# Corneal shapes of Chinese emmetrope and myopic astigmat

# aged 10-45 years.

(Running title: Corneal shape in emmetrope and myopic astigmat)

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## Abstract

**Purpose:** Myopia and astigmatism are highly prevalent in the Hong Kong Chinese. This study aimed to determine the effects of age and myopic astigmatism on the corneal shape factors in the Hong Kong Chinese.

**Methods:** One hundred subjects with compound myopic astigmatism (MA) or emmetropia (EM) were recruited from three age groups: 10-15yrs (n=32), 20-25yrs (n=37) and 40-45yrs (n=31). Refractive errors were measured by noncycloplegic subjective refraction. Corneal astigmatism and corneal shape factors were measured by the Scheimpflug-based Pentacam. The effects of age and refractive errors on the whole corneal shape (mean-P) and the semimeridian corneal shapes (semi-Ps) at the nasal, temporal, superior and inferior corneal quadrants (from corneal apex to 3mm peripheral cornea) were analyzed.

**Results:** Age had significant effects on the mean-P and semi-Ps (both p<0.001), with both EM and MA showing less prolate corneal shapes in older age groups. Partial correlation analyses adjusted for age showed that mean-P and semi-Ps were correlated with multiple refractive-error components (Pearson's r= -0.30 to -0.78, all p<0.05), with higher correlations found along the horizontal semi-Ps in MA (Pearson's r= +0.37 to -0.78, all p<0.01). Compared to EM, MA had more prolate temporal semi-Ps in all the three age groups (p<0.05). Strikingly, age and refractive errors also had significant impacts on the asymmetry of the corneal shape along the horizontal meridian.

**Conclusions:** Corneal shapes were influenced by age and myopic astigmatism in the Hong Kong Chinese. These results highlight the importance of controlling these factors when designing a study on the corneal shape.

## Introduction

Myopia and astigmatism frequently co-exist.<sup>1-5</sup> Earlier studies have shown that the presence of astigmatism in young children may promote the development of myopia.<sup>2, 6, 7</sup> More recently, several studies also indicate that higher magnitude of myopia increases the risk of having significant astigmatism.<sup>1, 4, 5</sup> While understanding the origins of the interaction between myopia and astigmatism is vital in developing effective clinical interventions, it is also important to understand the structural changes in those with myopic astigmatism when evaluating the effectiveness of a treatment regime. However, despite the high prevalence rates of myopia and astigmatism in the Asian populations,<sup>8-10</sup> very little is known about the structural characteristics of those with myopic astigmatism. For instance, although several studies have reported high prevalence rates of myopia (64%~83%<sup>11, 12-14</sup>) and astigmatism (21%~48%<sup>15, 16</sup>) in Hong Kong Chinese, it is unclear if the multiple structural<sup>17, <sup>18, 19</sup> and functional anomalies<sup>20-22</sup> found in myopic eyes are related to structural changes occurred at the anterior segment.</sup>

Unlike myopia, the primary structural correlates of which are the changes in eye's axial dimensions,<sup>23, 24</sup> the refractive (manifest) astigmatism is due to the differences in refractive powers across the different meridians of cornea and crystalline lens.<sup>25-27</sup> Several studies have indicated the dominant role of corneal astigmatism in the magnitude of refractive astigmatism: First, the magnitude and the vector components of refractive astigmatism are highly correlated with those of corneal astigmatism.<sup>28-30</sup> Second, the age-related change in refractive

astigmatism, i.e., from against-the-rule (ATR) to with-the-rule (WTR) astigmatisms during infancy and from WTR to ATR astigmatisms during late adulthood,<sup>5, 31-34</sup> appeared to be due to the changes in the corneal toricity with age.<sup>5, 31, 33</sup> Because peripheral visual experience could play an influential role on the refractive development,<sup>18, 35, 36</sup> it is important to characterize the structural changes in corneal parameters that are related to the eye's peripheral optics.

The corneal shape parameters, such as the corneal shape factor (P), asphericity (Q=P-1), and eccentricity ( $e=\sqrt{(1-P)}$ ), are developed to describe the changes in corneal curvature from corneal apex to the periphery by referring to different conic sections.<sup>37, 38</sup> While previous studies have shown that these corneal shape parameters may vary depending on age,<sup>39, 40</sup> refractive errors<sup>41-43</sup> and corneal astigmatism,<sup>41</sup> no study has focused on the effects of myopic astigmatism on the corneal shape. In light of the high prevalence rates and the close association of myopia and astigmatism from our recent study,<sup>5</sup> we aimed to determine the effects of age and myopic astigmatism on the corneal shape factors in the Hong Kong Chinese.

## Method

One hundred Chinese participants were recruited and stratified into three age groups: 10-15yrs (n= 32), 20-25yrs (n= 37) and 40-45yrs (n= 31). These three age groups were chosen to cover the periods when high prevalence rates of myopia and astigmatism were observed in the Hong Kong Chinese.<sup>5</sup> In each age group, similar numbers of participants with emmetropia (EM) and those with compound myopic astigmatism (MA) were recruited. Emmetropia was defined as spherical-equivalent refractive error (M) within  $\pm 0.75D$  with cylindrical power (Cyl)  $\leq 0.75D$ , and compound myopic astigmatism was defined as M≤-1.00D with Cyl≥1.00D. Rigid contact lens wearers and subjects who had previous history of ocular surgeries were excluded. Soft contact lens wearers were required to stop wearing contact lenses at least 24 hours before the eye examination. All subjects were recruited through advertisements posted in the campus or on the university's website. All procedures followed the Declaration of Helsinki and the protocol was approved by the Ethics Committee of The Hong Kong Polytechnic University.

After informed consent was obtained, a comprehensive eye examination was conducted by a registered optometrist. Non-cycloplegic subjective refractions were conducted using the maximum plus with maximum visual acuity as the endpoint, and only subjects whose best corrected visual acuity achieved at least logMAR 0.00 in both eyes were included. Refractive errors were decomposed into M, J0 and J45 astigmatic components using Fourier analyses.<sup>44</sup> Of the 47 MA subjects, the numbers of WTR (axis: 0°~30°

& 150°~180°), ATR (axis: 60°~120°) and oblique astigmatisms (axis: 30°~60° & 120°~150°) were 41, 3 and 3, respectively. Corneal health was evaluated by slit-lamp biomicroscopy. None of the participants had corneal pathologies or anomalies.

## **Corneal Shape Factors**

Corneal biometric parameters, including corneal astigmatism, semimeridian corneal shape factor (semi-P) and mean corneal shape factor (mean-P), were measured by the Pentacam's Scheimpflug-based tomography (software version 1.12, Oculus, Germany) using the 25-image mode. Three consecutive readings were taken as suggested by a previous study,<sup>45</sup> and averaged values were used for data analyses. Measurements were repeated until all measurements passed the 'quality specifications' (i.e., Analyzed Area, Valid Data, Lost Segments, Lost Seg. Continuous, 3D Model Deviation, Alignment (XY), Alignment (Z) and Eye Movement), as determined by the manufacturer's software. The corneal astigmatism and corneal shape factors were measured for the central 3mm and 6mm diameter zones, respectively. The corneal shape measurement was restricted to 6mm corneal diameter because measurements from a larger diameter were often affected by the upper eyelid. The nasal, temporal, superior, inferior semi-Ps and mean-P, which were measured along the two principal powered meridians, were extracted from the "Topometric Display" of the software. According to the manufacturer (personal communication), the semi-Ps were derived from the sagittal curvature with the apex of the conic section set at the corneal apex, and the mean-P was calculated as the averaged value of the four semi-Ps.

Figure 1 shows a representative Pentacam's topographic map (Figure 1) of a participant with astigmatism (Cyl= 2.25D) in this study, the two black lines represent the 6mm-diameter chords along the horizontal and vertical principal meridians and the interception of these two lines represents the corneal apex. The corneal shape factors are derived using the equation that describes a conic section:  $y^2 = 2r_0 - px^2$ , where  $r_0$  is the apical radius of curvature and p is the corneal shape factor.<sup>46</sup> In this example, the nasal, temporal, superior and inferior semi-Ps were 0.40, 0.68, 1.01 and 1.35, respectively; and the mean-P was 0.86. In this study, the mean standard deviations of the three consecutive measures of semi-Ps from all the subjects were 0.037 (95% CI: 0.031, 0.042), 0.038 (95% CI: 0.030, 0.046), 0.040 (95% CI: 0.033, 0.047) and 0.063 (95% CI: 0.054, 0.072) for the nasal, temporal, inferior and superior quadrants, respectively.

#### Statistical analysis

Only the data from the right eyes were used for analyses. The effects of age and refractive errors on the corneal shape were determined by twoway analysis of variances (ANOVAs). If a significant main effect was found, a Tukey's post-hoc test was carried out to determine which pair was significantly different. The associations between two variables were determined by Pearson's partial correlation analyses. All the statistical analyses were done using Minitab 15.1.30.0 (Minitab Inc., USA) with a significant level set at  $\alpha$ <0.05.

## Results

#### Demographic Information & Refractive Status

Table 1 summarizes the demographic information and refractive-error status of our subjects. There were no significant differences in the mean age (unpaired t-tests, p>0.05) or the proportions of different genders (Chi-square test, p=0.68) between the refractive groups in any of the three age groups. As expected, MA had significantly higher degrees of M, refractive and corneal Cyl and J0 than EM for all the three age groups (two-way ANOVAs, refractive-error effect, all p≤0.01; Tukey's post-hoc tests, all p<0.001). In addition, the MA in 20-25yrs age group had significantly higher M than the MAs in 10-15yrs and 40-45yrs age groups (two-way ANOVAs, age effect, p≤0.01; Tukey's post-hoc tests, p<0.05).

#### <u>Mean P</u>

Age (p<0.001) but not refractive error (p=0.38) had a significant effect on mean-P (two-way ANOVAs). In both the EM and MA groups, the 10-15yrs age groups had the most prolate cornea, followed by the 20-25yrs and the 40-45yrs age groups (all p<0.05). Because no significant differences in mean-P were found between the refractive groups in all the three age groups, all data were pooled for correlation analysis of mean-P and age. As shown in Figure 2, a direct and significant correlation was found between mean-P and age (r=0.58, p<0.001): the most and least prolate corneas were found in the 10-15yrs and the 40-45yrs age groups, respectively.

#### <u>Semi-P</u>

Semi-P was affected by both age and refractive errors (two-way ANOVAs, all p<0.001). With respect to the age effect, the 10-15yrs age group had a more prolate corneal shape than the 40-45yrs age group for all (Tukey's post-hoc tests, all p<0.03) except the inferior corneal quadrant (p=0.81) in both EM and MA. Furthermore, compared with the 40-45yrs age group, the 20-25yrs age group had significantly more prolate nasal cornea in EM (Tukey's post-hoc test, p= 0.001) and more prolate temporal cornea in both EM and MA (Tukey's post-hoc tests, both p<0.05). Figure 3 illustrates the significant effects of refractive errors on the semi-Ps for the four different corneal quadrants (two-way ANOVAs, all p<0.01). Specifically, MA consistently showed more prolate temporal corneas than EM for all the three age groups (Tukey post-hoc test, all p<0.05). Furthermore, MA had a more prolate nasal cornea than EM in the 40-45yrs age group but a less prolate inferior cornea than EM in both the 10-15yrs and 20-25yrs age groups (Tukey post-hoc tests, all p<0.02).

#### Correlations between corneal shape and refractive/corneal components

Because both mean-P and semi-Ps were affected by age, partial correlation analyses were conducted to determine if these two shape factors were correlated with the refractive and corneal components. Table 2 presented only those partial correlation coefficients (r) that were statistically significant after controlling for age. As shown, although significant correlations were found between both mean-P and semi-Ps with multiple refractive and corneal components, the correlations with semi-Ps were in general stronger than those with mean-P. Comparing across the four semi-Ps, it was also noted that stronger correlations were more frequently found along the horizontal than the vertical meridians. Furthermore, the nasal and temporal semi-Ps were significantly correlated with corneal Cyl and J0 in both MA and EM, and the correlations were always stronger in MA than those in EM.

#### Asymmetry of corneal shape along horizontal and vertical meridians

To illustrate the effects of age and refractive errors on the asymmetry of meridional corneal shape, Figure 4 connects the two semi-Ps along the (A) horizontal and (B) vertical meridians. Two-way ANOVAs showed that the 10-15yrs age group had significantly higher horizontal corneal asymmetry (i.e., temporal semi-P – nasal semi-P) than the 40-45yrs age group in EM (two-way ANOVA, age effect, p=0.001; Tukey post-hoc test, p=0.007); and EM had a significantly higher horizontal corneal asymmetry than MA in the 10-15yrs age group (two-way ANOVA, refractive-error effect, p=0.001; Tukey post-hoc test, p=0.001).

# Discussion

Our results showed that: 1) age and refractive errors can influence the corneal shape; and 2) compound myopic astigmatism altered regional corneal shapes especially along the horizontal principal meridian.

Age has a significant effect on the corneal shape factors in our study: the mean-P (Figures 3) and nearly all semi-Ps (Figure 4) were most prolate in the 10-15yrs age group, followed by the 20-25yrs and 40-45yrs age groups. A less prolate corneal shape with age was also noted in four previous studies,<sup>40,</sup> <sup>43, 47, 48</sup> but was not found in two other studies.<sup>39, 42</sup> In addition to the different instrumentations employed and the ethnic groups involved, we speculate that the distribution of subjects' age and/or refractive errors within each study may contribute to the discrepancy across studies. For instance, given the significant effects of age and myopic astigmatism on the corneal shape as shown in this study, it is possible that the disproportionate distributions of a particular age group and/or higher representations of a particular refractive status (e.g., emmetropia) had hidden the effect of age on the corneal shape in some of the previous studies. Thus, these results highlight the importance of controlling for age and refractive errors when recruiting subjects for a study on the corneal shape.

In addition to age, another important finding of this study is the effects of refractive errors on the regional corneal shape. As indicated by the partial correlation analyses in Table 2, subjects with higher degree of myopia and WTR refractive/corneal astigmatisms were found to have more prolate nasal and temporal corneal shapes. In this respect, previous studies have reported mixed effects of refractive errors on the corneal shape: some studies found a less prolate/more oblate corneal shape with myopia progression<sup>49, 50</sup> or increased magnitudes of myopia,<sup>43</sup> but other studies either found a more prolate corneal shape with increased myopia<sup>42</sup> or failed to find significant difference in corneal asphericity across emmetrope, hyperope and myope.<sup>41</sup> One possibility for the discrepancies found across different studies could be due to the different experimental designs including the age range involved, the classifications of refractive errors, and the diameter used to calculate the

corneal shape factors. It is also possible that the coexistence of astigmatism with myopia and hyperopia<sup>3, 5, 51</sup> has confounded the effects of refractive errors on the corneal shape. For instance, as shown in Table 2, corneal shapes were more strongly correlated with astigmatic components (Cyl and J0) than with M — whereas M is a parameter commonly used in previous studies to represent the refractive status. In this respect, earlier studies<sup>39, 52, 53</sup> and ours (Figure 4) have shown repeatedly that there are meridional variations in corneal shape. Recently, Nieto-Bona et al.<sup>41</sup> have shown that classifying their subjects according to their magnitude of corneal astigmatism, but not their M or corneal powers, led to significantly different corneal shapes. Taken together, these results indicate the significance of astigmatic components when interpreting the corneal shape parameters.

A novel finding from this study is the effects of age and refractive errors on the asymmetry of corneal shape along the horizontal meridian. As shown in Figure 4, significant differences in the nasal-temporal asymmetry were found between the 10-15yrs and the 40-45yrs of EM, and between EM and MA of the 10-15yrs age groups. In contrast, the superior-inferior asymmetry in corneal shape did not appear to be affected by age or refractive errors. The nasal-temporal asymmetry in local corneal powers was also reported previously in both Asian and Caucasian clinical subjects using two different corneal topographers,<sup>54, 55</sup> with the nasal cornea showing a more rapid peripheral flattening (more prolate) when compared to the temporal cornea a result similar to our 10-15yrs age group. Because cornea contributes to more than half of the eye's refractive power, it would be important to

determine the effects of asymmetric corneal shape on the central and peripheral refractive profile, especially during early eye growth. Recent studies using peripheral refractions and magnetic resonance images have repeatedly found nasal-temporal asymmetry in the posterior eye shape of the myopic humans,<sup>56, 57</sup> rhesus monkeys,<sup>58</sup> and marmosets (Totonelly KC, et al. IOVS 2008;49:ARVO E-Abstract 3589). Interestingly, when studying the effects of the magnitude of myopia on the changes in peripheral refraction in emmetropes and simple myopes (18-35yrs), it was found that myopia development had a stronger effect on the horizontal than the vertical peripheral refractions, and there was a tendency for the nasal-temporal asymmetry to decrease with higher magnitudes of myopia.<sup>59</sup> Because both of these trends were also noted in the corneal shape of our subjects (Figure 4), one may speculate that the changes in the anterior (i.e., corneal shape) and posterior eye shapes (i.e., peripheral refractions) are somehow correlated. For instance, given that the eye's posterior outer coat, the sclera, is undergoing structural remodeling during myopic eye growth,60, 61 it is likely that the regional change in corneal shape came about because of the stretch created by asymmetric posterior eye shape remodeling. Alternatively, because the alterations in corneal shape could contribute to the total ocular aberration, especially the spherical aberration,<sup>62</sup> it is also possible that the abnormal corneal shape precedes the myopia development. Although contradictory findings were reported on the role of initial corneal shape in promoting myopia development,<sup>49, 50</sup> further study is strongly in need given the limitation of representing the corneal shape as a whole by using a parameter such as mean-P.

To our knowledge, this is the first study that compares the corneal shape factors between MA and EM in a Chinese population with high prevalences of myopia and astigmatism; however, it has several limitations on the experimental design. First, this is not a population-based study and the sample size is relatively small. All participants were recruited through advertisements posted on campus or on university website and thus may be self-selected. Second, the non-cycloplegic subjective refraction technique was used to determine the refractive errors in this study. Although potential ocular accommodation had been minimized by using the maximum plus with maximum visual acuity approach during the subjective refraction, we cannot exclude the possibility that the magnitude of myopia might have been slightly over-estimated especially in the youngest age group. Nevertheless, our results showed that the corneal shape is closely associated with age and myopic astigmatism. Due to the dominant role of cornea on the central and the peripheral optics, it is important for the future study to consider the effects of age and refractive errors when designing an experiment on the corneal shape.

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Table 1. Demographic information and refractive-error components of EM andMA in the three age groups.

Verieblee	10-1	5 yrs	20-2	5 yrs	40-45 yrs		
variables	EM	MA	EM	MA	EM	MA	
Age (Yrs)	11.53±0.42	12.67±0.39	22.00±0.40	22.17±0.37	42.24±0.50	42.00±0.56	
Subjects number							
Total	17	15	19	18	17	14	
Male:Female	9:8	8:7	10:9	8:10	7:10	8:6	
M (D)	+0.10±0.07	-4.76±0.49	+0.00±0.08	-6.26±0.55	-0.04±0.08	-4.07±0.53	
Refractive astigmatism							
Cyl (D)	+0.18±0.04	+1.68±0.16	+0.26±0.06	+1.96±0.20	+0.32±0.05	+1.89±0.25	
J0 (D)	+0.04±0.02	+0.68±0.11	+0.03±0.04	+0.79±0.13	-0.11±0.03	+0.62±0.22	
J45 (D)	-0.01±0.02	-0.02±0.11	+0.04±0.02	+0.11±0.11	-0.04±0.02	+0.08±0.08	
Corneal astigmatism							
Cyl (D)	+1.06±0.07	+1.86±0.19	+1.05±0.09	+2.13±0.13	+0.79±0.11	+1.91±0.26	
J0 (D)	+0.48±0.04	+0.86±0.09	+0.47±0.05	+0.91±0.11	+0.35±0.05	+0.83±0.17	
J45 (D)	+0.11±0.04	-0.07±0.09	+0.13±0.04	+0.19±0.09	+0.00±0.04	+0.11±0.08	

Table 2. Partial correlation analyses between the corneal shape factors (mean P and semi-Ps) and refractive-error components after controlling for the age effects. Only significant Pearson's r are shown. Significant levels are represented as \* p<0.05, \*\* p<0.01, \*\*\* p<0.001.

Variables	Mean P		Superior		Inferior		Nasal		Temporal	
	EM	MA	EM	MA	EM	MA	EM	MA	EM	MA
M (D)	-0.30*	+0.31**						+0.37*		+0.40***
Refractive astigmatism										
Cyl (D)								-0.46***		-0.43**
J0 (D)		-0.44**				+0.38*		-0.75***	-0.53***	-0.73***
Corneal astigmatism										
Cyl (D)	-0.35*	-0.37*		+0.34*		+0.35**	-0.48***	-0.70***	-0.59***	-0.69***
J0 (D)	-0.33*	-0.46**		+0.30*		+0.33*	-0.45**	-0.78***	-0.60***	-0.77***

Note: J45 components were not correlated with any corneal shape factor.

# Figure legends.



Figure 1. A representative colored topographic map showing the semimeridian P values (semi-P) along the two principal meridians in a participant with astigmatism. The two black lines represent the horizontal and vertical principal meridians and the interception of these two black lines is the corneal apex. The values of the four semi-Ps (N, nasal; T, temporal; S, superior; and I, inferior) are shown at corresponding quadrants.



Figure 2. Effects of age on mean-P. Data for individual subjects are presented by smaller symbols in the background. The mean values ( $\pm$ SE) for different refractive-error groups are represented by the larger symbols. The solid line represents the regression line with the best linear fit, the equation and statistics for this line are inserted.



Figure 3. Semi-Ps (mean $\pm$ SE) as a function of age at different corneal quadrants. The oblate and prolate corneal shapes are indicated by semi-P values of greater and smaller than 1.0, respectively. Statistical significant differences, marked by asterisk, were frequently found between EM and MA along the horizontal meridians. Significant levels are represented as \* p<0.05, \*\* p<0.01, \*\*\* p<0.001.



Figure 4. Asymmetry of corneal shape along the horizontal and vertical meridians for different refractive-error groups as a function of age. The results of Tukey's Post-hoc tests comparing the magnitudes of semi-P's asymmetry (i.e., (Temporal – Nasal) or (Superior – Inferior)) between the two refractive-error groups for each age cohort (solid lines), or the two age cohorts for each refractive group (dashed lines), are inserted. Significant levels are represented as \*\*p<0.01, \*\*\*p<0.001.