

## Abstract

**Purpose:** To characterize and compare the corneal shapes and monochromatic aberrations in Chinese myopic adults with and without astigmatism.

**Methods:** Forty-six Hong Kong Chinese aged 50-70 years with compound against-the-rule myopic astigmatism (MA, n=18) or simple myopia (SM, n=28) were recruited. Corneal shapes were measured by a Scheimpflug-based corneal topographer: the semi-meridian corneal shape factors at the nasal, temporal, inferior, and superior corneal quadrants measured from the corneal apex to 3mm mid-periphery were analyzed. The ocular aberrations were measured by the COAS Shack-Hartmann wavefront aberrometer; the corneal aberrations were computed using the corneal topographic map data measured by the Medmont E300 corneal topographer; and the internal aberrations were calculated from the ocular and corneal aberrations.

**Results:** Compared to SM, MA had more oblate nasal and temporal corneal shapes and showed significantly more negative Y trefoil and more positive vertical coma. The asymmetry in corneal shape along the vertical principal meridian (inferior – superior) was significantly associated with the Y trefoil and vertical coma of the cornea, suggesting that this regional asymmetry in corneal shape may contribute to the ocular aberrations.

**Conclusions:** The significant relationships found between astigmatism, corneal shapes and monochromatic aberrations underscore the importance of taking corneal shape into account when correcting the optical defects in myopic Chinese adults with astigmatism.

**Keywords:** astigmatism; corneal shape; aberrations; myopia; refractive errors

## Introduction

The number of aging population (age  $\geq 65$  years) in the world is estimated to be dramatically increasing from about 524 million in the year 2010 to about 1.5 billion in the year 2050 (World Health Organization<sup>1</sup>). Of particular concern is the financial burden associated with the increased prevalence of astigmatism after age of forty<sup>2-8</sup> and the shift in astigmatic subtypes from with-the-rule (WTR) in younger age to against-the-rule (ATR) in older age.<sup>2, 9-11</sup> In Hong Kong Chinese, a population in which myopia (or short-sightedness) has become epidemic like many other Asian Chinese populations,<sup>12-14</sup> astigmatism is frequently associated with myopia and shows the characteristic changes with age.<sup>2, 15, 16</sup> Because visual performance is adversely affected by the presence of astigmatism as low as 1.00DC,<sup>17, 18</sup> and because visual quality is significantly degraded by the increasing higher-order aberrations (HOAs) in the aging eyes,<sup>19-24</sup> it is important to determine the structural correlates of astigmatism with age and its relation with the eye's overall optical quality.

Cornea contributes to more than two-third of the eye's refractive power. More importantly, not only is the corneal shape significantly correlates with age and refractive errors,<sup>25-30</sup> the asphericity of corneal shape has been demonstrated to alter the eye's HOAs.<sup>31, 32</sup> Previous studies usually measured the corneal shape as a whole or along a particular meridian. However, a recent study has shown that the corneal shape is not rotational symmetric and there are significant regional variations.<sup>33</sup> To investigate the effect of age and refractive errors on regional corneal shapes, we compared the semi-meridian corneal shape factors (nasal, temporal, superior and inferior quadrants) between the

myopic astigmats and emmetropes collected from three age cohorts (10-15 yrs, 20-25 yrs, and 40-45 yrs).<sup>27</sup> Our results indicated that the myopic astigmats exhibited a more prolate temporal corneal shape than the emmetropes in all the three age cohorts studied, and the higher degree of WTR astigmatism was found to be associated with more prolate in temporal and nasal corneal shape. However, because nearly all of the myopic astigmats had WTR astigmatism (44 out of 47) – an astigmatic subtype typically found in younger populations<sup>2, 34, 35</sup> – whether myopic astigmats with ATR astigmatism also exhibit similar changes in the corneal shape remains unclear.

An understanding of the biometry characteristics of the key ocular refractive components may facilitate the development of effective ophthalmic aids for common refractive errors. For example, the corneal shape and ocular aberrations have been taken into account in the development of advanced ophthalmic optical aids (e.g., the customized contact lenses<sup>36, 37</sup>; aspheric intraocular lenses<sup>38, 39</sup>) and corneal-ablation refractive surgery.<sup>40-42</sup> However, despite the fact that myopia is highly prevalent in the Asian Chinese populations<sup>2, 12-14</sup> and the global population is aging, very little is known on how astigmatism is related to the corneal shape and ocular aberrations in the aging myopes. The primary aim of this study was to characterize the corneal shape in the Chinese myopic adults (aged 50 to 70 years) with and without ATR astigmatism. Since we found significant effects of astigmatism on regional corneal shape, we further investigated whether the changes in

corneal shape were associated with the inter-subject variation in monochromatic aberrations.

## **Methods**

Forty six Hong Kong Chinese adults aged between 50 to 70 years old were recruited through advertisements posted in the campus or on the university's website. The participants were stratified into two groups according to their refractive errors – simple myopic group (SM, n=28) with spherical-equivalent refractive error (M)  $\leq -0.50\text{D}$  and astigmatism (Cyl)  $\leq 0.75\text{D}$ ; and compound myopic ATR astigmatic group (MA, n=18) with  $M \leq -0.50\text{D}$ ,  $\text{Cyl} \geq 1.00\text{D}$  and minus cylinder correcting axis  $= 90^\circ \pm 20^\circ$ . Spectacle prescriptions were determined using the non-cycloplegic subjective refractions with the maximum-plus-maximum-acuity<sup>43</sup> as the endpoint. The exclusion criteria were: 1) rigid contact lens wearers; 2) history of ocular surgeries; 3) diabetes mellitus; 4) any type of lens opacities worse than grade 2 (LOCSIII system<sup>44</sup>); and 5) best corrected visual acuity worse than logMAR 0.10 in any eye. All experimental procedures were approved by the ethics committee of The Hong Kong Polytechnic University, and the research was conducted according to the principles expressed in the Declaration of Helsinki.

### Ocular monochromatic aberrations

The ocular aberration (i.e., aberration of the whole eye) was measured using a Complete Ophthalmic Analysis System (COAS) Shack-Hartmann wavefront aberrometer (software version 1.44.12, Wavefront sciences, Inc., USA). One drop of 0.4% proparacaine and one drop of 1% tropicamide was instilled to

dilate the pupil. The ocular aberrations were measured after 30 minutes of drug instillation. Five repeated measurements were taken and averaged. The analyses of ocular aberrations, and also the corneal and internal aberrations, were restricted to 5mm pupil diameter because a larger pupil diameter cannot be achieved in 2 of our subjects.

#### Corneal monochromatic aberrations

Medmont E300 corneal topographer (Medmont Pty Ltd. Australia) was used to measure the corneal topography. Three repeated measurements were taken for each eye and the measurement was repeated until all the accuracy indexes were >95. The Vol-Pro (Sarver and Associates, Inc., USA), a commercially available computer software adopted the standards for reporting ocular aberrations,<sup>45</sup> was used to calculate the corneal aberrations from the corneal topographic map data. Following the standards for reporting the optical aberrations of the eyes, the line of sight (an imaginary line connecting the fixation point to the center of the entrance pupil) was selected as the reference axis for the determination of the corneal and ocular aberrations.<sup>45</sup> Specifically, when calculating the corneal aberrations from the corneal topographic maps, the pupil center was used as the origin of the Cartesian reference frame.<sup>45, 46</sup> The averaged values generated from the three corneal topographic map data were used for data analysis. To minimize the potential variation of aberrations caused by the changes of tear-air interface during the inter-blink intervals,<sup>47</sup> the corneal topography and ocular aberrations were measured immediately after blinks.

### Semi-meridian corneal shape factors

The details of protocol in measuring the semi-meridian corneal shape factors have been described elsewhere.<sup>27</sup> In brief, the corneal topography for each eye was constructed based on the 25 images captured by the Pentacam Scheimpflug camera system (Oculus, Germany). The “Topometric Display” of the manufacturer’s software generated four semi-meridian corneal shape factors calculated from the central 6mm-diameter chord, i.e., at the nasal, temporal, superior and inferior corneal quadrants. The semi-meridian corneal shape factors along the horizontal (close to 180°) and vertical (close to 90°) principal meridians were derived from the sagittal curvatures with the apex of the conic section set at the corneal apex. Three consecutive measurements, which passed all the ‘quality specifications’ as provided by the manufacturer’s software, were taken and averaged.

### Statistical analysis

Data from the right eyes (Total: n= 36; SM: n= 24; MA: n= 12) were used for analyses unless only the fellow eye (Total: n= 10; SM: n= 4; MA: n= 6) fulfilled the refractive-error inclusion criteria. The spectacle prescriptions from subjective refraction were decomposed into M, J0 and J45 using the power vector analysis.<sup>48</sup>

The internal aberration was calculated by subtracting the corneal aberration from the ocular aberration.<sup>46</sup> To compare the aberrations between the left and right eyes, the signs of the bilaterally asymmetrical Zernike terms (e.g., Z3, Z8, Z9, Z10, Z11) in the left eye were reversed.<sup>49, 50</sup> The aberration data were

presented as Zernike terms up to 6th radial order using the single indexing scheme.<sup>45</sup> The root mean square (RMS) of the total HOAs was calculated from the 3rd to the 6th order Zernike terms. Unpaired t-test was used to compare the difference between MA and SM. Pearson's correlation analyses were conducted to determine the correlation between two variables. Statistical analyses were done by using Minitab 15.1.30.0 (Minitab Inc., USA) with significance level set at  $\alpha < 0.05$ .

## **Results**

As expected, except the astigmatic components (Table 1), the demographic information and refractive status of MA and SM were comparable: MA had significantly higher magnitude of refractive Cyl and more negative refractive J0 (i.e., the minus cylindrical axis was oriented near 90°, ATR astigmatism) than SM (unpaired t-tests,  $t=9.04$  &  $-9.18$ ,  $DF=22$  &  $25$ , both  $p < 0.001$ ).

### Regional corneal shape factors

Our study provided further evidence that the presence of astigmatism could influence the regional corneal shape factors.<sup>27</sup> On average, the corneal shapes at the nasal and temporal quadrants were oblate in MA and prolate in SM with statistically significant differences (Fig. 1, unpaired t-tests,  $t=2.90$  &  $2.73$ ,  $DF=38$  &  $37$ , both  $p=0.01$ ), whereas the inferior and superior corneal shape factors were not significantly different between groups (unpaired t-tests,  $t=-1.68$  &  $0.80$ ,  $DF=41$  &  $35$ , both  $p \geq 0.10$ ). We also compared the asymmetry in corneal shape between MA and SM along the vertical (inferior – superior) and horizontal principal meridians (nasal – temporal). These two refractive-



error groups appeared to demonstrate an opposite pattern in corneal shape asymmetry along the vertical principal meridian (Fig. 1): on average, the corneal shape of MA was oblate at the superior quadrant and spherical at the inferior quadrant, whereas the corneal shape of SM was oblate at the inferior quadrant and spherical at the superior quadrant; however, the differences between groups were not statistically significant along both the vertical (unpaired t-test,  $t=-1.87$ ,  $DF=38$ ,  $p=0.07$ ) and horizontal principal meridians (unpaired t-test,  $t=0.33$ ,  $DF=30$ ,  $p=0.75$ ).

#### Horizontal/ vertical (H/V) and oblique astigmatism

When comparing the H/V astigmatism (Z5), the ocular and corneal H/V astigmatism of MA were more positive (i.e., more ATR astigmatism) than that of SM (Fig. 2a, unpaired t-tests,  $t=6.70$  &  $5.21$ ,  $DF=27$  &  $37$ ,  $p<0.001$ ), but the internal H/V astigmatism of MA and SM were both in positive values with no statistical difference (Fig. 2a, unpaired t-test,  $t=0.80$ ,  $DF=32$ ,  $p=0.43$ ). Probably because all participants in MA had ATR refractive astigmatism, there were no significant difference between SM and MA in the oblique astigmatism (Z3) of the ocular, corneal and internal components (Fig. 2b, unpaired t-tests,  $t=0.55\sim1.97$ ,  $DF=33\sim37$ ,  $p>0.05$ ).

The astigmatism of the whole eye showed stronger correlations with the corneal optics than the internal optics: the ocular H/V astigmatism (Z5) was strongly correlated with that of the corneal (Fig. 3a, Pearson's correlation,  $r=0.84$ ,  $p<0.001$ ) but not the internal optics (Fig. 3b, Pearson's correlation,  $r=0.15$ ,  $p=0.33$ ); the ocular oblique astigmatism (Z3) was moderately

correlated with that of the corneal (Fig. 4a, Pearson's correlation,  $r=0.50$ ,  $p<0.001$ ) and internal optics (Fig. 4b, Pearson's correlation,  $r=0.35$ ,  $p=0.02$ ). Our results suggested that the corneal astigmatism accounted for the variations of the ocular astigmatism (H/V astigmatism: 70.0%; oblique astigmatism: 23%) – this supports the previously published data that the age-related changes of the refractive astigmatism is mainly corneal in nature.<sup>2, 9-11</sup>

### Higher-order aberrations

We compared the individual ocular Zernike terms, from Z6 to Z14, between MA and SM (Fig. 5): in MA, the Y trefoil was more negative (Z6, unpaired t-test,  $t=-3.26$ ,  $DF=35$ ,  $p=0.003$ ) and the vertical coma was in opposite sign (Z7, unpaired t-test,  $t=2.70$ ,  $DF=43$ ,  $p=0.01$ ) when compared to SM; other Zernike terms and the total RMS of HOAs of the whole eye were not significantly different between groups (unpaired t-tests,  $t=-1.08\sim1.70$ ,  $DF=29\sim41$ , all  $p>0.10$ ). The RMS of the Y trefoil, but not the RMS of vertical coma (unpaired t-test,  $t=-1.21$ ,  $DF=43$ ,  $p=0.23$ ), was significantly higher in MA than that of SM (1.78 folds, unpaired t-test,  $t=2.72$ ,  $DF=28$ ,  $p=0.01$ ). The J0 astigmatic component was significantly correlated with both the Y trefoil (Pearson's correlation,  $r=0.37$ ,  $p=0.01$ ) and vertical coma (Pearson's correlation,  $r=-0.39$ ,  $p=0.007$ ).

### Y Trefoil and vertical coma

The Y trefoils of the whole eye and of the cornea were more negative in MA than those of SM (Fig. 6a, unpaired t-tests,  $t=-3.26$  &  $-3.06$ ,  $DF=35$  &  $29$ ,  $p\leq0.005$ ); the internal Y trefoils were not significantly different between groups

(unpaired t-test,  $t=-1$ ,  $DF=40$ ,  $p=0.33$ ). On the other hand, although the vertical coma of the whole eye was significantly different between SM and MA (Fig. 6b, unpaired t-test,  $t=2.70$ ,  $DF=43$ ,  $p=0.01$ ), those of the corneal and internal optics were not significantly different between groups (unpaired t-test,  $t=1.67$  &  $0.94$ ,  $DF=42$  &  $33$ ,  $p\geq 0.10$ ).

The cornea appeared to account for the variations of the Y trefoil (58%) and vertical coma (67%) of the whole eye: the ocular Y trefoil was correlated stronger with the corneal Y trefoil (Fig. 7a, Pearson's correlation,  $r=0.77$ ,  $p<0.001$ ) than that of the internal optics (Fig. 7b, Pearson's correlation,  $r=0.60$ ,  $p<0.001$ ); the ocular vertical coma was only significantly correlated with the vertical coma of the cornea (Fig. 8a, Pearson's correlation,  $r=0.82$ ,  $p<0.001$ ) but not that of the internal optics (Fig. 8b, Pearson's correlation,  $r=0.13$ ,  $p=0.40$ ).

#### Correlation between the regional corneal shape factors, Y trefoil and vertical coma

The asymmetry in corneal shape along the vertical principal meridian partially accounted for the variations of the Y trefoil (21%) and vertical coma of the cornea (47%): a more negative corneal shape asymmetry along the vertical principal meridian (i.e., more oblate corneal shape at the superior than the inferior quadrant), was associated with a more negative Y trefoil (Fig. 9a, Pearson's correlation,  $r=0.48$ ,  $p=0.001$ ) and a more positive vertical coma (Fig. 9b, Pearson's correlation,  $r=-0.69$ ,  $p<0.001$ ).

## Discussion

The current study confirms and extends the results of our previous study on the regional variations of corneal shape in younger myopic astigmats (10-45 years).<sup>27</sup> These two studies shared similar methodology with key differences in the recruitment of non-astigmatic group (current: simple myopes; previous: emmetropes), and the criteria for visual acuity (current: logMAR 0.10; previous: logMAR 0.00) and myopia (current:  $M \leq -0.50D$ ; previous:  $M \leq -1.00D$ ). Figure 10 plots the data from these two studies to illustrate the significant impacts of age on regional corneal shape in myopic astigmats and non-astigmats (simple myopes and emmetropes were represented using different symbols). In general, the corneal shapes appeared to become less prolate/more oblate with age at virtually all regions in subjects with or without astigmatism, despite the fact that the eldest non-astigmatic age group (50-70 years) was also having a simple myopic error. Of particular interest is the trend observed at the inferior cornea of the myopic astigmats (blue symbols in Figure 10, left panel): instead of becoming more oblate over time like the other three regions, the inferior corneal shape of the two eldest age groups actually became less oblate. It is worth noting that the proportions of astigmatic subtypes (i.e., WTR:ATR) vary across the four age groups in these two studies: while the two youngest age groups were having either WTR or oblique astigmatism, the two eldest age groups had higher proportions of ATR astigmatism (3 of 14 subjects in 40-45 age group, 18 of 18 subjects in 50-70 age group). Thus, it is possible that the changes in the proportion of astigmatic subtypes across the different age groups might have contributed to

the regional variations in corneal shape. To test this hypothesis, we analyze the correlations between J0 astigmatic component (a vector component which is sensitive to the changes in magnitude of WTR/ ATR astigmatism) and regional corneal shape by pooling all data from previous and current studies. Our results showed that the J0 astigmatic component was significantly correlated with all ( $p \leq 0.001$ ) except the superior corneal shape factor ( $r = -0.04$ ,  $p = 0.61$ ). Interestingly, whereas J0 astigmatic component was negatively correlated with the horizontal corneal shape factors ( $r$  for nasal =  $-0.66$ ,  $r$  for temporal =  $-0.77$ ; both  $p < 0.001$ ), it was positively correlated with inferior corneal shape factors ( $r = +0.22$ ,  $p = 0.001$ ). These results indicate that the differential changes in the corneal shape at different regions could potentially contribute to the changes in astigmatic subtypes with age.

An important finding in this study is that the asymmetry in superior-inferior corneal shape partially accounted for the corneal variations in the Y trefoil and vertical coma (Fig. 9), which could explain why MA showed more negative and higher RMS of Y trefoil and more positive vertical coma than SM. In this respect, two previous studies have investigated the associations between the refractive/corneal astigmatism and corneal<sup>51</sup> or ocular aberrations.<sup>52</sup> Similar to our finding, Zhao and coworkers<sup>51</sup> have found no significant association between the refractive astigmatism and spherical aberration. On the other hand, Wei, Chan and Tan<sup>52</sup> have reported that the refractive astigmatism was directly correlated with both the horizontal coma (Z8) and X trefoil (Z9), whereas our result showed significant correlations between J0 astigmatic component and the vertical coma and Y trefoil. However, it should be noted

that these two previous studies only analyzed the impacts of astigmatic magnitude (i.e., correcting cylindrical power) on the ocular aberrations and did not consider the axis of astigmatism. Although Wei, Chan and Tan<sup>52</sup> did not specify the astigmatic axis of their adult subjects, it is possible that subjects with WTR and ATR astigmatisms were both included according to their subjects' age range (21.5-52.8 years). Moreover, the difference in instruments employed (COAS vs. Zywave) and the pupil diameter analyzed (5mm vs. 6mm) are other possible explanations for the discrepancy between studies. As suggested by previous published data,<sup>53, 54</sup> the trend for the Y trefoil to shift in the negative direction and vertical coma to shift in the positive direction might be associated with the eyelid pressure acting on the corneal surface; however, because we did not measure the mechanical properties and morphology of the eyelid, this biomechanical factor needs further investigation.

It has been documented that the corneal astigmatism is partially compensated by the internal astigmatism to maintain a certain level of refractive astigmatism in the younger eyes with a variety of refractive errors.<sup>35, 55</sup> In our elder SM, the internal H/V astigmatism (in positive value, ATR), derived from mathematical calculation, also counterbalanced the corneal astigmatism (in negative value, WTR) and resulted in ocular H/V astigmatism of a lower value, although the compensation was, on average (reduced 5.4% of the RMS of corneal H/V astigmatism), lower than that of the younger eyes (reduced 41% of the RMS of corneal H/V astigmatism).<sup>55</sup> In contrast, our elder MA exhibited a much higher ocular H/V astigmatism than SM because both the corneal and internal H/V astigmatisms (increased 202.5% of the RMS of corneal H/V

astigmatism) in MA had the same sign (ATR), suggesting that the balance between the corneal and internal astigmatism were somehow broken.

Unlike the younger eyes (age: 24 to 38 years), in which the corneal HOAs are partially compensated by the internal optics to maintain certain levels of ocular HOAs,<sup>20, 46</sup> the aging eyes (age: >45 years) usually show an imbalance between the corneal and internal optics, leading to an increase of the ocular HOAs.<sup>20, 22, 30</sup> When compared with the previous studies,<sup>56, 57</sup> which measured the ocular aberrations (5mm pupil diameter) in younger populations (8-30 years) with mixed spherical refractive errors (i.e., from hyperopia,  $M \geq +1.00D$ , to moderate myopia,  $M \leq -5.00D$ ), our myopic aging subjects (SM:  $0.24 \pm 0.01 \mu m$ , MA:  $0.27 \pm 0.02 \mu m$ ) showed a higher RMS of the total HOAs ( $0.157 \pm 0.071$  to  $0.183 \pm 0.065 \mu m$ ).<sup>56, 57</sup> While factors including the magnitude of refractive error and the experimental protocol employed in these studies might have contributed to the differences between these studies, these results indicate that the optical quality is deteriorating in the aging eyes.<sup>20, 58-60</sup>

To our knowledge, this is the first study aimed to investigate the relationship between the regional corneal shape factors and HOAs in the aging Chinese myopic adults with and without ATR astigmatism; however, there are several limitations that worth noting. First, this study did not measure the visual performance related to the changes in in corneal shapes and HOAs. Although previous studies have documented that a more oblate corneal shape in the aging subjects increases both the on-<sup>31, 32</sup> and off-axis ocular aberrations,<sup>61</sup> it is possible that smaller pupil size in elderly, which was not measured in this

study, might have alleviated the consequences on visual performance. Second, even though we had applied the same reference axis when determining the corneal and ocular aberrations, because the corneal and ocular aberrations were measured separately using different instruments, the subtle differences in eye position or pupil alignment during measurements may influence the calculated results of internal aberration. Third, although we had attempted to minimize the effects of tear film by performing the corneal topography and ocular aberrations measurements immediately after blinks, we cannot rule out the potential contribution of the reduced tear film stability to the increased HOAs<sup>62</sup> in the aging eyes.

In conclusion, the presence of astigmatism in aging Chinese myopes is associated with changes in regional corneal shape and higher order ocular aberrations. To achieve the best optical quality, it is important to take this parametric changes into account when designing conventional/advanced ophthalmic aids or formulating refractive surgery strategy for this rapidly increasing population.



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## References

1. World Health Organization. Global health and aging. Geneva: World Health Organization; 2011.
2. Leung TW, Lam AKC, Deng L, Kee CS. Characteristics of astigmatism as a function of age in a Hong Kong clinical population. *Optom Vis Sci* 2012;89:984-92.
3. Sawada A, Tomidokoro A, Araie M, Iwase A, Yamamoto T. Refractive errors in an elderly Japanese population: the Tajimi study. *Ophthalmology* 2008;115:363-70.
4. Cheng CY, Hsu WM, Liu JH, Tsai SY, Chou P. Refractive errors in an elderly Chinese population in Taiwan: the Shihpai Eye Study. *Invest Ophthalmol Vis Sci* 2003;44:4630-8.
5. Liu YC, Chou P, Wojciechowski R, Lin PY, Liu CJL, Chen SJ, Liu JH, Hsu WM, Cheng CY. Power vector analysis of refractive, corneal, and internal astigmatism in an elderly Chinese population: the Shihpai Eye Study. *Invest Ophthalmol Vis Sci* 2011;52:9651-7.
6. Saw SM, Chan YH, Wong WL, Shankar A, Sandar M, Aung T, Tan DTH, Mitchell P, Wong TY. Prevalence and risk factors for refractive errors in the Singapore Malay Eye Survey. *Ophthalmology* 2008;115:1713-9.
7. Bourne RR, Dineen BP, Ali SM, Noorul HDM, Johnson GJ. Prevalence of refractive error in Bangladeshi adults: results of the National Blindness and Low Vision Survey of Bangladesh. *Ophthalmology* 2004;111:1150-60.
8. Kee CS. Astigmatism and its role in emmetropization. *Exp Eye Res* 2013;114:89-95.
9. Anstice J. Astigmatism—its components and their changes with age. *Am J Optom Arch Am Acad Optom* 1971;48:1001-6.
10. Hirsch MJ. Changes in astigmatism after the age of forty. *Am J Optom Arch Am Acad Optom* 1959;36:395-405.
11. Lyle WM. Changes in corneal astigmatism with age. *Am J Optom Arch Am Acad Optom* 1971;48:467-78.
12. He M, Zeng J, Liu Y, Xu J, Pokharel GP, Ellwein LB. Refractive error and visual impairment in urban children in southern China. *Invest Ophthalmol Vis Sci* 2004;45:793-9.
13. Lin LLK, Shih YF, Hsiao CK, Chen CJ. Prevalence of myopia in Taiwanese schoolchildren: 1983 to 2000. *Ann Acad Med Singapore* 2004;33:27-33.
14. Saw SM, Tong L, Chua WH, Chia KS, Koh D, Tan DTH, Katz J. Incidence and Progression of Myopia in Singaporean School Children. *Invest Ophthalmol Vis Sci* 2005;46:51-7.
15. Farbrother JE, Welsby JW, Guggenheim JA. Astigmatic axis is related to the level of spherical ametropia. *Optom Vis Sci* 2004;81:18-26.
16. Mandel Y, Stone RA, Zadok D. Parameters associated with the different astigmatism axis orientations. *Invest Ophthalmol Vis Sci* 2010;51:723-30.
17. Wolffsohn JS, Bhogal G, Shah S. Effect of uncorrected astigmatism on vision. *J Cataract Refract Surg* 2011;37:454-60.
18. Zheng GY, Du J, Zhang JS, Liu SB, Nie XL, Zhu XH, Tang XX, Xin BL, Mai ZB, Zhang WX. Contrast sensitivity and higher-order aberrations in patients with astigmatism. *Chin Med J (Engl)* 2007;120:882-5.
19. Applegate RA, Donnelly Iii WJ, Marsack JD, Koenig DE, Pesudovs K. Three-dimensional relationship between high-order root-mean-square wavefront error, pupil diameter, and aging. *J Opt Soc Am A Opt Image Sci Vis* 2007;24:578-87.

20. Artal P, Berrio E, Guirao A, Piers PA. Contribution of the cornea and internal surfaces to the change of ocular aberrations with age. *J Opt Soc Am A Opt Image Sci Vis* 2002;19:137-43.
21. Atchison DA, Markwell EL. Aberrations of emmetropic subjects at different ages. *Vision Res* 2008;48:2224-31.
22. Berrio E, Tabernero J, Artal P. Optical aberrations and alignment of the eye with age. *J Vis* 2010;10.
23. Brunette I, Bueno JM, Parent M, Hamam H, Simonet P. Monochromatic aberrations as a function of age, from childhood to advanced age. *Invest Ophthalmol Vis Sci* 2003;44:5438-46.
24. McLellan JS, Marcos S, Burns SA. Age-related changes in monochromatic wave aberrations of the human eye. *Invest Ophthalmol Vis Sci* 2001;42:1390-5.
25. Carney LG, Mainstone JC, Henderson BA. Corneal topography and myopia. A cross-sectional study. *Invest Ophthalmol Vis Sci* 1997;38:311-20.
26. Dubbelman M, Sicam V, Van der Heijde GL. The shape of the anterior and posterior surface of the aging human cornea. *Vision Res* 2006;46:993-1001.
27. Leung TW, Lam AKC, Kee CS. Corneal shapes of chinese emmetropes and myopic astigmats aged 10 to 45 years. *Optom Vis Sci* 2013;90:1258-66.
28. Nieto-Bona A, Lorente-Velázquez A, Montes-Micó R. Relationship between anterior corneal asphericity and refractive variables. *Graefes Arch Clin Exp Ophthalmol* 2009;247:815-20.
29. Atchison DA, Markwell EL, Kasthurirangan S, Pope JM, Smith G, Swann PG. Age-related changes in optical and biometric characteristics of emmetropic eyes. *J Vis* 2008;8:29.1-0.
30. Guirao A, Redondo M, Artal P. Optical aberrations of the human cornea as a function of age. *J Opt Soc Am A Opt Image Sci Vis* 2000;17:1697-702.
31. Calossi A. Corneal asphericity and spherical aberration. *J Refract Surg* 2007;23:505-14.
32. Kiely PM, Smith G, Carney LG. The mean shape of the human cornea. *J Mod Opt* 1982;29:1027-40.
33. Zhang Z, Wang J, Niu W, Ma M, Jiang K, Zhu P, Ke B. Corneal asphericity and its related factors in 1052 Chinese subjects. *Optom Vis Sci* 2011;88:1232-9.
34. Harvey EM, Dobson V, Clifford-Donaldson CE, Green TK, Messer DH, Miller JM. Prevalence of astigmatism in Native American infants and children. *Optom Vis Sci* 2010;87:400-5.
35. Tong L, Carkeet A, Saw SM, Tan DT. Corneal and refractive error astigmatism in Singaporean schoolchildren: a vector-based Javal's rule. *Optom Vis Sci* 2001;78:881-7.
36. Chernyak DA, Campbell CE. A System for the Design, Manufacture and Test of Custom Lenses With Known Amounts of High Order Aberrations. *Invest Ophthalmol Vis Sci* 2002;43.
37. Marsack J, Milner T, Rylander G, Leach N, Roorda A. Applying wavefront sensors and corneal topography to keratoconus. *Biomed Sci Instrum* 2001;38:471-6.
38. Montés-Micó R, Ferrer-Blasco T, Cerviño A. Analysis of the possible benefits of aspheric intraocular lenses: review of the literature. *J Cataract Refract Surg* 2009;35:172-81.
39. Packer M, Fine IH, Hoffman RS. Aspheric intraocular lens selection based on corneal wavefront. *J Refract Surg* 2009;25:12-20.

40. Gatinel D, Azar DT, Dumas L, Malet J. Effect of anterior corneal surface asphericity modification on fourth-order Zernike spherical aberrations. *J Refract Surg* 2014;30:708-15.
41. Koller T, Iseli HP, Hafezi F, Mrochen M, Seiler T. Q-factor customized ablation profile for the correction of myopic astigmatism. *J Cataract Refract Surg* 2006;32:584-9.
42. Stojanovic A, Wang L, Jankov MR, Nitter TA, Wang Q. Wavefront optimized versus custom-Q treatments in surface ablation for myopic astigmatism with the WaveLight ALLEGRETTO laser. *J Refract Surg* 2008;24:779-89.
43. Grosvenor T. Subjective refraction. In: Grosvenor S, editor. *Primary care optometry*. St. Louis, Mo: Butterworth-Heinemann/Elsevier, 2007: 209-23.
44. Chylack LT, Jr., Wolfe JK, Singer DM, Leske MC, Bullimore MA, Bailey IL, Friend J, McCarthy D, Wu SY. The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group. *Arch Ophthalmol* 1993;111:831-6.
45. Thibos LN, Applegate RA, Schwiegerling JT, Webb R, VSIA Standards Taskforce Members. Standards for reporting the optical aberrations of eyes. *J Refract Surg* 2002;18:S652-60.
46. Artal P, Guirao A, Berrio E, Williams DR. Compensation of corneal aberrations by the internal optics in the human eye. *J Vis* 2001;1:1-8.
47. Montés-Micó R, Alió JL, Muñoz G, Charman WN. Temporal changes in optical quality of air-tear film interface at anterior cornea after blink. *Invest Ophthalmol Vis Sci* 2004;45:1752-7.
48. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci* 1997;74:367-75.
49. Howland HC, Howland B. A subjective method for the measurement of monochromatic aberrations of the eye. *J Opt Soc Am* 1977;67:1508-18.
50. Smolek MK, Klyce SD, Sarver EJ. Inattention to nonsuperimposable midline symmetry causes wavefront analysis error. *Arch Ophthalmol* 2002;120:439-47.
51. Zhao H, Dai G-M, Chen L, Weeber HA, Piers PA. Spherical aberrations of human astigmatic corneas. *J Refract Surg* 2011;27:846-8.
52. Wei RH, Lim L, Chan WK, Tan DTH. Higher order ocular aberrations in eyes with myopia in a Chinese population. *J Refract Surg* 2006;22:695-702.
53. Buehren T, Collins MJ, Carney L. Corneal aberrations and reading. *Optom Vis Sci* 2003;80:159-66.
54. Ghosh A, Collins MJ, Read SA, Davis BA, Iskander DR. The influence of downward gaze and accommodation on ocular aberrations over time. *J Vis* 2011;11.
55. Kelly JE, Mihashi T, Howland HC. Compensation of corneal horizontal/vertical astigmatism, lateral coma, and spherical aberration by internal optics of the eye. *J Vis* 2004;4.
56. Carkeet A, Hai DL, Tong L, Mei Saw S, Tan DTH. Refractive error and monochromatic aberrations in Singaporean children. *Vision Res* 2002;42:1809-24.
57. Kwan WCK, Yip SP, Yap MKH. Monochromatic aberrations of the human eye and myopia. *Clin Exp Optom* 2009;92:304-12.
58. Amano S, Amano Y, Yamagami S, Miyai T, Miyata K, Samejima T, Oshika T. Age-related changes in corneal and ocular higher-order wavefront aberrations. *Am J Ophthalmol* 2004;137:988-92.
59. Artal P, Ferro M, Miranda I, Navarro R. Effects of aging in retinal image quality. *J Opt Soc Am A Opt Image Sci Vis* 1993;10:1656-62.

60. Calver RI, Cox MJ, Elliott DB. Effect of aging on the monochromatic aberrations of the human eye. *J Opt Soc Am A Opt Image Sci Vis* 1999;16:2069-78.
61. He JC. Theoretical model of the contributions of corneal asphericity and anterior chamber depth to peripheral wavefront aberrations. *Ophthalmic Physiol Opt* 2014;34:321-30.
62. Cho P, Yap M. Age, gender, and tear break-up time. *Optom Vis Sci* 1993;70:828-31.

## Figure legends

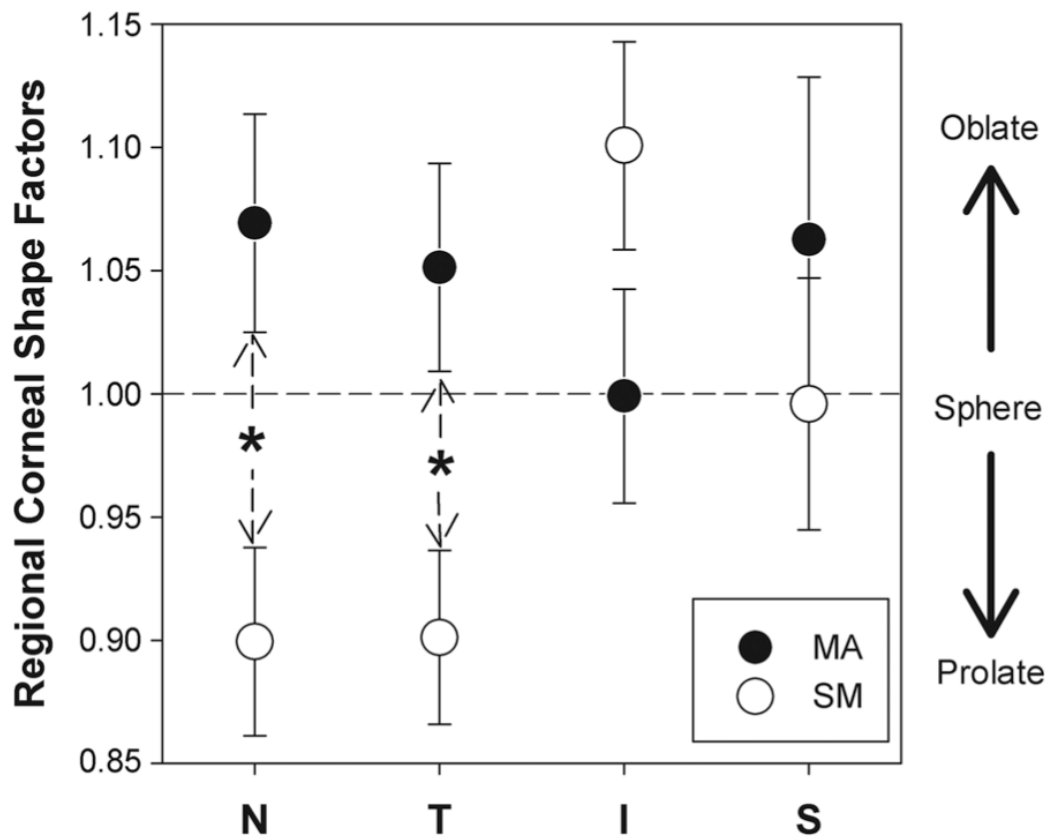


Figure 1. Comparisons of regional corneal shape factors (mean $\pm$ SE) between MA (filled circles) and SM (open circles) at the nasal (N), temporal (T), inferior (I) and superior (S) quadrants. The horizontal dashed line indicates where the cornea is spherical in shape (corneal shape factor = 1); the data above and below this line represent oblate (corneal shape factor >1) and prolate ellipses (corneal shape factor <1), respectively. The dashed arrow represents a significant difference between MA and SM, with the asterisk showing the significant level: \*  $p < 0.05$ .

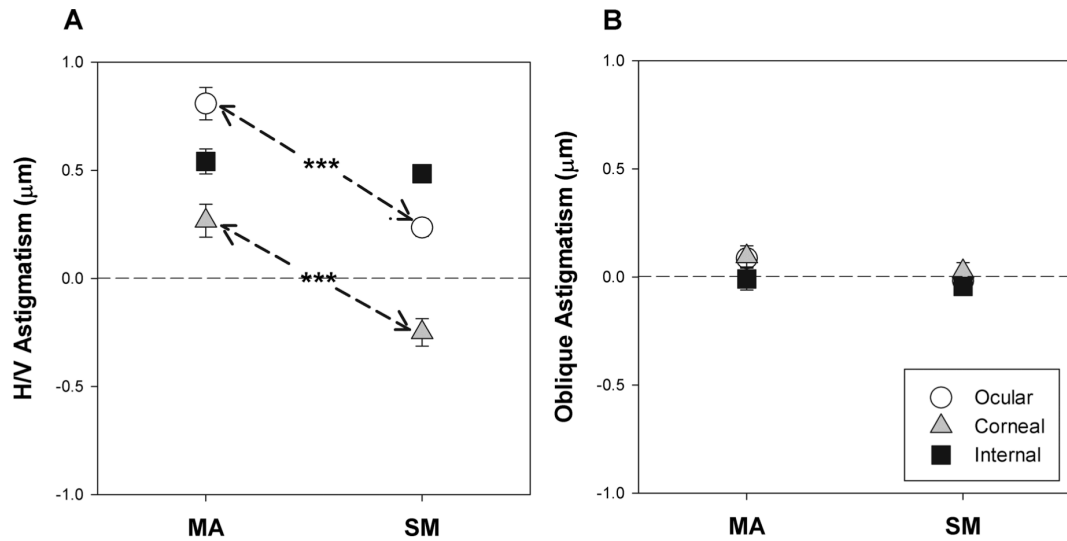


Figure 2. Comparisons of the ocular (circles), corneal (triangles) and internal (squares) astigmatism (mean $\pm$ SE) between MA and SM in 5mm pupil diameter: (a) H/V astigmatism; and (b) oblique astigmatism. The dashed arrow represents a significant difference between MA and SM, with the asterisk showing the significant level: \*\*\*  $p < 0.001$ . Note that some error bars were too small and were masked by the symbols.

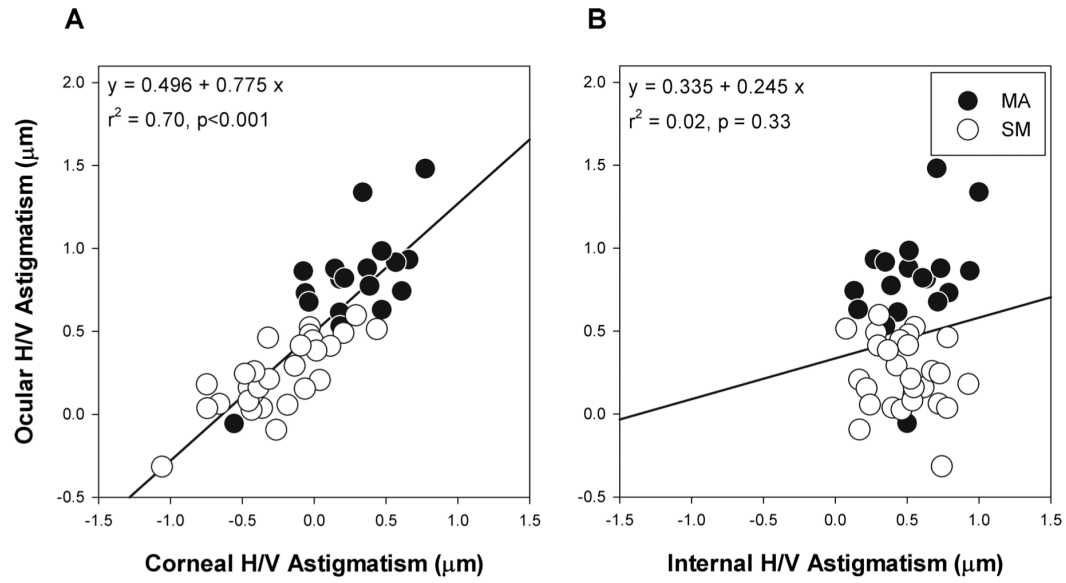


Figure 3. Correlations between the ocular H/V astigmatism with (a) the corneal H/V astigmatism, and (b) the internal H/V astigmatism in 5mm pupil diameter of MA (filled circles) and SM (open circles). The solid lines represent the regression line with the best linear fit, the equation and statistics for these lines are inserted.



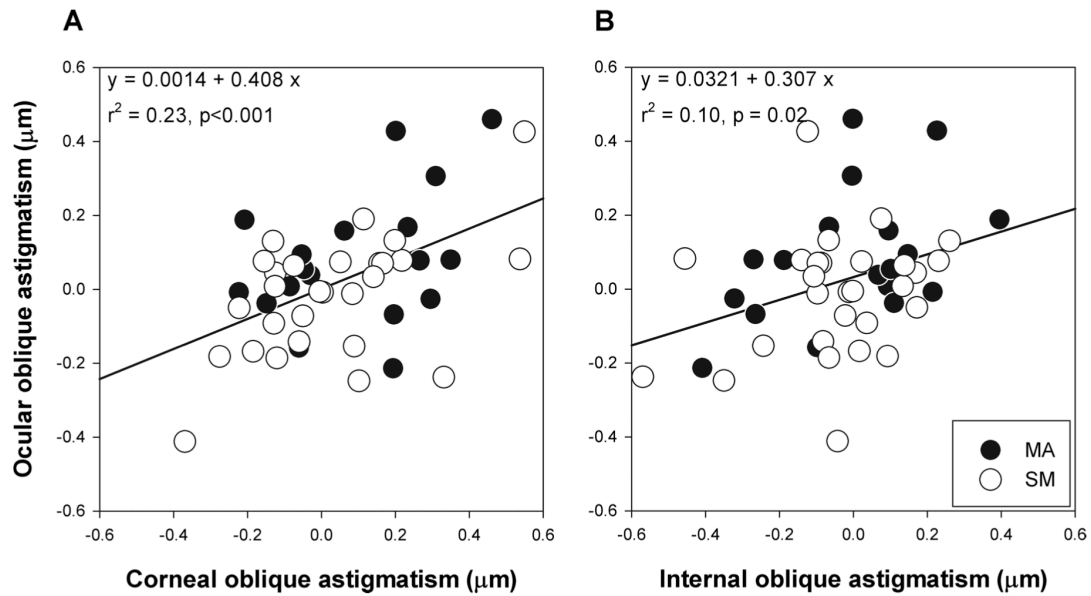


Figure 4. Correlations between the ocular oblique astigmatism with (a) the corneal oblique astigmatism, and (b) the internal oblique astigmatism in 5mm pupil diameter of MA (filled circles) and SM (open circles). The solid lines represent the regression line with the best linear fit, the equation and statistics for these lines are inserted.

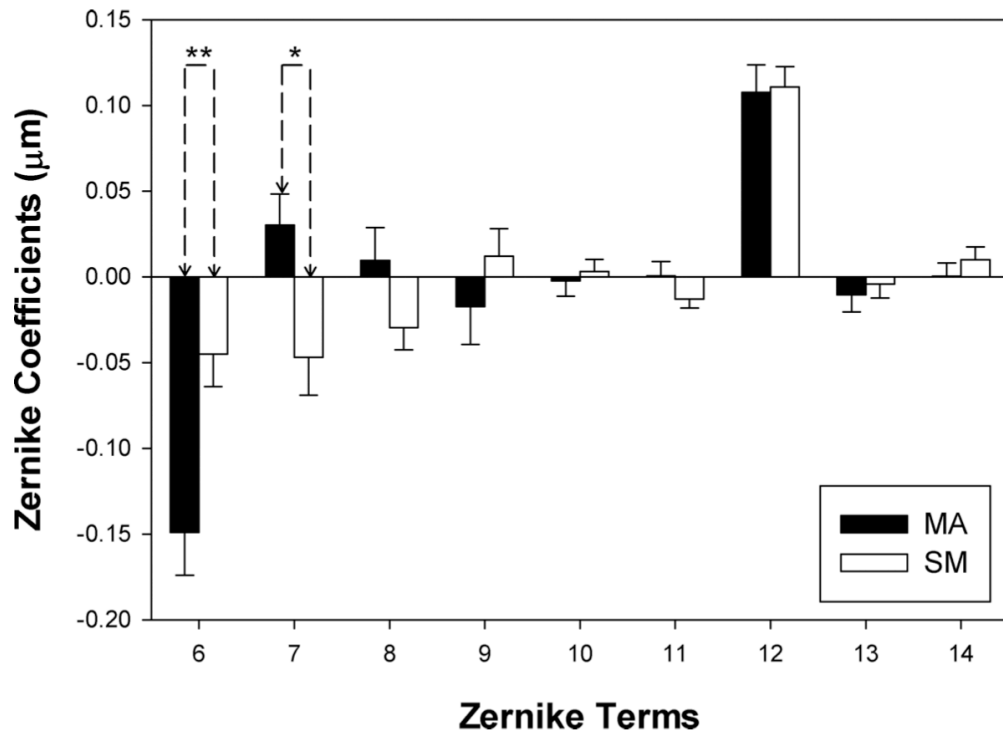


Figure 5. Comparisons of the ocular higher order Zernike terms, from Z6 to Z14 (mean $\pm$ SE), between MA (filled bars) and SM (open bars) in 5mm pupil diameter. The dashed arrow represents a significant difference between MA and SM, with the asterisk showing the significant levels: \*  $p < 0.05$ ; \*\*  $p < 0.01$ .

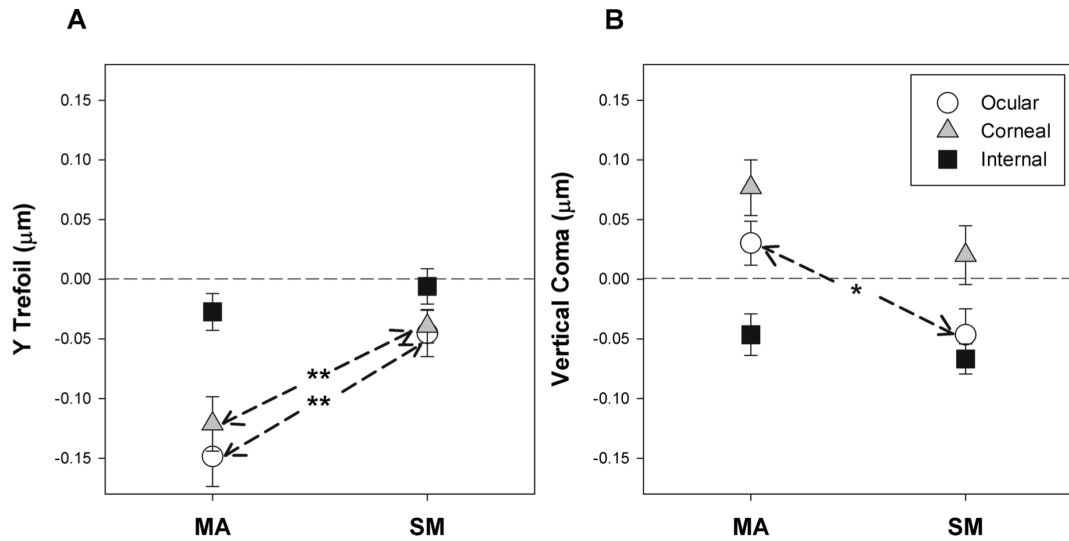


Figure 6. Comparisons of (a) Y trefoil and (b) vertical coma (mean $\pm$ SE) between MA and SM for the whole eye (circles), the corneal (triangles) and internal (squares) optics in 5mm pupil diameter. The dashed arrow represents a significant difference between MA and SM, with the asterisk showing the significant levels: \*  $p < 0.05$ ; \*\*  $p < 0.01$ .

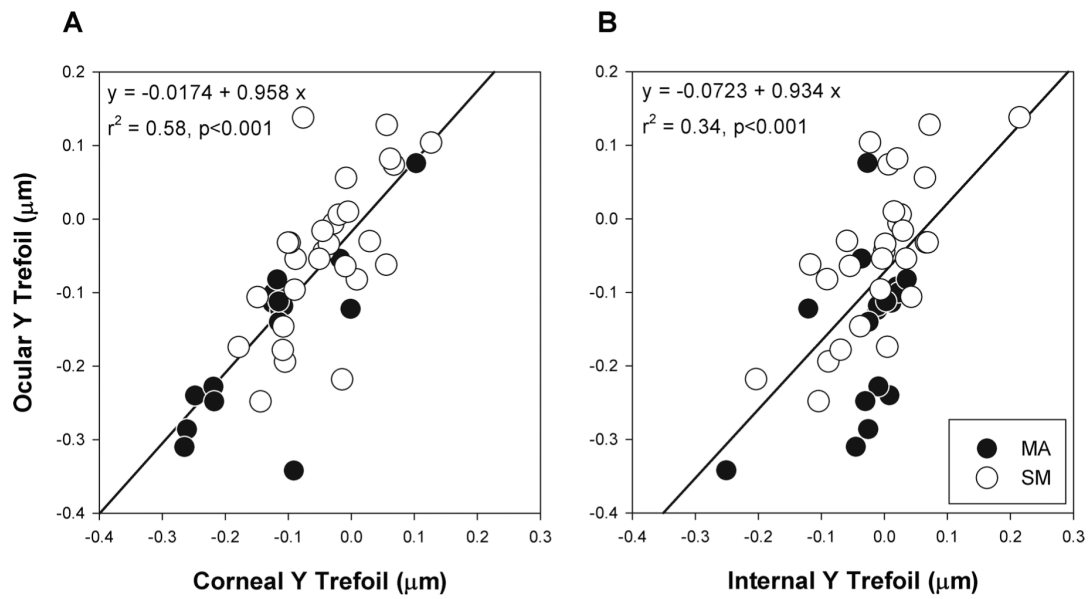


Figure 7. Correlations between the ocular Y trefoil with (a) the corneal Y trefoil, and (b) the internal Y trefoil in 5mm pupil diameter of MA (filled circles) and SM (open circles). The solid lines represent the regression line with the best linear fit, the equation and statistics for these lines are inserted.

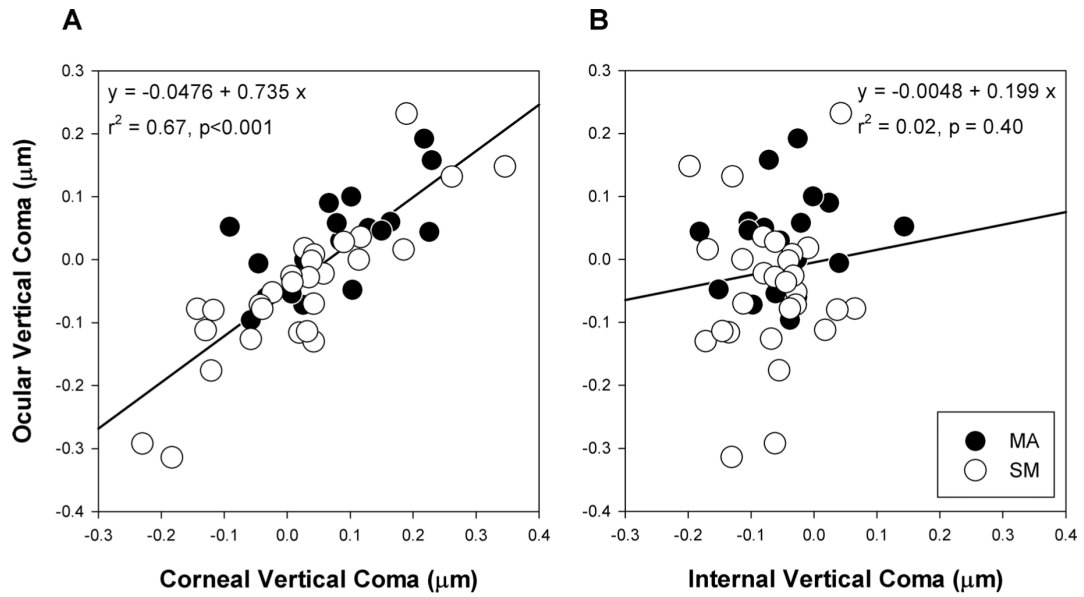


Figure 8. Correlations between the ocular vertical coma with (a) the corneal vertical coma, and (b) the internal vertical coma in 5mm pupil diameter of MA (filled circles) and SM (open circles). The solid lines represent the regression line with best linear fit, the equation and statistics for these lines are inserted.

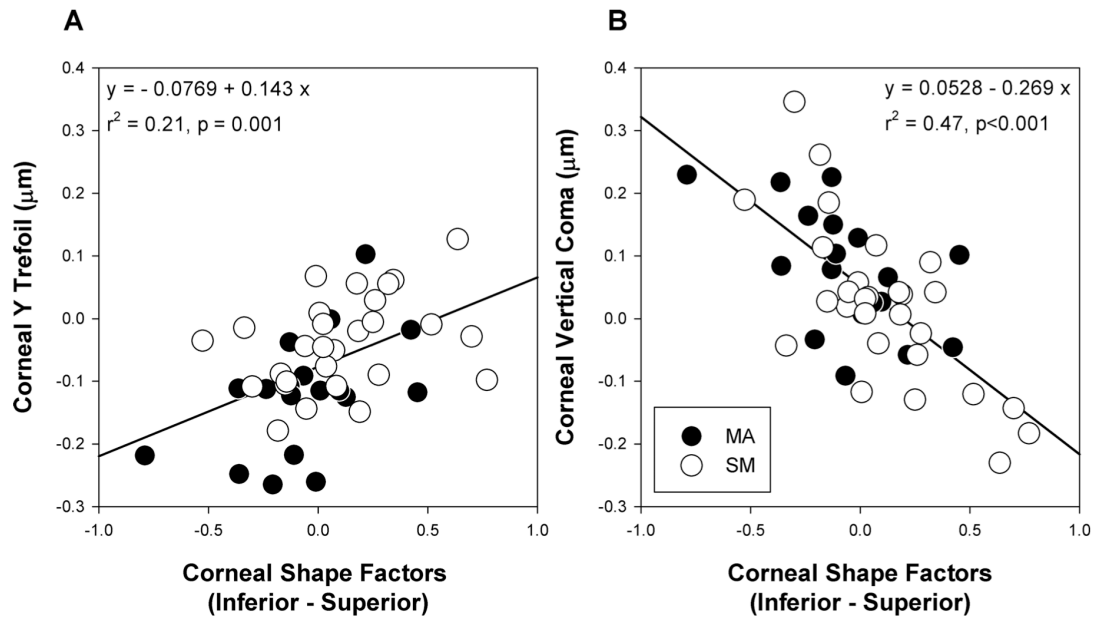


Figure 9. Correlations between (a) the corneal Y trefoil and (b) the corneal vertical coma in 5mm pupil diameter with the asymmetry in corneal shape along the vertical meridian (inferior – superior) in MA (filled circles) and SM (open circles). The solid lines represent the regression line with the best linear fit, the equation and statistics for these lines are inserted.

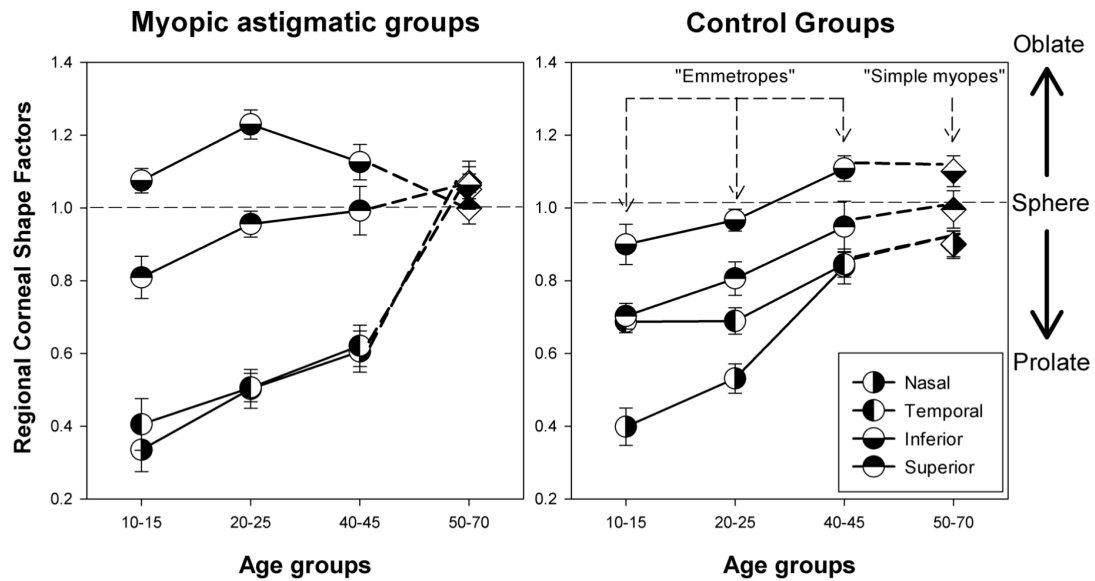


Figure 10. Changes in regional corneal shape factors (mean $\pm$ SE) as a function of age at the nasal (orange symbols), temporal (green symbols), inferior (blue symbols) and superior (red symbols) quadrants for the myopic astigmats (left) and controls (right). Note that the control groups were, respectively, emmetropes and simple myopes in our previous and current studies. The data from our previous <sup>25</sup> and current studies are represented in circles (connected with solid line) and squares (connected with dashed line), respectively. The horizontal dashed line represents a spherical cornea (corneal shape factor = 1); the data above and below this line represent oblate (corneal shape factor >1) and prolate corneas (corneal shape factor <1), respectively.

## Table

Table 1. Comparisons of demographic information and refractive status (mean±SE) between MA and SM.

Variables	MA	SM	p value
Age (Years)	57.56±1.20	55.71±0.94	0.23
M (D)	−2.03±0.40	−2.65±0.38	0.27
Refractive astigmatism			
Cyl (D)	1.51±0.11	0.41±0.05	<0.001
J0 (D)	−0.73±0.06	−0.12±0.03	<0.001
J45 (D)	−0.02±0.05	−0.01±0.03	0.77