

Retinal Nerve Fiber Layer Thickness in a Population of 12-Year-Old Children in Central China Measured by iVue-100 Spectral-Domain Optical Coherence Tomography: The Anyang Childhood Eye Study

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PURPOSE. To study the distribution of peripapillary retinal nerve fiber layer (RNFL) thickness in a population of 12-year-old children in central China using iVue-100 spectral-domain optical coherence tomography (SD-OCT).

METHODS. Twelve-year-old students ($n = 2105$) from four randomly selected middle schools in Anyang, China, participated in the study. Each child underwent ocular examinations, including optical biometry, cycloplegic autorefractometry, and SD-OCT (iVue-100). Glaucoma optic nerve head scan was performed to measure RNFL thickness. Only the children with a signal strength index higher than 45 were included in the analyses. Multivariate analyses were performed to examine the association of RNFL with demographic variables (e.g., sex, age, and body mass index [BMI]) and ocular variables (e.g., axial length and refractive error).

RESULTS. Optical coherence tomography scans of adequate quality were available for 1955 children (92.9%). The mean (SD) RNFL thickness was 103.08 (9.01) μm , with the mean (SD) thickest RNFL in the inferior quadrant (129.34 [14.90] μm), followed by the superior (126.19 [15.24] μm), temporal (82.98 [10.57] μm), and nasal (73.82 [13.89] μm) quadrants. The RNFL was thicker with shorter axial length ($\beta = -1.53$, $P < 0.0001$) and with higher hyperopia ($\beta = 0.90$, $P < 0.0001$). Girls had slightly thicker average RNFL thickness than boys ($P < 0.0001$). The RNFL thickness had no significant correlation with age or BMI.

CONCLUSIONS. This study establishes normative peripapillary RNFL values of 12-year-old Chinese children as measured by iVue-100 SD-OCT. The RNFL thickness decreased significantly with increasing axial length and higher myopia.

Keywords: retinal nerve fiber layer thickness, iVue-100, Chinese children, spectral-domain optical coherence tomography

Evaluation of retinal nerve fiber layer (RNFL) thickness is crucial in the diagnosis and follow-up of glaucoma severity and progression.^{1,2} Quantitative assessment of RNFL from traditional photography is often difficult and subjective,³ especially for children, which makes it a challenge to diagnose and manage childhood glaucoma. Optical coherence tomography (OCT), first described by Huang et al.,⁴ is a high-resolution cross-sectional imaging technique that provides RNFL thickness

in vivo measurements. It gives a depth image based on the reflections of different retina layers (B-scan) and uses an algorithm to determine and measure RNFL thickness. The OCT scan is quick, noncontact, and noninvasive, rendering it ideally suitable for children.

Previous studies⁵⁻¹⁰ have investigated RNFL thickness in children, but there has been no population-based study of Chinese children. The recently developed spectral-domain OCT

TABLE 1. Characteristics of Children With Versus Without OCT Scans

Characteristic	Children With OCT Performed, <i>n</i> = 1955	Children Without OCT Performed, <i>n</i> = 150	<i>P</i> Value
Sex, <i>n</i> (%)			
Female	979 (50.1)	76 (50.7)	0.89
Male	976 (49.9)	74 (49.3)	
Age, <i>y</i> , <i>n</i> (%) [*]			
<12	36 (1.8)	2 (1.3)	0.66
12-13	1870 (95.7)	145 (96.7)	
>13	45 (2.3)	3 (2.0)	
Spherical equivalent, mean (SD), D	-1.38 (1.95)	-3.30 (3.06)	<0.0001
Axial length, mean (SD), mm	24.07 (1.03)	24.89 (1.29)	<0.0001
Height, mean (SD), cm	154.92 (7.24)	155.98 (6.97)	0.08
Weight, mean (SD), kg	47.61 (10.71)	49.86 (11.74)	0.03
BMI, mean (SD), kg/m ²	19.71 (3.66)	20.35 (3.91)	0.06

* The data from four students were unavailable.

(SD-OCT) technology¹¹⁻¹⁴ with higher resolution and easier clinical application has improved the diagnostic accuracy in detecting early glaucoma. Its diagnosing capability and reproducibility have been proved in adults.^{14,15} In reviewing the contemporary literature, it was found that few researchers have applied this new technology in children.

In China, glaucoma is the third most avoidable cause of severe visual impairment and blindness in children.¹⁶ In our previous study,¹⁷ it was found that approximately 1% of rural adults 40 years or older have POAG, which is associated with increasing age, greater axial length, and higher myopia. The prevalence of POAG in China is likely to increase in the coming decades because of the rapid aging and a myopic shift of the Chinese population.^{17,18} Therefore, it is helpful to detect glaucoma early in patients and to monitor the changes in peripapillary RNFL thickness by establishing a database from large samples of children. The present study was a cross section of a cohort study that aimed to establish a database of peripapillary RNFL thickness in 12-year-old children in central China measured by iVue-100 (version 2.5.0.100; Optovue, Inc., Fremont, CA) SD-OCT and to evaluate the variation in RNFL thickness by demographic and ocular variables.

METHODS

Study Design and Population

The Anyang Childhood Eye Study (ACES) was a school-based cohort study designed to longitudinally observe the development of myopia and other ocular diseases among grade 1 and grade 7 students in urban areas of Anyang, Henan Province, central China.¹⁹ The study adhered to the Declaration of Helsinki and was approved by the ethics committee of Beijing Tongren Hospital, Capital Medical University, Beijing, China. Each student was asked for verbal assent, and informed written consent was obtained from at least one parent.

The ACES population consisted of two parts, grade 1 students in primary schools and grade 7 students in junior high schools. In total, there were 21 primary schools and 11 junior high schools in the Anyang urban area. The researchers applied stratified cluster sampling and randomly selected 11 primary schools and 4 junior high schools from which to draw samples for this study. The baseline examinations of the grade 7 students were performed during the first year of the study from October 2011 to December 2011. Follow-up examinations were conducted annually during the subsequent 2 years. The present study reports the baseline data collected from grade 7 students.

Ocular Examinations

All students were organized and led by their teachers to undergo comprehensive ocular examinations at the health examination station in Anyang Eye Hospital. The examinations were performed by ophthalmologists (B-DZ, S-ML, HL, YW, ZY, JF, and NW) and ophthalmological students (S-YL and M-TK), all of whom received formal training according to a standard operating procedure (SOP). The SOP was written for staff training before data collection. All examinations were required to be performed according to the SOP, which was supervised by an epidemiologist (S-YZ).¹⁹

TABLE 2. Distribution of RNFL Thickness Parameters in Right Eyes Among 1955 Students

RNFL Thickness Parameter, μ m	Mean (SD)	95% Confidence Interval	
		Lower Bound	Upper Bound
Average RNFL	103.08 (9.01)	102.68	103.48
Temporal	82.98 (10.57)	82.51	83.45
Superior	126.19 (15.24)	125.51	126.86
Nasal	73.82 (13.89)	73.20	74.44
Inferior	129.34 (14.90)	128.68	130.00
16 Sections [*]			
TU1	73.93 (10.30)	73.47	74.39
TU2	109.60 (19.30)	108.75	110.46
ST2	147.31 (21.77)	146.34	148.28
ST1	139.12 (23.48)	138.07	140.16
SN1	112.76 (20.34)	111.86	113.67
SN2	105.54 (18.20)	104.73	106.35
NU2	87.97 (17.23)	87.20	88.73
NU1	70.02 (15.54)	69.33	70.71
NL1	63.18 (14.18)	62.55	63.81
NL2	74.12 (15.94)	73.41	74.82
IN2	99.30 (17.93)	98.51	100.10
IN1	122.53 (23.20)	121.50	123.56
IT1	152.25 (21.86)	151.28	153.22
IT2	143.26 (23.11)	142.24	144.29
TL2	86.70 (16.42)	85.98	87.43
TL1	61.67 (7.70)	61.33	62.01

S, superior; N, nasal; U, upper; L, lower; I, inferior; T, temporal.

* Midpoints of 30° sections.

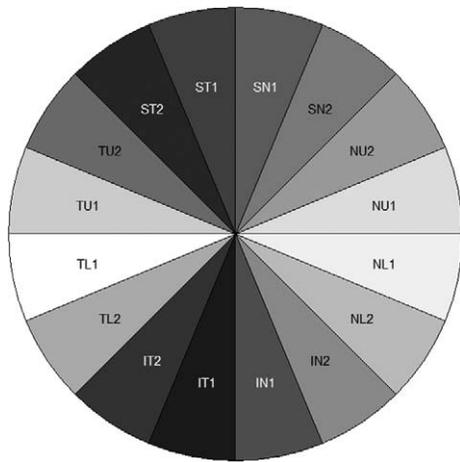


FIGURE 1. Pie graph showing RNFL mean thickness distribution of 16 sections in right eyes. The grayscale indicates RNFL thickness.

Height and weight were measured using an automatic and professional integrated set (UAL6X, UOSIM Co., Ltd, Dalian, China). Axial length was measured using an optical biometer (IOL Master; Carl Zeiss Meditec, Inc., Jena, Germany). The average of five repeated measurements was used for analysis. Cycloplegia was performed after the optical biometer measurements. Each student was first administered 1 drop topical anesthetic agent (Alcaine; Alcon, Fort Worth, TX) to alleviate discomfort, followed by 2 drops 1% cyclopentolate (Alcon) and 1 drop tropicamide (Mydrin P; Santen Pharmaceutical Co., Ltd., Osaka, Japan) at a 5-minute interval. Autorefraction (HRK-7000A; Huvitz Co., Ltd., Gyeonggi-do, Korea) was performed 30 minutes after administration of the last drop. The average of three measurements automatically obtained by the instrument was used for analyses. Hyperopia, emetropia, low myopia, moderate myopia, and high myopia were defined as spherical equivalents of at least +2.00 diopter (D), -0.5 D to less than +2.00 D, -0.50 D or less, -3.00 D or less, and -6.00 D or less in right eyes, respectively.

Peripapillary RNFL parameters in right eyes were measured by iVue-100 (Optovue, Inc.), a new-generation SD-OCT instrument that can be handheld for measurement. In this study, the OCT device was fixed on a table. Each student sat in front of the table to undergo OCT scans. The device uses a scanning laser diode to emit a scan beam with a mean (SD) wavelength of 840 (10) nm to provide images of ocular microstructures. The scan speed is 26,000 A-scans per second, 65 times faster than the Stratus OCT system (Carl Zeiss Meditec, Inc.). The axial length resolution is 5 μm, which is approximately twice as high as time-domain OCT.¹³

The optic nerve head (ONH) iVue-100 (Optovue, Inc.) protocol was used to obtain peripapillary RNFL imaging and parameters. It consists of 12 radial scans 3.4 mm in length (459 A-scans each) and 13 concentric ring scans ranging from 1.3 to 4.9 mm (429-969 A-scans each), all centered on the optic disc. The areas between the A-scans are interpolated, and various parameters are generated to describe the RNFL. All RNFL values were sampled from a fixed 3.45-mm diameter centered on the optic disc. The total scan time was 0.37 seconds. The outputs from the measurement were (1) average RNFL thickness; (2) temporal, superior, nasal, and inferior average RNFL thickness; and (3) 16 sections of the measuring circle around the ONH (each section was 22.5°).

This device uses a algorithmic type of image structure to obtain images for various layers. Image quality is described by

the signal strength index (SSI), which is based on the intensity of the reflected light. The SSI is displayed after each scan and ranged from near 0 (no signal) to approximately 90 (very strong signal). The greater the intensity (brightness) is, the higher the SSI is. Low signal strength can result in poor image resolution, lack of retinal detail, and an increase in segmentation errors (because there is little image structure for the algorithms to use). When the SSI is below the cutoff value, the image was labeled as poor, and the scan was retaken for improved signal strength. In this study, only the scans with an SSI higher than 45 (as suggested by the manufacturer) and labeled as good were used for analysis.

Statistical Analysis

Data in right eyes were included in the analyses using Statistical Analysis System software (SAS 9.2; SAS Institute Inc., Cary, NC). Multivariate regression analyses were used to assess the effect of age, body mass index (BMI), axial length, and refractive error on RNFL thickness. Analyses of covariance were used to evaluate sex differences, with adjustment for multiple variables.

RESULTS

Demographics

Of 2363 total students, 2267 (95.9%) consented to participate in the study. A total of 2105 students underwent iVue-100 (Optovue, Inc.) glaucoma ONH scan, and 150 children had scans with a low SSI, leaving data available for 1955 students (92.9% of those examined); these included 979 girls (50.1%) and 976 boys (49.9%). The mean (SD) age of these students

TABLE 3. Sex-Specific Distribution of RNFL Thickness Parameters

RNFL Thickness Parameter, μm	Male, n = 976	Female, n = 979	P Value
Average RNFL	102.13 (101.59-102.67)	104.03 (103.45-104.61)	<0.0001
Temporal	81.53 (80.92-82.13)	84.42 (83.72-85.13)	<0.0001
Superior	126.05 (125.12-126.98)	126.33 (125.34-127.31)	0.4226
Nasal	73.52 (72.65-74.39)	74.12 (73.25-74.99)	0.3708
Inferior	127.42 (126.56-128.29)	131.24 (130.26-132.23)	<0.0001
16 Sections*			
TU1	73.20 (72.59-73.82)	74.66 (73.98-75.33)	0.0291
TU2	106.29 (105.16-107.41)	112.91 (111.65-114.17)	<0.0001
ST2	145.00 (143.63-146.37)	149.61 (148.26-150.96)	<0.0001
ST1	141.16 (139.67-142.65)	137.08 (135.63-138.53)	0.0006
SN1	112.97 (111.71-114.24)	112.56 (111.27-113.84)	0.6736
SN2	105.05 (103.94-106.15)	106.04 (104.86-107.21)	0.1434
NU2	87.69 (86.63-88.76)	88.24 (87.15-89.33)	0.2826
NU1	69.79 (68.81-70.77)	70.24 (69.28-71.21)	0.5884
NL1	62.70 (61.80-63.60)	63.66 (62.78-64.54)	0.2509
NL2	73.89 (72.90-74.88)	74.35 (73.33-75.36)	0.6903
IN2	98.77 (97.69-99.85)	99.84 (98.67-101.01)	0.3051
IN1	120.75 (119.35-122.14)	124.31 (122.80-125.81)	0.0032
IT1	150.44 (149.15-151.74)	154.06 (152.62-155.49)	0.0012
IT2	139.73 (138.37-141.09)	146.78 (145.28-148.28)	<0.0001
TL2	84.94 (84.05-85.83)	88.46 (87.32-89.60)	<0.0001
TL1	61.67 (61.20-62.14)	61.67 (61.17-62.16)	0.3868

Data were adjusted for age, axial length, refractive error, and cluster sampling. Results are expressed as means (95% confidence intervals). S, superior; N, nasal; U, upper; L, lower; I, inferior; T, temporal.

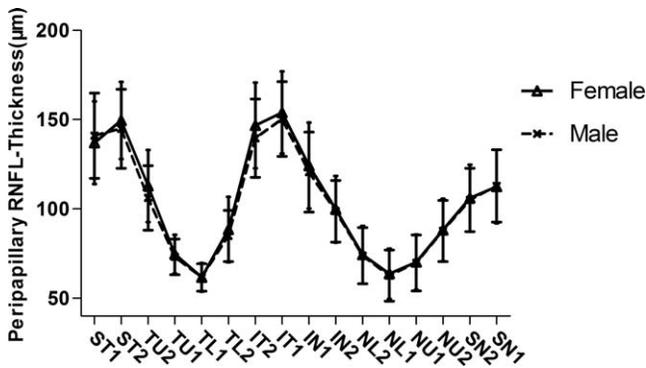


FIGURE 2. Graph showing sex differences in RNFL mean thickness of 16 sections in right eyes. Error bars denote SDs.

was 12.34 (0.58) years (age range, 10–16 years), and the mean (SD) spherical equivalent was -1.38 (1.95) D. Table 1 gives the details of children with versus without OCT performed. There were statistically significant differences in spherical equivalent and axial length between the two groups.

Distribution of RNFL Thickness

The overall distributions of RNFL thickness are given in Table 2. The mean (SD) RNFL thickness was 103.08 (9.01) μm and showed interindividual variability ranging from 72.01 to 150.07 μm . The average RNFL thickness varied by approximately 2-fold between the largest and the smallest thickness. The mean (SD) RNFL was thickest in the inferior quadrant (129.34 [14.90] μm), followed by the superior (126.19 [15.24] μm), temporal (82.98 [10.57] μm), and nasal (73.82 [13.89] μm) quadrants. Variation in the mean (SD) RNFL thickness also existed when separated by 16 individuals sections (each section was 22.5°), with the thickest (152.25 [21.86] μm) in the IT1 section and the thinnest (61.67 [7.70] μm) in the TL1 section (Table 2). The pie graph in Figure 1 shows these differences more intuitively.

The average RNFL thickness was 1.90 μm thicker in girls than in boys ($P < 0.0001$) after adjusting for age, axial length, refractive error, and cluster sampling. These sex-specific differences were statistically significant in the temporal (2.89 μm , $P < 0.0001$) and inferior (3.82 μm , $P < 0.0001$) quadrants but not in the superior (0.28 μm , $P = 0.42$) and nasal (0.60 μm ; $P = 0.37$) quadrants. The sex-specific differences in RNFL thickness of 16 sections are summarized in Table 3, and the tendency to sex variation is shown in Figure 2.

The RNFL thickness increased significantly with more positive spherical equivalent ($\beta = 0.90$, $P < 0.0001$) (Fig. 3A) and decreased significantly with increasing axial length ($\beta = -1.53$, $P < 0.0001$) (Fig. 3B) after adjusting for age, sex, BMI, and cluster sampling. Table 4 summarizes the correlation of refractive error and peripapillary RNFL thickness in each quadrant. The average, superior, nasal, and inferior thicknesses have negative correlations with refractive error. Table 5 gives the average RNFL thicknesses and those for the four quadrants by refractive error group after adjusting for age, sex, axial length, and BMI. No statistically significant correlations were found between RNFL thickness and age or BMI in multiple linear regression analyses.

DISCUSSION

Optical coherence tomography has become a widely used tool in clinical and scientific practice. Compared with older time-

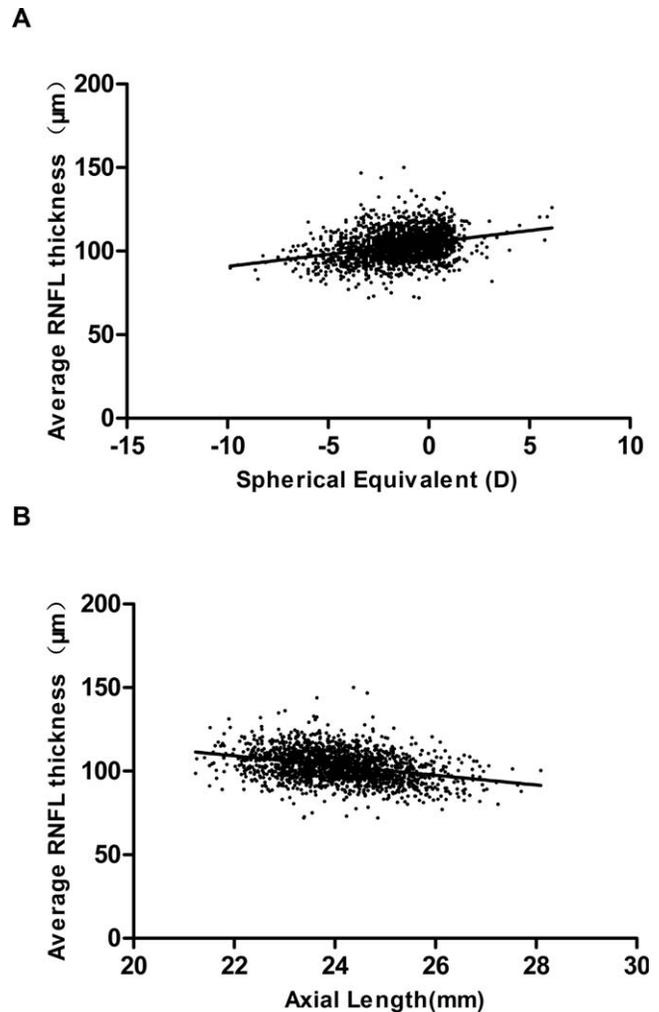


FIGURE 3. Scattergrams showing the relationship of average RNFL thickness in right eyes with (A) spherical equivalent ($\beta = 0.90$, $P < 0.0001$) and (B) axial length ($\beta = -1.53$, $P < 0.0001$) after adjusting for age, sex, BMI, and cluster sampling.

domain instruments, SD-OCT has greatly enhanced scan speed and resolution. However, the use of peripapillary RNFL thickness measurement by OCT has been limited in children because of the lack of normative data. To our knowledge, this is the first study to investigate peripapillary RNFL thickness in a large sample of Chinese children as measured with SD-OCT. In this cross section of the ACES, we found that in predominantly 12-year-old Chinese children the peripapillary mean (SD) RNFL thickness was 103.08 (9.01) μm . Children with longer eyeballs and higher myopia had thinner average RNFL thickness. Girls

TABLE 4. Correlation of Refraction and Peripapillary RNFL Thickness

RNFL Thickness Parameter, μm	Mean (SD)	Spherical Equivalent, mean (SD), D	r	P Value
Average RNFL	103.08 (9.01)	-1.38 (1.95)	-0.28	<0.0001
Temporal	82.98 (10.57)	-	0.13	<0.0001
Superior	126.19 (15.24)	-	-0.29	<0.0001
Nasal	73.82 (13.89)	-	-0.36	<0.0001
Inferior	129.34 (14.90)	-	-0.22	<0.0001

TABLE 5. RNFL Thickness Parameters by Refraction Group After Adjusting for Age, Sex, Axial Length, and BMI

RNFL Thickness Parameter, μm	Hyperopia, $n = 21$		Emmetropia, $n = 654$		Low Myopia, $n = 818$		Moderate Myopia, $n = 313$		High Myopia, $n = 26$	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Average RNFL	103.93	100.17–107.69	104.19	103.41–104.98	103.47	102.87–104.08	100.72	99.60–101.84	98.25	94.77–101.72
Temporal	80.24	75.62–84.86	81.98	81.02–82.95	83.47	82.72–84.22	84.98	83.60–86.35	85.69	81.42–89.97
Superior	121.50	115.12–127.88	128.73	127.40–130.06	126.75	125.72–127.78	121.29	119.38–123.19	114.65	108.75–120.54
Nasal	79.15	73.20–85.10	76.01	74.77–77.26	73.75	72.79–74.71	70.50	68.72–72.27	65.72	60.22–71.22
Inferior	134.84	128.51–141.17	130.03	128.70–131.35	129.92	128.90–130.95	126.14	124.25–128.03	126.92	121.07–132.77

CI, confidence interval.

had slightly thicker average RNFL thickness than boys ($P < 0.001$). Age and BMI were not related to average RNFL thickness.

Previous studies have reported OCT measurements of peripapillary RNFL thickness in children and adults (Table 6). Compared with that in other studies in children, the average RNFL thickness in the present study varied considerably and was similar to that of 12-year-old Australian children^{6,20} and Korean children.²¹ Compared with two previous studies^{9,10} in Chinese children, the average RNFL in the present study was thinner; this variation may primarily be a result of the different mean (SD) refractive status in children between the present study (-1.38 [1.95] D) and the other studies (1 to approximately -3 D with <1 -D astigmatism and -0.82 [1.33] D, respectively). In addition, the other studies measured children with wider age ranges (approximately 5–18 years and 6–17 years, respectively) and used an OCT system that differed from ours, which might also be potential sources of difference.

Peripapillary RNFL thickness seems to be ethnic specific.^{8,20,22–24} Samarawickrama et al.²⁰ reported that East Asian children generally had thicker RNFL than European Caucasian children at the ages of 6 years and 12 years. The average RNFL in the present sample was similar to that of European Caucasian children and was thinner than that of East Asian children. These differences were mainly because of the different mean refractive status of children in the two studies; the children of the ACES were more myopic (-1.38 D) than the East Asian children (-0.7 D) and the European Caucasian children ($+0.8$ D). Another reason might be the different instruments used in the two studies. We used SD-OCT, while the other study used the Stratus OCT system (Carl Zeiss Meditec, Inc.). In addition, a number of factors such as pupil size, the presence of lens opacity, and OCT signal strength have been reported to influence the measurement of RNFL thickness.²⁵ A notable finding in the present study was that the temporal RNFL thickness was thicker in Chinese than in Caucasians and that the nasal RNFL thickness was the opposite. These ethnic differences probably have a strong genetic basis because they can be demonstrated in children and in adults.^{5,8,10,22,26–28}

The average RNFL thickness was found to be thicker in the superior and inferior quadrants than in the temporal and nasal quadrants. This characteristic, called a “double-hump” configuration of peripapillary RNFL thickness, has been reported in previous studies^{7,10,21,29} of adults and children. The peripapillary RNFL thickness was usually thickest in the inferior rim, followed by the superior and nasal rims, and was thinnest in the temporal rim. This is known as the “inferior superior nasal temporal” pattern,³⁰ which reflects the nerve fibers converging to the ONH from the superior and inferior arcuate bundles. In the present study, RNFL was thickest in the inferior quadrant, followed by the superior and temporal quadrants, and the thinnest was in the nasal quadrant. Such a

phenomenon has been reported in other studies^{22,26,28} of Chinese adults. The order of RNFL thickness in the four quadrants has varied in studies.^{5,8,27} These inconsistencies between studies may be explained by ethnic differences.

Previous studies of RNFL thickness generally found no sex difference in children^{7,9,21} or adults.^{23,27,28} Huynh et al.⁵ reported significantly thicker average RNFL ($P = 0.007$) and inferior quadrant RNFL ($P = 0.02$) in boys than in girls after adjusting for age, height, axial length, ethnicity, and cluster sampling. In our study, we found that the average RNFL thickness and that in the temporal and inferior quadrants were significantly greater in girls. When separated by 16 sections, girls had thicker RNFLs in 10 sections, most of them located in the superior and inferior quadrants. However, these differences were small and may in part result from the overlying blood vessels.⁵

The relationship between axial length and RNFL thickness has been examined in several studies.^{5,22,28} Huynh et al.⁵ found a significant trend toward thinner RNFL with longer axial length in 6-year-old children. Knight et al.²² observed that axial length had a negative correlation with the mean RNFL thickness but had a positive correlation with the temporal quadrant RNFL thickness in 63 Chinese adults. Cheung et al.²⁸ reported that longer axial length was associated with thinner mean RNFL in a population-based study of Chinese adults. We found that the average RNFL thickness was significantly negatively correlated with axial length, which is consistent with previous studies.^{5,22,28}

The correlation of refractive error with RNFL thickness has been inconsistent in previous studies. Bowd et al.³¹ found that refractive error was not significantly associated with any RNFL parameters in 155 Caucasian individuals. Vernon et al.³² examined 31 highly myopic Caucasians and found no statistically significant association between the mean RNFL thickness and spherical equivalent ($P = 0.80$). Huynh et al.,⁵ Salchow et al.,⁷ and Qian et al.⁹ reported a positive correlation of the average RNFL thickness with refractive error in healthy children. Budenz et al.²⁷ and Cheung et al.²⁸ reported thinning RNFL with increasing severity of myopia in white and Asian adults. In this study, we found a significant positive correlation of the average RNFL thickness with refractive error in a low-myopia population. This means that as myopia increases RNFL thickness decreases and that as hypermetropia increases RNFL thickness increases. However, conclusions about the relationship between RNFL thickness and high myopia should be made prudently.

Studies^{22,23,27,29,33} have reported that RNFL thickness decreased as age increased. Budenz et al.²⁷ found that RNFL was thinner in older people, with a decline of approximately 2 μm per decade. Qian et al.⁹ and Salchow et al.⁷ reported that RNFL thickness tended to increase with age in a population younger than 18 years. In the present study, the average RNFL thickness had no correlation with age. However, the age range

TABLE 6. Previous Studies on RNFL Thickness Measured by OCT in Eyes of Healthy Children and Adults

Source	Instrument*	Ethnicity	Age, mean (SD) [range], y	Sample Size	Average RNFL, mean (SD), μm
Children					
Present study	iVue-100	Chinese	12.34 (0.58) [10-16]	1955	103.08 (9.00)
Ahn et al., ²¹ 2005	Stratus OCT	Korean	12.60 (2.13) [9-18]	72	105.53 (10.33)
Samarawickrama et al., ²⁰ 2010	Stratus OCT	White	6.7 (0.4)	762	102.99
		East Asian	6.5 (0.4)	155	106.9
		White	12.7	1050	103.33
		East Asian	12.7	216	105.72
		Black	8.6 (3.1) [3-17]	154	110.7 (8.84)
El-Dairi et al., ⁸ 2009	Stratus OCT	White	8.5 (3.1) [3-17]	109	105.9 (10.18)
Salchow et al., ⁷ 2006	Stratus OCT	92% Hispanic	9.7 (2.7) [4-17]	92	107.0 (11.1)
Leung et al., ¹⁰ 2010	Stratus OCT	Hong Kong Chinese	9.75 [6-17.6]	104	113.5 (9.8)
Qian et al., ⁹ 2011	Stratus OCT	Chinese	10.4 (2.7) [5-18]	199	112.36 (9.21)
Kee et al., ³⁷ 2006	Stratus OCT	Korean	8.5 [4-17]	84	108.8 (11.3)
Gire et al., ³⁸ 2010	Stratus OCT	French	9.68 (3.02) [4-15]	104	104.33 (10.22)
Children and adults					
Parikh et al., ³³ 2007	Stratus OCT	Asian Indian	11.1 (3.9) [5-20]	59	100.15 (10.8)
			24.7 (3.6) [20-35]	49	98.76 (12.7)
			41.65 (4.88) [35-50]	34	97.17 (10)
			55.58 (4.25) [50-75]	45	92.28 (9.56)
Adults					
Cheung et al., ²⁸ 2011	SD-OCT	Chinese	53.0 (6.4) [44-73]	542	97.62 (9.10)
Knight et al., ²² 2012	Cirrus HD-OCT	African descent	45.8 (15.6)	51	93.9 (1.2 SE)
		Chinese	44.8 (16.4)	63	96.4 (1.1)
		European descent	49.1 (18.3)	122	90.1 (0.8)
		Hispanic	39.1 (12.3)	35	95.6 (1.4)
		All	47.4 (15.8) [18-85]	328	100.1 (11.6)
Budenz et al., ²⁷ 2007	Stratus OCT	Black	47.13 (8.11)	42	114.86 (15.14)
Racette et al., ²⁴ 2005	Stratus OCT	White	49.18 (9.23)	34	108.50 (17.17)
Manassakorn et al., ³⁹ 2008	Stratus OCT	Thai	44.7 (12.2)	250	109.3 (10.5)
Kanno et al., ⁴⁰ 2010	Time domain-OCT	Japanese	44.0 (14.5) [20-84]	460	111.8 (10.0)
Wang et al., ⁴¹ 2011	RTVue	Chinese	34.65 (14.48)	62	109.76 (9.10)
Garas et al., ¹³ 2010	RTVue	White	54.0 (17.9)	14	106.7 (7.5)
Gonzalez-Garcia et al., ¹¹ 2009	RTVue		63.5 (10.2)	60	102.8
Mansouri et al., ¹⁵ 2012	iVue	All	22.9 (2.6) [20-27]	10	103.9 (8.3)
			53.9 (5.0) [50-66]	10	100.7 (3.9)
Bendschneider et al., ⁴² 2010	SD-OCT	White	[20-78]	170	97.2 (9.7)

* Instrument manufacturers are as follows: iVue-100 (version 2.5.0.100; Optovue, Inc., Fremont, CA), Stratus OCT (Carl Zeiss Meditec, Inc., Jena, Germany), Cirrus HD-OCT (Carl Zeiss Meditec, Inc.), RTVue (Optovue, Inc.), and iVue (Optovue, Inc.).

in our study was small, and most of the students were 12 years old. Another possible explanation is that RNFL thickness remains constant in early childhood and adolescence.^{6,10} A population-based study²⁸ of 542 healthy Chinese at a mean (SD) age of 53.0 (6.4) years using SD-OCT reported a mean (SD) RNFL thickness of 97.62 (9.10) μm , which was much thinner than our results in children.

Body mass index had no effect on RNFL thickness. Although some investigators have reported that BMI influences optic nerve parameters, few studies^{34,35} have detected an association with RNFL thickness. Cheung et al.²⁸ also reported that BMI did not influence RNFL measurements.

The strengths of this study include its large unbiased sample, school-based design, standardized examination, and detailed analyses. There were some limitations of our study. First, our sample was more myopic compared with samples in other studies. Although some epidemiological investigations have shown that the incidence of myopia among Chinese teenagers is high,³⁶ its influence on RNFL thickness is unclear. Refractive status should be considered when comparing RNFL thickness in different ethnic groups. Second, many examinations were performed in the ACES; to ensure an overall high

response rate, only a few OCT scans were performed in each student. One hundred fifty students (7.1%) were excluded because of a low SSI. Inclusion of this more myopic group might have affected the average RNFL thickness. Third, RNFL thickness measured by iVue-100 (Optovue, Inc.) did not correct for magnification, which might have affected the accuracy of the RNFL thickness. Fourth, we did not take into account the effect of optic disc size on RNFL thickness. Further studies should correct for magnification and add optic disc size as an influencing factor. Fifth, most children in this study were 12 to 13 years old. Therefore, the results cannot be applied to younger or older children. However, the results from primary schools and the annual follow-up investigations in the ACES will fill this void. Some children may be found to have glaucoma in the future but cannot be diagnosed and excluded at this stage. Therefore, follow-up of these children is necessary to clarify this issue.

In summary, in this school-based survey in central China, we used SD-OCT and found that the mean (SD) peripapillary RNFL thickness was 103.08 (9.01) μm in predominantly 12-year-old Chinese children. Peripapillary RNFL was thinner in longer or more myopic eyes. The thickest RNFL is located in

the inferior quadrant, followed by the superior, temporal, and nasal quadrants. Girls had slightly greater RNFL thickness than boys.

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References

- Sommer A, Miller NR, Pollack I, Maumenee AE, George T. The nerve fiber layer in the diagnosis of glaucoma. *Arch Ophthalmol*. 1977;95:2149-2156.
- Quigley HA, Katz J, Derick RJ, Gilbert D, Sommer A. An evaluation of optic disc and nerve fiber layer examinations in monitoring progression of early glaucoma damage. *Ophthalmology*. 1992;99:19-28.
- Herrmann J, Funk J. Diagnostic value of nerve fibre layer photography in glaucoma [in German]. *Ophthalmologie*. 2005; 102:778-782.
- Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991;254:1178-1181.
- Huynh SC, Wang XY, Rochtchina E, Mitchell P. Peripapillary retinal nerve fiber layer thickness in a population of 6-year-old children: findings by optical coherence tomography. *Ophthalmology*. 2006;113:1583-1592.
- Huynh SC, Wang XY, Burlutsky G, Rochtchina E, Stapleton F, Mitchell P. Retinal and optic disc findings in adolescence: a population-based OCT study. *Invest Ophthalmol Vis Sci*. 2008; 49:4328-4335.
- Salchow DJ, Oleynikov YS, Chiang MF, et al. Retinal nerve fiber layer thickness in normal children measured with optical coherence tomography. *Ophthalmology*. 2006;113:786-791.
- El-Dairi MA, Asrani SG, Enyedi LB, Freedman SF. Optical coherence tomography in the eyes of normal children. *Arch Ophthalmol*. 2009;127:50-58.
- Qian J, Wang W, Zhang X, et al. Optical coherence tomography measurements of retinal nerve fiber layer thickness in Chinese children and teenagers. *J Glaucoma*. 2011;20:509-513.
- 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: 95-99.
- Gonzalez-Garcia AO, Vizzeri G, Bowd C, Medeiros FA, Zangwill LM, Weinreb RN. Reproducibility of RTVue retinal nerve fiber layer thickness and optic disc measurements and agreement with Stratus optical coherence tomography measurements. *Am J Ophthalmol*. 2009;147:1067-1074, 1074.e1. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3465966/>. Accessed November 9, 2013.
- Menke MN, Knecht P, Sturm V, Dabov S, Funk J. Reproducibility of nerve fiber layer thickness measurements using 3D Fourier-domain OCT. *Invest Ophthalmol Vis Sci*. 2008;49: 5386-5391.
- Garas A, Vargha P, Hollo G. Reproducibility of retinal nerve fiber layer and macular thickness measurement with the RTVue-100 optical coherence tomograph. *Ophthalmology*. 2010;117:738-746.
- Leite MT, Rao HL, Zangwill LM, Weinreb RN, Medeiros FA. Comparison of the diagnostic accuracies of the Spectralis, Cirrus, and RTVue optical coherence tomography devices in glaucoma. *Ophthalmology*. 2011;118:1334-1339.
- Mansouri K, Liu JH, Tafreshi A, Medeiros FA, Weinreb RN. Positional independence of optic nerve head and retinal nerve fiber layer thickness measurements with spectral-domain optical coherence tomography. *Am J Ophthalmol*. 2012;154: 712-721.e1. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3806882/>. Accessed November 9, 2013.
- Gilbert C, Foster A. Childhood blindness in the context of VISION 2020: the right to sight. *Bull World Health Organ*. 2001;79:227-232.
- Liang YB, Friedman DS, Zhou Q, et al. Prevalence of primary open angle glaucoma in a rural adult Chinese population: the Handan Eye Study. *Invest Ophthalmol Vis Sci*. 2011;52:8250-8257.
- Song W, Shan L, Cheng F, et al. Prevalence of glaucoma in a rural northern China adult population: a population-based survey in Kailu County, Inner Mongolia. *Ophthalmology*. 2011;118:1982-1988.
- Li SM, Liu LR, Li SY, et al; Anyang Childhood Eye Study Group. Design, methodology and baseline data of a school-based cohort study in central China: the Anyang Childhood Eye Study [published online ahead of print October 25, 2013]. *Ophthalmic Epidemiol*. doi:10.3109/09286586.2013.842596.
- Samarawickrama C, Wang JJ, Huynh SC, et al. Ethnic differences in optic nerve head and retinal nerve fibre layer thickness parameters in children. *Br J Ophthalmol*. 2010;94: 871-876.
- Ahn HC, Son HW, Kim JS, Lee JH. Quantitative analysis of retinal nerve fiber layer thickness of normal children and adolescents. *Korean J Ophthalmol*. 2005;19:195-200.
- Knight OJ, Girkin CA, Budenz DL, Durbin MK, Feuer WJ. Effect of race, age, and axial length on optic nerve head parameters and retinal nerve fiber layer thickness measured by Cirrus HD-OCT. *Arch Ophthalmol*. 2012;130:312-318.
- Alasil T, Wang K, Keane PA, et al. Analysis of normal retinal nerve fiber layer thickness by age, sex, and race using spectral domain optical coherence tomography. *J Glaucoma*. 2013;22: 532-541.
- Racette L, Boden C, Kleinhandler SL, et al. Differences in visual function and optic nerve structure between healthy eyes of blacks and whites. *Arch Ophthalmol*. 2005;123:1547-1553.
- Cheung CY, Leung CK, Lin D, Pang CP, Lam DS. Relationship between retinal nerve fiber layer measurement and signal strength in optical coherence tomography. *Ophthalmology*. 2008;115:1347-1351, 1351.e1-2. [http://www.aajournal.org/article/S0161-6420\(07\)01290-0/abstract](http://www.aajournal.org/article/S0161-6420(07)01290-0/abstract). Accessed November 9, 2013.
- Mok KH, Lee VW, So KF. Retinal nerve fiber layer measurement of the Hong Kong Chinese population by optical coherence tomography. *J Glaucoma*. 2002;11:481-483.
- Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. *Ophthalmology*. 2007;114:1046-1052.
- Cheung CY, Chen D, Wong TY, et al. Determinants of quantitative optic nerve measurements using spectral domain optical coherence tomography in a population-based sample of non-glaucomatous subjects. *Invest Ophthalmol Vis Sci*. 2011;52:9629-9635.

29. Varma R, Bazzaz S, Lai M. Optical tomography-measured retinal nerve fiber layer thickness in normal Latinos. *Invest Ophthalmol Vis Sci.* 2003;44:3369-3373.
30. Jonas JB, Gusek GC, Naumann GO. Optic disc, cup and neuroretinal rim size, configuration and correlations in normal eyes [published corrections appear in *Invest Ophthalmol Vis Sci.* 1991;32:1893 and 1992;32:474-475]. *Invest Ophthalmol Vis Sci.* 1988;29:1151-1158.
31. Bowd C, Zangwill LM, Blumenthal EZ, et al. Imaging of the optic disc and retinal nerve fiber layer: the effects of age, optic disc area, refractive error, and gender. *J Opt Soc Am A Opt Image Sci Vis.* 2002;19:197-207.
32. Vernon SA, Rotchford AP, Negi A, Ryatt S, Tattersal C. Peripapillary retinal nerve fibre layer thickness in highly myopic Caucasians as measured by Stratus optical coherence tomography. *Br J Ophthalmol.* 2008;92:1076-1080.
33. Parikh RS, Parikh SR, Sekhar GC, Prabakaran S, Babu JG, Thomas R. Normal age-related decay of retinal nerve fiber layer thickness. *Ophthalmology.* 2007;114:921-926.
34. Zheng Y, Cheung CY, Wong TY, Mitchell P, Aung T. Influence of height, weight, and body mass index on optic disc parameters. *Invest Ophthalmol Vis Sci.* 2010;51:2998-3002.
35. Wong AC, Chan CW, Hui SP. Relationship of gender, body mass index, and axial length with central retinal thickness using optical coherence tomography. *Eye (Lond).* 2005;19:292-297.
36. He M, Zheng Y, Xiang F. Prevalence of myopia in urban and rural children in mainland China. *Optom Vis Sci.* 2009;86:40-44.
37. Kee SY, Lee SY, Lee YC. Thicknesses of the fovea and retinal nerve fiber layer in amblyopic and normal eyes in children. *Korean J Ophthalmol.* 2006;20:177-181.
38. Gire J, Cornand E, Fogliarini C, Benso C, Haouchine B, Denis D. Retinal nerve fiber layer in OCT 3: prospective study of 53 normal children [in French]. *J Fr Ophtalmol.* 2010;33:444-449.
39. Manassakorn A, Chaidaroon W, Ausayakhun S, Aupapong S, Wattanakorn S. Normative database of retinal nerve fiber layer and macular retinal thickness in a Thai population. *Jpn J Ophthalmol.* 2008;52:450-456.
40. Kanno M, Nagasawa M, Suzuki M, Yamashita H. Peripapillary retinal nerve fiber layer thickness in normal Japanese eyes measured with optical coherence tomography. *Jpn J Ophthalmol.* 2010;54:36-42.
41. Wang X, Li S, Fu J, et al. Comparative study of retinal nerve fibre layer measurement by RTVue OCT and GDx VCC. *Br J Ophthalmol.* 2011;95:509-513.
42. Bendschneider D, Tornow RP, Horn FK, et al. Retinal nerve fiber layer thickness in normals measured by spectral domain OCT. *J Glaucoma.* 2010;19:475-482.

APPENDIX

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