Ann Med Res

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journal page: www.annalsmedres.org

Compatibility of peripapillary choroidal thickness measurement between 4-point manual measurement and measurement by manual re-segmentation in eyes with and without glaucoma

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ARTICLE INFO

Keywords:
Peripapillary choroidal thickness
OCT
Glaucoma

Received: Jan 06, 2023
Accepted: Jul 27, 2023
Available Online: 25.08.2023

DOI:
10.5455/annalsmedres.2023.01.012

Abstract

Aim: To evaluate the compatibility of peripapillary choroidal thickness (PPCT) measurement using 4-point manual measurement and measurement by manual re-segmentation in glaucomatous and non-glaucomatous eyes.

Materials and Methods: A total of 270 eyes of 135 consecutive patients were included in the study. Of these, 79 eyes had glaucoma. Optical coherence tomography (OCT) images of peripapillary circle scans were investigated with Heidelberg Spectralis OCT. PPCT at the 3.4 mm circular line around the disc was measured by 2 techniques; manual 4-point measurement (PPCT-1) at temporal, superior, nasal and inferior sectors and by changing retinal nerve fiber layer (RNFL) segmentation lines manually using the editing function and obtaining automatic calculations (PPCT-2). **Compatibility of the 2 techniques and** correlations with RNFL measurements, age, sex, glaucoma presence, glaucoma drug usage, glaucoma stage, mean deviation, spherical equivalent (SE) and corneal thickness were investigated.

Results: The mean PPCT measured with the PPCT-1 technique was 149.44 ± 2.84 µm, while with the PPCT-2 technique, it was 159.51 ± 2.72 µm ($p<0.001$). There was a statistically strong positive correlation between PPCT-1 nasal and PPCT-2 nasal values (R: 0.875). Negative correlations were found between the 2 methods with age, SE, glaucoma stage and glaucoma drug usage.

Conclusion: Both of the measurement techniques are useful to evaluate PPCT.

Introduction

Spectral-domain optical coherence tomography (OCT) technology, also referred to as Fourier domain OCT, uses a super-luminescence diode and produces cross-sectional B-scan images of the retina. With this technology, B-scans are acquired and 3-dimensional images of the retina with high spatial resolution are constructed [1].

There are different scanning protocols like circle scan, line scan, and volume scan. For peripapillary retinal nerve fiber layer (RNFL) analysis, the circle scan is used. The Heidelberg Spectralis OCT system (Spectralis OCT; Heidelberg Engineering, Inc., Dossenheim, Germany) uses fovea to disc alignment technology correcting unwanted rotations; thus, improving the reproducibility of RNFL measurements and ensuring point-to-point thickness comparisons. Moreover, Tru-Track Active Eye Tracking enables the capture of multiple images in the same location [1].

A Bruch membrane opening (BMO)-centered OCT scan of the RNFL is taken in a circular pattern and the circle is unrolled and displayed as a horizontal OCT scan. This allows viewing of the peripapillary RNFL in a single shot. The scans have 3.9 axial and 11-micron lateral resolution. This information is displayed in temporal-superior-nasal-inferior-temporal (TSNIT) order (from left to right), generating a TSNIT thickness profile. The average thickness of the RNFL is calculated and displayed in the thickness profile and classification chart [1].

With advances in OCT technology, it is possible to visualize the choroid [2], which is a vascular layer supplying the outer retina [3], as well as the prelaminar portion of the optic nerve head [4,5]. Macular and peripapillary choroidal thickness measurements provide invaluable information about some retinal and optic nerve head diseases such as glaucoma [2].

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Since the peripapillary choroid is not as thick as in the macular region [6], the choroidoscleral junction is mostly discernable on OCT images of peripapillary circle scans in RNFL thickness profiles. With enhanced depth imaging (EDI), the quality of OCT images is enhanced by focusing on the outer retinal layer, choroid, and lamina cribrosa. EDI is available for all OCT images. But because automatic multilayer segmentation is not possible and reference data is not available for circle scans, RNFL classification is not possible with EDI [1].

There are OCT studies in the literature measuring peripapillary choroidal thickness (PPCT) with both manual and manual resegmentation. In this current study, we measured PPCT using two measurement techniques. One is a 4-point manual measurement using a distance measurement tool, and the other is a manual re-segmentation of the peripapillary circle scan. First of all, we aimed to investigate the compatibility of these two techniques. However, we also analyzed the relationship between PPCT measured by two techniques and RNFL, glaucoma, glaucoma drug use, vision, central corneal thickness (CCT), refraction, age, gender, intraocular pressure (IOP), and mean deviation (MD).

Materials and Methods

Study population and design

This study was approved by the local ethical committee with the registration number HNEAH-KAEK 2021/318-3365 and it adhered to the ethical principles stated in the Declaration of Helsinki. In this retrospective cross-sectional study, we investigated 270 peripapillary circle scans of 135 patients using Heidelberg Spectralis OCT between February and May 2022 at Sultan Abdulhamid Han Training and Research Hospital. For this study, the sample size was calculated as 105 when the G-Power was 95% power, 0.05 below the significance level, and the effect size was 0.5.

Patient recordings were investigated with ophthalmologic examination notes including refraction, IOP measurements with Goldmann applanation tonometry, biomicroscopic anterior, and dilated posterior segment evaluation. Demographic characteristics of the patients including age and sex were noted. Refractive status in spherical equivalent (SE) which is the sum of spherical refractive error and half of the cylinder, corneal thickness, IOP, glaucoma presence, glaucoma stage according to Hodapp-Parrish Anderson staging [7] using Goldmann visual field analysis, Swedish Interactive Threshold Algorithm Standard 24–2 (Humphrey visual field analyzer, Carl Zeiss Inc., Dublin, CA, USA), mean deviation of visual field results, and visual acuity on the Snellen Chart converted to LogMAR were examined and noted.

In the case of ocular hypertension (OHT) and glaucoma, visual field testing was investigated. The diagnosis of glaucoma is made based on specific optic disc findings, such as increased cupping, neuroretinal rim loss; focal notching, bayoneting, or nasalization of blood vessels accompanied by glaucomatous visual field loss and nerve fiber layer defects. IOP measurements were taken with applanation tonometry, corneal thickness measurements were obtained with pentacam (Oculus, Wetzlar, Germany), OCT scans were performed using Heidelberg Spectralis OCT (Spectralis OCT; Heidelberg Engineering, Inc., Dossenheim, Germany) with glaucoma application, and circle scans were conducted. After RNFL analysis, one grand mean and 6 sectorial RNFL thickness measurements were noted.

Figure 1. PPCT-1: peripapillary choroidal thickness measurement on OCT image of peripapillary circle scan; manual measurement from RPE-choroidoscleral junction. RPE: retinal pigment epithelium.

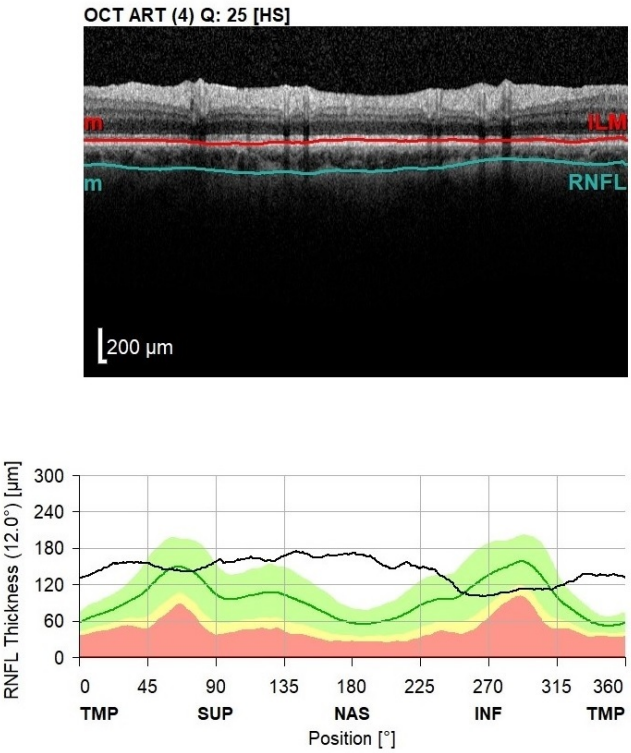

Figure 2. PPCT-2: On routine RNFL scan with segmentation editing function, the ILM line positioned is at RPE-Bruch membrane line and NFL repositioned to the choroidoscleral junction. Automatic calculation gives the 360o peripapillary thickness as one mean and 6 sectoral measurements. RNFL: retinal nerve fiber layer, ILM: internal limiting membrane, RPE: retinal pigment epithelium, NFL: nerve fiber layer.

Inclusion criteria

Patients aged above 40 years with RNFL scans with a quality score greater than or equal to 20 were included in the study. In the case of glaucoma or OHT diagnosis, patients using antiglaucomatous drugs or who had not started drug therapy were included. Phakic patients or patients with uncomplicated phacoemulsification history at least one year before were included.

Exclusion criteria

Patients with myopic or hypermetropic refractive error >4 diopters (D) or astigmatic refractive error >2D, inflammatory ocular diseases like uveitis, uncomplicated phacoemulsification history within 1 year, or complicated phacoemulsification history at any time, vitrectomized eyes, angle-closure glaucoma, maculopathy including intermediate and advanced age-related macular degeneration, diabetic retinopathy, and media opacities or other situations precluding OCT scan quality below 20 and scans where the choroidoscleral interface is not visible were not included into the study.

Measurements of peripapillary choroidal thickness

All measurements were made by Heidelberg Spectralis OCT (Spectralis OCT; Heidelberg Engineering, Inc., Dossenheim, Germany). Using the RNFL thickness map module, a circle scan was taken at 12^0 positioned approximately 3.4 mm from the center of the optic nerve head and an axial scan was taken in a circular pattern. Using the same OCT scan, choroidal thickness was measured by 2 techniques at different times by the same investigator blinded to previous results and patient characteristics.

Firstly, PPCT was measured manually at 4 points; temporal on the 0-180* axis, superior on the 90-270* axis, nasal on the 0-180* axis and inferior on the 90-270* axis (Figure 1). The perpendicular distance from retina pigment epithelium (RPE)-Bruch membrane complex to the discernable choroido-scleral junction was measured. These measurements were labeled as PPCT-1. If vessel shadowing precluded the measurements, nearest neighbor nasal or temporal measurements were completed. Results were recorded and overlays were deleted.

At a different time, the same scans were investigated with the RNFL thickness measurement module using the editing function for automatic segmentation lines by manually changing the internal limiting membrane (ILM) line repositioning the PRE-Bruch membrane complex and nerve fiber layer (NFL) line to the choroido-scleral junction (Figure 2). Automatic calculations of grand mean, temporo-superior, naso-superior, nasal, naso-inferior, temporo-inferior, and temporal choroidal thickness were noted and labeled as PPCT-2. The 2 methods of measurement were compared with each other. The compatibility of the two methods was investigated. The correlations of the 2 methods with age, sex, IOP, CCT, vision in LogMAR, glaucoma stage, MD, antiglaucoma drug usage, and spheric equivalent (SE) were investigated.

Statistical analysis

Data were evaluated with the statistical package program IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). Descriptive statistics are given as number of units (n), percent (%), mean, standard deviation (sd), standard error (SE), median (M), minimum (min), and maximum (max) values. The distribution of differences in numerical variables was evaluated with the Shapiro-Wilk test of normality. PPCT-1, PPCT-2, and RNFL values were compared with generalized linear mixed models (GLMM) according to gender and the presence of glaucoma. Pearson and Spearman's analyses were used according to the normality of the data for the correlation of numerical variables with each other. The relationship between PPCT-1, PPCT-2, and RNFL values was evaluated by partial correlation analysis. A value of $p<0.05$ was considered statistically significant.

Results

In the study, 270 eyes of 135 patients were evaluated. Of the patients, 55 (40.7%) were male and 80 (59.3%) were female. The age of the patients was between 50.0-92.0 years and the mean age was 70.4 ± 7.8 years. The number

Table 1. Characteristics of Patients (135 patients, 270 eyes).

Gender, n (%)	
Male	55 (40.7)
Female	80 (59.3)
Age, (years)	
Mean ± SD	70.4 ± 7.8
M (min-max)	70.0 (50.0-92.0)
SE	
Mean ± SE	0.511 ± 0.125
Vision in Logmar	
Mean ± SE	0.214 ± 0.026
IOP (mmHg)	
Mean ± SE	15.91 ± 0.28
Drug	
Mean ± SE	0.49 ± 0.07
CCT (µm)	
Mean ± SE	533.44 ± 3.08
MD	
Mean ± SE	-2.32 ± 0.49
Glaucoma, n (%)	
Negative	191 (70.7)
Positive	79 (29.3)
Glaucoma Stage, n (%)	
None	191 (70.7)
Mild	63 (23.3)
Moderate	11 (4.1)
Advanced	5 (1.9)

SD: Standard deviation, SE: Standard error, M: Median, min: Minimum, max: Maximum.

Characteristics of patients. Note that drug means a number of antiglaucomatous molecules used. SE: spherical equivalent, IOP: Intraocular pressure, CCT: central corneal thickness, MD: mean deviation in visual field.

Table 2. Comparison of PPCT-1, PPCT-2 and RNFL Values by Gender and Presence of Glaucoma.

	Gender			Glaucoma		
	Male	Female	p value	Negative	Positive	p value
	Mean±SE	Mean±SE		Mean±SE	Mean±SE	
PPCT-1						
Average	143.96 ± 5.59	151.29 ± 4.66	0.316	152.75 ± 3.78	136.08 ± 5.34	**0.003**
Temporal	143.67 ± 4.41	157.73 ± 6.33	0.152	155.88 ± 5.12	141.66 ± 6.81	**0.040**
Superior	162.88 ± 5.63	165.28 ± 4.69	0.744	168.16 ± 4.22	154.35 ± 6.91	0.092
Nasal	160.15 ± 7.61	164.97 ± 6.51	0.631	169.11 ± 5.24	147.77 ± 6.96	**0.003**
Inferior	119.87 ± 6.44	130.86 ± 5.51	0.197	131.58 ± 4.42	113.03 ± 5.95	**0.003**
PPCT-2						
Average	154.08 ± 5.48	164.92 ± 4.68	0.136	163.25 ± 3.78	153.43 ± 5.03	0.051
Temporal Superior	158.48 ± 5.50	171.25 ± 4.69	0.080	169.14 ± 3.92	157.64 ± 5.58	0.056
Nasal Superior	162.11 ± 5.91	175.60 ± 5.04	0.085	173.15 ± 4.15	161.78 ± 5.79	0.063
Nasal	163.24 ± 6.27	170.54 ± 5.35	0.378	171.39 ± 4.33	157.86 ± 5.91	**0.025**
Nasal Inferior	142.93 ± 6.19	153.48 ± 5.28	0.198	152.27 ± 4.29	141.31 ± 5.86	0.069
Temporal Inferior	138.48 ± 5.85	150.28 ± 4.99	0.128	148.14 ± 4.12	138.22 ± 5.71	0.097
Temporal	151.52 ± 5.74	164.25 ± 4.89	0.094	161.35 ± 4.03	152.62 ± 5.38	0.113
RNFL						
Average	90.68 ± 1.95	94.89 ± 1.61	0.099	98.84 ± 1.08	79.34 ± 1.54	**<0.001**
Temporal Superior	120.58 ± 3.21	120.12 ± 2.67	0.911	127.82 ± 1.91	100.21 ± 2.85	**<0.001**
Nasal Superior	103.02 ± 3.24	106.71 ± 2.71	0.385	110.50 ± 2.02	89.41 ± 2.87	**<0.001**
Nasal	68.15 ± 2.15	75.83 ± 1.81	**0.007**	78.07 ± 1.39	59.89 ± 1.97	**<0.001**
Nasal Inferior	100.28 ± 2.99	106.32 ± 2.50	0.124	110.31 ± 1.98	87.95 ± 2.91	**<0.001**
Temporal Inferior	127.99 ± 3.71	133.27 ± 3.10	0.277	140.26 ± 2.25	108.17 ± 3.26	**<0.001**
Temporal	67.52 ± 1.81	69.86 ± 1.51	0.321	71.88 ± 1.22	62.05 ± 1.74	**<0.001**

SE: Standard error, PPCT: Peripapillary choroidal thickness, RNFL: retinal nerve fiber layer,
Bold values indicate statistically significance.

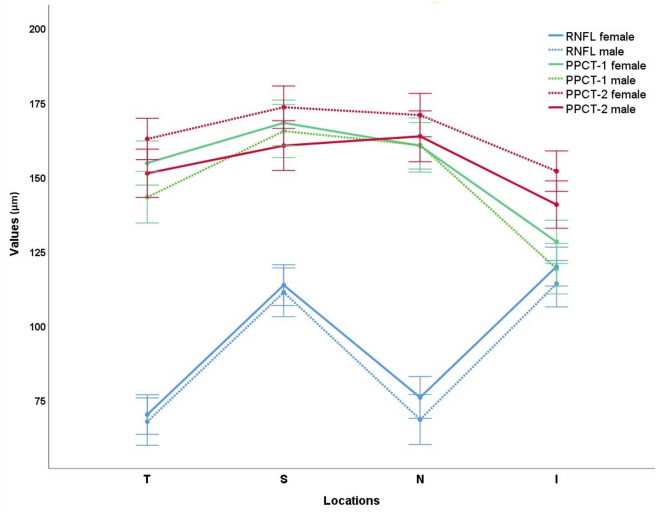

Figure 3. Peripapillary choroidal thickness measurements by PPCT-1 and PPCT-2 and RNFL measurements in µm in females and males. T: temporal, S: superior, N: nasal, I: inferior.

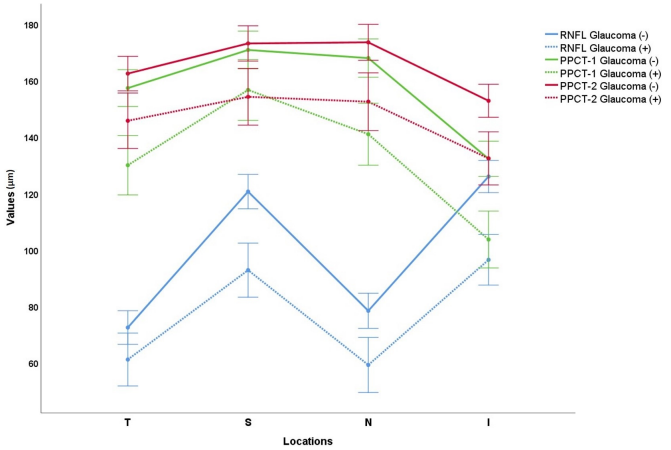

Figure 4. Peripapillary choroidal thickness measurements by PPCT-1 and PPCT-2 and RNFL measurements in eyes with glaucoma and without glaucoma. T: temporal, S: superior, N: nasal, I: inferior.

of eyes with glaucoma was 79 (29.3%). Of 270 eyes, 63 (23.2%) had mild, 11 (4.1%) had moderate, and 5 (1.9%) had advanced glaucoma. The characteristics of patients were summarized in Table 1.

The mean PPCT measurement in PPCT-1 was 149.44 ± 2.84 µm, and in PPCT-2 was 159.51 ± 2.72 µm ($p<0.001$).

We compared PPCT1, PPCT2, and RNFL values based on gender in 4 sectors using GLMM, which is seen in Fig-

Table 3. Correlation of PPCT-1 and PPCT-2 with characteristic variables.

		PPCT-1	PPCT-2
		Average	Average
Age	R	-0.209	**-0.192**
	P	0.001	**0.002**
SE	R	0.179	**0.223**
	P	0.004	**<0.001**
Vision in LogMAR	R	-0.090	**-0.152**
	P	0.152	**0.016**
IOP	R	-0.008	0.023
	P	0.896	0.721
CCT	R	0.175	0.131
	P	0.025	0.102
MD	R	0.083	0.042
	P	0.323	0.622
Drug	Rho	-0.168	**-0.157**
	P	0.007	**0.013**
Glaucoma Stage	Rho	-0.190	**-0.189**
	P	0.002	**0.003**

R: Pearson correlation coefficient; Rho: Spearman correlation coefficient.
Correlations of PPCT-1 and PPCT-2 with age, SE, Logmar, IOP, CCT, MD, antiglaucomatous drug number, and glaucoma stage. SE: spherical equivalent, IOP: Intraocular pressure, CCT: central corneal thickness, MD: mean deviation.

Table 4. Correlations for PPCT-1 and PPCT- 2.

	R	p	R*	p*
Average	**0.790**	**<0.001**	**0.763**	**<0.001**
Temporal	**0.766**	**<0.001**	**0.681**	**<0.001**
Superior	**0.396**	**<0.001**	**0.389**	**<0.001**
Nasal	**0.865**	**<0.001**	**0.875**	**<0.001**
Inferior	**0.822**	**<0.001**	**0.788**	**<0.001**

R: Pearson correlation coefficient, *Adjusted for gender, age, SE, glaucoma stage, Vision in LogMAR CCT, and drug usage by partial correlation analysis. SE: spherical equivalent, CCT: central corneal thickness.

ure 3. There wasn't any statistically significant difference in PPCT-1 and PPCT-2 values in men and women (Table 2). RNFL values in the nasal quadrant were statistically thicker in women than in men (75.83 ± 1.81 µm and 68.15 ± 2.15 µm, respectively; $p<0.05$). There was no significant gender difference between RNFL values in other quadrants (Table 2). The mean PPCT-1, PPCT-2 and RNFL values according to the presence of glaucoma are shown in Figure 4. Mean, temporal, nasal, and inferior PPCT-1 values were statistically significantly thinner in eyes with glaucoma than in eyes without glaucoma ($p<0.05$ for each). In PPCT-2 measurements, only the measurement in the nasal quadrant was statistically thinner in eyes with glaucoma ($p<0.05$). RNFL values in glaucoma were statistically lower in all quadrants as expected compared to eyes without glaucoma ($p<0.001$ for each) (Table 2).

The correlations of mean PPCT-1 and PPCT-2 with characteristic variables are summarized in Table 3. There were statistically weak negative correlations between age/antiglaucomatous drug use/glaucoma stage and mean PPCT-1/PPCT-2 measurements. There were statistically weak positive correlations between SE and average measurements of PPCT-1 / PPCT-2. Again, there was a statistically weak negative correlation between LogMAR and PPCT-2 avarage measurement, and a statistically weak positive correlation between CCT and PPCT-1 average measurement.

When we examine the correlation of the two methods according to the corrected R values, there were statistically strong positive correlations between PPCT-1 nasal and PPCT-2 nasal values; statistically good positive correlations between average, temporal, and inferior values; and a statistically weak positive correlation between superior values ($p<0.001$) (Table 4).

When the correlation of the 2 measurements with the RNFL measurements were analyzed, there were statistically weak positive correlations according to the corrected R values adjusted for gender, age, SE, glaucoma stage, LogMAR and drug usage between PPCT-1 nasal and RNFL nasal values (R: 0.217, $p<0.05$). There were statistically weak positive correlations between PPCT-2 average and RNFL average (R: 0.320, $p<0.05$) and between PPCT-2 superior and RNFL superior values (R: 0.276, $p<0.05$) (Table 5).

Discussion

In the current study, manual 4-point measurement in the temporal, superior, nasal, and inferior sectors in PPCT-1 and manual re-segmentation of OCT images of the peripapillary circle generated from 1536 A-scan measurements in PPCT-2 and automatic calculation of a mean and 6 sectors correlated well. PPCT-2 values were significantly higher in all measurements. This is probably because more points were measured at 1536, PPCT-2. In the PPCT-1 technique, the average value was calculated over only 4 measurements. Both measurement techniques produced a choroidal thickness pattern that was thicker superiorly/nasally and thinner temporally/inferiorly. Both measurements were similar in males and females.

The correlation analysis showed negative correlations between PPCT-1 average and age, glaucoma drug usage, and glaucoma stage. We found positive correlations with PPCT-1 mean measurement and SE and CCT. PPCT-2 average measurement was correlated negatively with age, glaucoma stage and glaucoma drug usage. PPCT-2 measurements were positively correlated with SE. We found higher vision levels (lower LogMAR values) were associated with higher PPCT-2 average values. Sector-to-sector correlation analysis showed a weak positive correlation between PPCT-1 nasal and RNFL nasal values PPCT-2 average and RNFL average and between PPCT-2 superior and RNFL superior values. In the PPCT-2 technique, OCT software calculates different segments of the same scans for RNFL measurement so correlation is better than the 4-point measurement of PPCT-1.

Table 5. Correlations of PPCT-1 and PPCT-2 with RNFL.

		PPCT-1				PPCT-2			
		R	p	R*	p	R	p	R*	p
RNFL	Average	**0.191**	**0.002**	0.076	0.466	**0.240**	**<0.001**	**0.320**	**0.002**
	Temporal	-0.035	0.593	0.041	0.705	-0.108	0.090	0.001	0.995
	Superior	0.052	0.420	-0.076	0.508	**0.220**	**<0.001**	**0.276**	**0.014**
	Nasal	0.172	0.007	**0.217**	**0.041**	**0.184**	0.004	0.176	0.098
	Inferior	**0.244**	**<0.001**	0.042	0.697	**0.272**	<0.001	0.153	0.153

R: Pearson correlation coefficient, *Adjusted for gender, age, SE, glaucoma stage, Vision in LogMAR, CCT, and drug usage by partial correlation analysis. SE: spherical equivalent, CCT: central corneal thickness.

Overall, we measured PPCT measurements, which are subject to many current studies related to glaucoma pathogenesis, with 2 different techniques. Mathematically, comparing a measurement taken from 4 points and the calculations made by the device from the 1536 A-scan measurement may not seem very feasible. However, PPCT 2 is technically more challenging and PPCT-1 can be preferred because it is faster. This study showed us that both techniques are in good correlation and the correlation between PPCT-1 and measurements such as age, SE, glaucoma stage, and average RNFL is close to PPCT-2.

In many studies, the pathophysiologic basis for development of glaucoma, optic nerve head supply and choroidal thickness were investigated [8-11]. But the role of choroidal thickness in glaucoma pathogenesis is still controversial. In the current study, the PPCT measurements were compared between the eyes with glaucoma and without glaucoma, with PPCT-1 measurements; there were statistically significant lower measurements for all sectors, except the superior sector, in glaucomatous eyes. In the superior sector, choroidal thickness measurements were thinner, but not statistically significant. The superior sector is the sector where focal glaucomatous defects may start. This result is somewhat unexpected if nerve fiber loss is associated with choroidal thickness loss. But the same sector is the place where most retinal blood vessels enter the disc. If there was vessel shadowing, the choroid was measured slightly nasally or temporally, whichever was nearest to 90°. This may have affected the results.

With PPCT-2 measurements, there were persistently lower measurements for eyes diagnosed with glaucoma, but the difference was only significant in the nasal sector. In our study population, the vast majority of eyes with glaucoma were early stage. Glaucoma starts with the focal loss of nerve fiber bundles and as glaucoma progresses, it turns into global loss. In this study, the PPCT-2 technique may not show early focal choroidal thickness loss, even if present. The PPCT-2 technique includes many measurement points that may not catch focal thinning.

Some previous studies found a negative correlation between IOP [12] and PPCT and some others did not [13]. We did not find any correlation with any of the measurement techniques. In our study, all eyes with glaucoma were using antiglaucomatous drugs and had controlled IOP. This may bias the probable correlation. In one multicenter study with a healthy young population, no correlation was found between PPCT and IOP [14]. In both techniques, we found a negative correlation with antiglaucomatous drug usage and glaucoma stage. But we found no correlation between MD and any PPCT measurements.

In the literature, Jiang et al. [15] found mean PPCT was 134 ± 53 µm in the Chinese population. They used Heidelberg Spectralis OCT, conventional RNFL scans and measured PPCT on a 3.4 mm circular scan at 8 points. They found no difference between men and women. They found thicker PPCT was significantly associated with younger age, shorter axial length, and better best-corrected visual acuity. They found no relationship between PPCT and CCT, IOP, and glaucomatous optic neuropathy. They determined a pattern that was thickest in the superior sector, followed by temporal, nasal and inferior sectors.

Oh et al. [16] measured PPCT using 3D-OCT (3D-OCT 1000 Mark II, software ver. 4.21, Top- con, Tokyo, Japan) in circle scan mode which provides RNFL thickness and retinal thickness. They changed the RPE segmentation line to the choroidoscleral junction, and calculated PPCT by subtracting retinal thickness from the re-segmented measurement. They found mean average choroidal thickness was 191 ± 62 µm in participants with mean age of 41 years. They found the temporal sector was thickest followed by superior, nasal and inferior sectors. They found a negative correlation between PPCT and increasing age.

Rhodes et al. [17] measured PPCT using Heidelberg Spectralis OCT by 48 radial volume scans centered on the optic nerve head using the EDI mode in patients of African and European descent. They calculated PPCT at five different locations away from the BMO (0-250 µ, 250-500 µ, 500-1000 µ, 1000-1500 µ). They found mean PPCT increased as the distance from the BMO increased. Patients of African descent had thicker PPCT. In both groups, they found a negative correlation between age and PPCT.

Hirooka et al. [18] reported PPCT measurements in normotensive glaucoma (NTG) patients. They measured PPCT with Heidelberg Spectralis OCT, using a circle scan in EDI mode, and they made manual 8-point measurements. They found mean PPCTs were 148.8 ± 53.3 µm and 128.1 ± 44.6 µm in normal and NTG subjects, respectively ($p = 0.04$). They found no correlation between IOP and choroidal thickness. They reported that RNFL thickness and PPCT measurements were not significantly correlated for any peripapillary location and no significant correlation was found between MD and mean peripapillary choroidal thickness.

In the report by Suh et al. [12] they investigated unilat-

eral normotensive glaucoma patients. They used Heidelberg Spectralis OCT with a 3.4-mm diameter peripapillary circle scan, standard protocol for RNFL assessment, centered on the optic disc, and represented as a linear strip for choroidal thickness. They measured PPCT by re-segmentation and retinal thickness function, as we did in PPCT-2 measurements. They reported that the average PPCT was not statistically significantly different in the glaucomatous and nonglaucomatous eyes of patients ($p = 0.52$). There was no definite difference between the choroidal thickness underlying the RNFL defect in glaucomatous eyes and the choroidal thickness of a compatible position in the contralateral normal eye, indicating that there was no correlation of RNFL with choroidal thickness. They found age ($p = 0.004$) and axial length ($p < 0.0001$) were negatively associated with peripapillary choroidal thickness.

There are some limitations of our study. Firstly, although our sample size is not small, the distribution of eyes with glaucoma is heterogeneous concerning the glaucoma stage and glaucoma type. Although we did not include most secondary glaucoma, we included open-angle glaucoma types including primary open-angle glaucoma, pseudoexfoliative glaucoma, normotensive glaucoma, and ocular hypertension. Moreover, we include the eyes using topical antiglaucomatous molecules or not starting yet. The results of the study may be more powerful with the homogeneous glaucoma type and stage or with a larger sample size of patients with glaucoma that allow us for subgroup analysis. One more limitation of our study that we already mentioned above is related to its design which is unable to show progressive choroidal changes in patients with glaucoma. Finally, we include both eyes of the subjects. Since the quantitative data of repeated measurements belonging to bilateral eyes were included in the study for comparisons, which were dependent variables indeed, we preferred to use GLMM to overcome the bias. GLMM provides us a very useful platform to evaluate both normally and non-normally distributed, dependent and independent, categoric and numeric variables to take into consideration at the same time and to detect the main effect of the variables.

Conclusion

In summary, both of our measurement techniques are compatible with the literature in that PPCT correlates negatively with age and SE, and there is no difference in PPCT by gender. Measurements with the PPCT-1 technique showed that PPCT was significantly thinner in most quadrants in glaucoma patients. In the measurements obtained with the PPCT-2 technique, PPCT was found to be thinner in all quadrants in eyes with glaucoma, while statistical significance was found only in the nasal quadrant. Therefore, the relationship between glaucoma and PPCT is still controversial. It has been reported in the literature that there is no relationship between choroidal thickness and IOP in healthy eyes, and we similarly did not find a relationship between PPCT and IOP in either measurement technique. However, we found negative correlations with the number of antiglaucomatous drug usages and glaucoma stage. The loss of choroidal thickness in glaucoma patients may be among the factors that cause the development and progression of glaucoma, or it may be a result of glaucoma. Prospective, multicenter studies are needed to further define the relationship between glaucoma and choroidal thickness.

Abbreviations

BMO: Bruch membrane opening

CCT: central corneal thickness

EDI: enhanced depth imaging

ILM: internal limiting membrane

IOP: intraocular pressure

MD: mean deviation

NFL: nerve fiber layer

OCT: optical coherence tomography

OHT: ocular hypertension

PPCT: Peripapillary choroidal thickness,

NFL: retinal nerve fiber layer

SE: spherical equivalent

Author contributions

Y.U. and N.T.D. were responsible for study design, data acquisition and analysis Y.U. wrote the manuscript. Both authors critically revised the manuscript and approved the final version.

Disclosure statement

Both authors report no conflicts of interest and they are responsible for the content and writing of this article.

Funding

No funding was received for this research.

Conflict of interest statement

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

This study was approved by the local ethical committee with the registration number of HNEAH-KAEK 2021/318-3365 (Date: 13.12.2021) and it adhered to the ethical principles stated in the Declaration of Helsinki.

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