·Clinical Research·

Peripapillary retinal nerve fiber layer thickness distribution in Chinese with myopia measured by 3D-optical coherence tomography

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Abstract

• AIM: To assess the effect of myopia on the thickness of retinal nerve fiber layer (RNFL) measured by 3D optical coherence tomography (3D -OCT) in a group of nonglaucomatous Chinese subjects.

• METHODS: Two hundred and fifty-eight eyes of 258 healthy Chinese myopic individuals were recruited and four groups were classified according to their spherical equivalent (SE): low myopia (*n*=42, -0.50<SE<-3.0D), moderate myopia (*n*=120, -3.0D≤SE<-6.0D), high myopia (*n*=58, -6.0D≤SE<-8.0D) and extreme high myopia (*n*=38, SE ≥-8.0D). The RNFL thickness profile including superior, nasal, inferior and temporal quadrant and each of the 12 clock-hour thicknesses were measured by 3D-OCT. The RNFL thicknesses among four sample groups were performed by one-way analysis of variance (one-way ANOVA) and least significant difference test (LSD test). Correlations between RNFL thickness and axial length/spherical equivalent were performed by linear regression analysis.

• RESULTS: The overall RNFL parameters shown significant differences between groups excluding 7, 9, 10, 11 o´clock hour thickness. The RNFL thickness of superior, nasal, inferior, average and 1, 2, 3, 4, 5, 6, 12 o´clock sectors were decreased with the increasing axial length and higher degree of myopia. In contrast, as axial length and the degree of myopia increased, the temporal and 8, 9 o´clock sectors thicknesses were increased. A considerable proportion of myopic eyes were classified as outside the normal limits. Six o´clock was the most notable of the total, which 43.4% were outside the normal limits.

• CONCLUSION: On the measurement of RNFL, the characteristics of RNFL with the change of the degree of myopia were observed. As the degree of myopia increases, the RNFL thickness measured by 3D -OCT including the average and superior, nasal, inferior sectors decreases. And due to the change of RNFL thickness, it should be considered when using OCT to access for the damage of glaucoma especially people with myopia.

• KEYWORDS: optical coherence tomography; myopia; retinal nerve fiber layer

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INTRODUCTION

At present, there is around 400 million Chinese (33% of the population, 1.5 times the world average) suffering from myopia. Its prevalence has increased markedly in recent years [1,2]. It is well known that myopia is a risk factor of glaucoma and myopic fundus changes may complicate the diagnosis and treatment. Assessment of the peripapillary retinal nerve fiber layer (RNFL) thickness has been an important approach for detecting structural damage in patients with glaucoma [3,4]. Therefore, it is urgent to establish the correlation between RNFL thickness and myopia, not only for understanding the characteristics of RNFL with the change of the degree of myopia, but also for using these characteristics to be identified with the early stage of glaucoma.

Table 1 Characteristics of the study population

Parameters	Low myopia	Moderate myopia	High myopia	Extreme myopia	P
n	42	120	58	38	
Age (a)	26.52±5.68	28.37±6.34	27.88±5.77	27.89±6.94	[1]0.434
Sex (M/F)	22/20	64/56	22/36	16/22	[2]0.206
Axial length (mm)	23.44±0.89	24.12±0.89	24.57±0.90	25.25±0.91	[1]<0.001
Spherical equivalent (D)	-1.99±0.52	-4.50±0.82	-6.75±0.58	-9.12±1.34	[3]<0.001

[1]P value and [2]P value among groups were performed by one-way ANOVA test and χ^2 tests, respectively. [3]P value was calculated between low, moderate and high myopia groups due to the heterogeneity of variance.

Optical coherence tomography (OCT) is an emerging ophthalmic examination which has been applied to measure the RNFL thickness. Compared with conventional time-domain OCT (TD-OCT), TOPCON 3D-OCT1000 which is a Spectral-domain OCT (SD-OCT) provided a higher resolution, dense grid mapping of the retinal, three-dimensional reconstruction of the scanned area and normative database of age-matched yellow race controls[5].

This large sample analysis was to investigate the variation of myopic patients' RNFL thickness as well as changes in some factors of influence. It is designed to improve the sensitivity and specificity of OCT on detecting RNFL structure and diagnosing the early stage of glaucoma.

SUBJECTS AND METHODS

Subjects Two hundred and fifty-eight healthy Chinese myopic individuals ranging in age from 18 to 49 years (mean±SD, 27.89±6.21 years) were recruited in this study from August 2010 to October 2011. All of the subjects for this study underwent a full ophthalmic examination including visual acuity, slit lamp examination (Topcon SL-1E Slit Lamp; Topcon Corp., Japan), refraction (Topcon RM-8800; Topcon Corp., Tokyo, Japan), intraocular pressure (Topcon NCT CT-80: Topcon Corp., Japan), axial length by contact ultrasound A-scan biometry (Cine Scan A/B scan; Quantel Medical Inc., France) and fundus photography (Canon CR6-45NM Fundus Camera; Canon Inc., Tokyo, Japan). The axial length (AL) of eye ranged from 21.52 to 27.18mm (mean±SD, 24.28±1.04). Then it was confirmed that all included eyes had no known ocular disease or diabetes, hypertension, craniocerebral injury and all that the intraocular pressure was lower than 18mmHg.

The subjects should have a spherical equivalent (SE) refractive error less than -0.50D in both eyes. SE is defined as sphere plus half-negative cylinder [sphere+(cylinder/2)]. The eyes were classified into low myopia (n=42, -0.5D<SE <-3.0D), moderate myopia (n=120, -3.0D≤SE<-6.0D), high myopia (n=58, -6.0D≤SE<-8.0D) and extreme high myopia (n=38, SE≥-8.0D; Table 1).

Methods

Optical coherence tomography scanning The TOPCON 3D-OCT1000 system (software version 3.12) was used to measure the peripapillary RNFL thickness, which can identify the disc centre automatically, acquire 27 000 A-scans per second and has a 5μm depth resolution in tissue. It provided a normative database of age-matched controls of yellow race. This tomography has the function of inputting the eye's axial length and the degree of myopia. The default axial length and refraction in every OCT scan are set to 24.39mm and 0D. In order to obtain the exact printout values, the two parameters should be input to the OCT before the examination.

The operator centered the circular scan on the optic nerve head (ONH) while the eye was fixated. Average measurements of three sequential circular scans of diameter 3.4mm centered on the optic disc were recorded. Parameters including superior, nasal inferior and temporal quadrant thicknesses and thicknesses for each of the 12 o'clock-hour positions were generated automatically in the analysis report. The superior clock hour was 12 o'clock. The others were plotted in a clockwise direction for a right eye and counterclockwise for a left eye.

All individuals should be scanned for several times in order to obtain three images met the conditions as follows: 1) image quality of at least 60; 2) the fundus images can be used to verify the scan location; 3) the optic disc located in the centre of scan circle. The individuals who have a peripapillary atrophy exceeding the scan circle were excluded. If one's optic disc also deviated from the centre of scan circle after several scans, this person would be excluded, as well. When we did comparison between the normative populations data with ours, scans with the highest quality was used for analysis.

Statistical Analysis Due to the measured parameters of both eyes in the subjects had a high degree of correlation and the result was no statistically different (P>0.05), we selected the one eye of each subject data randomly and used for statistical analysis.

Statistical analysis were performed on computer using the SPSS software (version 13.0; SPSS Science, Chicago, IL, USA); and a P<0.05 was considered statistically significant.

Table 2 RNFL thickness in different groups as measured by 3D-OCT

RNFL thickness (μm)	Low myopia	Moderate myopia	High myopia	Extreme high myopia	[1]P
Superior	140.52±18.02	135.68±14.10	128.02±13.62	125.18±15.49	<0.001
Nasal	105.69±14.94	90.33±14.49	87.59±14.11	87.59±14.11	<0.001
Inferior	155.81±14.93	150.80±16.53	148.00±14.77	144.68±19.75	0.017
Temporal	90.86±13.25	94.24±14.44	98.03±16.71	99.08±15.26	0.035
Average	123.22±8.11	117.76±9.09	115.41±7.49	114.42±11.12	<0.001
1 o'clock	132.02±21.64	126.78±18.06	116.34±18.22	112.29±16.85	<0.001
2 o'clock	120.29±17.65	104.58±18.80	100.47±18.94	101.58±20.28	<0.001
3 o'clock	93.38±13.39	82.20±15.12	80.10±13.69	82.11±14.43	<0.001
4 o'clock	103.45±21.26	84.68±16.08	82.33±17.82	82.34±16.82	<0.001
5 o'clock	139.79±26.80	129.63±24.21	121.76±24.47	116.97±23.66	<0.001
6 o'clock	175.31±25.28	166.83±28.76	158.50±25.92	155.50±30.65	0.004
7 o'clock	152.57±22.36	156.04±26.42	163.83±28.70	162.11±27.19	0.107
8 o'clock	87.74±15.11	90.73±15.74	95.59±18.59	96.87±18.34	0.028
9 o'clock	77.90±10.85	81.48±12.91	83.79±15.25	84.21±14.01	0.106
10 o'clock	106.98±17.30	110.50±20.27	114.90±21.97	116.24±20.22	0.111
11 o'clock	153.07±23.56	149.79±20.39	147.50±16.41	144.89±21.80	0.296
12 o'clock	136.67±26.70	130.62±21.94	119.90±20.31	118.74±24.07	<0.001

[1]*P* values were performed by one-way ANOVA tests.

Linear regression method was used to determine the correlation between RNFL thickness and continuous variables (axial length and spherical equivalent), and expressed as the Pearson coefficient of correlation (r). The gender between low myopia, moderate myopia, high myopia and extreme high myopia groups were compared by using the independent t-test. The RNFL thickness of four sample groups was performed by one-way analysis of variance (one-way ANOVA) and post hoc analysis, least significant difference test.

RESULTS

This study comprised 258 eyes of 258 Chinese myopic individuals (124 males, 134 females). The mean age, AL, and SE were 27.89±6.21 years (range, 18-49 year), 24.28±1.04mm (range, 21.52-27.18mm), -5.28±2.33D (range, -0.63 to -13.75 years), respectively. A significantly negative correlation between AL and SE was shown in Figure 1 (r=-0.66, P<0.001). The age and gender both had no significant difference between groups (P>0.05). However, there were statistical significances for AL and SE between groups (P<0.001, Table 1).

After the comparisons of the RNFL thickness, we found significant differences between groups excluding 7, 9, 10, 11 o'clock hour thickness (Table 2). The further test showed that the RNFL thickness of superior, nasal, inferior, average and 1, 2, 3, 4, 5, 6, 11, 12 o'clock sectors were decreased with the increasing AL and higher degree of myopia (Figures 2, 3). In contrast, as AL and the degree of myopia increased, the temporal and 8, 9 o'clock sectors thicknesses were increased. There was no statistically significant in 7, 10 o'clock sectors. Table 3 shows the comparisons of RNFL thickness between groups using least significant difference test. The low myopia group showed significantly thicker RNFL thickness than high and extreme high myopia group. However, there is no significant difference between high and extreme high myopia group. The correlations between RNFL thickness and AL/SE with 3D-OCT are shown in Table 4.

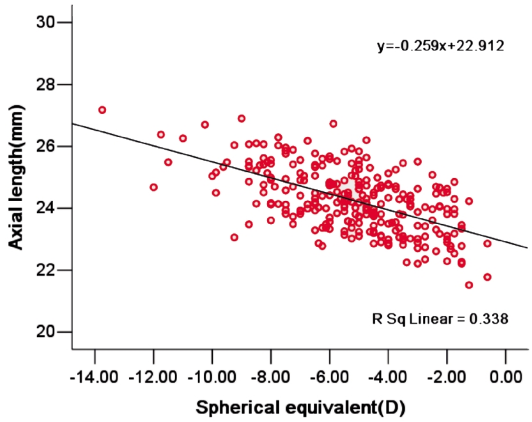

Figure 1 Scatter plots of the axial length and the spherical equivalent.

Figure 4 presents the proportion of eyes falling outside the normative range based on the database of OCT. The 6 o'clock was the location which had the largest number of people falling outside the normal limits. Of the myopic eyes, 43.4% was identified as outside the normative range at 6 o'clock.

DISCUSSION

In contrast to previous studies using older-generation OCT, we evaluated peripapillary RNFL thickness in this study basing on TOPCON 3D-OCT. We found that RNFL thickness decreased as the increasing degree of myopia and axial length except the temporal sector. On comparing the

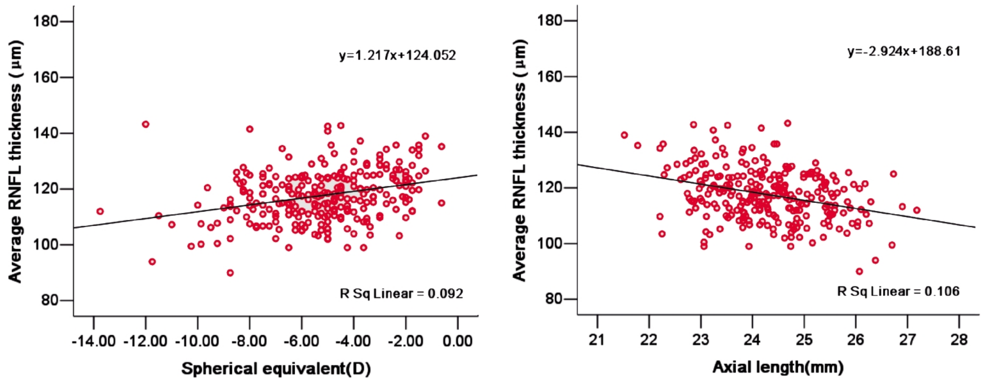

Figure 2 Scatter plots of the average RNFL thickness against the spherical equivalent and the axial length.

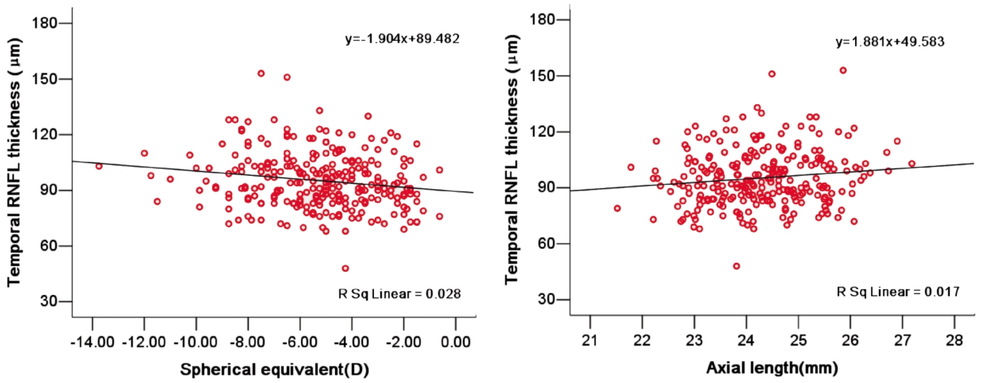

Figure 3 Scatter plots of the temporal RNFL thickness against the spherical equivalent and the axial length.

Table 3 Comparison of RNFL thickness in different groups by pos hoc analysis

	Low-moderate myopia	Moderate-high myopia	High-extreme high myopia	Low-high myopia	Low-extreme high myopia	Moderate-extreme high myopia
Superior	0.071	0.001	0.363	<0.001	<0.001	<0.001
Nasal	<0.001	0.239	0.705	<0.001	<0.001	0.557
Inferior	0.090	0.287	0.334	0.020	0.003	0.047
Temporal	0.207	0.113	0.738	0.018	0.015	0.083
Average	0.001	0.101	0.597	<0.001	<0.001	0.046
1 o'clock	0.116	0.001	0.296	<0.001	<0.001	<0.001
2 o'clock	<0.001	0.175	0.778	<0.001	<0.001	0.395
3 o'clock	<0.001	0.365	0.507	<0.001	0.001	0.972
4 o'clock	<0.001	0.403	0.997	<0.001	<0.001	0.475
5 o'clock	0.022	0.047	0.353	<0.001	<0.001	0.006
6 o'clock	0.092	0.063	0.607	0.003	0.002	0.030
8 o'clock	0.319	0.071	0.714	0.021	0.015	0.050
12 o'clock	0.139	0.004	0.807	<0.001	0.001	0.005

P values between groups were all performed by least significant difference test.

RNFL in different sectors and clock hours between four groups, positive results were observed as well.

As far as we know, the globe is elongated in myopic eyes. It results in thinning of the retina as it is stretched. And the RNFL thickness is thinner as well. However, most studies including ours were all demonstrated that the temporal RNFL thickness was increased with the increasing axial length and the degree of myopia. The only discrepancy between us was that the significant point was 8, 9 o'clock in our research compared with others' 8-10 o'clock[6] and 8-11 o'clock[7]. Most researchers supported the theory of a redistribution of RNFL as the axial length increases in length [6,7]. Kim *et al*[6] speculated that the retinal was dragged toward the temporal horizon as the axial length increases. We all knew that the papillomacular bundles exist in the temporal quadrant. The fibers of macular area walked upper and lower of the horizontal suture towards the optic disc. Whether it would lead to the temporal RNFL different from other quadrants, it still needed to be proved.

The default axial length in TOPCON 3D-OCT is 24.39mm, and a diameter of 3.4mm scanning circle centered on the optic disc during the scanning. The interesting issue in OCT measurement is the magnification effect in myopic eyes. Leung *et al*[7] indicated that it has been recognized that the

Table 4 Correlations between RNFL thickness and AL/SE with 3D-OCT

	Correlation with AL		Correlation with SE	
	r	*P*	*r*	*P*
Superior	-0.20	0.001	0.35	<0.001
Nasal	-0.30	<0.001	0.30	<0.001
Inferior	-0.37	<0.001	0.22	<0.001
Temporal	0.13	0.019	-0.17	0.003
Average	-0.33	<0.001	0.30	<0.001
1 o'clock	-0.16	0.004	0.36	<0.001
2 o'clock	-0.26	<0.001	0.27	<0.001
3 o'clock	-0.21	<0.001	0.21	0.001
4 o'clock	-0.33	<0.001	0.31	<0.001
5 o'clock	-0.39	<0.001	0.30	<0.001
6 o'clock	-0.33	<0.001	0.24	<0.001
7 o'clock	0.03	0.335	-0.13	0.156
8 o'clock	0.18	0.002	-0.17	0.002
9 o'clock	0.12	0.029	-0.15	0.009
10 o'clock	0.07	0.146	-0.13	0.111
11 o'clock	-0.17	0.004	0.15	0.007
12 o'clock	-0.12	0.032	0.27	<0.001

Correlations between RNFL and AL/SE were calculated by linear regression.

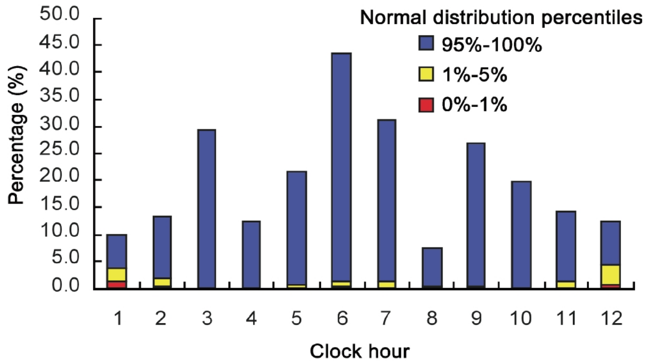

Figure 4 Bar chart of the percentage of eyes falling outside the normal limits classified as three parts.

existence of magnification effect could maximize the actual scanning radius (1.7mm), although one can input the individual's axial length and SE in OCT [8,9]. Varma *et al* [10] dissected 10 dead bodies and found that the edge of optic disc was the thickest place and RNFL thickness of the four sectors decreased with the increasing distances from the optic disc. Therefore, we speculated that would result in the underestimation of RNFL thickness on account of the RNFL thickness decreases at increasing distances from the optic disc. However, some researchers proposed that as the existence of association between optic disc size and SE, the RNFL is not necessary to be measured farther from the disc margin[11,12]. Jonas[11] reported that the optic disc size depends on the refractive error with an increase in highly myopia eyes. In other words, the myopic eye had a larger optic disc. Due to the correlation between optic disc and refractive error, we considered that the magnification effect caused by the increasing axial length can be compensated.

It is not clear whether age can affect RNFL thickness. Budenz *et al* [13] examined normal participants ranging in age between 18 and 85 years, and found that RNFL thickness varies significantly with age, ethnicity. However, a research including 91 myopic subjects from 4 to 17 years concluded that age was not correlated with RNFL thickness as measured by Stratus OCT after adjustment for refraction. In our research, the age range was from 18 to 49 years [14]. We analyzed and found no significant difference between age and the thickness of RNFL after SE adjustment. Nevertheless, due to the narrow range of age, we could not definite about the correlation.

TOPCON 3D-OCT involved a normative database of Asian population and provided information on the normal limits of RNFL thickness. Based on the normative database, we can identify the ocular disease involving RNFL even the retinal thickness. Leung *et al* [5] have shown that a large percentage of Chinese myopic eyes were classified outside normal limits on the nasal sectors (from 12 to 6 o'clock). In this study, we found a considerable proportion of subjects' RNFL thickness located outside the normal limits, as well. The 6 o'clock was the most notable of the total. Therefore, further research on the RNFL measurements in myopic eyes should be done. And it is necessary to establish a database involved healthy subjects with myopia.

In patients with myopia, the ratio of normal-tension glaucoma and suspected glaucoma was significantly higher than the rest, while in patients with open-angle glaucoma, myopia accounted for 46.9% [15]. Mitchell *et al* [16] found a strong correlation between open-angle glaucoma and myopia, with an odds ratio of 2.3 in eyes with low myopia and 3.3 in eyes with moderate-to-high myopia. Therefore, it is necessary to assess the myopia patients with RNFL thinning in order to identify whether it is caused by myopia or glaucoma, and reduce the ratio of misdiagnosis of the early glaucoma.

A possible source of bias in present study was that highly myopic eyes usually show a characteristic appearance of the peripapillary atrophy. Considering of this reason, we had excluded 11 individuals whose peripapillary atrophy exceeded the scan circle. However, we could not speculate whether the RNFL thickness of some individuals with the peripapillary atrophy inside the scan circle was influenced. Therefore, a further research is necessary in this regard.

In summary, the study analyzed the relationship between SE/AL and RNFL parameters measured with TOPCON 3D-OCT, and found individuals with highly myopia had thinner RNFLs, except for the temporal quadrant. According to this study, we believed that 3D-OCT not only can be used for tracking the course of myopia, but also for assessing the clinical suspected glaucoma with myopia accurately.

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