Posterior Retinal Contour in Adult Human Anisomyopia

Nicola S. Logan,[1] *Bernard Gilmartin,*[1] *Christine F. Wildsoet,*[2] *and Mark C. M. Dunne*[1]

Purpose. It is well documented that myopia is associated with an increase in axial length or, more specifically, in vitreous chamber depth. Whether the transverse dimensions of the eye also increase in myopia is relevant to further understanding of its development.

Methods. The posterior retinal surface was localized in two-dimensional space in both eyes of young adult white and Taiwanese-Chinese iso- and anisomyopes ($N = 56$), from measured keratometry, A-scan ultrasonography, and central and peripheral refraction ($\pm 35°$) data, with the aid of a computer modeling program designed for this purpose. Anisomyopes had 2 D or more interocular difference in their refractive errors, with mean values in their more myopic eyes of −5.57 D and in their less myopic eyes of −3.25 D, similar to the means of the two isomyopic groups. The derived retinal contours for the more and less myopic eyes were compared by way of investigating ocular shape changes that accompany myopia, in the posterior region of the vitreous chamber. The presence and size of optic disc crescents were also investigated as an index of retinal stretching in myopia.

Results. Relative to the less myopic eyes of anisometropic subjects, the more myopic eyes were more elongated and also distorted into a more prolate shape in both the white and Chinese groups. However, the Chinese eyes showed a greater and more uniform relative expansion of the posterior retinal surface in their more myopic eyes, and this was associated with larger optic disc crescents. The changes in the eyes of whites displayed a nasal–temporal axial asymmetry, reflecting greater enlargement of the nasal retinal sector.

Conclusions. Myopia is associated with increased axial length and a prolate shape. This prolate shape is consistent with the proposed idea that axial and transverse dimensions of the eye are regulated differently. The observations that ocular shape changes are larger but more symmetrical in Chinese eyes than in eyes of whites warrant further investigation. (*Invest Ophthalmol Vis Sci.* 2004;45:2152–2162) DOI:10.1167/iovs.03-0875

Myopia is now a very common condition, with its prevalence having increased in recent decades, and is now approaching 39% in young adolescents in Western society[1] and 84% in Taiwanese-Chinese children.[2,3] Apart from juvenile-onset myopia, the onset of myopia may occur as a delayed, adult-onset condition. The late-onset form of myopia has been strongly linked with specific occupational demands for sustained and demanding near vision tasks.[4,5] The rising prevalence of myopia has significant economic and social implications, resulting in renewed interest in methods for ameliorating myopia.

The development of effective treatment strategies for myopia requires a clear understanding of what governs the onset and progression of myopia and the underlying biological processes. That genes have been identified only for high myopia (>6 D)[6–10] and not for lower levels of myopia suggests that high myopia represents a distinct class of the disorder. It is conjectured that lower levels of myopia represent a more complex trait, with genetic factors determining susceptibility to provocative visual environmental factors and thus myopia.[4,9,11–16]

Critical to the progress in myopia research has been animal studies that allow direct and controlled experimental manipulation of the visual environment,[17,18] with an interesting corollary emerging between the myopia resulting from imposed hyperopic defocus in very young animals[17,19] and lags of accommodation evident in myopia in children.[20] These findings converge on the additional observation that form deprivation can also be induced in adolescent animals.[21,22] As in humans, there are also reports of optic disc crescents and other signs of retinal stretching coupled with high myopia in mammalian eyes,[23,24] and in limited commentary covering eye shape changes in animal studies, there is evidence of an axial bias to the changes. The latter parallels are consistent with similarities in the scleral structure and composition of mammals and primate eyes; for example, both mammalian and primate eyes have fibrous scleras. That similar mechanisms underlie myopic growth in these cases is consistent with the common finding of exaggerated scleral changes at the posterior pole compared with the more anterior regions of myopic eyes in tree shrew[25–27] monkey,[28,29] and humans.[30] In the chick, which is also widely used in animal studies of myopia, the sclera has an additional cartilaginous layer, potentially limiting the general applicability of derived models for scleral growth. Nonetheless, a posterior (axial) bias to biochemical changes in the sclera has also been reported in myopic chick eyes.[31]

The paucity of information concerning the nature of myopic eye growth in humans reflects, in part, the lack of accessible in vivo techniques. Most published data relate to in vitro measurements taken from highly myopic eyes after enucleation.[32] In contrast, in the present study we used a computational procedure to compare in young adult Taiwanese-Chinese and white iso- and anisomyopes, biometric correlates of ocular shape derived from central and peripheral refractive error data. It is well documented that off-axis measurements of refractive error differ considerably from foveal (on-axis) refractive error measurements by an amount that depends on the degree of eccentricity from the fixation point and the nature of the on-axis refractive error.[33–36] Ferree and Rand[37] were both the first to make such measurements and the first to suggest that it may be possible to describe the shape of the retinal surface from peripheral refraction data. Subsequently, Dunne[38] and Logan et al.[39] developed their proposal to derive the

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TABLE 1. Profile of Young Adult Subjects Participating in the Study

	White		Chinese	
	Anisomyopia	**Isomyopia**	**Anisomyopia**	**Isomyopia**
Gender				
Male	7	6	8	8
Female	7	8	6	6
Age range (y)	18–26	18–26	14–26	20–25
Range of refractive error (D)	−0.25 to −8.00	0 to −6.75	−0.25 to −9.00	0 to −7.25

computational model used in the present study to derive two-dimensional posterior retinal contours from refraction, corneal curvature, and axial biometry measurements.[38,39] Our strategy of comparing the two eyes of anisomyopes avoids the confounding influence of differences in genetic background—the less myopic eye serving as an inherent experimental control. Presumably these eyes are exposed to the same visual (environmental) influences. Although anisomyopia is uncommon in eyes of whites, with only approximately 1.5% of the population having interocular differences of 2 D or more,[40] its prevalence approaches 4% in Taiwanese-Chinese eyes.[41]

Optic disc crescents are more common in myopic eyes, with more myopic eyes tending to have larger optic disc crescents.[42,43] These trends are consistent with the notion that optic disc crescents are a product of retinal stretching. The present study also assessed the relationship between optic disc crescent diameters and refractive error and the influence of ethnicity and interocular refractive differences.

In summary, the present study focused on the ocular shape differences related to myopia in anisomyopes. We were also interested in whether there are shape differences that might imply structural differences between white and Chinese eyes that go hand in hand with the greater susceptibility of Chinese eyes to myopia and anisomyopia. We also investigated whether the structural correlates of isomyopia are the same as those for anisomyopia. We found that ocular shape varied with the amount of myopia, in both isomyopes and anisomyopes. We also noted differences in the magnitude and symmetry of shape changes related to ethnicity.

METHODS

Subjects

A total of 56 young adult subjects participated in this study, which included four subgroups: white (Wh) and Taiwanese-Chinese (TCh) anisomyopes and white and Taiwanese-Chinese isomyopes. Each group comprised 14 subjects. The Chinese subjects were either born in Taiwan of Chinese parents or born in Australia or the United Kingdom of parents who were born in Taiwan of Chinese parents. Table 1 summarizes the profile of these groups. All anisomyopic subjects had interocular differences in spherical equivalent refractive errors of 2 D or more, with the less myopic eye having at least 0.12 D of myopia. All isomyopes had interocular differences of 0.50 D or less. The two isomyope groups were matched in terms of the mean refractive errors, and these means correspond closely to the equivalent values for the less myopic eyes of the two anisomyope groups. All subjects had less than 2 D of astigmatism. Most (93%) had less than 0.75 DC, and all had binocular single vision. None of the anisomyopia was secondary to ocular disease. All four groups were matched approximately in age and gender. Most of the Chinese subjects ($n = 18$) were examined at Queensland University of Technology (QUT; Brisbane, Australia). All other subjects were examined at Aston University (Birmingham, UK). The Ethics Committees of Aston University and QUT approved the study, and the study conformed to the tenets of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from subjects after the nature of the study was explained to them.

Ocular Biometric Measurements

A full optometric eye examination was performed before data collection. Assessments included objective and subjective refractions, visual acuity, oculomotor balance, binocularity, amplitude of accommodation, ophthalmoscopy, and slit lamp biomicroscopy. Experimental data collection comprised central and peripheral refractions, A-scan ultrasonography, and keratometry. Both the right and left eyes of all subjects were measured. Eyes were cyclopleged with 1% tropicamide (1 drop of approximately 50 μL; Minims; Chauvin Pharmaceuticals, Romford, UK) for refraction and ultrasonography measurements. Cycloplegia was first confirmed by monitoring accommodative amplitude. Initial baseline values were obtained using the push-up method before drug instillation. Residual accommodation of less than 0.4 D has been reported in young myopes with this tropicamide dose regimen,[44] and similar effects were observed in the present study.

Central (on-axis) and peripheral (off-axis) refractions were measured with an open-field objective infrared (IR) autorefractor (Canon R-1; Canon US, Lake Success, NY). This autorefractor has been used extensively in human refractive error and accommodation research.[45–48] It was interfaced with a computer (MacIntosh; Apple Computer, Cupertino, CA) to allow electronic collection of the refraction data. Refraction measurements were taken sequentially: central-to-nasal followed by central-to-temporal, along the horizontal meridian at 5° intervals out to a minimum of 30° eccentricity (maximum of 40°). These peripheral data were obtained by having subjects fixate appropriately spaced circular targets on an arc 50 cm away. Subjects were secured in a headrest and instructed to change fixation by moving their eyes only. The targets were color coded to aid identification, and the nonfixating eye was occluded. Typically, eyes show increasing astigmatism with increasing eccentricity, reflecting the oblique path of light rays traversing the optics of the eye. From recorded peripheral refraction data, values for the tangential plane (i.e., for rays traveling in the plane of oblique incidence, horizontal rays) and the sagittal plane (i.e., for rays traveling at right angles to the plane of oblique incidence, vertical rays) were calculated, as required for the computing scheme. The average of the latter refractions that delimit the interval of Sturm defines the spherical equivalent refractive error and their difference, the amount of astigmatism. A minimum of five readings was collected for each eccentricity to derive these data. Unless otherwise indicated, refraction data are reported in terms of equivalent spherical refractions.

Axial length data were recorded from cyclopleged eyes with a biometric instrument (Omega Compu-Scan Biometric Ruler; Storz International, St. Louis, MO) This instrument includes a hand-held focused, solid tip, 10-MHz probe and automatically discards measurements with a standard deviation greater than 0.1 mm. A minimum of 10 readings were recorded and averaged. The subject was required to fixate a spotlight at a distance of 6 m during measurement,[49] with corneas anesthetized with 1 drop of topical 0.4% benoxinate HCl (Minims; Chauvin Pharmaceuticals) beforehand.

Central corneal curvature data were recorded with a keratometer (Bausch and Lomb, Tampa, FL). Three readings were taken for each principal meridian and used to obtain a grand average.

Computation of Retinal Contours

The computing scheme used to generate the two-dimensional retinal contours in individual eyes, has been described and evaluated elsewhere.[38,39] A brief description of each stage in this process is included herein.

The first stage involves the generation of an eye model, comprising three axially aligned spherical surfaces (one corneal surface and two crystalline lens surfaces) separated by homogenous ocular media of assumed refractive index. The model made use of corneal radius and refractive errors for the horizontal meridian which were derived by vector analysis from keratometry and on-axis refraction data. Ocular axial distances (A-scan ultrasonography: anterior chamber depth, crystalline lens thickness, and vitreous chamber depth) were also used. Anterior and posterior crystalline lens radii were computed, in the absence of phakometric data, using a scheme originally devised by Bennett[50] and later modified by Royston et al.[51]

The second stage involved calculating peripheral refractions in the eye model for each of the eccentricities (field angles) used in measurements. Meridional-Coddington ray-tracing formulas[52] were used to calculate peripheral refraction in the model eye. At each field angle, a chief ray was traced out of the eye starting from its intersection with the retinal surface (given an initial retinal radius of curvature of 12 mm). The chief ray was accompanied by a pair of infinitesimally close rays (one sagittal, the other tangential), allowing emergent vergence to be calculated for both the sagittal and tangential meridians. With a reversal of sign, these vergences equated to the sagittal and tangential refractive errors.

The third stage involved adjusting corneal asphericity in the model eye to achieve a perfect match between the measured and calculated peripheral astigmatism at each field angle. This was necessary to account for the effects on peripheral astigmatism of unmeasured parameters such as the gradient refractive index structure of the crystalline lens and the misalignment of ocular surfaces. It was achieved by treating the corneal surface as an ellipse that could be defined by an apical radius of curvature (set to the average value obtained by keratometry) and a conic constant (that determines the degree to which the corneal surface steepens or flattens in the periphery). For each chief ray, the corneal conic constant was adjusted, keeping the apical radius constant, until the measured and calculated peripheral astigmatic values were equal. This procedure generates a model cornea that is described by a single apical radius of curvature and multiple conic constants, one for each chief ray. It is important to note that the conic constants derived in this manner bear no direct relationship with the single conic constant obtained with corneal topography.

The fourth and final stage involved adjusting the position of the retinal surface locally, for each chief ray, until a perfect match arose between the measured and calculated sagittal refractive error. The use of the sagittal refractive error allowed compensation for any measured central astigmatism; specifically, sagittal peripheral refraction was adjusted, at each field angle, by an amount equal to the central astigmatism. The output of this final stage was a series of paired coordinates defining the position of the retinal surface. One coordinate represents the distance between the corneal vertex and a plane containing the eccentric retinal point and perpendicular to the anteroposterior axis of the model eye. For brevity, this is referred to as the "distance from the cornea." The other coordinate represents the distance within the latter plane between the eccentric retinal point and the anteroposterior axis of the model eye. Because the anteroposterior axis strikes the retina at the fovea, this coordinate is referred to as the "distance from the fovea."

The coordinate system allowed graphic representation of the shape of the posterior retinal surface (Fig. 1) and thus visualization of differences between eyes—for example, in the case of anisomyopia. The use of the corneal apex as the reference point, also allowed the amount of expansion posteriorly of the retinal surface to be characterized. The use of a retinal coordinate system referenced to the fovea would have allowed us to determine only retinal shape changes. To quantify interocular differences in posterior segment shape, we derived a parameter called the index of differential posterior stretch (IDPS, see Fig. 1). Mathematically, this represents the difference in the area under a curve fitted to the retinal coordinates of the less myopic eye subtracted from the area under the curve fitted to retinal coordinates of the more myopic eye. Third-order polynomial functions were used for this purpose. To quantify any nasal-to-temporal asymmetry in these shape differences (e.g., compare Fig. 1A with 1B), a separate IDPS for the nasal and temporal halves of the retina was calculated and a ratio derived. Interocular differences in the relative enlargement of the retinal surface in the axial and transverse directions were also characterized. Axial differences were calculated by subtracting the axial length of the less myopic eye from that of the more myopic eye, whereas transverse differences were calculated by subtracting the width of the retina corresponding to maximum measured field angles (i.e., transverse chord diameter), of the less myopic eye from the more myopic eye. The ratio of the transverse-to-axial differences is least when axial enlargement is proportionately larger.

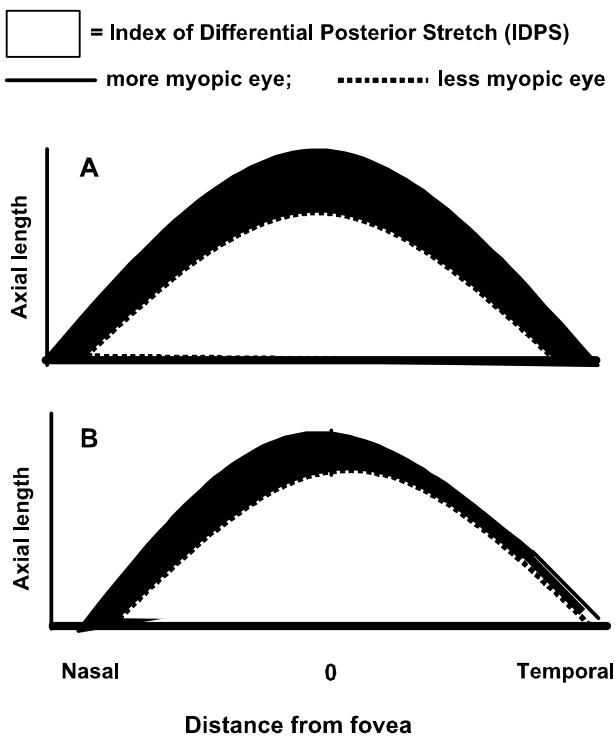

FIGURE 1. Retinal contours derived from peripheral refractive error data. The *x*-axis describes the distance from the fovea in the nasal and temporal directions; the *y*-axis describes the distance of the retinal surface from the cornea. IDPS stretch corresponds to the area between the retinal contours of the more myopic and less myopic eyes. (**A**) Uniform expansion in the more myopic eye. (**B**) A differential expansion of the nasal retinal sector; this asymmetry is expressed as the ratio of IDPSs derived separately for the nasal and temporal sectors.

Measurement of Optic Disc Crescents

Two different approaches were used to obtain the dimensions of optic discs and optic disc crescents, based on location. For subjects seen at Aston University, optic disc and optic crescent diameters were measured by retinal tomography with a scanning laser ophthalmoscope (Heidelberg Retinal Tomograph [HRT]; Heidelberg Engineering GmbH, Heidelberg, Germany). The distance measure option on the HRT biometric menu was used for this purpose. For subjects examined at QUT,

TABLE 2. Biometric Data for More Myopic (M) and Less Myopic (m) Eyes of the Anisomyopes and Isomyopes

Ocular Component	Anisomyopes		Isomyopes	
	M	m	M	m
Whites				
Refractive error (D)	−5.57 ± 1.75*	−3.25 ± 1.74*	−3.32 ± 2.29	−3.09 ± 2.26
Axial length (mm)	25.57 ± 1.27*	24.69 ± 1.17*	24.19 ± 1.02	24.09 ± 1.03
Anterior chamber depth (mm)	3.77 ± 0.11	3.82 ± 0.09	3.67 ± 0.18	3.66 ± 0.18
Lens thickness (mm)	3.60 ± 0.20	3.59 ± 0.16	3.61 ± 0.11	3.55 ± 0.24
Vitreous chamber depth (mm)	18.19 ± 1.32*	17.27 ± 1.19*	16.91 ± 0.95	16.87 ± 0.80
Corneal radius (mm)	7.57 ± 0.31	7.57 ± 0.30	7.61 ± 0.31	7.62 ± 0.31
Chinese				
Refractive error (D)	−5.24 ± 2.14*	−2.65 ± 2.03*	−4.24 ± 2.35	−4.04 ± 2.32
Axial length (mm)	25.90 ± 1.34*	24.61 ± 1.17*	24.89 ± 0.92	24.85 ± 0.90
Anterior chamber depth (mm)	3.69 ± 0.14	3.72 ± 0.16	3.78 ± 0.16	3.80 ± 0.10
Lens thickness (mm)	3.43 ± 0.26	3.44 ± 0.20	3.62 ± 0.19	3.62 ± 0.20
Vitreous chamber depth (mm)	18.78 ± 1.50*	17.45 ± 1.42*	17.49 ± 0.77	17.43 ± 0.75
Corneal radius (mm)	7.76 ± 0.29	7.78 ± 0.31	7.67 ± 0.34	7.65 ± 0.34

Data are the mean ± SD. M, more myopic; m, less myopic.
* Significant interocular differences ($P < 0.001$).

a nonmydriatic retinal camera (Topcon TRC-45N; Topcon Europe, IJssel, The Netherlands) was used to obtain photographic slides that were then analyzed by projection onto graph paper. The optic disc diameter was measured in the horizontal meridian, and the crescent diameter was measured from the horizontal edge of the optic disc to the edge of the crescent along the longest diameter. In all cases, the size of the crescent was expressed as a ratio of the crescent width to optic disc diameter.[43]

Statistical Analyses

Of most interest were the influences of ethnicity and anisometropia on eye shape and other ocular parameters. A two-way factorial ANOVA was initially applied using ethnicity (Chinese and white) and refractive group (anisomyopia and isomyopia) as the factors on difference data (i.e., more myopic eye minus less myopic eye). Further analyses used a three-factor split-plot ANOVA with ethnicity and refractive group as the main plot factors, along with a third subplot factor of retinal sector (nasal versus temporal). Correlation analyses were also performed on some of the data.

RESULTS

Table 2 shows the mean central (on-axis) refractive error, corneal radius of curvature, and axial ocular component data for the more and less myopic eyes in each of the two white and Taiwanese-Chinese groups. Overall, there were no ethnicity-based differences in any of these parameters and no group effect of corneal curvature, anterior chamber depth, and lens thickness, although, as expected, there was a significant group (i.e., anisomyopia and isomyopia) effect of refractive error and vitreous chamber depth. Interocular differences in refractive error and axial length correlated strongly in the two anisomyopic groups ($r^2 = 0.78$ white, $r^2 = 0.62$ Chinese; Fig. 2), this outcome being typical of findings in previous studies.[53–55] Together, these results imply that the documented anisomyopia results from differences in the vitreous chamber dimensions of related eyes.

Peripheral Refractions

Figure 3 shows for the right eyes of all subjects the peripheral refraction data for 30° eccentricity in the nasal visual field normalized to the foveal value. At this peripheral location, most eyes showed relative hyperopia, the mean in the white and Chinese groups being similar: +0.99 ± 1.54 D and +1.01 ± 0.79 D, respectively. Both groups also showed increases in relative hyperopia, with increasing myopia centrally.

Retinal Contours and Eye Shape

Figures 4A and 4B show the mean retinal coordinate data for the more and less myopic eyes of the white and Chinese anisomyopes, respectively, and Figures 4C and 4D show the equivalent plots for the white and Chinese isomyopes. While both anisomyopic groups showed a readily distinguishable outward (posterior) displacement (i.e., more enlarged in both axial and transverse dimensions) of the retinal surface of their more myopic eyes relative to that of their less myopic eyes, there were also ethnicity-related differences in the pattern of ocular shape change. Specifically, the eyes of whites exhibited a nasal–temporal asymmetry that was not evident in the Chinese eyes. In the white group, the outward displacement of the retinal surface of the more myopic eyes was largely confined to the nasal retinal sector. In contrast, the temporal contours of the same eyes tended to overlap. The difference between the Chinese and white groups was in the latter temporal sector that was expanded, like the nasal sector, in the more myopic Chinese eyes, rendering the changes overall more axially symmetric in the Chinese group.

Derived IDPS allowed statistical analysis of the effects of anisometropia and the interacting influence of ethnicity. As predicted, anisomyopes recorded greater IDPS values than isomyopes (Chinese: +14.51 ± 7.83 mm^2 vs. +1.16 ± 4.65 mm^2; white: +13.04 ± 5.67 vs. +1.83 ± 3.42 mm^2). The latter refractive group differences were highly significant (three-factor, split-plot ANOVA, $P < 0.0001$); however, ethnicity-based differences were not significant ($P = 0.58$). The second-order interaction between sector and refraction also was not significant, although the third-order interaction (ethnicity-sector-refraction) was significant ($P < 0.01$). The IDPS correlated only poorly with the degree of anisomyopia ($P = 0.13$). The latter data for individual subjects are plotted in Figure 5. Visual inspection of these data indicate differences between isomyopes and anisomyopes as expected, but little difference related to ethnicity.

The ratio of transverse chord diameter to axial length is shown plotted against central refractive error in all right eyes in Figure 6. If the posterior retinal surface expands uniformly in both axial and transverse directions during myopic growth, then this ratio will be stable and its correlation with refractive error weak. The mean ratio in the white subjects was 0.80 ±

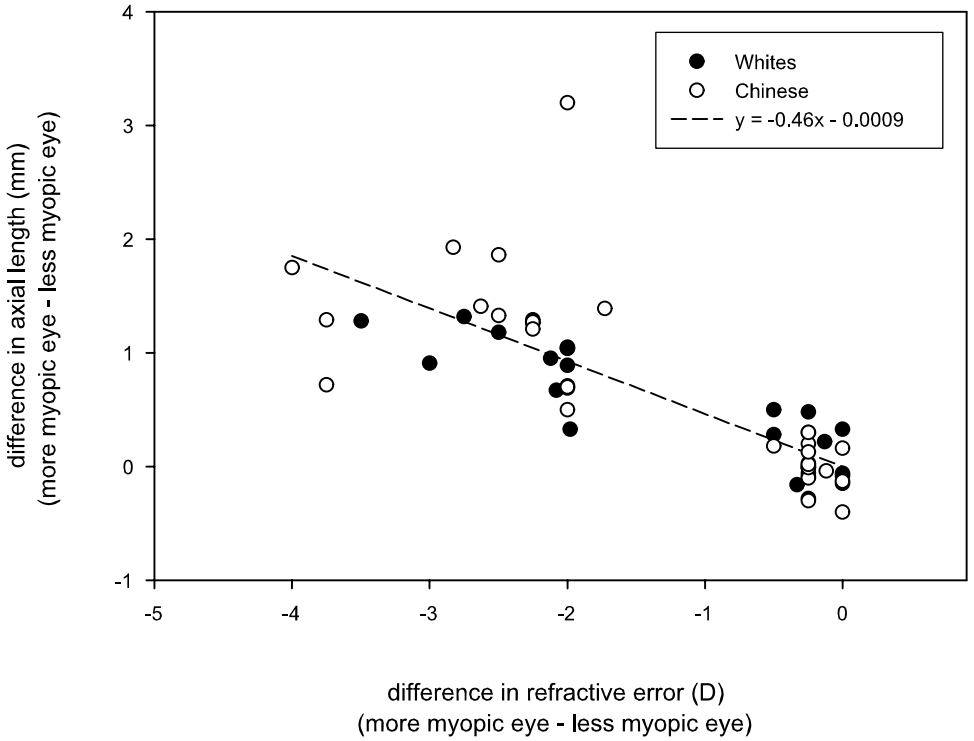

FIGURE 2. Interocular differences in mean spherical refractive error plotted against interocular differences in axial length for both white and Chinese aniso- and isomyopes.

0.05, and a similar mean value was found for the Chinese subjects, 0.82 ± 0.07, with no significant difference between the white and Chinese groups ($P = 0.4$). However, in the Chinese subjects this ratio decreased, with higher levels of myopia indicating a disproportionately greater axial elongation. In other words, the more myopic eyes had a more prolate shape to the posterior segment. The trend is significant in the Chinese subjects ($P < 0.05$) and remains significant ($P < 0.05$) if the criteria for inclusion is myopia of 0.50 D or more. No significant relationship was found for the white groups ($P = 0.3$). This difference suggests an ethnicity-related difference in the patterns of myopic growth, with Chinese eyes showing a more consistent axial bias.

Optic Disc Crescents in Anisomyopia

Shown in Figures 7A and 7B are individual ratios of optic disc crescent width to disc diameter plotted as a function of central refractive error for the right eyes of white and Chinese subjects. These parameters are significantly correlated in the case

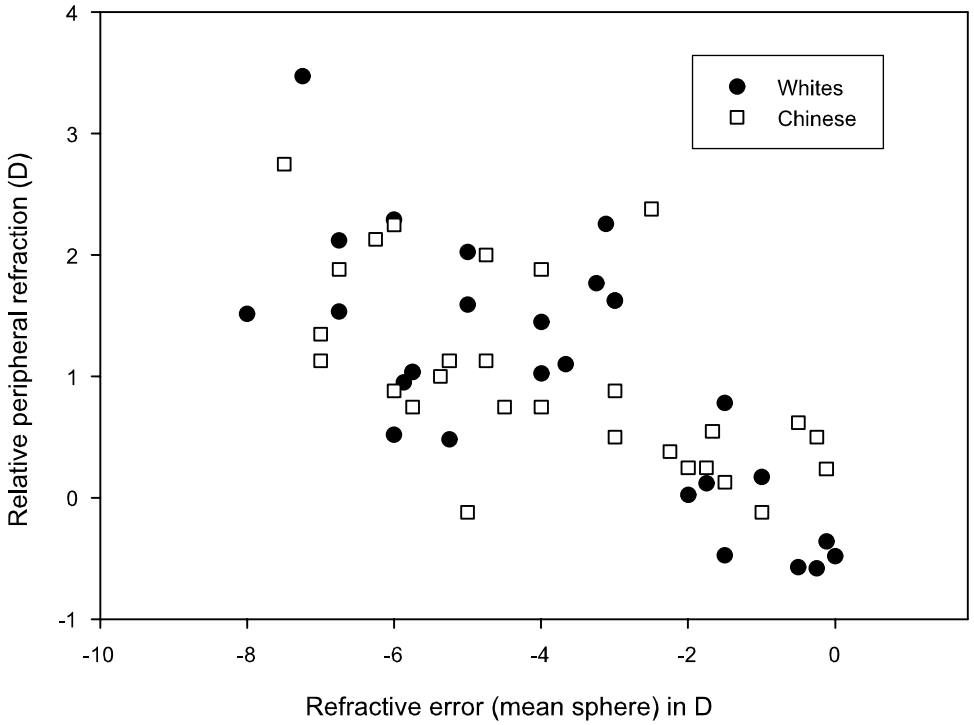

FIGURE 3. The relative peripheral refractive error shown as differences between the spherical equivalent refractions measured off-axis at 30° eccentricity in the nasal visual field and on-axis (at the fovea) in the right eyes of all subjects. Note that the peripheral refractions became more hyperopic with increasing on-axis myopia.

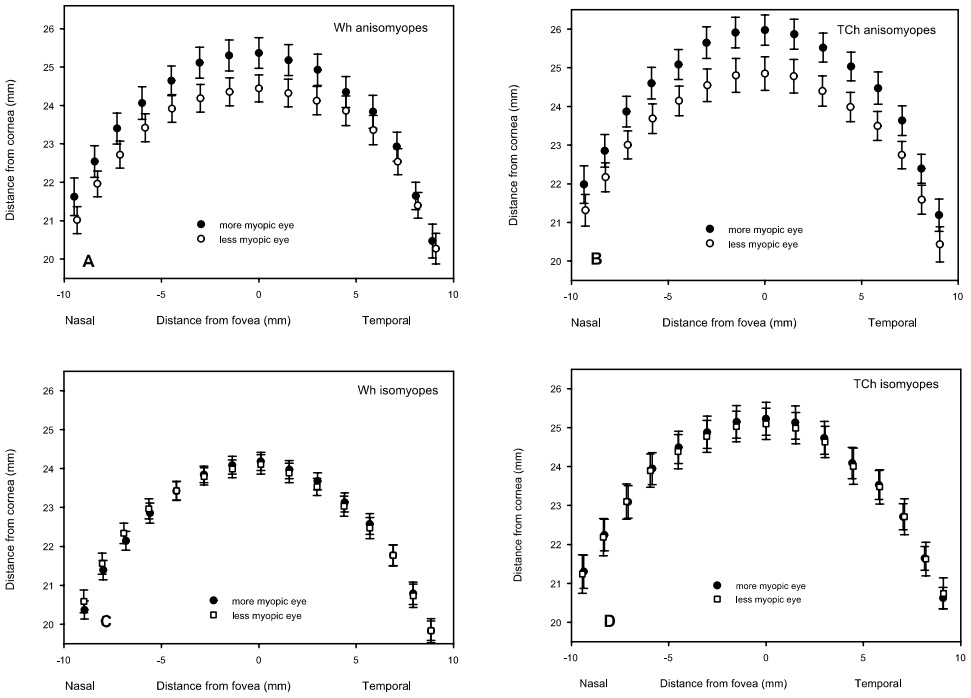

FIGURE 4. Retinal contours derived from refraction data measured out to 35° (~10 mm) nasally and temporally. Mean data with standard errors are shown for (**A**) anisomyopic and (**C**) isomyopic whites and (**B**) anisomyopic and (**D**) isomyopic Chinese. The contours of the more myopic eyes of both anisomyopic groups showed significant outward displacement that was greatest around the posterior pole and relatively greater at the nasal than the temporal retina in the white group.

of Chinese myopes ($r = -0.54$, $P < 0.01$) but not in the white myopes ($r = -0.21$, $P = 0.5$). Interocular differences (Figs. 7C, 7D) in the same parameters also correlated significantly in the Chinese anisomyopes ($r = -0.68$, $P < 0.01$) but not for the white anisomyopes ($r = -0.11$, $P = 0.6$). Together these data provide further evidence of ethnicity-related differences in growth patterns in myopia.

DISCUSSION

In this study, we combined peripheral refraction data with a new modeling technique to examine the ocular shape associated with the development of myopia to obtain further insight into the progression of myopia in humans. In past related studies, conjectures about shape changes have been based directly on these refraction data. The technique used derives retinal contours from peripheral refraction data. An important feature of the present study is the inclusion of anisomyopes, which offers the possibility of comparing eyes with different amounts of myopia under conditions that control for genetic variability. The mean interocular difference in eye size in these subjects was 1.39 mm, confirming the axial origin of the anisomyopia and also providing reasonable sensitivity to test for asymmetries in eye-shape changes involving the posterior

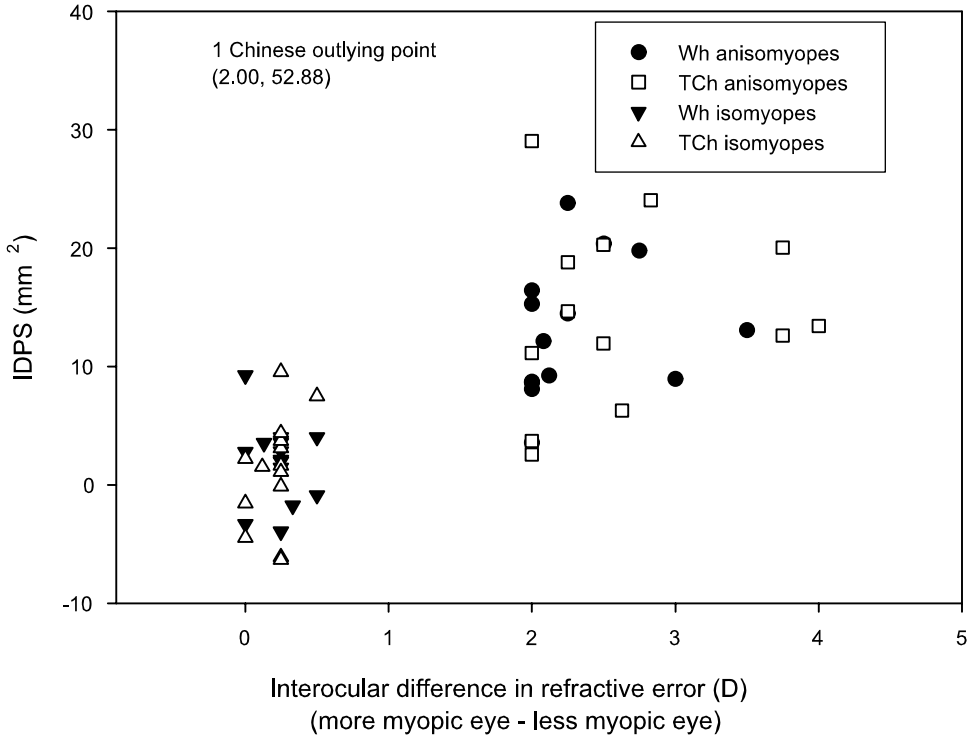

FIGURE 5. IDPS plotted against interocular difference in on-axis spherical equivalent refractive errors for both white and Chinese anisomyopes and isomyopes.

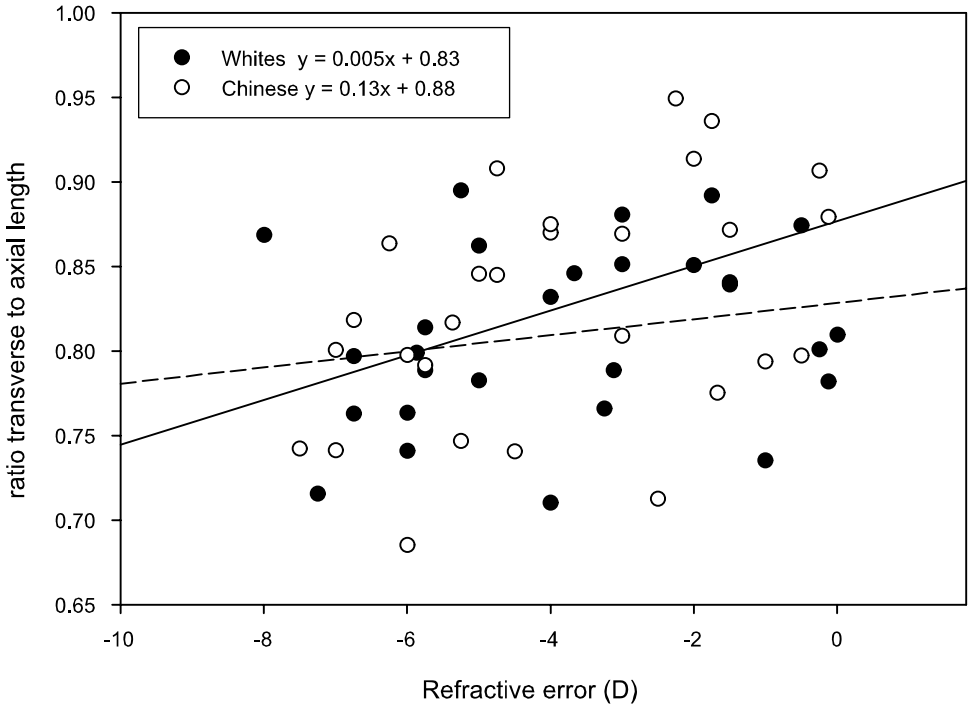

FIGURE 6. Ratio of transverse chord diameter to axial length plotted against spherical equivalent refractive errors in right eyes of all subjects. Regression lines are shown for the white (*dashed*) and Chinese (*solid*) subjects.

segment, where the axial differences arose. The posterior segment changes were coupled to ocular shape changes: There was a bias toward greater axial elongation in increasing myopia compared with lateral (equatorial) expansion that was most evident in Taiwanese-Chinese eyes, even though the two ethnic groups were matched in refractive error. In the Chinese ethnic group, signs of retinal stretching evident from the size of optic disc crescents also mirrored interocular differences in refractive error, with differences increasing with the level of anisometropia. White but not Taiwanese-Chinese anisomyopes exhibited a significant nasal-to-temporal asymmetry in the ocular shape changes, reflecting a relatively reduced expansion of the temporal retinal sector.

Structural Correlates of Myopia

No evidence was found to support a contribution from the anterior ocular segment to the anisomyopic error, although our measurements were limited to central corneal curvature and anterior chamber depth. Interocular differences in both parameters were not significant for either the white or the Chinese anisomyopes. There were also no apparent ethnic differences

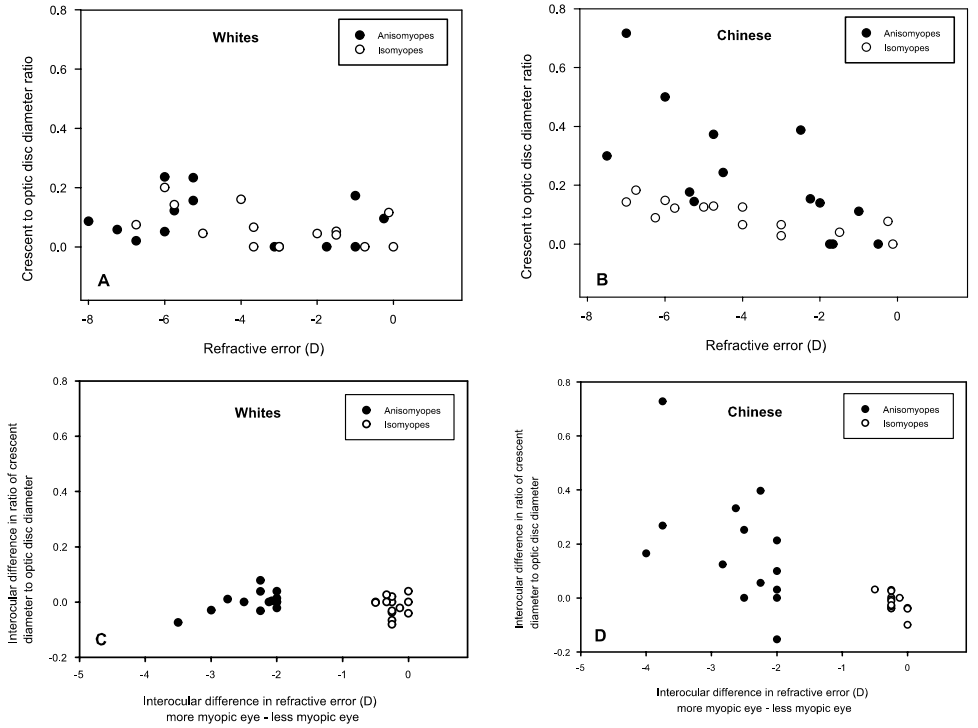

FIGURE 7. Ratio of crescent diameter to optic disc diameter against spherical equivalent refractive error for right eyes of (**A**) all white myopes and (**B**) all Chinese myopes. Interocular differences in ratio of crescent diameter to optic disc diameter plotted against interocular differences in spherical equivalent refractive errors for (**C**) white and (**D**) Chinese subjects. Only the Chinese anisomyopes show significant refractive error-dependent differences in this ratio—that is, an increase with increasing myopia.

in corneal curvature. In the first case, our findings are consistent with previous cross-sectional studies on myopes showing that the anterior segment of the eye does not account for the dioptric error in myopia,[56] although there are other reports of corneal steepening in highly myopic eyes.[57] The mean refractive errors of the more myopic eyes of our anisomyopes were under −6 D in both ethnic groups, possibly explaining why no related corneal curvature changes were found. However, our finding in relation to ethnic differences is also at odds with reports of Chinese eyes having steeper central corneal curvatures than eyes of whites. The latter discrepancy may reflect differences in instrumentation and thus the area of cornea sampled. Our different subject source, differences in age and refractive profiles, and the relatively small size of our sample may also be contributing factors.[58,59]

Although myopia is generally considered to be axial in nature, such conclusions are typically based on monocular data from individual subjects.[60–64] Results in both white and Chinese eyes from the present study agree with these earlier studies. Furthermore, whereas it does not necessarily follow that anisomyopia has the same structural correlates as myopia, generally, this was the finding of the present study (i.e., the more myopic eyes of anisomyopes were longer than their fellow eyes). The latter result is also consistent with previous studies.[40,65] Thus, anisomyopes can be considered in structural terms to be a genuine subset of myopia.

Peripheral Refraction

In most eyes, the most peripheral refractive errors were hyperopic relative to their central (on-axis) refractive errors. This finding is in agreement with previous studies (Love J, et al. *IOVS* 2000;41:ARVO Abstract 1592).[53,66] Higher on-axis myopia was also associated with higher relative hyperopia in the periphery, and this finding is consistent with those in the study by Seidemann et al.,[66] who also used young adult subjects. In this case, the peripheral refractive errors of myopes exhibited relatively more hyperopia compared with those of emmetropes.

Posterior Segment Shape

Whereas more myopic eyes exhibited proportionately greater overall enlargement of the vitreous chamber than did less myopic eyes, there was an axial bias to these changes, giving a more prolate shape in the more myopic eyes. This posterior segment shape change with myopia was evident in both white and Chinese eyes, although more exaggerated in the Chinese eyes, and is in agreement with conclusions based on peripheral refraction data for both children and adults in other recent related studies on eyes of whites (Love J, et al. *IOVS* 2000;41: ARVO Abstract S302).[53,66] However, it must also be acknowledged that shape changes described in this study and related studies are confined to a relatively small area spanning the posterior fovea 60° in the present study.

Although the present study made use of peripheral refraction data to determine ocular shape indirectly, the conclusion reached that myopic eyes take on prolate shapes is supported by other studies employing a variety of optical and nonoptical approaches. For example, in one study, enucleated highly myopic eyes are described to have prolate shapes, although these eyes tended also to be older eyes and frequently manifested staphylomas.[67] Myopic eyes are also reported to be have generally larger axial diameters compared with their transverse (equatorial) diameters in another very early study employing an x-ray technique to generate visual phosphenes.[68] However, this study included very high myopia, up to −16 D. More direct measurement of ocular shape is now possible both with modern optical methods such as laser Doppler interferometry (LDI),[69] optical low-coherence reflectometry (OLCR),[70] magnetic resonance imaging (MRI),[71] and computerized tomography (CT).[72] In one such study using OLCR[73] in children, myopic eyes were reported to have steeper retinas than did emmetropic and hyperopic eyes. However, these more direct optical methods have some of the same limitations of field size as the method used in the present study. MRI does not have the latter limitation, and a study using MRI[71] reports ocular dimensions along anteroposterior, equatorial, and vertical axes in myopes as well as emmetropes and hyperopes. In contrast to our finding, they report an overall equatorial bias to ocular shape in myopes as well as in two other refractive groups. Indeed, they found no differences between the ocular shapes between the three refractive groups. Differences in refractive error cannot explain this discrepancy between our studies, as the mean refractive error of their myopic group (−6.54 D) closely corresponds to the means for the more myopic eyes of our two anisomyopic groups (−5.57 and −5.24 D, respectively). This discrepancy may represent another example of an ethnic difference in myopic growth patterns, although ethnic details are not provided in the MRI study. Furthermore, in another study making use of CT scans to obtain ocular shape information in a large sample (255) of children in China,[72] the ratio of the anteroposterior axis to the horizontal transverse axis was found to vary with refractive error type consistent with the notion that myopes have more prolate eye shapes. Specifically, myopes had a ratio greater than unity, whereas the ratio in hyperopes was less than unity and that in emmetropes was approximately 1. An alternative explanation for the discrepancy in the findings of the MRI study compared with the other cited studies may lie in the technique itself. The accuracy of the MRI technique used in the latter study is not given although image resolution obtained with standard diagnostic MRI is 0.33 mm, corresponding to a dioptric value of approximately 1 D. In comparison, errors with the computational methods have been given to be less than ±0.37 D.[38]

The asymmetry in the changes to the posterior segment in myopic eyes noted here and elsewhere (axial changes greater than transverse changes) presumably reflects regional differences in scleral growth patterns and suggests that the axial and transverse dimensions of the eye are regulated differently. Scleral biochemical and histologic data from animal myopia studies also point to differential regulation, with the posterior sclera consistently exhibiting the greatest changes with induced myopia.[24,26,28,29]

A local retinal mechanism provides the most parsimonious solution to this problem, as it allows for regional control and there are data from both chick and tree shrew to support this proposal (using half diffusers and lenses[24,73–75] or using optic nerve section or blockade of retinal ganglion cell action potential[76–78]). Examples in nature that may reflect regional control include lower-field myopia, which has been reported in birds and amphibians (Love J, et al. *IOVS* 2000;41:ARVO Abstract S302).[53,66,79] In lower animals, it is speculated that this lower-field myopia serves to keep the ground in focus while the animals perform other visual functions. It may at the same time represent a regional growth response to the hyperopic defocus experienced early in life. Noting that near work has long been implicated in the development of myopia,[80] a stronger growth signal emanating from the central foveal region and acting on the underlying sclera would be consistent with the fovea's high acuity and thus greater sensitivity to defocus. However, Seidemann et al.[66] have argued from a biomechanical perspective that the visual experience and associated growth responses of more peripheral regions have most influence over the location of the posterior pole and others have gone farther to speculate that retinal steepness may provide a predictor of development of myopia.[70]

Mechanical factors involving the choroids, extraocular muscles, and sclera have also been the subject of speculation as determinants of ocular shape. In unrelated studies, Greene[81] used modeling to demonstrate that the posterior sclera of the eyes is subject to significant stress during contraction of the oblique extraocular muscles, and van Alphen[82] demonstrated in an in vitro study of semidissected eyes, that the choroid provides a greater restraining influence on equatorial expansion when IOP is increased. Observations from in vitro studies of human eyes also indicate that the posterior sclera is inherently more susceptible to stretching than the anterior sclera,[83,84] although this difference may reflect the differential effects of growth signals reaching the sclera. The relevance of the latter data may also be called into question because it relates to highly myopic eyes. Nonetheless, that the posterior sclera is more stretchable is also suggested by recently published indirect evidence of prolate shape changes induced by accommodation.[85] The latter report is of further interest as nearwork and, in particular, accommodation have long been linked to the development of myopia.[80]

Although both the white and Chinese groups showed ocular shape changes in the posterior section of the eye, there are differences in these shape changes related to ethnicity that were evident in the anisomyopia data. Compared with the eyes of whites, the Chinese eyes show both a greater amount of posterior shape change and also display greater overall axial symmetry to the shape changes (i.e., the shape in both the nasal and temporal meridians is concordant; Fig. 5). In eyes of whites, the expansion with increasing myopia was largely limited to the nasal sector. The reason for this ethnic-based difference is unclear. There may be inherent asymmetries in the scleras of eyes of whites that are not present in Chinese eyes that could result in nasal–temporal differences in the rates of expansion. For examples, thinner scleras expand elastically at a greater rate than thicker sclera when subjected to the same IOP.[86] An alternative choroidal explanation is also plausible. Animal studies report choroidal thinning along with scleral changes in myopic eyes (chick,[87] marmoset,[88] monkey,[89] tree shrew[90]), and there are also reports of choroidal thinning coupled to high myopia in humans.[32] Any asymmetry in such thinning is likely to be reflected in differences in the protection afforded to the sclera against the stretching influence of IOP.[82]

None of these explanations provides a ready reason for the nasal–temporal asymmetry in ocular shape noted in our white subjects. Drawing on an analogy with lower-field myopia, an environmental influence linked to near vision and the operation of emmetropization would predict the opposite pattern of asymmetry. An additional weakness of this explanation is that it offers no explanation for the ethnic differences reported herein.

Retinal Stretching

In high myopia, clinical signs of stretching are widely recognized as an increasingly tessellated appearance of the fundus and the presence of optic disc crescents.[42,43] Optic disc crescents occur when the pigmented choroid becomes detached from the margin of the optic disc. Previous studies have shown the prevalence of optic disc crescents to be correlated with both axial length and refractive error, being more prevalent in larger and/or highly myopic eyes.[43] An interesting aspect of the results found in this study is the high positive correlation between interocular differences in size of the optic disc crescents and myopia evident in the Chinese anisomyopia data but not in the equivalent white data. This ethnicity difference may reflect the greater overall ocular shape changes exhibited by Chinese eyes or alternatively suggest ultrastructural differences in the region surrounding of the optic nerve head or in the choroid more generally.

In summary, our study of anisomyopes served to provide further confirmatory evidence of the axial as opposed to refractive nature of myopia in humans. The increasingly prolate shape to the retinal contours that occurs in increasing myopia also points to a local axial (posterior) bias to the underlying scleral growth process. In developing potential treatments for the control of myopia, it is important to understand the origin of this bias. It is also important to understand why myopic Chinese eyes show a greater, more axially symmetric enlargement of the vitreous chamber than do eyes of whites, as this could be associated with their greater susceptibility to myopia.

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