

Corneal Thickness Profile and Posterior Corneal Astigmatism in Normal Corneas

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Purpose: To analyze the influence of corneal thickness profile on posterior corneal astigmatism (PA).

Design: Prospective, observational study.

Subjects: We included 418 normal subjects (213 men and 205 women) ranging in age from 6 to 93 years (49.0±23.4 years, mean ± standard deviation) in this study.

Methods: Anterior and posterior corneal topography were evaluated using 3-dimensional anterior segment optical coherence tomography. Pericentral corneal thickness (PCT) in each quadrant (superior, inferior, nasal, and temporal) was measured, and average PCT in the vertical (superior + inferior) and horizontal (nasal + temporal) directions was calculated. Posterior corneal astigmatism was calculated as (1) assumed PA based on the anterior corneal curvature measurement and the keratometric index and (2) actual PA derived from the direct measurement of posterior corneal curvature.

Main Outcome Measures: Corneal thickness distribution and the difference between assumed and actual PA.

Results: The PCT was significantly greater in the vertical (546.0±31.8 μm) than in the horizontal direction (542.6±31.7 μm) ($P < 0.0001$), and the difference between them was significantly correlated with subject age ($r = 0.518$, $P < 0.0001$). The difference between assumed and actual PA significantly correlated with the discrepancy between vertical and horizontal PCT ($r = 0.819$, $P < 0.0001$), as well as subject age ($r = 0.533$, $P < 0.0001$).

Conclusions: Corneal thickness is greater in the vertical than in the horizontal direction, making the PA more against-the-rule pattern than calculated on the basis of the anterior corneal curvature measurement only. Such discrepancy is more prominent in older patients. *Ophthalmology* 2015;122:1072-1078 © 2015 by the American Academy of Ophthalmology.

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A precise measurement of corneal refractive power is of vital clinical importance to obtain optimal postoperative refraction after cataract surgery. The keratometer is the device most commonly used to evaluate corneal curvature, but it measures only the curvature of the anterior corneal surface. To estimate the total corneal refractive power without directly measuring the posterior corneal curvature, the keratometric index was introduced.¹ The keratometric index is used on the basis of the premise that the anterior and posterior corneal curvatures have a constant and linear relationship.^{2,3} However, this premise is not always true because the anterior-posterior curvature ratio varies from eye to eye,^{2,3} making the keratometric index not necessarily accurate in all cases.

With the growing popularity of toric intraocular lenses to correct preexisting corneal astigmatism at the time of cataract surgery,⁴⁻⁶ accurate evaluation of corneal astigmatism has become more important. Previous studies evaluated the contribution of posterior corneal astigmatism (PA) to total corneal astigmatism with Scheimpflug cameras^{7,8} and anterior segment optical coherence tomography (AS-OCT),⁹ and reported that keratometric astigmatism (KA) may misinterpret actual total corneal astigmatism. That is, in eyes with with-the-rule (WTR) astigmatism, KA overestimated total corneal astigmatism, whereas in eyes with against-the-rule (ATR) astigmatism, KA underestimated total corneal astigmatism.⁷⁻⁹

Several studies have evaluated pachymetry mapping on the annular ring around the corneal apex in normal eyes¹⁰⁻¹³ and demonstrated that the corneal thickness profile is not uniform depending on the radial direction. Such nonuniformity of corneal thickness distribution influences the anterior-to-posterior ratio of corneal curvature and thus jeopardizes the validity to calculate corneal refraction using the keratometric index, but those factors have not been investigated. Especially if the anterior and posterior corneal curvatures lack mutual linearity, estimation of PA and KA based on the measurements of anterior corneal curvature alone can be misleading.

In this study, we examined the corneal thickness distribution in the 4 quadrants (superior, inferior, nasal, and temporal) and compared the thickness profile in vertical and horizontal directions. We calculated PA as (1) assumed PA derived from the anterior corneal curvature and the keratometric index and (2) actual PA based on the direct measurement of posterior corneal curvature. We then assessed the association of subject age with the discrepancy between assumed and actual PA values.

Methods

Study Group

This study followed the tenets of the Declaration of Helsinki. Subjects were recruited from the University of Tsukuba Hospital and Ito

Eye Clinic between April 2010 and August 2013. The inclusion criteria were as follows: eyes with spherical equivalent between -10.0 and $+3.0$ diopters (D) and with no history of ocular surgery or contact lens wear. Eyes with corneal diseases (e.g., keratoconus, corneal dystrophy) were excluded. Those with eyelid, orbit, or conjunctival diseases that could affect the corneal shape were also excluded. When bilateral eyes were eligible, data from the right eye were used for the analyses. The research was approved by the Institutional Review Board of University of Tsukuba Hospital, and informed consent was obtained from all subjects.

Three-Dimensional Anterior Segment Optical Coherence Tomography

Corneal topography was performed by experienced examiners (Y.U., M.M., and M.I.) using a 3-dimensional AS-OCT (SS-1000, CASIA, Tomey Corp, Nagoya, Japan), which is a 1310-nm swept-source optical coherence tomography (OCT) with a scan speed of 30 000 axial scans per second.¹⁴ During 1 scan, 16 cross-sectional corneal images were obtained in 0.34 seconds, with a 10.0-mm scan range diameter. Each image consisted of 512 telecentric A-scans.¹⁵ The anterior and posterior corneal height and pachymetry data were computed for each measurement point. During the noncontact scan, subjects self-fixated on a target to align the center of their corneas for measurements. All measurements were repeated at least twice to obtain clear images of the anterior and posterior corneal surfaces, and the best image was chosen by the examiner for data analyses.

Pachymetry

From the pachymetry, central corneal thickness (CCT) was recorded, and the pericentral corneal thickness (PCT) in each quadrant (superior, inferior, nasal, and temporal) was calculated as the average corneal thickness in each quadrant on the annular ring that was 3 mm in diameter around the corneal apex (Fig 1). The vertical corneal thickness was defined as the average PCT in superior and inferior quadrants, and the horizontal corneal thickness was defined as the average PCT in nasal and temporal quadrants.

Posterior Corneal Astigmatism

The PA was calculated by 2 ways: (1) assumed PA derived from the anterior corneal curvature and the keratometric index and (2) actual PA based on the direct measurement of posterior corneal curvature.

The keratometric power is calculated as the simulated total corneal power using the keratometric index (1.3375) and the radius of anterior corneal curvature. In this study, the assumed PA was computed from the keratometric power on the basis of the following assumptions: the ratio of anterior corneal power to posterior corneal power is constant, and thus the ratio of posterior corneal power to keratometric power is also constant.

$$\text{keratometric power} = (1.3375 - 1.0)/r(a)$$

$$\text{posterior corneal power} = (1.336 - 1.376)/r(p)$$

$$\text{*keratometric index} = 1.3375$$

$$\text{refractive index of the aqueous humor} = 1.336$$

$$\text{refractive index of the cornea} = 1.376$$

$$r(a), \text{ radius of anterior corneal curvature}$$

$$r(p), \text{ radius of posterior corneal curvature}$$

$$\text{posterior to keratometric power ratio (posterior corneal power/keratometric power)}$$

$$= (1.336 - 1.376) \times r(a)/(1.3375 - 1.0) \times r(p)$$

$$= -0.119 \times r(a)/r(p)$$

$$\text{refractive power of the posterior cornea}$$

$$= -0.119 \times r(a)/r(p) \times \text{keratometric power}$$

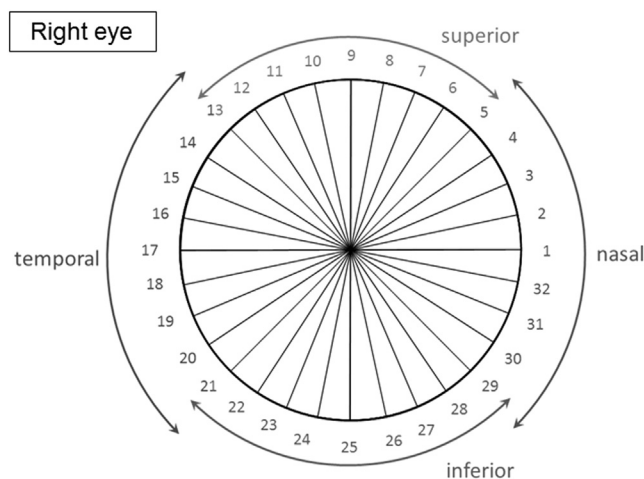


Figure 1. The pericentral corneal thickness in each quadrant (superior, inferior, nasal, and temporal) was calculated as the average corneal thickness in each quadrant on the annular ring that was 3 mm in diameter around the corneal apex.

The magnitude of KA was calculated from the keratometric powers on the steepest and flattest meridians. According to this formula, the magnitude of assumed PA was computed: assumed PA = $[0.119 \times r(a)/r(p)] \times KA$. The axis of assumed PA and the axis of KA are orthogonalized to each other.

The actual PA was calculated from the posterior corneal curvatures on the steepest and flattest meridians, as directly measured with the 3-dimensional AS-OCT.

All measurements including PA were based on the data from the annular ring that was 3 mm in diameter around the corneal apex. The type of anterior corneal astigmatism was categorized into WTR, ATR, and oblique. The astigmatism was judged to be WTR when the steepest meridian was between 60° and 119° . That with the steepest meridian of 0° to 29° or 150° to 180° was considered to be ATR, and all others were regarded as oblique. The relationship between the magnitude of KA and the actual PA was analyzed in each type of anterior corneal astigmatism.

Using vector analysis, double-angle plots were generated and the difference in vectors between the assumed and actual PA was calculated. The magnitude of vector difference between the assumed and the actual PA was analyzed in relation to the difference in corneal thickness between the vertical and horizontal directions, as well as subject age.

Statistical Analysis

The PCT in the superior, inferior, nasal, and temporal quadrants was compared using 1-way analysis of variance with Bonferroni multiple comparison. The magnitude of actual PA was compared among eyes with anterior WTR, ATR, and oblique astigmatism. The vertical and horizontal corneal thicknesses were compared using the paired *t* test. The assumed and actual PA were also compared. The CCT, PCT in each quadrant, difference in corneal thickness between the vertical and horizontal directions, and magnitude of vector difference between the assumed and the actual PA were analyzed in relation to age using the Pearson correlation test. In each type of anterior corneal astigmatism, the relationship between KA and actual PA was also analyzed. The magnitude of vector difference between the assumed and the actual PA was analyzed in relation to the difference in corneal thickness between the vertical and horizontal directions. *P* values <0.05 were

Table 1. Correlation between Corneal Thickness and Age

	Mean \pm SD	P Value* (Correlation Coefficient)
CCT	530.7 \pm 31.5 μ m	0.0386 ($r = -0.101$)
PCT		
Superior quadrant	554.6 \pm 33.4 μ m	0.5324
Inferior quadrant	537.4 \pm 31.2 μ m	0.0032 ($r = -0.144$)
Nasal quadrant	548.9 \pm 32.1 μ m	0.0289 ($r = -0.107$)
Temporal quadrant	536.2 \pm 31.6 μ m	0.0112 ($r = -0.124$)
Vertical corneal thickness	546.0 \pm 31.8 μ m	0.0766
Horizontal corneal thickness	542.6 \pm 31.7 μ m	0.0176 ($r = -0.116$)
Difference (vertical – horizontal)	3.4 \pm 1.8 μ m	<0.0001 ($r = 0.518$)

CCT = central corneal thickness; PCT = pericentral corneal thickness; SD = standard deviation.

*Correlation between corneal thickness and age using the Pearson correlation coefficient.

considered statistically significant. Statistical analyses were conducted using StatView version 5.0 (SAS Inc, Cary, NC).

Results

In total, 418 participants (213 men and 205 women) were enrolled in this study, ranging in age from 6 to 93 years (49.0 \pm 23.4 years, mean \pm standard deviation). The spherical equivalent of the eyes was between -10.0 and $+2.90$ D (-2.15 ± 2.90 D).

Table 1 shows pachymetry data and their correlation with subject age. The PCT was significantly greater in the superior quadrant than in the nasal ($P = 0.0111$), inferior ($P < 0.0001$), and temporal quadrants ($P < 0.0001$). The PCT in the nasal quadrant was significantly larger than that in the inferior ($P < 0.0001$) and temporal quadrants ($P < 0.0001$). There was no significant difference in PCT between the nasal and temporal quadrants.

Among the 4 quadrants, PCT was the greatest in the superior, nasal, and inferior quadrants in 337 eyes (80.6%), 71 eyes (17.0%), and 10 eyes (2.4%), respectively. The PCT was the smallest in the temporal, inferior, and nasal quadrants in 258 eyes (61.7%), 158 eyes (37.8%), and 2 eyes (0.5%), respectively.

There was significant correlation between age and CCT ($r = -0.101$, $P = 0.0386$). Age of the subjects showed significant correlation with PCT in the inferior, nasal, and temporal quadrants, but not with PCT in the superior quadrant (Table 1).

The vertical corneal thickness was significantly greater than the horizontal corneal thickness, and the difference between them was significantly correlated with subject age ($r = 0.518$, $P < 0.0001$) (Fig 2).

Keratometric astigmatism, assumed PA, and actual PA are presented in Table 2. In all subjects, there was a significant difference between the assumed and the actual PA ($P < 0.0001$). When measurement results are compared according to the type of anterior corneal astigmatism, the actual PA was significantly greater in eyes with WTR astigmatism than in those with ATR ($P < 0.0001$) and oblique astigmatism ($P < 0.0001$). The actual PA was significantly greater in eyes with oblique astigmatism

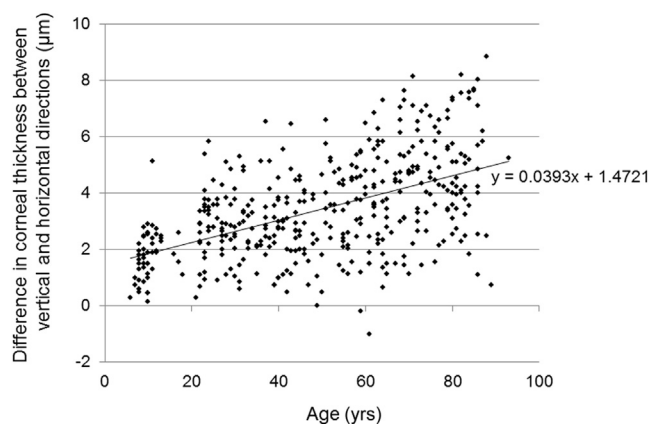


Figure 2. Subject age showed a significant correlation with the difference between vertical and horizontal corneal thickness (Pearson's correlation coefficient, $r = 0.518$, $P < 0.0001$).

than in those with ATR astigmatism ($P = 0.0002$). There was a significant correlation between the magnitude of KA and the actual PA in the WTR group ($r = 0.764$, $P < 0.0001$) (Fig 3A) and ATR group ($r = -0.294$, $P = 0.0019$) (Fig 3B), but not in the oblique astigmatism group ($r = 0.263$, $P = 0.0841$) (Fig 3C).

Figures 4 and 5 are the double-angle plots showing assumed and actual PA. The vector difference between the assumed and the actual PA was 0.23 ± 0.10 D at an axis of $178\pm 8^\circ$, the magnitude of which showed a significant correlation with subject age ($r = 0.533$, $P < 0.0001$) (Fig 6).

Figure 7 shows scatterplots demonstrating the difference in corneal thickness between vertical and horizontal directions versus the magnitude of vector difference between the assumed and actual PA. There was a significant correlation between them ($r = 0.819$, $P < 0.0001$).

Discussion

In the past, topographic studies of corneal posterior surface have been conducted using scanning-slit topography and Scheimpflug cameras, but similar measurements became possible recently with OCT-based topography. The advent of Fourier-domain OCT drastically shortened the measurement time, and swept-source AS-OCT with a faster scan rate significantly reduced the influence of motion artifacts.¹⁶ Jhanji et al¹⁷ reported that swept-source AS-OCT, which is the same device we used in the current study, had better reproducibility coefficients and intraclass correlation coefficients in the assessment of corneal thickness than scanning-slit topography. Szalai et al¹⁸ also used the same swept-source AS-OCT and reported that the repeatability of corneal thickness measurements was comparable with that of Scheimpflug cameras. These reports confirm the validity of corneal thickness measurements with swept-source AS-OCT.

Although many previous studies have investigated CCT,^{19–26} there has been a paucity of information on PCT in living human eyes because PCT is difficult to measure in situ. Recently, developments of the Scheimpflug camera and AS-OCT have led to more precise and easier measurements

Table 2. Corneal Astigmatism

	All Subjects	Type of Anterior Corneal Astigmatism		
		WTR (266 Eyes)	ATR (108 Eyes)	Oblique (44 Eyes)
KA (D)				
Mean magnitude	1.05±0.68	1.13±0.70	0.98±0.65	0.70±0.40
Mean vector	0.47 (Axis 88°)	1.06 (Axis 90°)	0.88 (Axis 1°)	0.11 (Axis 73°)
Assumed PA (D)				
Mean magnitude	0.15±0.10	0.16±0.10	0.14±0.09	0.10±0.06
Mean vector	0.06 (Axis 178°)	0.15 (Axis 0°)	0.12 (Axis 91°)	0.02 (Axis 163°)
Actual PA (D)				
Mean magnitude	0.31±0.14	0.36±0.13	0.20±0.09	0.29±0.09
Mean vector	0.29 (Axis 178°)	0.35 (Axis 178°)	0.16 (Axis 2°)	0.26 (Axis 177°)

ATR = against-the-rule; D = diopters; KA = keratometric astigmatism; PA = posterior corneal astigmatism; WTR = with-the-rule.

of PCT,^{12,13} which allow detailed assessments of PCT in vivo.^{10–13} Studies using these devices by Khoramnia et al,¹⁰ Zheng et al,¹¹ Li et al,¹² and Huang et al¹³ showed that PCT tended to be greater in the superior direction. However, statistical comparisons of PCT among the 4 quadrants have not been conducted.^{10–13} In this study, we compared PCT in the 4 quadrants and discussed the difference in corneal thickness between the vertical and horizontal directions. It was found that the cornea was thicker in

the vertical than in the horizontal direction, which can explain why the posterior cornea surface tends to be more ATR astigmatic than the anterior corneal surface, as demonstrated by recent studies.^{7–9}

As for the age-related change in CCT, many studies have reported that human corneas become thinner with age,^{19–24} but there have been several conflicting reports.^{11,13,25} In regard to PCT, few studies have referred to the detailed relationship between PCT and age.^{11,13} Zheng et al¹¹ and

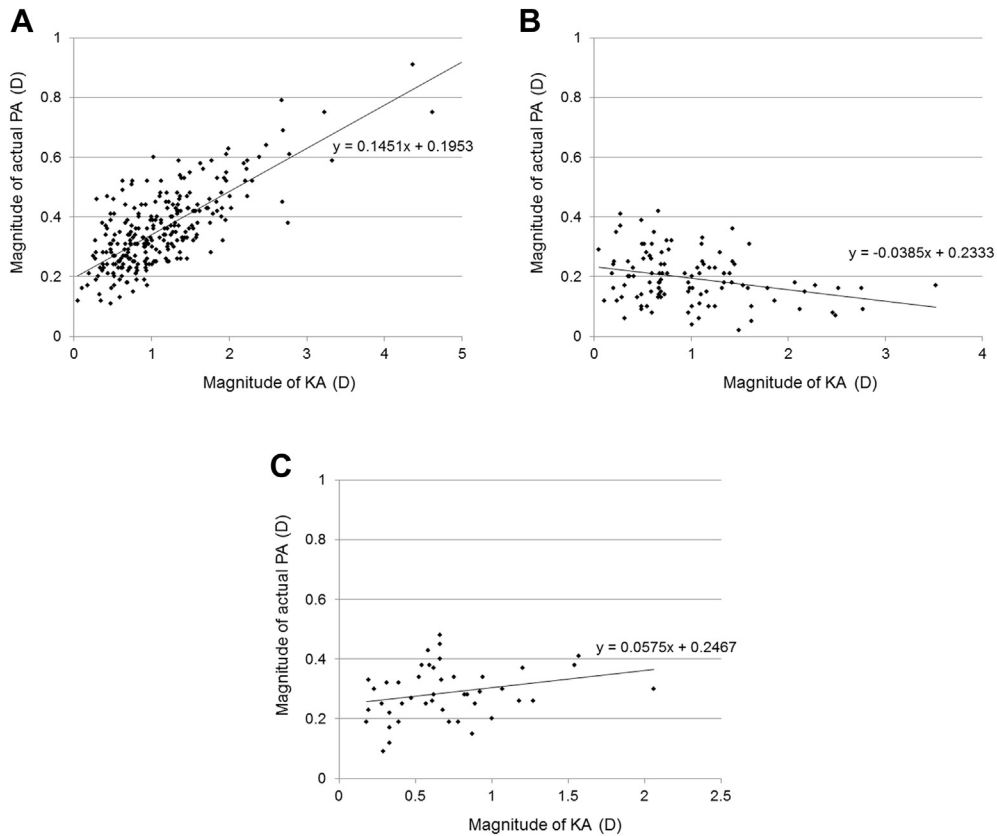


Figure 3. There was a significant correlation between the magnitude of keratometric astigmatism (KA) and actual posterior corneal astigmatism (PA) in eyes (A) with with-the-rule (WTR) astigmatism ($r = 0.764, P < 0.0001$) and (B) against-the rule (ATR) astigmatism ($r = -0.294, P = 0.0019$), but not in those with oblique astigmatism ($r = 0.263, P = 0.0841$; C). D = diopters.

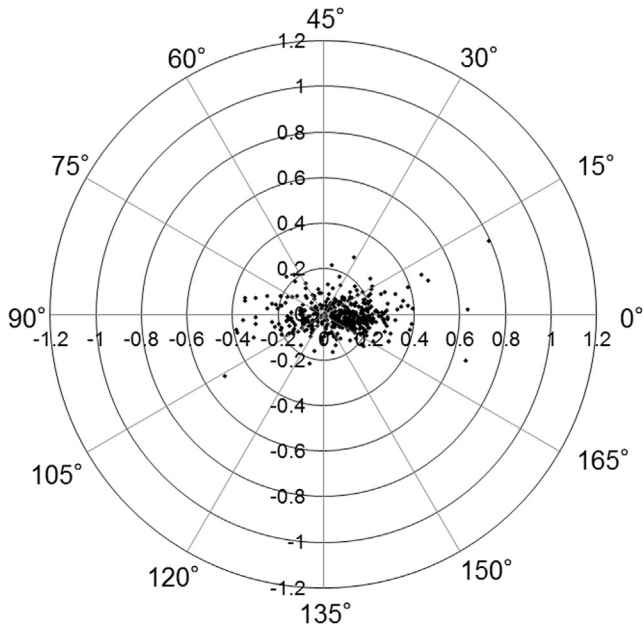


Figure 4. Double-angle plot of assumed posterior corneal astigmatism (each ring = 0.2 diopters [D], outer ring = 1.2 D). Data are mostly scattered around the center.

Huang et al¹³ reported that no correlation was found between age and CCT, as well as PCT. In this study, we found that PCT in the inferior, nasal, and temporal quadrants showed a significantly negative correlation with aging, whereas PCT in the superior quadrant did not. The age-related microstructural changes of the normal cornea

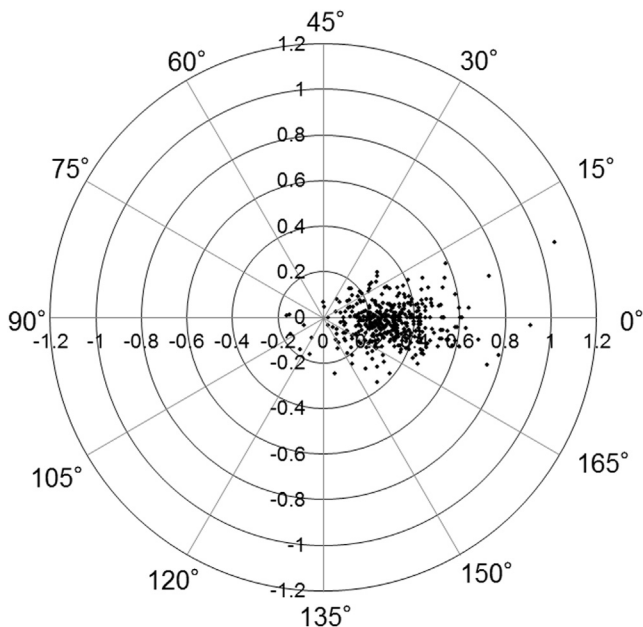


Figure 5. Double-angle plot of actual posterior corneal astigmatism (PA) (each ring = 0.2 diopters [D], outer ring = 1.2 D). Data are scattered mostly to the right of the center, indicating that actual PA tends to have an against-the-rule pattern.

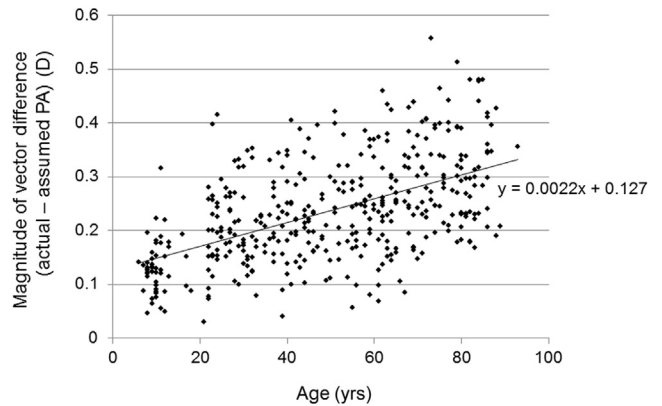


Figure 6. A significant correlation between age and magnitude of vector difference (actual – assumed posterior corneal astigmatism [PA]) (Pearson correlation coefficient, $r = 0.533$, $P < 0.0001$). D = diopters.

were investigated with laser scanning in vivo confocal microscopy.^{25,26} Niederer et al²⁵ reported that the density of the sub-basal nerve fiber, keratocytes, and endothelial cells declined with age, and Germundsson et al²⁶ reported that Bowman’s layer became thinner with age. These changes may be the source of reduction in CCT and PCT with age, as observed in our study. In addition, the presence of the upper eyelid may play a role by protecting the upper cornea from some age-related changes, such as dehydration. This can result in the regional discrepancy in corneal thickness, especially between the vertical and horizontal directions in older subjects. Further studies should be conducted to elucidate these points.

With the use of the Scheimpflug camera, Ho et al⁷ and Koch et al⁸ measured both the anterior and posterior corneal curvatures and revealed that the amount of actual PA was greater in eyes with anterior WTR astigmatism

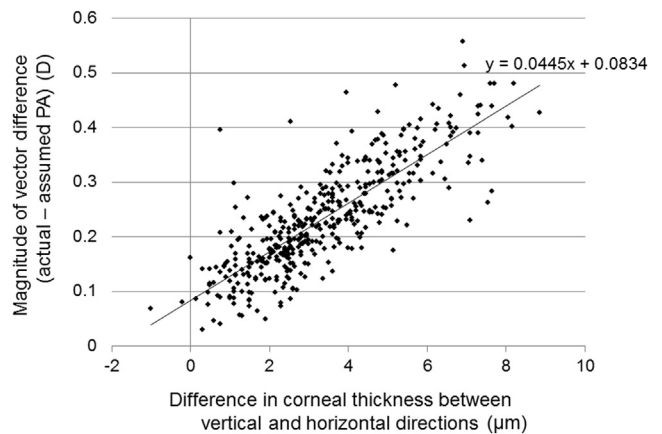


Figure 7. Difference in vertical and horizontal corneal thickness showed a significant correlation with magnitude of vector difference (actual – assumed posterior corneal astigmatism [PA]) (Pearson correlation coefficient, $r = 0.819$, $P < 0.0001$).

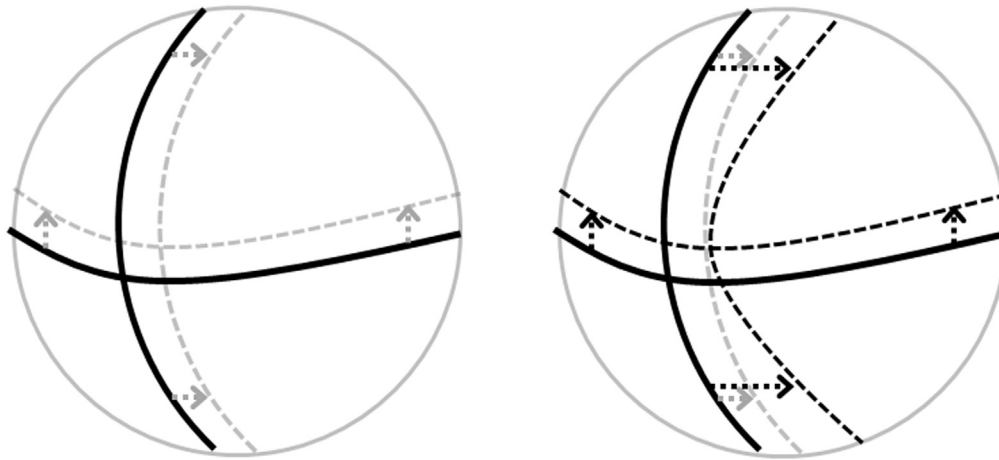


Figure 8. Left: The keratometric index is used on the assumption that the corneal thickness profile is uniform across the cornea. Right: In reality, the cornea is thicker in the vertical than in the horizontal direction (black dotted arrow), making the posterior cornea more against-the-rule astigmatic than when calculated using the anterior corneal curvature and keratometric index.

than in those with ATR. In this study, we showed similar findings using a swept-source AS-OCT. Ho et al⁷ and Koch et al⁸ also evaluated the error produced by estimating total corneal astigmatism from anterior corneal measurements only. They used vector analysis to calculate the error and reported that the anterior corneal measurements underestimated total corneal astigmatism by 0.28 D at 177° and 0.22 D at 180°, respectively.^{7,8} However, we focused on PA in the current study and assessed the error produced by estimating PA from anterior corneal measurements only. It was found that the vector difference between the assumed and the actual PA was 0.23 D at 178°, which is highly consistent with the results of the mentioned studies.^{7,8}

The magnitude of vector difference between the assumed and the actual PA was significantly correlated with the difference in the vertical and horizontal corneal thickness. Keratometric power is calculated using the keratometric index and anterior corneal curvature on the basis of the premise that the corneal thickness profile is uniform. The simulated posterior corneal curvature is thus presumed to have a constant and linear relationship with the anterior corneal curvature (Fig 8, left). However, we found that the cornea was significantly thicker in the vertical than in the horizontal direction. That is, the actual posterior corneal curvature is steeper than the simulated posterior corneal curvature in the vertical direction (Fig 8, right). Because the posterior corneal surface has negative power, a steeper posterior corneal curvature in the vertical direction results in increased ATR astigmatism. This explains why KA can misinterpret actual total corneal astigmatism in many cases.

Study Limitations

First, because this study was a cross-sectional evaluation, we may not have been able to demonstrate the actual age-related changes in the normal corneas. To investigate the

exact influence of age on normal corneas, longitudinal studies would be ideal. Second, in our study, pachymetric and astigmatic analyses were performed only on the annular ring that was 3 mm in diameter around the corneal apex. Although Ho et al⁷ also evaluated anterior astigmatism and PA on the 3-mm zone, Holladay et al²⁷ suggested that 4.5 mm is the ideal measurement zone to determine central corneal power on the basis of Scheimpflug imaging in eyes undergoing corneal refractive surgery. Thus, evaluation of corneal thickness profile on the 4.5-mm annular ring might be more ideal. In addition, Kamiya et al²⁸ reported that not only the magnitude of astigmatism but also pupil size can affect the uncorrected visual acuity in astigmatic eyes. Therefore, it will be intriguing to perform pachymetric and astigmatic analyses on circles covering different diameters in accordance with the individual pupil sizes, which might be the theme of future studies. Third, only swept-source AS-OCT was used to evaluate corneal thickness in this study. Although swept-source AS-OCT is reported to have precision comparable to or better than that of scanning-slit topography¹⁷ and Scheimpflug cameras,¹⁸ there have been no direct comparisons of corneal thickness measurements, especially in the peripheral cornea, between AS-OCT and Scheimpflug imaging devices.

In conclusion, we found that the corneal thickness profile is not uniform depending on the location and direction of the cornea. Corneal thickness especially is greater in the vertical than in the horizontal direction, making the posterior cornea more ATR astigmatic than estimated on the basis of anterior corneal measurements only and the keratometric index. In addition, this study indicated that the lack of uniformity of the corneal thickness profile becomes larger with age, and thus the discrepancy between the assumed and the actual PA is more prominent in older patients. We hope these findings will add some helpful information to our understanding of corneal physiology and clinical practice in cataract and refractive surgery.

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Abbreviations and Acronyms:

AS-OCT = anterior segment optical coherence tomography; **ATR** = against-the rule; **CCT** = central corneal thickness; **D** = diopters; **KA** = keratometric astigmatism; **OCT** = optical coherence tomography; **PA** = posterior corneal astigmatism; **PCT** = pericentral corneal thickness; **WTR** = with-the-rule.

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