

Regional Variations in the Relationship between Macular Thickness Measurements and Myopia

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PURPOSE. To investigate the relationship between myopia and macular thickness, as measured by optical coherence tomography.

METHODS. A total of 143 normal subjects comprising 80 eyes with high myopia (spherical equivalent [SE] < -6.0 D), 37 eyes with low to moderate myopia (SE between -6.0 and -0.5 D), and 26 nonmyopic eyes (SE > -0.5 D) were analyzed in this cross-sectional study. Total average, foveal, and inner and outer average macular thicknesses measured by the StratusOCT (Carl Zeiss Meditec Inc., Dublin, CA) were compared among the three diagnostic groups. Associations between macular thickness and refractive error/axial length were evaluated by linear regression analysis.

RESULTS. The minimum foveal and average foveal (1-mm ring on the OCT retinal thickness map) thicknesses were significantly greater, and the outer ring macular (3-6-mm) thicknesses significantly lower in the high myopic eyes than in the low to moderate myopic and nonmyopic eyes. No significant difference was found in the inner ring (1-3-mm) macular thickness measurements among the groups. There was a positive correlation between the axial length and the average foveal thickness ($r = 0.374$, $P < 0.001$). Negative correlations were found between axial length and the average outer ring macular thickness ($r = -0.471$, $P < 0.001$) and total average macular thickness ($r = -0.311$, $P < 0.001$).

CONCLUSIONS. Retinal thickness is related to refractive error/axial length in normal subjects with regional variations in correlation within the 6-mm macular region. Analysis of macular thickness in the evaluation of macular diseases and glaucoma should be interpreted only in the context of refractive errors and the location of measurement. (*Invest Ophthalmol Vis Sci.* 2007;48:376-382) DOI:10.1167/iovs.06-0426

Myopia is a very prevalent condition, and, in many developed countries, complications related to high myopia are a major cause of blindness. It has been shown in histopathological studies that there is increasing scleral and retinal thinning with myopia.^{1,2} In myopic eyes, the globe is enlarged with increase in axial length and the stretching beyond normal

dimensions may result in thinning of the retina. With the availability of modern imaging technologies, in vivo measurements of retinal thickness have been made possible, and the relationship between myopia and retinal thickness has been examined.³⁻⁷ Of interest, contrary to the histopathologic findings, in vivo imaging studies have not identified an association between retinal thickness and the axial length of the eye. Lim et al.³ measured the macular thickness with horizontal and vertical linear scans with the first generation of OCT (OCT 1; Carl Zeiss Meditec, Inc., Dublin, CA) in myopic subjects and concluded that average macular thickness did not vary with myopia. This is in agreement with an earlier study by Wakitani et al.,⁴ who used a similar study design with the second generation of OCT (Humphrey 2000 OCT system; Carl Zeiss Meditec, Inc.). In a recent study, Zou et al.,⁵ using a retinal thickness analyzer (RTA; Talia Technology Ltd., Neve-Lian, Israel), found no significant difference in any of the RTA-measured parameters between emmetropic and myopic eyes. Although reduced retinal thickness was demonstrated in eyes with axial length greater than 24 mm in the RTA study by Chan et al.,⁶ no significant correlation was detected between axial length/refractive error and retinal thickness.

The disparity may stem from the relatively low scanning resolution and small sampling density of the measuring devices used in the earlier studies. Both OCT 1 and OCT 2000 allow 100 A-scans in a linear scan with axial resolution of ~12 to 15 μm , and only two to four linear scans over the macular region were captured in previous studies.^{3,4} Although a higher sampling density can be achieved with RTA with 16 optical sagittal cross sections 187 μm apart covering an area of 3 mm^2 , the lower axial resolution (52 μm) and the longer scanning time with the RTA compared with the OCT may render retinal thickness measurements less accurate. Currently, the StratusOCT (Carl Zeiss Meditec, Inc.) is the only commercially available imaging device that allows axial scanning resolution less than 10 μm for measurement of retinal thickness. In this study, we re-examined the relationship between retinal thickness and myopia with the StratusOCT to see whether it would support the histologic and clinical observations.

METHODS

Subjects

One hundred forty-three Chinese patients who met the inclusion criteria were consecutively recruited during the period from October 2005 to March 2006 at the University Eye Center, The Chinese University of Hong Kong. All subjects underwent a full ophthalmic examination including visual acuity, refraction, intraocular pressure measurement with Goldmann tonometry, dilated fundus examination with stereoscopic biomicroscopy of the optic nerve head under slit lamp, indirect ophthalmoscopy, refraction, and A-scan ultrasound biometry. Other than refractive error, all included eyes had no concurrent disease and had best corrected visual acuity of at least 20/40. Subjects were divided into three diagnostic groups according to refractive status: (1) high myopia (spherical equivalent < -6.00 D); (2) low to moderate

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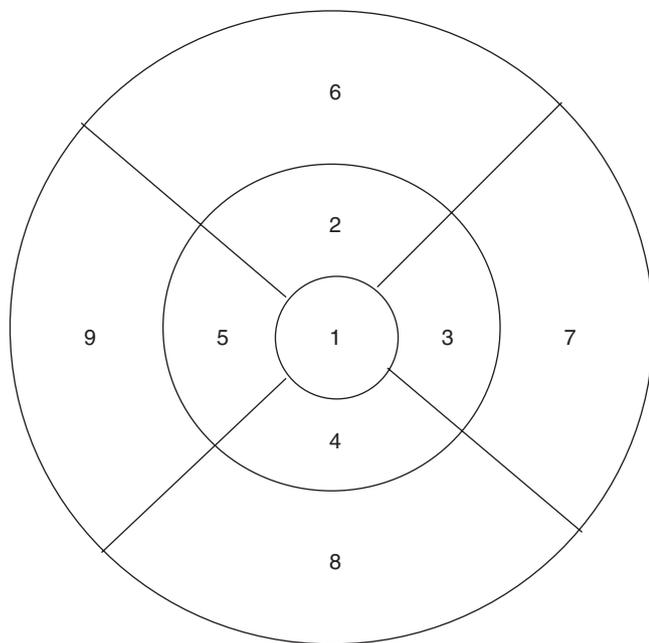


FIGURE 1. Macular thickness map topology. The diameters of the three concentric circles are 1, 3, and 6 mm. Area 1 represents the fovea; areas 2, 3, 4, and 5 form the inner ring; and areas 6, 7, 8, and 9 form the outer ring.

myopia (spherical equivalent between -0.50 and -6.00 D); and (3) nonmyopia (spherical equivalent between > -0.50 and $+3.50$ D). Subjects with clinical evidence of myopic macular degeneration, intraocular pressure more than 21 mm Hg, visual field defects (see below), history of intraocular surgery, refractive surgery, neurologic diseases or diabetes were excluded. In one randomly selected eye, optical coherence tomography was performed. The study was conducted in accordance with the ethical standards stated in the Declaration of Helsinki and approved by the local clinical research ethics committee, with informed consent obtained.

Optical Coherence Tomography

Optical coherence tomography was performed with OCT version 3 (StratusOCT; Carl Zeiss Meditec, Inc.). Retinal thickness over the macula was delineated in the scan as the distance between the first signal from the vitreoretinal interface and the signal from the anterior boundary of the retinal pigment epithelium. The fast macular thickness scanning protocol was used, in which six 6-mm lines (oriented 30° apart) in a radial spokelike pattern are acquired in a continuous auto-

ated sequence. Each of the six linear scans is composed of 128 equally spaced, transverse A-scans. The calculation of macular thickness is based on the 6-mm retinal thickness map analysis printout. The map is composed of nine sectorial thickness measurements in three concentric circles with diameters of 1, 3, and 6 mm (Fig. 1). The area bounded by the outer (6-mm) and middle (3-mm) circles forms the outer ring, and the area bounded by the middle (3-mm) and inner circles (1-mm) forms the inner ring. The inner and outer rings are divided into four quadrants: superior, nasal, inferior, and temporal. The central 1-mm circular region represents the foveal area. Total average macular thickness, average and four-quadrant macular thicknesses in the inner (1–3 mm) and outer (3–6 mm) rings, and the central 1-mm fovea thickness were analyzed in the study. High reproducibility of retinal thickness measurements by StratusOCT has been demonstrated in other studies.^{8,9} All the scans had signal strength of at least 7. In addition, all the macular images were checked to ensure that the foveal depression was evident in the center of the scan. No abnormal vitreoretinal traction or retinoschisis was identified. Two subjects were excluded because of the incidental finding of a lamellar macular hole.

Visual Field Testing

Standard visual field testing was performed with the static automated white-on-white threshold 24-2 SITA standard strategy (Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc.). A visual field was defined as reliable when fixation losses and false-positive and -negative rates were less than 25%. A visual field defect was defined as having three or more significant ($P < 0.05$) non-edge-contiguous points with at least one at the $P < 0.01$ level on the same side of the horizontal meridian in the pattern deviation plot and classified as outside normal limits in the Glaucoma Hemifield Test.

Statistical Analysis

Statistical analyses were performed (SPSS version 11.0; SPSS Inc., Chicago, IL), and differences in macular measurements among the three diagnostic groups were evaluated by one-way analysis of variance. Associations between macular measurements and spherical equivalent/axial length and age were examined by linear regression analysis and expressed as the Pearson correlation coefficient. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 143 eyes with spherical equivalent ranging from $+3.25$ to -18.13 D (mean \pm SD = -6.13 ± 4.52) and axial length ranging from 21.10 to 31.10 mm (mean = 25.77 ± 1.86) were analyzed. High correlation was found between axial length and spherical equivalent ($r = -0.879$; $P < 0.001$). The refractive error and axial length distribution in each diagnostic

TABLE 1. Baseline Data of the Three Diagnostic Groups with 95% Confidence Intervals

	High Myopia	Low to Moderate Myopia	Nonmyopia	P
Number of subjects	80	37	26	
Spherical equivalent (D)	-9.5 ± 2.2 (-9.96 – -8.97)	-3.9 ± 1.5 (-4.43 – -3.44)	1.0 ± 1.1 (0.59 – 1.49)	$<0.001^*$
Axial length (mm)	27.0 ± 1.1 (26.74 – 27.23)	25.1 ± 1.0 (24.75 – 25.42)	23.0 ± 1.1 (22.60 – 23.46)	$<0.001^*$
Sex (male/female)	36/44	11/26	14/12	0.133†
Age (y)	37.5 ± 8.1 (35.70 – 39.30)	37.9 ± 13.1 (33.49 – 42.24)	48.4 ± 14.7 (42.49 – 54.36)	$<0.001‡$

Data within parentheses represent 95% confidence intervals.

* Analysis of variance.

† χ^2 test

‡ Analysis of variance with Bonferroni connection. Significant differences were noted between nonmyopic and high-myopic groups ($P < 0.001$) and nonmyopic versus low-moderate myopic groups ($P < 0.001$).

TABLE 2. Correlations between Macular Measurements and Spherical Equivalent, Axial Length, and Age

	Spherical Equivalent		Axial Length		Age	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Foveal minimum	-0.332	<0.001	0.371	<0.001	0.143	0.088
Average foveal (1 mm)	-0.320	<0.001	0.374	<0.001	0.071	0.400
Temporal inner macula	0.135	0.108	-0.099	0.241	-0.062	0.464
Superior inner macula	0.116	0.167	-0.043	0.606	-0.025	0.763
Nasal inner macula	0.031	0.715	-0.040	0.637	-0.025	0.770
Inferior inner macula	0.138	0.100	-0.095	0.259	-0.010	0.909
Average inner macula	0.114	0.174	-0.078	0.353	-0.034	0.638
Temporal outer macula	0.537	<0.001	-0.537	<0.001	-0.010	0.903
Superior outer macula	0.401	<0.001	-0.372	<0.001	-0.052	0.534
Nasal outer macula	0.241	0.004	-0.266	0.001	0.041	0.629
Inferior outer macula	0.472	<0.001	-0.495	<0.001	0.097	0.247
Average outer macula	0.465	<0.001	-0.471	<0.001	0.023	0.784
Total macular thickness	0.316	<0.001	-0.311	<0.001	0.031	0.710

group is shown in Table 1. The mean age of the nonmyopic group (48.4 ± 14.7 years) was significantly higher than that of the high myopic (37.5 ± 8.1 years; $P < 0.001$) and low to moderate myopic (37.9 ± 13.1 ; $P = 0.001$) groups, but no significant correlation was detected between age and any of the macular measurements (Table 2). No significant difference was found in gender distribution among the groups ($P = 0.133$).

Table 3 presents the macular measurements stratified by gender. The minimum foveal thickness, average foveal (1-mm) thickness, and the superior, temporal and average inner ring

macular thicknesses were significantly lower in the women. There was no significant difference in total average and outer ring macular thicknesses between the genders.

Total and regional macular thickness measurements in each group are summarized in Table 4. Although no significant difference in inner ring macular thicknesses was found among the groups, the average outer ring macular thickness was significantly lower in the high myopic eyes than the low to moderate myopic ($P = 0.015$) and the nonmyopic ($P < 0.001$) eyes. In contrast, the average foveal (1-mm) thickness was significantly higher in the high myopic eyes than in the other

TABLE 3. Gender Differences in Macular Thickness Measurements with 95% Confidence Intervals

	Women	Men	<i>P</i> *
Age (y)	39.01 ± 11.16 (36.56-41.46)	40.34 ± 12.32 (37.19-43.50)	0.501
Spherical equivalent (D)	-6.33 ± 4.28 (-7.27--5.39)	-5.85 ± 4.85 (-7.09--4.61)	0.530
Axial length (mm)	25.55 ± 1.72 (25.17-25.93)	26.07 ± 2.01 (25.56-26.59)	0.098
Foveal minimum	164.20 ± 21.58 (159.45-168.94)	180.93 ± 26.16 (174.23-187.63)	<0.001
Average foveal (1 mm)	197.87 ± 21.91 (193.05-202.68)	217.51 ± 26.27 (210.78-224.24)	<0.001
Temporal inner macula	262.49 ± 15.52 (259.08-265.90)	270.41 ± 17.59 (265.91-274.91)	0.005
Superior inner macula	276.74 ± 16.28 (273.17-280.32)	285.62 ± 18.92 (280.78-290.47)	0.003
Nasal inner macula	277.70 ± 16.58 (274.05-281.34)	283.98 ± 38.97 (274.00-293.97)	0.192
Inferior inner macula	273.90 ± 16.66 (270.24-277.56)	277.21 ± 22.61 (271.42-283.00)	0.315
Average inner macula	272.70 ± 14.75 (269.47-275.95)	279.31 ± 19.74 (274.25-284.36)	0.024
Temporal outer macula	218.11 ± 17.14 (214.34-221.88)	220.80 ± 17.48 (216.33-225.28)	0.358
Superior outer macular	240.99 ± 17.73 (237.09-244.88)	243.49 ± 19.73 (238.44-248.54)	0.427
Nasal outer macula	263.90 ± 20.30 (259.44-268.36)	262.34 ± 20.94 (256.98-267.71)	0.655
Inferior outer macula	233.34 ± 18.32 (229.32-237.37)	232.87 ± 18.38 (228.16-237.58)	0.879
Average outer macula	239.10 ± 16.08 (235.56-242.63)	239.88 ± 16.69 (235.60-244.15)	0.777
Total macular thickness	244.91 ± 15.00 (241.61-248.20)	249.00 ± 16.63 (244.74-253.26)	0.125

Data are mean micrometers \pm SD.

* Independent *t*-test.

TABLE 4. Macular Measurements (μm) in the 3 Diagnostic Groups

	High Myopia (<i>n</i> = 80)	Low to Moderate (<i>n</i> = 37)	Nonmyopia (<i>n</i> = 26)	<i>P</i> *
Foveal minimum	178.91 \pm 26.99 (172.91-184.92)	160.68 \pm 17.96 <i>P</i> < 0.001‡ (154.69-166.66)	163.19 \pm 18.88 <i>P</i> = 0.011† (155.57-170.82)	<0.001
Average foveal (1 mm)	213.41 \pm 26.63 (207.49-219.34)	196.54 \pm 24.03 <i>P</i> = 0.002‡ (188.53-204.55)	198.00 \pm 17.43 <i>P</i> = 0.019† (190.96-205.04)	0.001
Temporal inner macula	264.23 \pm 16.39 (260.58-267.87)	267.22 \pm 18.48 <i>P</i> > 0.999 (261.05-273.38)	269.00 \pm 15.76 <i>P</i> = 0.634 (262.63-275.37)	0.390
Superior inner macula	278.85 \pm 17.17 (275.03-282.67)	281.00 \pm 18.48 <i>P</i> > 0.999 (274.84-287.16)	285.04 \pm 19.36 <i>P</i> = 0.385 (277.22-292.86)	0.308
Nasal inner macula	279.88 \pm 34.46 (272.21-287.54)	279.84 \pm 18.13 <i>P</i> > 0.999 (273.79-285.88)	282.69 \pm 18.96 <i>P</i> > 0.999 (275.03-290.35)	0.901
Inferior inner macula	273.68 \pm 18.48 (269.56-277.79)	276.43 \pm 21.85 <i>P</i> > 0.999 (269.15-283.72)	278.77 \pm 18.77 <i>P</i> = 0.744 (271.19-286.35)	0.472
Average inner macula	274.16 \pm 17.38 (270.29-278.02)	276.12 \pm 17.21 <i>P</i> > 0.999 (270.38-281.86)	278.88 \pm 17.38 <i>P</i> = 0.690 (271.86-285.89)	0.471
Temporal outer macula	212.33 \pm 13.93 (209.22-215.43)	221.92 \pm 15.16 <i>P</i> = 0.004‡ (216.86-226.97)	236.81 \pm 16.34 <i>P</i> < 0.001† (230.21-243.41)	<0.001
Superior outer macula	236.18 \pm 15.62 (232.70-239.65)	244.43 \pm 15.94 <i>P</i> = 0.047‡ (239.12-249.75)	256.77 \pm 21.91 <i>P</i> < 0.001† (247.92-265.62)	<0.001
Nasal outer macula	259.29 \pm 19.27 (255.00-263.58)	264.38 \pm 22.30 <i>P</i> = 0.603 (256.94-271.81)	273.77 \pm 18.31 <i>P</i> = 0.005† (266.37-281.16)	0.006
Inferior outer macula	226.24 \pm 14.94 (222.91-229.56)	235.76 \pm 17.86 <i>P</i> = 0.009‡ (229.80-241.71)	250.65 \pm 15.87 <i>P</i> < 0.001† (244.25-257.06)	<0.001
Average outer macula	233.51 \pm 12.92 (230.63-236.38)	241.64 \pm 15.62 <i>P</i> = 0.015‡ (236.43-246.85)	254.50 \pm 16.51 <i>P</i> < 0.001† (247.83-261.17)	<0.001
Total macular thickness	242.84 \pm 14.09 (239.71-245.98)	248.40 \pm 15.72 <i>P</i> = 0.198 (243.16-253.64)	255.90 \pm 17.12 <i>P</i> = 0.001† (248.98-262.81)	0.001

Data are mean micrometers \pm SD.

* One way analysis of variance.

† Statistically significant difference between nonmyopic and high-myopic eyes after Bonferroni post hoc test.

‡ Statistically significant difference between low to moderate myopic and high-myopic eyes after Bonferroni post hoc test.

groups (low to moderate myopia, *P* = 0.002; nonmyopia, *P* = 0.019).

The relationships between macular thickness and refractive error/axial length were analyzed by using linear regression analysis (Table 2). Total macular thickness decreased with increasing axial length (*r* = -0.311; *P* < 0.001) and negative spherical equivalent (*r* = 0.316, *P* < 0.001; Fig. 2). Analyses on the individual quadrants identified significant correlations only in the outer ring macular thicknesses. Average foveal thickness, in contrast, increased with increasing axial length (*r* = 0.374; *P* < 0.001) and negative spherical equivalent (*r* = -0.320; *P* < 0.001; Fig. 3). Table 5 presents the linear regression analysis results in the age group 23 to 28 years. This group was analyzed because it represented the youngest age group in a narrow age range. A similar pattern of correlations was observed, and significant correlations were evident between the average macular thickness and axial length/refractive error.

DISCUSSION

Contrary to histologic findings and clinical observations that retinal thinning or chorioretinal atrophy is more common in myopia,^{2,10-12} the correlation between average macular thickness and myopia has been found to be insignificant in previous in vivo imaging studies.³⁻⁷ With the use of the StratusOCT (Carl Zeiss Meditec, Inc.), which provides a higher axial scanning resolution and sampling density, we found that there was a negative correlation between total macular thickness and axial length (positive correlation with spherical equivalent) and a positive correlation between foveal thickness and axial length (negative correlation with spherical equivalent).

In myopic eyes, the elongation of the globe leads to mechanical stretching and thinning of the retina. It is conceivable that the extent of the elongation would be related to the degree of retinal thinning. The lack of correlation between axial length/refractive error and retinal thickness in previous

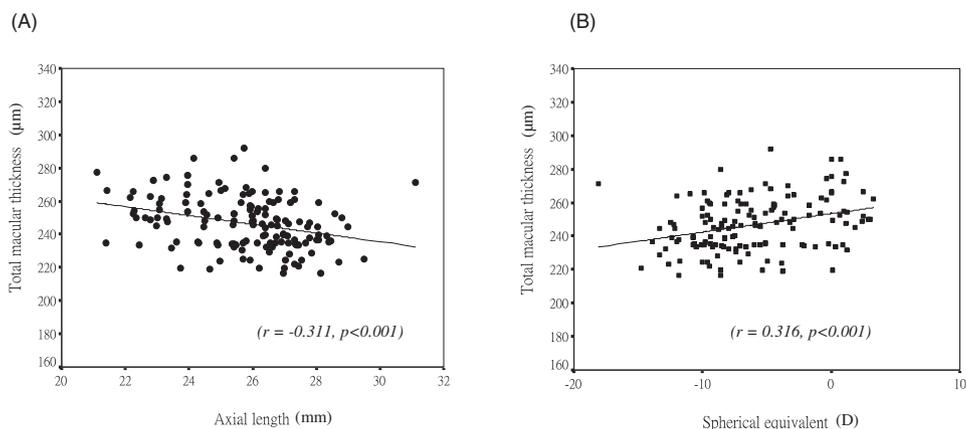


FIGURE 2. Scatterplots of total macular thickness against axial length (A) and spherical equivalent (B).

studies had been attributed to various causes. In a OCT macular thickness study, Wakitani et al.⁴ proposed that the periphery, rather than the central retina, is thinner in myopic eyes. The absence of large blood vessels and optic fibers could render the peripheral retina less resistant to traction and stretch, and the decrease in peripheral retinal thickness may compensate for the stretching force over the entire retina to preserve the central retinal thickness. This conclusion is supported by Lim et al.,³ who also suggested that retinal thinning in myopia is more common in the peripheral retina. In the present study, we found that the outer ring (3–6 mm), but not the inner ring (1–3 mm), macular thicknesses decreased in eyes with a greater degree of myopia. Similarly, the negative correlations found between the outer ring but not the central retinal thicknesses and axial length agreed with the hypothesis that the retinal thickness in the most central area is preserved in high myopia.

It is interesting to note that although the outer ring macular measurements decreased with axial length, the foveal minimum and foveal (1-mm) thickness increased. In fact, Lim et al.³ also reported a positive correlation between axial length and minimum foveal thickness. However, they suggested that it was the poorer and off-foveola fixation in highly myopic eyes that accounted for the association. In this study, the central fixation was confirmed in each patient by observing the location of the foveal depression at the center of each macular scan. Therefore, off-foveola fixation was highly unlikely with the present data. Although myopic foveoschisis could result in foveal thickening, none of the recruited subjects was found to have this, and those with macular abnormalities had been excluded from the study. Our findings of increased minimum foveal/foveal (1-mm) thickness with axial length may be related

to the retinomotor movements of the photoreceptors. In a form-deprivation myopia animal model, it was observed that the photoreceptor outer segments were elongated.¹³ However, this increase in foveal thickness could also be an early sign of vitreoretinal traction in highly myopic eyes. A longitudinal follow-up study would be needed to address this question fully.

In this study, the minimum foveal, average foveal (1-mm), and average inner ring macular thicknesses were significantly lower in the women (Table 3). These findings are in agreement with several studies,^{14–16} suggesting an influence of gender on absolute central retinal thickness measurements. The reduced foveal thickness in women is compatible with the observation that they have a higher risk of development of macular holes,^{17,18} as the sequence of macular hole development has been suggested to begin with foveal thinning, although the exact pathogenesis is still unclear.¹⁹ And yet, if foveal thinning represents a risk factor, it would be difficult to explain why highly myopic eyes had greater foveal thickness than did with low to moderate myopic and nonmyopic eyes (Table 4), because it is well known that macular hole development is more common in high myopia. However, as mentioned, the increase in foveal thickness could also be an early subclinical sign of vitreoretinal traction in highly myopic eyes. The incomplete and abnormal vitreous detachment and liquefaction that are more commonly found in high myopic eyes are probably more causative in the pathogenesis of macular holes.

In the present study, although there was a relatively wide age spectrum (23–77 years), age was found to have no significant correlation with any of the macular thickness parameters, in line with findings in other studies,^{5–7,20} although a few have

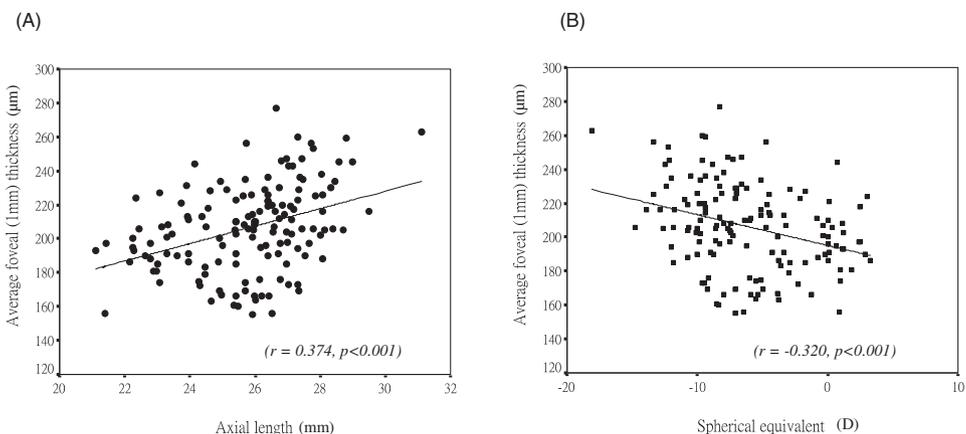


FIGURE 3. Scatterplots of average foveal (1-mm) thickness against axial length (A) and spherical equivalent (B).

TABLE 5. Correlations between Macular Measurements and Spherical Equivalent/Axial Length in a Subgroup of 29 Young Subjects Ages 23–28 Years

	Spherical Equivalent		Axial Length	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Mean Age (y) (95% CI)		25.97 ± 1.59 (25.36–26.57)		
Mean axial length (mm) (95% CI)		25.88 ± 1.62 (25.26–26.50)		
Mean spherical equivalent (D) (95% CI)		−5.64 ± 3.93 (−7.14–−4.15)		
Foveal minimum	−0.313	0.099	0.392	0.035
Average foveal (1 mm)	−0.195	0.310	0.276	0.148
Temporal inner macula	0.460	0.012	−0.357	0.057
Superior inner macula	0.459	0.012	−0.325	0.085
Nasal inner macula	0.333	0.078	−0.219	0.254
Inferior inner macula	0.616	<0.001	−0.443	0.016
Average inner macula	0.517	0.004	−0.372	0.047
Temporal outer macula	0.700	<0.001	−0.593	0.001
Superior outer macula	0.630	<0.001	−0.463	0.011
Nasal outer macula	0.414	0.026	−0.334	0.077
Inferior outer macula	0.622	<0.001	−0.598	<0.001
Average outer macula	0.637	<0.001	−0.534	0.003
Total macular thickness	0.588	0.001	−0.463	0.011

suggested that macular thickness decreases with age.^{21,22} Similar direction of correlations between the minimum foveal thickness, outer macular thickness, total macular thickness, and axial length were observed in the youngest age group (23–28 years) which supports these associations are robust (Table 5). The finding of negative correlation between the inner macular thickness and axial length/spherical equivalent in the youngest age group compares favorably with a recent epidemiology study in children by Huynh et al.,²³ who reported that retinal thinning with increasing axial length occurs in the outer and inner macular regions, but not in the central macula. However, the reason for the difference in the regional correlations between different age groups remains obscure. Further study with a larger sample size is needed to investigate whether there are age-related patterns in the correlations between macular thickness and axial length/refractive error.

Nevertheless, the findings in the present study are important in helping clinicians to understand the pattern of regional variations in macular thickness in myopia. The observations suggest that refractive error should be a consideration in the interpretation of retinal thickness normograms, and, as the current normative database in the StratusOCT database does not take this into account, clinicians should be aware of the effect of refractive error when evaluating the significance of a particular macular thickness in aiding diagnosis and monitoring of diseases such as diabetic macular edema or glaucoma in patients with myopia.

The limitation of the StratusOCT macular thickness map is that it is derived from only six linear scans over a 360° area in the transverse plane. Mathematical interpolations are used to derive thickness estimations for the spaces in between. However, the macular thickness map is the only analysis protocol available in the StratusOCT that provides regional macular thickness measurements and is widely used in clinical practice. Another limitation relates to magnification in myopic eyes. The default axial length and refraction in every OCT scan is 24.46 mm and 0.0 D, respectively. Although one can input the patient's axial length and refractive correction (spherical equivalent), they have no impact on magnification during scanning. Because the scan length in the fast/standard macular thickness scanning protocols cannot be adjusted in the StratusOCT, the actual scan length in a myopic eye could be longer than 6 mm, because of the magnification's effect (as a result of the change in refractive power and axial length), although the actual

thickness measurement in the axial direction does not depend on these factors. Although the magnification's effect is minimal on the measurement of central macular or foveal thickness, it may lead to slight underestimation of thickness in the peripheral retina. As a result, the strength of the correlation between outer macular thicknesses and axial length or spherical equivalent may be reduced. Nevertheless, the findings in this study are clinically relevant and important in the interpretation of OCT macular thickness measurements, since the 6-mm fast/standard macular thickness scans have become the standard scanning approach in clinical practice and in clinical studies.

In summary, there are regional variations of association between macular thickness and myopia with positive correlation between axial length and foveal thickness and negative correlation with the outer ring (3–6 mm) macular thickness. The fact that the outer ring (3–6 mm) dominates 75% of the 6-mm macular region results in the observation that the average macular thickness (6-mm) decreases with increasing degree of myopia. Evaluation of macular thickness in macular diseases and glaucoma should always be interpreted in light of the degree of refractive error and the region of measurement.

References

- Apple DJ, Fabb MF. *Clinicopathologic Correlation of Ocular Disease: a Text and Stereoscopic Atlas*. St. Louis: CV Mosby; 1978;39–44.
- Yanoff M, Fine BS. *Ocular Pathology: A Text and Atlas*. Philadelphia: Harper & Row; 1982;513–514.
- Lim MC, Hoh ST, Foster PJ, et al. Use of optical coherence tomography to assess variations in macular retinal thickness in myopia. *Invest Ophthalmol Vis Sci*. 2005;46:974–978.
- Wakitani Y, Sasoh M, Sugimoto M, et al. Macular thickness measurements in healthy subjects with different axial lengths using optical coherence tomography. *Retina*. 2003;23:177–182.
- Zou H, Zhang X, Xu X, et al. Quantitative in vivo retinal thickness measurement in Chinese healthy subjects with the retinal thickness analyzer. *Invest Ophthalmol Vis Sci*. 2006;47:341–347.
- Chan CM, Yu JH, Chen LJ, et al. Posterior pole retinal thickness measurements by the retinal thickness analyzer in healthy Chinese subjects. *Retina*. 2006;26:176–181.
- Gobel W, Hartmann F, Haigis W. Determination of retinal thickness in relation to the age and axial length using optical coherence tomography. *Ophthalmology*. 2001;98:157–162.
- Paunescu LA, Schuman JS, Price LL, et al. Reproducibility of nerve fiber thickness, macular thickness, and optic nerve head measure-

- ments using StratusOCT. *Invest Ophthalmol Vis Sci.* 2004;45:1716-1724.
9. Gurses-Ozden R, Teng C, Vessani R, et al. Macular and retinal nerve fiber layer thickness measurement reproducibility using optical coherence tomography (OCT-3). *J Glaucoma.* 2004;13:238-244.
 10. Spencer WH. *Ophthalmic Pathology: an Atlas and Textbook.* 3rd ed. Philadelphia: WB Saunders; 1985;395-400.
 11. Curtin BJ, Karlin DB. Axial length measurements and fundus changes of the myopic eye. *Trans Am Ophthalmol Soc.* 1970;68:312-334.
 12. Curtin BJ. The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc.* 1977;75:67-86.
 13. Liang H, Crewther DP, Crewther SG, et al. A role for photoreceptor outer segments in the induction of deprivation myopia. *Vision Res.* 1995;35:1217-1225.
 14. Massin P, Vicaud E, Haouchine B, et al. Retinal thickness in healthy and diabetic subjects measured using optical coherence tomography mapping software. *Eur J Ophthalmol.* 2002;12:102-108.
 15. Hee MR, Puliafito CA, Duker JS, et al. Topography of diabetic macular edema with optical coherence tomography. *Ophthalmology.* 1998;105:360-370.
 16. Wong AC, Chan CW, Hui SP. Relationship of gender, body mass index, and axial length with central retinal thickness using optical coherence tomography. *Eye.* 2005;19:292-297.
 17. Evans JR, Schwartz SD, McHugh JD, et al. Systemic risk factors for idiopathic macular holes: a case-control study. *Eye.* 1998;12:256-259.
 18. The Eye Disease Case-Control Study Group. Risk factors for idiopathic macular holes. *Am J Ophthalmol.* 1994;118:754-761.
 19. Morgan CM, Schatz H. Involutional macular thinning: a pre-macular hole condition. *Ophthalmology.* 1986;93:153-161.
 20. Chan A, Duker JS, Ko TH, et al. Normal macular thickness measurements in healthy eyes using Stratus optical coherence tomography. *Arch Ophthalmol.* 2006;124:193-198.
 21. Alamouti B, Funk J. Retinal thickness decreases with age: an OCT study. *Br J Ophthalmol.* 2003;87:899-901.
 22. Kanai K, Abe T, Murayama K, et al. Retinal thickness and changes with age. *Nippon Ganka Gakkai Zasshi.* 2002;106:162-165.
 23. Huynh SC, Wang XY, Rochchina E, et al. Distribution of macular thickness by optical coherence tomography: findings from a population-based study of 6-year-old children. *Invest Ophthalmol Vis Sci.* 2006;47:2351-2357.