Anatomy and Pathology/Oncology

Retinal Thickness and Axial Length

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PURPOSE. To examine the relationships between axial length and foveal and peripheral retinal thickness.

METHODS. Using optical coherence tomography, foveal retinal thickness was measured in participants of the population-based Beijing Eye Study without optic nerve or macula diseases. Inner and outer nuclear layer thickness as surrogate for retinal thickness was assessed in the fundus periphery in human globes enucleated due to malignant uveal melanoma or painful glaucoma.

RESULTS. The study included 1117 individuals with a mean age of 64.2 ± 9.7 years (range: 50–93 years) and mean axial length of 23.4 ± 1.04 mm (range: 20.29–28.68 mm). In multivariate analysis, thicker central foveal thickness was associated with male sex (P < 0.001; standardized regression coefficient beta: −0.13; nonstandardized regression coefficient B: −5.84; 95% confidence interval (CI): −8.56, −3.13); urban region of habitation (P = 0.02; beta: 0.07; B: 3.56; 95% CI: 0.55, 6.57); thinner lens thickness (P = 0.01; beta: −0.08; B: −5.11; 95% CI: −9.01, −1.21); and longer axial length (P < 0.001; beta: 0.13; nonstandardized regression coefficient B: 3.13; 95% CI: 2.41, 5.17). In the same multivariate model, superior, inferior, and temporal foveal thickness was not significantly associated with axial length (P = 0.26, P = 0.19, P = 0.08, respectively), while thicker nasal foveal thickness was associated with longer axial length (P = 0.009; beta: 0.09; B: 1.50; 95% CI: 0.37, 2.62). In the histomorphometric part of the study including 52 eyes (sagittal diameter: 27.0 ± 4.2 mm; range: 22–37 mm), mean thickness of the inner and outer nuclear layers at the equator and at the midpoint equator/posterior pole decreased with longer axial length (P < 0.001; beta: −0.48; and P = 0.02; beta: −0.44, respectively).

CONCLUSIONS. Myopic axial globe elongation was associated with retinal thinning in the equatorial and pre-equatorial region, while foveal retinal thickness was mostly unaffected by axial length. It suggests that axial elongation takes place predominantly in the equatorial and pre-equatorial region of the eye.

Keywords: retinal thickness, axial elongation, myopia, axial length, Beijing eye study

The prevalence of myopia has been increasing worldwide, with the steepest rise in frequency in the young generations in East and Southeast Asia.1 Assuming that the so-called “school myopia” is similar to adult myopia with an increased likelihood of myopic retinopathy and glaucomatous optic neuropathy, myopia could become the worldwide leading cause for irreversible visual impairment and blindness as these younger generations age.2,3 It is thus imperative that the process of myopization be better understood.

Previous investigations revealed that the myopic enlargement of the globe was predominantly an axial elongation while the horizontal globe diameter and vertical globe diameter increased only by a fraction of the increase in axial length.4,6 Studies also showed that the disc-fovea distance increased with longer axial length, while the length of macular Bruch’s membrane length did not differ between axially elongated eyes and eyes with a normal axial length.7 The increase in the disc-fovea distance was predominantly due to the development and enlargement of parapapillary gamma zone defined as an area free from Bruch’s membrane at the temporal optic disc border.7,8 If the length of Bruch’s membrane in the macular region did not elongate with longer axial length, the assumption was made that the thickness of the retina in the macular region should not be affected by axial elongation, since the retinal pigment epithelium with attached photoreceptors is anchored to Bruch’s membrane. It would fit with reports that best corrected visual acuity was independent of axial length in eyes without myopic retinopathy.9 We therefore conducted this study to address the question: Parallel to the length of Bruch’s membrane, is retinal thickness in the foveal region independent...
of axial length? We chose a population-based recruitment of the study participants to reduce the possibility of a selection bias by a referral of patients.

Previous experimental studies have suggested that the peripheral retina participates in eye growth regulation.\textsuperscript{10-13} Other investigations postulated a model in which the myopic enlargement of the globe was mainly an axial elongation, changing the globe shape from a sphere to an elongated tube with two hemispheres at its ends. In that hypothetical model, the myopic globe enlargement would occur mainly by an elongation of the globe walls in the retroequatorial region. If the latter model of a myopia-associated elongation of the lateral globe walls was correct, one would infer that the retina in the equatorial and pre-equatorial regions in contrast to the macular retina would decrease in thickness with longer axial length. To test that assumption, we carried out, as the second part of our study, a histomorphometric examination of the peripheral retinal thickness in human enucleated globes. We took enucleated globes since in vivo measurements of the peripheral retinal thickness were not available and technically difficult to obtain.

**Methods**

The Beijing Eye Study 2011 was a population-based cross-sectional study in Northern China. The medical ethics committee of the Beijing Tongren Hospital approved the study protocol and all participants gave informed written consent. The only eligibility criterion for inclusion into the study was an age of 50+ years. Out of 4403 eligible individuals, 3468 (78.8%) individuals participated in the survey. Mean age was 64.6 ± 9.8 years (median, 64 years; range, 50–93 years). Among the 3468 subjects, 1633 (47.1%) individuals lived in the rural region and 1835 (52.9%) individuals lived in the urban region. The study was described in detail previously.\textsuperscript{3,14}

All study participants underwent an interview with standardized questions on socioeconomic parameters, physical activity, and known major systemic diseases. An ophthalmic examination included measurement of best corrected visual acuity, slit lamp examination of the anterior segment, tonometry, biometry using optical low-coherence reflectometry (Lenstar 900 Optical Biometer; Haag-Streit, 3098 Koeniz, Switzerland), and photography of the cornea, lens, macula, and optic disc. Using spectral-domain optical coherence tomography (OCT) Spectralis; Heidelberg Engineering Co., Heidelberg, Germany) with the enhanced-depth imaging modality, we obtained images of the fovea. Using the scan running through the fovea, we measured the thickness of the subfoveal chorioid. Retinal thickness was measured by spectral-domain (SD)-OCT (iVue; Optovue Inc., Fremont, CA, USA) in a randomized subgroup of the study population. Retinal thickness was determined mainly based on the automatic alignment of the retina layers. The alignment was checked by an ophthalmologist, who was masked from other parameters, and known major systemic diseases. An ophthalmic examination included measurement of best corrected visual acuity, slit lamp examination of the anterior segment, tonometry, biometry using optical low-coherence reflectometry (Lenstar 900 Optical Biometer; Haag-Streit, 3098 Koeniz, Switzerland), and photography of the cornea, lens, macula, and optic disc. Using spectral-domain optical coherence tomography (OCT) Spectralis; Heidelberg Engineering Co., Heidelberg, Germany) with the enhanced-depth imaging modality, we obtained images of the fovea. Using the scan running through the fovea, we measured the thickness of the subfoveal chorioid. Retinal thickness was measured by spectral-domain (SD)-OCT (iVue; Optovue Inc., Fremont, CA, USA) in a randomized subgroup of the study population. Retinal thickness was determined mainly based on the automatic alignment of the retina layers. The alignment was checked by an ophthalmologist, who was masked from other measurement data specific to the study participant. Manual adjustment was carried out (e.g., in the case of a retinal surface abnormality in eyes with an epiretinal membrane or with a vitreoretinal traction). Full retinal thickness was defined as the distance between the inner limiting membrane and the apical boundary of the retinal pigment epithelium. Central foveal thickness was defined as the thickness of the retina in the center of the foveal pit. All techniques applied in the study have been described in detail previously.\textsuperscript{3,13,15}

Inclusion criteria for the present study were the availability of OCT data of the macular retina and the absence of glaucomatous optic nerve damage; diabetic retinopathy; retinal vein occlusion; early, intermediate, or late age-related macular degeneration; and myopic retinopathy as defined recently.\textsuperscript{16} Only one eye per subject was included into the study.

For the histomorphometric part of the study, we examined human globes which had been fixed in a solution of 4% formaldehyde and 1% glutaraldehyde immediately after enucleation. The globes had been enucleated due to malignant melanomas or due to painful end-stage glaucoma. After measuring the sagittal, horizontal, and vertical globe diameters, a segment running through the optic nerve head and the pupil was cut out of the fixed globes, dehydrated in alcohol, embedded in paraffin, sectioned for light microscopy, and stained by the periodic-acid-Schiff method or with hematoxylin-eosin. The meridional direction of the segment depended on the location of the tumor in the group of eyes with a malignant choroidal melanoma. In all other globes, the sections were horizontally oriented. For all eyes, one section with a thickness of 8 μm and which ran through the central part of the optic nerve head was taken for further evaluation. The landmark used to identify the posterior pole was the macula characterized by a multilayered retinal ganglion cell layer. The equator was defined as the region with the longest coronal globe diameter. Using a light microscope with an built-in millimeter scale, an objective with a magnification of ×25, and an ocular with a magnification of ×10, the thickness of the inner nuclear layer and outer nuclear layer of the retina was measured at the equator, at the midpoint between the posterior pole and the equator, and at the midpoint between the equator/posterior pole midpoint and the posterior pole. We used the thickness measurements of the inner and outer nuclear layers instead of the total retinal thickness since some eyes showed some artefactual changes in the plexiform layers. The technique has been described recently.\textsuperscript{17}

A commercially available statistical software package (SPSS for Windows, version 22.0; IBM-SPSS, Inc., Chicago, IL, USA) was used for the statistical analysis. We first calculated the mean and standard deviations of the main outcome parameters. In a second step of the analysis, we performed univariate analyses of potential associations between the foveal thickness and other ocular and general parameters. In a third step, we carried out a multivariate analysis, with foveal thickness as dependent variable and as independent variables all those parameters which were significantly associated with foveal thickness in the univariate analysis. We then dropped step by step those parameters from the list of independent parameters, which either showed a high collinearity or which were no longer significantly associated with foveal thickness. All P values were 2-sided and were considered statistically significant when the values were less than 0.05. We calculated the standardized regression coefficient beta, the nonstandardized regression coefficient B, and its 95% confidence interval (CI).

**Results**

The study included 1117 individuals (639 women) with a mean age of 64.2 ± 9.7 years (median: 63.0 years; range: 50–93 years) and a mean refractive error of −0.14 ± 1.82 diopters (DL median: 0.25 D; range: −11.75 to +6.00 D). Mean axial length was 23.4 ± 1.04 mm (median: 23.31 mm; range: 20.29–28.68 mm). Compared with the nonparticipants (n = 2351; 1324 women), the individuals participating in this study did not differ significantly in age (64.2 ± 9.7 years versus 64.8 ± 9.9 years; P = 0.07); sex (P = 0.63); anterior chamber depth (2.49 ± 0.49 mm versus 2.49 ± 0.50 mm; P = 0.99); lens thickness (4.57 ± 0.34 mm versus 4.56 ± 0.34 mm; P = 0.72); refractive error (−0.27 ± 2.26 D versus −0.17 ± 2.02 D; P = 0.23); intraocular pressure (14.4 ± 2.6 mm Hg versus 14.5 ± 2.8 mm Hg; P = 0.13). The individuals included into the present study compared with those not included had a
TABLE 1. Associations Between Central Foveal Thickness (Center of the Foveal Pit) as Measured by SD-OCT* and Ocular and Systemic Parameters in the Beijing Eye Study 2011 (Univariate Analysis)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P Value</th>
<th>Standardized Regression Coefficient</th>
<th>Nonstandardized Regression Coefficient</th>
<th>95% CI of B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>0.04</td>
<td>0.06</td>
<td>0.14</td>
<td>0.01, 0.27</td>
</tr>
<tr>
<td>Sex</td>
<td>&lt;0.001</td>
<td>-0.18</td>
<td>8.04</td>
<td>-10.6, -5.5</td>
</tr>
<tr>
<td>Rural/urban region</td>
<td>&lt;0.001</td>
<td>0.12</td>
<td>5.93</td>
<td>2.92, 8.95</td>
</tr>
<tr>
<td>Body height, cm</td>
<td>&lt;0.0001</td>
<td>0.16</td>
<td>0.43</td>
<td>0.27, 0.59</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>0.02</td>
<td>0.07</td>
<td>0.15</td>
<td>0.02, 0.25</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior corneal curvature radius, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central corneal thickness, µm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>&lt;0.001</td>
<td>-0.11</td>
<td>-1.28</td>
<td>-1.99, -0.57</td>
</tr>
<tr>
<td>Lens thickness, mm</td>
<td>0.004</td>
<td>-0.09</td>
<td>-2.35</td>
<td>-4.15, -0.54</td>
</tr>
<tr>
<td>Lens refractive power, D</td>
<td>&lt;0.001</td>
<td>-0.22</td>
<td>-2.45</td>
<td>-3.08, 1.78</td>
</tr>
<tr>
<td>Optic disc area, mm²</td>
<td>0.002</td>
<td>-0.10</td>
<td>-5.40</td>
<td>-8.77, -2.03</td>
</tr>
<tr>
<td>Neuroretinal rim area, mm²</td>
<td>0.93</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choroidal thickness, µm</td>
<td>&lt;0.001</td>
<td>-0.13</td>
<td>-0.04</td>
<td>-0.04, -0.02</td>
</tr>
<tr>
<td>Fundus tessellation degree</td>
<td>&lt;0.001</td>
<td>0.15</td>
<td>2.65</td>
<td>1.63, 3.66</td>
</tr>
<tr>
<td>Epiretinal membrane</td>
<td>0.10</td>
<td>0.06</td>
<td>1.32</td>
<td>-0.25, 2.89</td>
</tr>
<tr>
<td>Intraocular pressure, mm hg</td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Optovue, Inc.

significantly higher level of education (4.3 ± 0.9 versus 3.8 ± 1.1; P < 0.001); came more often from an urban region (76% versus 41.9%; P < 0.001); had a larger anterior corneal curvature radius (7.65 ± 0.25 mm versus 7.60 ± 0.25 mm; P < 0.001); thicker central corneal thickness (535 ± 32 µm versus 531 ± 33 µm; P = 0.005), and longer axial length (23.4 ± 1.04 mm versus 23.2 ± 1.18 mm; P < 0.001).

In univariate analysis, thicker central foveal thickness was associated with older age (P = 0.04); male sex (P < 0.001); urban region of habitation (P < 0.001); taller body height (P < 0.001); heavier body weight (P = 0.02); lower depression score (P = 0.05); higher level of education (P < 0.001); lower blood concentration of low-density lipoproteins (P = 0.01); and cholesterol (P = 0.002); more myopic refractive error (P < 0.001); longer axial length (P < 0.001); longer anterior corneal curvature radius (P < 0.001); deeper anterior chamber depth (P < 0.001); thicker lens thickness (P = 0.004); higher refractive power of the lens (P < 0.001); smaller optic disc area (P = 0.002); thinner subfoveal choroidal thickness (P < 0.001); and higher degree of fundus tessellation (P < 0.001; Table 1).

In the multivariate analysis, we first dropped from the list of independent parameters refractive error (variance inflation factor [VIF]: 117) and blood concentration of cholesterol (VIF: 7.5). We then deleted parameters that were no longer significantly associated with foveal thickness: depression score (P = 0.96); age (P = 0.87); cognitive function score (P = 0.87); body height (P = 0.84); body weight (P = 0.79); level of education (P = 0.48); anterior corneal curvature radius (P = 0.57); refractive lens power (P = 0.59); anterior chamber depth (P = 0.26); blood concentration of low-density lipoproteins (P = 0.10); fundus tessellation (P = 0.19); and optic disc area (P = 0.10). In the final model, thicker central foveal thickness was associated with male sex (P < 0.001); urban region of habitation (P = 0.02); thinner lens thickness (P = 0.01); thinner subfoveal choroidal thickness (P = 0.04), and longer axial length (P < 0.001; Table 2). If we added presence of epiretinal membranes to the list of independent variables, thicker central foveal thickness remained to be significantly associated with male sex (P < 0.001; beta: -0.13; B: -5.71; 95% CI: -8.73, -2.69); urban region of habitation (P = 0.04; beta: 0.07; B: 3.66; 95% CI: 0.19, 7.13); thinner lens...
thickness \( (P = 0.006; \text{beta: } -0.11; \text{B: } -6.68; \text{95\% CI: } -11.0, -2.32) \); and longer axial length \( (P < 0.001; \text{beta: } 0.18; \text{B: } 3.66; \text{95\% CI: } 2.14, 5.19) \), in addition to the presence of an epiretinal membrane \( (P = 0.01; \text{beta: } 0.09; \text{B: } 12.0; \text{95\% CI: } 2.72, 21.13) \).

Subfoveal choroidal thickness was no longer significantly \( (P = 0.08) \) associated with central foveal thickness in that model. If eyes with epiretinal membrane were excluded from the analysis, thicker central foveal thickness was associated with male sex \( (P < 0.001) \), urban region of habitation \( (P = 0.04) \), thinner lens thickness \( (P = 0.004) \), and longer axial length \( (P < 0.001) \), while subfoveal choroidal thickness was not significantly \( (P = 0.08) \) associated with central foveal thickness in that model.

If in the model central foveal retinal thickness was replaced by the retinal thickness measurements obtained in the other foveal regions, the relationship between retinal thickness and axial length remained true only for the nasal quadrant \( (P = 0.009; \text{beta: } 0.09; \text{B: } 1.50; \text{95\% CI: } 0.37, 2.62) \), while superior foveal retinal thickness, inferior foveal retinal thickness, and temporal foveal retinal thickness were not significantly associated with axial length \( (P = 0.26, P = 0.19, \text{and } P = 0.08) \).

To get information about the retinal thickness in the fundus periphery and since OCT images of the peripheral retina were not available, we examined histological slides of 34 eyes of 34 individuals with an age of 57.7 ± 21.7 years (range: 24–88 years). Mean sagittal diameter was 27.0 ± 4.2 mm (median: 25.75 mm; range: 22–37 mm); mean horizontal diameter was 24.30 ± 1.8 mm (median: 24.0 mm; range: 22–27 mm); and mean vertical globe diameter was 23.4 ± 1.5 mm (median: 24 mm; range: 22–26 mm). The globes had been enucleated due to malignant uveal melanomas \( (n = 9) \) or due to painful end-stage glaucoma \( (n = 25) \).

Mean thickness of the outer nuclear layer decreased significantly with longer axial length in the equatorial region \( (P = 0.001; \text{beta: } -0.55; \text{equation of the regression line:} \text{thickness outer nuclear layer} = -1.08 \times \text{axial length [mm]} + 54.9 \text{; Fig. 1}) \). In a similar manner, thickness of the outer nuclear layer at the midpoint equator/posterior pole decreased.
significantly with longer axial length \((P = 0.04; \beta = 0.37)\); equation of the regression line: thickness outer nuclear layer \(= 63.72 - 1.07 \times \text{axial length} \, [\text{mm}] + 63.7\), while the statistical significance of this association was lower than the significance of the previous one (Fig. 2). Outer nuclear layer thickness measurements taken closer to the posterior pole were not significantly associated with axial length \((P = 0.52)\). If the diagnosis was added to the regression analysis, it was not significantly \((P = 0.70)\) associated with the thickness of the nuclear retinal layer, while the association between the thickness of the outer nuclear layer in the equatorial region and axial length remained significant \((P = 0.009)\).

In a similar manner, mean thickness of the inner nuclear layer and outer nuclear layer combined and determined in the equatorial region decreased significantly with longer axial length \((P = 0.004; \beta = -0.48)\); equation of the regression line: thickness outer nuclear layer \(= -1.49 \times \text{axial length} \, [\text{mm}] + 84.5\). Also, mean thickness of the inner nuclear layer and outer nuclear layer combined and measured at the midpoint equator/posterior pole decreased significantly with longer axial length \((P = 0.02; \beta = -0.44)\); equation of the regression line: thickness outer nuclear layer \(= -1.65 \times \text{axial length} \, [\text{mm}] + 99.6\). Thickness measurements of both nuclear layers taken closer to the posterior pole were not significantly associated with axial length \((P = 0.28)\). If the diagnosis was added to the regression analysis, it was not significantly associated with the thickness of the nuclear retinal layers.

**DISCUSSION**

In our population-based study, thicker central foveal thickness and nasal foveal thickness were associated with male sex, urban region of habitation, thinner lens thickness, thinner subfoveal choroidal thickness, and longer axial length. In the same multivariate model, superior foveal retinal thickness, inferior foveal thickness, and temporal foveal thickness were not significantly associated with axial length. In the histomorphometric study, outer and inner nuclear layer thickness in the equatorial region and at the midpoint equator/posterior pole decreased significantly with longer axial length, while thickness measurements taken closer to the posterior pole were not significantly associated with axial length. The in vivo measurement of retinal thickness in the foveal region and the histomorphometric assessment of the retinal thickness in enucleated human globes showed that longer axial length was associated with a retinal thinning in the fundus periphery while retinal thickness in the center of the foveal pit did not decrease with longer axial length. It suggested that axial elongation took place predominantly in the equatorial and pre-equatorial region of the eye.

Our results that foveal retinal thickness did not decrease with longer axial length agreed with findings obtained in previous studies. In the population-based Handan Study on 2230 healthy Chinese aged 50 years and older, central foveal thickness was positively correlated with axial length.\(^{18}\) Using swept-source OCT, Wang and colleagues\(^{19}\) measured the foveal retinal thickness in 146 healthy volunteers and found higher values for men than for women, but no association with axial length. Examining 194 emmetropic or myopic children aged 6 to 17 years, Chen and colleagues\(^{20}\) reported a thicker foveal thickness in children with moderate to high myopia than in children with emmetropia or low myopia. In an investigation by Wu and colleagues,\(^{21}\) mean foveal thickness \((P < 0.0001)\) and in the fovea with a diameter of 1 mm \((P = 0.006)\) was significantly greater in 80 highly myopic eyes than in 40 nonmyopic eyes. Interestingly, the mean retinal thickness in the inner and outer macular area (superior, nasal, inferior, or temporal) was significantly thinner in the highly myopic group.
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than in the nonhighly myopic group. Song and colleagues reported that the mean foveal thickness increased ($P < 0.001$) with longer axial length, while in the inferior and temporal region of the inner macular ring and in all quadrants of the outer macular ring average macular thickness and macular volume decreased with longer axial length. As in our study, foveal thickness was higher in men than in women. In partial contrast to our study, Hwang and Kim found that mean foveal thickness, inner/out macular thickness, and macular volume decreased and foveal thickness increased with longer axial length. In the Sydney Childhood Eye Study, Huynh et al. examined children aged 6 years and reported that the inner and outer macula, but not the central fovea, showed significant thinning with increasing axial length. Luo and colleagues assessed 104 Chinese schoolchildren aged 11 to 12 years and found that children with moderate myopia (myopic refractive error at least $-3.0$ D) had thinner quadrant-specific macular thickness (except in the inferior and superior inner quadrants) than children with low myopia (myopic refractive error $< -3.0$ D) and children with no myopia. Total macular volume was negatively associated with axial length.

Retinal thickness in the midperiphery has been recently measured in one study by Wenner and colleagues. After pupil dilation, the peripheral retina was scanned in 50 individuals (age: 19–50 years; axial length: 21–27 mm) by a spectral-domain OCT at 4500, 5500, 6500, 7500, and at 9000 μm eccentricity from the fovea and from the optic nerve head. In multiple regression analysis, peripheral retinal thickness decreased with longer axial length. These results agree with our histomorphometric measurements showing a decrease in the thickness of the retinal nuclear layers with longer axial length.

The finding that retinal thickness when measured in the fundus periphery decreased with longer axial length, but when measured in the foveal region increased with, or was statistically independent of axial length, agrees with the notion that myopic enlargement of the globe occurs predominately by axial elongation of the globe walls in the midperiphery. This notion is supported by findings obtained in other studies. A change in globe shape from a sphere to a more axially elongated form was described as early as in 1899 by Heine and later by others. Unpublished data also suggests a sagittal bias to eye enlargement in myopia (own data). Interestingly, the equatorial to retroequatorial region is the area where the sensory part of the mechanism for emmetropization has been presumed. Studies revealed that a defocus of the image on the retina was detected in the peripheral region.

The notion that the eye walls in the midperiphery elongate in the process of myopic globe enlargement fits with the finding that the thickness of the retina in the foveal region did not decrease with longer axial length as shown in our and previous studies.

Correspondingly, the length of macular Bruch’s membrane did not enlarge with longer axial length. The finding that foveal retinal thickness did not decrease with longer axial length also agreed with the observation that best corrected visual acuity was independent of axial length in eyes without myopic retinopathy.

It has remained elusive why thicker foveal thickness was associated with urban region of habitation in our study population (Table 2). One of the reasons for the association might have been differences between the urban study population and the rural study population in parameters that were not determined in the study but which might have influenced foveal thickness. One may also take into account that the association between thicker foveal thickness and rural region of habitation was relatively weak with an error probability of 2% to 4%.

Potential limitations of our study should be taken into account. First, our study on the central foveal retinal thickness measurements had a minimum age limit of 50 years so that the findings of our study cannot directly be applied to younger individuals. The difference in the results of the association of perifoveal retinal thickness with axial length between our study including adults and other investigations including children may be because of the difference in age between the study populations. Second, the increase in foveal retinal thickness with longer axial length as found in our and other studies may not be because of anatomical parameters but because of an optical artefact—if the magnification of the retinal image by the optic media of the eye and by the optical elements of the imaging OCT was not fully taken into account. Third, we could have measured the peripheral retinal thickness using the OCT technology as has also been carried out by Wenner and colleagues for the periphery. Using the OCT, however, it would not have been possible to examine the equatorial region of the globe which was the most interesting one since the zone of axial elongation has been presumed to be there. Fourth, our study was not a longitudinal investigation so that any conclusions drawn were based on the assumption that data obtained in a cross-sectional analysis would reflect on a longitudinal development. Only a follow-up study can ultimately address this question whether in axially elongating eyes the central retinal thickness remains unchanged while the retina in the equatorial periphery gets thinner. Fifth, the model proposed in the introduction ignored the process of eye enlargement, which involves an increased scleral remodeling and subsequent surface area expansion under the existing intraocular pressure. One would expect to find the greatest scleral expansion in areas where scleral remodeling is greatest and/or the sclera is thinnest. Sixth, the globes included into the histomorphometric part of our study had been enucleated due to uveal malignant melanomas or painful glaucoma. Since these diseases may have affected the thickness of the outer and inner nuclear layers of the retina, it might have been questionable whether the findings from these diseased eyes could be transferred on normal eyes. The authors performed the measurements of the retinal nuclear layer thickness only in those regions which were evidently not primarily affected by the uveal tumors. Also, glaucoma primarily affects the retinal ganglion cell layer while the nuclear layers are, if at all, affected to a much lower degree. If the diagnosis of glaucoma or uveal melanoma was added to the statistical analysis in our study, the results of the statistical analysis remained unchanged: the association between lower thickness of the equatorial outer nuclear layer and longer axial length remained significant ($P = 0.009$), while the diagnosis was not significantly ($P = 0.70$) associated with the thickness of the nuclear retinal layer. Seventh, the histomorphometric part of our study included only a relatively small number of globes so that the statistical power of the sample size was relatively low. It holds true for the lack of a statistically significant association between axial length and the thickness of the outer nuclear layer or inner nuclear layer of the retina measured at the posterior pole.

In conclusion, myopic axial elongation of the globe was associated with a thinning of the retina in the equatorial and pre-equatorial regions, while central foveal retinal thickness in the fovea did not decrease with longer axial length. It suggests that axial elongation takes place predominantly in the equatorial and pre-equatorial region of the eye, while the foveal region is less affected. This finding may be of interest for elucidating the process of emmetropization and myopization.
Retinal Thickness and Axial Length

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