Impact of Ethnicity on the Correlation of Retinal Parameters with Axial Length

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PURPOSE. To examine whether the relationship of axial length (AL) to retinal nerve fiber layer (RNFL) and macular parameters measured by optical coherence tomography (OCT) differs according to ethnicity.

METHODS. As part of the Sydney Myopia Study, 2353 children from grade 7 (age range, 11.1–14.4 years) completed detailed ocular examinations in the 2004–2005 school year. AL was measured with noncontact interferometry and Stratus OCT was performed (Carl Zeiss Meditec, Jena, Germany).

RESULTS. East Asian children displayed larger AL correlations with average RNFL, inferior RNFL, nasal RNFL outer macula, and macular volume (r = −0.25, −0.36, −0.31, −0.35, and −0.31, respectively; P < 0.001) than did Caucasian children (r = −0.14, −0.20, −0.12, −0.17, and −0.13 respectively; P < 0.001). Positive correlations between the temporal RNFL and AL were found only among East Asian and South Asian children (r = 0.28, P < 0.001; and r = 0.27, P = 0.03, respectively). In Caucasian children, the foveal minimum and central macula correlated significantly with AL (r = 0.11 and r = 0.13, respectively, P ≤ 0.001).

CONCLUSIONS. Retinal parameters measured by OCT correlated with AL, and the extent of this correlation varied by ethnicity. It may therefore be that ethnicity should be considered when interpreting OCT scans on individuals with AL outside the usual range. (Invest Ophthalmol Vis Sci. 2010;51:4977–4982) DOI:10.1167/iovs.10-5226

Optical coherence tomography (OCT) is used increasingly for the diagnosis and monitoring of ocular conditions, as it permits quantitative as well as qualitative assessment of retinal parameters. Quantitative measurement of retinal parameters using OCT has shown great potential to delineate pathology from physiology. Therefore, an accurate understanding of normal variation in different populations and ethnicities is important in using the full potential of this technology.

It has now been widely reported that Stratus OCT (Carl Zeiss Meditec, Jena, Germany) retinal measurements correlate with axial length (AL). In addition, there have been some reports of ethnic differences in retinal parameters measured by Stratus OCT, showing that Caucasians have a thicker central macula and a thinner retinal nerve fiber layer (RNFL) than do East Asian or African-American subjects. However, there are very few reports on whether the correlations between retinal parameters and AL vary by ethnicity. To our knowledge, only El-Dairi et al. have reported on this relationship. In their study of 286 healthy children (age range, 3–17 years), they showed that both RNFL and macular parameters were associated with AL in eyes of Caucasian, but not in those of African-American, subjects.

Examination of the relationship between AL and retinal parameters is important, as it allows clinicians to consider the context of retinal findings in individuals with AL outside the usual range. The purpose of this study was to explore the effect of AL on RNFL and macular measurements by Stratus OCT in different ethnic groups in a healthy adolescent population.

METHODS

The Sydney Myopia Study (SMS) is a population-based survey that was undertaken to evaluate childhood ocular conditions. The study was approved by the University of Sydney Human Research Ethics Committee. New South Wales Department of Education and Training, and the Catholic Education office. Written informed consent from one parent and verbal assent from each child were obtained before the examinations. The study adhered to the tenets of the Declaration of Helsinki. The study methods are described in detail elsewhere.

The city of Sydney was geographically stratified into deciles of different socioeconomic status (SES), based on the Australian Bureau of Statistics 2001 national census. Two schools were selected from the top SES decile, and the remainder randomly selected from the bottom nine deciles, with a proportional mix of public (n = 18) and private or religious schools (n = 3). All eligible year-7 students from these 21 high schools were invited to participate. The examinations were conducted in the 2004–2005 school year.

Examination

The ocular examination was conducted on both eyes of each participant by a group consisting of ophthalmologists, other medical practitioners, optometrists, and orthoptists. Visual acuity (VA) was assessed monocularly with a logarithm of minimum angle of resolution (log-MAR) chart, read at 244 cm (8 feet). Subjective refraction was performed to determine best corrected VA in children in whom presenting VA was <0.02 logMAR units. AL measurement was performed with a noncontact partial coherence laser interferometry (OILMaster; Carl Zeiss Meditec). Cycloplegia was achieved with cyclopentolate 1% and tropicamide 1% administered twice (5 minutes apart); in addition, phenylephrine 2.5% was used if adequate mydriasis (≥6 mm) was not achieved. Autorefraction (Canon RK-F1; Canon, Tokyo, Japan) was performed at least 25 minutes after application of the eye drops.

Optical Coherence Tomography

The Stratus OCT (OCT3, software ver. 4.0.1; Carl Zeiss Meditec) obtains cross-sectional retinal tomographic scans, that have been found to
be highly reproducible.\textsuperscript{18–20} OCT scans were conducted after cyclopia with the fast scan protocol, to measure macular and peripapillary RNFL parameters. The macular scans consisted of six radial scans each with 128 A-scans over a 6-mm distance. This macular thickness map was divided into three concentric areas with boundaries at 0.5, 1.5, and 3 mm from the scan center, termed the central, inner, and outer macula, respectively. The average of five macular scans was used in the analyses. The peripapillary RNFL was scanned with 256 A-scans arranged in a 3.4-mm radius circle centered on the optic disc, with the average of three circular scans used in analysis.

### Questionnaires

A comprehensive 193-item questionnaire was completed by the parents. Questions included demographic information, ocular and general medical history, and birth parameters. Ethnicity was self-reported by the participants’ parents, by choosing from a list of ethnicities including Caucasian (European), East Asian, Indian/Pakistani/Sri Lankan, African, Melanesian/Polynesian, Middle Eastern, Indigenous Australian, and South American and other. A child was considered to belong to a specific ethnic group if both parents self-identified with a common ethnicity; otherwise, the child was classified as having mixed ethnicity.

### Statistical Analysis

Only scans that were complete and had a signal strength greater than 5 were used in our analyses. To compare various characteristics (age, sex, refractive error, visual acuity, height, weight, and axial length) of participants with those of nonparticipants, we used the $\chi^2$ test of proportions and the $t$ test to compare means between groups. Means and standard deviations of retinal parameters and correlation coefficients of AL with retinal parameters were calculated. Partial correlation coefficients with adjustments for age, sex, height, and ethnicity were calculated for the whole sample. $R_{\text{max}}$ for retinal parameters with increasing AL was calculated using regression models with medians of quintiles for AL as independent variables. The Bonferroni correction was applied to all correlations (SAS software, ver. 9.1.3; SAS Institute, Cary, NC).

### Results

#### General and Retinal Characteristics

Of 3144 eligible children, 2353 were tested; for the others ($n = 791$), either we did not obtain parental consent for the child to participate in the study or the child was absent from school on days that testing was performed. Those with eye diseases ($n = 16$) including congenital glaucoma, optic nerve hypoplasia, microphthalmos, congenital nystagmus, and cortical blindness due to cerebral palsy and those with amblyopia ($n = 44$) were excluded. Of the remaining children, there were 2152 (91%) and 2068 (88%), respectively, with adequate-quality RNFL and macular scans; the characteristics of the included and excluded children are shown in Table 1. Subjective refraction was performed in 372 of the children. The four largest ethnic groups, Caucasian ($n = 1243$), East Asian ($n = 300$), South Asian ($n = 109$) and Middle Eastern ($n = 149$), considered separately from those of European Caucasian ethnicity, were used for the ethnicity-specific analyses.

East Asian, South Asian, and Middle Eastern children all had significantly longer AL than did the Caucasian children ($P < 0.001, <0.001$, and 0.002, respectively; Table 2). These subgroups also had significant differences in RNFL and macular thickness when compared with those of the Caucasian group. For example, the East Asian children had significantly thicker temporal and superior RNFL and thinner nasal RNFL than did the Caucasian children ($P < 0.001$).

#### Correlations

Partial correlation coefficients of the associations between retinal parameters and AL for the whole group, adjusted for age, sex, height, and ethnicity, are presented in Table 3. The average, inferior, nasal, and superior RNFL all correlated negatively with AL, whereas the temporal RNFL had a small positive correlation ($r = 0.12$, all $P \leq 0.001$). Inner macula, outer macula, and macular volume were all negatively correlated with AL ($P < 0.001$). Foveal minimum and central macular thickness were not significantly correlated with AL ($P > 0.05$).

AL correlations with retinal parameters, stratified by ethnicity, are shown in Table 4. Average, inferior, and nasal RNFL correlated negatively with AL in both Caucasian and East Asian children, with the East Asian children displaying larger correlations for these parameters ($r = -0.25$, $-0.36$, and $-0.31$, respectively, $P < 0.001$). Among both the East Asian and South Asian children, the temporal RNFL correlated positively with AL ($r = 0.28, P < 0.001$; and $r = 0.27, P = 0.03$, respectively). In the Caucasian children, there was only a very small positive correlation between AL and the temporal RNFL ($r = 0.08, P = 0.004$). The superior RNFL weakly correlated with AL only in the Caucasian children ($r = -0.08, P = 0.03$). We found no

### Table 1. Characteristics of Children with Included and Excluded Scans of the RNFL and Macula

<table>
<thead>
<tr>
<th></th>
<th>Included ($n = 2092$)</th>
<th>Excluded ($n = 202$)</th>
<th>Included ($n = 2031$)</th>
<th>Excluded ($n = 263$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr†</td>
<td>12.7 ± 0.4</td>
<td>12.7 ± 0.4</td>
<td>12.7 ± 0.4</td>
<td>12.7 ± 0.4</td>
</tr>
<tr>
<td>Boys, n (%)</td>
<td>1086 (51.9)</td>
<td>77 (38.1)*</td>
<td>1052 (51.8)</td>
<td>111 (42.2)*</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1263 (60.4)</td>
<td>107 (53.0)*</td>
<td>1224 (60.3)</td>
<td>146 (55.5)</td>
</tr>
<tr>
<td>East Asian</td>
<td>300 (14.3)</td>
<td>41 (20.3)*</td>
<td>291 (14.3)</td>
<td>50 (19.0)*</td>
</tr>
<tr>
<td>South Asian</td>
<td>109 (5.2)</td>
<td>18 (8.9)*</td>
<td>107 (5.3)</td>
<td>20 (7.6)</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>149 (7.1)</td>
<td>13 (6.4)</td>
<td>146 (7.2)</td>
<td>16 (6.1)</td>
</tr>
<tr>
<td>Other‡‡</td>
<td>271 (13.0)</td>
<td>25 (11.4)</td>
<td>263 (13.0)</td>
<td>31 (11.8)</td>
</tr>
<tr>
<td>SER†</td>
<td>0.51 ± 0.17</td>
<td>0.16 ± 0.15*</td>
<td>0.52 ± 0.14</td>
<td>0.16 ± 0.16*</td>
</tr>
<tr>
<td>VA, correct letters†</td>
<td>56.35 ± 5.81</td>
<td>55.55 ± 6.75</td>
<td>56.4 ± 5.6</td>
<td>55.2 ± 7.8*</td>
</tr>
<tr>
<td>AL, mm‡</td>
<td>23.39 ± 0.81</td>
<td>23.41 ± 0.91</td>
<td>23.38 ± 0.81</td>
<td>23.45 ± 0.91</td>
</tr>
<tr>
<td>Height, cm‡</td>
<td>156.1 ± 7.88</td>
<td>156.6 ± 7.6</td>
<td>156.1 ± 7.9</td>
<td>156.3 ± 7.5</td>
</tr>
<tr>
<td>Weight, kg†</td>
<td>50.31 ± 13.04</td>
<td>49.20 ± 11.86</td>
<td>50.39 ± 13.09</td>
<td>48.90 ± 11.72</td>
</tr>
</tbody>
</table>

† SER, spherical equivalent; VA, logMAR visual acuity.
* $P < 0.05$ included versus excluded children.
† Mean ± SD.

- **SER**, spherical equivalent; **VA**, logMAR visual acuity.
- * $P < 0.05$ included versus excluded children.
- † Mean ± SD.
significant AL correlations with RNFL parameters in the subgroup of Middle Eastern children.

The foveal minimum and central macular thickness had significant AL correlations in the Caucasian children. (r = 0.11, P = 0.001; and r = 0.13, P < 0.001, respectively). The inner macula had a negative AL correlation only in the East Asian children (r = −0.16, P = 0.05), whereas outer macular thickness had negative correlation with AL in all ethnicities. Macular volume showed negative correlations in Caucasian, East Asian, and Middle Eastern children (Table 4).

**DISCUSSION**

We found significant AL correlations with RNFL and macular parameters in a large adolescent population. Temporal RNFL correlated positively with AL, whereas other RNFL quadrants had a negative correlation with AL. Further, the inner and outer macular thickness and macular volume correlated negatively with AL. Although these overall patterns were seen in the different ethnic subgroups, there were differences in the magnitude of the correlations between groups. We were unable to find significant correlations for most parameters in South Asian and Middle Eastern children, examined separately from European Caucasian and East Asian children.

**RNFL Thickness**

Previous reports have largely indicated a negative AL correlation with the RNFL, as shown in Table 5. Direct comparison with these earlier studies is difficult because of differences in the measurement protocols and statistical analyses used. However, only two studies failed to show a statistically significant negative AL correlation with the RNFL. In one of these studies, Hoh et al. used OCTI technology rather than Stratus OCT and ultrasound biometry rather than a noncontact optical biometer; in the other study, Vernon et al. examined a very small sample (n = 31).

An explanation of RNFL thinning with increasing AL is that longer eyes have a larger area over which retinal ganglion cell axons are spread, resulting in a thinner RNFL. A second possible explanation is that this finding represents an artifact of OCT scanning. As OCT is an optical system, the scan circle projected onto the retina in longer eyes is larger than the scan circle in shorter eyes. As suggested in previous reports, this enlarged scan circle could lead to an underestimation of RNFL thickness, as the RNFL thickness decreases with increasing distance from the disc margin.

Few studies have been conducted to examine the relationship of AL to RNFL thickness in different quadrants. The finding that the temporal RNFL positively correlates with AL and negatively with myopia has recently been reported and is in keeping with our findings. In two studies, the investigators failed to find an AL correlation with the temporal RNFL. In one, Rauscher et al. studied a small sample (n = 28), and in the other, Leung et al. included subjects covering a very wide age range (22–60 years), a known confounder for RNFL thickness, which could have explained the discrepancy with our findings.

A possible explanation for an AL-related increase in the temporal RNFL thickness was provided by Kim et al. who suggested that the retina may be dragged toward the temporal horizon as the AL increases, resulting in a thickened RNFL from the overlapping of nerve fiber bundles at the temporal sector. This hypothesis is in agreement with our finding of a thicker temporal RNFL in eyes with longer AL.

**Macular Thickness**

Table 6 provides a summary of findings from other studies on the correlation of AL with macular OCT parameters. Both inner and outer macular thicknesses were found to have negative correlations with AL by some investigators, findings that are in agreement with ours. Wakitani et al. using the older generation OCT (Humphrey 2000 OCT; Carl Zeiss Meditec), failed to find an AL correlation with inner macular thickness. The different scanning protocol for this system results in scans not directly comparable to Stratus OCT, so we could not compare the findings.
TABLE 4. Correlation Coefficients of Retinal Parameters with AL Stratified for Ethnicity

<table>
<thead>
<tr>
<th>Source</th>
<th>OCT Version</th>
<th>Ethnicity</th>
<th>Age (y)</th>
<th>n</th>
<th>Correlation of Average RNFL with AL</th>
<th>Correlation Coefficient</th>
<th>Regression Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huynh et al.</td>
<td>Stratus</td>
<td>Mixed</td>
<td>5–7</td>
<td>1765</td>
<td>Negative*</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Budenz et al.</td>
<td>Stratus</td>
<td>Mixed</td>
<td>18-85</td>
<td>328</td>
<td>Negative</td>
<td>NR</td>
<td>$-2.24; P &lt; 0.0001$</td>
</tr>
<tr>
<td>Nagai-Kusuhara et al.</td>
<td>Stratus</td>
<td>Japanese</td>
<td>20-65</td>
<td>162</td>
<td>Negative</td>
<td>NR</td>
<td>$-1.77; P = 0.011$</td>
</tr>
<tr>
<td>Hoh et al.</td>
<td>OCT 1</td>
<td>Chinese/Malay/Indian</td>
<td>19-24</td>
<td>152</td>
<td>No correlation</td>
<td>0.03; $P = 0.75$</td>
<td>NR</td>
</tr>
<tr>
<td>Leung et al.</td>
<td>Stratus</td>
<td>Chinese</td>
<td>22-60</td>
<td>115</td>
<td>Negative</td>
<td>$-0.31; P = 0.0001$</td>
<td>NR</td>
</tr>
<tr>
<td>Vernon et al.</td>
<td>Stratus</td>
<td>Caucasian (UK)</td>
<td>35-60</td>
<td>31</td>
<td>No correlation†</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>El-Dairi et al.</td>
<td>Stratus</td>
<td>Caucasian (US)§</td>
<td>5-17</td>
<td>154</td>
<td>Negative</td>
<td>$-0.27; P &lt; 0.001$</td>
<td>NR</td>
</tr>
<tr>
<td>Sony et al.</td>
<td>Stratus</td>
<td>Indian</td>
<td>20-70</td>
<td>146</td>
<td>No correlation</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR, not reported.

* $P_{\text{trend}} < 0.0001$.

† Tendency for mean RNFL to decrease with increasing AL ($P = 0.17$).

§ Caucasian subgroup of 286 children. No correlation of AL with RNFL reported for whole group.
In summary, AL affected OCT-measured retinal parameters in our population. We demonstrated that there is overall thinning of RNFL and macular parameters with increases in AL. The strengths of these correlations appeared to be more prominent in the East Asian children than in the Caucasian children. Therefore, ethnicity may be a consideration when interpreting OCT scans on individuals with AL outside the usual range.

References


