The effect of myopia on retinal nerve fibre layer measurement: a comparative study of spectral-domain optical coherence tomography and scanning laser polarimetry

Geng Wang, Kun Liang Qiu, Xie Hui Lu, Li Xia Sun, Xu Jian Liao, Hong Ling Chen, Ming Zhi Zhang

ABSTRACT
Background/aim To evaluate the effect of myopia on retinal nerve fibre layer (RNFL) thickness measurement by using spectral domain optical coherence tomography (Cirrus HD OCT) and scanning laser polarimetry with enhanced corneal compensator (GDx ECC).
Methods One hundred and forty-nine eyes of 149 myopic subjects were recruited and subdivided into three groups according to their refractive errors: high myopia group (spherical equivalent (SE) $> -6$ D); moderate group ($-3 \text{D} \leq \text{SE} > -6$ D); low group ($-0.5 \text{D} \leq \text{SE} > -3$ D). RNFL thickness was measured by Cirrus High Definition (HD) OCT and GDx ECC. Associations between RNFL thickness and axial length/SE were evaluated by using Pearson correlation analysis.
Results Average RNFL thickness measured with Cirrus OCT correlated significantly with axial length ($r = -0.322$, $p < 0.001$) and SE ($r = -0.291$, $p < 0.001$). No significant correlation was detected between RNFL thickness and axial length/SE. Average RNFL thickness measured with GDx ECC correlated with axial length ($r = -0.068$, $p = 0.407$) and SE ($r = 0.109$, $p = 0.187$). There was no significant relationship between RNFL thickness and axial length/SE.
Conclusion Average RNFL thickness measured with Cirrus HD OCT decreases as the degree of myopia increases while no such correlation was detected in GDx ECC. Histological studies are warranted to further our understanding of the relationship between RNFL thickness and myopia.

INTRODUCTION
Since myopia is a worldwide common ocular disorder that can increase the risk of primary open angle glaucoma (POAG) two- to threefold, the diagnosis of POAG in myopic patients is important. Myopic eye is associated with tilted optic disc, increased intraocular pressure (IOP), and visual field defects. All these factors make the clinical diagnosis of POAG in myopic patients challenging. It has been shown that retinal nerve fibre layer (RNFL) thinning may be an early sign of glaucomatous damage. Measurement of RNFL thickness has been emerging as an important diagnostic technology for glaucoma. It is therefore important to establish the relationship between RNFL thickness and myopia.

Both optical coherence tomography (OCT) and scanning laser polarimetry (SLP) have been developed to measure in vivo RNFL thickness objectively. Studies with the instruments based on these two technologies have been performed to evaluate the relationship between myopia and RNFL thickness. Using OCT-1, Hoh et al did not find any significant association between RNFL thickness and axial length/SE, while recent studies based on OCT 3 (StratusOCT; Carl Zeiss Meditec Inc, Dublin, CA, USA; the time domain technology) have reported a negative relationship between RNFL thickness and axial length. However, no such evident correlation between RNFL and myopia was found in a recent study based on SLP with variable corneal compensator (GDx VCC). Thus, the association between RNFL thickness and myopia is controversial.

It has been shown that spectral domain optical coherence tomography (Cirrus High Definition (HD) OCT; Carl Zeiss Meditec, Dublin, California, USA) and SLP with enhanced corneal compensation (GDx ECC), which are the latest commercially available versions of OCT and SLP, respectively, have superior performance over conventional OCT and SLP with variable corneal compensation (GDx VCC). The aim of this study was to evaluate the relationship between myopia and RNFL thickness using Cirrus HD OCT and GDx ECC. To date, no study has used SLP and OCT concurrently to evaluate the relationship between RNFL thickness and myopia. It is unclear whether myopia can lead to the discrepancy of RNFL measurements between SLP and OCT. Simultaneous use of these two technologies will be helpful for further understanding of the relationship between RNFL thickness and myopia.

MATERIALS AND METHODS
Subjects
One hundred and sixty-six Chinese subjects were recruited from June 2009 to October 2009. One eye from each subject was randomly selected. All subjects received complete ophthalmic examinations in the Joint Shantou International Eye Center, which included visual acuity, IOP measured by Goldmann applanation tonometry, axial length measured by IOL Master (Carl Zeiss Meditec Inc, Jena, Germany), refraction and dilated fundus stereo examination. For each subject, RNFL thickness was measured with Cirrus HD OCT and GDx ECC by three experienced technicians. All subjects were subdivided into three groups according to refractive error: high myopia group (SE $> -6$ D); moderate group ($-3 \leq \text{SE} > -6$ D); low group ($-0.5 \leq \text{SE} > -3$ D).

Inclusion and exclusion criteria
All the included eyes had an SE of less than $-0.5$ D and no other concurrent diseases. Subjects with
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best corrected visual acuity of less than 20/40, IOP >21 mmHg, family history of glaucoma, intraocular surgery, myopic macular degeneration, clinical evidence of glaucoma, parapapillary atrophy (PPA) extending the circle of OCT RNFL scan, refractive surgery, age <18 years, neurological diseases or diabetes were excluded.

Visual field testing
All visual field tests were performed with the static automated white-on-white threshold 24-2 SITA standard strategy (Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc, Dublin, CA, USA). A visual field test was considered to be reliable when fixation loss, false positive and false negative were all <20%. 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 horizontal meridian in the pattern deviation plot and classified as outside normal limits in the glaucoma hemi-field test. All the visual field tests of included eyes were within normal limits (147 eyes) or general reduction of sensitivity (two eyes) in the glaucoma hemi-field test (GHT).

Cirrus HD OCT imaging
Cirrus HD OCT (software version 3.0.0.64) uses the technology of spectral-domain optical coherence tomography. The parapapillary RNFL thickness was measured by Cirrus HD OCT using Optic Disc Cube 200×200 protocol. The software of the instrument provided a built-in algorithm that can locate the centre of the optic disc even if it is not well centred in the scan image. The software identified the disc centre by finding a dark spot near the centre of the scan that has a shape and size consistent with a range of optic discs. A calculation circle of 3.46 mm in diameter consisting of 256 A-scans then is positioned automatically around the optic disc. Eye movements were monitored by reading real-time fundus images. Images with misaligned vessels within the scanning circle were excluded and retaken. The signal for the scanned retina was uniform with minimum signal strength of seven. The mean RNFL thickness of 360° and each quadrant was derived from the analysis printout generated by Cirrus HD OCT.

GDx ECC scanning
SLP with GDx ECC (software version 5.5.0; Carl Zeiss Meditec Inc, Dublin, CA, USA) was used to scan and analyse RNFL thickness. Scans were accepted when quality scores assessed by the software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight and the typical scan score (TSS) exported from the GDx software were no less than eight. The images had even illumination. The raw data were exported from the instrument. The parameters of superior, inferior and the temporal superior nasal inferior temporal (TSNIT) average RNFL thickness were collected.

Statistical analysis
The statistical analyses were performed with commercially available software (SPSS ver. 15.0; SPSS Inc, Chicago, IL, USA). Pearson correlation was used to study the correlation between average RNFL thickness and axial length/SE. The average RNFL thickness values were compared among groups using one-way ANOVA. A p value <0.05 was considered statistically significant.

RESULTS

This study involved 166 subjects. Seventeen subjects were excluded for the following reasons: unreliable visual field tests (7), extended PPA (1), unacceptable OCT scans (5), SLP with low scan quality (5) or typical scan score (1). One hundred forty-nine eyes from 149 subjects (64 women and 89 right eyes) met our criteria after exclusion. The mean age, SE and axial length were 23.00 (95% CI 22.52 to 23.69, range 18.02—40.05) years, −5.05 (95% CI −4.70 to −5.40, range −1.00—11.13) D and 25.58 (95% CI 25.41 to 25.76) mm, respectively. SE correlated significantly with axial length (r = −0.762, p<0.001). The characteristics of the three subgroups were presented in table 1. Significant differences were detected in SE (p<0.001) and axial length (p<0.001) among groups. No significant differences were found for age, sex, visual field mean deviation and pattern SD among groups. One hundred and forty-seven subjects had a visual field identified as ‘normal visual field’ by GHT. Two subjects had a visual field identified as ‘general reduction of sensitivity’ by GHT.

Table 1 Characteristics of the high, moderate and low myopia groups

<table>
<thead>
<tr>
<th></th>
<th>Low myopia (n = 30)</th>
<th>Moderate myopia (n = 66)</th>
<th>High myopia (n = 53)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE (D)*</td>
<td>−2.17±0.55</td>
<td>−4.41±0.71</td>
<td>−7.48±1.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Axial length (mm)*</td>
<td>24.50±0.73</td>
<td>25.32±0.70</td>
<td>26.52±0.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>23.00±3.53</td>
<td>22.62±3.61</td>
<td>23.48±5.24</td>
<td>0.547</td>
</tr>
<tr>
<td>MD (dB)*</td>
<td>−1.85±0.94</td>
<td>−2.02±1.00</td>
<td>−2.27±0.95</td>
<td>0.140</td>
</tr>
<tr>
<td>PSD (dB)*</td>
<td>1.43±0.22</td>
<td>1.44±0.23</td>
<td>1.46±0.26</td>
<td>0.780</td>
</tr>
<tr>
<td>Sex (n female/n male)</td>
<td>20/10</td>
<td>33/33</td>
<td>32/21</td>
<td>0.258</td>
</tr>
</tbody>
</table>

Values are mean ± SD. High myopia: (SE = −6 D); moderate myopia: (−3 D ≤ SD > −6 D); low myopia: (−0.5 D ≤ SE > −3 D).

*One-way ANOVA test.

**t** test.

SE, spherical equivalent; MD, mean deviation of visual field; PSD, pattern SD of visual field.
DISCUSSION

In current study, we found a significant correlation between 360° average RNFL thickness and axial length/SE by Cirrus HD OCT. In addition, significant correlations were found between RNFL thickness and axial length/SE in the superior, inferior and temporal quadrants using Cirrus HD OCT. However, we did not find any significant relationship between RNFL thickness (including average and sectorial thickness) and axial length/SE using GDx ECC.

The Cirrus OCT results in current study accord with previous studies based on Stratus OCT but are in contrast to those of the study based on OCT-1. The earlier generations of OCT that are based on the technology of time domain OCT, OCT-1 has lower A-scan resolution than Stratus OCT and Cirrus OCT. It has been reported that Stratus OCT had superior performance in RNFL measurement compared with OCT-1, providing images with fewer artefacts and higher quality. A recent study has shown that Cirrus OCT had lower variability and better reproducibility for RNFL thickness in each clock hour except in the temporal quadrant (8–11 o’clock). It has been shown that elongation of the globe occurs in myopic eyes. The thicker RNFL observed in the temporal quadrant may be due to the redistribution of RNFL. Further studies are needed to clarify the correlation between axial length and peripapillary RNFL thickness in the temporal quadrant. Because of the sectorial variation of RNFL thickness observed in myopic eyes, the diagnosis of glaucoma based on RNFL measurement with OCT should be judged with caution. A normative database built on a myopic cohort is needed for the diagnosis of glaucoma in myopic eyes with OCT.

In the previous studies based on SLP, no correlation was found between RNFL thickness and axial length. According to Kremmer et al., RNFL thickness was related to SE but not axial length. Ozdek et al. also reported the correlation between SE and RNFL thickness. It should be noted that both studies used the early generation of SLP without VCC. It has been shown that measurement of RNFL thickness by SLP with fixed corneal compensator (FCC) was less reliable than GDx VCC. Recently, Vetrugno et al. found no correlation between RNFL thickness and SE in 86 myopic eyes (mean refractive error −3.9±1.5 D, range −2.00−−8.25 D) using GDx VCC. Of note, data on axial length and TSS were not mentioned in the study. It has been demonstrated that atypical retardation patterns (ARPs) are associated with myopia and can cause inaccurate measurement. In the study by Qiu et al., fewer ARPs were observed with GDx ECC than with GDx VCC. However, ARPs can still exist in GDx ECC measurements in highly myopic eyes. To reduce the influence of ARPs, images with TSS <80 were excluded in the current study. The sample size in the current study may be inadequate to reveal a statistically

Table 2 Correlations between RNFL thickness and axial length/SE with cirrus OCT (one-way ANOVA and Pearson analysis results)

<table>
<thead>
<tr>
<th></th>
<th>Superior RNFL (µm)</th>
<th>Nasal RNFL (µm)</th>
<th>Inferior RNFL (µm)</th>
<th>Temporal RNFL (µm)</th>
<th>Average RNFL (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 30)</td>
<td>(n = 66)</td>
<td>(n = 53)</td>
<td>(n = 53)</td>
<td>(n = 149)</td>
</tr>
<tr>
<td>Low myopia</td>
<td>127.70 ± 22.72</td>
<td>67.03 ± 10.60</td>
<td>133.57 ± 12.83</td>
<td>79.80 ± 9.46</td>
<td>102.00 ± 8.78</td>
</tr>
<tr>
<td>Moderate myopia</td>
<td>117.88 ± 15.36</td>
<td>63.00 ± 11.64</td>
<td>124.00 ± 15.86</td>
<td>82.32 ± 14.08</td>
<td>96.79 ± 8.11</td>
</tr>
<tr>
<td>High myopia</td>
<td>113.57 ± 16.30</td>
<td>64.26 ± 10.47</td>
<td>117.25 ± 17.29</td>
<td>85.83 ± 17.01</td>
<td>95.17 ± 8.93</td>
</tr>
<tr>
<td>p Value</td>
<td>0.002</td>
<td>0.255</td>
<td>&lt;0.001</td>
<td>0.166</td>
<td>0.002</td>
</tr>
<tr>
<td>Correlation with axial length (r (p value)) (n = 149)</td>
<td>0.32 (&lt;0.001)</td>
<td>0.10 (0.210)</td>
<td>0.37 (&lt;0.001)</td>
<td>0.29 (&lt;0.001)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD.

OCT, optical coherence tomography; RNFL, retinal nerve fibre layer; SE, spherical equivalent.
significant correlation between average RNFL thickness and axial length/SE with GDx ECC. However, the coefficients of the correlations were relatively small. The possible but weak correlation between RNFL thickness and axial length/SE under SLP may not have much clinical value.

We consider the discrepancy of the results to be due to the different technologies employed by the two instruments. OCT measures the difference in time of the reflected light projected by the instrument. The difference in time is then transferred into difference in distance to form the transverse image of retina. RNFL is then identified and measured by the software combined with the instrument. A fixed scanning circle with diameter of 3.46 mm is used to measure the parapapillary RNFL thickness. It was reported that displacement of the scanning circle in Stratus OCT, which utilised manual placement of scanning circle, resulted in decreased RNFL measurement.18 Although Cirrus HD OCT can automatically locate the scanning circle, eccentric placement cannot be totally eliminated. One subject in the current study was excluded for an obviously eccentric scanning circle. The margin of optic disc is difficult to identify with PPA, which is more common in high myopic eyes. This may have resulted in displacement of the scanning circle and thinner RNFL measurement in high myopic eyes. Another important issue in OCT measurement is the magnification effect in myopic eyes. According to the formulae $t = p x s$ and $q = 0.01306(x - 1.82)$, where $t$ stands for the actual retinal parameter, $p$ for the magnification factor related to the camera of OCT, $s$ for the reported transverse measurement in OCT, $q$ for the inherent magnification factor of the eye and $x$ for the axial length, the actual diameter of the circle may be larger than 3.46 mm in eyes with longer axial length.19 But the myopic eye may also have a larger optic disc.20 Although RNFL thickness decreases as the distance from optic disc increases, the measurements may not necessarily be thinner in highly myopic eyes. In contrast, SLP
calculated birefringence was 0.27 degrees/m by SLP and histological thickness in primates. The birefringence has been determined by comparing RNFL retardation in SLP. Histological studies are needed to establish the relationship between RNFL and SE/axial length, which are more common in high myopia, but it is unclear whether this birefringent constant will fit myopic eyes. Studies have shown that the birefringent property of RNFL varied at different locations surrounding the optic disc. Previous studies have shown that the high scleral reflectivity may be one cause of ARPs, which result in higher apparent RNFL values. Thus, we excluded images with TSS <8 to reduce the influence of ARPs, which are common in the myopic eye. The influence of ARPs cannot be eliminated. Since ARPs are more common in high myopia, it was still a possible reason for the negative correlation between RNFL and SE/axial length in SLP. Histological studies are needed to establish the relationship between myopia and RNFL thickness.

There are several limitations of the present study. One potential limitation is the relatively narrow age range (18.02–40.05 years) of our study cohort. Thus, our results may not apply to elder myopic subjects. It is not clear whether age will influence RNFL thickness. In the present study, the age range was narrow but matched in each group. This may reduce the influence of age on RNFL measurements. We did not exclude subjects with general reduced sensitivity of visual field, as we were concerned that the general reduction of sensitivity might be caused by myopia but not glaucoma. It has been demonstrated that myopia is associated with visual field defects. Myopic eyes with borderline visual fields or even outside normal limits may be caused by myopia instead of glaucoma. Our criteria may exclude the otherwise healthy myopic eyes, and this may bias our results. Only two subjects with visual fields of ‘general reduction of sensitivity’ in GHT were included in this study. The results did not change when we analysed the data excluding these two subjects.

Although sectorial variation of RNFL thickness was observed in myopic eyes, average RNFL thickness measured with Cirrus HD OCT decreased as the degree of myopia increased. However, no significant correlation was detected between RNFL thickness measured with GDx ECC and axial length/SE. Histological studies are warranted to further our understanding of the relationship between RNFL thickness and myopia.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the Joint Shantou International Eye Center of Shantou University and the Chinese University of Hong Kong, Shantou. The study was designed following the ethical standards of the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

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