Ganglion Cell-inner Plexiform Layer Thickness Measured by Cirrus High-definition Optical Coherence Tomography Enhances Glaucoma Diagnosis in Patients with Moderate or High Myopia

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ABSTRACT

Objective: To assess the diagnostic ability of Cirrus high-definition optical coherence tomography (HD-OCT) parameters in patients with moderate or high myopia for detecting glaucoma, and to compare the thickness of the macular ganglion cell-inner plexiform layer (GC-IPL) in glaucomatous and normal eyes in both types of myopia.
Materials and Methods: This prospective study enrolled moderately (spherical equivalent -3.00 to -6.00 diopters) and highly (spherical equivalent ≤ -6.00 diopters) myopic patients without (controls) and with (study) glaucoma. Cirrus HD-OCT was used to determine the thickness of the peripapillary retinal nerve fiber layer (RNFL) and the GC-IPL. The area under the receiver operating characteristic curve was analyzed to evaluate the glaucoma detection capability of each Cirrus HD-OCT parameter.
Results: Seventy eyes (31 moderate myopia, 39 high myopia) were included. The parameters with the best diagnostic ability were minimum GC-IPL, inferior RNFL and average RNFL thickness in moderately myopic eyes, and average RNFL, inferior RNFL and inferotemporal GC-IPL thickness in highly myopic eyes. All parameters were thinner in glaucomatous than in normal eyes in both groups.
Conclusion: Although macular GC-IPL thickness demonstrated high ability to detect glaucoma in patients with moderate or high myopia, it should be used in combination with other structural imaging and functional assessments for diagnosing glaucoma.

Keywords: Ganglion cell-inner plexiform layer thickness; glaucoma; myopia; Cirrus high-definition optical coherence tomography (Siriraj Med J 2022; 74: 284-293)

INTRODUCTION

Glaucoma was reported to be the major cause of irreversible blindness and the second most prevalent cause of moderate and severe visual impairment.[1,2] Numerous risk factors lead to the development of glaucoma, and myopia is one of them.[3] Globally, myopia prevalence is increasing, and approximately 5 billion people will be affected by 2050, especially in East and Southeast Asia. In addition to uncorrected myopia itself, pathologic ocular complications from myopia or its comorbidities, such as myopic macular degeneration, choroidal neovascularization, and glaucoma, can lead to increased medical and economic

burden.[4,5] A previous study reported that myopic eyes had a two to three times higher risk of having glaucoma[6], and high myopic eyes had a nearly six-fold increased risk of having primary open-angle glaucoma.[7] Thus, early detection and treatment of glaucoma in myopia is crucial for preventing disease progression.[8]

Previous study reported that detection of structural abnormalities, i.e., retinal nerve fiber layer (RNFL) defects, may develop four to six years before the onset of visual field abnormalities.[9] As a consequence, recent advances in ocular imaging, especially spectral-domain optical coherence tomography (SD-OCT), which is a frequently used structural imaging, may greatly contribute to the early detection and treatment of glaucoma. Previous studies used peripapillary RNFL thickness as a measurement of RGC axon loss to detect glaucoma, and since approximately 50% of RGCs are located in the macular region, and the inner retinal layers are preferentially affected by glaucomatous damage[10,11], further studies have assessed macular parameters to aid in glaucoma diagnosis. Previous studies demonstrated that the thickness of macular ganglion cell complex (GCC) generated by an RTVue SD-OCT (Optovue, Fremont, CA, USA), and the thickness of macular ganglion cell-inner plexiform layer (GC-IPL) by Cirrus high-definition optical coherence tomography (HD-OCT) with ganglion cell analysis (GCA) algorithm (Carl Zeiss Meditec, Jena, Germany) yielded glaucoma detection ability similar to peripapillary RNFL thickness; however, they found GC-IPL thickness measurement not be confounded by the variation in RNFL.[10-14]

Evaluation of RGC loss using various techniques of structural imaging has been continuously improved to achieve more accuracy in glaucoma detection, and with better reproducibility. However, diagnosing glaucoma in myopic eyes is still difficult since anatomical distortion of the optic nerve head (ONH) (e.g., tilted disc, large peripapillary atrophy) can mystify ophthalmologists to differentiate between glaucomatous damage and myopia-related optic disc changes. Therefore, objective structural quantification may have a role in diagnosing glaucoma in myopia.[15-17] Leung, et al. reported that, when using Cirrus HD-OCT, temporally converged superior and inferior RNFL bundles were detected in myopic eyes, which resulted in abnormal RNFL measurement.[18] Additionally, a previous study concluded that optic disc and cup margin detection errors were likely to be found in myopic eyes.[15] Thus, particular care must be taken when interpreting RNFL thickness map and neuroretinal rim measurement obtained by SD-OCT in myopic eyes. Analysis of macular parameters has been proposed as an alternative method for diagnosing glaucoma to avoid misdiagnosis of glaucoma via the influence of optic disc variation in myopia.

The thickness of the GC-IPL is a macular parameter that has been studied in various research. Choi, et al. demonstrated that in highly myopic eyes, GC-IPL has a diagnostic potential for glaucoma that is comparable to RNFL thickness.[19] In a previous study, the inferotemporal GC-IPL thickness was found to have the largest area under the receiver operating characteristic (AuROC) curve, suggesting that it might be utilized as an effective preperimetric glaucoma detection parameter in myopia.[20]

Since the normative databases in SD-OCT do not include data from highly myopic subjects, diagnosis of glaucoma in these patients is still somewhat difficult.[21] Moreover, differences in the severity of myopia can affect the GC-IPL thickness measurement. Seo, et al. concluded that GC-IPL in all sectors were thinner in high myopes compared to low and moderate myopes.[22] Akashi, et al. reported that GC-IPL thickness had a high AuROC curve value for distinguishing highly myopic glaucomatous eyes from normal eyes in patients with and without high myopia (spherical equivalent (SE) ≤ -6.00 diopters).[23] Accordingly, this study aimed to determine the diagnostic capability of Cirrus HD-OCT parameters for diagnosing glaucoma in patients with moderate (SE -3.00 to -6.00 diopters) or high myopia (SE ≤ -6.00 diopters), and to compare macular GC-IPL thickness between glaucomatous and normal eyes in both types of myopia.

MATERIALS AND METHODS

This prospective, comparative cross-sectional study was conducted at Siriraj Hospital, was approved by the Committee for the Protection of Human Participants in Research of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand [EC 103/2014], and was registered in the Thai Clinical Trials Registry (identification number TCTR20210726001). This study followed to the tenets of the Declaration of Helsinki. Each subject provided a written informed consent before enrollment.

This study was performed in the ophthalmology outpatient clinic of Siriraj Hospital during February 2014 to December 2018. Patients aged older than 20 years with SE ≤ -3.00 diopters (D) and best spectacles-corrected visual acuity of 20/40 or better were eligible for inclusion. Subjects with retinal or macular pathology, vision-associated systemic or neurologic diseases, receiving drugs known to affect the macula (e.g., chloroquine, ethambutol), previous intraocular surgery or laser within 1 month, inability to cooperate with the examination,

and/or having an allergic reaction to the eye drops used in the study protocol were excluded. Participants visiting the ophthalmology outpatient clinic who met these criteria were enrolled in this study with written informed consent. Only one eye was randomly selected in the final analysis if both eyes met all research eligibility criteria.

All recruited patients underwent a complete ophthalmic examination, which consisted of assessment of visual acuity (VA), refractive error measured by autorefractor (ARK-530A; NIDEK, Aichi, Japan) and recorded as spherical equivalents (SE), intraocular pressure (IOP) measurement obtained with Goldmann applanation tonometry, slit-lamp and dilated fundus examination, gonioscopy, axial length obtained using a biometer (IOL Master 500; Carl Zeiss Meditec), OCT RNFL and GC-IPL parameter measurement by Cirrus HD-OCT software version 6.0.0.599 (Carl Zeiss Meditec), and visual field test by Humphrey visual field analyzer (Carl Zeiss Meditec) using the 24-2 Swedish interactive threshold algorithm (SITA) strategy.

Enrolled subjects were classified into either the moderately or highly myopic groups. Moderate and high myopia were defined as SE -3.00 D to -6.00 D and ≤ -6.00 D, respectively. Within each of those two groups, patients were further subdivided into either glaucoma (study) or normal (control) groups. Using the reference standard[24], glaucomatous eyes were defined as eyes with glaucomatous optic neuropathy with corresponding abnormal visual field tests. Glaucomatous optic neuropathy was defined as enlarged cupping ≥ 0.5 vertical cup/disc (C/D) ratio or an asymmetrical vertical C/D ratio greater than 0.2. Glaucomatous visual field defect was defined as any one of the following: a cluster of ≥ 3 non-edge adjacent points in one hemifield of pattern deviation plot with a probability < 5%, and including at least 1 point with a probability < 1%; a pattern standard deviation (PSD) showing a probability < 5%; or, a glaucoma hemifield test (GHT) showing outside normal limits. Normal subjects were moderately and highly myopic patients who visited ophthalmology outpatient clinic with mild cataract, dry eyes or eye check up and without glaucoma, which defined as those with an IOP ≤ 21 mmHg, no glaucomatous optic neuropathy, and without detectable visual field defect. The visual field of the normal group must not meet any of the aforementioned criteria for glaucomatous visual field defect and a GHT showing within normal limits, a mean deviation (MD) and PSD within the 95% confidence limit. OCT measurements are not considered as part of the examinations to include a patient in the normal control group.

Cirrus HD-OCT measurement

Two scans were obtained through a dilated pupil, one peripapillary RNFL scan and one macular scan (optic disc cube 200x200 protocol and macular cube 512x128 protocol, respectively). Macular scan measured GC-IPL thickness within a 6x6x2 mm cube centered at the fovea using the GCA algorithm, and the measurements were generated into the minimum, average, and 6 sectorial parameters (Inferotemporal, inferior, inferonasal, superonasal, superior and superotemporal). The optic disc cube protocol measured peripapillary RNFL thickness through a 6x6x2 mm cube, after which the measurements were analyzed into the average and the 4 quadrant thicknesses (temporal, superior, nasal, and inferior). Scans with a signal strength lower than 6 on either macular GC-IPL or peripapillary RNFL scan, visible eye movement, decentration, artifacts from blinking, and/or image distortion from anatomical abnormalities were discarded. Measurement values were analyzed via comparison with the device's normative database, and the results were visually described as a color-coded significance map with the colors green, yellow, and red indicating normal, borderline, and abnormal, respectively. There was no cutoff point of OCT value to define glaucoma, but it was used in combination with structural and functional tests to enhance glaucoma diagnosis.

Statistical analysis

Patient characteristics are reported as mean plus/minus standard deviation (SD) for normally distributed continuous data, and as frequency and percentage for categorical variables. Peripapillary RNFL and GC-IPL thicknesses were compared between the glaucoma and normal groups using unpaired *t*-test, and were compared among 4 groups using 1-way analysis of variance (ANOVA) by Tukey HSD or Games-Howell. The ability of a factor to detect glaucoma was assessed by the AuROC curve. All statistical analyses were performed using PASW Statistics software version 26. A *p*-value < 0.05 indicates statistically significant.

RESULTS
Subjects

Seventy eyes were included and categorized into 4 groups, as follows: moderately myopic normal group (*n*=16), highly myopic normal group (*n*=16), moderately myopic glaucomatous group (*n*=15), and highly myopic glaucomatous group (*n*=23). Patient demographic and baseline characteristics compared between glaucomatous and normal eyes in the moderate and high myopia groups

are presented in Table 1. The mean age of the moderately myopic group was 47.55±14.51 years (range from 22 to 68 years), and 19 were female (61.29%). The mean age of the highly myopic group was 45.69±15.02 years (range from 21 to 70 years), and 22 were female (56.41%). No significant differences were found in age, VA, IOP, or SE between normal and glaucomatous eyes in both the moderate and high myopia groups.

Cirrus HD-OCT measurement

Macular GC-IPL and peripapillary RNFL thicknesses as evaluated by Cirrus HD-OCT compared between glaucomatous and normal eyes in the moderate and high myopia groups are demonstrated in Table 2. No patients were excluded for poor quality scans. In both groups, all of the RNFL thickness parameters, except for the nasal region in both groups (moderate myopia $p=0.700$, and high myopia $p=0.831$) and the temporal region in the highly myopic group ($p=0.118$), were significantly thinner in glaucomatous than in the normal eyes (all $p<0.05$).

Comparison of macular GC-IPL thickness between glaucomatous and normal eyes in both the moderate and high myopia groups revealed statistically significant differences in minimum, average, and all sectors of macular GC-IPL thickness (all $p<0.05$), except for the superonasal GC-IPL sector in both the moderate and high myopia groups ($p=0.282$ and 0.614, respectively), and the superior GC-IPL sector in the high myopia group ($p=0.443$).

Diagnostic ability

All of the AuROC values of macular GC-IPL and peripapillary RNFL thickness in both the moderate and high myopia groups were above 0.5 (Table 3). In the moderately myopic group, the best parameters for distinguishing glaucomatous eyes from normal eyes were minimum GC-IPL, inferior RNFL, and average RNFL thicknesses (AuROC: 0.963, 0.925 and 0.919, respectively) (Fig 1). In the highly myopic eyes, average RNFL, inferior RNFL, and inferotemporal GC-IPL thicknesses (AuROC: 0.980, 0.962 and 0.905, respectively) demonstrated the best diagnostic ability for differentiating glaucoma from normal eyes (Fig 2).

TABLE 1. Patient demographic and baseline characteristics compared between normal and glaucomatous eyes in the moderate and high myopia groups.

	Moderately myopic group (n = 31)			Highly myopic group (n = 39)		
	Normal (n =16)	Glaucoma (n =15)	*P* value*	Normal (n =16)	Glaucoma (n =23)	*P* value†
Female, n (%)	11 (68.8)	8 (53.3)	0.38	12 (75)	10 (43.5)	0.10
Age, years	43.56 (13.47)	51.80 (14.80)	0.53	42.50 (15.19)	47.91 (14.83)	0.82
VA, logMAR	0.07 (0.09)	0.11 (0.11)	0.85	0.09 (0.10)	0.10 (0.10)	1.00
IOP, mmHg	15.69 (1.85)	14.33 (2.38)	0.55	14.56 (2.94)	13.65 (2.48)	0.82
SE, D	-4.39 (0.87)	-4.57 (0.99)	1.00	-7.61 (1.14)	-8.40 (4.79)	0.95
AL, mm	25.51 (0.89)	25.14 (1.25)	0.95	26.42 (0.81)	27.69 (1.49)	<0.01
MD, dB	-0.87 (1.49)	-5.10 (4.20)	<0.01	-1.35 (0.99)	-6.27 (3.56)	<0.01
PSD, dB	1.47 (0.25)	5.25 (3.65)	<0.01	1.67 (0.56)	5.60 (3.64)	<0.01

Data are given as mean (SD).
Abbreviations: VA; visual acuity, IOP; intraocular pressure, SE; spherical equivalent, AL; axial length, MD; mean deviation, PSD; pattern standard deviation
* Value for comparison of normal and glaucomatous eyes in moderately myopic group
† Value for comparison of normal and glaucomatous eyes in highly myopic group

TABLE 2. Peripapillary RNFL and macular GCIPL thickness as measured by Cirrus HD-OCT compared between normal and glaucomatous eyes in the moderate and high myopia groups.

	Moderately myopic group (n = 31)			Highly myopic group (n = 39)		
	Normal (n =16)	Glaucoma (n =15)	*P* value*	Normal (n =16)	Glaucoma (n =23)	*P* value†
RNFL thickness parameters, µm						
Average	97.31 (8.13)	72.73 (14.00)	<0.001	89.81 (7.07)	70.96 (7.38)	<0.001
Superior	119.75 (16.18)	89.13 (18.50)	<0.001	103.50 (16.74)	81.39 (14.03)	<0.001
Nasal	68.63 (9.17)	63.20 (11.01)	0.700	65.63 (12.38)	61.48 (12.01)	0.831
Inferior	120.19 (20.87)	77.67 (21.23)	<0.001	114.13 (15.86)	74.13 (15.02)	<0.001
Temporal	80.50 (11.17)	61.27 (17.26)	0.001	75.69 (8.06)	65.74 (13.65)	0.118
Macular GC-IPL parameters, µm						
Average	80.88 (6.64)	71.33 (8.02)	0.004	75.88 (4.26)	67.17 (9.13)	0.004
Minimum	79.44 (6.73)	61.87 (8.73)	<0.001	73.19 (7.48)	58.52 (12.06)	<0.001
ST	80.50 (6.28)	71.33 (8.73)	0.019	76.25 (4.12)	67.78 (10.99)	0.015
S	81.69 (7.29)	70.40 (9.83)	0.047	77.44 (4.79)	71.13 (16.82)	0.443
SN	83.00 (7.04)	75.60 (10.31)	0.282	78.19 (5.91)	73.22 (14.42)	0.614
IN	82.00 (6.19)	71.93 (8.56)	0.001	74.56 (6.06)	67.04 (6.53)	0.007
I	78.50 (6.97)	66.47 (8.08)	0.001	73.50 (4.18)	61.04 (10.37)	<0.001
IT	79.88 (6.87)	66.00 (9.51)	<0.001	75.69 (5.00)	62.96 (8.49)	<0.001

Data are given as mean (SD).
Abbreviations: ST; superotemporal, S; superior, SN; superonasal, IN; inferonasal, I; inferior, IT; inferotemporal
* Value for comparison of normal and glaucomatous eyes in moderately myopic group
† Value for comparison of normal and glaucomatous eyes in highly myopic group

DISCUSSION

This study aimed to demonstrate the diagnostic performance of OCT parameters, including peripapillary RNFL and macular GC-IPL thickness obtained by Cirrus HD-OCT, to detect glaucoma in moderately and highly myopic patients. We found the capability of macular GC-IPL thickness parameters for discriminating between glaucomatous and normal eyes to be high and comparable to peripapillary RNFL thickness in both myopia severity groups.

Diagnosing glaucoma in myopic patients can be a challenge due to anatomical variations in the optic disc and retina, such as tilted disc, nasal elevation, temporal flattening, rotation, posterior staphyloma, and large peripapillary atrophy, can make it difficult for clinicians to distinguish between structural damage from glaucoma and anatomical changes due to myopia.[15,16] In addition to the difficulties in making a clinical diagnosis by direct visualization of ONH or optic disc photographs, structural evaluation via peripapillary RNFL parameters obtained by SD-OCT can also demonstrate inaccuracies of measurement. Hwang, *et al.* reported that neuroretinal rim measurement errors were observed in myopic patients when using Cirrus HD-OCT.[15] Leung, *et al.* concluded that increasing

TABLE 3. The AuROC value (SE) for each Cirrus HD-OCT parameter, which indicates the strength of that parameter for distinguishing between normal and glaucomatous eyes, in the moderate and high myopia groups.

	Moderately myopic group (n = 31)	Highly myopic group (n = 39)
RNFL thickness parameters, µm		
Average	0.919 (0.057)	0.980 (0.018)
Superior	0.892 (0.058)	0.855 (0.064)
Nasal	0.648 (0.108)	0.548 (0.093)
Inferior	0.925 (0.045)	0.962 (0.027)
Temporal	0.850 (0.077)	0.795 (0.076)
Macular GC-IPL parameters, µm		
Average	0.842 (0.073)	0.887 (0.058)
Minimum	0.963 (0.031)	0.897 (0.065)
ST	0.810 (0.086)	0.891 (0.057)
S	0.838 (0.075)	0.760 (0.079)
SN	0.756 (0.091)	0.758 (0.082)
IN	0.823 (0.077)	0.832 (0.074)
I	0.881 (0.059)	0.904 (0.054)
IT	0.894 (0.055)	0.905 (0.053)

Data are given as AUROC (SE).
Abbreviations: ST; superotemporal, S; superior, SN; superonasal, IN; inferonasal, I; inferior, IT; inferotemporal
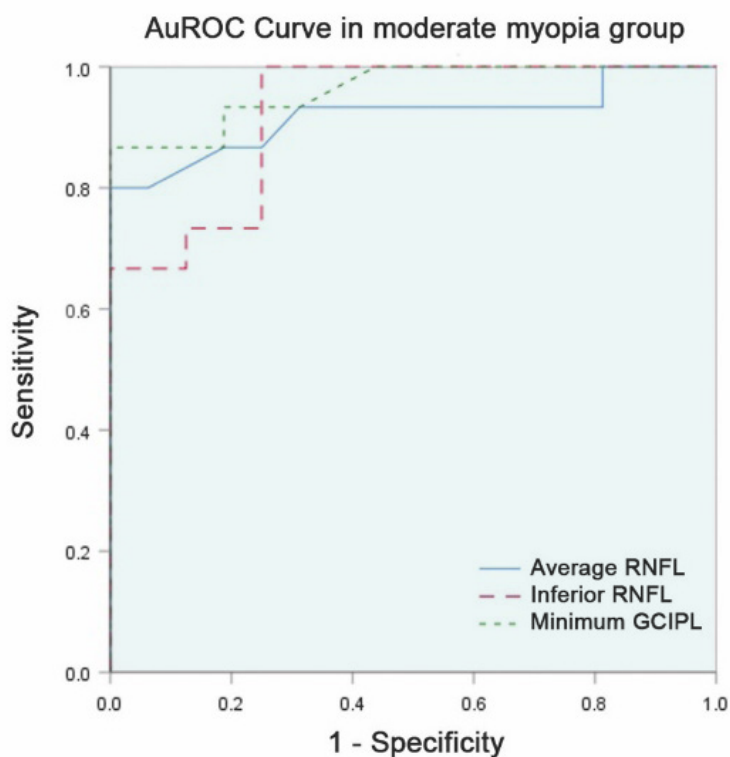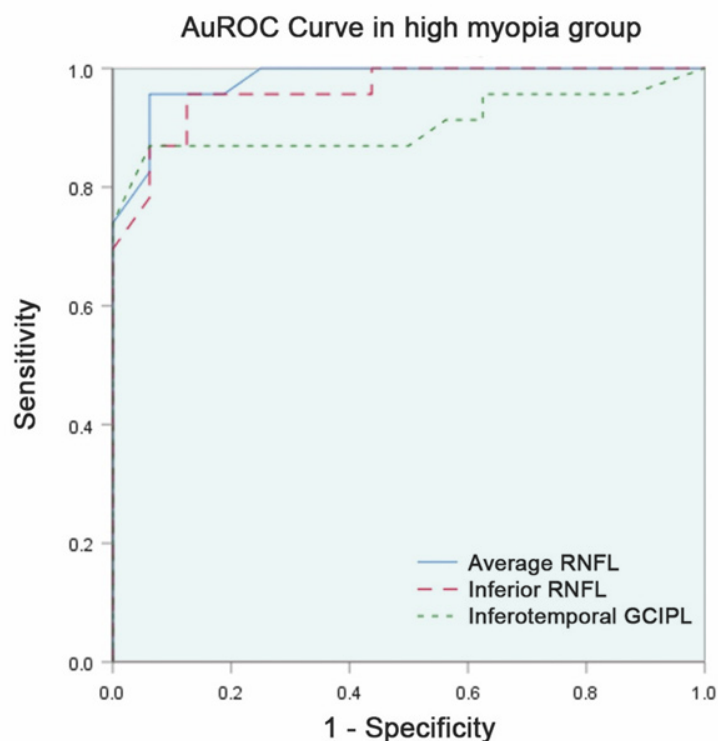

Fig 1. The area under the receiver operating characteristic (AuROC) curve for the 3 best parameters by Cirrus HD-OCT for distinguishing between normal and glaucomatous eyes in the moderate myopia group.
Abbreviations: RNFL; peripapillary retinal nerve fiber layer, GCIPL; macular ganglion cell-inner plexiform layer.

Fig 2. The area under the receiver operating characteristic (AuROC) curve for the 3 best parameters by Cirrus HD-OCT for distinguishing between normal and glaucomatous eyes in the high myopia group.
Abbreviations: RNFL; peripapillary retinal nerve fiber layer, GCIPL; macular ganglion cell-inner plexiform layer.

severity of myopia associated with temporally converged superotemporal and inferotemporal bundles of RNFL, which led to abnormal measurement of RNFL.[18] Kim, *et al.* reported that in healthy eyes, false-positive OCT RNFL findings were influenced by smaller disc areas and longer axial lengths, and these factors are usually found in myopic eyes.[25]

In contrast to the limitations of RNFL measurement for diagnosing glaucoma in myopic patients, macular parameters, which are less affected by the optic nerve head variations found in myopia, have good diagnostic ability and their application has been reported in several studies.[14,19,20,23,26-28] Kim, *et al.* reported the effectiveness of using GCC thickness, composed of inner plexiform layer, ganglion cell layer, and RNFL, measured by RTVue SD-OCT for diagnosing glaucoma in myopic eyes to be similar to the diagnostic results obtained from using peripapillary RNFL thickness.[27] Previous study found that global loss volume from GCC algorithm was the best parameter for differentiating between highly myopic glaucoma and nonglaucoma subjects.[28] Despite its advantages, recent study showed the RNFL in myopic eyes to be thinner than the RFNL in normal eyes[23], so the results of macular GCC thickness may be confounded by these variations of RNFL in myopic subjects.

When excluding RNFL measurement, another macular parameter, GC-IPL thickness, was introduced. Previous study reported that in highly myopic subjects, macular GC-IPL thickness demonstrated a similar capability to identify glaucoma as the RNFL thickness. In the highly myopic group (SE -6.00 to -20.00 D), they found the SD-

OCT parameters with the highest AuROC values to be inferior RNFL and inferotemporal GC-IPL thicknesses (AuROC: 0.906, 0.852, respectively). In the non-highly myopic eyes (SE -0.25 to -6.00 D), the best AuROC values were average RNFL (AuROC: 0.920) and minimum GC-IPL thicknesses (AuROC: 0.908).[19] Seol, *et al.* found GC-IPL thickness at inferotemporal sector to be the best parameter for detecting preperimetric glaucoma in both the non-highly myopic (SE -0.50 to -6.00 D; AuROC: 0.747) and highly myopic groups (SE ≤ -6.00 D; AuROC: 0.737).[20] These results are consistent with our findings. In our study, minimum GC-IPL, inferior RNFL, and average RNFL thicknesses (AuROC: 0.963, 0.925, and 0.919, respectively) were the parameters with the best diagnostic performance in the moderately myopic group. In the highly myopic group, average RNFL, inferior RNFL, and inferotemporal GC-IPL thicknesses (AuROC: 0.980, 0.962, and 0.905, respectively) were the best parameters for detecting glaucoma.

The parameters that demonstrated the greatest AuROC in the moderately myopic eyes (mean SE: -4.48 ± 0.92 D) in our study were similar to those identified in the non-highly myopic group (mean SE: -2.46 ± 1.69 D) in previous study[19]; however, greater AuROC values were found in our study. Since increasing severity of myopia temporally converges the inferior and superior RNFL bundles and brings them closer to the macula[18], using macular parameters may be an appropriate tool for detecting glaucomatous damage in eyes with a higher severity of myopia. Moreover, previous study reported the glaucoma diagnostic ability of macular GCA to be

influenced by the angular distance between the RNFL defect and the fovea, which means that defects located far from the fovea may be difficult to detect with GCA maps.[29] In the moderately myopic group, the AuROC for minimum GC-IPL thickness was the highest in our study, and higher than that reported from previous study, and this may be due to a greater degree of myopia, as discussed above.

In the high myopia group, we found average RNFL, inferior RNFL, and inferotemporal GC-IPL thickness to have the greatest AuROC values, which is consistent with previous studies.[19,20] However, among all of the SD-OCT parameters, the RNFL parameters showed the best AuROC values. Despite the higher degree of myopia, it remains unclear why the RNFL parameters have superior diagnostic ability. Of interest, recent studies reported several factors specific to highly myopic eyes that may reduce the reliability of GC-IPL measurements. Kim, *et al.* reported that in eyes with myopic tilted disc, increasing degree of optic disc torsion corresponded with distortion of the posterior pole contour[30], which may imply that GC-IPL measurement in high myopes could be influenced by anatomical misalignment in the macular area. Furthermore, although GC-IPL thickness assessments in highly myopic eyes demonstrated satisfying long-term reproducibility, various factors, such as retinal thinning caused by chorioretinal atrophy and posterior staphyloma from myopia-related changes, may significantly influence reproducibility.[31] In addition to thinning of the macular region from stretching of the posterior globe, abnormal macular thickening or macular retinoschisis may also develop in highly myopic eyes.[32] These factors will eventually confound GC-IPL evaluation, so caution must be exercised when interpreting GC-IPL thickness in high myopia.

The current study demonstrated that all of the parameters obtained by SD-OCT were thinner in glaucomatous than in normal eyes in both moderately and highly myopic patients. Among the normal eyes, RNFL and GC-IPL thickness parameters were both lower in high myopes than in moderate myopes. In contrast to our findings, Seo, *et al.* reported that temporal RNFL thickness analyzed by Cirrus HD-OCT was significantly greater in highly myopic normal eyes than moderately myopic normal eyes, which could be attributed to the temporalization of RNFL when the degree of myopia and axial length increase.[22] Further studies that include more normal subjects in both groups may confirm these hypotheses. Thinning of RNFL and GC-IPL thicknesses in higher severity myopia could be artifactual findings due to the ocular magnification effect. A recent study showed

that the significant negative correlation found between OCT parameters (GC-IPL and RNFL thicknesses) and axial length was the result of ocular magnification effect since the area scanned by OCT was greater in elongated globes.[33,34] Therefore, further study using magnification correction factors is needed to remedy this limitation, and to avoid misdiagnosis of glaucoma in patients with myopia.

Since the prevalence of myopia is increasing globally, and especially in Asia[17], data collection from various population groups is needed to construct normative databases for myopia, which will enhance our ability to diagnose glaucoma in myopic patients. Previous studies were mainly conducted in Korean, Japanese, and Chinese participants.[14,18-20,22,23,26] To the best of our knowledge, this is the first study to investigate the common structural imaging parameters and their diagnostic abilities in different severities of myopia in Thai population. These results from different ethnic groups provide clinically useful data that can be used to develop myopia-specific normative databases for general population. One of the strengths of this study is that we enrolled normal subjects in both myopia severity groups so that AuROC values could be generated to satisfactorily detect glaucoma among myopic patients. However, according to the Hodapp, Parish, and Anderson criteria[35], the glaucomatous eyes included in this study were classified as having early to moderate defects, which means that our findings may not be applicable to eyes with greater or lesser severity of glaucoma damage. Future study evaluating the diagnostic performance of these parameters for differentiating different severities of glaucoma is warranted.

Limitations

There are certain limitations to this study that should be mentioned. First, the study population size was relatively small, and this may have given our study insufficient statistical power to identify all statistically significant differences and associations between groups. Additional studies in a larger number of participants may be needed confirm and/or improve the validity of our results. Second, GC-IPL thinning in myopic glaucoma patients was not necessarily detected by HD-OCT measurement. Because the Cirrus HD-OCT equipment utilized in this research assessed macular GC-IPL thickness inside a 6x6x2 mm cube centered at the fovea, the presence of any glaucomatous defect away from this area might not be detected by this algorithm, as shown in Fig 3. Measurement of a larger field of the macula may optimize the glaucoma diagnosis, even in patients with myopia.
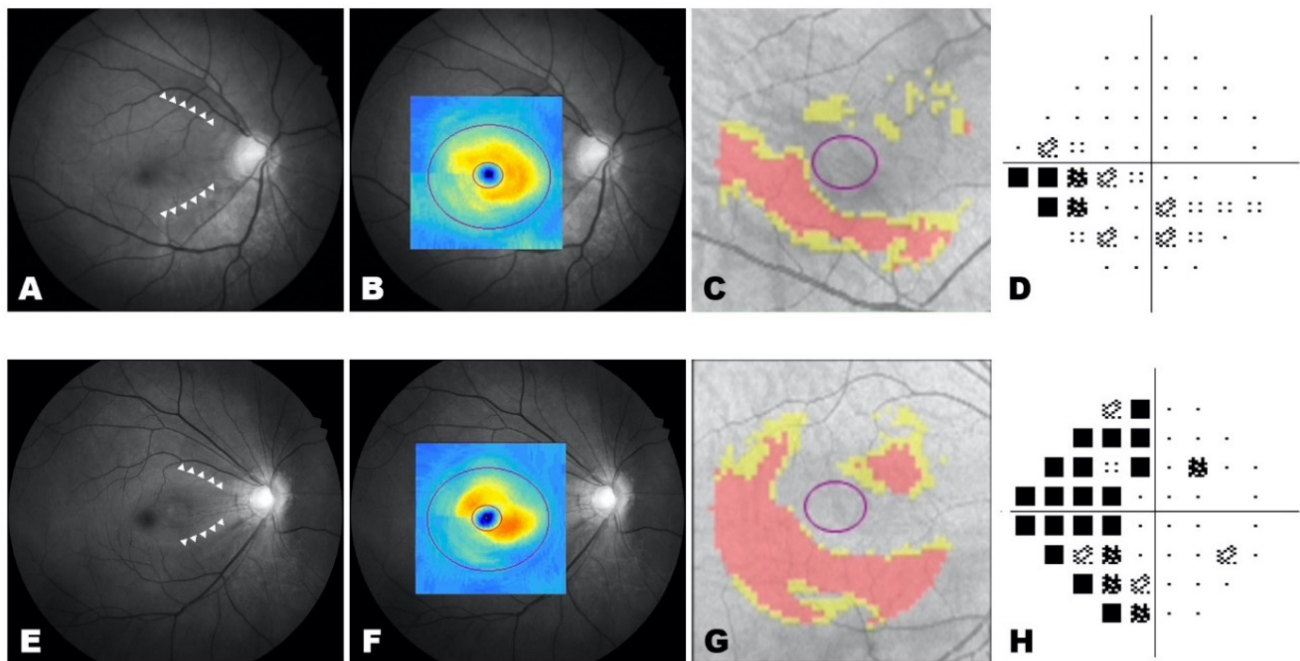
Fig 3. An example of a moderate myopia patient, and a high myopia patient.

Moderately myopic patient (A-D). Right eye; SE -5.00 D, AL 26.68 mm, HVF MD -2.00 dB.

(A) Red-free fundus photograph showed multiple RNFL defects (arrow heads). Generalized RNFL thinning in the inferior retina was observed as the choroidal vessels became clearly visible, so the RNFL defect was more easily detected in the superior hemifield than in the inferior hemifield.

(B) Detection of inferior defect on GCIPL thickness map indicated that the superior defect was located away from the macular area, thus the scanned area of the GCIPL thickness map was unable to include the superior defect into the analysis.

(C) The GCIPL deviation map was consistent with the thickness map.

(D) HVF pattern deviation map showed inferior arcuate scotoma and early superior nasal step both of which correspond with the RNFL defects. Of note, GCA could not detect abnormality in the superior hemifield despite mild inferior field loss.

Highly myopic patient (E-H). Right eye; SE -6.00 D, AL 27.23 mm, HVF MD -7.20 dB.

(E) Red-free fundus photograph showed multiple RNFL defects (arrow heads) in both the superior and inferior hemifields.

(F) The GCIPL thickness map was able to detect both superior and inferior hemifield defect, and the inferior defect was much more severe than superior defect.

(G) The findings of the GCIPL deviation map were consistent with those of the GCIPL thickness map.

(H) HVF pattern deviation map showed double arcuate scotomas, and severe defect was found in the superior visual field, which corresponds with the observed RNFL defects and GCA.

CONCLUSION

Macular GC-IPL thickness demonstrated high ability to detect glaucoma in patients with moderate or high myopia and thus can enhance glaucoma diagnosis in both groups of myopic patients. However, it should be utilized in conjunction with a comprehensive clinical examination, additional structural imaging modalities, and functional assessments to elucidate a more precise diagnosis of glaucoma in myopia.

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Conflict of interest declaration

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