Table 5 shows the sector AUROC values calculated for the separation of glaucoma and normal eyes. The AUROC of the RNFLT values ranged between 0.506 (sector 3; temporal area) and 1.000 (sector 5; inferotemporal area). The AUROC of MP sensitivity values ranged between 0.591 (sector 12; superior area) and 0.981 (sector 5′; inferotemporal area). The AUROC of cpRNFLT sector 12 was significantly greater than that of the corresponding MP sensitivity at sector 12 and sector 12′ ($P < 0.05$). For the other sectors, no statistically significant difference was found ($P > 0.10$ for all comparisons). Clinically significant diagnostic ability (AUROC significantly better than the line of 0.5) was found for 6 of the 12 cpRNFLT sectors (50%) and 11 of the 24 MP sensitivity sectors (45.8%).

Discussion

In the current pilot study, we evaluated the diagnostic performance of circumpapillary MP testing in early and moderate glaucoma. MP is a relatively new technology, which has been shown to provide clinically useful information on the macular function in AMD and glaucoma [1, 7–10]. However, since glaucoma is typically a disease of the elderly, the macula often also suffers from early AMD or other diseases [1, 2, 7], which reduce the ability of MP to detect the glaucomatous functional damage. Circumpapillary MP made along a circle of 3.45 mm diameter that is centered on the disc center does not involve the macula. Thus, the results are theoretically not influenced by macular pathologies. In addition, the measuring circle used for circumpapillary MP corresponds to the measuring circle used in SD-OCT for RNFLT measurement, which potentially enables the

Table 5 Area under receiver-operating characteristic curves for cpRNFLT and circumpapillary retinal sensitivity, respectively

cpRNFL sector number	Normal versus Glaucoma		MP-3 sector number	Normal versus glaucoma	
	cpRNFLT			Circumpapillary MP sensitivity	
	AUROC (SE)	*P* value		AUROC (SE)	*P* value
1	0.890 (0.092)	< 0.0001**	1	0.909 (0.068)	< 0.0001**
			1′	0.825 (0.092)	0.0004**
2	0.766 (0.125)	0.03**	2	0.682 (0.130)	0.1622
			2′	0.740 (0.116)	0.0384**
3	0.506 (0.153)	0.97	3	0.734 (0.122)	0.06
			3′	0.727 (0.121)	0.06
4	0.825 (0.130)	0.01**	4	0.675 (0.137)	0.2019
			4′	0.714 (0.120)	0.0741
5	1.000 (0.000)	< 0.0001**	5	0.903 (0.076)	< 0.0001**
			5′	0.981 (0.022)	< 0.0001**
6	0.935 (0.067)	< 0.0001**	6	0.825 (0.100)	0.0011**
			6′	0.812 (0.098)	0.0015**
7	0.545 (0.149)	0.7596	7	0.740 (0.112)	0.0312**
			7′	0.740 (0.119)	0.0435**
8	0.656 (0.149)	0.2956	8	0.753 (0.130)	0.0507
			8′	0.617 (0.150)	0.4362
9	0.558 (0.155)	0.7070	9	0.656 (0.127)	0.2214
			9′	0.714 (0.124)	0.0843
10	0.734 (0.122)	0.0554	10	0.714 (0.121)	0.0762
			10′	0.649 (0.139)	0.2836
11	0.701 (0.136)	0.1384	11	0.773 (0.110)	0.013**
			11′	0.844 (0.090)	0.0001**
12	0.961 (0.043)	< 0.0001**	12	0.591* (0.143)	0.5250
			12′	0.610* (0.135)	0.4121

Two MP test points correspond to one RNFLT sector. The corresponding test point locations and RNFLT sectors have the same number, but each second MP test point location clockwise is marked with a comma. For example, cpRNFLT sector 1 corresponds to MP test point location 1 and 1′

AUROC area under receiver-operating characteristic curve, *SE* standard error, *cpRNFLT* circumpapillary retinal nerve fiber layer thickness

*$P<0.05$ for comparison of corresponding cpRNFLT, **indicates that the AUROC was significantly better than 0.5

investigator to compare the corresponding structural damage (sector RNFLT) and functional deterioration (MP sensitivity). These aspects suggest that circumpapillary MP testing may be a useful additional test to SD-OCT and visual field examination, for the detection of glaucoma. To our knowledge, the clinical usefulness of circumpapillary MP was not evaluated prior to the current investigation (Figs. 2, 3).

The most important result of our study is that circumpapillary MP has a diagnostic accuracy and AUROC values that are similar to those found with SD-OCT for cpRNFLT, for each circumpapillary sector, respectively. The best separation was found for the inferotemporal and superotemporal circumpapillary sectors with both methods, and significant structure–function correlations were found for these regions and the superonasal area. Since early glaucomatous structural damage typically occurs both inferotemporally and superotemporally in primary open-angle and normal tension glaucoma [14, 15]; and the

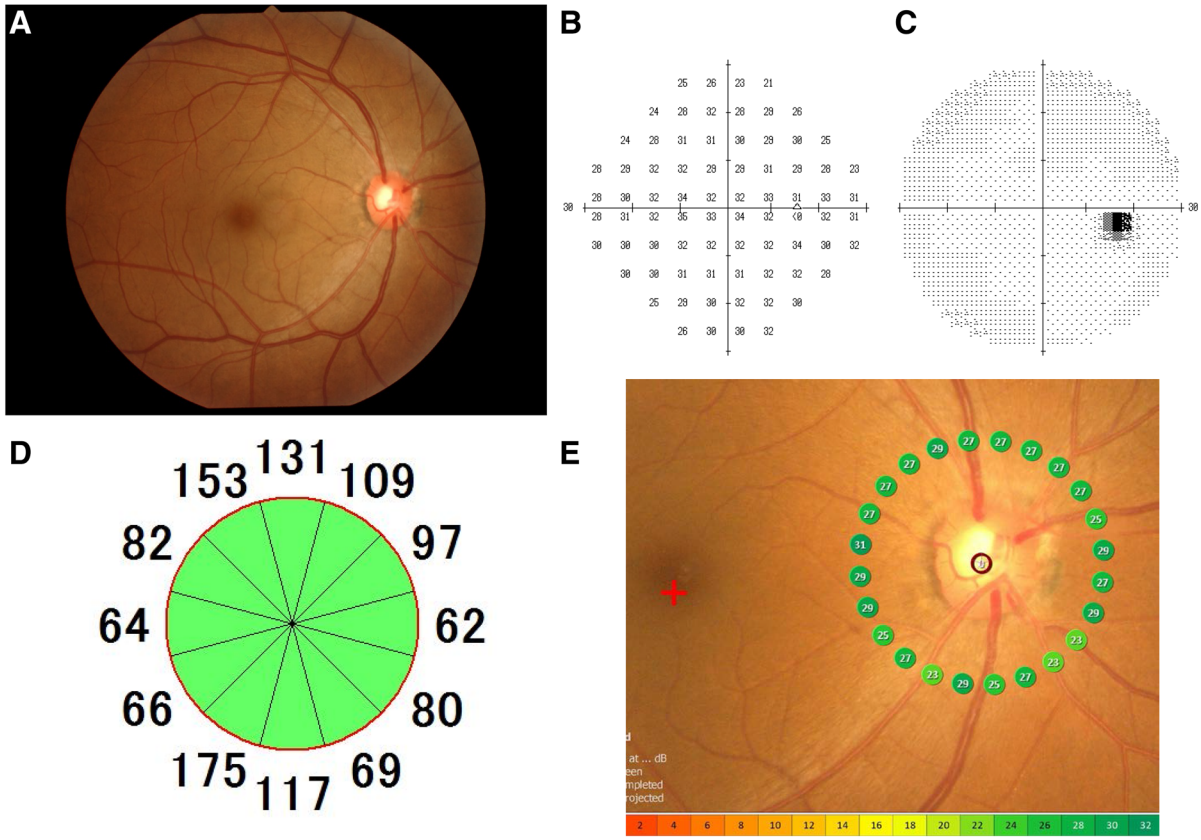

Fig. 2 Color fundus photograph (**a**), Humphrey 30-2 SITA visual field (**b**, gray scale; **c**, threshold sensitivity values), RS-3000 spectral-domain optical coherence tomographic (SD-OCT) image with the 12 retinal nerve fiber layer sectors (**d**), and the 24 circumpapillary microperimetry sensitivity sectors (**e**) of a normal right eye 66-year-old female subject

MP sensitivity reductions spatially corresponded to the sector RNFL thinning measured with SD-OCT, we believe that our MP results hinted at the early glaucomatous damage locations. This suggests that circumpapillary MP could be a clinically useful method for the detection of early-to-moderate glaucoma, at least when conventional perimetry and macular MP cannot provide sufficient information due to macular diseases. Since MP technology offers fixation control during the examination, the reliability of the result can also be objectively characterized.

It is also important to note that the test time for MP (4.4 min on average) was statistically and clinically significantly shorter than that of the 30-2 SITA visual field test (7.2 min on average). The shorter test time, which is attributed to the lower number of test points compared to the SITA test, and the assistance of the eye tracking function of the instrument, represents a clinical advantage when inexperienced patients or patients with cooperation problem are investigated.

Our study has limitations. The number of participants was low, and all participants were Japanese primary open-angle glaucoma or normal-tension glaucoma patients. The glaucoma eyes had early or moderate glaucomatous deterioration, and no severe glaucoma cases and pre-perimetric glaucoma eyes were included. We did not include any eyes with any macular disease. Therefore, no conclusion from our study can be made on patients with other ethnicities and glaucoma types, very early or very late glaucomatous damage, and coexisting macular pathology. Since no direct spatial correspondence between the circumpapillary MP locations and the SITA visual field test point locations has been established, we could not investigate the relationship of sector MP sensitivity and individual visual field location sensitivity values.

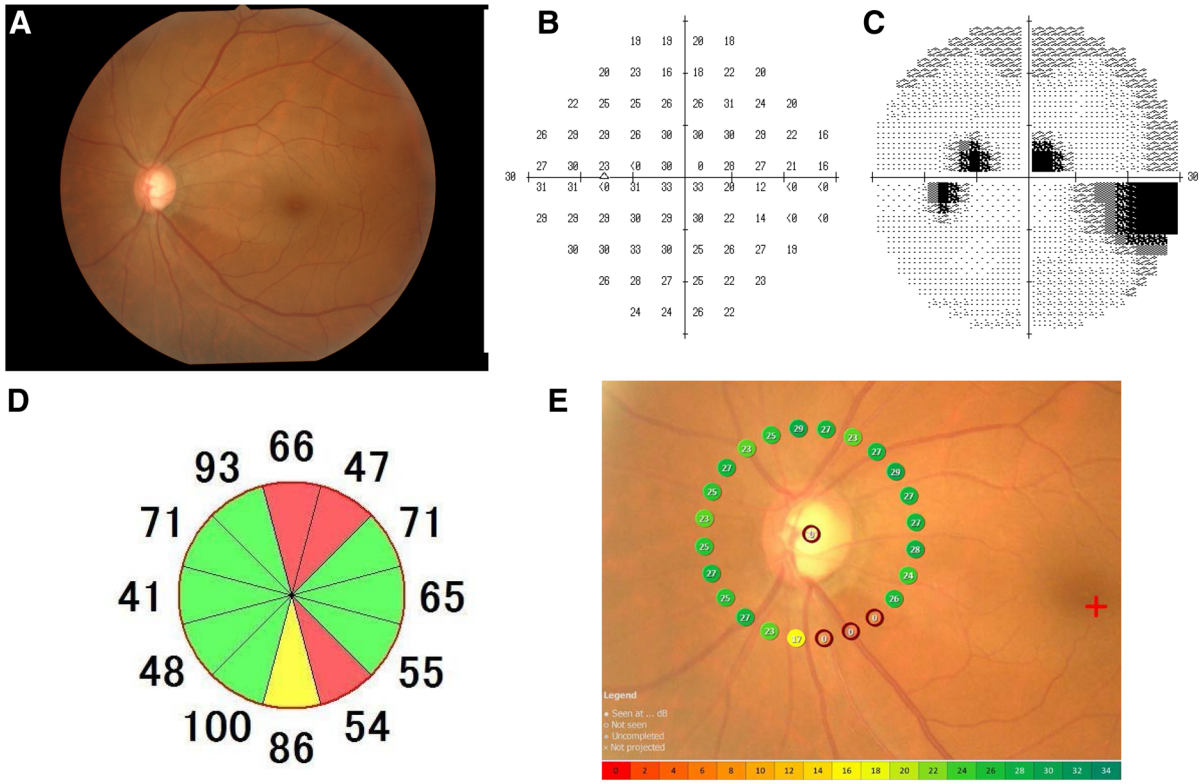

Fig. 3 Color fundus photograph (**a**), Humphrey 30-2 SITA visual field (**b**, gray scale; **c**, threshold sensitivity values), RS-3000 SD-OCT image with the 12 retinal nerve fiber layer sectors (**d**), and the 24 circumpapillary microperimetry sensitivity sectors (**e**) of the glaucomatous left eye of a 59-year-old female primary open-angle glaucoma patient. The superior and inferotemporal structural damage (neuroretinal rim loss on **a** and retinal nerve fiber layer thinning on **d**) spatially corresponds with the inferior nasal step and the superior paracentral sensitivity reduction shown by the Humphrey visual field (**b**, **c**). The circumpapillary microperimetry test (**e**) shows a significant sensitivity reduction inferotemporally around the disc

In conclusion, our pilot study showed that circumpapillary MP has a favorable diagnostic performance to detect early and moderate glaucoma in Japanese eyes. The diagnostic accuracy was similar to that of SD-OCT cpRNFLT. The correlation between cpRNFLT and circumpapillary MP sensitivity was very high for the inferotemporal and superotemporal circumpapillary areas, and the test time was significantly shorter than that with the 30-2 SITA test. These results suggest that circumpapillary MP is a fast, easy to perform, and potentially useful diagnostic test for glaucoma. Circumpapillary MP is probably less sensitive to detect very early glaucomatous changes than cpRNFLT; therefore at the current level of information, we do not recommend it as a general surrogate of cpRNFLT measurement. However, further investigations on larger populations with various ethnicities and coexisting macular diseases are necessary to establish the clinical value of circumpapillary MP for glaucoma detection.

Compliance with ethical standards

Conflict of interest Gábor Holló is a consultant of Optovue Inc and Zeiss. The other authors declare no conflict of interest.

Human and animal rights The Kyorin University Hospital Institutional Review Board for Human Research approved the study protocol, and the study conduct adhered to the tenets of the Declaration of Helsinki.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Ooto S, Suzuki M, Vongkulsiri S, Sato T, Spaide RF (2015) Multimodal visual function testing in eyes with nonexudative age-related macular degeneration. Retina 35:1726–1734
2. Dal Vecchio M, Lavia C, Nassisi M, Grignolo FM, Fea AM (2016) Microperimetric assessment after epiretinal membrane surgery: 4-year follow-up. J Ophthalmol. https://doi.org/10.1155/2016/7030791
3. Cennamo G, Vecchio EC, Finelli M, Velotti N, de Crecchio G (2015) Evaluation of ischemic diabetic maculopathy with fourier-domain optical coherence tomography and microperimetry. Can J Ophthalmol 50:44–48
4. Kim YH, Yun C, Kim JT, Kim SW, Oh J, Huh K (2014) The correlation between retinal sensitivity assessed by microperimetry and contrast sensitivity in diabetic macular oedema. Br J Ophthalmol 98:1618–1628
5. Battu R, Khanna A, Hegde B, Berendschot TT, Grover S, Schouten JS (2015) Correlation of structure and function of the macula inpatients with retinitis pigmentosa. Eye 29:699–702
6. Igarashi N, Matsuura M, Hashimoto Y, Hirasawa K, Murata H, Inoue T, Obata R, Aihara M, Asaoka R (2016) Assessing visual fields in patients with retinitis pigmentosa using a novel microperimeter with eye tracking: the MP-3. PLoS ONE. https://doi.org/10.1371/journal.pone.0166666
7. Wu Z, Ayton LN, Luu CD, Guymer RH (2014) Relationship between retinal microstructures on optical coherence tomography and microperimetry in age-related macular degeneration. Ophthalmology 121:1445–1452
8. Hirooka K, Misaki K, Nitta E, Ukegawa K, Sato S, Tsujikawa A (2016) Comparison of macular integrity assessment (MAIA^{TM}), MP-3, and Humphrey field analyzer in the evaluation of the relationship between the structure and function of the macula. PLoS ONE. https://doi.org/10.1371/journal.pone.0151000
9. Sato S, Hirooka K, Baba T, Tenkumo K, Nitta E, Shiraga F (2013) Correlation between the ganglion cell-inner plexiform layer thickness measured with cirrus HD-OCT and macular visual field sensitivity measured with microperimetry. Investig Ophthalmol Vis Sci 54:3046–3051
10. Rao HL, Januwada M, Hussain RS, Pillutla LN, Begum VU, Chaitanya A, Senthil S, Garudadri CS (2015) Comparing the structure–function relationship at the macula with standard automated perimetry and microperimetry. Investig Ophthalmol Vis Sci 56:8063–8068
11. Rao HL, Hussain RS, Januwada M, Pillutla LN, Begum VU, Chaitanya A, Senthil S, Garudadri CS (2016) Structural and functional assessment of macula to diagnose glaucoma. Eye 31:593–600
12. Kita Y, Holló G, Kita R, Horie D, Inoue M, Hirakata A (2015) Differences of intrasession reproducibility of circumpapillary total retinal thickness and circumpapillary retinal nerve fiber layer thickness measurements made with the RS-3000 optical coherence tomograph. PLoS ONE 10(12):e0144721. https://doi.org/10.1371/journal.pone.0144721
13. Kita Y, Soutome N, Horie D, Kita R, Holló G (2017) Circumpapillary ganglion cell complex thickness to diagnose glaucoma: a pilot study. Indian J Ophthalmol 65:41–47
14. Lee WJ, Na KI, Kim YK, Jeoung JW, Park KH (2017) Diagnostic ability of wide-field retinal nerve fiber layer maps using swept-source optical coherence tomography for detection of preperimetric and early perimetric glaucoma. J Glaucoma 26:577–585
15. Chen HY, Wang TH, Lee YM, Hung TJ (2005) Retinal nerve fiber layer thickness measured by optical coherence tomography and its correlation with visual field defects in early glaucoma. J Formos Med Assoc 104:927–934