Macular Ganglion Cell-Inner Plexiform Layer, Ganglion Cell Complex, and Outer Retinal Layer Thicknesses in a Large Cohort of Chinese Children

Lu Cheng,1–3 Mingjin Wang,1 Junjie Deng,2,3 Minzhi Lv,1 Wenhan Jiang,4 Shuyu Xiong,2,3 Sifei Sun,5 Jianfeng Zhu,1 Haidong Zou,1–3 Xiangui He,1,4 and Xun Xu1–3

1Department of Preventative Ophthalmology, Shanghai Eye Disease Prevention and Treatment Center, Shanghai Eye Hospital, Shanghai, China
2Department of Ophthalmology, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, China
3Shanghai Key Laboratory of Fundus Disease, Shanghai, China
4School of Public Health, Fudan University, Shanghai, China
5Jiading Center for Disease Prevention and Control, Shanghai, China

CORRESPONDENCE: Xiangui He, Department of Preventative Ophthalmology, Shanghai Eye Disease Prevention and Treatment Center, Shanghai Eye Hospital, No. 380 Kangding Road, Shanghai 200040, China; xianhezi@163.com.
Xun Xu, Department of Ophthalmology, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, China; drxuxun@sjtu.edu.cn.

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PURPOSE. The purpose of this study was to describe the normative values, distribution patterns, and correlated factors of macular ganglion cell-inner plexiform layer (GCIPL), ganglion cell complex (GCC), and outer retinal layer (ORL) thicknesses in Chinese children.

METHODS. A sample of 3000 healthy children with different refractive status aged 6 to 19 years was consecutively examined. Demographics were recorded, and a comprehensive ophthalmic examination including refractive error and axial length (AL) was taken from all participants. The GCIPL, GCC, and ORL thicknesses were measured using swept source-optical coherence tomography (OCT), and multiple linear regression was used to determine which factors were associated with the thickness of each layer.

RESULTS. The average thickness was 77.00 ± 4.78 μm (95% confidence interval [CI]: 69.56–84.56 μm) in the GCIPL, 107.68 ± 5.95 μm (95% CI: 98.45–117.21 μm) in the GCC, and 178.57 ± 9.02 μm (95% CI: 164.33–192.56 μm) in the ORL. Multiple regression analysis indicated that GCIPL thickness was associated with sex (β = 0.168, P < 0.001), age (β = 0.126, P < 0.001), axial length (β = −0.181, P < 0.001), and refractive error (β = 0.233, P < 0.001). Age (β = 0.154, P < 0.001), sex (β = 0.102, P < 0.001), and refractive error (β = 0.149, P < 0.001) were associated independently with GCC thickness after adjusting for the other factors. Furthermore, age (β = 0.100, P < 0.001), sex (β = 0.163, P < 0.001), AL (β = −0.283, P < 0.001), and refractive error (β = 0.207, P < 0.001) were the independent factors associated with ORL thickness.

CONCLUSIONS. The present study established a normative pediatric database for macular layer thicknesses in healthy Chinese children, advancing the ability of OCT in diseases diagnosis and monitoring among children.

Keywords: optical coherence tomography, ganglion cell-inner plexiform Layer, ganglion cell complex, outer retinal layer, children
healthy children has been reported,\textsuperscript{24,25} this value is not representative for condition of an individual layer.

In the present study, we aimed to establish the normative macular GCIPL, GCC, and ORL thicknesses profile in a large cohort of Chinese children using swept source-OCT (SS-OCT) to describe their topographic distributions in different macular sectors and to determine the demographic and ocular factors associated with them.

**METHODS**

**Setting and Participants**

The study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Shanghai General Hospital, Shanghai Jiao Tong University. Twelve primary and middle schools were randomly selected using cluster sampling. All students were screened for enrollment in January 2016. Children were excluded if (1) there were intraocular surgeries or pathologies, including amblyopia (best-corrected visual acuity < 20/25), strabismus, ptosis, congenital cataracts, glaucoma, and fundus diseases according to self-reported history or ophthalmic examination; (2) they were unwilling or unable to cooperate; (3) the OCT images were still poor after being retaken (including poor alignment, signal strength index < 60, black lines across the image due to blinks, or motion artifacts); (4) the parents were unwilling or unable to give written consent; or (5) the participant was unwilling or unable to give verbal assent. The research team consisted of one ophthalmologist, five optometrists, two public health physicians, and two nurses. The investigation site was located within the schools. The experimental protocol was explained to all participants, and written informed consent was provided by their parents or other guardians.

**Research Methods**

Participant age and sex were recorded from state-issued identification cards, and their heights and weights were measured. Body mass indexes (BMIs) were calculated. Each participant underwent a comprehensive ophthalmic examination, including an evaluation of visual acuity, a sensorimotor examination, slit-lamp biomicroscopy, tonometry, cycloplegic refraction, and a fundus examination. These examinations were followed by ancillary testing, including axial length (AL), corneal curvature, and SS-OCT. Visual acuity was measured using a retro-illuminated Early Treatment of Diabetic Retinopathy Study (ETDRS) chart at a distance of 4 m. Cycloplegia was achieved by administering one drop of topical 0.5% proparacaine (Alcaine; Alcon, Fribourg, Switzerland), followed by two doses of 1% cyclopentolate (Cyclogyl; Alcon), applied 5 minutes apart. After 30 minutes, if the pupils were still reactive to light and the pupil size was estimated to be less than 6 mm, a third drop of cyclopentolate was administered. Corneal curvature and refraction measurements were performed with a desk-mounted auto-refractor (model KR-8900; Topcon, Tokyo, Japan), and spherical equivalent refraction (SER) was used to classify the refractive status. Hyperopia was defined as SER ≥ 0.5 diopters (D) and myopia as SER ≤ –0.5 D. Myopia was further categorized into high myopia (SER ≤ –5.0 D), moderate myopia (5.0 D < SER ≤ –3.0 D), and mild myopia (–3.0 D < SER ≤ –0.5 D). The IOP was measured by a noncontact tonometer (model NT-4000; Nidek, Inc., Fremont, CA, USA) before dilation, and the AL was measured using noncontact optical biometry (IOL Master, version 5.02; Carl Zeiss Meditec, Oberkochen, Germany).

SS-OCT (model DRI-OCT-1 Atlantis; Topcon) with a lateral resolution of 10 μm and a depth resolution of 8 μm was used to measure the thickness of retinal layers. A single technician performed the SS-OCT image acquisitions between 9 and 11 AM to reduce the impact of diurnal variation. Scans were retaken if poor alignment, low signal strength (signal strength index < 60), blinks (black lines across the image), or motion artifacts (shearing or breaks of the vessel pattern) were noticed. GCIPL thickness was defined as the distance from the interface between the nerve fiber layer and ganglion cell layer to the interface between the inner plexiform layer and inner nuclear layer. GCC was defined as the distance between the internal limiting membrane and the interface between the inner plexiform layer and inner nuclear layer, as the sum of RNFL and GCIPL. ORL thickness was defined as the distance from the interface between the inner plexiform layer and inner nuclear layer to the interface between the RPE and the Bruch membrane (Fig. 1). All acquired images were inspected, and if automatic segmentation errors and foveal centration errors occurred, manual segmentation or determination of foveal center was performed, based on anatomic features. The ETDRS grid was applied accordingly, which divided the macula into nine sectors of three concentric circles centered on the fovea.
Thicknesses of the GCIPL, GCC, and ORL within each subfield were calculated automatically. To illustrate the effects of the ocular magnification on the macular thickness measurements, another group of 150 children was randomly selected from the same schools as the original group. They underwent a SS-OCT examination and a conducted magnification correction through the Topcon built-in software, using a modification of the Littmann’s method by determining the axial length before the image capture.26,27

### Table 1. General Characteristics of the 3000 Participants

<table>
<thead>
<tr>
<th>Parameter (n = 3000)</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>11.67 ± 3.44</td>
<td>11</td>
<td>6</td>
<td>19</td>
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<tr>
<td>Weight, kg</td>
<td>43.39 ± 16.52</td>
<td>41.10</td>
<td>16.30</td>
<td>130.00</td>
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<tr>
<td>Height, cm</td>
<td>148.68 ± 17.18</td>
<td>148.00</td>
<td>109.00</td>
<td>193.00</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>18.89 ± 3.80</td>
<td>18.32</td>
<td>10.84</td>
<td>40.57</td>
</tr>
<tr>
<td>UVA</td>
<td>0.59 ± 0.36</td>
<td>0.63</td>
<td>0.025</td>
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<tr>
<td>AL, mm</td>
<td>24.04 ± 1.31</td>
<td>23.88</td>
<td>19.88</td>
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<td>SER, D</td>
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<td>-0.50</td>
<td>-1.18</td>
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<tr>
<td>IOP, mm Hg</td>
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<td>16.00</td>
<td>9.00</td>
<td>25.00</td>
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<tr>
<td>Corneal curvature, D</td>
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UVA, uncorrected visual acuity.

### Table 2. Macular GCIPL, GCC, ORL Thickness Profiles for Normal Children

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<th>Layer</th>
<th>Subfield</th>
<th>Mean ± SD</th>
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<th>25th</th>
<th>75th</th>
<th>95th</th>
<th>Minimum</th>
<th>Maximum</th>
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<td>73.92</td>
<td>79.89</td>
<td>84.56</td>
<td>42.33</td>
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<td>Center</td>
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<td>61</td>
<td>13</td>
<td>91</td>
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<tr>
<td></td>
<td>Parafoveal</td>
<td>93.01 ± 6.03</td>
<td>84</td>
<td>89.25</td>
<td>96.5</td>
<td>102.5</td>
<td>42.25</td>
<td>117.75</td>
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<td>Perifoveal</td>
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<td>40.25</td>
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<td>104</td>
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<td>106.73 ± 8.34</td>
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<td>T2</td>
<td>167.35 ± 9.97</td>
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<td>157.05 ± 10.27</td>
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<td>173</td>
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</table>

### Statistical Analysis

SAS (version 8.0; SAS Institute, Cary, NC, USA) and MedCalc (version 19.0.7; MedCalc Software, Ostend, Belgium) was used for all the statistical analyses, and all data were doubly entered independently by two research associates; all discrepancies were adjudicated. Although data were acquired from both eyes, only the right eye data were used for statistical analysis to avoid intereye dependencies. The parameters used for analyzing the three layers (GCIPL/GCC/ORL) in the macular...
were nine sectoral thicknesses, parafoveal (average of inner-ring quadrants) or perifoveal (average of outer-ring quadrants) thickness, and overall macular thickness, calculated as the weighted average of the sectoral macular thickness measurements, using the following formula: \( \frac{1}{36} \text{center} + \frac{1}{18} \text{(sum of inner-ring quadrants’ thickness)} + \frac{3}{16} \text{(sum of outer-ring quadrants’ thickness)} \). The characteristics observed are presented as the mean ± SD for normally distributed continuous variables and as rates for categorical data. The data distribution was examined using the Kolmogorov-Smirnov test. All SS-OCT measurements were normally distributed, and intergroup differences were tested by \( t \)-test or ANOVA; comparisons of macular thicknesses with and without magnification correction were made using paired-samples \( t \)-test. Categorical variables were compared using the \( \chi^2 \) test. Stepwise multiple regression analysis was performed to determine the independent factors related to the average thickness of each layer. Linear regression analysis was used to analyze the relationship between the thickness of each layer and SER, AL, and age.

**RESULTS**

**General Characteristics**

A total of 5046 school children aged 6 to 19 years participated in the study, and 3000 eyes from 3000 children (1553 boys and 1447 girls) were included in the analyses. Reasons for exclusion were ocular diseases (35 participants with amblyopia according to self-reported history or best corrected visual acuity results, 3 participants with strabismus found by ophthalmic examination, 1 participant with myopic pathologic findings through fundus examination), poor SS-OCT images (10 participants), and poor cooperation (3 participants). The demographic characteristics of the 3000 included participants are shown in Table 1, and the histograms are presented in Supplementary Figure S1.

**Normative Thicknesses and Distributions of Macular GCfPL, GCC, and ORL**

For each of the thickness parameters, data normality was assessed, and all parameters were normally distributed. Normative ranges of each parameter were constructed by determining the values corresponding to the 5th to 95th percentiles. The mean GCfPL, GCC, and ORL thicknesses were 77.00 ± 4.78 μm (5th–95th percentile range, 69.56–84.56 μm), 107.68 ± 5.95 μm (5th–95th percentile range, 98.45–117.21 μm), and 178.57 ± 9.02 μm (5th–95th percentile range, 164.33–192.56 μm). Table 2 shows the macular GCfPL, GCC, and ORL thickness measurements according to the ETDRS maps, and histograms of the central, parafoveal, perifoveal, and overall thicknesses are shown in Supplementary Figure S2. Both the macular layer thicknesses and total macular thickness (calculated by the sum of GCC and ORL thicknesses) measured in the present study were greater than those measured in adults, where SS-OCT was also used. The topographic distribution patterns for the macular GCfPL, GCC, and ORL thicknesses are presented as thickness maps (Fig. 2). The GCfPL thickness of the parafoveal region was thicker than that of the perifoveal region. This was consistent with the anatomical distribution that ganglion cell densities reach 32,000 to 38,000 cells/mm² in a horizontally oriented elliptical ring 0.4 to 2.0 mm from the foveal center. In the perifoveal region, GCfPL thickness in the nasal sector exceeded that in the temporal sector, and the superior sector exceeded the inferior sector, which is also consistent with the distribution of RGC in the peripheral retina. The differences between GCfPL and GCC distributions reflect the distribution of macular RNFL, of which the thickness decreased from the nasal sector toward the temporal sector horizontally. The maximum ORL thickness was located in the parafoveal region followed by the central region. In both the parafoveal and perifoveal regions, the ORL thickness in the nasal sector exceeded that in the temporal sector, and the superior sector exceeded the inferior sector, similar to GCfPL.

**Factors Associated With Macular GCfPL, GCC, and ORL Thicknesses**

We conducted a multiple regression analysis to explore which factors are related to the thickness of each macular layer. Among the factors included, age, sex, AL, and SER were significantly and independently related to the macular GCfPL and ORL thicknesses, and only age, sex, and SER were related...
to the macular GCC thickness (Table 3). This analysis showed that boys had thicker GCIPL, GCC, and ORL than girls, and the thicknesses of all three layers increased slightly with age and SER, whereas GCIPL and ORL thicknesses decreased with increasing AL. Additionally, according to the standardized coefficient, the factor most closely related to the GCIPL thickness was SER, for the GCC thickness it was age, and for the ORL thickness it was AL. Considering that AL is not always available clinically and sphere error is highly related to AL, we also conducted a multiple regression analysis using sphere and cylinder error instead of AL and SER, and the results are shown in Supplementary Table S1.

Next we performed a linear regression analysis to determine the relationships of SER, AL, and age with GCIPL, GCC, and ORL thicknesses (Fig. 3). Linear regression analysis revealed a positive correlation between SER and GCIPL, GCC, and ORL thicknesses. According to the model, every 1-D increase in SER is associated with a 0.61-μm (95% confidence interval [CI], 0.54–0.67 μm) increase in GCIPL thickness, a 0.15–μm (95% CI, 0.07–0.24 μm) increase in GCC thickness, and a 1.44–μm (95% CI, 1.28–1.57 μm) increase in ORL thickness. The linear correlation analysis also revealed a negative correlation between AL and GCIPL and ORL thicknesses. Every 1-mm increase in AL is associated with a 0.97–μm (95% CI, 0.84–1.10 μm) decrease in GCIPL thickness.

**FIGURE 3.** Linear relationships between macula layer thickness and SER, AL, and age. (A) Correlations of macular GCIPL, GCC, and ORL thickness with SER. It is shown that SER correlates positively with GCIPL, GCC, and ORL thicknesses. ORL thickness is affected the most. (B) Correlations of macular GCIPL, GCC, and ORL thickness with AL. The GCIPL and ORL thicknesses are correlated negatively with the AL. No significant correlation is found between GCC thickness and AL. (C) Correlations of macular GCIPL, GCC, and ORL thickness with age. There is a positive effect of age on the GCC thickness but a negative effect on the GCIPL and ORL thicknesses.

**TABLE 3.** Demographic and Ocular Independent Variables Associated With Thicknesses of the GCIPL, GCC, and ORL

<table>
<thead>
<tr>
<th>Layer</th>
<th>Factors</th>
<th>Standardized Coefficient</th>
<th>Unstandardized Coefficient</th>
<th>95% CI</th>
<th>P Value</th>
<th>VIF</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCIPL</td>
<td>Intercept</td>
<td>93.129</td>
<td>86.203, 98.018</td>
<td>&lt;0.001*</td>
<td>0.129</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.126</td>
<td>0.180</td>
<td>0.126, 0.257</td>
<td>&lt;0.001*</td>
<td>1.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.158</td>
<td>1.655</td>
<td>1.209, 2.126</td>
<td>&lt;0.001*</td>
<td>1.948</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SER</td>
<td>0.233</td>
<td>0.457</td>
<td>0.366, 0.624</td>
<td>&lt;0.001*</td>
<td>1.871</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AL</td>
<td>−0.181</td>
<td>−0.675</td>
<td>−0.884, −0.396</td>
<td>&lt;0.001*</td>
<td>1.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.034</td>
<td>0.044</td>
<td>−0.000, 0.101</td>
<td>0.099</td>
<td>1.409</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP</td>
<td>−0.005</td>
<td>−0.010</td>
<td>−0.064, 0.062</td>
<td>0.773</td>
<td>1.012</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corneal curvature</td>
<td>−0.001</td>
<td>−0.002</td>
<td>−0.091, 0.087</td>
<td>0.965</td>
<td>1.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCC</td>
<td>Intercept</td>
<td>107.775</td>
<td>99.809, 115.433</td>
<td>&lt;0.001*</td>
<td>0.135</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.154</td>
<td>0.280</td>
<td>0.164, 0.358</td>
<td>&lt;0.001*</td>
<td>1.948</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.102</td>
<td>1.283</td>
<td>0.725, 1.873</td>
<td>&lt;0.001*</td>
<td>1.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SER</td>
<td>0.149</td>
<td>0.376</td>
<td>0.189, 0.563</td>
<td>&lt;0.001*</td>
<td>1.871</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AL</td>
<td>−0.080</td>
<td>−0.174</td>
<td>−0.392, 0.253</td>
<td>0.646</td>
<td>1.333</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.056</td>
<td>0.074</td>
<td>0.009, 0.143</td>
<td>0.042</td>
<td>1.409</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP</td>
<td>−0.045</td>
<td>−0.029</td>
<td>−0.112, 0.056</td>
<td>0.518</td>
<td>1.012</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corneal curvature</td>
<td>0.003</td>
<td>0.009</td>
<td>−0.108, 0.126</td>
<td>0.881</td>
<td>1.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORL</td>
<td>Intercept</td>
<td>228.698</td>
<td>216.934, 240.463</td>
<td>&lt;0.001*</td>
<td>0.178</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.100</td>
<td>0.280</td>
<td>0.149, 0.411</td>
<td>&lt;0.001*</td>
<td>1.948</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.163</td>
<td>3.161</td>
<td>2.448, 3.875</td>
<td>&lt;0.001*</td>
<td>1.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SER</td>
<td>0.207</td>
<td>0.801</td>
<td>0.546, 1.057</td>
<td>&lt;0.001*</td>
<td>1.871</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AL</td>
<td>−0.283</td>
<td>−2.086</td>
<td>−2.572, −1.600</td>
<td>&lt;0.001*</td>
<td>1.333</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.063</td>
<td>0.161</td>
<td>0.060, 0.262</td>
<td>0.002</td>
<td>1.409</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP</td>
<td>−0.064</td>
<td>−0.052</td>
<td>−0.178, 0.074</td>
<td>0.416</td>
<td>1.012</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corneal curvature</td>
<td>−0.006</td>
<td>−0.033</td>
<td>−0.229, 0.163</td>
<td>0.741</td>
<td>1.006</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VIF, variance expansion factor.

* Independent factors significantly associated with the GCIPL/GCC/ORL thicknesses in the regression models.
and a 2.55-μm (95% CI, 2.30–2.78 μm) decrease in ORL thickness. The linear correlation analysis demonstrated a small but statistically significant positive effect of age on GCC thickness but a negative effect on GCIPL and ORL thicknesses. This resulted from the correlation between age, SER, and AL. After adjustment for SER and AL, as demonstrated by the multiple regression, the effects of age on GCIPL, GCC, and ORL thicknesses were all positive.

### Macular GCIPL, GCC, and ORL Thicknesses for Different Demographic and Ocular Status

Sex, age, SER, and AL appeared to be the major confounding factors for macular GCIPL, GCC, and ORL thicknesses according to the multiple regression analysis; therefore, we also provided the thickness profile of each layer for different sex, age, SER, and AL status (Supplementary Tables S2–S4). Through the subfield analysis, we found that age, SER, and AL had different effects on different sectors. Perifoveal thicknesses of the three layers were lesser in children with a larger degree of myopia, greater age, and longer axis; however, the differences were less significant or even opposite in the parafoveal region, whereas the central sector thicknesses had exactly the opposite tendency. The trends for thicknesses of individual macular layers were consistent with that for total macular thickness as reported in a previous study.24

### Magnification Effect Analysis

During the ocular magnification correction process, 150 children (77 boys and 73 girls) were recruited and 1 boy was excluded due to poor images. The mean age, AL, SER, and corneal curvature were 11.50 to 7.65 D, respectively. The histograms are shown in Supplementary Figure S3. There was no significant difference in age, sex, SER, AL, and corneal curvature between these two groups of children, and the distributions of the demographic characteristics were quite similar as well, suggesting the 149 children could represent the entire group.

The Bland-Altman plot showed that apart from several extreme values, most of the thickness differences with and without the magnification correction were of less than 5 μm; the before/after amendment differences of the whole area were only a few micrometers, which were relatively small considering the measurement error (Figs. 4–6). No significant difference was found in the GCIPL, GCC, and ORL thicknesses with and without magnification correction in all nine sectors of the ETDRS grid (Table 4). Multiple regression analysis showed that AL and sex were significantly related to the macular GCIPL and ORL thicknesses both before and after magnification correction (Supplementary Table S5). In the subgroup analysis according to AL status (Supplementary Table S6), only the AL ≤ 23 mm group presented significant difference in the GCIPL and GCC thicknesses with and without magnification correction. Therefore, we consider the magnification effect on the individual macular layer thickness measurement and the relationship with other factors to be minimal in the current study.

### DISCUSSION

Measurement of individual macular layer through OCT is especially useful for children with glaucoma, neuroophthalmologic, or retinal diseases because it provides high-resolution, objective, and quantitative assessments of RGCs and the outer retina. Profiles of macular layer thicknesses in normal children can provide references for defining abnormal thinning, thickening, or change of thickness distribution patterns.

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**Table 4.** Comparisons of Macular GCIPL, GCC, and ORL Thicknesses Before and After Magnification Correction

<table>
<thead>
<tr>
<th>Layer</th>
<th>Subfield</th>
<th>Before/After (μm)</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCIPL</td>
<td>Center</td>
<td>46.66/46.99</td>
<td>−0.327 (−1.245, 0.591)</td>
<td>0.483</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>93.62/93.23</td>
<td>0.393 (−0.125, 0.912)</td>
<td>0.136</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>90.46/90.17</td>
<td>0.287 (−0.204, 0.777)</td>
<td>0.250</td>
</tr>
<tr>
<td></td>
<td>S1</td>
<td>93.35/93.11</td>
<td>0.240 (−0.311, 0.791)</td>
<td>0.391</td>
</tr>
<tr>
<td></td>
<td>H1</td>
<td>93.47/93.25</td>
<td>0.220 (−0.300, 0.740)</td>
<td>0.405</td>
</tr>
<tr>
<td></td>
<td>N2</td>
<td>71.21/71.09</td>
<td>0.127 (−0.342, 0.595)</td>
<td>0.594</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>70.89/70.95</td>
<td>−0.067 (−0.512, 0.378)</td>
<td>0.768</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>67.31/67.19</td>
<td>0.113 (−0.388, 0.655)</td>
<td>0.621</td>
</tr>
<tr>
<td></td>
<td>L2</td>
<td>59.50/59.76</td>
<td>−0.260 (−0.771, 0.251)</td>
<td>0.316</td>
</tr>
<tr>
<td>GCC</td>
<td>Center</td>
<td>56.25/56.74</td>
<td>−0.487 (−1.678, 0.705)</td>
<td>0.421</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>118.61/118.19</td>
<td>0.427 (−0.312, 1.160)</td>
<td>0.256</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>111.22/111.05</td>
<td>0.167 (−0.419, 0.752)</td>
<td>0.575</td>
</tr>
<tr>
<td></td>
<td>S1</td>
<td>119.75/119.77</td>
<td>−0.013 (−0.702, 0.676)</td>
<td>0.970</td>
</tr>
<tr>
<td></td>
<td>H1</td>
<td>123.29/122.89</td>
<td>0.407 (−0.381, 1.195)</td>
<td>0.309</td>
</tr>
<tr>
<td></td>
<td>N2</td>
<td>124.48/124.57</td>
<td>−0.093 (−0.504, 0.320)</td>
<td>0.656</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>95.43/95.45</td>
<td>−0.013 (−0.540, 0.513)</td>
<td>0.960</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>112.13/112.07</td>
<td>0.053 (−0.359, 0.465)</td>
<td>0.798</td>
</tr>
<tr>
<td></td>
<td>L2</td>
<td>105.50/105.61</td>
<td>−0.113 (−0.577, 0.350)</td>
<td>0.630</td>
</tr>
<tr>
<td>ORL</td>
<td>Center</td>
<td>181.67/181.80</td>
<td>−0.127 (−0.663, 0.360)</td>
<td>0.608</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>191.08/191.49</td>
<td>−0.407 (−0.917, 0.104)</td>
<td>0.118</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>187.69/187.37</td>
<td>0.320 (−0.132, 0.772)</td>
<td>0.164</td>
</tr>
<tr>
<td></td>
<td>S1</td>
<td>189.89/189.76</td>
<td>0.127 (−0.475, 0.728)</td>
<td>0.678</td>
</tr>
<tr>
<td></td>
<td>H1</td>
<td>184.38/184.51</td>
<td>−0.127 (−0.650, 0.397)</td>
<td>0.653</td>
</tr>
<tr>
<td></td>
<td>N2</td>
<td>164.47/164.99</td>
<td>−0.520 (−1.138, 0.098)</td>
<td>0.098</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>164.11/164.23</td>
<td>−0.113 (−0.610, 0.384)</td>
<td>0.653</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>166.53/166.22</td>
<td>0.307 (0.150, 0.763)</td>
<td>0.186</td>
</tr>
<tr>
<td></td>
<td>L2</td>
<td>153.82/153.78</td>
<td>0.040 (−0.412, 0.492)</td>
<td>0.861</td>
</tr>
</tbody>
</table>
associated with pediatric diseases. In the present study, we provide the normative database for macular layer thicknesses in a large cohort of Chinese children using Topcon SS-OCT, showing the thickness distribution patterns and their correlated factors.

Macular layer thickness profiles with different OCT equipment have been reported in normal subjects (Table 5). However, most of the studies were conducted in adults, and using normative thickness data from the adults may affect the accuracy of disease diagnosis among children. As shown through the comparison of studies using the same Topcon SS-OCT device, the GCIPL, GCC, and ORL of children reported in the current study were considerably thicker than those of the adults.

Although a study reported macular layer thicknesses in normal children using Spectralis SD-OCT, the sample size was relatively small and was conducted in Caucasians. As ethnicity has been reported to be a determinant factor in macular layer thicknesses and high myopia was less common in Caucasians, data from the Caucasians may not be suitable for the Asians. Moreover, the database provided in the previous study is only applicable to the Spectralis OCT, because measurements are not interchangeable between different OCT device. The current study produced a normative pediatric database for Topcon SS-OCT device in the Asian population, compensating some deficiencies of previous studies.

FIGURE 4. Bland–Altman plot for macular GCIPL thicknesses before and after magnification correction. The Bland–Altman plot shows the mean difference in different subfields before and after magnification correction (solid line) and limits of agreement (dashed line). C, central macula; S1, inner superior; I1, inner inferior; N1, inner nasal; T1, inner temporal; S2, outer superior; I2, outer inferior; N2, outer nasal; T2, outer temporal.
Measurements of focal abnormalities in the macular layer thicknesses are more reliable indicators of diseases than overall change. An overall thinning of the GCIPL or GCC could be due to normal population variation, myopic retinal degeneration, or aging. A focal defect or thickening, however, would be highly unlikely in the absence of glaucoma or diabetic retinopathy, as well as other specific diseases. Therefore, the subfield analysis and thickness maps for the macular GCIPL, GCC, and ORL are valuable. In the present study, we also described the topographical distributions of GCIPL, GCC, and ORL according to the ETDRS grid, which were demonstrated to be consistent with both the retinal anatomy and the results of other studies.

Many studies have investigated demographic and ocular factors that affect macular thickness, such as age, sex, SER, AL, corneal curvature, BMI, and IOP. In the current study, we demonstrated that the macular GCIPL, GCC, and ORL thicknesses of children were significantly associated with age, sex, SER, and AL. We also provided the macular thickness profiles based on sex, age, SER, and AL status. However, the variations among different sex, age, SER, or AL groups were relatively small, especially the GCIPL and GCC, considering the depth resolution (8 μm) and measurement error (average test-retest variation of 2.89 μm for GCIPL, 3.21 μm for GCC, and 5.79 μm for ORL in reproducibility confirmation) of SS-OCT described in our previous study. Low variability across...
different demographic and ocular status could alleviate the interference from these factors unrelated to diseases. For example, pRNFL has been demonstrated to reduce significantly with increase in the degree of myopia; hence, it was difficult to distinguish glaucoma in high-myopia populations according to the normative pRNFL value. Therefore, measurements of macular layers, especially the GCIPL and GCC, are well-suited for disease diagnosis and monitoring.

The ocular magnification effect is one of the important compounding factors affecting both the individual macular thickness measurement and the relationship with other factors. Unfortunately, the magnification was not corrected before the image capture of the 3000 participants and the Topcon SS-OCT device is not designed to correct the magnification after imaging. We recruited another group of 149 children to be able to illustrate the effects of ocular magnification on the macular thickness measurements. The results of the magnification effect analysis in the current study suggested that the impact of the magnification effect on the individual macular layer thickness measurement and the relationship with other factors were minimal. In future studies, we are going to perform the magnification correction before the image capture, thus expecting more accurate results.

Strengths of the present study include the large sample size and school-based design, which make the study population representative because the attendance rate of primary and
### Table 5. Comparison of Representative Studies Concerning Macular Layer Thicknesses Measured by OCT in Healthy Subjects

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Instruments</th>
<th>Ethnicity</th>
<th>Sample Size</th>
<th>Age Mean (SD)</th>
<th>Average GCIPL, l</th>
<th>Average GCC, l</th>
<th>Average ORL, l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>Children</td>
<td>Topcon SS-OCT</td>
<td>Chinese</td>
<td>3000</td>
<td>11.67 (3.44) [6–19]</td>
<td>1447:1553</td>
<td>77.00 (4.78)</td>
<td>107.68 (5.95)</td>
</tr>
<tr>
<td>Yanni et al.</td>
<td>Children</td>
<td>Spectralis SD-OCT</td>
<td>Caucasians</td>
<td>83</td>
<td>45:38</td>
<td>60–15</td>
<td>84.6,*</td>
<td>79.7†</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>Adults</td>
<td>Topcon SS-OCT</td>
<td>Korean</td>
<td>60</td>
<td>23:37</td>
<td>20</td>
<td>73.56</td>
<td>104.89</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>Adults</td>
<td>Topcon SS-OCT</td>
<td>Mixed</td>
<td>22</td>
<td>15:7</td>
<td>15</td>
<td>70.5 (5.86)</td>
<td>107.9 (8.1)</td>
</tr>
<tr>
<td>Ueda et al.</td>
<td>Adults</td>
<td>Cirrus HD-OCT</td>
<td>Japanese</td>
<td>102</td>
<td>40:62</td>
<td>15</td>
<td>80.3 (5.86)</td>
<td>115.2 (6.95)</td>
</tr>
<tr>
<td>Mwanza et al.</td>
<td>Adults</td>
<td>Cirrus HD-OCT</td>
<td>Mixed</td>
<td>282</td>
<td>133:149</td>
<td>18–84</td>
<td>82.1 (5.62)</td>
<td>70.6</td>
</tr>
<tr>
<td>Demirkaya et al.</td>
<td>Adults</td>
<td>Topcon SD-OCT</td>
<td>Caucasians</td>
<td>120</td>
<td>63:57</td>
<td>18–81</td>
<td>70.6</td>
<td></td>
</tr>
<tr>
<td>Nieves-Moreno et al.</td>
<td>Adults</td>
<td>Spectralis SD-OCT</td>
<td>Caucasians</td>
<td>74</td>
<td>69.39</td>
<td>61.95 (9.58)</td>
<td>102.24</td>
<td></td>
</tr>
</tbody>
</table>

* Macular layer thicknesses of the parafoveal nasal area.
† Macular layer thicknesses of the parafoveal temporal area.
‡ Cirrus HD-OCT scan only provides macular layer thicknesses of the parafoveal area.

In summary, the present study provided normative values, distribution patterns, and correlated factors for thicknesses of macular GCIPL, GCC, and ORL in a large cohort of children 6 to 19 years of age. Numerous pediatric disorders affecting the retina and optic nerve can be identified according to the normative profiles provided in the current study.

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**References**


