Measuring Retinal Thickness and Visual Acuity in Eyes with Different Types of Astigmatism in a Cohort of Hong Kong Chinese Adults

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Purpose. The purpose of this study was to investigate optical coherence tomography (OCT)-measured retinal thickness (RT) and best-corrected distance visual acuity (BCDVA) in eyes with different types of astigmatism.

Methods. This is a case-control study of 101 participants stratified into With-The-Rule (WTR; $n = 41$), Against-The-Rule (ATR; $n = 25$), and control ($n = 35$) groups by noncycloplegic subjective refraction. Inclusion criteria were ages between 18 and 45 years, spherical-equivalent (SE) refraction ≥ -10.00 diopters (D), negative cylindrical power (CYL) ≤ -0.75 D with axes of 0 to 30 degrees/150 to 180 degrees for WTR and 60 to 120 degrees for ATR, or CYL ≥ -0.25 D for controls. Participants suffering from ocular diseases related to retinal defects, having a history of ocular surgery, with BCDVA >0.10 LogMAR, or poor OCT imaging quality were excluded. Fovea-centered scans were performed using spectral-domain OCT (SD-OCT), and RT automatically measured by the inbuilt software. Only right eyes were analyzed. Groups were matched for age, gender, SE, axial length, and corneal curvature.

Results. One-way ANOVA showed a significant difference in both BCDVA ($P = 0.039$) and macular RT ($P = 0.028$) among the three groups. Bonferroni's post hoc test revealed statistically significant between-group differences in BCDVA (WTR vs. controls, $P = 0.041$), as well as in RT at inner-nasal (WTR vs. ATR, $P = 0.034$) and outer-temporal subfields (WTR vs. controls, $P = 0.042$). BCDVA was positively associated with macular RT ($r = 0.206$, $P = 0.041$) after adjusting for age, gender, and axial length.

Conclusions. Greater RT and poorer BCDVA were found in eyes with WTR astigmatism. Our findings suggest that the effect of astigmatism on retinal thickness and BCDVA may vary depending on not only magnitude, but also axis of astigmatism.

Keywords: astigmatism, retinal thickness (RT), visual acuity, optical coherence tomography (OCT)

Astigmatism, a common refractive error, is attributable to differential refractive powers across different meridians and, consequently, each point of an object is refracted into light spreading between two line foci with specific, typically orthogonal, orientations. Most infants are born with significant astigmatism,[1–3] either With-The-Rule (WTR; greatest refractive power in the vertical meridian) or Against-The-Rule (ATR; greatest refractive power in the horizontal meridian). Several population based studies have reported that the predominant type of astigmatism in Chinese infants is WTR, with the proportion of affected infants ranging from 72% to 97%.[4–6] Astigmatism declines substantially throughout infancy and childhood,[7–9] but its prevalence increases during the adolescence,[9,10] then appears to stabilize during adulthood,[11,12] before increasing again in old age.[12,13]

It has been hypothesized that degradation of retinal image quality produced by natural or optically imposed astigmatism disrupts defocus-guided emmetropization,[14] and potentially interferes with refractive development and progression of myopia. This hypothesis is supported by studies in both chicks[15–17] and monkeys[18–20] that demonstrated an altered course of emmetropization with imposed astigmatism, although the end point varied across studies. In humans, significant positive associations between the presence of astigmatism and the prevalence or later development of myopia have been observed in several cross-sectional and longitudinal studies.[21–24]

With respect to the effects of the astigmatic axis on eye growth, studies in chicks[17,25] and monkeys[20] have demonstrated an influence of astigmatism on the development of axial length (AL) and refraction according to its axis orientation, supporting the hypothesis that orientation-dependent image blur received by the retina may perturb emmetropization.[26,27] In humans, it has been reported that children with ATR astigmatism were more likely to develop myopia later in life[21] or have a more rapid progression of myopia,[28] and young adults with high myopia had greater odds of WTR astigmatism.[12,29] Recent experimental studies in human eyes

have also shown that even 60 minutes of exposure to WTR and ATR astigmatic defocus using +3.00 diopters (D) cylindrical lenses could trigger bidirectional changes in choroidal thickness[30] and refractive astigmatism,[31] suggesting that an orientation-dependent signaling pathway is in place.

Emerging evidence has indicated that the retina plays an essential role in the development of astigmatism,[16] probably via the orientation-selective cells to decode the orientation-dependent visual signals.[32] Whereas more investigation is required to understand the mechanism of astigmatism-related eye growth, previous research has reported abnormal retinal electrophysiological responses in astigmatic eyes. Flitcroft et al.[33] recorded flash electroretinographic (ERG) signals from 123 children with reduced vision and found that highly astigmatic (cylindrical power [CYL] <−1.50 D) children had abnormal flash ERG responses more frequently than low or non-astigmatic children. In contrast, our recent study in chicks showed that multifocal ERG responses were significantly correlated with WTR or ATR astigmatism experimentally induced by sphero-cylindrical lenses (−6.00 DS/−8.00 DC). Specifically, in chicks that developed ATR astigmatism, the magnitude of induced astigmatism was inversely correlated with the amplitude of the induced component (IC) of the multifocal ERG signal, which predominantly reflects the inner retinal response.[34] In contrast, the magnitude of induced WTR astigmatism was directly correlated with increased IC amplitude (Vyas SA, Lakshmanan Y, Chan HHL, Leung TW & Kee CS. Experimentally induced myopia and myopic astigmatism alter retinal electrophysiology in chickens. *Sci Rep*. 2022;12:21180, https://doi.org/10.1038/s41598-022-25075-8). Although previous studies focused heavily on functional measurements, such as retinal electrophysiology, less is known about how retinal structures vary in eyes with different types of astigmatism.

In healthy myopic[35,36] and highly myopic populations,[37] the flash and multifocal ERG responses are directly correlated with the retinal thickness determined by optical coherence tomography (OCT), with the retina being thinner in eyes with lower amplitude and/or higher latency of ERG responses. However, even though previous clinical studies have reported a direct relationship between ERG response and retinal thickness,[35–37] and astigmats more commonly display abnormal ERG signals,[33] it remains unclear whether retinal thickness profiles differ between astigmatic eyes and those of non-astigmats. This study aimed to characterize the OCT-measured retinal thickness in a Chinese adult population with either WTR or ATR astigmatism and compare it with non-astigmatic control eyes. The study also determined whether the retinal thickness variation across astigmatic groups was associated with the best-corrected distance visual acuity (BCDVA). It is worth noting that OCT is a noninvasive and accurate method for measuring the retinal thickness profile and is widely applied for detection of various retinal abnormalities and disease management. This study aimed to provide insights into the orientation-dependent, visually guided optical defocus mechanisms in human eyes and highlight the potential differences in retinal thickness in astigmatic eyes. If astigmatism disturbs retinal thickness during development, it should also be considered in interpreting retinal OCT data in clinical settings.

Methods

This case-control study was approved by the Ethics Committee of The Hong Kong Polytechnic University (HKPU; HSEARS20201201003) and conducted in accordance with the Declaration of Helsinki.

Study Population

The study analyzed the OCT and clinical data of Chinese adults in Hong Kong. As the majority of Chinese adults in Hong Kong exhibit WTR astigmatism,[12] all available participants with ATR astigmatism were identified from records of patients attending the Optometry Clinic of HKPU between January 2013 and January 2021, according to the inclusion criteria (see below). Study participants with WTR and non-astigmats (controls) were then identified by matching their age, gender, and refractive state with those of the ATR participants. Of the 3611 records reviewed, 156 fulfilled the inclusion criteria and were divided into WTR astigmatism, ATR astigmatism, and control groups.

Inclusion and Exclusion Criteria

Inclusion criteria for astigmatic participants were: age between 18 and 45 years; spherical-equivalent (SE) refraction ≥−10.00 diopters (D); and CYL ≤−0.75 D with cylindrical axes of 0 to 30 degrees/150 to 180 degrees for WTR, and of 60 to 120 degrees for ATR, which were determined by subjective refraction. Inclusion criteria for the control group were: age between 18 and 45 years; SE ≥−10.00 D; and CYL ≥−0.25 D. Because the prevalence of astigmatism, particularly ATR, increases after age 45,[12] probably due to the aging effects on the cornea and crystalline lens, this study excluded older adults to prevent these confounding factors from affecting the data interpretation. Exclusion criteria also included: any coexisting or previous ocular disease, including glaucoma and retinal anomalies, cataract and precataractous lens changes, and keratoconus; and history of ocular or retinal surgery. Study participants with BCDVA worse than 0.10 LogMAR, and those with poor OCT imaging quality or unavailable clinical data were also excluded.

Of the 156 participants who fulfilled the inclusion criteria, 55 were excluded due to ocular disease ($n = 24$), history of ocular or retinal surgery ($n = 7$), BCDVA worse than 0.10 LogMAR ($n = 1$), or poor OCT image and unavailable data ($n = 23$). A total of 101 participants were included for final analysis. None of the participants reported a history of myopia control interventions, in particular, orthokeratology or rigid contact lenses that might affect corneal astigmatism. The flowchart for inclusion and exclusion of the study cohort is presented in Figure 1.

Eye Examinations and Measurements

All study participants received a comprehensive eye examination performed by the registered optometrists in the Optometry Clinic of HKPU. Noncycloplegic subjective refraction was conducted using the maximum plus with maximum visual acuity as the end point,[38] in which sphere, cylinder, and axis were recorded. BCDVA was determined with Snellen visual acuity charts and converted into the logarithm of the minimal angle of resolution (LogMAR) for statistical analysis. The AL was obtained with a non-contact optical biometer (IOL Master, Carl Zeiss Meditec, Jena, Germany), and a minimum of three measurements were taken for every participant. The means of these three measurements were used for data analysis. Refractive errors were converted into SE, J0, and J45 astigmatic components using Fourier analyses.[39] The two astigmatic components,

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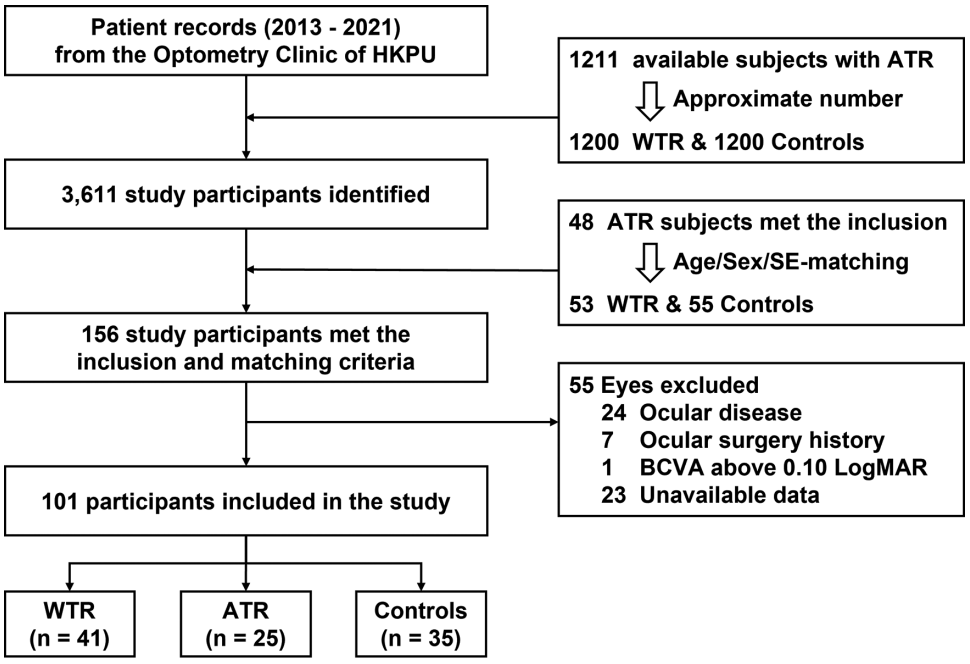

Figure 1. Flowchart for inclusion and exclusion of study cohort. WTR, With-The-Rule astigmatism; ATR, Against-The-Rule astigmatism; BCDVA, best-corrected distance visual acuity.

J0 and J45, represented astigmatism using power vectors, allowing the incorporation of the magnitude and axis of all forms of astigmatism for statistical analysis. In the equations, S is spherical power, C is negative cylindrical power, and α is cylindrical axis.

$$SE = S + \frac{C}{2}$$

$$J_0 = -\frac{C}{2} \times \cos 2\alpha$$

$$J_{45} = -\frac{C}{2} \times \sin 2\alpha$$

OCT Imaging

OCT images were obtained with a spectral-domain OCT (Spectralis OCT, Heidelberg Engineering Inc., Heidelberg, Germany) using a macular volume scan, centering on the fovea formed by 49 horizontal B-scans (512 A-scans per B-scan). The OCT images were acquired by averaging at least 15 frames of B-scan images, with the eye movement tracked by the build-in TruTrack Active Eye Tracking technology to reduce speckle noise and minimize eye motion artifacts. Transverse ocular magnification was adjusted by the Spectralis software based on the mean corneal radius of curvature and SE for each eye. Only OCT images with a signal-to-noise (SNR) ratio of >15 dB and without significant blurring or artifacts affecting the retinal layer segmentation were included for further analyses.

Retinal Thickness Measurements

Retinal thickness within the central 6-mm circle was automatically measured by the inbuilt Heidelberg segmentation software (Heidelberg Eye Explorer). The software delineated different retinal boundaries, including Inner Limiting Membrane (ILM) and Basal Membrane (BM), between which the distance represented the retinal thickness. The retinal segmentation of each B-scan and the grid alignment of each eye were checked, and segmentation errors were manually corrected by a masked imaging analyst. Manual correction was only performed for apparent detectable errors visible on quick inspection (e.g. ILM or BM delineation error). In total, OCT of nine eyes (8.9%) were manually corrected, and no more than five B-scan frames were corrected in each case. The intra-class correlation coefficients (ICCs) between retinal thicknesses (RTs), measured by automatic segmentation with and without manual correction, ranged from 0.917 to 0.977 (all $P < 0.001$; Supplementary Table S1), suggesting good reliability of RT measurements in this study.

A traditional macular grid defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) was used for RT analysis. The ETDRS grid divided the macula into nine sections, including a central 1-mm circle representing the foveal area, a 3-mm diameter inner ring, and a 6-mm diameter outer ring. The inner and outer rings were divided into four quadrants: superior, nasal, inferior, and temporal. A demonstration of ETDRS grid is presented in Supplementary Figure S1.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics (version 26; IBM Corp., Armonk, NY, USA). Due to the highly correlated biometric parameters and OCT-measured RTs between the right and left eyes (Pearson's correlations, range = 0.76 to 0.98, all $P < 0.001$; Supplementary Table S2), only data from the right eyes were used for data analysis. All values are expressed as mean (SD), median (range), or proportions as appropriate. One-way analysis of variance (ANOVA) test was performed to compare the demographic and biometric characteristics among different types of astigmatism (WTR, ATR, and controls). The analysis of covariance (ANCOVA) test was performed to

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compare the retinal thickness across groups, with age, sex, and AL adjusted as the covariates. If a significant main effect was found in ANOVA or ANCOVA, a Bonferroni's pairwise post hoc test was carried out to determine which pair was significantly different. The partial eta-squared (η_p^2) value was calculated to indicate the effect size in ANOVA and ANCOVA tests: small effect, $\eta_p^2 = 0.01$ to 0.06; medium effect, $\eta_p^2 = 0.06$ to 0.14; and large effect, $\eta_p^2 > 0.14$.[40] The associations among RT, BCDVA, and astigmatic components J0 and J45 were determined by Pearson's partial correlation analysis, with adjustment for age, sex, and AL. A two-sided P value of less than 0.05 was considered statistically significant.

Results

Demographic and Biometric Characteristics

In total, data of 101 right eyes from 101 study participants were analyzed. Data were grouped according to their astigmatic magnitude and axis: WTR, $n = 41$; ATR, $n = 25$, and controls, $n = 35$. The demographic information and biometric characteristics of the study cohort are shown in Table 1. The groups were similar for age, gender, SE, AL, corneal curvature, and intraocular pressure (all $P > 0.05$).

Best-Corrected Distance Visual Acuity in Different Types of Astigmatism

BCDVA values were -0.015 ± 0.058, -0.034 ± 0.054, and -0.048 ± 0.060 LogMAR in WTR, ATR, and control groups, respectively (see Table 1). One-way ANOVA showed a significant difference in BCDVA in these three groups ($P = 0.039$, $\eta_p^2 = 0.066$), and Bonferroni's post hoc test further revealed that the difference in BCDVA between WTR and control groups was significant ($P = 0.041$, $\eta_p^2 = 0.065$). Correlation analysis showed that BCDVA was negatively associated with the magnitude of astigmatism ($r = -0.233$, $P = 0.021$), but not with J0 or J45 astigmatic components (both $P > 0.05$), when controlled for age, sex, and AL.

Retinal Thickness in Different Types of Astigmatism

The whole macular and subfield RTs in eyes with different types of astigmatism are shown in Figure 2 and Table 2. The mean (SD) of whole macular RTs were 307.54 ± 11.57, 301.60 ± 7.90, and 302.12 ± 10.46 µm in WTR, ATR, and control groups, respectively. The mean (SD) of RTs in the central subfield (fovea) were 269.59 ± 17.21, 262.36 ± 17.92, and 265.80 ± 21.56 µm in WTR, ATR, and control groups, respectively. The WTR group showed a thicker retina in all sectors compared with the ATR and control groups, reaching a statistically significant level in the whole macula ($P = 0.028$, $\eta_p^2 = 0.073$), inner-superior ($P = 0.042$, $\eta_p^2 = 0.065$), inner-nasal ($P = 0.036$, $\eta_p^2 = 0.067$), and outer-temporal ($P = 0.026$, $\eta_p^2 = 0.074$) subfields, after controlling for age, sex, and AL. Bonferroni's post hoc tests showed that the between-group differences in RT at inner-nasal (WTR vs. ATR, $P = 0.034$, $\eta_p^2 = 0.068$) and outer-temporal (WTR vs. control, $P = 0.042$, $\eta_p^2 = 0.070$) were statistically significant.

In these 101 eyes, RT was negatively associated with the J0 astigmatic component, reaching statistical significance in the whole macular region ($r = -0.267$, $P = 0.037$), inner-superior ($r = -0.268$, $P = 0.037$), and inner-nasal subfields ($r = -0.347$, $P = 0.006$) after adjusting for age, sex, and AL. No significant correlation was found between RTs and astigmatic magnitude nor J45 astigmatic component in any sector (all $P > 0.050$). The correlations between RT and J0 and J45 astigmatic components are shown in Supplementary Table S3.

Correlations Between BCDVA and Retinal Thickness

BCDVA was positively associated with RT in all sectors, reaching statistical significance in the whole macular region

Table 1. Demographic Information and Biometric Characteristics of Study Cohort

	Astigmatism			
	WTR	ATR	Controls	*P* Value*
No.	41	25	35	
Age, y	31.9 (8.1)	32.2 (8.2)	31.1 (7.5)	0.854
Sex (M/F)	18/23	7/18	13/22	0.331
Axial length, mm	26.41 (1.14)	26.47 (0.98)	26.49 (1.18)	0.995
Corneal curvature, mm	7.80 (0.30)	7.81 (0.34)	7.87 (0.32)	0.694
Spherical equivalent, D	−4.49 (3.27)	−4.61 (3.52)	−4.13 (2.98)	0.830
Spherical power, D				0.937
Mean (SD)	−3.88 (3.20)	−4.07 (3.54)	−4.08 (2.98)	
Median (Range)	−2.75 (−9.00, 0.00)	−3.00 (−9.50, 0.00)	−2.75 (−9.25, 0.25)	
Cylindrical power, D				<0.001
Mean (SD)	−1.22 (0.38)	−1.07 (0.32)	−0.11 (0.13)	
Median (Range)	−1.25 (−2.00, −0.75)	−1.00 (−1.75, −0.75)	0.00 (−0.25, 0.00)	
Component J_0	−0.60 (0.20)	0.42 (0.16)	0.01 (0.06)	<0.001
Component J_{45}	0.03 (0.22)	0.16 (0.27)	0.01 (0.05)	0.013
BCDVA (LogMAR)	−0.015 (0.058)	−0.034 (0.054)	−0.048 (0.060)	0.039
IOP (mm Hg)	14.42 (2.68)	14.89 (3.06)	15.60 (2.72)	0.250

All data were expressed as mean (SD) for continuous variables or proportions for categorical variables unless stated otherwise.

WTR, With-The-Rule astigmatism; ATR, Against-The-Rule astigmatism; D, diopter; BCDVA, best-corrected distance visual acuity; IOP, intraocular pressure.

* The *P* value was calculated using 1-way ANOVA test among three groups.

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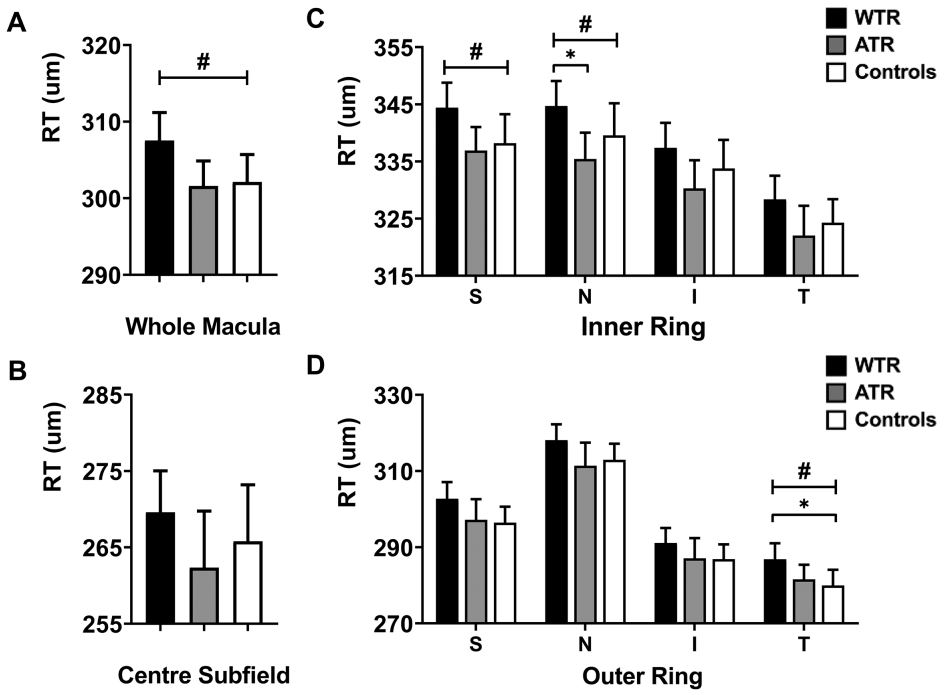

Figure 2. Retinal thickness in eyes with different types of astigmatism. OCT-measured retinal thickness at (**A**) the whole macular, (**B**) foveal region, (**C**) inner, and (**D**) outer ring of the measured region in eyes with different types of astigmatism. WTR, With-The-Rule astigmatism; ATR, Against-The-Rule astigmatism; RT, retinal thickness; S, superior; N, nasal; I, inferior; T, temporal. # Significant differences ($P < 0.05$) across three groups using 1-way ANCOVA test adjusted for the age, sex, and axial length. * Significant differences ($P < 0.05$) between paired groups (Bonferroni's post hoc test).

Table 2. Retinal Thickness in Eyes With Different Types of Astigmatism

	Astigmatism				
	WTR	**ATR**	**Controls**	***P* Value***	***P* Value†**
Retinal thickness, mean (SD)					
Whole macula	307.54 (11.57)	301.60 (7.90)	302.12 (10.46)	**0.028**	–
Central subfield	269.59 (17.21)	262.36 (17.92)	265.80 (21.56)	0.282	–
Inner ring (3 mm)					
Superior	344.41 (13.86)	336.92 (9.97)	338.20 (14.74)	**0.042**	–
Nasal	344.71 (13.84)	335.44 (11.15)	339.57 (16.32)	**0.036**	**W-A, 0.034**
Inferior	337.39 (13.88)	330.28 (11.95)	333.77 (14.56)	0.124	–
Temporal	328.37 (13.10)	322.04 (12.62)	324.29 (14.93)	0.147	–
Outer ring (6 mm)					
Superior	302.73 (13.82)	297.20 (13.11)	296.46 (12.18)	0.087	–
Nasal	318.10 (13.19)	311.40 (14.68)	312.94 (12.39)	0.106	–
Inferior	291.12 (12.40)	287.08 (12.88)	286.89 (11.24)	0.200	–
Temporal	286.85 (13.26)	281.56 (9.34)	279.97 (11.95)	**0.026**	**W-C, 0.042**

WTR, With-The-Rule astigmatism; ATR, Against-The-Rule astigmatism.

* The *P* value calculated by 1-way ANCOVA analysis across three groups, with age, sex, and axial length used as covariates for adjustment.

† The *P* value calculated using Bonferroni's pairwise post hoc test, only significant differences are listed. W-A, WTR vs. ATR; W-C, and WTR vs. controls.

($r = 0.206$, $P = 0.041$) and four quadrants in the outer ring of the measured ETDRS grid ($r = 0.199$ to 0.243, $P = 0.016$ to 0.049) after adjusting for age, sex, and AL. Correlations between BCDVA and RTs in the whole cohort are shown in Figure 3 and Supplementary Table S3.

The association between BCDVA and RT was also investigated in eyes with different types of astigmatism for stratification analysis. In the WTR group, BCDVA was positively correlated with RT for the whole macular region (r = 0.338, $P = 0.038$) and four quadrants in the outer ring of the ETDRS grid ($r = 0.340$ to 0.485, $P = 0.002$ to 0.041), after adjusting for age, sex, and AL. However, no significant correlation between BCDVA and RT in either the whole macular region or individual subfields was noted in the ATR and control groups. Stratification analysis for correla-

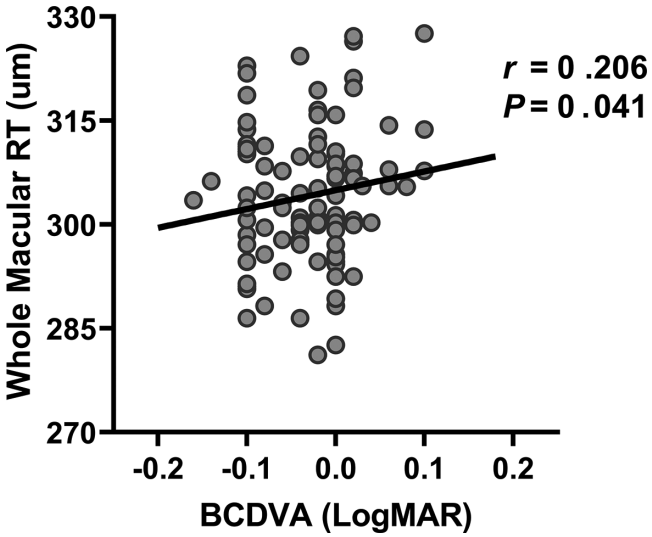

Figure 3. Correlation between BCDVA and retinal thickness in the whole cohort. Associations between RT and BCDVA were obtained by Pearson's partial correlation analysis after adjusting for age, sex, and axial length. BCDVA, best-corrected distance visual acuity; RT, retinal thickness.

tions between BCDVA and RTs are shown in Supplementary Table S4.

Discussion

Using OCT imaging technology, this study reports, for the first time, the influence of different types of astigmatism on RT and its relationship with visual acuity in a Chinese adult population. Both retinal thickness and BCDVA differed significantly between different types of astigmatism, with the thickest retina and poorest BCDVA found in eyes with WTR astigmatism. In addition, a significant correlation of increased BCDVA and increased retinal thickness was observed. However, stratification analysis revealed that this significant correlation only applied to the WTR group. Our findings suggest that the effect of astigmatism on RT and BCDVA may vary depending on not only the magnitude, but also on the axis of astigmatism.

Orientation-dependent optical cues associated with astigmatism may play an important role in ocular growth, affecting not only changes in axial length and refractions,[20,21,28] but also chorioretinal structure.[17,30] Hoseini-Yazdi et al.[30] imposed 60 minutes of WTR and ATR astigmatic blurs to 18 healthy young adults using +3.00 D cylindrical lenses and observed bi-directional changes in choroidal thickness measured using OCT, significant thickening with imposed WTR, and thinning with ATR astigmatism. In contrast, after imposing WTR and ATR astigmatic blurs to chicks using sphero-cylindrical lenses for a week, Vyas and Kee[17] found a significant choroidal thickening in chicks with ATR treatment, but not in the WTR treatment group. Most recently, Chan et al. reported bi-directional changes in refractive astigmatism in young adults ($n = 19$) exposed to only 60 minutes of either WTR or ATR astigmatic blur using +3.00 D cylindrical lenses. The J0 astigmatism became less positive (from +1.53 DC to +1.28 DC) in the WTR condition and less negative (from –1.33 DC to –0.94 DC) in the ATR condition, suggesting compensatory responses to minimize the astigmatic blur at the outset of the experiment.[31] Taken together, these findings are consistent with orientation-dependent modulation of astigmatic errors, as a component of refractive error development.

In the current study, when RT was obtained by SD-OCT and compared between eyes with different types of astigmatism, it was observed that WTR astigmats showed a significantly thicker retina in the macula compared with the ATR and control groups. This finding has not been previously reported. In Vyas and Kee's study,[17] no difference in axial RT measured by A-scan ultrasonography was found between chicks with induced WTR and ATR astigmatism, which was in agreement with the current study (foveal thickness, $P > 0.05$). However, perifoveal RTs were not measured in that chick study.[17]

When analyzing the regional retinal thickness, post hoc analyses revealed that WTR astigmats had a thicker retina along horizontal meridian than the ATR and control groups, reaching statistically significance for the inner nasal and outer temporal regions. Humans are often born with a substantial degree of hyperopia.[41,42] This hyperopic defocus is known to trigger the eye to grow toward the focal plane, thereby reducing the refractive error and finally achieving the emmetropic state ("emmetropization").[43] In a hyperopic eye with WTR astigmatism, the horizontal line focus is formed closer to the retina than the vertical line focus, creating a horizontally oriented blur visual signal at the retinal plane (i.e. each point object becomes an ellipse with a horizontal major axis). With respect to the retinal neural processing pathway, the ganglion and amacrine cells of many vertebrates are orientation-selective, responding more robustly to a preferred orientation.[32,44] In the peripheral retina, the preferred orientation of these orientation-selective cells appears to lie in parallel to the radial orientation (e.g. the orientation-selective cells in the nasal and temporal retina prefer horizontally oriented stimuli).[45–47] Thus, these cells at the nasal and temporal retina are more likely to receive optical signals of their preferred orientation under the hyperopic-astigmatic WTR condition compared to those in the superior and inferior retina. The orientation-dependent optical blur created by astigmatism may influence retinal structural development and lead to meridional differences in RT.

However, it is worth noting that this hypothesis does not seem to work for the insignificant difference in regional RT between the ATR and control groups, and the current retrospective study did not monitor the retinal structural changes longitudinally. Thus, further longitudinal clinical studies or animal research is required to confirm the above speculation about the effects of astigmatism on RT changes. In addition, whereas on-axis astigmatism dominates in the central visual field, off-axis astigmatism increases in the mid to far peripheral regions[48] and largely determines the characteristics of peripheral retinal defocus, consequently affecting peripheral RT and local eye growth in those regions. However, this study only investigated the RT at the macular region (central 6-mm diameter, approximately 20 degrees of the central visual field). Although peripheral refraction data was unavailable in the current study, the relative off-axis astigmatism, which was calculated using the data provided by Atchison, Pritchard, and Schmid (2006),[48] appears to be negligible across the 6-mm central retina (within −0.302 DC, see Supplementary Material for details). Thus off-axis astigmatism likely had limited impact on the RT data reported here.

Nevertheless, further investigation would be worthwhile to determine whether and how off-axis astigmatism, in terms of its magnitude, axis, and asymmetry, influences the retinal defocus pattern in mid to far peripheral regions and contributes to subsequent retinal structural development. Future studies should take into account peripheral refractions and would also benefit from wide-field OCT measurements. They would also benefit from more detailed analysis of retinal images and the inclusion of choroidal thickness data.

Because of the limitation of the cross-sectional design, the causal relationship between astigmatism and RT cannot be addressed in this study. Because a thicker retina was also found to be associated with a poorer BCDVA, it is also possible that participants in different astigmatic groups had different early visual experiences, which may have affected retinal structure and function, and subsequently, the course of emmetropization, resulting in different amounts and types of astigmatism in their later life. Popa et al.[16] recently showed that whereas chicks could develop astigmatism to partially compensate for the optically imposed cylindrical errors by +4.00 DS/−8.00 DC lens, such compensatory astigmatism could not be induced when the retinal circuit was destroyed by intravitreal injection of 20 μL excitotoxin mixture (2 μmol N-methyl-D-aspartate, 0.2 μmol quisqualic acid, 0.2 μmol kainic acid; could destroy most of the retinal interneurons, mainly amacrine cells), indicating the necessity of a healthy retina for normal astigmatic compensation. Further investigation is required involving both clinical and laboratory studies, to verify our speculation and understand the mechanism controlling RT in astigmatic eyes.

Several studies have reported that astigmatism influences the optical measurements obtained by OCT,[49,50] which was suggested to be attributable to an ocular magnification effect caused by corneal astigmatism. The optical distortion due to the magnification factor may alter scan distance and lead to changes in RT measurement. In this study, both corneal curvature and refraction were first matched across groups (see Table 1), and entered in the Spectralis software to minimize the influence of any astigmatism-related magnification factor on OCT measurement. According to the Spectralis technical guidelines, a 0.1 mm difference in corneal radius of curvature will only induce a 0.8% error in lateral measurement.[51] Based on the corneal curvature for individual groups in this study, the deviation of transverse magnification calculated from the mean corneal radius of curvature and from each power meridian should be less than 1%. Notably, a previous study found only negligible changes (<1 um) in macular thickness measured by the OCT immediately after participants wore −3.25 DC astigmatic soft contact lenses to induce WTR and ATR astigmatism.[49] Taken together, the potential optical magnification effects of corneal astigmatism on OCT measurement of RT cannot explain the increased RT in the WTR group of the current study.

In this study, BCDVA differed significantly among the WTR, ATR, and control groups, eyes with WTR astigmatism having poorest BCDVA. In this regard, many studies observed a reduction of visual acuity with increasing astigmatic magnitude,[52,53] but the influence of astigmatic axis on visual acuity remains controversial.[52,54–58] In contrast to the current study, astigmatism in most previous studies was optically induced by a cylindrical lens,[52,54] refractive surgery,[55,56] or computer simulation,[57,58] and the different study designs adopted may have led to varying findings. For instance, the neural effect of astigmatic blur could be influenced by the axis of astigmatic blur, the magnitude and axis of a subject's natural astigmatism, and even the types of stimuli (optical defocus vs. simulated blur).[59] Importantly, a population-based study[53] in China observed a higher prevalence of visual impairment (defined as BCDVA ≤0.7) in WTR astigmats, when the astigmatism was ≥0.75 D, which is in agreement with our findings with a similar study population (i.e. Chinese with naturally occurring astigmatism).

Astigmatism during childhood may result in a form of meridian-specific visual impairment ("meridional amblyopia"),[60,61] which is a result of abnormal development in the primary visual cortex and may lead to visual deficits across a range of visual functions.[61–63] Several studies suggested subtle increases in RT of amblyopic eyes (BCDVA >0.3 LogMAR).[64,65] Indeed, children born with WTR astigmatism, which is the predominant form in Chinese infants,[4–6] are prone to developing amblyopia when it is not corrected during childhood.[63] Although none of the participants reported amblyopia in the current study, whether the thicker retina and poorer BCDVA observed in our WTR group were by-products of amblyopia remains unanswered. Notably, despite the significant differences in BCDVA across groups, all participants had BCDVA better than 0.10 LogMAR, and the difference across groups ranged only from 1 to 2 letters, which may not be detectable in clinical practice.

Analysis revealed that BCDVA was positively associated with RT after adjusting for age, sex, and AL, and reached statistical significance in the whole macular and outer rings of the measured regions. In this respect, several studies have reported associations between macular RT and visual acuity, but the directions of associations varied.[66–71] In amblyopic eyes, an increased macular thickness has been associated with poorer visual acuity.[64] Yen et al.[72] hypothesized that amblyopia might disrupt the postnatal development of the macula, including the normal decline in the number of retinal ganglion cells[73] and axons,[74] resulting in a thicker macula than non-amblyopic eyes. However, other studies have observed a reverse association in normal emmetropic[69,70] and myopic[71] eyes, with a thicker retina corresponding to better visual acuity. Presumably, a thicker macula might reflect more densely packed retinal neurons (e.g. photoreceptors and ganglion cells), thereby increasing the Nyquist frequency and so improving visual acuity. However, neither explanation above can fully explain the findings in the current study.

A noticeable difference in this study compared to previous reports, is that we stratified participants into WTR, ATR, and non-astigmatic control groups. It should be noted that the inverse relationship between retinal thickness and BCDVA only existed in the WTR group, but not in the ATR or control groups in the stratification analyses (see Supplementary Table S4). Further studies involving a detailed analysis of individual retinal layers and multifocal electrophysiological recordings are needed to investigate the origin of observed RT changes and their association with functional changes. Furthermore, this study only included participants with BCDVA better than 0.1 LogMAR, whereas other studies[69–71] recruited participants with poorer BCDVA (up to 1.0 LogMAR). Thus, the insignificant correlation in the ATR and control groups may be due to the restricted BCDVA range.

To our knowledge, this is the first study that has compared the RT and BCDVA between different types of astigmatism (WTR, ATR, and controls) by closely matching participants' other characteristics in a Chinese adult population. Our findings suggest that the astigmatic magnitude and

axis influence retinal development, and astigmatism should be considered in the clinical management of ocular diseases related to retinal abnormalities and when interpreting OCT data. However, our design has several limitations. First, this is not a population-based study, as study participants were drawn from an existing patient base, and the sample size may be inadequate to detect all of the different patterns of RT and BCDVA among three types of astigmatism using a stratification analysis. The limited sample size in each group may explain why a significant correlation of RT and BCDVA was found in the WTR astigmats, but not in the ATR and control groups. Second, this work was a cross-sectional study and, thus, did not investigate the causal relationship between astigmatism and RT. A longitudinal study should be performed to further investigate how the astigmatic axis plays a role in RT and visual acuity development in human eyes. Third, manual correction for automatic segmentation may potentially introduce some bias for retinal thickness measurements. Although the ICCs between RT measured with and without manual correction indicated good reliability, a second independent evaluator or a more robust automatic approach for retinal segmentation should be considered in future studies to minimize potential measurement bias. Fourth, participants' history of refractive correction in childhood was unavailable in this retrospective study, and we cannot rule out the possibility that the reduced visual acuity could be due to abnormal visual development during childhood. A pinhole visual acuity test to distinguish between optical and neural contributions to the reduced visual acuity was not performed.

Conclusions

Greater RT and poorer best-corrected distance visual acuity were found in eyes of Chinese adults with WTR astigmatism, compared with those in the ATR and control groups. The findings suggest that the astigmatic magnitude and axis influence retinal structure and function. However, the underlying mechanism has yet to be investigated. Further longitudinal studies are needed to investigate retinal structural and functional changes in astigmatic children.

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Investigative Ophthalmology & Visual Science

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