Comparing the ganglion cell complex and retinal nerve fibre layer measurements by Fourier domain OCT to detect glaucoma in high myopia

Na Rae Kim,[1] Eun Suk Lee,[1] Gong Je Seong,[1] Sung Yong Kang,[2] Ji Hyun Kim,[1] Samin Hong,[1] Chan Yun Kim[1]

[1]Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea
[2]Department of Ophthalmology, Asan Medical Center, University of Ulsan, College of Medicine, Seoul, Korea

Correspondence to
Dr Chan Yun Kim, Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, 134 Shinchon-dong, Seodaemun-gu, Seoul 120-752, Korea; kcyeye@yuhs.ac

Accepted 22 June 2010
Published Online First 30 August 2010

ABSTRACT

Aim To compare the diagnostic ability to detect glaucomatous changes between peripapillary retinal nerve fibre layer (RNFL) thickness and the macular ganglion cell complex (GCC) in highly myopic patients using Fourier domain optical coherence tomography.

Methods Participants, consecutively enrolled from January 2009 to June 2009, were imaged with RTVue-100 (NHM4 and MM7 scan). The sensitivity and specificity of a colour code less than 5% (red or yellow) for glaucoma diagnosis were calculated. Area under the receiver operator characteristic (AUROC) curves were generated to assess the ability of each parameter to detect glaucomatous changes.

Results 73 normal controls and 77 glaucoma patients were included. Participants were categorised as 105 non-high myopes (spherical equivalent >-6.0 dioptres) and 45 high myopes (Spherical equivalent ≤-6.0 dioptres). The GCC thickness showed a strong correlation with RNFL thickness (correlation coefficient=0.763, $p<0.001$) in all participants. The sensitivity from superior GCC colour code was significantly higher than that from superior RNFL ($p=0.019$). The ability to detect glaucomatous changes in the highly myopic group by examining the average GCC thickness (AUROC, GCC; 0.889) was higher than when examining RNFL thickness (AUROC, RNFL; 0.825); however, there was no statistical significance ($p=0.442$).

Conclusions The ability to diagnose glaucoma with macular GCC thickness was comparable with that with peripapillary RNFL thickness in high-myopia patients. Macular GCC thickness measurements may be a good alternative or a complementary measurement to RNFL thickness assessment in the clinical evaluation of glaucoma in patients with high myopia.

INTRODUCTION

Optical coherence tomography (OCT) has allowed in vivo quantitative analysis of the peripapillary retinal nerve fibre layer (RNFL), and measuring the RNFL has been useful for diagnosing glaucoma.[1 2] However, the normal variation of the peripapillary RNFL and pathological peripapillary changes make that diagnosis of glaucoma difficult when interpreting OCT peripapillary RNFL measurements by comparing them with the normative database.

Glaucoma is characterised by selective loss of retinal ganglion cells (RGC).[3–5] Because the macular region contains more than 50% of all the RGCs, assessing ganglion cell changes in the macular region may be useful for diagnosing glaucoma instead of measuring peripapillary RNFL thickness.[6–8] RTVue-100 (Optovue, Fremont, California) is a commercially available OCT device with Fourier-domain (FD) technology. FD-OCT can measure the thickness of the macular ganglion cell complex (GCC) layer, which extends from the internal limiting membrane to the inner nuclear layer and includes the ganglion cell layer.

Although a few studies have detected glaucoma in highly myopic patients using peripapillary RNFL measurements, little is known about the relation between myopia and macular GCC thickness or the diagnostic ability of GCC measurement in myopia. In this study, we used FD-OCT to compare measuring macular GCC and peripapillary RNFL thickness to diagnose glaucoma in highly myopic patients.

METHODS

Participants

Participants were consecutively enrolled from the Glaucoma-Cataract Clinic of Severance Hospital from January 2009 to June 2009. Glaucoma patients with or without high myopia were consecutively enrolled as they presented, and normal controls were sequentially matched. The study was approved by our institutional review board and complied with the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants.

Axial ocular dimensions were measured using partial laser interferometry (IOL master, Carl Zeiss Meditec, Jena, Germany). Non-cycloplegic refraction was measured using an autorefractor (RK-3, Canon USA, Lake Success, New York) and was further refined subjectively by experienced ophthalmologists. Refraction data were converted to spherical equivalents, which were calculated using the spherical dioptre (D) plus one-half the cylindrical dioptric power. Participants were divided into two groups according to refractive errors: the high myopia group (spherical equivalent, ≤-6.00 D) and the non-high myopia group (spherical equivalent, >-6.00 D). Automated visual-field examinations (Humphrey visual field analyser with SITA standard 24-2, Carl Zeiss Meditec, Dublin, California) were performed. All eyes underwent applanation tonometry, gonioscopy, stereoscopic optic disc photography, red-free RNFL photography and RTVue FD-OCT after pupillary dilation to a minimum diameter of 5 mm on the same day. Peripapillary RNFL and perifoveal

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.

GCC thickness measurements were obtained using RTVue-100 by the same operator.

Glaucomatous eyes were defined as those with a glaucomatous visual field defect confirmed by two reliable visual field examinations and by the appearance of a glaucomatous optic disc irrespective of the level of intraocular pressure. A field defect was defined as having three or more significant ($p<0.05$) non-edge contiguous points with at least one at the $p<0.01$ level on the same side of the horizontal meridian in the pattern deviation plot, classified as outside normal limits in the glaucoma hemifield test, and confirmed with at least two visual field examinations. Glaucoma in myopia has been described to cause a variety of field defects.[9 10] In this study, the same definition regarding the field defect was applied to both highly and non-highly myopic eyes, and highly myopic eyes with any atypical non-glaucomatous field defect such as an enlarged blind spot, superotemporal peripheral defect or generalised reduction were excluded.

Normal eyes were defined as those with no family history of glaucoma in a first-degree relative, no history or evidence of intraocular surgery, and no retinal pathological features. Normal eyes also had an intraocular pressure of 21 mm Hg or lower, normal-appearing optic nerve heads (ONHs), and normal visual field tests, irrespective of the amount of spherical equivalents.

Participants with a narrow angle, media opacity, prior history of ocular surgery, diabetes mellitus, or other diseases affecting the visual field were excluded.

OCT measurements

The average thickness of the GCC and RNFL was measured using RTVue-100 (software version: 4.0.5.39), which acquires 26 000 A scans per second and has a 5 μm depth resolution in tissue. The RNFL thickness was determined by the nerve head map 4 mm diameter (NHM4) mode, which measures RNFL thickness by recalculating data along a 3.45 mm diameter circle around the optic disc using a map created from en face imaging utilising six circular scans ranging from 2.5 to 4.0 mm in diameter (587 or 775 A scans each) and 12 linear data inputs (3.4 mm length, 452 A scans each). Disc area measurements were also obtained using the NHM4 mode.

GCC parameters were obtained by the MM7 protocols, centred 1 mm temporal to the fovea. This protocol uses one horizontal line with a 7 mm scan length (934 A scans) followed by 15 vertical lines with a 7 mm scan length and 0.5 mm interval (800 A scans). The GCC thickness was measured from the internal limiting membrane to the inner plexiform layer boundary. The focal loss volume as the integral of deviation in areas of significant focal GCC loss and global loss volume as the sum of negative fractional deviation in the entire area were also computed. Images with a Signal Strength Index less than 35 with overt misalignment of the surface detection algorithm or with overt decentration of the measurement circle location were excluded.

The results from the comparison of RNFL and GCC thickness to normative data were illustrated with a stoplight colour scheme for each protocol. RNFL and GCC thicknesses in the normal range were represented by green backgrounds, those that were abnormal at the 5% level were represented by yellow backgrounds, and those that were abnormal at the 1% level were represented by red backgrounds.

Statistics

When data from both eyes were eligible for analysis, only one eye from each patient was randomly selected and used for data analysis.

To evaluate the relationship of spherical equivalents and axial lengths against RNFL and GCC profiles, Pearson correlation coefficients of demographic variables with OCT parameters were calculated in normal controls. Abnormal RNFL thicknesses displayed as a yellow or red colour on a colour scale (less than 5%) based on the normative database in RTVue were used to calculate sensitivity and specificity (%). The sensitivity and specificity of OCT parameters for detecting glaucoma were compared using the χ^2 test or Fisher exact test. To compare the diagnostic ability of RNFL and GCC in both highly myopic and non-highly myopic groups, area under the receiver operator characteristic curves were generated to assess the ability of each parameter to detect glaucomatous changes. Differences in AUROC between RNFL and GCC were tested for statistical significance by a previously described method.[11]

Statistical analysis was performed using SPSS for Windows (version 12.0.0; SPSS, Chicago, Illinois). A p value of less than 0.05 was accepted as statistically significant.

RESULTS

Participants

During the enrolment period, a total of 355 eyes from 196 individuals who agreed to participate were examined. Eleven eyes were excluded because of poor OCT images due to low signal strength (<35, n=11). Sixteen eyes were excluded because of improper OCT images due to scan decentration (RNFL, n=1; GCC, n=13) or the presence of an epiretinal membrane (n=2).

Table 1 Characteristics of subjects

	Highly myopic group (N=45)			Non-highly myopic group (N=105)			
	Normal (N=24)	Glaucoma (N=21)	p Value*	Normal (N=49)	Glaucoma (N=56)	p Value†	p Value‡
Age (years)	41.83±12.44	42.67±16.32	0.847	52.39±15.55	56.02±14.90	0.225	<0.001
Females, no (%)	16 (66.7%)	7 (30.4%)	0.026	26 (53.1%)	25 (44.6%)	0.389	0.776
Intraocular pressure (mm Hg)	15.25±2.97	13.14±2.63	0.016	14.01±3.86	13.45±3.36	0.427	0.361
Central corneal thickness (μm)	544.07±38.94	563.35±36.34	0.165	544.08±31.44	539.37±39.74	0.637	0.116
Spherical equivalents (dioptres)	−8.41±3.00	−9.25±3.70	0.406	−1.35±2.10	−1.25±2.08	0.810	<0.001
Axial length (mm)	26.87±1.40	27.72±1.97	0.117	24.34±1.09	24.22±1.22	0.603	<0.001
Anterior chamber depth (mm)	3.56±0.54	3.72±0.63	0.396	3.43±0.65	3.32±0.58	0.401	0.024
Mean deviation (dB)	−3.99±3.84	−8.56±5.82	0.003	−2.43±1.78	−9.49±7.41	<0.001	0.946
Pattern standard deviation (dB)	2.95±2.39	7.85±4.76	<0.001	2.53±1.34	7.75±4.16	<0.001	0.924
Visual field index (%)	94.74±8.56	79.84±19.09	0.004	97.94±2.27	75.73±25.61	<0.001	0.608
Disc area by RTVue (mm^2)	2.61±0.68	2.31±0.52	0.120	2.57±0.52	2.58±0.57	0.958	0.360

The data are given as the mean±SD.
*Value for comparing normal and glaucoma in the highly myopic group.
†Value for comparing normal and glaucoma in the non-highly myopic group.
‡Value for comparing high myopia and non-high myopia.

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.

Table 2 Peripapillary retinal nerve fibre layer thickness obtained using RTVue

	Highly myopic group (N=45)			Non-highly myopic group (N=105)			
	Normal (N=24)	Glaucoma (N=21)	p Value*	Normal (N=49)	Glaucoma (N=56)	p Value†	p Value‡
Signal strength	56.82±6.87	53.36±11.00	0.222	58.54±8.46	56.13±8.91	0.160	0.195
Average (μm)	106.37±13.97	84.01±19.20	<0.001	111.27±13.52	87.48±17.43	<0.001	0.453
Superior (um)	111.08±17.75	92.71±24.42	0.006	115.62±16.15	94.19±22.26	<0.001	0.674
Inferior (μm)	101.65±14.71	75.30±16.57	<0.001	106.90±12.68	80.39±16.72	<0.001	0.343
SN1 (μm)	114.46±31.49	106.81±28.29	0.399	126.53±18.90	99.96±27.81	<0.001	0.770
SN2 (μm)	109.67±29.69	100.43±30.72	0.311	118.65±18.88	97.48±30.00	<0.001	0.691
NU2 (μm)	83.83±23.66	72.38±23.70	0.113	92.61±22.42	81.45±24.50	0.017	0.059
NU1 (μm)	69.46±24.42	58.05±20.33	0.099	73.69±20.29	67.14±19.63	0.096	0.108
NL1 (μm)	61.33±19.13	57.33±17.37	0.469	69.47±16.17	63.36±16.87	0.062	0.029
NL2 (μm)	71.63±24.39	67.86±19.96	0.577	81.53±17.06	71.84±18.21	0.006	0.064
IN2 (μm)	98.29±27.97	93.57±23.13	0.544	114.37±19.03	91.79±21.33	<0.001	0.146
IN1 (μm)	123.00±25.17	96.19±25.75	0.001	130.49±24.76	95.80±26.05	<0.001	0.780
IT1 (μm)	135.71±29.20	82.76±34.65	<0.001	150.20±23.29	90.38±31.36	<0.001	0.320
IT2 (μm)	136.13±37.54	76.52±27.91	<0.001	138.43±23.49	88.25±30.50	<0.001	0.634
TL2 (μm)	108.21±31.19	66.91±15.29	<0.001	95.16±18.92	75.84±23.52	<0.001	0.449
TL1 (μm)	76.46±22.94	62.91±15.29	0.027	75.76±17.97	65.73±19.75	0.008	0.938
TU1 (μm)	91.83±27.23	70.24±23.38	0.007	84.69±17.93	70.23±19.57	<0.001	0.297
TU2 (μm)	122.37±32.84	91.86±33.56	0.003	112.96±21.30	89.61±23.68	<0.001	0.195
ST2 (μm)	156.33±32.78	122.43±40.57	0.003	157.41±24.68	124.09±31.65	<0.001	0.890
ST1 (μm)	141.75±32.16	119.52±35.87	0.034	158.35±27.25	125.86±33.36	<0.001	0.122

*Value for comparing normal and glaucoma in the highly myopic group.
†Value for comparing normal and glaucoma in the non-highly myopic group.
‡Value for comparing high myopia and non-high myopia.
IN, inferonasal; IT, inferotemporal; NL, nasal lower; NU, nasal upper; SN, superonasal; ST, superotemporal; TL, temporal lower; TU, temporal upper.

Five eyes in which an erroneous RNFL or GCC profile of 0.0 μm were measured with an OCT algorithm (RNFL, n=3, GCC, n=2), and four eyes in which a reversed cross-sectional image caused algorithm failure of the GCC scan were excluded from analysis. Ten eyes were further excluded because of unacceptable quality of stereoscopic disc photography or red-free RNFL photography (n=3) or unreliable visual fields (n=7).

A total of 150 eyes from 150 individuals were included in the analysis. Patients were categorised into two groups: the non-highly myopic (n=105) and highly myopic groups (n=45). There were 73 normal controls and 77 open-angle glaucoma patients. The mean age of the participants was 50.69±15.90 years (range 22–77 in the high myopia group; 22–78 in the non-high myopia group). Table 1 summarises the demographic characteristics.

OCT measurements

The GCC thickness showed strong correlations with RNFL thickness (correlation coefficient=0.763, p<0.001). The average, superior and inferior RNFL thicknesses were significantly different between normal and glaucomatous eyes in both the highly and non-highly myopic group (all p<0.05). In the highly myopic group, significant differences were found in the RNFL thickness from the IN1 to the ST1 sector (corresponding to temporal half region), but not in the SN1 to the IN2 sector (corresponds to nasal half region) between normal and glaucomatous eyes. For the non-highly myopic group, there was a significant difference in the RNFL measurements for all sectors, except the NU1 to the NL1 sector. When comparing RNFL thickness between the high myopic group and the non-highly myopic group, only the NL1 sector showed a significant difference (p=0.029) (table 2).

The average, superior and inferior GCC thicknesses were significantly different between normal and glaucoma eyes in both non-high myopes and high myopes (all p<0.05). Focal loss volume and global loss volume were also different between normal and glaucoma. When comparing GCC parameters between high myopia and non-high myopia, focal loss volume only showed a significant difference (p=0.015) (table 3).

Table 3 Perimacular ganglion cell complex parameters obtained using RTVue

	Highly myopic group (N=45)			Non-highly myopic group (N=105)			
	Normal (N=24)	Glaucoma (N=21)	p Value*	Normal (N=49)	Glaucoma (N=56)	p Value†	p Value‡
Signal strength	60.96±8.86	58.17±13.41	0.408	62.79±8.97	63.32±9.12	0.766	0.050
Average (μm)	93.11±9.95	75.78±10.01	<0.001	93.70±9.45	79.28±9.13	<0.001	0.650
Superior (μm)	93.67±9.90	78.19±14.03	<0.001	93.11±11.02	82.22±11.18	<0.001	0.711
Inferior (μm)	92.72±11.64	73.42±9.72	<0.001	93.71±10.05	76.35±10.70	<0.001	0.764
Focal loss volume (%)	4.03±4.28	11.97±8.53	<0.001	1.79±2.50	7.20±3.91	<0.001	0.015
Global loss volume (%)	11.62±7.11	26.32±9.57	<0.001	8.96±5.61	21.29±8.33	<0.001	0.099

*Value for comparing normal and glaucoma in the highly myopic group.
†Value for comparing normal and glaucoma in the non-highly myopic group.
‡Value for comparing high myopia and non-high myopia.

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.

Relationship of demographic variables with RNFL and GCC in normal eyes

Table 4 shows the correlation among demographic variables including biometric and refractive error and the OCT parameters among different hemispheres measured with OCT in normal controls. In the highly myopic group, the superior RNFL thickness was significantly associated with age (correlation coefficient=−0.472, p=0.020). Peripapillary RNFL and macular GCC parameters obtained using RTVue were not significantly associated with both axial length and spherical equivalent.

Diagnostic performance of RNFL and GCC

An inferior RNFL colour code showed a significantly higher sensitivity than superior RNFL thickness in both highly myopic and non-highly myopic group (p=0.047 and 0.018, respectively). Sensitivity from a superior GCC and inferior GCC colour code was not different in either group. In the high myopia group, the sensitivity from a superior GCC colour code was significantly higher than that from superior RNFL (p=0.019). The abnormal colour code from more than one sector of the octametric RNFL map and from global loss volume of GCC showed the best sensitivity, and the abnormal colour code from the superior RNFL thickness showed the best specificity in the highly myopic group (table 5).

Table 6 shows the ROC curve areas with 95% CIs. AUROC curves of GCC and RNFL did not show any significant differences in either the non-high myopia or the high myopia groups (average RNFL vs average GCC, superior RNFL vs superior GCC, and inferior RNFL vs inferior GCC; p=0.422, 0.354 and 0.675 in the high myopia group; p=0.653, 0.652 and 0.913 in the non-high myopia group, respectively). Macular GCC parameters showed higher AUROC curves than RNFL in the high myopia group for detecting glaucoma; however, there was no statistical significance (figure 1A). In the non-highly myopic group, the AUROC curves of average RNFL thickness and average GCC comparing normal with glaucomatous eyes were also similar (figure 1B). The best parameter for discriminating normal and glaucomatous eyes was inferior GCC thickness obtained from in the highly myopic group and focal loss volume of GCC in the non-highly myopic group.

DISCUSSION

In this study, we investigated the diagnostic ability of OCT to detect glaucomatous changes in highly myopic and non-highly myopic eyes. We examined whether macular GCC thickness or peripapillary RNFL thickness had a better diagnostic ability in these participants. Macular GCC thickness showed comparable AUROC curves to peripapillary RNFL thickness for determining glaucoma in high-myopia patients.

Although some studies have shown that there is no association between myopia and peripapillary RNFL thickness,[12 13] others have reported that peripapillary RNFL measurements using OCT in myopic eyes may not be reliable due to peripapillary changes and thinner RNFL thickness than in the normal population.[14–19] A thin polar RNFL could be incorrectly attributed to a glaucomatous change if one does not account for the effect of axial length or refractive error.[18] In addition, the normative database for Stratus OCT excludes extremes in refractive error.[18] In contrast to previous studies using older-generation OCTs,[12–19] we evaluated peripapillary RNFL thickness using FD-OCT and evaluated macular GCC thickness parameters which are not provided with TD-OCT. The normative data from RTVue-100 had 2.8% myopes equal or

Table 4 Pearson correlation coefficients of the relationship between optical coherence tomography parameters and age, axial length, and refractive errors in normal controls (N=73)

	Normal subjects with high myopia (N=24)					Normal subjects without high myopia (N=49)				
	Age (year)	CCT (μm)	SE (dioptres)	Axial lengths (mm)	Disc area (mm^2)	Age (year)	CCT (μm)	SE (dioptres)	Axial lengths (mm)	Disc area (mm^2)
Retinal nerve fibre layer										
Average	−0.353 (0.091)	0.000 (0.999)	0.321 (0.126)	−0.339 (0.114)	0.003 (0.989)	−0.275 (0.056)	−0.372 (0.074)	−0.121 (0.408)	−0.050 (0.742)	0.360* (0.011)
Superior	−0.472* (0.020)	0.051 (0.864)	0.306 (0.146)	−0.334 (0.120)	0.010 (0.963)	−0.260 (0.071)	−0.405 (0.050)	−0.130 (0.372)	−0.057 (0.704)	0.360* (0.011)
Inferior	−0.101 (0.639)	−0.057 (0.846)	0.241 (0.258)	−0.256 (0.238)	−0.007 (0.976)	−0.257 (0.074)	−0.294 (0.164)	−0.094 (0.522)	−0.032 (0.834)	0.308* (0.031)
Ganglion cell complex										
Average	0.170 (0.428)	−0.061 (0.837)	−0.247 (0.245)	0.222 (0.310)	−0.270 (0.201)	−0.239 (0.098)	−0.124 (0.564)	0.050 (0.731)	−0.032 (0.835)	0.142 (0.329)
Superior	0.141 (0.511)	0.094 (0.749)	−0.185 (0.386)	0.118 (0.591)	−0.142 (0.508)	0.317* (0.027)	−0.173 (0.419)	−0.050 (0.733)	0.052 (0.732)	0.087 (0.554)
Inferior	0.182 (0.394)	−0.162 (0.581)	−0.239 (0.260)	0.255 (0.239)	−0.323 (0.124)	−0.124 (0.397)	−0.083 (0.698)	0.092 (0.529)	−0.088 (0.561)	0.186 (0.201)

The data are given as the Pearson correlation coefficients with p value in parenthesis.
*p value <0.05.
CCT, central corneal thickness; SE, spherical equivalents.

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.

Table 5 Sensitivity and specificity (%) with 95% CI of retinal nerve fibre layer and ganglion cell complex parameters compared with the normative database of RTVue

	Highly myopic group (N=45)		Non-highly myopic group (N=105)			
	Sensitivity	Specificity	Sensitivity	Specificity	p Value†	p Value‡
Retinal nerve fibre layer						
Average	76.19 (52.8 to 91.8)	75.00 (53.3 to 90.2)	71.43 (57.8 to 82.7)	89.80 (77.8 to 96.6)	0.676	0.097
Superior	52.38 (29.8 to 74.3)	87.50 (67.6 to 97.3)	51.79 (38.0 to 65.3)	89.80 (77.8 to 96.6)	0.963	0.768
Inferior	85.71 (63.7 to 97.0)	58.33 (36.6 to 77.9)	76.79 (63.6 to 87.0)	87.76 (75.2 to 95.4)	0.390	0.004
≥1/16 sector	100.00 (83.9 to 100.0)	33.33 (15.6 to 55.3)	98.21 (90.4 to 100.0)	51.02 (36.3 to 65.6)	0.538	0.154
Ganglion cell complex						
Average	90.48 (69.6 to 98.8)	58.33 (33.6 to 77.9)	78.57 (65.6 to 88.4)	79.59 (65.7 to 89.8)	0.228	0.056
Superior	85.71 (63.7 to 97.0)	66.67 (44.7 to 84.4)	64.29 (50.4 to 76.6)	83.67 (70.3 to 92.7)	0.067	0.099
Inferior	85.71 (63.7 to 97.0)	62.50 (40.6 to 81.2)	83.93 (71.7 to 92.4)	83.67 (70.3 to 92.7)	0.847	0.044
Focal loss volume (%)	95.24 (76.2 to 99.9)	54.17 (32.8 to 74.4)	85.71 (73.8 to 93.6)	75.51 (61.1 to 86.7)	0.247	0.065
Global loss volume (%)	100.00 (83.9 to 100.0)	41.67 (22.1 to 63.4)	91.07 (80.4 to 97.0)	67.35 (52.5 to 80.1)	0.157	0.036
p Value*						
Average	0.214	0.221	0.383	0.161		
Superior	0.019	0.086	0.180	0.372		
Inferior	>0.999	0.768	0.341	0.564		

*Value for comparing sensitivity and specificity between retinal nerve fibre layer and ganglion cell complex parameters.
†Value for comparing sensitivity between high myopia and non-high myopia group.
‡Value for comparing specificity between high myopia and non-high myopia group.

worse than −5.0 dioptres.[20] In this study, peripapillary RNFL and macular GCC thickness from RTVue were not associated with either axial length or spherical equivalence.

RTVue directly measures the thickness of the inner three retinal layers with improved resolution and provides an analysis of the percentage loss of these layers compared with a normative database. It is expected to target the cells directly affected by glaucoma in the area of their highest concentration. A recent study showed that macula GCC parameters obtained with FD-OCT produce comparable AUROC curves as circumpapillary RNFL measurements obtained with TD-OCT.[21 22] Because the axonal fibres arising from individual RGCs coming from all RGC populations converge towards the ONH, any loss in the RNFL may be most readily detected in the peripapillary region. This anatomy may be the reason for the comparable diagnostic ability of RNFL and GCC measurements.

We wondered whether perimacular GCC assessment is advantageous over peripapillary RNFL measurements in the high myopia group. In our study, macular GCC thickness measurements obtained from RTVue showed higher AUROC curves than peripapillary RNFL thickness measurements in highly myopic patients for detecting glaucoma; however, the difference was not statistically significant. With regard to the sensitivity of the colour code provided by OCT, the sensitivity from the superior GCC colour code was significantly higher than that from superior RNFL. Previous studies using Stratus OCT reported that the superior area from the quadrant map demonstrated the strongest negative correlation between axial length and RNFL thickness.[17 19] Thinned RNFL along the superior peripapillary area in highly myopic eyes could have resulted in lower sensitivity from the superior hemifield RNFL colour code, while the superior hemifield GCC colour code was less affected

Table 6 Area under receiver operating characteristic curve values with 95% CIs between normal and glaucomatous eyes

	Mean±SE (95% CI)		
	Highly myopic group (N=45)	Non-highly myopic group (N=105)	p Value†
Retinal nerve fibre layer			
Average	0.825±0.065 (0.699 to 0.952)	0.861±0.037 (0.789 to 0.934)	0.630
Superior	0.736±0.079 (0.582 to 0.890)	0.788±0.046 (0.698 to 0.877)	0.570
Inferior	0.881±0.051 (0.781 to 0.980)	0.884±0.033 (0.820 to 0.948)	0.961
Ganglion cell complex			
Average	0.889±0.046 (0.798 to 0.980)	0.883±0.032 (0.820 to 0.946)	0.915
Superior	0.829±0.062 (0.708 to 0.950)	0.758±0.048 (0.664 to 0.852)	0.365
Inferior	0.909±0.043 (0.825 to 0.993)	0.889±0.032 (0.826 to 0.952)	0.709
Focal loss volume (%)	0.837±0.058 (0.724 to 0.951)	0.902±0.031 (0.841 to 0.964)	0.323
Global loss volume (%)	0.885±0.050 (0.787 to 0.982)	0.893±0.030 (0.833 to 0.952)	0.891
p Value*			
Average	0.422	0.653	
Superior	0.354	0.652	
Inferior	0.675	0.913	

*Value for comparing areas under the receiver operator characteristic curves between retinal nerve fibre layer and ganglion cell complex parameters.
†Value for comparing high myopia and non-high myopia.

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.

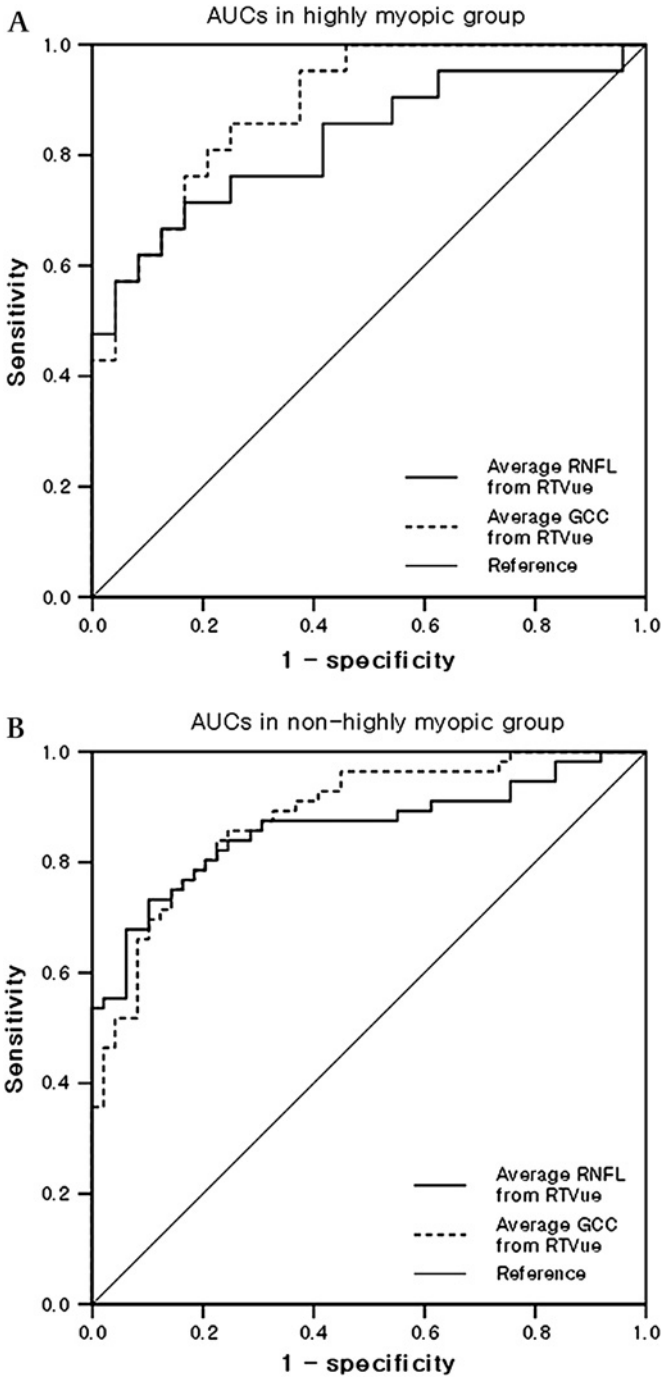

Figure 1 Area under the receiver operator characteristic curves (AUC) of average retinal nerve fibre layer thickness (RNFL) and the average ganglion cell complex (GCC) thickness obtained using RTVue optical coherence tomography in (A) the highly myopic group and (B) the non-highly myopic group.

by refractive errors. Further investigation of these properties is needed. Although the diagnostic ability of the GCC parameter was not superior to RNFL parameters in high myopia subjects, GCC and RNFL parameters can be complementary.

In the past, most investigators have focused on the comparison of measurements at the macula and the optic disc. This was due in part to the fact that most commercial imaging instruments yielded one or the other. Now, many techniques are available for obtaining both measurements in one session. The perifoveal region yields information on the ganglion cells and their axons located at the centre of the macula, which are represented in perimetry only by a few points at the centre of the visual field, whereas the peripapillary region reflects the entire retina. The time course of the disease and for treatment decisions may differ between an eye with a well-preserved central macula and damaged peripheral retina, and one with damage in both areas. By including both regions, it may be possible to gain new knowledge on the process of glaucomatous damage through an additional role for measuring GCC in glaucoma assessment.

In this study, we used RNFL and GCC thickness of the superior and inferior hemisphere. RTVue-100 provides the RNFL and GCC thickness of each retinal hemisphere. Measurements of each hemisphere are more reasonable than measurements of the quadrant sections including superior, inferior, temporal and nasal quadrants, since glaucomatous damage follows hemispheres.

There were several limitations to this study, including a relatively small sample size. A possible source of bias was that highly myopic eyes usually show a characteristic appearance of the ONH with shallow cupping, a large myopic crescent and bright fundus pigmentation, and the typical morphology may have made the examiners assume that the eye was highly myopic. This study was conducted with only Asian participants, and there may be differences among ethnic groups. The participants in this study were somewhat different from those in practice, because we excluded highly myopic eyes with any atypical visual-field defect, including an enlarged blind spot, superotemporal peripheral defect or generalised reduction.

In conclusion, this study used new-generation FD-OCT and found that peripapillary RNFL thickness and macular GCC thickness from FD-OCT were not related with axial length and spherical equivalence. Macular GCC thickness had a comparable discriminating power for detecting glaucoma compared with RNFL thickness in both the non-highly myopic group and the highly myopic group. Macular GCC thickness measured by FD-OCT may be a good alternative or complementary to RNFL thickness assessment for detecting glaucoma in cases of high myopia. A more accurate parameter representing RGC loss in the perimacular area could improve the capability for glaucoma diagnosis in highly myopic eyes in the future.

Funding This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (No 2009-0076736).

Competing interests None.

Patient consent Obtained.

Ethics approval Ethics approval was provided by the Severance Hospital, Seoul, Korea.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Huang ML,** Chen HY. Development and comparison of automated classifiers for glaucoma diagnosis using Stratus optical coherence tomography. *Invest Ophthalmol Vis Sci* 2005;**46**:4121–9.
2. **Parikh RS,** Parikh S, Sekhar GC, *et al*. Diagnostic capability of optical coherence tomography (Stratus OCT 3) in early glaucoma. *Ophthalmology* 2007;**114**:2238–43.
3. **Garway-Heath DF,** Caprioli J, Fitzke FW, *et al*. Scaling the hill of vision: the physiological relationship between light sensitivity and ganglion cell numbers. *Invest Ophthalmol Vis Sci* 2000;**41**:1774–82.
4. **Harwerth RS,** Carter-Dawson L, Shen F, *et al*. Ganglion cell losses underlying visual field defects from experimental glaucoma. *Invest Ophthalmol Vis Sci* 1999;**40**:2242–50.
5. **Zeimer R,** Asrani S, Zou S, *et al*. Quantitative detection of glaucomatous damage at the posterior pole by retinal thickness mapping. A pilot study. *Ophthalmology* 1998;**105**:224–31.
6. **Ishikawa H,** Stein DM, Wollstein G, *et al*. Macular segmentation with optical coherence tomography. *Invest Ophthalmol Vis Sci* 2005;**46**:2012–17.

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.

7. **Tan O,** Li G, Lu AT, *et al*. Mapping of macular substructures with optical coherence tomography for glaucoma diagnosis. *Ophthalmology* 2008;**115**:949—56.
8. **Van Buren JM.** *The Retinal Ganglion Cell Layer: A Physiological-Anatomical Correlation in Man and Primates of the Normal Topographical Anatomy of the Retinal Ganglion Cell Layer and its Alterations with Lesions of the Visual Pathways*. Springfield, IL: Charles C Thomas, 1963.
9. **Nicolela MT,** Drance SM. Various glaucomatous optic nerve appearances: clinical correlations. *Ophthalmology* 1996;**103**:640—9.
10. **Greve EL,** Furuno F. Myopia and glaucoma. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1980;**213**:33—41.
11. **Hanley JA,** McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983;**148**:839—43.
12. **Hoh ST,** Lim MC, Seah SK, *et al*. Peripapillary retinal nerve fiber layer thickness variations with myopia. *Ophthalmology* 2006;**113**:773—7.
13. **Salchow DJ,** Oleynikov YS, Chiang MF, *et al*. Retinal nerve fiber layer thickness in normal children measured with optical coherence tomography. *Ophthalmology* 2006;**113**:786—91.
14. **Budenz DL,** Anderson DR, Varma R, *et al*. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. *Ophthalmology* 2007;**114**:1046—52.
15. **Kashiwagi K,** Tamura M, Abe K, *et al*. The influence of age, gender, refractive error, and optic disc size on the optic disc configuration in Japanese normal eyes. *Acta Ophthalmol Scand* 2000;**78**:200—3.
16. **Leung CK,** Mohamed S, Leung KS, *et al*. Retinal nerve fiber layer measurements in myopia: an optical coherence tomography study. *Invest Ophthalmol Vis Sci* 2006;**47**:5171—6.
17. **Leung MM,** Huang RY, Lam AK. Retinal nerve fiber layer thickness in normal Hong Kong Chinese children measured with optical coherence tomography. *J Glaucoma* 2010;**19**:95—9.
18. **Rauscher FM,** Sekhon N, Feuer WJ, *et al*. Myopia affects retinal nerve fiber layer measurements as determined by optical coherence tomography. *J Glaucoma* 2009;**18**:501—5.
19. **Vernon SA,** Rotchford AP, Negi A, *et al*. Peripapillary retinal nerve fibre layer thickness in highly myopic Caucasians as measured by Stratus optical coherence tomography. *Br J Ophthalmol* 2008;**92**:1076—80.
20. **Sinai MJ,** Garway-Heath DF, Fingeret M, *et al*. The role of ethnicity on the retinal nerve fiber layer and optic disc area measured with Fourier domain optical coherence tomography [abstract]. *Invest Ophthalmol Vis Sci* 2009;**50**(Suppl):P4785.
21. **Seong M,** Sung KR, Choi EH, *et al*. Macular and peripapillary retinal nerve fiber layer measurements by spectral domain optical coherence tomography in normal-tension glaucoma. *Invest Ophthalmol Vis Sci* 2010;**51**:1446—52.
22. **Tan O,** Chopra V, Lu AT, *et al*. Detection of macular ganglion cell loss in glaucoma by Fourier-domain optical coherence tomography. *Ophthalmology* 2009;**116**:2305—14 e1—2.

BMJ Group, supporting you throughout your career…

At BMJ Group we have resources available to you at every stage of your career.

Whether you are a medical student or doctor in training looking to keep up with the latest news and prepare for exams, or a qualified doctor who wants the latest medical information, to attend conferences, or looking for your next job, BMJ Group has something to offer. For the latest information on all of our products and services register to receive email updates at

group.bmj.com/registration

BMJ student BMJ BMJJournals BMJCareers BMJEvidence Centre BMJLearning The BMJ Group Awards

Br J Ophthalmol: first published as 10.1136/bjo.2010.182493 on 30 August 2010. Downloaded from http://bjo.bmj.com/ on 23 April 2018 by guest. Protected by copyright.