Association Between Retinal Thickness of 64 Sectors in Posterior Pole Determined by Optical Coherence Tomography and Axial Length and Body Height

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Purpose. We determined a significant correlation between the retinal thickness (RT) in 64 cells or sectors of the posterior pole, and the axial length (AL) and the body height (BH).

Methods. A prospective, observational cross-sectional study of 64 right eyes of 64 healthy volunteers (mean age, 26.0 ± 4.5 years; range, 22–39 years). The RT within the central 24° area was measured in the Spectralis spectral domain-optical coherence tomographic (SD-OCT) images. The correlations between the RT and the AL or the BH were determined by linear regression analyses.

Results. The mean ± SD of the AL was 25.04 ± 1.30 mm, and that of the BH was 167.2 ± 8.5 cm. The RTs of the central four cells around the fovea were not significantly correlated with the AL. The RTs of 54 cells were significantly and negatively associated with the AL (r = −0.25 to −0.56, P < 0.05). In contrast, the RTs of the central to temporal eight cells were significantly and positively correlated with the BH (r = 0.26–0.37, P < 0.05). The RTs of 56 cells were not significantly correlated with the BH.

Conclusions. The RT of the posterior retina, except in the fovea, decreased as AL elongated, and those of the central temporal areas were significantly correlated with the BH. Thus, the AL and BH must be considered when the RT is evaluated. The 64-sector analysis on OCT is useful to assess the detailed changes of RT affected by them. (http://www.umin.ac.jp/ctr/index.htm number, UMIN000007154.)

Keywords: myopia, body height, retinal thickness, fovea

Evidence has been accumulating that the retinal thickness (RT) determined by optical coherence tomography (OCT) is an important parameter for diagnosing different types of retinal diseases. The RT can be measured noninvasively in the OCT images, not only to determine its relationship to other biophysical parameters of the body, but also to evaluate the effectiveness of treatments.1–5 To take advantage of this technology, which can determine the RT repeatedly and noninvasively, it is essential to determine the RT of normal subjects to construct a normative database. There is good evidence that the RT is affected by degree of reflection of the retinal structures, axial length (AL) of the eye, and age.4–18 Understanding how these parameters affect the RT is essential for evaluating the pathologic conditions of the eyes, and also that of eyes with high myopia. In biomedical measurements of any structure of the body, the relationship of the structure to the body size is important. Thus, there is a significant relationship between the AL of the eye and the body height (BH).19–21 This is important especially when RT measurements are made with the spectral-domain OCT (SD-OCT), because it can measure the RT with a resolution of micrometers.22–24 As best we know, the relationship between the RT in different sectors or cells of the posterior pole of the eye and the BH of healthy subjects has not been reported.

To study the effect of early treatment on the retina of eyes with diabetic retinopathy, the Early Treatment Diabetic Retinopathy Study (ETDRS) group divided the posterior pole of the eye into nine macular sectors; the fovea, four inner ring sectors, and four outer ring sectors. This sectoring is used frequently to evaluate local retinal changes in eyes with different retinal diseases. It has been reported that the thickness of the fovea was not correlated significantly with the AL, but the thickness of the perimacular sectors were correlated negatively with the AL.7,8,14,17,18 Although, this is an artificial areal sectoring, and it may not necessarily be the optimal way to sector the posterior pole of the eye. For example, the RT of a specific area can be influenced by the presence of blood vessels and the retinal nerve fiber layer, and the influence of these structures would be masked when the sector is large. Thus, these characteristics in a focal area would not necessarily be detected when only nine relatively large sectors are analyzed. To differentiate the data between the normal and diseased eyes more accurately, it is necessary to obtain more detailed data from normal retinas.

A more detailed sectoring of the posterior pole of the eye has been developed. The Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) can calculate the RT of 64 sectors or cells within the central 24° area obtained by a posterior pole asymmetry (PPA) scan (Fig. 1A).25,26 The 64-cell map may be better than the ETDRS nine macular sector map (Fig. 1B) for investigating the relationships between the RT and other factors that might affect the RT. To the best of our knowledge, there are no studies determining the
study was conducted as a part of this study. An analysis of the optic disc and the retinal nerve fiber in myopic and myopic eyes was used for the analyses. In the end, the right eyes of 64 individuals (42 men and 22 women) were used for the analyses. Five other eyes were excluded because of segmentation error in the RT. One eye was excluded due to a superior segmental optic disc anomaly; known systemic diseases, such as hypertension and diabetes; presence of visual field defects; and prior refractive or intraocular surgery. None of the eyes was initially excluded as determined by examining their medical history were included. All of the eyes had a standard ocular examination, including slit-lamp biomicroscopy of the anterior segment; ophthalmoscopy of the ocular fundus; IOP measured with a pneumotonometer (CT-80; Topcon, Tokyo, Japan); and the AL measured with the AL-2000 ultrasound instrument (Tommy Corporation, Nagoya, Japan). The refractive error (spherical equivalent) was measured with the Topcon KR8800 autorefractometer/keratometer (Topcon). All eyes were examined by a single examiner (TY) in the main part of the study, but, additionally, 17 eyes were examined by a second examiner (YK) as described in the Supplementary Material. Just before the eye examination, the BH was measured with the participants standing without shoes by a single examiner (KY). The body weight also was measured without excess clothing and shoes by two examiners (MT and KN).

The RT was measured with the Spectralis SD-OCT (Heidelberg Engineering) using the images obtained by PPA scans. In this protocol, the OCT instrument automatically draws a horizontal line connecting the center of the fovea and the center of the optic disc as a reference line. Then, 61 line scans (1024 A scans/line) parallel to the reference line within the central 35 ° × 30 °, and five overlapping B-scan/image were taken. The embedded OCT software determined the distance between the internal limiting membrane and the Bruch’s membrane, and recorded it as the RT. Then, 3-dimensional (3D) RT maps were made. The quality of the scans was indicated by a color scale at the bottom of the scan images, where it had to be in the green range to be considered a good quality scan. In addition, the SD-OCT macular map provided a color scale representation of the topographic RT, which helped evaluate the image quality. We examined all of the B-scan images of each eye to determine whether there were any segmentation errors in the images. The following criteria were used to identify segmentation errors in the B-scan: obvious disruption or abrupt changes of the detected border for 5% consecutive or 20% cumulative of the entire image. Five eyes were excluded because of segmentation error in the RT. The average RT of each 8 × 8 (3° × 3°) sector, which made up of the 64 sectors, was determined (Fig. 1A).

### Methods

All of the procedures used conformed to the tenets of the Declaration of Helsinki. A written informed consent was obtained from all subjects after an explanation of the procedures to be used. The study was approved by the Ethics Committee of Kagoshima University Hospital, and it was registered with the University Hospital Medical Network (UMIN) clinical trials registry (CTR). The registration title was, ‘‘Morphological analysis of the optic disc and the retinal nerve fiber in myopic eyes’’ and the registration number was UMIN000007154. A detailed protocol is available at https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=00007154/language=J. The present study was conducted as a part of this study.

### Subjects

This was a cross-sectional, prospective, observational study. We examined 72 eyes of 72 individuals between February 1, 2011 and February 20, 2012. Volunteers with no known eye diseases as determined by examining their medical history were included. All of the eyes had a standard ocular examination, including slit-lamp biomicroscopy, ophthalmoscopy, and OCT; best-corrected visual acuity of ≥0.1 logarithm of the minimum angle of resolution (logMAR) units; and IOP ≤21 mm Hg. The exclusion criteria were eyes with known ocular diseases, such as glaucoma, staphyloma, and optic disc anomaly; known systemic diseases, such as hypertension and diabetes; presence of visual field defects; and prior refractive or intraocular surgery. None of the eyes was initially excluded as determined by examining their medical history were included. A total of 72 Japanese volunteers was screened for this project. One eye was excluded due to a superior segmental optic disc hypoplasia, and two eyes because of prior refractive surgery. Five other eyes were excluded because of segmentation error in the RT. In the end, the right eyes of 64 individuals (42 men and 22 women) were used for the analyses.

### Measurement of AL, Refractive Error, and RT of 64 Sectors in Posterior Pole

All of the eyes had a standard ocular examination, including slit-lamp biomicroscopy of the anterior segment; ophthalmoscopy of the ocular fundus; IOP measured with a pneumotonometer (CT-80; Topcon, Tokyo, Japan); and the AL measured with the AL-2000 ultrasound instrument (Tommy Corporation, Nagoya, Japan). The refractive error (spherical equivalent) was measured with the Topcon KR8800 autorefractometer/keratometer (Topcon). All eyes were examined by a single examiner (TY) in the main part of the study, but, additionally, 17 eyes were examined by a second examiner (YK) as described in the Supplementary Material. Just before the eye examination, the BH was measured with the participants standing without shoes by a single examiner (KY). The body weight also was measured without excess clothing and shoes by two examiners (MT and KN).

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### Interobserver and Intervisit Reproducibility

Interobserver and intervist reproducibility was investigated in the right eyes of 17 young healthy Japanese volunteers. The interobserver or the intervisit correlation coefficients were calculated using a 2-way mixed-effects model for measurements of absolute agreement. The interobserver correlation coefficients of 64 cells RT were greater than 0.97 (range, 0.974–0.999; median, 0.990; Supplementary Fig. S1). The intervisit correlation coefficients of 64 cells RT were greater than 0.93 (range, 0.939–0.998; median, 0.988; distribution Supplementary Fig. S2). The interobserver and intervist reproducibility of the PPA scan was excellent. Therefore, one scan was sufficient to measure the mean RT of 64 cells in the PPA scan. A detailed description of the methods and results is presented as supplementary materials with Supplementary Figures S1 and S2.

### Table: Participants Data

<table>
<thead>
<tr>
<th>Age, y</th>
<th>26.0 ± 4.5</th>
<th>22–39</th>
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</thead>
<tbody>
<tr>
<td>Sex, M/F</td>
<td>42/22</td>
<td></td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
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<td>−14.25–0.00</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>25.0 ± 1.3</td>
<td>22.4–28.2</td>
</tr>
<tr>
<td>Body height, cm</td>
<td>167.3 ± 8.5</td>
<td>149.5–185.5</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>63.8 ± 13.2</td>
<td>42.7–119.0</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.6 ± 3.4</td>
<td>16.9–40.3</td>
</tr>
</tbody>
</table>
The mean ± SD RTs (in micrometers) for the 64 cells in the posterior pole of the eye. F, fovea; D, optic disc.

**Statistical Analyses**

All statistical analyses were performed with the SPSS statistics 21 for Windows (SPSS, Inc., IBM, Somers, New York). The relationships between the AL, BH, and refractive error were determined by calculating the Pearson coefficients of correlation. The relationships between the RT of each of the 64 cells and the AL or BH were determined by calculating the Pearson coefficients of correlation. The relationships between any two variables, for example, RT and AL, were investigated by partial correlation analysis after excluding the effects of the third variable (BH).

**Results**

The demographic information of the patients is presented in the Table. The mean ± SD of the age was 26.0 ± 4.5 years, and the mean refractive error (spherical equivalent) was −4.1 ± 3.1 diopters (D). The mean AL was 25.0 ± 1.3 mm, and the mean BH was 167.3 ± 8.5 cm. The mean RTs of the 64 cells are shown in Figure 2.

**Pearson’s Correlation Coefficients Between BH, AL, and Refractive Error**

The refractive error and AL were significantly and negatively correlated (R = −0.79, P < 0.001). The BH (R = 0.19, P = 0.14) and the body mass index (BMI) were not significantly correlated with the AL (R = 0.24, P = 0.06). The body weight was significantly and positively correlated with the AL (R = 0.26, P = 0.038).

**Pearson’s Correlation Coefficient and Partial Correlation Coefficient Between RT of Each of 64 Cells and AL and BH**

The RTs of the four cells surrounding the fovea were not significantly correlated with the AL. The RTs of 54 cells were significantly and negatively correlated with the AL (R = −0.25 to −0.56, P < 0.05). In contrast, the RTs of the eight temporal cells around the fovea were significantly and positively correlated with the BH (R = 0.26–0.37, P < 0.05). The RTs of 56 cells were not significantly associated with the BH (Fig. 3).

The body weight was significantly correlated with the RT of three cells (R = 0.26–0.31, P < 0.05). However, these cells were distributed randomly with no obvious pattern. We concluded that the RTs are not significantly correlated with the body weight. Thus, these three cells were excluded from the following analyses. The BMI was not significantly associated with the RT of any of the 64 cells.

After excluding the effect of the BH, partial correlation analysis showed that the correlations between the RT of the 64 cells and the AL were similar to those determined by the Pearson’s correlation analyses. In contrast, after excluding the effect of the AL, the number of cells in which there was a significantly correlation between the RT and the BH increased from eight to 19 sectors (R = 0.26–0.39, P < 0.05, Fig. 4). The cells not significantly associated with the AL not only were distributed in the central area, but also extended in an arch-like line from the optic disc area along the lower temporal arcade (Figs. 3, 4).

**Discussion**

We investigated the RT of young healthy subjects using smaller sectors (3° × 3°) in a larger area (24°) of the posterior pole than that examined in earlier studies.7,8,14,17,18 As a result, we obtained several new findings. First, the RTs of the eight temporal cells of the fovea and its lateral neighbors were significantly and positively correlated with the BH, and the RTs of the other 56 cells were not significantly associated with the BH (Fig. 3B). Even after excluding the effect of AL, partial correlation coefficient analysis showed that the cells corresponding to the central and temporal retina were significantly correlated with the BH (Fig. 4B). We concluded that the foveal sectors and the sectors temporal to the fovea are thicker, and the thickness increases as BH increases in young Japanese individuals.

On the other hand, most of the other sectors were not significantly associated with the BH. The exact reason for this was not determined, but earlier studies and our results showed that the thickness of the perimacular area decreases significantly with an increase in the AL of the eye.7,8 So, this effect may cancel out the thicker retina in taller individuals.

The macular thickness was not significantly associated with the AL, so that a thicker retina should be present regardless of the increased AL.
the AL. The sectors temporal to the fovea were the areas of thinner retinal nerve fiber layer originally. Thus, the change of retinal nerve fiber layer with axial elongation may contribute minimally in this area. This structural feature may be due to this finding. This information could not have been obtained without using an analysis of these highly sectored areas.

In terms of the AL, the RTs of the four foveal sectors (6° × 6°) were not significantly associated with the AL, but the RT of 54 other cells was significantly and negatively associated with the AL. These findings are partly compatible with the previous reports using the nine-sectoring method. In the nine sector studies, no correlation was found between AL and the thickness of central macular areas, which corresponded to the four foveal sectors of the 64-sector grid.\(^{14,17}\) Studies of young subjects using the nine-sectoring method showed that the retinal thinning with increasing AL occurred in the outer and inner macular regions, but not in the central macula.\(^{7,8}\)

Most population-based studies have shown a significant positive correlation between the BH and AL of the eye.\(^{19–21}\) However, we found that there was no significant correlation between the BH and AL. We cannot explain this discrepancy; however, similar discrepancies sometimes are observed even in large population studies. For example, the central corneal thickness was significantly correlated with BH in the Tajimi Study,\(^{29}\) but not so in the Central India Eye and Medical Study.\(^{31}\) This discrepancy should be studied in a future study with a larger number of subjects. In addition, this discrepancy might have arisen because our population tended to be more myopic with longer AL; the mean AL of this study was 25.0 mm, but it was less than 24 mm in other studies. Also, our study sample had a narrow age distribution. These may the causes for the nonsignificant correlation between the BH and AL.

To our knowledge, this is the first study to investigate the relationship between the BH and RT, and a positive and significant correlation between the RT of the macula and BH was found. However, additional studies with a larger sample size and measurements of the thicknesses of the individual retinal layers are needed to determine whether there are patterns in the correlations between individual retinal layer thicknesses and the AL.

Our results and those of earlier studies showed that the thinning of the retina with increasing AL was not present in the central macular area.\(^{7,8,14,17,18}\) These findings suggested that there may be a mechanism to maintain the central RT stable even with an elongation of the AL. The maintenance of central RT would be important for the development of normal visual function. However, this was a cross-sectional study, and the elongation of the AL was not really evaluated. To answer this question, a cohort longitudinal study of the same group of individuals is necessary.

We used sectorialized measurements for the AL and BH. The distribution of the sectors with significant correlations between the AL or the BH and RT had a regularity that was similar to earlier findings. Therefore, we concluded that these findings were valid. Another limitation was that the study population was made up of young Japanese volunteers who are known to belong to the most myopic group in the world.\(^{29}\) Thus, our results describe the characteristics of young myopic eyes, but might not necessarily hold for older and nonmyopic populations. Additionally, the number of female participants was smaller than that of male participants (42 men versus 22 women). We performed the same analysis by sex; however, the effect of sex could not be observed clearly, probably due to the small number of female participants (See Supplementary Materials). An epidemiologic study should help generalize the present results to other populations.

In summary, we found that the RTs of the fovea and temporal retina are correlated positively with the BH. The RT of the most posterior polar sectors decreased as the AL elongated. However, there was no significant correlation between the AL and RT of the four foveal sectors. With an advancement of OCT, more accurate and representative normative databases are needed to make correct diagnosis and management of retinal diseases. The present information would be of great help for this purpose. Thus, we concluded that the macular RTs are distributed with region-specific variations. These data should be valuable when interpreting macular parameters for diagnosis and monitoring of disease severity and progression.

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References


