Original Article

Effect of myopia and optic disc area on ganglion cell-inner plexiform layer and retinal nerve fiber layer thickness

Sunil Ganekal, Sadhwini MH, Shivanna Kagathur

Purpose: The aim of this work was to study the impact of myopia and different optic disc areas on ganglion cell-inner plexiform layer (GCIPL) and retinal nerve fiber layer (RNFL) thickness profiles in myopic patients by spectral-domain optical coherence tomography (SD-OCT). **Methods:** This was a cross-sectional study of 100 eyes of 50 myopic individuals. All patients underwent complete ophthalmic evaluation and SD-OCT examination. According to spherical equivalent (SE), patients were divided into M1, M2, and M3 (low, moderate, and high myopia group). According to optic disc area values, patients were divided into D1, D2 and D3 (small, medium and large disc groups). Average GCIPL and RNFL thickness recorded globally and separately for all quadrants and also according to 12 clock hours and analyzed with respect to different myopic groups, optic disc area groups, and axial length. **Results:** Quadrantic RNFL thickness profiles and their average RNFL thickness were significantly thinner in high myopic group compared to low myopic group, except for the temporal quadrant ($P < 0.05$). Average RNFL and RNFL thickness of all quadrants were significantly thicker in the large disc group than in the small disc group ($P < 0.05$). Average GCIPL and GCIPL thicknesses of all sectors were significantly thinner in high myopic group compared to low myopic group ($P < 0.05$). No significant correlation was observed between GCIPL and disc area changes. Average RNFL thickness correlated significantly with SE (3.667 μm/diopter), axial length (–5.3805 μm/mm) and optic disc area (9.4617 μm/mm^2). Also, average GCIPL thickness correlated statistically significantly with SE (1.6807 μm/diopter) and axial length (–2.626 μm/mm). **Conclusion:** Myopia and axial length significantly reduce RNFL and GCIPL thickness profiles but the optic disc area significantly increases RNFL thickness, but not GCIPL thickness.

Key words: GCIPL, myopia, optic disc area, RNFL

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Myopic eyes have an enlarged optic disc with large cup-to-disc ratios and larger areas of peripapillary atrophy and localized retinal nerve fiber layer (RNFL) defects. The structural changes result in the fragility of the supporting tissue in the lamina cribrosa and in dynamic imbalance due to structural changes in the surroundings of the ONH.[1] The influence of high myopia on ganglion cell complex (GCC) may be less than that on RNFL.[2] Spectral-domain optical coherence tomography (SD-OCT) helps measure the thickness of each layer of retina and implies that the thinning of the inner retina in the macula is due to the loss of ganglion cells.[3] Myopia has been identified as an independent and strong risk factor for primary open-angle glaucoma.[4]

In myopic glaucoma, both myopic changes and glaucomatous changes are thought to be present, and it is often difficult to clearly distinguish the two types of changes, leading to misdiagnosis of glaucoma.[5] Our aim was to use OCT to detect changes in RNFL and ganglion cell-inner plexiform layer (GCIPL) in myopic individuals. Myopia leads to a decrease in thickness in RNFL and could represent a predisposing factor for the future development of glaucoma. However, there are conflicting results regarding the effect of myopia on ganglion cell layer at macula. Hence, we did this study to determine the effect of increasing myopia and optic disc area on GCIPL thickness profiles in healthy young adults.

Methods

A cross-sectional study was conducted on healthy myopic individuals. IRB approval was obtained, and the research adhered to the tenets of the Declaration of Helsinki. One hundred eyes of 50 myopic healthy individuals aged between 20 and 40 years with best-corrected visual acuity (BCVA) of ≥ 6/12 were included in the study. Informed consent was taken from all the patients. Patients with any media opacity, degenerative myopia, with glaucoma or ocular hypertension, congenital optic disc defects, ocular anomalies which affect GCIPL and RNFL, ocular trauma, and previous ocular surgeries were excluded from the study.

All patients underwent complete ophthalmic evaluation; BCVA was converted to spherical equivalent. Axial length was

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measured with optical biometry (IOLMaster™ version 700, Carl Zeiss Meditec, Germany); dilated fundus evaluation was done with fundus photography. OCT examination was performed on both eyes with CIRRUS HD-OCT 500 (Carl Zeiss Meditec, Inc. Dublin, California). Standardized OCT protocols were used to measure RNFL and GCIPL thickness. Macular cube scan (512 × 128) was used to measure GCIPL thickness in macular area and Optic disc cube/3D scan (200 × 200) was used to measure RNFL thickness and optic disc area [Fig. 1]. Good-quality OCT scans with sufficient signal strength (>6) were taken for analysis.

The subjects were grouped as follows: According to spherical equivalent (SE) values, M1—low myopia group (SE < –3.0D), M2—moderate myopia group (–3.0D < SE < –6.0D), and M3—high myopia group (–6.0D < SE < –8.0D). According to optic disc area values: D1—Small disc group (disc area <2.0 mm^2), D2—medium disc group (2.0 mm^2 < disc area <2.5 mm^2), and D3—large disc group (disc area > 2.5 mm^2). Average RNFL thickness recorded globally, separately for superior, inferior, nasal, and temporal quadrants and also according to 12 clock hours and analyzed with respect to different myopic groups, optic disc area groups, and axial length. Average GCIPL thickness recorded globally and separately for superior, superonasal, inferonasal, inferior, inferotemporal, and superotemporal sectors and analyzed with respect to different myopic groups, optic disc area groups, and axial length.

Data were analyzed using Epi-info software version 7.2.0.1. Sociodemographic characteristics were described using frequency and proportions. Ocular measurements were described using descriptive statistics. Frequency distribution was done using bar diagram, pie chart, line diagram, box, and whisker plot. Bivariate analysis used to test the difference of measurements in various myopic individuals, GCIPL, RNFL, and disc area groups was tested using analysis of variance (ANOVA). All tests of significance were interpreted at α error of 5%. A value of $P < 0.05$ was considered statistically significant. Correlation between various ocular measurements was tested using scatter plot and correlation coefficient. Simple linear regression was used to assess the covariance of each variable with respect to the other. Multiple linear regression was performed to predict the change in RNFL and GCIPL thickness using SE, axial length, and disc area as independent variables.

Results

The mean age was 26.44 ± 4.321 years. There were 52 men and 48 women. Of the total 100 eyes, based on the degree of refractive error, 37 eyes were in M1 group, 39 were in M2 group, and 24 were in the M3 group. In the disc area categorization, 59 eyes were included in D1 group, 34 were included in D2 group, and 7 were included in D3 group. Mean SE was –3.94 ± 2.019 diopters. Mean optic disc area was 2.04 ± 0.315 mm^2. Mean axial length was 24.38 ± 1.179 mm. Average RNFL thickness in M1, M2, and M3 groups are shown in Table 1. As the SE increased, the average RNFL thickness decreased. Significant thinning of RNFL noted as the degree of myopia increased in all quadrants except for temporal quadrant, which shows an increase in thickness in M3 than M2.

RNFL thickness according to clock hours was also analyzed in comparison with M1, M2, and M3 groups [Fig. 2]. RNFL thickness at 1, 2, 5, 6, 7, and 12 O'clock hours showed a decrease in thickness with $P < 0.05$. RNFL thickness at 8, 9, 10, and 11

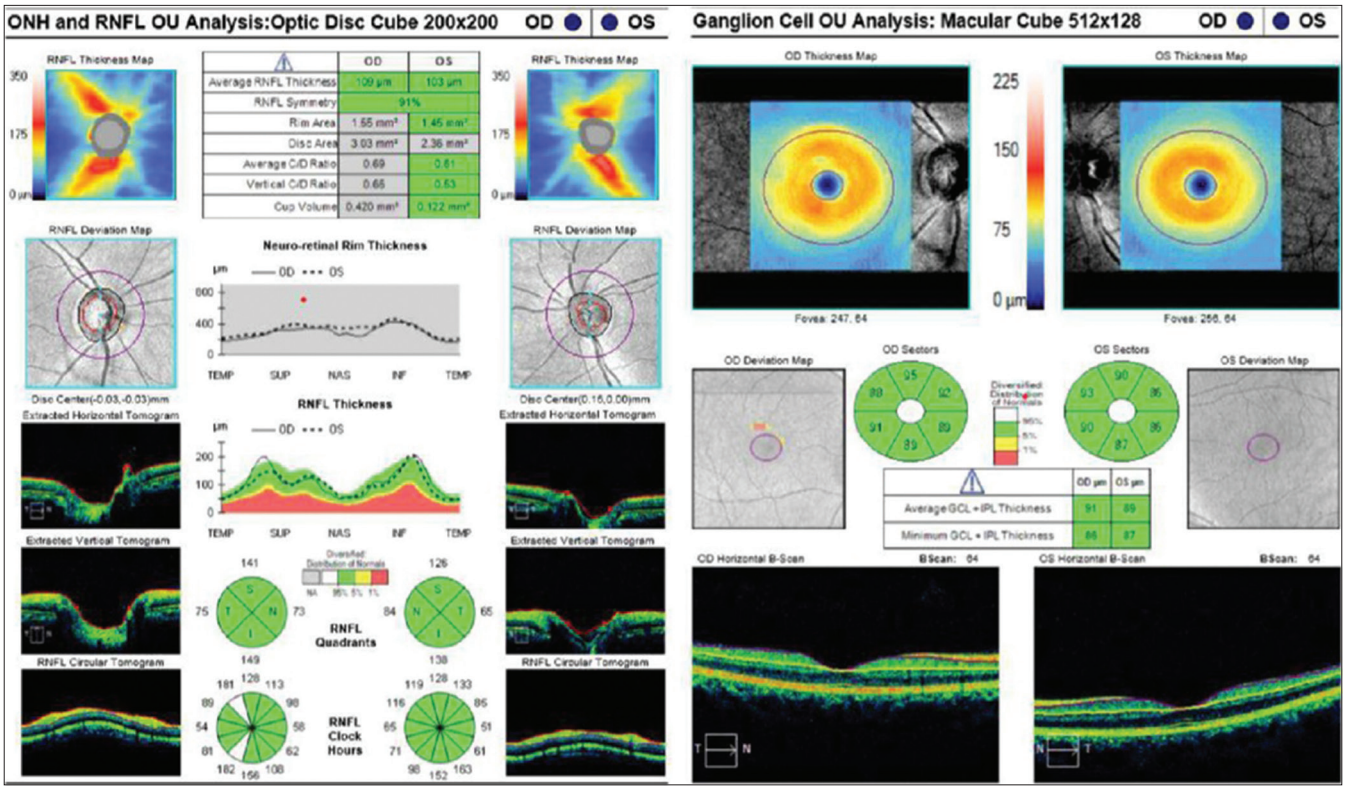

Figure 1: Representative OCT images (RNFL and GCIPL measurements)

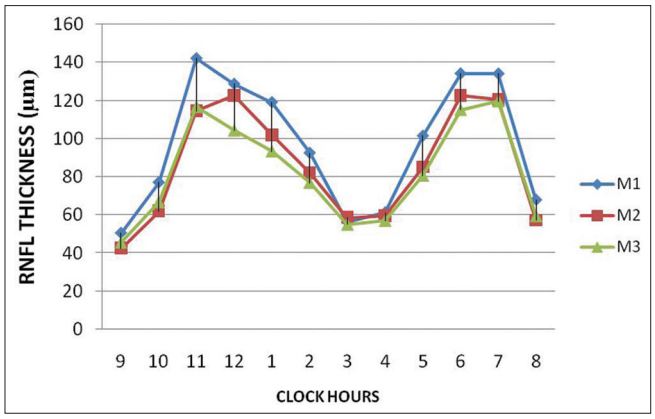

Figure 2: Line graph showing clock hour RNFL thickness profile among M1, M2, and M3

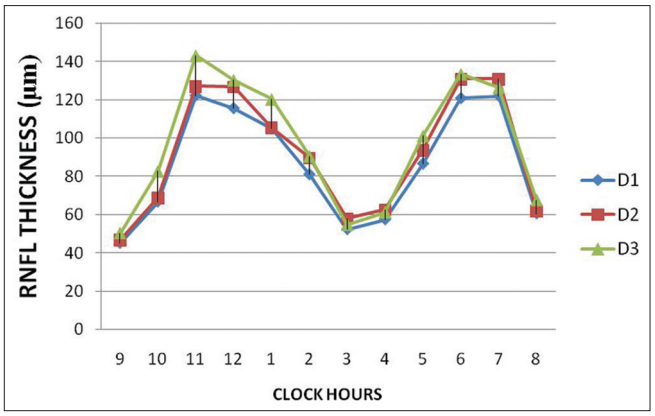

Figure 3: Line graph showing clock hour RNFL thickness profile among D1, D2, and D3

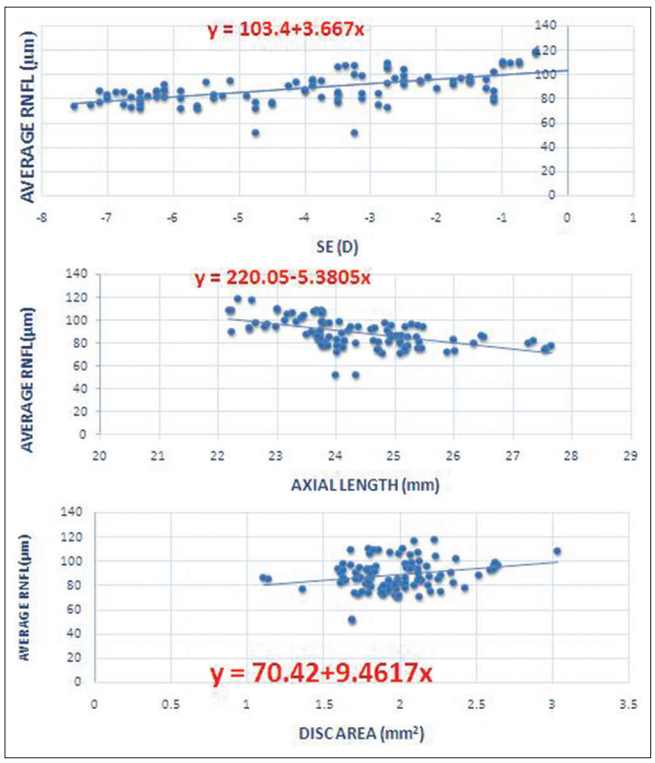

Figure 4: Scatter plot of simple linear regression between average RNFL and SE, axial length and optic disc area

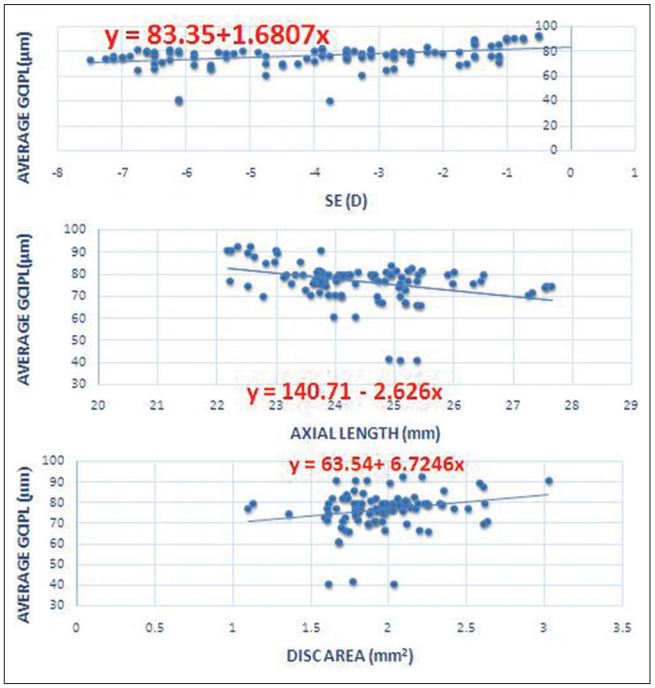

Figure 5: Scatter plot of simple linear regression between average GCIPL and SE, axial length and optic disc area

O′ clock hours showed an increase in thickness in M3 than M2 with a $P < 0.05$. However, RNFL thickness at 3 and 4 O′clock hours was not statistically significant. RNFL thickness profile was compared with D1, D2, and D3 and the results are shown in Table 2. Average RNFL and RNFL in different quadrants were thicker in large disc group as compared to small disc group. RNFL thickness according to clock hours were analyzed in comparison to D1, D2, and D3 [Fig. 3]. RNFL thickness at 2, 3, and 10 O′ clock hours showed an increase in thickness ($P < 0.05$). RNFL thickness at other clock hours also showed an increase in thickness but was not statistically significant.

Average GCIPL thickness was compared with M1, M2, and M3 [Table 3]. As the SE increased GCIPL became thinner. When RNFL thinning was compared with GCIPL thinning in each myopic group, RNFL thinning was more pronounced than GCIPL thinning, but both were statistically significant. GCIPL thickness profile was compared with D1, D2, and D3, as shown in Table 4. Ganglion cell layer and inner plexiform layer were not affected by change in optic disc size. In our study, axial length of each eye was compared with the average RNFL and average GCIPL. The increase in axial length causes thinning of RNFL with a strong negative correlation ($r = –0.532$) and thinning of GCIPL with moderate negative correlation ($r = –0.342$).

A statistically significant correlation was observed between average RNFL and SE ($P < 0.001$). Scatter plot of simple linear regression of average RNFL in relation to SE, Axial length and optic disc area is shown in Fig. 4. For every 1 diopter change in SE, there was 3.667 µm thinning in RNFL layer. For every 1 mm change in axial length, there was –5.3805 µm change in

Table 1: Comparison of RNFL thickness (average and different quadrants) with subgroups based on SE

RNFL thickness (μm)	M1 (*n*=37)	M2 (*n*=39)	M3 (*n*=24)	ANOVA F	*P*
RNFL average	97.68±10.84	85.10±12.32	81.96±5.14	20.86	<0.001
RNFL superior	129.59±12.093	112.28±19.484	105.25±9.719	22.296	<0.001
RNFL nasal	70.70±7.965	65.08±11.396	61.83±5.888	7.586	0.001
RNFL inferior	124.35±19.184	109.41±18.893	105.08±10.673	11.030	<0.001
RNFL temporal	64.59±10.291	53.51±8.956	57.58±8.541	13.426	<0.001

Table 2: Comparison of RNFL thickness (average and different quadrants) with subgroups based on optic disc area

RNFL thickness (μm)	D1 (*n*=59)	D2 (*n*=34)	D3 (*n*=7)	ANOVA F	*P*
RNFL average	86.15±12.36	92.18±12.01	97.57±6.19	4.68	0.011
RNFL superior	113.95±18.74	118.97±16.39	133.14±5.27	4.13	0.019
RNFL nasal	63.36±9.10	70.56±9.56	71.57±4.58	8.07	0.001
RNFL inferior	109.80±18.22	119.15±20.20	123.00±12.21	3.62	0.030
RNFL temporal	57.90±11.03	58.59±10.04	64.43±6.43	1.22	0.301

Table 3: Comparison of GCIPL thickness (average and different sectors) with subgroups based on SE

GCIPL thickness (μm)	M1 (*n*=37)	M2 (*n*=39)	M3 (*n*=24)	ANOVA F	*P*
Average GCIPL	80.81±7.29	74.85±7.78	73.58±10.79	6.977	0.001
GCIPL Superior	81.43±11.81	75.54±7.94	75.13±10.80	4.107	0.019
GCIPL supero-nasal	84.03±6.39	77.15±9.16	75.54±11.67	8.368	0.000
GCIPL infero-nasal	81.19±7.50	76.36±8.22	74.17±11.02	5.377	0.006
GCIPL inferior	77.70±8.59	74.13±8.09	70.58±11.98	4.314	0.016
GCIPL infero-temporal	79.89±8.14	73.64±8.28	74.33±12.04	4.906	0.009
GCIPL supero-temporal	78.51±8.30	72.21±7.95	72.54±10.01	6.012	0.003

Table 4: comparison of GCIPL thickness (average and different sectors) with subgroups based on Optic disc area

GCIPL Thickness (μm)	D1 (*n*=59)	D2 (*n*=34)	D3 (*n*=7)	ANOVA F	*P*
Average GCIPL	75.25±8.89	78.47±8.64	81.00±8.83	2.313	0.104
GCIPL superior	76.47±9.53	79.59±9.07	77.71±21.47	0.943	0.393
GCIPL Supero-Nasal	77.54±9.88	81.12±9.12	85.43±5.28	3.149	0.047
GCIPL infero-nasal	76.56±8.99	79.29±8.71	78.43±11.90	1.002	0.371
GCIPL inferior	73.17±9.71	76.65±9.54	76.71±8.51	1.602	0.207
GCIPL infero-temporal	74.93±9.60	76.97±9.86	82.00±6.68	1.923	0.152
GCIPL supero-temporal	73.27±9.04	76.09±8.33	78.86±11.12	1.909	0.154

RNFL layer. For every 1 mm^2 change in optic disc area, there was 9.4617 μm change in RNFL layer. As seen previously, comparison between average RNFL and optic disc area was statistically significant ($P = 0.011$)

Scatter plot of simple linear regression between average GCIPL and SE, axial length and optic disc area are shown in Fig. 5. A statistically significant correlation was observed between average GCIPL and SE ($P = 0.001$). It is evident that for every 1 diopter change in SE, there is 1.6807 μm change in GCIPL layer. For every 1 mm change in axial length, there is –2.626 μm change in GCIPL layer. As seen before, there was a moderate negative correlation between both the variables. For every 1 mm^2 changes in optic disc area, there is 6.724 μm change in GCIPL layer. However, from the previous comparison between average GCIPL and optic disc area, it was seen that it was not statistically significant ($P = 0.104$).

Discussion

Early detection of glaucoma can be made by assessing RNFL and GCIPL measurements. Sam Seo *et al*.[6] showed that myopia can significantly affect GCIPL and RNFL thickness and the optic disc size has a significant influence on RNFL thickness. Hence, there is a need to look into this clinically significant correlation. Wei-Wei Wang *et al*.[7] showed that RNFL and GCIPL thicknesses become thinner with advancing age. Ageing effect on OCT parameters in our study was minimized by enrolling only young patients aged between 20 and 40 years.

In accordance with previous studies,[6-10] our study also showed that as the SE increased there was thinning of RNFL.

RNFL thickness at 8, 9, 10, and 11 O'clock hours showed an increase in thickness in M3 group compared to M2 group due to dragging of the retina towards temporal horizon. Hence, significant RNFL thinning was seen in all quadrants, except in temporal quadrant.

Similar to study by Savini G *et al*.,[11] our study also showed that RNFL was thicker in large discs as compared to small disc group. Increase in RNFL thickness in nasal, inferior, and superior quadrant was statistically significant ($P < 0.05$). The reason for this could be, smaller the disc one tend to include more area beyond the Peripapillary RNFL in the scanning circle leading to underestimation of RNFL. RNFL thickness in different clock hours was also compared with small(D1), medium(D2) and large (D3) disc groups. At 2,3 and 10 0' clock hours increase in RNFL thickness was seen which was statistically significant ($P < 0.05$). Similar to previous studies by Giacomo Savini *et al*.[12] and Chau-Yin Chen *et al*.,[13] our study also showed a strong negative correlation between axial length and RNFL thickness. This implies that an increase in axial length causes thinning of RNFL.

Studies by Wei-Wei Wang *et al*.[7] and Min Woo Lee *et al*.[14] showed that GCC thickness were significantly thinner in myopia. Similarly, our study also showed GCIPL thinning in moderate and high myopias (M2 and M3) and thinning was seen in all sectors. This could be due to the stretching effect from an elongated eye. In our study, average GCIPL thickness in relation to optic disc size had no correlation ($P = 0.104$) similar to study by Sam Seo *et al*.[6] Thus, change in optic disc size did not affect GCIPL thickness. Studies by Victor T. Koh *et al*.[15] and Jean-Claude Mwanza *et al*.[16] showed significant thinner average GCIPL thickness in association with longer axial length in the magnitude of 1.06% per each millimeter increase in axial length. Our study also showed that increase in axial length causes thinning of GCIPL with moderate correlation.

Simple linear regression analysis in our study revealed average RNFL thickness to be correlated significantly with SE (3.667 μm/diopter), axial length (–5.3805 μm/mm), and optic disc area (9.4617 μm/mm^2). Additionally, simple linear regression analysis revealed average GCIPL thickness to be correlated statistically significantly with SE (1.6807 μm/diopter) and axial length (–2.626 μm/mm). There was, however, no significant correlation between average GCIPL thickness and disc area. Multiple linear regression analysis of RNFL and GCIPL thickness with SE, axial length, and disc area as independent variables revealed that SE and axial length shown to have a significant effect on RNFL and GCIPL thickness profiles. But optic disc area failed to do so.

Conclusion

In our study, the effect of myopia is more pronounced on RNFL thinning than on GCIPL thinning. However, effect of change in disc area was only seen on RNFL thickness but not on GCIPL thickness. Our results, therefore, indicate the importance of careful interpretation of the current OCT maps in cases of eyes with varying myopic degree and optic disc area.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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