# OCULAR BIOMETRIC INVESTIGATION OF ANISOMETROPIA

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## SUMMARY

Anisometropia exists whenever there is a difference in refractive error between a pair of eyes. Approximately 2.5% of the UK population have 2D or more anisometropia. The thesis investigates principally a subset of anisometropia, namely anisomyopia, which has an incidence of approximately 1%. Despite substantial research in the field of human myopia, studies to date have provided only limited insight into the mechanisms underlying its aetiology and development. It is known that a consistent feature of myopia is an increase in axial length which matches the dioptric error, such that a 1 mm increase in axial length produces 2 to 3D of myopia. Consequently the inter-eye discrepancy in anisomyopia is generally attributed to differences in length of the posterior vitreous chamber. The reasons as to how or why anisometropia develops remain unclear. The thesis aims to define further the biometric correlates in anisometropic eyes in order to provide a structural foundation for propositions concerning the development of ametropia.

Biometric data are presented for 40 anisometropes and 40 isometropic controls drawn from Caucasian and Chinese populations. Eye shape with respect to different refractive errors was investigated by calculating retinal contours for up to 80° of the posterior globe. The contours were derived from a series of biometric and peripheral refraction data using a specially designed computational method. An open-view infra-red optometer was used to measure both central and peripheral refractive error.

The principal finding was that the main structural correlate of myopia is an increase in axial rather than equatorial dimensions of the posterior globe. This finding has not been previously reported for *in vivo* work on humans. The computational method described in the thesis is a more accessible method for determination of eye shape than current imaging techniques such as magnetic resonance imaging or laser Doppler interferometry (LDI). Retinal contours derived from LDI and computation were shown to be closely matched.

Corneal topography revealed no differences in corneal characteristics in anisometropic eyes which supports the finding that anisometropia arises from differences in vitreous chamber depth.

The corollary to axial expansion in myopia, that is retinal stretch in central regions of the posterior pole, was investigated by measurement of disc-to-fovea distances (DFD) using a scanning laser ophthalmoscope. DFD was found to increase with increased myopia which demonstrates the primary contribution made by posterior central regions of the globe to axial expansion.

The ocular pulse volume and choroidal blood flow, measured with the Ocular Blood Flow Tonograph, were found to be reduced in myopia; the reductions were found to be significantly correlated with vitreous chamber depth. The thesis includes preliminary data on whether the relationship arises from the influx of a blood bolus into eyes of different posterior volumes or represents actual differences in choroidal blood flow.

Accommodation has often been implicated in the onset and development of myopia although its aetiological significance is equivocal. Following measurements of amplitude of accommodation, stimulus-evoked and tonic accommodation the thesis presents data which show that accommodation response is independent of the biometric differences that occur in anisomyopia. This is further confirmation that the ocular consequences of anisometropia are restricted to the posterior, rather than anterior, sections of the globe.

The results presented in this thesis show the utility of computed retinal contour and demonstrate that the structural correlate of myopia is axial rather than equatorial expansion of the vitreous chamber. The technique is suitable for large population studies and its relative simplicity makes it feasible for longitudinal studies on the development of ametropia in, for example, children.

**Key Words:** anisometropia, myopia, retinal contour, biometry, peripheral refraction

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## CONTENTS

## LIST OF TABLES

## LIST OF FIGURES

## LIST OF APPENDICES

# CHAPTER 1

## DEVELOPMENT OF THE EYE AND REFRACTIVE ERROR

### *Introduction*

To understand the developmental anomaly of anisometropia, the general points on ametropia need to be reviewed. Much of the literature discussed in this chapter concerns ametropia in incidence and developmental terms. The different theories on the aetiology of myopia have been reviewed as anisomyopia is generally assumed to be a subset of myopia.

### 1.1 *Refractive error*

Emmetropia in the human eye is dependent upon the optimum correlation between the radii of curvature of the cornea and the crystalline lens surfaces, the refractive indices of the ocular media, the anterior and vitreous chamber depths and the lens thickness. As the eye grows it must, in order to remain emmetropic, maintain a co-ordinated relationship between these components, so that the focal length of the optics is conjugate with the axial length of the eye. Any discrepancy between co-ordination of the ocular components results in a refractive error.

The refractive error of the eye is an anomaly of the refractive state in which, in the absence of accommodation, the image of objects at infinity is not formed on the retina. Myopia exists if the image falls in front of the retina and hypermetropia when the image falls behind the retina. The eye is deemed emmetropic when the image of an object at infinity falls on the retina. The refractive error is the resulting correlation of the ocular components (Sorsby, Benjamin and Sheridan (1961). Figure 1.1 shows the classical depiction of an emmetropic and myopic eye.



Figure 1.1 Two eyes of one individual superimposed: one emmetropic and the other -15D myopic, after Duke-Elder (1970).

### 1.1.1 *Distribution of refractive error*

Sorsby and various colleagues (Sorsby *et al.*, 1957; Sorsby, Benjamin and Sheridan,1961) have shown that the refractive error in an adult population does not follow a normal (Gaussian) distribution that is evident for other human parameters such as height (Goss *et al.*, 1990). Interestingly they found that the ocular components of corneal radius, anterior chamber depth and lens power all have a Gaussian distribution. The ocular component axial length, like that of refractive error, has a leptokurtic distribution (see figure 1.2).

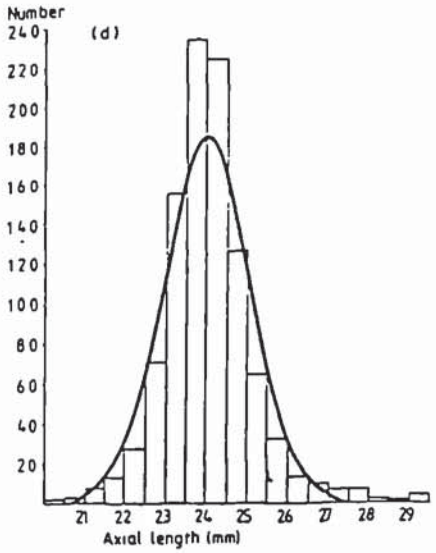



Figure 1.2 after McBrien and Barnes (1984).

At birth, infant eyes have been found to exhibit a normal distribution of refractive errors (see § 1.1.2). As the eye develops during childhood, there appears to be an active process which integrates the changing curvatures of the cornea and lens, and the thickness changes of the lens with the increasing axial length to eliminate or minimise refractive error. Evidence for a control mechanism in the development of refractive error has also come from the greater than expected frequency of emmetropia in an adult population. The process by which emmetropia is achieved and maintained, despite changes in all ocular components through growth, has been termed emmetropisation (McBrien and Barnes, 1984).

### 1.1.2 *Refractive error at birth*

*Cross-sectional studies*

The refractive error of the neonate was measured by Cook and Glasscock (1951) using retinoscopy under atropine cycloplegia. The results from 1000 infants revealed a wide distribution of refractive error at birth (see figure 1.3). Goldschmidt (1969) refracted 356 full-term infants under atropine cycloplegia. The findings agreed with those by Cook and Glasscock in that a large distribution of refractive errors was observed. The range extended from -9 to +8D, with 24% of the infants having myopia. The mean refractive error was +0.62D.

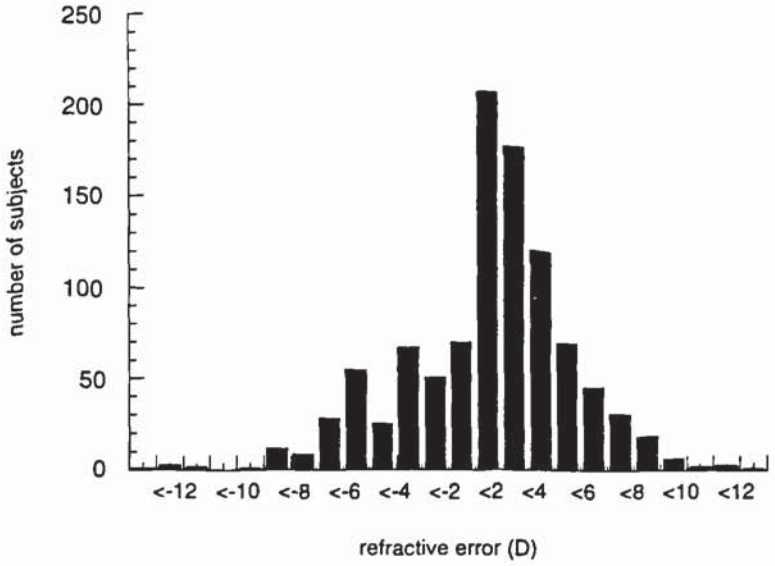



Figure 1.3 Distribution of refractive error in new-borns (drawn from data by Cook and Glasscock (1951)).

The difficulty in obtaining parental consent for infants undergoing cycloplegic refraction led Mohindra (1977) to develop a technique of near retinoscopy which does not require the use of a cycloplegic drug. The technique involves non-cycloplegic retinoscopy which is performed in a dark room while the infant watches the retinoscope light. Using this method they refracted 400 full-term infants between birth and 5 years of age. For infants aged 0 to 4 weeks they found a Gaussian distribution of refractive error with a range of -14 to +12D. This range narrowed to -3 to +4D by the age of 2.5 to 5 years. Grosvenor (1987) reported that Mohindra and Held's graphical results depicted a prevalence of myopia of about 50% at 0 to 4 weeks which decreased to 15% by 2.5 to 5 years. He suggested that the prevalence of myopia may however be artificially high owing to the lack of cycloplegia used.

*Longitudinal studies*

The refractive error of 210 newborn infants was measured by Thompson (1987) within their first week of life. She found that at birth almost 80% of the neonates had 1D or more hypermetropia. The average spherical equivalent refractive error was +2.75D (sd ±2.60). As in previous studies, a wide range of refractive errors was observed, ranging from -4.50 to +9.75D. The longitudinal study revealed that by the age of 12 months the refractive error distribution had decreased to a range of -2.25 to +4D.

Longitudinal change in refractive error in 113 infants during the first year of life was also investigated by Wood, Hodi and Morgan (1995). They found an increase in spherical equivalent refractive error from near emmetropia at 2 weeks of age to 2.6D of hypermetropia at 12 weeks. This finding is interesting in that it was observed in 75% of the infants and has not been recorded by previous researchers. A wide spread in the distribution of the differences in refractive error

between weeks 2 and 12 was found; for 95% confidence intervals the range of refractive error was +4.37 to -1.83DS. By 12 months of age this distribution of refractive error had decreased to become leptokurtic as seen in the adult population.

The rate of emmetropisation in human infancy was investigated by Saunders, Woodhouse and Westall (1995). They refracted 22 infants during the first 6 months of life and then again when the infants were between 12 and 17 months old using a modified version of Mohindra's near retinoscopy technique (see § 1.1.2). They found that the rate of emmetropisation occurred more rapidly with high refractive errors. Myopia was not observed in any infant.

These results are consistent with the finding of a non-Gaussian distribution of refractive error in an adult population and the theory of emmetropisation. Emmetropisation is thought to be a process whereby an active mechanism regulates the growth of one or more of the ocular parameters through feedback in response to the state of the retinal image (McBrien and Barnes, 1984).

## 1.2 *Growth of the eye*

The average axial ocular dimensions and corneal power have been documented by many researchers for both infants (see Table 1.1) and adults (see Table 1.2). The changes in axial length and corneal power that occur during the first year of life are responsible for the large decrease in ocular power; from 90D at birth to 75D at 12 months of age.

Table 1.1 A summary of previous literature on the axial dimensions of the infant eye, redrawn from Wood, Mutti and Zadnik (1996).

| *Author* | *n* | *Age* | *ACD (mm)* | *LT (mm)* | *AL (mm)* |
|---|---|---|---|---|---|
| Gernet (1964) | 36 (70 eyes) | 1-5 days | 2.9 | 3.4 | 17.1 |
| Luyckx (1966) | 52 (104 eyes) | 4-7 days | 2.6 | 3.7 | 17.6 |
| Larsen (1971a,b,d) | 80 (160 eyes) | 1-5 days | 2.4 | 4.0 | 16.6 |
| Fledelius (1992) | 25 | 37-43 weeks (gestational age) | 2.6 | 3.8 | 17.3 |

ACD, anterior chamber depth; LT, lens thickness; AL, axial length

Table 1.2. A summary of previous literature on the corneal and axial dimensions of the adult eye.

| *Author* | *n* | *Age (years)* | *CR (mm)* | *ACD (mm)* | *LP (D)* | *AL (mm)* |
|---|---|---|---|---|---|---|
| Tron (1934) | 275 | | 7.86* | 3.27 | 20.44 | 25.25 |
| Stenström (1948) | 1000 eyes | 20-35 | 7.78* | 3.68 | 17.35 | 24.00 |
| Sorsby *et al.* (1957) | 194 eyes | 20-50 | 7.72* | 3.47 | 20.71 | 23.94 |
| Fledelius (1982a,b) | 36 males | 18 | 7.95 | 4.03 | 3.53** | 24.19 |
| Fledelius (1982a,b) | 31 females | 18 | 7.82 | 3.89 | 3.58** | 23.74 |

CR, corneal radius; ACD, anterior chamber depth; AL, axial length; LP, lens power; *, calculated from corneal power using a refractive index of 1.336; **, lens thickness (mm).

*Axial length*

The eye grows rapidly in early childhood with an increase in axial length from approximately 18 mm at birth to 23 mm by the age of 3 (Sorsby, Benjamin and Sheridan, 1961). Based on visual optics principles, a 1 mm increase in axial length is known to correlate with a myopic shift of approximately 2 to 3D (Erickson, 1991). According to Sorsby and colleagues growth of the eye during infancy incurs a change in axial length of 5 mm. Theoretically this increase in axial length would induce 10 to 15D of myopia. This degree of myopic shift is not observed in normal development suggesting that a compensatory mechanism by the other ocular components exists, such as thinning of the crystalline lens and corneal flattening.

The average axial length of the adult eye is approximately 24 mm. This suggests that the eye grows only 1 mm from the age of 3 to around 13 years of age. It is interesting that this relatively slow phase of ocular growth coincides with the period of maximum body growth (Sorsby and Leary, 1970).

*Corneal curvature*

Research has indicated that the majority of corneal growth occurs pre-natally (Scammon and Wilmer, 1950) and nearly all post-natal growth has been found to occur within the first few years of life (Sorsby, Benjamin and Sheridan, 1961). The cornea of the neonate is generally assumed to be 3 to 5D steeper than that of a child (Sorsby, Benjamin and Sheridan, 1961). Wood, Mutti and Zadnik (1996) found that the mean corneal radius of curvature for 19 infants aged 3 to 18 months was 7.76 mm (43.5D), with a range from 7.35 to 8.46 mm. This finding is in conflict with other reports which have recorded steeper corneal powers in infants. Inagaki *et al.* (1985) found a mean corneal power of 7.05 mm (range 6.63 - 7.74 mm) on 22 infants with a gestational age of 37 - 43 weeks.

Cross-sectional results from a longitudinal study of myopia were investigated by Zadnik *et al.* (1993). They found that the corneal power varied non-systematically within 0.75D in 530 children between the ages of 6 and 12 years. Mean corneal power was 43.75D at 6 years of age and 43.91D at 12 years of age.

Fledelius (1982) carried out a longitudinal study of ophthalmic changes in 67 full-term subjects from age 10 to 18 years. He reported that there was no significant change in corneal radius over this period. The average value of corneal radius for the 36 male subjects was found to be 7.93 ± 0.27 mm for the 10 year olds and 7.95 ± 0.27 mm for the 18 year olds. At both ages the range of corneal radius was 7.5 to 8.5 mm.

The investigations suggest that adult values of corneal radius (Table 1.2) are reached by the age of 3 years and remain relatively stable throughout life.

*Anterior chamber depth*

Cross-sectional studies have shown that the anterior chamber depth (ACD) increases from birth to adolescence while the eye is growing. Larsen (1971a) measured ACD using ultrasound on 80 neonates and 846 children aged 6 months to 13 years. He reported that the ACD increased 0.9-

1.0 mm from birth to 1.5 years, 0.3-0.4 mm from the age of 1 to 7 years and almost 0.1 mm from 8 to 13 years. Previous studies have shown that the anterior chamber has normally reached its maximum depth by approximately 15 years of age (Larsen, 1971a; Sorsby, Benjamin and Sheridan, 1961; Sorsby and Leary 1970). Few changes have been recorded in the ACD from adolescence to about the age of 30 years. From the age of 30 years a monotonic decrease in ACD has been found to occur as crystalline lens fibres are continually added (Weale, 1982). Typical values for anterior chamber depth are 3 to 4 mm.

Goss and Erickson (1990) looked at the effects of changes in ACD on refractive error. They calculated these effects using a schematic eye. They stated that typical changes in ACD in the human eye are approximately 0.1 mm in magnitude. Changing the ACD by this amount in the schematic eye produced small changes in refractive error (<0.2D). They concluded that the ACD does not appear to be a major contributing factor in the development of refractive error.

*Crystalline lens*

The refractive index of the crystalline lens is thought to be heterogeneous, increasing monotonically from its surface to the nucleus. The gradient refractive index of the crystalline lens contributes much to the optical power of the eye. Unfortunately there is no knowledge of the refractive index distribution within the crystalline lens as no method exists to measure the refractive index directly *in vivo*. Physiological variation in the refractive indices of the gradient index crystalline lens is generally assumed to be negligible (Weale, 1982).

The decrease in ocular power that occurs during the first year of life cannot be accounted for by the changes in axial length and corneal curvature. The crystalline lens must therefore contribute to the decrease in overall power of the eye.

The majority of research into ocular biometry has used schematic models of the lens to predict the eye's optical properties. Wood, Mutti and Zadnik's (1996) study has disputed the schematic eye values for crystalline lens radii and equivalent refractive index for the infant eye. Wood, Mutti and Zadnik (1996) measured crystalline lens parameters in infants using a video-based keratophakometer. Results were obtained from 19 infants ranging in age from 3 to 18 months. The median refractive error was found to be +1.5D. Ultrasonography measurements were not obtained on the infants and axial ocular dimensions documented by Larsen (1971a, 1971b, 1971d) were used to calculate the crystalline lens radii. The median values for the anterior and posterior lens radii were 8.7 and 5.6 mm respectively. These values are much flatter than those of the Lotmar (1976) schematic infant eye. In order to produce a lens power to correlate with the flatter lens radii and the assumed values for axial dimensions, Wood, Mutti and Zadnik suggested that a greater equivalent refractive index was required. In his schematic eye Lotmar used a value of 1.43. The authors found a median equivalent refractive index of 1.49. They concluded that the majority of changes in lens power during infancy may be the result of a decrease in equivalent index.

The crystalline lens is known to continually grow throughout life. In adults it increases in thickness and the lens surfaces become steeper (Brown, 1974; Koretz *et al.*, 1989). Theoretically these changes would incur a myopic shift in the older eye. The fact that the majority of these ageing eyes do not become more myopic suggests a compensatory mechanism is involved. The adults who do develop myopia have a corresponding increase in axial length of the eye (Hemenger, Garner and Ooi, 1995; McBrien and Adams, 1997). Hemenger, Garner and Ooi (1995) studied age-related changes in the refractive index distribution of the human ocular lens. They calculated a gradient index parameter for 2 age groups using biometric data and a gradient index model of the lens. They found that the gradient index for the older age group (49 to 61 years) was flatter near the lens centre and steeper towards the lens surface than that for the younger age group (19 to 31 years). They concluded that in the crystalline lens, the changes in gradient index compensated for the changes in surface curvatures and thickness that occur with age.

### 1.3 *Development of ametropia*

Ametropia is generally believed to develop when there is a failure in the emmetropisation process. An anomaly in the correlation of the ocular components will result in a refractive error.
Sorsby *et al.* (1957) found that the majority of refractions within the range of +6 to -4D showed values for individual components that were within the range seen in emmetropia. They described these refractive errors as correlation ametropias as they believed that it was a failure in the correlation between the components that produced the ametropia. In high refractive errors, the value of one component was found to fall outside the emmetropic range. This anomalous component was usually axial length and the degree of ametropia was found to correspond to the anomaly in axial length. This group of refractive errors was termed component ametropias.

#### 1.3.1 *Myopia development*

Myopia develops when either an increased axial length is uncompensated by a decrease in corneal power or the crystalline lens power is too great for the cornea and axial length correlation. The dioptric error in myopia has been found to be consistently related to an increase in axial length or more specifically the vitreous chamber depth (Erickson, 1991).
In contrast to the large decrease in ocular power that occurs during the first year of life (see § 1.1.2), myopia usually develops during a period of relatively slower ocular growth (Larsen, 1971a, 1971b, 1971c and 1971d; Zadnik *et al.*, 1993); the prevalence of myopia increasing from about 2% as children enter school to approximately 15% by the age of 15 years (Blum, Bettman and Peters,1959).

### 1.3.2 *Prevalence of myopia*

Study of the prevalence of myopia reveals a wide variation in figures reported in the published literature. These variations arise from differences in population samples and from discrepancies in methodology. The prevalence of myopia has also been found to change significantly with age. Premature infants demonstrate a higher frequency of myopia (Dobson *et al.*, 1981) compared to full-term infants (see § 1.1.2). An increase in the incidence of myopia from the age of 5 to 20 years has been reported, with a subsequent decrease after the third decade of life (Laird, 1991; Phelps Brown, 1996).

The incidence of myopia has been found to vary between racial groups, but is approximately 25% of a general population (Fledelius, 1983). The frequency of myopia is particularly high in industrialised countries and rarely occurs in population groups of a lower academic level (Garner *et al.*, 1985). Even within a single racial or cultural group, the prevalence has been found to vary greatly with occupation (see table 1.3) (Goldschmidt, 1968); students having a greater prevalence of myopia than persons whose work entails little near vision activity. Zylbermann, Landau and Berson (1993) examined the influence of study habits on myopia in 870 genetically screened Jewish teenagers. They found a significantly higher prevalence and degree of myopia in a group of 139 Orthodox Jewish male students. Orthodox schooling consists of long periods of sustained near vision in conjunction with a swaying habit which is believed to aid concentration. A longitudinal study on the development of myopia in a specific occupational group (clinical microscopists) was investigated by McBrien and Adams (1997). They recorded that 45% of the 332 eyes in the study became myopic (≥0.37D) during the 2 year period.

Table 1.3 Comparison of myopia prevalence in six occupational categories by Goldschmidt (1968), redrawn from Curtin (1985).

| | | No. of myopes (%) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | No. of cases | Degree of myopia | | | | | | Total |
| Category* | examined | ≤1.50 | 1.75-2.5 | 2.75-6.5 | 6.75-9 | >9 | Total | >1.5 |
| 1 | 419 | 8.6 | 11.5 | 16.5 | 1.9 | 0.2 | 38.7 | 30.1 |
| 2 | 634 | 7.7 | 4.4 | 6.5 | 1.0 | — | 19.6 | 11.8 |
| 3 | 144 | 6.2 | 5.6 | 8.3 | — | — | 20.1 | 13.9 |
| 4 | 340 | 6.2 | 4.1 | 4.7 | 0.3 | — | 15.3 | 9.1 |
| 5 | 1301 | 4.2 | 1.9 | 2.2 | — | 0.2 | 8.5 | 4.3 |
| 6 | 753 | 2.8 | 1.3 | 1.5 | — | 0.1 | 5.7 | 2.9 |
| 7 | 60 | 5.0 | 5.0 | 3.3 | 1.7 | 1.7 | 16.7 | 11.7 |
| Total | 3651 | 5.3 | 3.7 | 4.9 | 0.4 | 0.2 | 14.5 | 9.2 |

*Category
1 Students
2 Clerks, shop assistants
3 Contractors, musicians, draftsmen, technicians, students of less demanding subjects such as art, agriculture, journalism
4 Electricians, photographers, metalsmiths, laboratory assistants, shoemakers, tailors, compositors
5 Bakers, carpenters, butchers, waiters, chefs, painters, bookbinders
6 Labourers, chauffeurs, farmers, postmen, seamen, fishermen
7 Miscellaneous occupations

### 1.3.2a *Prevalence variations in ethnic populations*

The variation in myopia among different populations has been shown in many studies (Borish, 1970; Curtin, 1985).

Laatikainen and Erkkila (1980) in a study on 411 Finnish school children reported a prevalence of myopia of 1.9% in children aged 7-8 years. This prevalence increased to 21.8% in 14 -15 year olds. Another Finnish study by Mäntyjärvi (1983) found that the prevalence of myopia in 9000 children increased from 0.8% in 7 year olds to 22.8% in 15 year olds.

Variations in prevalence of myopia have also been found within the Caucasian population. Comparisons between Jews and non-Jews have revealed a higher prevalence of myopia in the Jewish population (reviewed in Borish (1970)).

Epidemiological studies on remote populations in Arctic regions have revealed an inordinately high increase in myopia prevalence in the present generation compared to previous generations (Johnson, 1988).

An unusually high prevalence of myopia has been reported in Asian populations. In a study on 383 Hong Kong Chinese school children, Lam and Goh (1991) found the prevalence of myopia to increase from 30% at 6-7 years of age to 50% (girls) and 70% (boys) at 16-17 years of age. Other Chinese populations studies have recorded high prevalences of myopia. Lin *et al.* (1996)

reported that for Taiwanese children the prevalence of myopia was 11.8% at 6 years of age. This prevalence was found to increase to 55.5% by the age of 12 and to 75.9% at 15 years of age. Another study by Lin *et al.* (1996) examined the ocular components in 345 Taiwanese medical students, aged 18 - 21 years at the start of the study. They found that 92.8% of the students were myopic (≥ 0.25D). The students were examined 5 years later and were found to have a mean increase in degree of myopia -0.70 ±0.65D with a corresponding increase in axial length, the other ocular components were found to remain relatively unchanged. The prevalence of myopia increased from 92.8% to 95.8%.

The prevalence of myopia in Tibetan and Melanesian children have been found to be much lower than that in other Asian populations. In 400 Tibetan children aged 6 to 16 years, Garner *et al.* (1995) found a prevalence of myopia of 3.9%. The refractive error of 95.5% of the children was in the range -0.50 to +1.50D. The findings were similar in the Melanesian children (Garner *et al.*, 1985).

### 1.3.2 *Progression of myopia*

Most myopia is of juvenile onset (Grosvenor, 1987) and once it appears it increases steadily until the middle or late teens. Childhood myopia progression usually results from an increase in axial length of the eye. Sorsby and colleagues (1961 and 1970) and Larsen (1971d) suggested that axial length stops increasing by about 13 years of age. Both studies had limited data for subjects beyond 13 years of age and limited numbers of myopes. Goss and Winkler (1983) studied 299 patient records with a minimum of 4 refractions recorded between the ages of 6 and 24 years. The requisite for myopia was at least -0.50D. They found that the average age of cessation of myopia progression was 15.25 years in females and 16.5 years in males.

Goss and Cox (1985) noted that the average amount of myopia for a sample of optometry practice patients stabilised at about the same age as the median height from growth norms for US children. They postulated that myopia development and biochemical growth factors in the eye may be related to hormone levels affecting body growth.

*Longitudinal studies of myopia progression*

Cross-sectional studies are of little value in attempting to predict the rate of progression and degree of myopia in an individual. Longitudinal investigations provide better insight into these changes.

Fledelius (1981a) studied the changes in refraction between the ages of 10 and 18 years in a group of 137 Danes. He found that the myopes showed the most marked refractive change during adolescence. An increase in refraction in the direction of myopia occurred in 93% of the population. The median change was -1.75D in myopes, -0.70D in emmetropes and -0.50D in hypermetropes.

The most static eyes in the sample showed an axial elongation of 0.4-0.5 mm during adolescence. This was regarded as the basic growth that has to occur in relation to puberty. The

finding conflicts with Sorsby and colleagues (1961 and 1970) investigations who found no such increase in axial elongation due to puberty.

An initial study on myopia progression was made by Jensen (1991) on children aged 9-12 years and the follow-up was performed 8 years later (Jensen, 1995). Data was obtained on age of onset of myopia, degree of myopia, intraocular pressure, fundus changes, phoria status, nearpoint of convergence and accommodation in 124 children. Age of onset of myopia was the only parameter that correlated with the development of a high degree of myopia; an age of onset of less than 7 years resulted in a mean refractive error of -6.60D. The rate of myopia progression was not related to the age of onset of myopia.

## 1.4 *Aetiology of myopia*

Past literature on the aetiology of refractive errors have debated the nature versus nurture proposition with no definitive outcome. There is some evidence to support the belief that myopia under is genetic control (see § 1.4.1) but it is widely agreed that environmental factors may have some influence on myopia development (see § 1.4.2 and 1.4.3). Near work, diet and fibrile diseases have all been implicated in the development of myopia.

### 1.4.1 *Genetic influence*

The complexity of the eye and its refractive components is such that its growth is considered to be under elaborate genetic control. The code which guides the development of an organism is contained in the genes. A trait which requires both the presence of only one specific allele (heterozygous condition) to be expressed is referred to as dominant. A trait which requires both corresponding loci to have the same form of allele (homozygous condition) to be expressed is recessive. Monogenic inheritance of these sorts is usually studied by the examination of pedigrees. Through the use of pedigree studies, a particular trait can be followed through several family generation and an attempt can be made to assign a particular mode of inheritance. Multifactorial, or polygenic, inheritance differs from monogenic inheritance in that more than one gene is responsible for shaping characteristics (Grice *et al.*, 1996).

Evidence exists to suggest that genetics is a fundamental determinant of the refractive state. The distribution of myopia among races and ethnic groups, its prevalence in families and comparative studies in twins all support the idea that hereditary factors influence the development of ocular refraction (Curtin, 1985). Myopia has been classified as dominant, recessive, incomplete penetrance (i.e. not always expressed) (de Jong, Oostra and de Faber, 1993), X-linked (Haim, Fledelius and Skarsholm, 1988) and polygenic (Grice *et al.*, 1996).

*Twin Studies*

The relative effect of heredity and environment on refractive error can best be investigated using co-twin controls. Identical twins are single-ovum (monozygotic) individuals, the product of a single conception which splits in two at an early stage within the womb, thus leading to two individuals with identical genetic make-up. Binovular twins develop from two separately fertilised ova (dizygotic). Their genetic make-up tends only to be as similar as that of ordinary siblings. The general consensus is that if a significant amount of similarity, or concordance, exists between a pair of twins then this would indicate that genetic background is a major factor in determining ametropia (Chen, Cohen and Diamond, 1985).

Refractive error and its components in twins was assessed by Sorsby, Sheridan and Leary (1962). They reported that 70.5% of 78 monozygotic twins had less than 0.5D difference in refractive error. This similarity was found in only 30% of 40 dizygotic twins. In the monozygotic twins concordance between individual ocular components varied between 53 and 85%. Concordance between all ocular components was found in only 16.7% of these twins.

Chen, Cohen and Diamond (1985) compared genetic and environmental effects on the development of myopia in Chinese twin children. They examined 361 same-sex twin pairs aged between 10 and 15 years. Zygosity was determined by Mendelian traits. Studying and reading habit was assessed from the co-twins and their parents by questionnaires. They found that both genetic (zygosity) and environmental (reading and study habit) factors were significantly related to myopia development. A significant additive gene-environment interaction was found to correlate with myopia. The authors suggested that this finding indicates that the genetic expression may be modified by the environment.

### 1.4.2 *Accommodation*

Near work has been implicated in the aetiology of myopia (McBrien and Millodot, 1986). Various researchers have attempted to correlate accommodation differences with refractive error.

Myopes have been shown to demonstrate poorer than normal accommodation (McBrien and Millodot, 1986) especially in childhood (Gwiazda *et al.*, 1993). McBrien and Millodot (1986) reported a reduced mean gradient for the accommodative stimulus response function in late-onset myopes compared to emmetropes. Yet it is unclear whether the accommodative lag in myopes is the cause or the result of their refractive error. However Gwiazda *et al.* (1993) suggested that poor accommodation appears to accompany the development of myopia rather than precede it. It is questionable whether the small magnitude of the observed differences in accommodative response in myopes are related to the development of axial myopia.

### 1.4.3 *Risk factors for development of myopia*

The factors associated with the higher prevalence of myopia that is evident in Chinese populations (see § 1.3.2a) are unknown. One common feature to Hong Kong and Taiwan is the intensive education system. This system may require more near work activity which has often

been implicated as a high risk environmental factor for the development of myopia (see § 1.4.2). Most of the recent research in myopia has been concerned with the risk factors in the prediction for myopia development.

*Ratio of axial length to corneal radius*

The relationship between axial length and corneal radius (AL/CR ratio) has been suggested to be an index to indicate the extent to which axial elongation has occurred in a specific eye (Grosvenor, 1988). Grosvenor stated, based on data from Gullstrand's exact schematic eye, that the AL/CR ratio for an emmetropic eye was approximately 3.0. Therefore, for a myopic eye the AL/CR ratio would be expected to be greater than 3.0 and less than 3.0 for a hyperopic eye. Goss and Jackson (1993) in a longitudinal study on 8 to 12 year old children who were all emmetropic at the start of the investigation, examined the change in Al/CR ratio over a 3 year period. They found that those children who became myopic had an initial Al/CR ratio of greater than 3.0 whereas few children with an AL/CR ratio less than 3.0 became myopic.

*Clinical findings before the onset of myopia*

A series of investigations by Goss and Jackson (1995) have assessed discrepancies in clinical findings before the onset of myopia. A group of 87 emmetropic schoolchildren were examined at 6 monthly intervals for a period of 3 years. They investigated AL/CR ratio, zone of clear binocular vision, heterophoria and parental history of myopia. An AL/CR ratio of greater than 3.0 was found in the children who became myopic (29 children) compared to those who remained emmetropic (58 children) (Goss and Jackson, 1995). A more convergent zone of clear single binocular vision was found in the children who became myopic than in those who remained emmetropic (Goss and Jackson, 1996). They also found a lower value of positive relative accommodation in the became myopic group. Investigations into heterophoria revealed that an eso (convergent) shift in the near phoria was associated with the onset of myopia(Goss and Jackson, 1996b). However, the specificity of a near phoria as a risk factor for myopia development was not as high as parameters such as AL/CR ratio and positive relative convergence.

*Family history of myopia*

Family history of myopia has often been suggested as a risk factor for the development of myopia. The relationship between parental history of myopia and onset of myopia was assessed in a group of 87 initially emmetropic schoolchildren (Goss and Jackson, 1996c). The children were examined in 6 monthly intervals for a period of 3 years. They found a significant association between parental history and onset of myopia, the risk was greater if both parents were myopic than if one parent was myopic.

Three risk factors for myopia development a) refractive error at school entry, b) refractive error in infancy, c) parental history of myopia were investigated by Mutti and Zadnik (1995). They re-analysed data from Hirsch (1964), Gwiazda *et al.* (1993), and new data from the Orinda

longitudinal study of myopia (Zadnik *et al.*, 1993). They found that the best predictor for myopia was a refractive error that was more myopic than +0.50D at school entry (probability 0.53 for a prevalence of myopia of 15%). The predictive powers of infant refractive error and parental history of myopia were found to be lower (0.20 - 0.28).

### 1.4.4 *Animal models of myopia*

#### 1.4.4a *Experimental myopia in animals*

A diverse number of animal studies have succeeded in inducing experimental myopia by monocular deprivation using techniques such as lid-suture, corneal opacification and opaque goggles. It is from these animal models of anisomyopia that the process of emmetropisation can be studied. Animal studies were mainly introduced by Wiesel and Raviola (1977) who discovered that a degraded retinal image produced exaggerated ocular axial elongation in monkeys. Control studies, using dark-reared lid-sutured monkeys, have shown that form-deprivation rather than local effects of temperature or pressure is responsible for the development of myopia. Myopia has since been produced in several species by form-deprivation, these include the tree shrew (e.g. (McKanna and Casagrande, 1981; Norton and McBrien, 1992)), monkey (e.g. (Wallman and McFaddan, 1995)), marmoset (e.g. (Troilo, 1996)), cat (e.g. (Wilson and Sherman, 1977)) and chick (e.g. (Wildsoet and Wallman, 1995)). In humans, chronic degradation of the visual image before 3 years of age has led to axial myopia (Curtin, 1985). The myopia produced is expressed mainly as an increase in vitreous chamber depth and appears to be independent of species.

Chickens are the most frequently studied animal model as they have rapid eye growth and good optical quality. They can develop up to approximately 20D of axial myopia in 1 week and can compensate imposed defocus of 4D in 3 days. Mammalian models of myopia, for example tree shrews and monkeys, have an advantage over the avian models as they have a closer evolutionary relationship to humans, however, they have a longer developmental time and the degree of experimental myopia produced is less (Norton and McBrien, 1992).

Animal models have provided evidence that eye growth is, in part, visually controlled by a mechanism that depends upon local analysis of a retinal image without communication to the brain. Optic nerve section and form-deprivation have produced myopia in monkeys and chicks (Raviola and Wiesel, 1985; Troilo, Gottlieb and Wallman, 1987). Whereas, the control experiment, optic nerve section without visual deprivation resulted in a small hyperopic eye in the chick. Wallman *et al.* (1987) applied white translucent occluders selectively to either the nasal or temporal retina of developing chicks and found that excessive ocular growth occurred in the part of the eye corresponding to the deprived field.

The growing eye of a chick can compensate for imposed refractive error by readjusting axial eye growth rates when normal vision is restored (Wallman *et al.*, 1981). However, when the lids of

macaque monkeys are opened after a period of lid fusion, before completion of eye growth, the inter-eye difference in refractive error remains stable (Wiesel and Raviola, 1977).

Various researchers have shown that it is possible to manipulate the early refractive development of chick eyes by defocusing the retinal image with both concave and convex lenses (e.g. (Schaeffel, Glasser and Howland, 1988)). The chick eye was found to respond accurately to imposed defocus of between -10 and +15D by developing a refractive error of the same magnitude and sign as the imposed lens. Astigmatic defocus was produced in chick eyes by Irving, Callender and Sivak (1995). Corneal power changed selectively in response to the defocusing lens. They found that the axis of the induced astigmatism coincided with the axis of the inducing lens, however the amount of astigmatism produced was always less than that of the inducing lens. Variable results in the compensation for refractive defocus were produced with slit apertures. Decreased aperture size and non-circular aperture shape resulted in increasing inaccuracy in response to the imposed defocus. Irving, Callender and Sivak (1995) suggested that these results indicated that deprivation myopia and defocus induced refractive errors are different processes.

Wildsoet and Wallman (1995) investigated choroidal and scleral mechanisms of compensation to lens-induced refractive errors in chicks. They found that both the vitreous chamber depth and choroidal thickness altered to compensate for the imposed spectacle lens defocus and both reversed their changes in growth once the defocusing lenses were removed. Optic nerve section was, in contrast to results from form-deprivation myopia experiments, found to prevent myopia in response to negative lenses. They suggested that in order to compensate for hyperopia communication via the central nervous system is required.

A recent paper by Hung *et al.* (1995) has raised controversial issues in the management of refractive errors in young children. Hung *et al.* fitted infant monkeys with low powered spectacle lenses (-6 to +6D) in front of one eye. All the lens treated monkeys (n=10) developed anisometropia of at least 1D. They also monitored, for each monkey, which eye was used for focusing and they found that the monkeys used their lens-covered eye for vision when positive lenses were fitted but used their uncovered eye when negative lenses were worn. By using this fixation strategy the monkey exerts the minimum amount of accommodative effort to obtain a clear retinal image. The non-fixating eye is rendered hyperopic for near distances. With positive lenses, the lens-covered eye was found to have a reduction in the rate of vitreous chamber elongation and an increase in hyperopia. Whereas with negative lenses, the lens covered eye showed a relative increase in rate of axial growth and a corresponding myopic refractive error. On removal of the lenses, Hung *et al.* found a recovery response to reduce the induced anisometropia. They concluded that monkeys have a monocular emmetropisation mechanism which allows compensation for interocular differences in refractive error. They argued that full correction of refractive errors in very young children may impede the normal emmetropisation mechanism.

These findings support Medina's (1987) model of emmetropisation. Medina assumed a feedback control mechanism which implied that correcting myopia increased its progression. However, no data was presented to support the prediction.

### 1.4.4b *Pharmacological alterations in animal models of myopia*

The effect of form-deprivation on ocular growth has shown axial length to be the main structural correlate which is independent of species. However, the underlying retinal mechanisms and biochemical factors involved in form-deprivation myopia are not as yet understood. Various retinal substances that have been implicated in the development of form-deprivation myopia include acetylcholine, dopamine, basic fibroblast growth factor and vasoactive intestinal peptide (VIP). Pharmacological studies in animal models of myopia have attempted to modify eye growth by using various agonists and antagonists of these substances.

The retinal peptide VIP has been found in both the central and peripheral nervous systems and has been localised to a subset of amacrine cells in the chick retina (Fukuda *et al.*, 1981). Raviola *et al.* (1991) found an increase in the level of retinal immunoreactive VIP in the form-deprived eyes of neonatal rhesus macaques. Both the lid-sutured and contralateral eyes had the same distribution of amacrine cells thus suggesting that deprivation of visual input may cause an increase in VIP synthesis.

Pickett Seltner and Stell (1995) investigated the effect of VIP in the development of form-deprivation myopia in the chick. They found that daily injections of VIP reduced but did not eliminate form-deprivation myopia. VIP is known to be labile *in vivo* and some hydrolysed fragments have been found to act as VIP antagonists. Pickett Seltner and Stell found that a more stable form of VIP had no effect on the development of myopia whereas two VIP antagonists eliminated the myopia but with different efficacies. They concluded that VIP may be involved with both normal ocular development and in the development of myopia.

Another retinal neuropeptide, substance P, has been investigated by Stone *et al.* (1990). They found no difference in immunochemical reactivity in sutured and non-sutured eyes of monkeys.

The effect of fibroblast growth factors (bFGF) on the growth of the chick eye was studied by Rohrer *et al.* (1993). They injected bFGF into monocularly occluded chick eyes and discovered that excessive eye growth was attenuated in the occluded eyes in a dose-dependent manner. bFGF was found to have no effect on the unoccluded eyes. They suggested that bFGF may be involved in the pathogenesis of myopia by modulating the action of scleral growth regulators.

The work of Stone *et al.* (1990) investigated postnatal control of avian ocular growth in respect to dopaminergic mechanisms. They found that in neonatal chicks, intraocular injections of the dopamine agonist apomorphine reduced the expected axial elongation in lid-sutured eyes in a dose-dependent manner. They also discovered that apomorphine was geometrically selective in that the exaggerated equatorial growth that occurs in visual deprivation was not reduced by application of the drug. From this result they suggested that the axial and equatorial dimensions of the eye are regulated independently in chicks. Rohrer, Spira and Stell (1993) found similar

results in apomorphine and form-deprivation experiments in chicks. They also deduced from intravitreal versus subconjunctival administrations of apomorphine, that the intraocular site at which the form-deprivation myopia is blocked by the drug, resided in the retina or the pigment epithelium, but not the sclera.

Iuvone *et al.* (1989) examined the levels of retinal dopamine and its metabolite 3,4-dihydroxyphenylacetic acid (DOPAC) in monkeys as a function of age and monocular deprivation. They found that the level of dopamine increases in the first month of life but thereafter remained relatively stable. Light deprivation by an opaque contact lens reduced levels of dopamine and DOPAC relative to the unoccluded contralateral eye.

Visual degradation has been produced in chicks by both translucent occluders and by spectacle lenses. The response to the degradation of the retinal image is known to vary with method. Translucent occluders have produced exaggerated axial myopia whereas the response to spectacle lenses has depended on whether the lens was positive or negative. Schaeffel *et al.* (1994) investigated the response of the dopaminergic mechanisms in both lens-induced and deprivation myopia. They used 6-hydroxy dopamine (6-OHDA) which is known to inhibit dopaminergic pathways in the retina. They found that 6-OHDA suppressed the development of deprivation myopia whereas the same dose had no effect on the lens-induced myopia. They suggested that deprivation myopia and lens-induced myopia may occur due to different mechanisms.

Acetylcholine is another known retinal neurotransmitter and studies have investigated the interaction of muscarinic agents in experimental myopia. Stone, Lin and Laties (1991) administered both selective and non-selective muscarinic drugs to unilateral form-deprived chicks. They found that the non-selective antagonist atropine and the M1 selective antagonist pirenzepine both attenuated the axial elongation but did not prevent the increase in equatorial diameter that occurs with form-deprivation myopia. Research has shown that M1 muscarinic receptors are not found on the ciliary muscles and iris in mammals (Honkanen, Howard and Abel-Latif, 1990). They suggested that these results provide evidence for developing future research with selective M1 muscarinic antagonists as the debilitating side effects of pupil dilation and cycloplegia that occur with non-selective muscarinic antagonists will be avoided. Leech, Cottriall and McBrien (1995) have shown that form-deprivation myopia in chicks can be prevented with daily intravitreal injections of the M1 antagonist pirenzepine.

These pharmacological studies on chicks and monkeys have demonstrated that alterations in neurochemical transmitters have been induced by visual deprivation. Whether these biochemical alterations also occur in human myopia has yet to be investigated.

### 1.4.5 *Altered visual input in humans*

Human correlates of the high myopia produced in animals by form-deprivation are believed to exist in humans with eyelid and other ocular anomalies. The retinal image degradation, in early

infancy, caused by lid ptosis (O'Leary And Millodot, 1979), congenital cataracts (von Noorden and Lewis, 1987) and neonatal eyelid closure (Hoyt *et al.*, 1981) have been associated with high refractive errors, and in particular myopia. This form-deprivation myopia has been found to correlate with axial elongation of the eye.

Gee and Tabbara (1988) assessed the effect of form-deprivation in humans by measuring axial length with ultrasonography in patients with corneal opacification. The study comprised 79 patients, 39 with unilateral or bilateral corneal scars and 40 control patients. They found a statistically significant difference in axial lengths of eyes with bilateral corneal scars compared with eyes with normal corneas. The eyes with corneal opacifications had longer axial lengths. In patients with unilateral corneal scars, the eye with the scar was longer than the contralateral eye. A significant correlation with age of onset of corneal opacification and axial length was also noted. Eyes with corneal scars that occurred before 7 years of age were found to be longer than eyes where the onset of opacification was later. They concluded that the results are consistent with those from form-deprivation animal experiments where an altered visual input in a young animal leads to an increase in axial length and the development of myopia. This work is in agreement with a study by Rabin, van Sluyters and Malach (1981) who compared the incidence of myopia in 108 humans subjected to various ocular anomalies in early life. Both monocular and binocular cases of visual deprivation were examined. Causes of deprivation included congenital cataracts, retrolental fibroplasia, congenital optic atrophy, and juvenile macular dystrophy. They found that the mean refractive error of aphakic subjects (+9.30D) had shifted towards myopia compared to the mean refractive error of control subjects who were aphakic as a result of senile cataract (+11.49D). In the bilateral cases of deprivation, the prevalence of myopia was significantly greater than that for a general population. The 7 subjects with monocular deprivation were all anisomyopic with the deprived eye the more myopic eye.

Calossi (1994) found that an increase in axial length occurred in response to deprivation by infantile traumatic cataract. He assessed 13 patients who had suffered unilateral traumatic cataract between the ages of 2 and 16 years. In all patients he found that the affected eye had a greater axial length than the uninjured eye, this difference in axial length was greater in patients who had suffered an injury at an earlier age.

The association between axial length, refractive error and optic nerve hypoplasia was investigated by Weiss and Ross (1992). They examined 14 patients with unilateral optic nerve hypoplasia and found 9 of them to have an interocular difference in refractive error of 1D or more, the affected eye being the more myopic. They also found that 9 of 11 patients with asymmetric bilateral optic nerve hypoplasia had more myopia in the more affected eye.

Merriam, Ellis and Helveston (1980) assessed the correlation between congenital blepharoptosis, anisometropia and amblyopia in 65 patients. Anisometropia of 1.25D or more in sphere or 1.00D or more cylinder was present in 8 patients with unilateral blepharoptosis. In only 3 of these 8 cases, the deprived eye was the more myopic eye.

The relationship between disease-associated vision deprivation and spherical refractive errors in 256 children aged 1-16 years was investigated by Nathan *et al.* (1985). A control group of 1023 age-matched schoolchildren was also assessed. They found that diseases associated with the development of myopia correlated with peripheral or peripheral and central visual impairment, such as nystagmus, aniridia, retinopathies and optic atrophy. Diseases that affected foveal vision, for example albinism and maculopathies, resulted in mild hypermetropia (+0.80D). They concluded that the study showed emmetropia to be dependent on normal retinal images in human infants. If visual deprivation occurred before the age of 8 or 9 years then ametropia developed. Interestingly they found that hypermetropia was produced if the onset of visual impairment was in the first three years of life but was not congenital whereas myopia developed if the deprivation occurred at other ages except in cases where the macular function was specifically affected.

Other studies on visual deprivation and the development of myopia in humans have found conflicting results. Von Noorden and Lewis (1987) assessed the biometry measurements in 10 unilateral cataract patients and 2 complete unilateral ptosis patients. The axial length of the eye with the cataract was found to be longer than the contralateral eye in 7 of the 10 patients. In the 2 patients with unilateral ptosis, the axial length of the deprived eye was shorter than that of the contralateral eye. They concluded that visual deprivation in humans results in more variable responses than in animals.where the deprivation leads to axial elongation and myopia.

Miller-Meeks, Bennett and Keech (1980) investigated anisomyopia development secondary to vitreous haemorrhage in 11 children. Of the 11 children, 7 acquired vitreous haemorrhage before the age of 1 and 6 years of these children had anisomyopia with the affected eye being the more myopic. The range of anisomyopia was 1.37 to 10.75D. The degree of myopia was found to correlate with the age of onset and duration of the vitreous haemorrhage. The other 4 cases of vitreous haemorrhage occurred between the ages of 2 and 12 years and none of these children had anisomyopia.

Till (1983) examined 31 patients with unilateral ptosis aged 18 months to 10 years to determine the presence of any anisometropia. She found 18 (58%) of the 31 cases to have anisometropia of 1D or more, with the ptosed eye being the more ametropic. However, in only 6 of these 18 cases was the ptosed eye more myopic than the contralateral eye.

*Effect of spectacles on human visual development*

Ingram *et al.* (1991) investigated the process of emmetropisation and its relationship to squint and amblyopia in a spectacle-treated group and a non-treated group of children. Data was obtained from 287 children aged 6 months at the start of the investigation who had +4D or more hypermetropia in one or more meridia of either eye. The children were randomly allocated to either the no treatment group or to the group that were prescribed spectacles at 6 months of age. There were 143 children in the no treatment group and 144 in the spectacle-treated group. They noted that prescribing spectacles at 6 months of age may have impeded the process of

emmetropisation, although the results were not significant. Their criteria deemed emmetropisation had occurred if the refractive error reduced to +3.50D or less. They sub-divided the spectacle-treated group into those children who wore their spectacles continuously and those with poor compliance. They found that the hypermetropic error of the children who wore their spectacles continuously was significantly less likely to reduce than hypermetropia in the other two groups. The results of this study are interesting as they suggest that correcting refractive errors in children as young as 6 months of age may disrupt the normal process of emmetropisation.

### 1.4.6 *Application of animal models of myopia to human myopia*

Various aspects of human myopia have been studied and evidence for both a genetic-based theory of myopia development and an environmental influenced theory has been produced. The limitations of human myopia research, for example difficulties in completing longitudinal studies and ethical problems, and the discovery of visual deprivation-induced myopia in animals has led to the majority of myopia research being conducted on the animal model of myopia (Wildsoet, in press). Parallels have been drawn between the induced myopia in animals with human myopia. Whether the animal models of myopia correlate with human myopia is questionable. Zadnik and Mutti (1995) have reviewed the animal myopia literature with respect to its relationship to human myopia. They reported that the myopia induced in animals by deprivation is of a much greater magnitude than the myopia that develops in children. They also stated that the time period over which myopia was induced in animals differed from developmental myopia in children. They concluded that if the assumption that eye growth is modulated by similar biochemical factors in both animals and humans holds then the results of pharmacological studies on animal eye growth may be applicable to human myopia development.

Saunders, Woodhouse and Westall (1995) examined the rate of emmetropisation in 22 human infants. Refractive error was measured during the first 6 months of life and then again between 12 and 17 months of age. They found that the rate of emmetropisation was greater in those eyes with the greater initial refractive errors. They suggested that the results confirmed that the animal models of myopia are appropriate models to apply to human myopia development, as rate of recovery of induced ametropia in animals is also related to the magnitude of the induced refractive error.

However, there does not appear to be a correlation of the animal model of myopia with the occurrence of late onset myopia which develops in an otherwise healthy eye.

### 1.4.7 *Attempts to arrest the progression of myopia*

Many techniques have been advocated to reduce the rate of increase of myopia. The techniques include wearing bifocals (Goss and Grosvenor, 1990) and daily instillation of cycloplegics (Gimbel, 1973). These treatments are all based on the theory that prolonged accommodation results in

myopia development. Other treatments include wearing contact lenses (Winkler and Kame, 1995), daily instillation of antiglaucoma agents (Jensen, 1991), and visual training (Gilmartin, 1991).

Although the results from these and numerous other studies suggest that there does not appear to be any method by which the rate of myopia progression may be arrested or reduced, these findings are not definitive.

### 1.5 *Summary*

Myopia is a common condition in Industrialised Western society and in Asian populations. The prevalence of myopia in the UK is approximately 25% for 18 year-old students and rises to approximately 70% for Chinese 18 year-old students.

The main structural correlate of myopia is an increase in axial length of the posterior vitreous chamber that matches approximately the dioptric error.

Various factors have been implicated in the development of myopia, such as accommodation, increased IOP, a genetic predisposition and nutrition.

Animal models of myopia have been studied to provide some insight into myopia development. Results from these animal studies of refractive development suggest that an active process of emmetropisation is capable of detecting and compensating for imposed defocus.

Several methods, for example wearing bifocals and instillation of cycloplegics and anti-glaucoma agents, have been utilised in the attempt to reduce the rate of progression of myopia with little success.

Clearly longitudinal human studies are required to determine possible risk factors for the development of myopia.

# CHAPTER 2

# THE INCIDENCE AND AETIOLOGY OF ANISOMETROPIA

## 2.1 THE INCIDENCE OF ANISOMETROPIA

### 2.1.1 *Definition*

Anisometropia exists whenever there is a difference in refractive error between a pair of eyes. Most individuals have some discrepancy in interocular refractive error, with the term anisometropia reserved for an interocular difference of clinical significance (Borish, 1970). However, no standard criterion exists for defining anisometropia. In children, anisometropia that is of clinical significance is an interocular difference that may have the development of amblyopia or strabismus as a sequelae, and has been proposed to be as low as 1D (Ingram, 1979; Ingram and Barr, 1979). In adults, a level of 2D anisometropia can be considered clinically significant as it may cause asthenopia due to aniseikonia or inequalities in prismatic effects, especially in the vertical meridian, of the right and left lenses (Borish, 1970).

Anisometropia can be found in various forms of ametropia and may be subdivided according to refractive error: anisomyopia exists whenever both eyes are myopic; anisohyperopia where both eyes are hyperopic; when one eye is myopic and the other hyperopic the condition is termed antimetropia; in the case of unequal astigmatism, the ametropia is termed astigmatic anisometropia.

### 2.1.2 *Prevalence and Progression of Anisometropia*

The lack of a common criterion for defining anisometropia has led to difficulties in quantifying its prevalence. Some investigators have taken an asymmetry as low as 0.5D (e.g.(Stevens, 1960)), whereas others have taken 3D or more to represent significant anisometropia (Jackson, 1960). The matter is further complicated in that some authors have considered mean spherical differences (Parssinen, 1990) whilst others have compared meridional asymmetry (Hirsch, 1967). The incidence of anisometropia has been assessed in a number of studies using eye hospital patients as the patient sample (de Vries, 1985) whereas other investigations have sampled a general population (Laird, 1991). Clearly the prevalence of anisometropia will vary according to the criterion adopted and the sample studied. Table 2.1 reflects this variation.

Table 2.1 Prevalence of anisometropia expressed as a percentage of the sample population, modified from Laird (1991).

| Population age (yrs) | Investigators | Prevalence (%) |
|---|---|---|
| Premature infants | Fulton *et al.* (1981)[a] | 32.0 (N=146) |
| Full term infants | Zonis and Miller (1974)[b] | 17.3 (N=300) |
| | Fulton *et al.* (1980)[a] | 18.0 (N=640) |
| 1 to 6 | Hirsch (1952)[c] | 1.0 (N=1166) |
| | Ingram (1979)[c] | 6.5 (N=1648) |
| | Ingram and Barr (1979)[b] | 8.5 to 8.8 (N=148) |
| | Mayer *et al.* (1982)[d] | 4.0 (N=291) |
| 5 to 12 | Flom and Bedell (1985)[b] | 3.4 (N=2762) |
| 5 to 17 | Blum *et al.* (1959)[a] | 3.5 (N=1221) |
| 13 to 19 | Hirsch (1952)[c] | 2.4 (N=1040) |
| | Hirsch (1967)[b] | 6.0 (N=359) |
| | Laatkinen and Erkkila (1980)[a] | 3.6 (N=411) |
| | de Vries (1985)[e] | 4.0 (N=1356) |
| | Kehoe (1942)[b*] | 11.9 |
| | Giles (1950)[c*] | 7.4 (N=2500) |
| | Lebensohn (1957)[c*] | 10.0 |
| | Martinez (1977)[c] | 10.7 (N=2000) |
| | Fledelius (1984)[a] | 9.0 (N=1200) |

Superscripts indicate criteria for anisometropia
[a]0.50D sphere
[b]1.00D in corresponding meridians
[c]1.00D sphere
[d]2.00D cylinder of sphere
[e]not known
*Cited by Borish (1970)

### 2.1.2a *General population*

In a general clinical population the prevalence of anisometropia is around 10% for an interocular refractive error difference of 1D or more in spherical equivalent form. However, the prevalence decreases to 2.5% when anisometropia is defined as an interocular difference of 2D or greater (Laird, 1991).

Woodruff and Samek (1977) carried out an extensive screening programme on the refractive states of the Amerind Indian population in Ontario. They investigated 4018 subjects across a wide age range (0 to >90 years), although more than 50% of the population was under twenty years of age. Defining anisometropia as an interocular difference of 1D or more, they found that 7.24% were anisometropic whereas 52.2% of the subjects had an interocular difference of 0.25D or less. 1.24% of the population had anisometropia of 2D or more.

Fledelius (1984) assessed the prevalence of anisometropia and astigmatism in 1416 Danish hospital patients aged 16 - 85 years, in response to supermarkets selling spherical reading spectacles with equal powers on both sides. Anisometropia of 1D or more, in spherical equivalent form, was present in 9% of the patients. This prevalence decreased to 1.3% for an interocular refractive error difference of 3D or more.

The prevalence of anisometropia in a Chinese population is approximately 20% (personal communication Dr C. F. Wildsoet) and reflects their high incidence of myopia (see § 1.3.2a).

### 2.1.2b *Infant and childhood studies*

*Cross-sectional studies*

A number of researchers have measured the refractive error of newborn infants although little consideration has been given to any right and left eye asymmetries. Thompson (1987) determined the refractive error in both eyes of 210 newborn infants. She found that the level of anisometropia ranged from zero to 3.25D. Anisometropia of 1D or more was found in 21.5% of the infants. This incidence decreased to 14.4% for more than 1D of anisometropia and decreased further to 3.4% for anisometropia greater than 2D. The data was analysed in terms of spherical equivalent refractive errors. A similar incidence of anisometropia in newborn infants was found by Zonis and Miller (1974). They measured the refraction in 300 full-term Israeli infants at 48-72 hours after birth. Cycloplegic refractions revealed anisometropia of 1D or more in 17.3% of the infants. The incidence of anisometropia of 2D was found to be 3%. The majority of the anisometropes were anisohyperopic (85%) with the remainder being anisomyopic and antimetropic.

Gwiazda *et al.* (1993) undertook a longitudinal study of refractive error in 72 children for a period of at least 9 years. The children were first refracted between birth and 6 months by near-retinoscopy after Mohindra (1977). They found that 2 (2.78%) of the 72 children had anisometropia in the first six months. However, the level of anisometropia was not specified nor was the progression of the anisometropia discussed.

Bruce *et al.* (1991) assessed the incidence of refractive error and binocular vision anomalies in 699 infants, recruited randomly from general medical practitioners' records, in two age groups, 9-12 months and 30-36 months. They defined anisometropia as a difference of more than 1D between the two eyes in any meridian. A low incidence of anisometropia was found, 1% in the younger infants and 2.1% in the older infants.

The prevalences of anisometropia in an infant population that have been discussed above are summarised in table 2.2.

Table 2.2. Prevalence of anisometropia expressed as a percentage of the sample population

| Age group | Investigators | Anisometropia | % | N |
|---|---|---|---|---|
| newborn | Thompson (1987) | ≥ 1D | 21.5 | 210 |
| 48-72 hrs after | Zonis and Miller | ≥ 1D | 17.3 | 300 |
| birth | (1974) | ≥ 2D | 3.0 | |
| 9 - 12 mths | Bruce *et al.* (1991) | > 1D | 1.0 | 699 |
| 0 - 12 mths | Wood, Hodi and Morgan (1995) | > 1D | 1.3 | 113 |

Fulton *et al.* (1980) in a cross-sectional study to determine cycloplegic refractions in infants and young children, refracted 640 children whose ages ranged from birth to 160 weeks. They recorded that 82% of the children had no difference in spherical equivalent refraction between left and right eyes. However, the criteria defining interocular differences was not given. Fulton *et al.* represented the right and left eye differences in refraction in graphical form, however, no values for the level of anisometropia was given. In another study, Fulton, Hansen and Petersen (1982) examined 298 children with a myopic spherical equivalent refractive error of 0.25D or greater. The children were aged from birth to 10 years. They found that 74 (24.8%) of the children had anisometropia of 1D or more in spherical equivalent refractive error. In a study on premature infants Dobson *et al.* (1981) showed that a higher incidence of myopia and anisometropia occurs in premature infants compared to full-term infants. Only 20.5% of the premature infants showed an interocular difference of less than 0.25D, in spherical equivalent, compared with 91.9% of the full-term infants (Fulton *et al.*, 1980). The incidence of anisometropia was 32% for an interocular difference of 1D or more. Other studies on refraction in premature infants, for example Shapiro *et al.* (1980), have shown that by the time the infants are 6 months old the mean refractive errors for premature and full-term infants do not differ.

Flom and Bedell (1985) analysed data from 2762 children from kindergarten through to school grade 6. They found 94 (3.4%) of the children to have anisometropia of 1D or more in either pair of corresponding meridians. A similar prevalence of anisometropia was found by Laatikainen and Erkkilä (1980) who measured the refractive error in 411 non-selected school children aged 7 - 15 years. Anisometropia, of more than 1D in spherical equivalent form, was present in 3.6% of the children.

De Vries (1985) screened hospital records for anisometropic children born in 1972. He defined anisometropia as an interocular difference in refractive error of 2D or more in spherical or cylindrical power. Of 1356 children born in that year, 64 (4.7%) were anisometropic. However, it is not clear from the literature at what age the incidence of anisometropia was assessed in the children. Laird (1991) has recorded the prevalence of anisometropia found in de Vries' study to be 4% for an age-range of 13 to 19 years, and has stated that no definition for anisometropia was given. De Vries determined the progression of anisometropia in patients without ocular disease

and who were refracted on at least three occasions. The children were followed for a minimum of 2 years, some for 8 years. The amount of anisometropia was found to remain constant in 18 children, increase in 5 and decrease in 4. De Vries suggested that the study showed anisometropia to be stable in children. However, he has not supported this suggestion with statistical analysis of the data.
The investigations discussed above are summarised in table 2.1.

*Longitudinal studies*
Cross-sectional studies have shown the prevalence of anisometropia in children to be independent of age suggesting that anisometropia is stable throughout childhood (de Vries, 1985; Ingram, 1979). This research has been contraindicated by longitudinal studies which have shown variations in anisometropia in individuals (Ingram and Barr, 1979; Wood, Hodi and Morgan, 1995).

Thompson (1987), in addition to her cross-sectional study on refractive error of newborn infants, obtained longitudinal anisometropic data on 12 infants who were refracted at birth, three and six months. The mean level of anisometropia in the newborn was 0.61D which decreased to 0.19D by six months, most of the alteration was found to occur by three months (0.22D).
Ingram and Barr (1979) measured the changes in refraction in 148 children from the age of 1 to 3.5 years. Anisometropia, of 1D or more in sphere or cylinder, was found in 12 children at the age of 1. Over the next 2.5 years, the anisometropia in 7 subjects disappeared and a further 8 developed anisometropia.
The changeability of anisometropia in a selected population of astigmatic children to ascertain those children at risk for developing amblyopia was assessed by Abrahamsson, Fabian and Sjöstrand (1990). They refracted 310 children with 1D or more astigmatism in at least one eye. The children were refracted annually for a period of three years from the age of one. Anisometropia of 1D or more in any meridian was found in 18.7% (58 out of 310) of the children on at least one test session. Astigmatic anisometropia was found in 4 cases. No mention was made to the subsets of anisohyperopia and anisomyopia. All the anisometropic cases, except one, were orthophoric and had no signs of pathology. At the first test session 11% of the children were anisometropic of 1D or more, this prevalence varied little with age. They followed the initial anisometropic group over the 3 year testing period and found a continuous decrease in the number of anisometropic cases at all levels of anisometropia. In the majority of the 58 anisometropic cases, the anisometropia originated from the different rates of emmetropisation in the two eyes. They found that the anisometropia that may be generated during the emmetropisation process can be of a magnitude of at least 3D. Anisometropia of 3D in adults usually originates from differences in axial length (Sorsby, Leary and Richards, 1962). However, the importance of axial length, corneal steepness and lens powers as causal factors were not studied by Abrahamsson, Fabian and Sjöstrand due to a lack of data.

In a further study, Abrahamsson and Sjöstrand (1994) followed the refractive change in 20 children with 3D or more of anisometropia at 1 year of age. They measured the refractive error every 6 months for a period of 9 years. The refractive error was fully corrected at 2.5 years of age and any amblyopia was treated by occlusion therapy. They found that all the children remained anisometropic throughout the testing period, however, in 70% of the cases the anisometropia decreased with 50% becoming amblyopic. In the remaining 6 cases, the amount of anisometropia increased and all 6 children developed amblyopia. Abrahamsson and Sjöstrand concluded that the presence of anisometropia of 3D or more at 1 year of age suggests that the anisometropia is permanent but it is not necessarily an indication for the development of amblyopia.

Almeder, Peck and Howland (1990) conducted a longitudinal study on a volunteer population of 686 children aged 3 months to 9 years. They defined anisometropia as an interocular spherical difference of greater than 0.62D or a cylindrical difference of more than 0.75D. They found 19 (2.8%) non-strabismic anisometropic subjects. Of these subjects, 8 were seen either once or the anisometropia only appeared at their last testing session. In the other 11 subjects, the anisometropia had decreased to within normal limits by the next examination. From these results they estimated that the prevalence of persistent anisometropia was 0% in infants. Owing to the discrepancy between their results and previous data on the prevalence of anisometropia in children, the authors doubted whether their sample was representative of the general population. Therefore, they screened 374 Head Start and first-grade children using the same methods and criteria as used for the volunteer population. The prevalence of anisometropia in this group was 1.9%. No significant difference was found in the frequencies of anisometropia observed in the two populations. They concluded that this finding may in part reflect the fact that anisometropia is largely transient in young children.

Gomez and Fern (1991) in response to Almeder, Peck and Howland's findings, investigated the prevalence of anisometropia in paediatric patients who attended their clinic. They reviewed 807 records and as expected they found that the prevalence of anisometropia in this clinical population was higher than that in a general population. Anisometropia, of 1D or greater, was present in 7.5% of the cases. As this study was cross-sectional in nature, no information on the persistency of anisometropia was obtained.

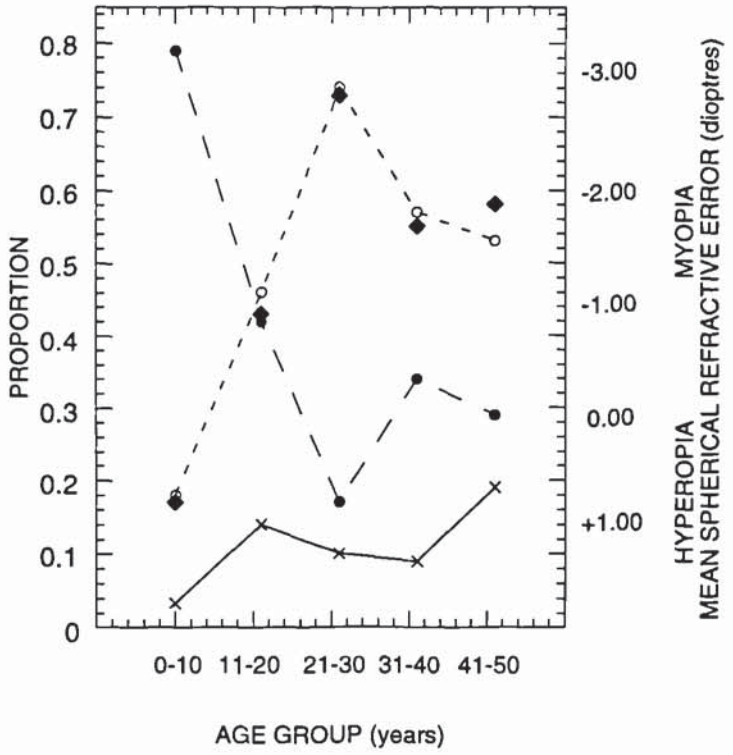
Hirsch (1967) used data from the Ojai longitudinal study on refractive error to assess the incidence of anisometropia. The 359 children all had 11 or 12 consecutive years of semiannual refractions. The children were aged between 5 and 7 years at the first examination and between 16 and 19 years at the last. Hirsch defined anisometropia as an interocular refractive error difference of 1D or more. He found that 2.5% (9 out of 359) of the 5 - 7 year olds had anisometropia, 8 cases were persistent and in the other case, the anisometropia decreased. Another 12 children were isometropic upon entering school but developed anisometropia throughout the study. The prevalence of anisometropia in the 16-19 years olds was found to be 5.6%.

A longitudinal study on 113 infants was carried out by Wood, Hodi and Morgan (1995). They examined the infants from birth over the first year of life in 3 month intervals. They found that anisometropia over 1D was rare and only presented at 6 (1.3%) individual examinations. Any anisometropia subsequently disappeared in children under 6 months of age. Only 2 children of 6 months or older were found to have anisometropia.

### 2.1.3 *Nature of ocular growth in anisometropia*

Various studies have noted the prevalence of anisometropia during and beyond adolescence. In the population as a whole there is a shift towards more myopic refractive errors through adolescence - the aetiology of which has been studied by many authors, for example (Curtin, 1985; Gilmartin and Winfield, 1995; Goss and Wickham, 1995). This shift towards myopia is also reflected in the number of cases of anisomyopia compared to anisohyperopia. The ratio between the two varies between studies: Schapero (1971), on the basis of Brock's (1962) figures, found the incidence of anisomyopia to be 3 times more prevalent than anisohyperopia; Jampolsky *et al.* (1955) analysed the refractive data from 200 non-strabismic anisometropes and found that the occurrence of anisomyopia was twice that of anisohyperopia. Sorsby, Leary and Richards (1962) in their study on the optical components of anisometropia in 68 patients found that the number of anisometropic subjects with myopia was 1.68 times the number of those with hyperopia. In a study of patients with very high levels of anisometropia (not less than 5D of anisometropia), Sanfilippo, Muchnick and Schlossman (1978) found1 in 30 patients to have hyperopia in their more ametropic eye.
Laird (1991) in a comprehensive review of 731 anisometropes with an interocular difference of 2D or more in the vertical meridian, assessed the distribution of anisometropia with respect to age. The subjects were aged between 3 and 50 years. He subdivided the data into 10-year intervals and into anisomyopia, anisohyperopia and antimetropia. He found that the proportion of anisomyopes increased up to age 30. Beyond the age of 30, the proportion of anisohyperopes increased. He postulated that the increase in relative prevalence of anisomyopia occurred either by an increase in the number of myopes or by an increase in the degree of myopia. To investigate the cause, Laird compared the proportion of anisomyopes, anisohyperopes and antimetropes in each decade with the mean change in refraction for each decade of the group as a whole. Figure 2.1 shows this comparison. Laird concluded that the increase in relative proportion of anisomyopia correlated with an increase in the degree of myopia occurring with age. However, this study was cross-sectional in nature and no consideration has been given to any differences in sample sizes for each age division.

Figure 2.1 Relative proportions of anisometropic subgroups with respect to age, redrawn after Laird (1991).




Variations in the proportion of the various anisometropic /antimetropic categories, presented for each 10-year age group. Anisomyopes are depicted by open circles, anisohyperopes by black dots, and antimetropes by crosses. These variations are compared with the mean change in refractive error with age (diamond symbol).

Gomez and Fern (1991) assessed the prevalence of anisometropia in 807 children with respect to age. As can be seen from figure 2.2 the prevalence of anisometropia of 1D or more, increases with increasing age.

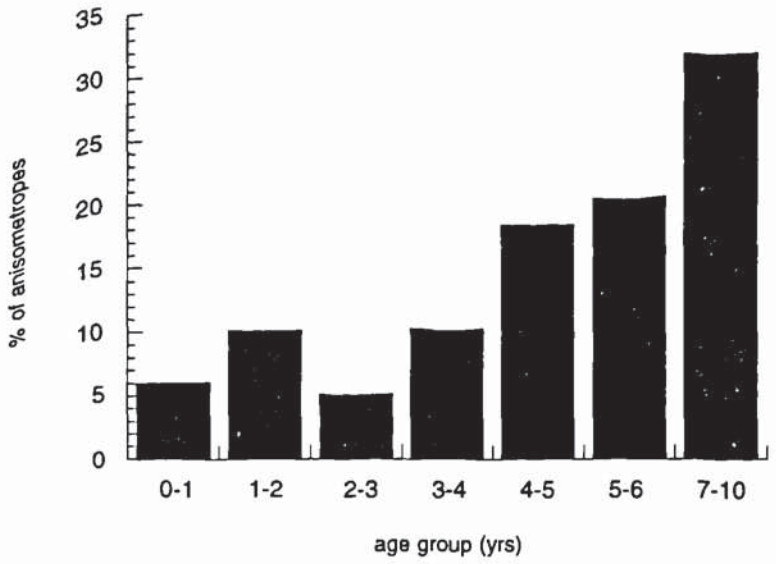
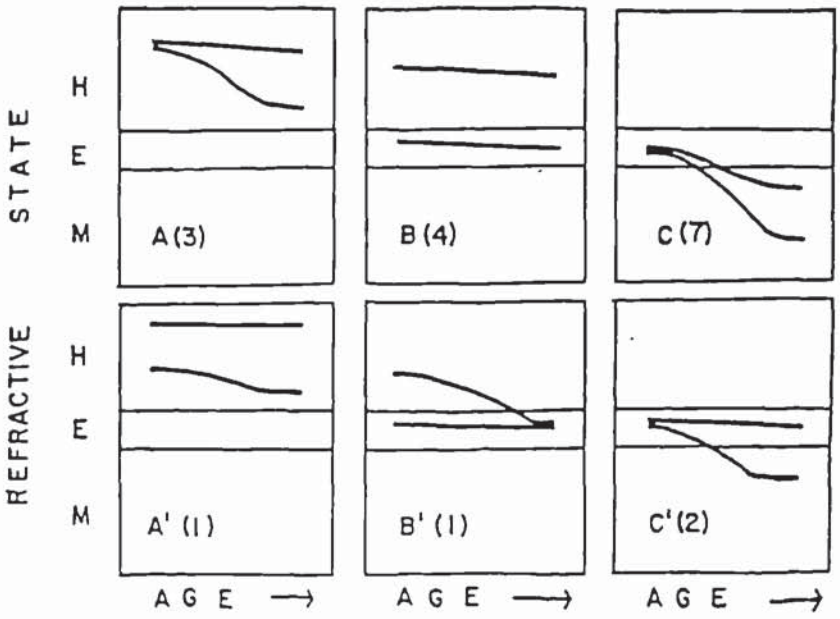



Figure 2.2 The prevalence of anisometropia with age, after Gomez and Fern (1991).

Individual growth patterns in anisometropia were investigated by Hirsch (1967), (see figure 2.3). In the Ojai longitudinal study on refractive error, Hirsch found that no two anisometropic children followed the same pattern of growth. However, four general trends emerged that described almost all of the children. The first trend described hyperopic eyes. Three hyperopic subjects had no anisometropia at the start of the study but developed it at an older age. One subject had anisometropia at the start with the amount increasing over the study period. The second trend represented five subjects who were hyperopic in one eye and emmetropic in the other eye. Four of the subjects remained anisometropic throughout the study period while the other subject became emmetropic in the hyperopic eye. The third trend applied to myopes. This was the largest group with nine subjects who were initially emmetropic but developed different degrees of myopia in both eyes (7 subjects) or developed myopia in only one eye (2 subjects). The fourth trend described astigmatic anisometropia which was found in three subjects.

The investigations have shown that the amount of anisometropia is variable throughout a person's lifetime and may either increase or decrease in nature.

Figure 2.3 Growth patterns in anisometropia, after Hirsch (1967).



## 2.2 THE AETIOLOGY OF ANISOMETROPIA

The finding that anisomyopia is around 2 to 3 times more common than anisohyperopia (see § 2.1.3) must be accounted for by any general theory of isometropic myopia development. Hirsch (1967) remarked that anisomyopia is an enigma for any theory of myopia.

### *Ocular components in anisometropia*

The refractive error of an eye is the resultant combination of the optical properties of the ocular components: e.g. radii of curvature of the cornea and crystalline lens surfaces, the refractive indices of the ocular media, the anterior and vitreous chamber depths and lens thickness. It has been demonstrated in § 1.1.1 that development and change of these components is correlated in such a way as to produce emmetropisation in eyes from birth to adulthood, which leads to the characteristic leptokurtotic distribution of refractive error. There is a propensity for a degree of symmetry in refractive error between a pair of eyes. The isometropic nature of the two eyes was investigated by Kehoe (1942), who demonstrated the frequency of vertical anisometropia in 1000 random cases. He found that the empirical was centred more around the zero ordinate than would be expected by chance factors.

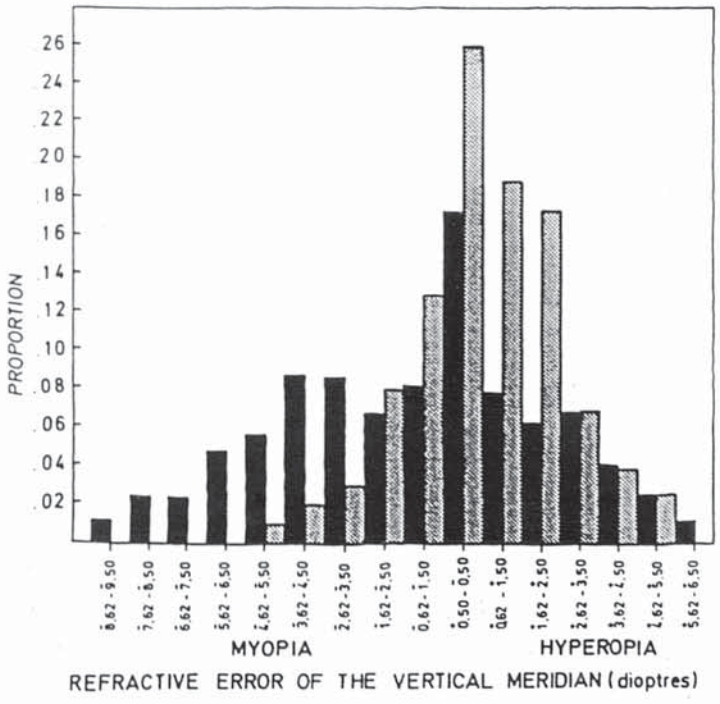



Figure 2.4 Prevalence of anisometropia in the vertical meridian, after Laird (1991).

Studies have recorded that the incidence of interocular refractive error asymmetry occurs in approximately 9% of the population for an interocular difference of 1D or more, and in approximately 2.5% of the population for an interocular difference of 2D or more (see § 2.1.2). In anisometropia, in addition to the development of ametropia by a possible failure in the emmetropisation process, the concordance between right and left eye refractive error has been disrupted. The distribution of ocular components contributing to anisometropia has been investigated by several researchers. The most comprehensive study was carried out by Sorsby, Leary and Richards (1962), who assessed the distribution of the different optical components in 68 anisometropes. The degree of anisometropia ranged from 2 to 15D. From analysis of the results, it was found that the different ocular components did not contribute equally to the anisometropia. Axial length was found to be the predominant factor in anisometropia, with the range of interocular differences in axial length extending beyond 15D. However, in low degrees of anisometropia, i.e. 2-3D, the anisometropia arose from differences in axial length associated with differences in lenticular and corneal powers. Moderate amounts of anisometropia, i.e. 3-5D, were mainly axial in origin with some degree of lenticular involvement. In the highest degrees of anisometropia (>5D), axial length was the predominant factor.

Fledelius (1981b) measured the refractive components in aniso- and isometropia by ultrasonography and keratometry. The subjects comprised 28 anisometropes with an interocular refractive error difference of greater than 1D, and 63 isometropes with 0.50D or less interocular difference in refraction. His results agreed with those of Sorsby, Leary and Richards (1962) in that anisometropia was mainly axial in nature.

Otsuka, Sugata and Araki (1981) analysed data from Araki, Otsuka and Sugata (cited in (Otsuka, Sugata and Araki, 1981)) and Sorsby, Leary and Richards (1962) by comparing the mean difference in biometric measurements in a pair of eyes. They proposed that their method for data calculation was an improvement on comparing correlation coefficients or distribution curves, as differences due to age and sex could mainly be eliminated. They concluded that the aetiology of low, medium and high anisometropia occurs principally from elongation of the axial length.

Reference to the literature has indicated that the cornea does not appear to contribute significantly to anisometropia. In all cases corneal power has been measured by conventional methods. Waardenburg (1930) found that only rarely do the powers of the two corneas show a difference in excess of 1D even with substantial degrees of anisometropia. In Sorsby, Leary and Richards' (1962) investigations, similar results were found. They noted that the range of differences in corneal power did not extend beyond 2D for 68 subjects with a range of 2 to 15D anisometropia. The difference in corneal power between a pair of eyes was sufficient to account for the anisometropia in 3 cases. The degree of anisometropia in these 3 cases were all of a low order, ranging from 2.4 to 2.8D. In another 10 cases the cornea contributed, up to a maximum of 2D, to reduce the anisometropia.

The contribution of lenticular power to anisometropia has been investigated by Tron (1933). In a study of 22 cases of anisometropia ranging from 2-13D, he found that in 14 cases the interocular difference in lens power exceeded the experimental error of 1D. In 4 of the 14 cases, the interocular discrepancy in lens power was found to be the determining component for the anisometropia. Using the technique of phakometry, Sorsby, Leary and Richards found 4 cases of anisometropia that were mainly lenticular in origin, these cases were confined to the lower degrees of anisometropia, 2-5D. Their results revealed the lenticular power to have a maximum difference of 3.75D between a pair of eyes.

These investigations have shown that in addition to the axial elongation that occurs in anisometropia, there is a failure in the normal adaptive mechanism that correlates the ocular components.

### 2.2.2 *IOP and ametropia*

Although the relationship between intraocular pressure (IOP) and anisometropia has been investigated by several researchers, the results are ambiguous. Tomlinson and Phillips (1970) found a statistically significant positive correlation between axial length and IOP, in that the eye with the longer axial length had the higher intraocular pressure. The age range of the 75 subjects was 18 to 27 years with a refractive error range of -7D to +4.75D. This finding agrees with Wallace and Lovell (1969) who found a raised IOP in myopes compared to hypermetropes in a study of 574 people aged 35 to 74 years in Jamaica. However, as the subjects were isometropes and from different races, the variabilities of race, sex, time of day and blood pressure may influence the results. Abdalla and Hamdi (1970) compared applanation tonometry measurements in 760 emmetropic and myopic eyes. Emmetropia incorporated refractions between +2 and -2D. Myopic subjects were classified into two groups; those with myopia ranging from -2 to -6D, and those with myopia greater than -6D, all subjects had less than 2D astigmatism. The subjects ranged in age from 11 to over 50 years. They found the mean values for intraocular pressure to be higher in myopes than in emmetropes but the differences were not always significant in all age groups. Age, sex, season, time of day and systemic blood pressure are all known to affect intraocular pressure. Bengtsson (1972), allowed for these influences and found no difference in IOP between different refractive groups in 1624 people aged 8 years or older. Tomlinson and Phillips (1972) examined 13 anisometropic children aged 8-16 years from a school eye service clinic. Anisometropes were chosen to provide a control for the influence of sex, season, time of day and blood pressure. They found that the eye with the greater axial and vitreous length had the significantly higher ocular tension. However, conflicting results were found by Bonomi, Mecca and Massa (1982) who studied the IOP in 137 anisometropes with unilateral high myopia, using applanation tonometry. High myopia was defined as a refractive error greater than 5D. The contralateral eye was hyperopic, emmetropic or had myopia less than 5D. They found no difference in intraocular pressure in a pair of eyes and concluded that high myopia is neither a cause nor a consequence of ocular hypertension.

Quinn *et al.* (1995) investigated the association of intraocular pressure and myopia in children attending a paediatric hospital. They obtained reliable IOP readings in 321 children with a pneumatonometer. The mean age of the subjects was 9.8 years with a range of 1 month to 19 years. Myopia was defined as a spherical equivalent of more than -1D. Their results indicated that IOP may be higher in myopic than non-myopic eyes, a weak positive correlation was found ($p < 0.1$ for the right eyes and $p < 0.05$ for the left eyes).

### 2.2.3 *The development of anisometropia and amblyopia*

Amblyopia is a developmental anomaly and is commonly defined as a reduced visual acuity not correctable by optical means and not attributable to structural or pathological anomalies of the eye. Reduced visual acuity is often described as a visual acuity of 6/9 or less (Schapero, 1971). The incidence of amblyopia depends on the criteria defining amblyopia, testing method, co-operation of the patients and the sample chosen. Amblyopia has been found to affect between 2 and 5% of the general population (von Noorden, 1967). Amblyopia is known to frequently occur with anisometropia although the cause and effect relationship has not been well defined.

Generally anisometropic amblyopia arises due to a bilateral symmetric accommodation mechanism occurring in a pair of eyes with unequal refractive errors. Under experimental conditions unequal accommodation of a pair of eyes has been stimulated by both asymmetrical convergence to a maximum of 0.9D (Marran and Schor, 1994) and by anisometropic stimuli to a maximum of 2D (Marran and Schor, 1995). Carlin *et al.* (1996) found no such aniso-accommodation.
In uncorrected anisometropia, the far point for each eye differs therefore only one of the two eyes receives a clear retinal image at any one time. In anisomyopia, there exists a distance for each eye that will produce a clear retinal image without accommodation. In contrast, hypermetropic subjects must accommodate to produce a clear image for all object distances. Anisohyperopes are assumed to exert the minimum amount of accommodation that will give a clear retinal image in the less hypermetropic eye resulting in the more hypermetropic eye never receiving a clear retinal image. Thus, in a pair of eyes, one retinal image will be blurred during the critical period of development leading to inadequate stimulation of the foveal sustained neurons which results in amblyopia (Ciuffreda, Levi and Semmlow, 1991). The effects of not obtaining a clear retinal image have been shown by visual deprivation experiments in animals (see § 1.4.4a). In the same way visual deprivation due to unequal refractive errors may alter the development of the visual system, the effect being greater in infants than in adults. Visual deprivation in children up to approximately 6 years of age often leads to amblyopia. Therefore, in young children uncorrected anisohyperopia may lead to a reduced visual acuity in the more hyperopic eye (Jampolsky *et al.*, 1955; Tanlamai and Goss, 1979).

The studies described below are concerned with anisometropia in non-strabismic amblyopes.

Flom and Bedell (1985) found that in anisometropic amblyopic children the average acuity in the amblyopic eye was 6/18. This average acuity dropped to 6/28 for amblyopes with both anisometropia and strabismus.

Corrected visual acuity in anisometropes was investigated by Jampolsky *et al.* (1955). Their subjects consisted 200 private patients with 1D or more anisometropia in spherical or cylindrical form. They found that among non-strabismic anisometropes, amblyopia was more prevalent and the inter-eye acuity difference was greater in anisohyperopes than in anisomyopes.

Kutschke, Scott and Keech (1991) examined 124 patients with 1D or more anisometropia and amblyopia aged 11 to 111 months. Their results agreed with those of Jampolsky *et al.* that hypermetropic differences in refractive error are more amblyogenic than myopic differences. Kutschke, Scott and Keech also found a relationship between initial vision and best vision obtained after treatment with spectacles or occlusion therapy, but neither factor was related to the degree of anisometropia.

The outcome of amblyopia treatment in 122 patients with anisohyperopic amblyopia without strabismus was investigated by Sen (1982). The degree of anisohyperopia in the subjects ranged from 1.5D to 9D in spherical equivalent form. The patients ranged in age from 6 to 20 years. He found that improvement in visual acuity after amblyopia treatment was greater in the younger subjects (aged 6 to 12 years) than in the older subjects (13 to 20 years). Anisometropes of 4D or less with an initial visual acuity of 6/24 or better were found to have a better prognosis than anisometropes with an inter-eye difference of greater than 4D. A similar study investigating anisometropic amblyopia and outcomes of treatment was carried out by Kivlin and Flynn (1981). They examined 67 anisometropic patients with an inter-eye refractive error difference of -18.75 to +6.25D and no strabismus. They found significant correlations between initial vision, degree of anisometropia and visual acuity after treatment. Kivlin and Flynn found amblyopia to be equal in hypermetropes and myopes with similar degrees of anisometropia. Their results conflict with those by Jampolsky *et al.*, who found denser amblyopia in hypermetropic patients compared to myopic patients.

In 18 cases of bilateral anisomyopia of 1D or more, Phillips (1959) found only one patient to have strabismus and none to be amblyopic. No information regarding the mean degree of anisomyopia was presented. Judging from the results of previous studies, if these cases of anisomyopia were all of low degrees of anisometropia then a low incidence of amblyopia would be expected. Phillips suggested that amblyopia was not present in the anisomyopes as the age of onset of anisomyopia may have been later than the critical period in which amblyopia develops.

*Anisometropia in infants*

Some studies have shown that the majority of infantile anisometropia is transient and poses little risk for development of amblyopia (Almeder, Peck and Howland, 1990; Wood, Hodi and Morgan, 1995) (see § 2.1.2b). Almeder, Peck and Howland (1990) found little persistence in infant anisometropia. They suggested that if persistent anisometropia is rarer than supposed, most

adult anisometropia may be the result rather than the cause of amblyopia. It has been suggested that infantile anisometropia that is persistent is associated with an interocular difference in axial length (Abrahamsson, Fabian and Sjöstrand, 1990). This group of anisometropes have a 1 in 4 risk of developing amblyopia. Birch, Stager and Everett (1995) claimed that few children in these studies had refractive errors greater than 1.5D. They investigated the refractive error in 39 infants with 1D or more anisometropia at the age of 1.5 years and reassessed them at 4 years of age. They found that only 25% of the children with an initial refractive error less than ±3D were still anisometropic at 4 years of age. Of the infants with an initial refractive error of ±3D or more, 82% were still anisometropic at the age of 4. They concluded that the combination of anisometropia and a refractive error of greater than ±3D was a significant risk factor in the development of amblyopia. Ingram and Walker (1979) assessed the risk factors for development of amblyopia and strabismus in pre-school children. They found that anisometropia of 1D or more was significantly associated with the child developing a strabismus or amblyopia in the more ametropic eye 2 or more years later.

*Incidence of amblyopia in anisometropia*

The prevalence of monocular amblyopia among 167 Thai and 472 American anisometropes was assessed by Tanlami and Goss (1979). The Thai anisometropes had an inter-eye refractive error difference of 2D or more and the Americans had anisometropia of 1D or more. The depth of amblyopia was found to vary directly with the degree of anisometropia (Tanlamai and Goss, 1979). The incidence of amblyopia (VA 6/9 or less) was found to be 100% in meridional anisohyperopes with 3.5D or more interocular difference and 100% in meridional anisomyopes with 6.5D or more difference in inter-eye refractive error (see figure 2.5). Similar incidences occurred for spherical equivalent differences in refractive error. Lower levels of anisometropia revealed smaller proportions of amblyopia. They found no significant difference in incidence of amblyopia in the Thai and American groups.

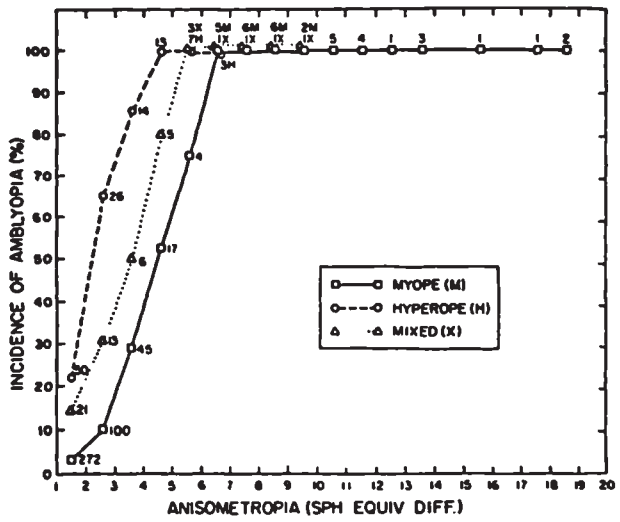



Figure 2.5 Incidence of amblyopia in anisometropia, after Tanlamai and Goss (1979).
The incidence of amblyopia in all myopic, mixed and hyperopic subjects with anisometropia calculated on the basis of difference in spherical equivalents and expressed in dioptres.

Schapero (1971) concluded that the eye with the greater refractive error, whether it was hypermetropic, myopic or astigmatic, was generally the amblyopic eye. The refractive error changes in amblyopic eyes are not well understood. Friedman, Neumann and Abel-Pelag (1985) found a statistically significant relationship between amblyopic and non-amblyopic eyes of non-strabismic patients treated with spectacles before the age of 3 years and reassessed at 7 years. They assessed 39 patients with marked ametropia, that is 5D or more spherical ametropia or 2.5D or more astigmatism in either eye, at 1-2.5 years and followed them until the age of 7 years. The non-amblyopic eye showed a significantly higher frequency of myopic shift (17 out of 21 patients) than the amblyopic eye (6 out of 16 patients). Their sample included 6 patients with anisometropia of 3D or more, 5 of whom had amblyopia in the more ametropic eye. Lepard (1975) found a similar result for 55 strabismic amblyopes between the mean ages of 4 and 14 years.

Investigations on anisometropia and its association with amblyopia have revealed no consistent pattern that could suggest which parameter may be the causative factor. Results have indicated that it is usually the more ametropic eye that is the amblyopic eye although the correlation between depth of amblyopia and degree of anisometropia is equivocal. Many other factors appear to be associated in the cause and effect relationship, the major one being binocularity.

### 2.2.4 *Anisometropia and strabismus*

Strabismus along with amblyopia has been linked to anisometropia and the association between them is not fully understood. Studies have shown that monocular visual deprivation can induce a shift in refraction in the deprived eye resulting in anisometropia (see § 1.4.5). Thus it is possible that the asymmetry in refractive errors may be the result rather than the cause of the strabismus.

Von Noorden (1967) stated that when both amblyopia and strabismus occur in anisometropic cases, it is difficult to tell which is the causative factor and which is the resultant factor.

A comparison between 40 non-strabismic anisohyperopes and 53 strabismic anisohyperopes was made by Phillips (1959). He found that the refractive error of the less ametropic eye was significantly greater in the strabismic group compared to the non-strabismic group. Degree of anisometropia, incidence of astigmatism and sex ratio were found to be similar in the two groups. However, the patients in the first group were older and the baseline refraction was based on an estimate of their refractive error at the age of 7 years.

In 865 patients with strabismus Phelps and Muir (1977) found the incidence of anisometropia of greater than 1.50D to be 9.4%. They then reviewed another 20,096 consecutive patients from their optometry practice to assess the incidence of anisometropia, strabismus and amblyopia. They found 5.3% of the patients to have strabismus, 3.6% had anisometropia and 0.6% had both anisometropia and strabismus.

Ciuffreda, Levi and Semmlow (1991) suggested that anisometropia probably causes the initial amblyopia, which leads to strabismus and a further deepening of the amblyopia. Sanfilippo, Muchnick and Schlossman (1978) found a high correlation between extent of amblyopia and the

binocular relationship in 30 patients with high anisometropia (≥5D). They noted that the greater the degree of amblyopia the more likely the patient was to be strabismic. Patients with small degrees of amblyopia were usually phoric. No correlation was found between the strength of the binocular relationship and amount of anisometropia. These results suggest that it is feasible that the anisometropia may be the primary cause of the amblyopia which then induces the strabismus. Conversely, Lepard (1975) described anisometropia which developed as a result of strabismus with the fixing eye becoming more myopic with age. Similarly, in a study of 61 amblyopic children Nastri *et al.* (1984) found that the refractive error developed at a different rate in the amblyopic eyes compared to the fixing eyes. The dominant eye became more myopic (or decreased in amount of hypermetropia) while the amblyopic eye remained virtually unchanged. These investigations suggest an alternative sequence of events to the hypothesis already suggested. Theoretically the existence of strabismus could cause amblyopia followed by the development of anisometropia which may lead to an increase in degree of amblyopia.

### 2.2.5 *Anisometropia and astigmatism*

Many studies have demonstrated a significant correlation between the incidence of anisometropia and the incidence of astigmatism.

In a cycloplegic refraction of 1648 1 year-old children, Ingram (1979) found the incidence of anisometropia of greater than 1D to be 6.5%. He noted that the anisometropia was significantly associated with bilateral hypermetropia. The correlation between anisometropia and astigmatism of +1.50D or more in one or both eyes had a greater statistical significance. These findings were followed up by a longitudinal study (Ingram and Barr, 1979) which assessed the changes in refraction between the ages of 1 and 3.5 years. A similar association between anisometropia and astigmatism was also found at these ages.

A study by de Vries (1985) of a hospital population of children found that 60 out of 64 patients with anisometropia had an astigmatic component of greater than 1D.

Research has indicated that anomalous form vision may trigger the development of myopia in the developing eye (see § 1.4.5). A frequent anomaly is astigmatic ametropia where a defocused image occurs due to the cylindrical error. If astigmatism in infants is left uncorrected amblyopia may result. Fulton, Hansen and Petersen (1982) assessed the relationship between astigmatism and myopia in 298 myopic children aged from birth to 10 years. They found that the children with the higher cylindrical errors, notably of oblique orientation, had the higher degrees of myopia. In children 3 years-old or younger, myopia progressed in eyes with ≥1DC. Myopia continued to increase in those children with ≥3DC until 8 years of age. They noted that patients (n=74) with 1D or more spherical equivalent anisometropia showed no trend for progression of myopia in either eye. Longitudinal data was not obtained on all children and no mention is given to any cylindrical error in the anisometropes. This suggests that anisometropia may result from form-deprivation by unilateral astigmatism, where the astigmatic eye becomes more myopic than the non-astigmatic eye.

### 2.2.6 *Anisometropia and stereopsis*

Stereoacuity is the smallest amount of horizontal retinal image disparity that enables the perception of relative depth or stereopsis. It is measured in seconds of arc.

In uncorrected anisometropia the two eyes usually have unequal visual acuity. Blurred vision will normally exist in the more ametropic eye. Research indicates that impairment in stereopsis may be related to the amount of blur and hence to degree of anisometropia. Ong and Burley (1972) demonstrated that experimentally induced anisometropia progressively degraded stereoacuity. They found that the depth error approximately doubled for artificially induced anisometropia of 0.75D. The depth error was found to be greater for myopic defocus.

Ingram and Walker (1979) suggested that binocular degradation may be associated with relatively small amounts (1D) of anisometropia. The same degree of refractive error presented symmetrically as myopia or hypermetropia produced no such deficit. Simons (1984) found that stereoacuity was reduced twice as much by monocular degradation of the image contrast than an equivalent reduction of the image contrast in both eyes.

The relationship between experimentally induced anisometropia and binocularity has also been investigated by Brooks, Johnson and Fischer (1996). Unilateral myopia, hypermetropia or astigmatism was induced in 19 subjects using trial lenses. Binocular status was assessed with the Titmus stereotest, Worth four-dot fusion and Bagolini lenses. They found that binocular function decreased in all subjects with increasing degrees of anisometropia. Significant loss of stereopsis with 1D of anisometropia occurred in some subjects with only 7 subjects retaining a stereoacuity of 40 arc seconds. They suggested that the mechanisms underlying the loss in stereopsis may involve foveal suppression, with a correlation between degree of anisometropia and extent of suppression.

While many reports have suggested that relatively low amounts of monocular blur severely reduce or eliminate stereopsis, others have reported the retention of stereoacuity in clinically significant anisometropia. Cooper and Feldman (1978) assessed the binocularity in 10 anisometropic amblyopes with a random-dot stereogram. Anisometropia was defined as an inter-eye refractive error difference of 0.75D or greater. They found that 5 of the anisometropes passed the test with a range of anisometropia of 0.75 to 4.50D. No difference in amount of anisometropia, refractive error or degree of amblyopia was found between those who passed the test and those who failed. Lovasik and Szymkiw (1985) examined the effects of induced aniseikonia, anisometropia, accommodation, retinal illuminance and pupil size on stereoacuity. Their study incorporated 50 experienced observers whose stereopsis was measured by the Titmus stereotest and the Randot test. The effects of induced anisometropia was examined by placing positive lenses in 0.50D steps before the dominant eye in a random sequence. They found that monocular blur caused a more rapid decrease in stereopsis than induced aniseikonia, with 1D of induced anisometropia, stereopsis of 40 arcsec could be maintained. The majority of observers were found to maintain moderate stereopsis with 2D of anisometropia. These results

differ from those of Peters (1969) who reported that 4 out of his 5 subjects were unable to maintain stereopsis with 1D of monocular blur.
These investigations have mainly concentrated on artificially inducing anisometropia in adults. Whether the binocular sensory effects demonstrated in these experiments are applicable to the loss in binocularity that may accompany anisometropia in children has yet to be ascertained.

### 2.2.7 *Aniseikonia*

The term aniseikonia describes a difference in size or shape of the ocular images of a pair of eyes. The degree of aniseikonia is determined by the whole visual system, which includes the retinal image size, anatomical placement of the retinal elements and the physiological and psychological alterations to the retinal image in reaching the visual cortex (Borish, 1970; Millodot, 1986).
As previously discussed in § 2.1.1 anisometropia may be classified in terms of its aetiology; axial anisometropia results from unequal axial lengths whereas refractive anisometropia results from differences in the powers of the ocular components. Clinically significant degrees of anisometropia (>2D) are usually axial in nature (Sorsby, Leary and Richards, 1962).
Optical correction of anisometropia may induce differences in retinal image size with a 5% difference in retinal image size traditionally considered to be the limit of tolerance for binocular vision (Duke-Elder, 1970).
The generally accepted view is that the inequalities in right and left image size may be reduced by correcting axial anisometropia at the anterior focal plane of the eye. This principle, known as Knapp's Law (1869) has often been used when selecting an optimal correction for anisometropia. Spectacles have been used to correct axial anisometropia, whereas contact lenses have been used in the correction of refractive anisometropia.

Several studies have found substantial amounts of aniseikonia in anisometropes corrected with spectacle lenses. Refractive anisometropia, that is misplacement of the lens from the anterior focal point of the eye, or inter-eye differences in anatomy may have contributed to the apparent failure of Knapp's Law.
Rose and Levinson (1972) measured aniseikonia in 11 subjects with at least 1D of anisometropia. The refractive error was corrected with both spectacle and contact lenses. Less aniseikonia was found with contact lenses than with spectacles. They assumed that the more myopic eye was stretched at the posterior pole compared to the contralateral eye. From this they concluded that the larger retinal image which occurs in the more myopic eye stimulates a similar number of receptors than the smaller retinal image in the less myopic eye.

Bradley, Rabin and Freeman (1983) investigated the origins of aniseikonia in 7 anisometropes while differences in retinal image size were kept to a minimum. The degree of anisometropia in the subjects ranged from 5 - 20D. A dichoptic size matching task was used to assess the amount

of aniseikonia. They found large amounts of aniseikonia, the amount of which correlated significantly with the degree of anisometropia. The anisomyopes all recorded the smaller image in their more ametropic eye compared to the anisohyperopes who observed a larger image in their more ametropic eye. Ultrasonography was performed on 2 subjects to confirm that the anisometropia was axial in nature. As the retinal image size was equal in both eyes, they concluded that the aniseikonia must result from non-optical interocular differences. They investigated this hypothesis by examining the retina and the shape of the globe. B-scan ultrasonography was obtained on 2 subjects and comparisons of the right and left eyes were made. The anterior part of the right and left eyes were found to be symmetrical, whereas the posterior part of the globes differed in size. Bradley, Rabin and Freeman concluded that the retina may have stretched in the more myopic eye as the retina has to cover a greater area in this eye. However, the exact orientation of the B-scan images are not known and may result in discrepancies in the measurements. To obtain more information on retinal stretching, they photographed the fundus at different eccentricities along the horizontal meridian in several subjects. The photographs depicted that the more myopic eye was usually associated with signs of retinal stretching such as scleral crescents, pale non-uniform fundus and visible choroidal vessels. They found that the degree of aniseikonia correlated with the amount of observed retinal stretching.

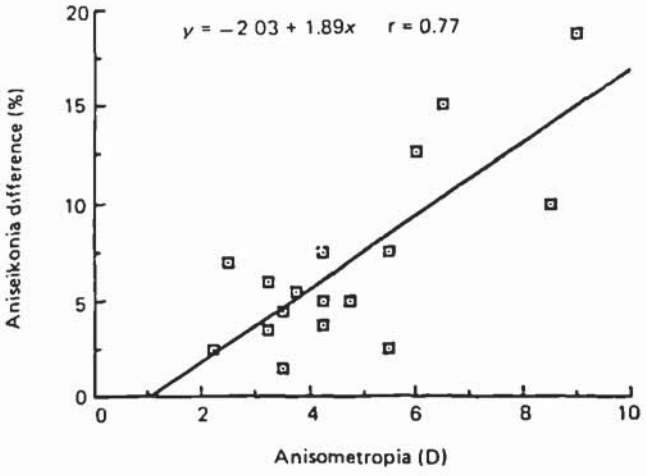



Figure 2.6 Aniseikonia in anisometropes with spectacles and contact lenses after Winn *et al.* (1988).

Winn *et al.* (1988) conducted a more comprehensive study based on Bradley, Rabin and Freeman's hypothesis. The study comprised 18 anisometropes with a minimum interocular difference in refractive error of 2D. Ultrasonography measurements revealed that the anisometropia in 17 subjects was axial in nature. Aniseikonia was measured, using a haploscope, with the refractive error corrected with both spectacle and contact lenses. They found that in 17

of the 18 subjects less aniseikonia was produced with contact lenses than with spectacles. In agreement with Bradley, Rabin and Freeman's results, they concluded that the non-optical factors must be the major contributors in production of aniseikonia.

It may be that whilst anisometropia exists in an individual, the visual system may adapt to the difference in retinal image size. In view of these findings the clinical management of axial anisometropia may need to be reviewed. If the ocular system has compensated for the anisometropia by having the larger retinal image fall on a similar number of receptors as the contralateral eye, then axial anisometropia may be better corrected with contact lenses than spectacles.

### 2.3 *Summary*

Reviewing the literature reveals no standard definition of anisometropia. Most frequently anisometropia is expressed in terms of an arbitrary difference in dioptric power between a pair of eyes.

The existence of two types of anisometropia can be deduced from the literature. One caused by temporal irregularities in the emmetropisation process. The other type appears to have a different origin, that is due to differences in axial length, and is persistent.

Despite substantial research in the field of human myopia, studies to date have provided only limited insight into the mechanisms underlying myopia development. It is known that a consistent feature of myopia is an increase in axial length that matches the dioptric error such that a 1 mm increase in axial length produces around 2 to 3D of myopia (Erickson, 1991; Grosvenor and Scott, 1993). The inter-eye refractive error discrepancy in anisomyopia is normally attributed to differences in axial length of the posterior vitreous chamber (Sorsby, Leary and Richards, 1962).

The reasons as to how or why anisometropia develops remain unclear. Studies on the prevalence and progression of anisometropia suggest that the condition does not develop in a consistent manner for all individuals. The crystalline lens appears to be involved in some cases, for example in those eyes which became more hyperopic over a period of time during which the contralateral eye became less hyperopic (Laird, 1991). There is also evidence which suggests that the lens was implicated in artificially induced anisometropia in animals (Hendrickson and Rosenblum, 1985; McKanna and Casagrande, 1981). However it is clear that in the majority of cases anisometropia results from differences in vitreous chamber depth. Much of the research into anisometropia has been concerned with cross-sectional studies which have been useful in ascertaining prevalence figures. These investigations are unable to provide information on growth patterns in anisometropia. The few longitudinal studies that have been completed suggest that anisometropia may be transient in infants (Almeder, Peck and Howland, 1990; Wood, Hodi and Morgan, 1995). If childhood anisometropia only exists temporarily as the eye develops then this finding questions the clinical judgement of correcting anisometropia in

children. In attempting to address this question particular attention should be given to the recent animal research on young monkeys by Hung, Crawford and Smith (1995) and Hung and Smith (1996) where correction of refractive errors impeded the normal emmetropisation process (see § 1.4.4a). Unfortunately if anisometropia is left uncorrected then the associated anomalies of amblyopia and strabismus may develop. Research has as yet been unable to clarify fully the cause and effect relationship between anisometropia, amblyopia and strabismus. Another clinical factor to be considered in correction of anisometropia is aniseikonia. It appears that the visual system adapts to the differences in retinal image size that occurs with anisometropia. These findings suggest that the clinical management of anisometropia needs to be reassessed.

# CHAPTER 3

# PERIPHERAL REFRACTION

### *Introduction*

Measurements of peripheral refraction have been found to correlate with ametropia. Various researchers have discussed to possibility of determining the shape of the retinal surface by measurement of peripheral refraction. However, no study has addressed the relationship between ametropia, peripheral refraction, retinal contour and biometric data.

## 3.1 *Aberrations of the eye*

The eye, in common with most refracting systems, is subject to a number of aberrations which affect the resolution and quality of the image formed. These aberrations include spherical aberration, chromatic aberration, coma, oblique astigmatism, field curvature and distortion (Charman, 1983). In the peripheral field, objects are imaged by obliquely incident rays of light which are limited principally by the pupil. Rays in the plane of oblique incidence converge first and produce tangential line foci and rays travelling at right angles to the plane of oblique incidence converge to produce sagittal line foci. For a given object distance, foci arising from pencils of light entering the eye from all directions lie on two curved surfaces referred to as the tangential and sagittal image shells (Dunne, 1995). The dioptric distance between the two image shells, denoted the interval of Sturm, specifies the amount of peripheral astigmatism for a specific field angle. For a typical human eye these image shells fall either side of the retina (Ferree, Rand and Hardy, 1931; Millodot, 1981) (see figure 3.1).

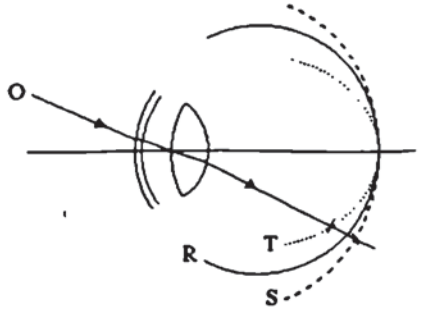



Figure 3.1 An oblique ray bundle, O, forming tangential, T, and sagittal images, after Dunne (1995).

Oblique astigmatism has been studied by various researchers both in human eyes, e.g. (Dunne and Barnes, 1990; Ferree, Rand and Hardy, 1931; Millodot, 1981) and in schematic eyes (Dunne and Barnes, 1987; Le Grand, 1967; Lotmar, 1971). Most peripheral refraction measurements have been obtained by retinoscopy or optometers. However, Millodot and Lamont (1974) also used a subjective method to measure peripheral astigmatism and found the results to agree

closely with objective measurements obtained from the same subjects. Their subjective method consisted of a bracketing technique using spherical lenses with the subjects viewing a Landolt C. Most measurements have been taken along the horizontal meridian although Rempt, Hoogerheide and Hoogenboom (1971) have also investigated peripheral refraction in the vertical meridian (see § 3.1.1).

### 3.1.1 *Measurements of peripheral astigmatism in real eyes*

In 1801, Young (1801) was the first to consider that light incident on the cornea and lens at an oblique angle would cause astigmatism. The first recorded measurements of peripheral astigmatism in the human eye has been attributed to Parent (1881, cited in Le Grand (1967)). He measured the amount of astigmatism by retinoscopy at eccentricities of 15° and 45° horizontally and found 0.50D and 2.75D respectively. Ferree, Rand and Hardy (1931) measured peripheral refraction in twenty-one eyes using a Zeiss refractometer. Measurements were taken in either 5° or 10° intervals along the horizontal meridian out to a maximum of 60° nasally and temporally. Peripheral refraction was represented pictorially and classified into three types.

### 3.1.1a *Classification of peripheral astigmatism*

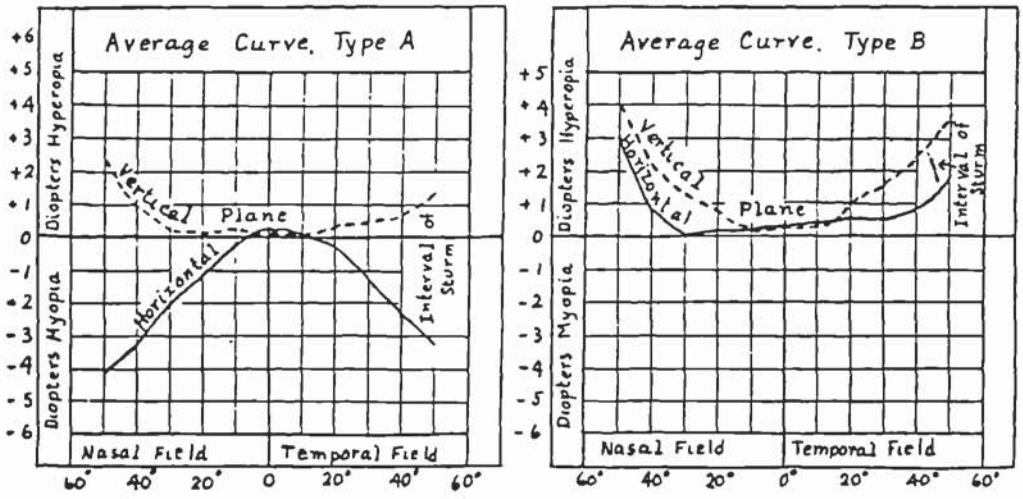



Figure 3.2 Showing the peripheral refraction types A and B after Ferree, Rand and Hardy (1931).

In type A, the horizontal meridian became more myopic with increasing eccentricity and the vertical meridian more hyperopic. The interval of Sturm varied over a large range of dioptres, for example, at an eccentricity of 50° the amount of astigmatism ranged between subjects from 2.50D to 8.75D. Of the 21 eyes examined, 12 had peripheral refraction of type A.

In type B, the eye became *less* myopic in the horizontal meridian with increasing field angle and more hyperopic in the vertical meridian. This type of peripheral refraction resulted in small intervals of Sturm, ranging only from 0.25D to 3.12D at an eccentricity of 50°. Type B peripheral refraction was found in 6 of the 21 subjects.

In the third type, type C, the peripheral refraction was asymmetrical with a considerable difference in the interval of Sturm between nasal and temporal meridia (Ferree, Rand and Hardy, 1932). Three eyes were recorded to have peripheral refraction of type C. Ferree, Rand and Hardy have postulated that the asymmetry in peripheral refraction between the nasal and temporal meridia may be due to i) asymmetry in the shape of the nasal and temporal halves of the eyeball, ii) asymmetry in position of the lens about the anteroposterior plane of the eye or iii) a combination of (i) and (ii).

Leibowitz, Johnson and Isabelle (1972) in an investigation of peripheral motion detection, measured peripheral refraction up to an eccentricity of 80° using retinoscopy. The three subjects in their study showed intersubject variation in peripheral refractive error, similar to the types of peripheral refraction demonstrated by Ferree, Rand and Hardy.

Rempt, Hoogerheide and Hoogenboom (1971) measured peripheral refraction in both eyes of 442 pilots by retinoscopy. Measurements were taken along the horizontal meridian at 0°, 20°, 40° and 60° eccentricity, in some cases refraction was also measured at 10°, 30° and 50°. Results were represented in a diagrammatic form, similar to that used by Ferree, Rand and Hardy which they named a skiagram. Peripheral refraction was measured to determine whether a correlation could be found between different types of skiagrams and central refraction. The skiagrams were classified into 5 types.

Type I exhibited a small interval of Sturm and showed peripheral refraction to become less myopic with increasing degrees of eccentricity. Type I was most frequently seen in myopic eyes, 91 (64.5%) of the 141 myopic eyes in the study had a type I skiagram.

Type II depicted peripheral refraction to become more hyperopic in the vertical meridian and remain relatively stable in the horizontal meridian.

Type III showed marked asymmetry in the peripheral refraction for nasal and temporal meridia and appeared to occur only in near emmetropic eyes. Rempt, Hoogerheide and Hoogenboom have described types II and III to be intermediate types of skiagrams.

Type IV showed the refraction in the horizontal meridian to become more myopic with increasing eccentricity whereas the refraction in the vertical meridian became more hyperopic. This resulted in a large interval of Sturm and thus a high degree of peripheral astigmatism.

Type IV was the most frequent type of skiagram to occur (50.9% of all eyes) and 62.2% of emmetropic eyes exhibited this type of skiagram. Type V was found only to exist in hyperopic eyes and showed peripheral refraction to become less hyperopic towards the periphery. In most cases both eyes had similar skiagrams. However, there were 20 pairs of eyes that exhibited different skiagrams for each eye, of these cases 14 were anisometropic. Another 9 anisometropes had similar skiagrams in both eyes.

Rempt, Hoogerheide and Hoogenboom also measured peripheral refraction in the vertical meridian in 7 eyes. In 4 cases where there was a symmetrical skiagram in the horizontal meridian, the skiagram in the vertical meridian was similar. The other 3 cases had an asymmetrical horizontal skiagram but depicted less asymmetry in the vertical meridian.

### 3.1.1b *Relationship between ametropia and type of skiagram*

Hoogerheide, Rempt and Hoogenboom (1971) followed the refractive development of 214 pilots over a number of years to assess the risk of development of myopia. They compared the type of skiagram found at the initial test to the final refractive error. It was assumed that the general appearance of the skiagram is inborn and that it does not change in type during a lifetime. Using the same classifications as Rempt, Hoogerheide and Hoogenboom (1971), they found that of the 160 emmetropic or hyperopic pilots that showed no myopic shift in refractive error, 66% had peripheral refraction skiagrams of type IV. Of the 28 pilots who were hyperopic and showed a refractive error shift towards myopia but remained either hyperopic or emmetropic, 40% belonged to type I. In 9 originally hyperopic pilots who became myopic, 45% had type I skiagrams. 77% of 17 emmetropic pilots who became myopic had type I skiagrams. From these results, Hoogerheide, Rempt and Hoogenboom concluded that the type of skiagram may indicate whether the refractive error will show a myopic shift.

Millodot and Lamont (1974) measured peripheral refraction in 3 subjects using three different techniques: retinoscopy, refractometry and a subjective method. Measurements were made in 10 intervals, along the horizontal meridian, to an eccentricity of 60° in the temporal field. They found retinoscopy readings to be unreliable beyond an eccentricity of 50°. However, the three techniques showed good qualitative agreement in peripheral refraction measurements. Millodot (1981) investigated the relationship between ametropia and the type and degree of peripheral refraction. A Topcon refractometer was used to measure refractive error in 10° intervals along the horizontal meridian in both eyes of 32 subjects. 30 eyes were myopic and ranged from -1.00D to -7.87D (spherical equivalent), 13 eyes were near emmetropic (-0.99D to +0.74D) and 19 eyes were hypermetropic ranging in refractive error from +0.75D to + 4.50D. Millodot found that the *amount* of astigmatism was not systematically different between the refractive groups. Peripheral astigmatism increased with eccentricity in 57 of the 62 eyes similar to type A that has been described by Ferree, Rand and Hardy (1931). The amount of astigmatism increased from 0D at the fovea to approximately 4D at an eccentricity of 60°. Peripheral astigmatism remained constant with increasing eccentricity in 5 eyes (type B) and 9 of the 62 eyes were classified as type C, where the amount of astigmatism differed considerably in the nasal and temporal meridia. Millodot found that the amount of astigmatism was almost independent of the central refractive error, however, the inter-subject variation in peripheral refraction was related to central ametropia. Charman and Jennings (1982) commented on Millodot's work and noted that the results were as expected. They postulated that as the differences in ametropia are principally due to differences in axial length then, assuming that the retinas of all eyes are at the same position at the equator of the globe, all eyes would have similar refractive errors at large peripheral angles.

### 3.1.2 *Measurement of Peripheral Astigmatism in Schematic Eyes*

Various researchers have determined theoretical peripheral astigmatism values using schematic eyes. A schematic eye is a model consisting of a centred system of spherical surfaces which represents the optical system of a normal eye based on average dimensions of the human eye. Many eye models have been produced as no single model can approximate all eyes due to the gradient index nature of the crystalline lens, individual variations in dimensions with age, and asymmetries in the ocular system.

Most schematic eyes have been small-angle paraxial models with restricted numbers of surfaces separating homogeneous optical media. The first accurate schematic eye has been attributed to Listing (1851, cited in (Smith, 1995)), whose model consisted of a single corneal surface and a homogeneous lens. Gullstrand's No.1 schematic eye had six refracting surfaces with a high index (1.406) homogeneous nucleus surrounded by a lower index (1.386) cortex. Data was given for both an unaccommodated and accommodated version of the schematic eye. Gullstrand also devised a simplified schematic eye (No. 2 eye) with one corneal and two lenticular surfaces (Emsley, 1963).

These paraxial models are unable to predict ocular aberrations or the performance of the eye away from the optical axis. More sophisticated models of ocular dioptrics have been designed which include aspheric surfaces and homogeneous media. Lotmar's (1971) four-surfaced schematic eye had aspheric anterior corneal and posterior lenticular surfaces. Drasdo and Fowler (1974) produced a wide-angle schematic eye model. It consisted of a single aspheric corneal surface and two spherical lens surfaces and was used to predict the projection of the visual field onto the retina.

An alternative approach to using aspheric surfaces was the use of non-uniform refractive indices in the lens. Pomerantzeff *et al.* (1972) devised a wide-angle model of the eye to include a lens cortex with 100 layers, to represent the eye's imaging properties on and off axis. Blaker, (1980) in an attempt to produce an adaptive model of the eye, developed a model in which the crystalline lens had a gradient-index structure. It was used to investigate the optical parameters of the eye in various states of accommodation, by defining an accommodative index.

*Theoretical values for peripheral astigmatism*

Theoretical values for peripheral astigmatism have been calculated in schematic eyes. Le Grand (1967) was interested in how the quality of the retinal image varied with eccentricity, that is the distance of the image from the fixation point. He calculated the amount of astigmatism in the periphery of the eye using a spherical three surfaced schematic eye. Astigmatism was calculated along the horizontal meridian in 10° intervals both nasally and temporally. The theoretical values ranged from 0D at 0° eccentricity to 11.29D nasally and 7.52D temporally at an eccentricity of 50°. The values derived for astigmatism were considerably greater than those obtained experimentally. Table 3.1 shows values for peripheral astigmatism, the calculated results are from

Le Grand (1967) and the experimental results are the mean values taken from the data by Ferree, Rand and Hardy (1931).

Table 3.1 Theoretical and experimental peripheral astigmatism (in dioptres), after Le Grand (1967).

| Eccen- | Sagittal Surface | | | | Tangential Surface | | | |
|---|---|---|---|---|---|---|---|---|
| tricity | Nasal side | | Temporal side | | Nasal side | | Temporal side | |
| deg | Calc. | Exptl. | Calc. | Exptl. | Calc. | Exptl. | Calc. | Exptl. |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 10 | 0.28 | -0.05 | 0 | 0.04 | -0.47 | -0.44 | 0 | -0.15 |
| 20 | 0.85 | -0.02 | 0.28 | 0.43 | -1.40 | -1.33 | -0.47 | -0.56 |
| 30 | 1.71 | 0.27 | 0.85 | 0.5 | -2.81 | -2.19 | -1.40 | -1.52 |
| 40 | 2.84 | 1.02 | 1.71 | 0.75 | -4.68 | -3.48 | -2.81 | -2.60 |
| 50 | 4.27 | 2.39 | 2.84 | 1.43 | -7.02 | -4.35 | -4.68 | -3.39 |

Measurements are in dioptres; calc, calculated; exptl, experimental.

Le Grand based his calculations on spherical surfaces, homogeneous indices of refraction and emmetropia. He suggested that the discrepancy in the theoretical and experimental results was either due to the peripheral flattening of the cornea and posterior surface of the lens or to the layered structure of the crystalline lens. Lotmar (1971) calculated peripheral astigmatism using a schematic eye with an aspheric corneal surface and an aspheric back surface of the crystalline lens. This schematic eye produced values for peripheral astigmatism that were much closer to empirical results, although still larger. Lotmar and Lotmar (1974) came to the same conclusion when they compared these calculations with the data from Rempt, Hoogerheide and Hoogenboom. The use of aspheric surfaces for the cornea and back surface of the lens reduced the discrepancy in empirical and theoretical values of peripheral astigmatism. Lotmar (1971) suggested that the residual difference indicates that the dioptric system of the eye may have some form of compensatory mechanism, such as peripheral flattening of the cornea or variations in the refractive index or curvature of the crystalline lens, to reduce peripheral astigmatism. However, Millodot and Lamont (1974) found no appreciable difference in peripheral astigmatism in real eyes when the aspheric cornea was fitted with a spherical contact lens.

### 3.1.3 *Modelling of peripheral astigmatism*

With regard to Millodot and Lamont's finding, Dunne and Barnes (1987) modelled peripheral astigmatism by manipulating crystalline lens curvature and refractive index in their schematic eye. A four-surfaced schematic eye with a two-surfaced, monoindical lens was derived and manipulated to produce the same amounts of peripheral astigmatism that is found in real eyes whose pupil dimensions, central refraction and biometry measurements are known. The

manipulation of the schematic eye involved the assumption of lens surface parameters which did not correlate with those of real eyes. This was more evident in eyes with low amounts of peripheral astigmatism, which occurs in many myopic eyes, where the astigmatism could only be modelled by the use of unrealistically flat aspheric lenticular surfaces. However, when the model was adjusted to produce correct amounts of peripheral astigmatism, overcorrection of spherical aberration resulted. An overestimation of spherical aberration also occurred with Lotmar's (1971) schematic eye and with the gradient index schematic eye of Pomerantzeff (1972). Dunne and Barnes concluded that both spherical aberration and peripheral astigmatism cannot be correctly modelled in schematic eyes at any one time. Kooijman's (1983) schematic eye has produced realistic values of peripheral astigmatism up to eccentricities of 30° along with correct values for spherical aberration.

Dunne and Barnes (1990) have expanded on the work of theoretical calculations of peripheral astigmatism in schematic eyes by modelling peripheral refraction which has been measured in eyes with known optical surface parameters. A three-surfaced schematic eye was derived using a computer scheme after Leary and Young (1968) and from measured ocular component data from individual eyes. Dunne and Barnes found that modelling peripheral astigmatism measured in eyes with known optical biometry, produced results that matched the upper limits of experimental data to eccentricities of at least 40°. They concluded that aspheric surfaces and monoindical crystalline lenses appear to model peripheral astigmatism adequately.

### 3.2 *Retinal shape changes in ametropia*

Ferree and Rand (1933) considered the position of the oblique astigmatic image shells to be affected by subtle changes in retinal shape. They discussed the possibility of determining the shape of the retinal surface by measurement of peripheral refraction. Charman and Jennings (1982) have also suggested that the variation in type of peripheral astigmatism as found by Rempt, Hoogerheide and Hoogenboom (1971) and by Millodot (1981) may be attributed to retinal shape differences. Charman (1983) suggested that the differences in the skiagrams of types II, IV and V found by Rempt, Hoogerheide and Hoogenboom, could be attributed to differences in the shape and position of the retina with the optical components having a constant form. Whereas, variations in the ocular components may account for the reduction in peripheral astigmatism in types I and III.

Dunne, Barnes and Clement (1987) attempted to correlate peripheral astigmatism with retinal shape. They devised a model for expressing retinal shape changes in ametropia. Their model, which incorporated an elliptical retinal surface of constant equatorial radius, produced the types of peripheral astigmatism that have been found experimentally.

### 3.3 *Determination of retinal contour*

Previous work on retinal shape changes in ametropia led Dunne (1995) to develop a computing method to determine retinal contour from peripheral refraction and biometry measurements

In summary, the program generates a spherical three-surfaced schematic model of the eye based upon a subject's keratometry, A-scan ultrasonography and central refraction data. The formulae used to generate the schematic eye have been taken from Bennett (1988) and Royston, Dunne and Barnes (1989). At each eccentricity at which peripheral refraction is measured, the asphericity of the cornea is adjusted until the calculated values of peripheral astigmatism match those measured. The retinal curvature is then adjusted until the calculated sagittal refractive error matches the measured value. Retinal surface co-ordinates are then derived for that specific field angle. The process is repeated for several field angles to produce a set of co-ordinates that describe retinal contour. However, to date, this technique has not been validated against *in vivo* methods of determining retinal contour.

Other methods have been described for measuring retinal contour. Hitzenberger (1991) has described the use of laser Doppler interferometry (LDI) to measure retinal shape *in vivo.* However, the measurements require conversion from optical to geometric lengths and the instrument is not commercially available. Schmid *et al.* (1994) have used a modified version of Hitzenberger's LDI to measure retinal shape in 6 eyes out to 20° nasally and temporally from the fovea. They found the retinal shape profiles to display considerable inter-individual variation. They suggested that these eye shapes may lead to a new classification of myopia. Cheng *et al.* (1992) have used high resolution magnetic resonance imaging (MRI) to measure ocular dimensions along the antero-posterior, equatorial and vertical axes. As MRI gives a cross-sectional image of the eye, it is theoretically possible to calculate the shape of the retina from the image. None of these studies have attempted to correlate retinal shape with refractive error and other biometric measurements.

### 3.4 *Summary*

Off-axis measurements of refractive error have demonstrated inter-individual variation in amount of peripheral astigmatism. These peripheral refraction measurements can be categorised according to the type of skiagram. Several studies have found that the skiagram correlated with central refractive error with the majority of myopes exhibiting different skiagrams to emmetropes.

Investigators have suggested that the shape of the posterior globe may be determined from peripheral refraction measurements. Dunne (1995) has developed a computing technique that derives retinal contour from ray-tracing formulae, schematic eye parameters and measured values of peripheral refraction and biometric data.

The computational technique has not been applied to subjects with a range of refractive error to correlate retinal shape with refractive and biometric data.

### 3.5 *Aims and objectives of the thesis*

The paucity of information concerning the nature of myopic eye growth in humans reflects, in part, the lack of suitable and accessible *in vivo* techniques. The thesis aims to apply a new and specially designed computational technique to derive retinal contour and thus eye shape using a population of anisometropes.

The literature has revealed that anisometropia arises in a pair of eyes with similar anterior segment components but with different vitreous chamber lengths. The aims of the thesis are to investigate further the nature of the biometric correlation with peripheral refraction and retinal contour in anisometropia. The contribution of corneal topography, accommodation and ultrasound data to the development of anisometropia will be assessed.

Factors to be considered in the aetiology of myopia development are intraocular pressure and choroidal blood flow. The thesis aims to assess these parameters with regard to a correlation between them and refractive error.

Racial differences in prevalence of myopia have been reported in the literature. The thesis examines two racial groups, Caucasians and Chinese, to ascertain any discrepancies between them.

The thesis aims to provide further insight into the growth of the eye in the development of myopia and provide suggestions for a new predictive factor for the development of myopia.

# CHAPTER 4

# INSTRUMENTATION AND SUBJECTS

Subject details are provided in Appendix 1. The subjects comprised 2 major groups, Caucasian and Chinese. The Caucasian subjects were recruited by screening the first year entrants to Aston University in October 1993 and 1995 and from the Optometry students. The Chinese subjects were mainly recruited from a private practice owned by a visiting lecturer to the Optometry School at Queensland University of Technology, Brisbane, Australia. The remainder of the Chinese subjects were students of Aston University. Ethical clearance was acquired for all experimental procedures and informed consent was obtained from all subjects prior to any experimental testing.

## 4.1 *Biometry measurements*

Ocular biometry, keratometry and refraction measurements were obtained on all subjects participating in the experimental programme. Each subject underwent an eye examination prior to any experimental procedures. The eye examination included cycloplegic retinoscopy with 1% tropicamide HCl (*Chauvin, Minims*), subjective refraction, oculomotor balance, ophthalmoscopy, slit-lamp examination, stereopsis and intraocular pressure measurements.

### 4.1.1 *Keratometry*

A keratometer is an optical instrument which measures the central radius of curvature of the anterior surface of the cornea, over an annular area of approximately 3 mm (Bennett and Rabbetts, 1989). The principle of the keratometer is based on the reflection by the anterior corneal surface, the first Purkinje image, of an illuminated pattern of known size. The size of the reflected image from the patterns, or mires, is measured and the radius of curvature calculated. The amount of corneal astigmatism present is the algebraic difference between the radii of curvature measured in the two principal meridians. The central radius of curvature is measured between two points on either side of the keratometer axis. The assumption is made that the surface between these two points is spherical. It is known that the normal cornea is not spherical but flattens off in the periphery.

The effect of eye movements on the results is reduced by a doubling system incorporated into the instrument. Conventional keratometers have been found to measure the sagittal radius of curvature (Douthwaite and Burek, 1995).

Typical keratometry values for a normal population range from 7.20 - 8.40 mm with a mean of 7.78 ± 0.25 mm (Guillon, Lydon and Wilson, 1986).

Keratometry readings were measured with a Zeiss keratometer. This instrument has variable doubling and is a 2 position keratometer. The optics of the keratometer include collimated mires and a telecentric system to eliminate errors due to poor focusing.

The keratometer was calibrated and the calibration checked periodically with ball bearings of known diameters. For each subject, three sets of readings were taken along the 2 principal meridians of each eye and the results averaged to give a mean and a tangential reading of corneal curvature.

### 4.1.2 *A-Scan ultrasound*

Ultrasonography is widely used as a diagnostic technique and in measurement of the ocular dimensions. Ultrasonic waves are generated by electrically stimulating a small transducer. These sound waves are reflected by interfaces where there is a change in density of the medium of the ocular components. The frequency of the sound waves is typically 10 - 20 Hz which is above the range of human audibility. Increasing the frequency improves the resolution and reveals thinner and more anterior structures. A lower frequency results in better penetration of the ocular media. The two methods most commonly used in ophthalmic applications are time-amplitude (A-scan) and intensity modulated (B-scan) ultrasonography. A-scan is one-dimensional whereas B-scan gives a two-dimensional image but with a decrease in resolution. A B-scan image of the eye is more difficult to interpret than an A-scan image. Axial dimensions of the eye are usually measured with A-scan ultrasonography. Four reflections are displayed on the oscilloscope; the first from the cornea, the second and third from the anterior and posterior surfaces of the crystalline lens respectively, and the fourth is a series of reflections from the internal posterior surface of the eye. The series of reflections result from the different layers of the retina. The 'elapsed' or total time taken by the ultrasonic wave reflected from an interface to return to its point of origin is converted to distance in millimetres, using the assumed velocities of sound in the ocular media. The assumed velocities will vary according to instrument used. The Storz Omega uses a velocity of 1550 mm $s^{-1}$.

Axial length was measured with a Storz Omega Compu-Scan Biometric Ruler (Storz International, St. Louis) using a solid tip, 10 MHz focused transducer. The instrument takes a series of 512 readings in 0.5s, the fast sampling time reducing the effects of eye movements. The assumed velocities of sound in the ocular media for the Storz Omega ultrasound are 1550 $mms^{-1}$.
The ultrasound instrument in addition to the axial length measurements, provides separate values for anterior chamber depth, lens thickness and vitreous chamber depth components.
Prior to ultrasound measurements, the A-scan probe was sterilised with an alcohol swab (*Medi-Swab*) and the subject's corneas were anaesthetised with topical instillation of 0.4% benoxinate HCl (*Chauvin, Minims*). The subject fixated a spotlight at a distance of 6m, as a spotlight or a Snellen letter viewed at 6m have been found to be the preferred fixation conditions for obtaining

accurate measurements (Steele, Crabb and Edgar, 1992). The effects of accommodation were minimised as the subject was cyclopleged with 1% tropicamide (*Chauvin, Minims*). The probe was hand-held and removed from the cornea between measurements to ensure that each measurement was distinct from the previous one. A minimum of 10 measurements were taken per eye. All measurement had a standard deviation of less than 0.1 mm, the instrument has an option for rejecting any readings with a standard deviation of 0.1 mm or greater, which was employed.

The calibration of the A-scan was checked periodically using the plastic calibration block supplied. No statistically significant difference in measurements for the first and last calibration checks was found.

Attempts were made to determine the shape of the eye with B-scan measurements. However, the exact orientation of the image was unknown making it impossible to obtain repeatable readings.

### 4.2 *Refractive error measurement*

A substantial part of the research in this thesis is based on the measurement of refraction both centrally and peripherally and for different conditions of accommodation. The experimental design required an objective method of measuring refractive error which would allow stimuli to be presented to the subjects in a range of different locations. Three different autorefractors were assessed. A Canon R-1, a Nidek AR 800 and a Hartinger optometer were used to measure refractive error centrally and at 15° and 30° both nasally and temporally in 5 subjects, which was repeated 5 times. The data are presented in Appendix 2. The Nidek is positioned very close to the subjects' eye and thus different fixation stimuli cannot be successfully introduced. The Hartinger is capable of moving around the subject in order to measure refractive error at different eccentricities. However, the experimental time is much greater than for automated instruments. The Canon R-1 was the autorefractor of choice as it provides a binocular open-field of view extending 18° vertically and 50° horizontally.

#### 4.2.1 *Infra-red optometers*

The first infra-red (IR) instrument capable of measuring objective refraction was designed by Collins (1937, cited in Bennett and Rabbetts, 1989) whose refractionometer forms the basis of more recent optometers. Collins' optometer assessed the quality of the retinal image by projecting it onto a negative mask, this had the effect of transmitting maximum light output when the quality of the image was optimal. The signal-to-noise ratio was increased by optical chopping of the retinal signal which produced an alternating current in comparison to direct current from extraneous sources. Charman (1976) has comprehensively reviewed the Collins optometer.

IR optometers have two main advantages over other optometers such as the Hartinger (Zeiss Jena). The measuring beam is invisible to the subject thus accommodation is controlled more easily and pupillary constriction is reduced by the absence of a bright target. Pupil constriction

results in an increase in depth-of-focus which may induce accommodative changes (Hennessy, 1975; Ward and Charman, 1985).

IR optometers are based on the principle of grating focus, retinoscopy or Scheiner disc. The grating focus principle is the most common technique employed. A grating target is illuminated by IR light and is imaged on the retina. The image reflected back from the retina is passed through a mask and the intensity detected. As the optimum focus of the retinal image is approached, the intensity of the reflected IR light increases. The Canon Autoref R-1 is based on this design.

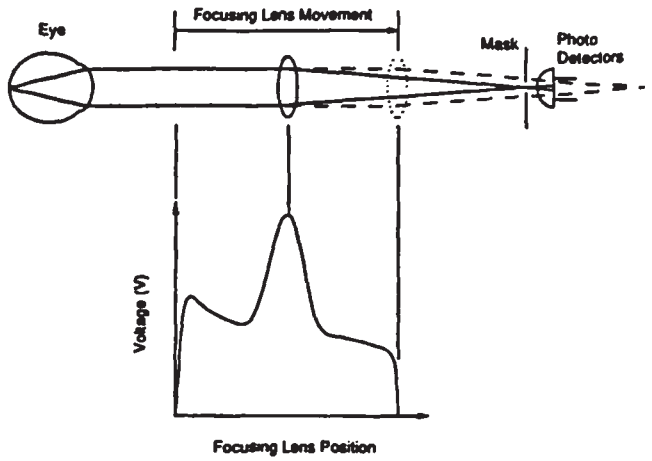



Figure 4.1 Figure on generation of Canon waveform after Davies *et al.* (1995).

#### 4.2.1a *The Canon Autoref R-1*

The Canon Autoref R-1 is an infrared (IR) autorefractor, although no longer manufactured, it was introduced by Canon Europa, Holland in 1981 to provide objective, static refractive error measurements of a clinical population.

A video camera transmits a magnified image of the subject's eye to a TV screen, which assists in alignment of the instrument and in checking fixation of the subject. An important feature of the instrument is the facility for good alignment. The alignment system of the Canon utilises a stationary, internal ring-shaped mark and the first Purkinje image from the subject's eye. The Canon was unique among other commercial autorefractors in that it provides a binocular open-field of view extending 18° vertically and 50° horizontally. This open-field minimises instrument myopia and is one of the major advantages of the Canon over other commercially available autorefractors (Hennessy, 1975). This feature has developed the Canon as a research instrument especially in the measurement of accommodation response, as an objective measurement of the ocular response to stimuli at specific distances from the eye can be made. Pugh and Winn (1988) have modified the Canon to provide continuous recordings of refractive error measurements. These modifications allow the focusing system to be disabled and adjusted manually. Manual adjustment of the lens results in a change in the vergence of light reaching the

photodectors which may be predicted from the lens position. In continuous mode of operation, the refractive error measurements are directly related to the magnitude of the output signal. The modification of a continuous mode of operation has enabled the microfluctuations in the accommodation response to be measured (Winn *et al.*, 1990).

The accuracy of the instrument in a clinical environment has been evaluated (Matsumura, 1983; McBrien and Millodot, 1985). The manufacturers claim an operating range of ±15.00 D for spherical power and ±7.00 D for the cylindrical. Power increments are in 0.12 D steps and cylinder axes in 1° steps. The measurement procedure is completed in 0.2 s and a sphero-cylindrical measure of the subject's refractive error is displayed on the TV monitor and can be printed onto heat sensitive paper.

#### 4.2.1b *Mode of operation*

The Canon operates on the principle of grating focus (Matsumura, 1983). A square-wave grating is imaged on the subject's retina while focusing lenses are driven along the optical axis of the measurement system. Maximum output of the photodetectors is obtained when the retinal image is optimally in focus and the time taken for the output to reach a maximum is measured, this time is then converted to a dioptric value of refractive error. The Canon simultaneously measures in three meridians separated by 60°, using three sets of photodetectors. The signal is transformed into a d.c. voltage waveform using signal conditioning circuitry. The relative location of the maximum voltage peak from each photodetector occurs for the position of best-focus of the reflected beam on the detector masks. The Canon calculates a sphero-cylindrical measure of refractive error using algorithms described by Matsumura *et al.* (1983).

All IR optometers have a limiting pupil diameter, the manufacturers of the Canon have specified a minimum of 2.9 mm in the static mode of operation. For continuous recording a minimum pupil diameter of 3.8 mm is required. For diameters greater that 2.9 mm, the instrument has the advantage of being pupil independent in its static mode of operation, as it uses *relative* location rather than magnitude of each peak photodetector output to calculate refraction.

As the pupil diameter reduces to less than 2.9 mm, the signal returning from the eye becomes too attenuated to give a reliable measurement of refractive error (see § 4.2.2). For pupil diameters less than 2.9 mm, the Canon is unable to locate the position of the position of maximum output for the three photodiodes and an error reading is obtained (Winn *et al.*, 1989).

### 4.2.2 *Peripheral Refraction*

The Canon was modified to measure peripheral refraction by the addition of an arc placed horizontally on top of the main body of the instrument at a distance of 50 cm from the subject's eyes. Fixation targets were coloured spots set at 5° intervals along the arc to a maximum of 40° both nasally and temporally.

It is documented (Winn *et al.*, 1989) that the signal returning from the eye to the Canon becomes attenuated as the pupil diameter approaches the minimum limiting level (see § 4.2.1b). Whether a similar effect occurs as angle of eccentricity increases was investigated. The gradient of the output of one photodiode was calculated for each angle at which peripheral refraction was measured. The results indicate that the peripheral refraction measurements are real and are not an artefact from an attenuated signal (see Appendix 3).

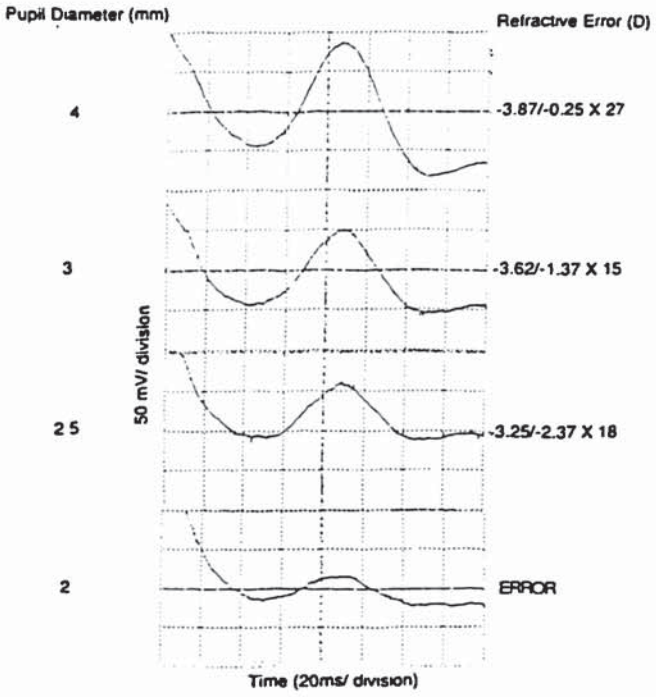



Figure 4.2 Pupil size and output of Canon, after Winn *et al.* (1989).

### 4.2.3 *Accommodation*

Amplitude of accommodation was measured using a high contrast (90%), black-on-white nearpoint card, with 6/9 print. The nearpoint card was mounted at eye level on an optical bench with the subject positioned on a chinrest at one end of the optical bench. Both push-up and push-down methods were used to assess the amplitude of accommodation (Rosenfield and Cohen, 1995).

Objective measurements of accommodation were obtained with the Canon, utilising the open field-of-view design of the instrument, and a Badal system.

A minimum pupil diameter of 2.9 mm is required for the Canon to calculate accurate refractive errors. In young eyes near vision tasks normally cause a reduction in pupil diameter as accommodative demand increases. This reduction in pupil diameter limits the accommodative demand that can be imposed on subjects. An error reading is obtained with the Canon if the accommodation level is such that the associated pupil constriction results in a pupil diameter that

is less than the limiting level of the instrument. Careful selection of subjects along with manipulation of lighting levels and level of accommodative stimulus can maintain pupil diameters above 2.9 mm. The use of mydriatic drugs to increase pupil diameter is undesirable as they can have unpredictable effects on the accommodation mechanism. Cyclopentolate HCl 0.1% (*Chauvin, Minims*), an anti-muscarinic, has been found to reduce the steady-state accommodation response at all stimulus levels (Mordi *et al.*, 1986). Amplitude of accommodation has been recorded to be reduced by approximately 1.39D (11%) with the instillation of phenylephrine 2.5%, a sympathomimetic (Gimpel, Doughty and Lyle, 1994).

An interface (designed and distributed by Steve Spadafore, Franklin and Marshall College, PO Box 3003, Lancaster, PA 17604) was used to connect the printer port of the Canon to a Macintosh Classic computer in order that the refraction data could be measured and recorded successively.

### 4.3 *Fundus morphology*

Fundus morphology changes in the myopic eye are well documented (Curtin, 1985). The myopic eye is often associated with scleral crescents, generalised tessellation, choroidal atrophy, pallor of the fundus and posterior staphylomae. An objective method of recording the image of the fundus was required to quantify morphological changes with refractive error. The technique of scanning laser ophthalmoscopy was employed to provide a computerised method of recording and analysing the data.

#### 4.3.1 *Scanning laser ophthalmoscopy*

The first scanning laser ophthalmoscopes were developed more than 15 years ago (Webb, Hughes and Pomerantzeff, 1980). They used two-dimensional scanning to project a rectangular line pattern on the retina. More recent developments incorporate additional scanning detection and a confocal optical system (Webb, Hughes and Delori, 1987). The scanning laser ophthalmoscope (SLO) was originally designed to image the fundus with much lower levels of illumination than with conventional means of viewing the fundus. The maximum irradiance at the retina being approximately one-hundredth of the irradiance of a fundus camera eliminating the requirement for dilation. Since the development of the SLO it has found many and varied uses including imaging of the fundus, microperimetry and electrophysiology (Mainster *et al.*, 1982) and assessment of reading performance in patients with low vision (Culham *et al.*, 1992).

#### 4.3.2 *Heidelberg Retina Tomograph*

The Heidelberg Retina Tomograph (Heidelberg Engineering, Heidelberg, Germany) is a confocal scanning laser ophthalmoscope developed mainly for the study of the optic nerve head with special reference to glaucoma (Burk, Roherschneider and Volcker, 1990). The Heidelberg Retina Tomograph (HRT) was designed for three dimensional imaging and three dimensional

measurements of the posterior segment of the eye *in vivo* . By using a confocal imaging system, the illuminated light source is focused to a single point of the object being examined. A confocal imaging system permits only light from the point illuminated to be detected, any light from out-of-focus planes or scattered light are suppressed. The light source used in the HRT is a laser operating at a wavelength of 670 nm.

Single two-dimensional section images are recorded and digitised in a 256 x 256 pixel frame and displayed in real time on the computer monitor. The scanned field can be set to 10 x 10, 15 x 15 or 20 x 20 degrees in size. The focal plane location can be varied between -12 D to +12 D in 0.25 D increments. Outside of this range images may be taken through the patient's spectacles. A three-dimensional image of the retina is scanned and recorded as series of 32 section images at 32 different focal planes. The depth over which the 32 images extends can be adjusted between 0.5 mm and 4.0 mm in 0.5 mm increments. The time taken for acquisition of a complete series is 1.6 seconds. The maximum irradiance at the retina is 0.5 mW/cm.

Image analysis is performed using the software of the computer system. The topography image is determined from the original data and eye movements are automatically compensated by the software by aligning the bifurcations of the blood vessels. The topography image consists of 256 x 256 picture elements each of which represents an individual height measurement at the corresponding location. The properties of the individual eye examined are used to calibrate absolute values for the height measurements. The topography image is the basis for analysing the properties of the structure scanned. Data analysis options include planimetric and stereometric measurements and analysis of topographic changes of the structures examined.

### *4.3.3 Heidelberg Retina Flowmeter*

The Heidelberg Retina Flowmeter (Heidelberg Engineering, Heidelberg, Germany) is a non-invasive method for assessing retinal blood flow. Heidelberg Retina Flowmeter (HRF) combines the techniques of confocal laser scanning and laser Doppler flowmetry.

The retina is scanned using an infrared laser, with a wavelength of 780 nm, in two dimensions. The frequency of the light reflected form moving red blood cells is shifted due to the optical Doppler effect and interferes with light reflected from stationary objects. The HRF measures the variation in light intensity through time at each point in a two dimensional field by multiple scanning. The frequency shift is computed and used as a measure of the amount and velocity of retinal blood cells.

Measurements of retinal blood flow were obtained from 2 subjects. However, the results were difficult to interpret (see Appendix 11).

## 4.4 Topographic Mapping System

Corneal topography instruments are generally used in a clinical environment to assess corneal changes after refractive surgery, corneal graphs and disease and in the fitting of contact lenses (Stevenson, 1992).

Corneal topography systems are based on the principles of keratoscopy. Keratoscopy consists of examining the reflection by the cornea of a pattern of alternating black and white concentric rings. The advent of computer-assisted photokeratoscopy have computers to analyse the photographed keratoscopy data. These instruments are generally known as corneal topography systems. Examples of commercially available systems are the EyeSys 2000 Corneal Analysis System (EyeSys Laboratories, Houston, TX, USA) and the TMS-1 (Computer Anatomy Inc., New York NY, USA). Corneal topography systems are able to generate corneal curvature measurements over both central and peripheral areas of the cornea which provides a more comprehensive description of corneal curvature. The computer algorithms produce a map of the corneal surface. A colour coding scheme is usually applied to these maps with different corneal powers represented by different colours, blue denoting low powers and red indicating high powers (Maguire, Singer and Klyce, 1987). Other measurements such as simulated K readings, the major astigmatic meridians and actual dioptric power measurements at each point.

Both the EyeSys and TMS-1 corneal topography systems have been used to assess corneal curvature in this thesis. The EyeSys measures corneal curvature at 16 positions along each of the 360 semi-meridians, whereas the TMS-1 instrument measures the curvature at 25 points along each of the 256 semi-meridians.

### 4.5 Ocular Blood Flow

The ocular blood flow (OBF) tonograph (OBF Labs, Cleverton, UK) is a non-invasive, objective method of measuring ocular blood flow. The OBF measures pulsatile choroidal blood flow. The pulsatile flow represents 75 to 85% of the total choroidal blood flow (Langham *et al.*, 1989; Riva *et al.*, 1994) and thus is a reliable parameter for evaluating choroidal circulation.

The OBF system allows continuous measurement of intraocular pressure (IOP) using a pneumatonometer described by Langham (1978). An air flow circulates in the probe, the contact end of which is a distensible film. A cyclic variation in IOP occurs, the ocular pulse, with each contraction of the heart. The distensible film moves in response to the ocular pressure and consequently alters the flow of air in the probe. These changes in air flow due to the ocular pulse are recorded and digitised by the computer software to generate pulses.

The pulsatile choroidal blood flow is calculated from the pulsatile variations in IOP, the pulse volume, and the heart rate. Several assumptions exist in the calculation of the OBF: 1) the outflow of blood from the eye is steady and non-pulsatile, 2) no reflux of blood occurs, 3) the blood vessels do not collapse, and 4) the IOP is recorded correctly and is transferred into a volume (Krakau, 1992).

Impaired vascular circulation is believed to be involved in pathology of the retina, the optic nerve head and the choroid (Langham *et al.*, 1991; Langham and Krammer, 1990). Research has indicated that the choroidal circulation is reduced in eyes with long axial lengths i.e. myopic eyes (James *et al.*, 1991).

### 4.6 *Drugs utilised in the experimental procedures*

The anti-muscarinic tropicamide HCl 1% (*Chauvin, Minims*) was used to provide cycloplegia and mydriasis in all subjects. Dilation was required to obtain peripheral refraction measurements. Ultrasound measurements were performed under cycloplegia to prevent an error in the lens thickness data arising from a lens which was accommodating.

Benoxinate HCl 0.4% (*Chauvin, Minims*) was the topical anaesthetic used for ultrasonography and ocular blood flow measurements.

# CHAPTER 5

# BIOMETRIC CORRELATES IN ANISOMETROPIA

## 5.1 *Introduction*

It is well documented that off-axis measurements of refractive error differ considerably from refractive measurements made along the optical axis (see § 3.1.1). The amount by which the off-axis refraction differs from that measured centrally depends upon the degree of eccentricity from the fixation point (Ferree, Rand and Hardy, 1931; Rempt, Hoogerheide and Hoogenboom, 1971). The graphical representation of sagittal and tangential refractive error against degree of eccentricity has been termed a skiagram by Rempt, Hoogerheide and Hoogenboom (1971). Peripheral refraction measurements were first classified into three different types according to amount of oblique astigmatism by Ferree, Rand and Hardy (1931). Rempt, Hoogerheide and Hoogenboom extended this work and further classified peripheral refraction measurements into 5 types of skiagrams (see § 3.1.1a). Various researchers have attempted to correlate the type of skiagram with refractive error (Hoogerheide, Rempt and Hoogenboom, 1971; Millodot, 1981). It has been demonstrated that type I skiagram (after Rempt, Hoogerheide and Hoogenboom), which depicts low amounts of peripheral astigmatism, is associated with myopic refractive errors. Whereas a skiagram of type IV, having a large interval of Sturm peripherally, has been found to correlate with emmetropia.

Ferree and Rand (1933) suggested that it may be possible to describe the shape of the retinal surface from measurements of peripheral refraction (see § 3.2). Dunne (1995) developed this proposal to derive a computing method to determine retinal contour shape from peripheral refraction and biometry measurements (see § 3.3).

*Purpose of present study*

It is widely known that the dioptric error in myopia is correlated with an increase in the axial length of the eye (see § 1.3). It is not known whether equatorial dimensions of the eye are likewise correlated with myopia. In anisomyopia, the discrepancy in inter-eye refractive error can normally be attributed to differences in axial length of the vitreous chamber. The present study has measured peripheral refraction and biometric data in both anisometropes and isometropes to derive retinal contours for both eyes of the subjects. Anisometropic subjects have been used in this study as they offer an unique opportunity to investigate the potential for differences in ocular components in eyes with a significant difference in refractive error. The difference in refractive error encountered in an anisometropic individual is greater than the degree of myopia which could be expected to occur in a longitudinal study over a period of three years. The

environmental influences which have been encountered by the subject are assumed to be constant for both eyes. By comparing right and left eyes, differences in ocular components may be assessed without consideration of intersubject variability arising from different environmental factors.

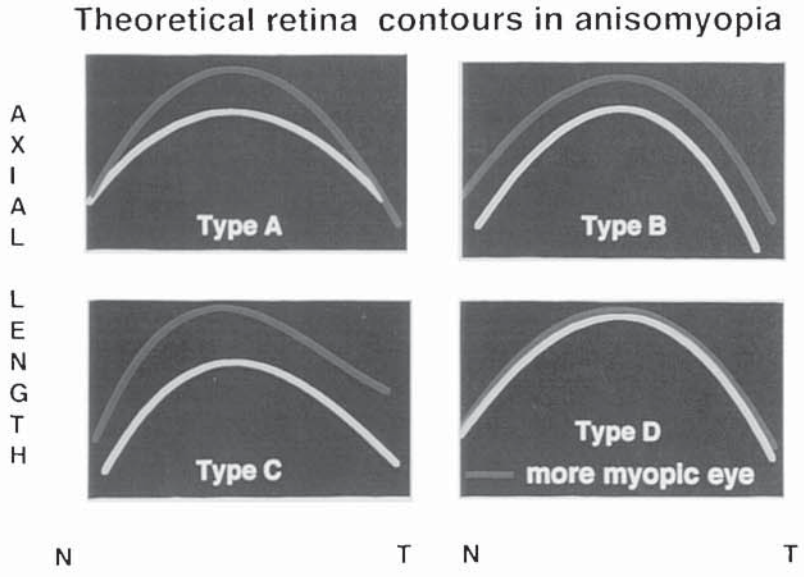



Figure 5.01 Theoretical retinal contours in anisometropia.

There are four possible profiles of retinal contour that may be envisaged in anisometropia (figure 5.01). 1) axial elongation only of the vitreous chamber in the more myopic eye with intersection of the two retinal contours in both nasal and temporal peripheral loci (type A); 2) the more myopic eye showing both longitudinal and transverse symmetrical expansion in the vitreous chamber i.e. overall expansion of the globe (type B); 3) some form of asymmetrical growth could occur in the more myopic eye with intersection of the two retinal contours in either the nasal or temporal periphery with no intersection of the peripheral retinal contours in the other half of the retina (type C); 4) the anisometropia may be refractive in nature and thus similar retinal contours may be found in both eyes (type D).

The present study uses Dunne's (1995) computing technique on a number of anisometropic subjects to ascertain the distribution of the shape of the retinal contours with regard to the categories above. Comparison of right and left eye retinal contours in anisometropes may lead to a better understanding of the growth of the eye in myopia.

*Ocular component analysis by vergence contribution*

Ocular components are traditionally expressed in surface powers and their axial separations in the eye. The differences in nomenclature used to assess the ocular components leads to difficulties in assessing their contribution to the total refractive system of the eye. Leary (1981) suggested a

method to determine the contribution of each ocular component by expressing it as a percent of the back vertex power of the anterior segment of the eye. He calculated back vertex power by ray-tracing a wavefront through the eye from the cornea and establishing the change in vergence through the each ocular component. This method did not account for the effects of vitreous chamber depth and Erickson (1984) has devised an alternative vergence method to incorporate the effects of vitreous chamber depth. Erickson's method traced the wavefront from the eye's far point rather than from optical infinity as suggested by Leary. Including the effect of the vitreous chamber depth causes a dampening effect on the other ocular components.

## 5.2 *Methods*

*Subjects*

The subjects used in the study were either of Caucasian or Chinese origin. Data from these two groups were analysed separately. The majority of the Chinese subjects were examined at Queensland University of Technology, Brisbane, Australia, following a research fellowship award. In Brisbane there is a large immigrant Chinese community with a prevalence of anisometropia of approximately 20% compared with a 2.5% prevalence in the UK. All other subjects were examined at Aston University, Birmingham, UK. The subjects were classified according to their interocular difference in refractive error. Anisometropia was defined as an inter-eye refractive error difference of 2D or more, spherical equivalent. Isometropia was defined as a interocular refractive error difference of 0.50D or less, spherical equivalent. All subjects had less than 2D of astigmatism, the majority had less than 0.75DC. They were all non-strabismic and had some degree of binocularity and no amblyopia. None of the anisometropia was secondary to ocular disease. Age range of subjects was 15 to 26 years.

The subject numbers totalled 20 Caucasian anisometropes, 20 Caucasian isometropes, 20 Chinese anisometropes and 20 Chinese isometropes.

The control isometropic group matched the anisometropes for age, and range of refractive error. The ratio of male to female was similar in both groups.

The Caucasian anisometropic group included 12 anisomyopes, 4 anisohyperopes and 4 antimetropes. Whereas the Chinese anisometropes were all anisomyopic.

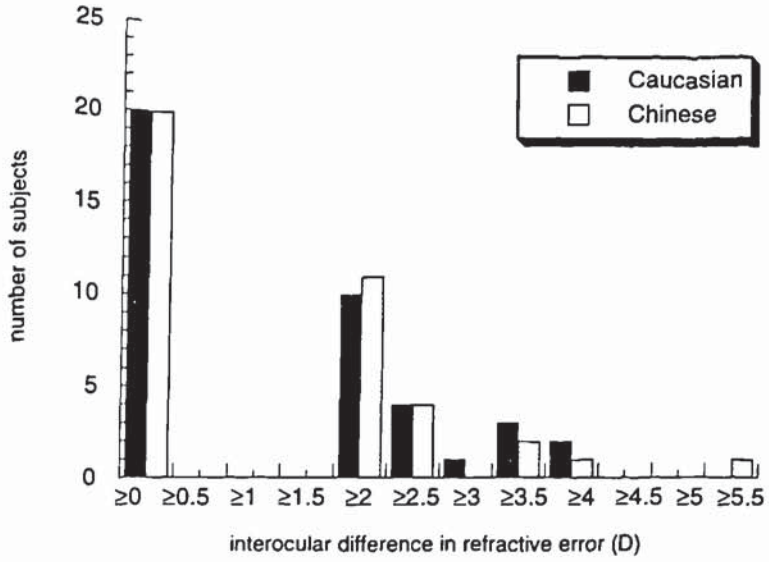



Figure 5.02 Histogram showing the distribution of interocular difference in refractive error in both the Caucasian and Chinese subjects.

*Experimental procedure*

A full optometric eye examination was carried out prior to experimental testing (see § 4).

Central and peripheral refraction, A-scan ultrasound and keratometry measurements were obtained on both the right and left eyes of all subjects. Cycloplegia and mydriasis were induced by topical installation of 1% tropicamide (*Minims*, Chauvin Pharmaceuticals). Both refraction and ultrasound data were obtained under cycloplegia. An initial base-line measurement of accommodation was made using a push-up rule prior to the instillation of tropicamide. The depth of cycloplegia was assessed by monitoring the reduction in amplitude of accommodation.

Central and peripheral refraction were measured with a Canon R-1 open-field objective IR autorefractor (see § 4.2). Data was obtained centrally and along the horizontal meridian at 5° intervals out to 35° both temporally and nasally. The fixation targets were alternate orange and yellow coloured spots set in an arc in 5° intervals at a distance of 50 cm from the subject's eyes. The subject's head was secured in place by the head and chin rests of the autorefractor and by a strap attached to its headrest. Subjects were instructed to change fixation by movement of their eyes only. A minimum of 5 readings were taken at each fixation point. An interface (designed and distributed by Steve Spadafore, Franklin and Marshall College, PO. Box 3003, Lancaster, PA 17604, USA.) was used to connect the printer port of the Canon to the Macintosh Classic computer in order that the refraction at each fixation point could be measured and recorded successively. The data for each fixation point was averaged and values for sagittal refractive error and interval of Sturm were calculated.

Biometric measurements of the ocular components were taken with a Storz Omega ultrasound device (Storz International, USA). The fixation target was a spotlight placed at a distance of 6m (, 1992). A focused, solid tip, 10 MHz probe was used. Benoxinate HCl (0.4%) was the topical anaesthetic used prior to the ultrasound measurements. A minimum of 10 readings with the A-scan were obtained. Any measurements with a standard deviation greater than 0.1 mm were discarded in accordance with the recommendations of the operation manual. Corneal curvature was measured using a keratometer, with three readings taken along each principle meridian. The instrument used for the Caucasian subjects and the Chinese subjects examined at Aston University was a Zeiss keratometer. The measurements taken from the Chinese subjects examined at QUT, Brisbane were made with a Bausch and Lomb keratometer.

The mean value for each measured parameter was used as the input data in the retinal contour computer program. Details of the individual biometric data are given in Appendix 3.

Repeatability of this technique has been assessed by repeating the measurement cycle 10 times on both eyes of one anisomyopic subject. Each measurement cycle consisted of keratometry, A-scan ultrasonography and central and peripheral refraction. There was a minimum of 30 min between each measurement cycle and a maximum of 1 week.

### 5.3 *Results*

Data was analysed in order to compare the ocular components, peripheral refraction and retinal contours. The retinal contours were generated using Dunne's computing scheme (1995), (see § 3.3). For one anisomyopic subject 10 retinal contours were derived for both the right and left eyes and standard deviations from the mean were calculated.

*Biometric measurements*

The mean ocular component measurements for the right eye are reported in Table 5.1.

Right and left eye results have been analysed separately to eliminate any effect of inter-eye correlation that may occur between a pair of eyes (Ray and O'Day, 1985).

Results from ultrasonography show that the anterior chamber depth and lens thickness are similar in both the Caucasian and Chinese eyes. The data shows that the Chinese subjects have a more myopic mean refractive error than the Caucasian subjects. This finding is reflected in the axial lengths of the 2 races with the Chinese having a longer axial length.

Table 5.1 Mean biometric measurements for both eyes of the Caucasian and Chinese subjects.

| | Caucasian | | Chinese | |
|---|---|---|---|---|
| Ocular component | R | L | R | L |
| Rx (D) | -2.05 (± 3.37) | -2.18 (± 3.17) | -4.73 (± 3.02) | -4.74 (± 3.10) |
| AL (mm) | 24.19 (± 1.50) | 24.22 (± 1.39) | 25.26 (± 1.33) | 25.37 (± 1.39) |
| ACD (mm) | 3.69 (± 0.18) | 3.70 (± 0.17) | 3.79 (± 0.11) | 3.70 (± 0.15) |
| LT (mm) | 3.60 (± 0.15) | 3.59 (± 0.15) | 3.55 (± 0.24) | 3.54 (± 0.24) |
| VCD (mm) | 16.77 (± 1.36) | 16.79 (± 1.30) | 17.92 (± 1.32) | 18.13 (± 1.45) |
| CR (mm) | 7.66 (± 0.29) | 7.66 (± 0.28) | 7.73 (± 0.31) | 7.73 (± 0.30) |

Rx, refractive error; AL, axial length; ACD, anterior chamber depth; LT, lens thickness; VCD, vitreous chamber depth; CR, corneal radius; ± equals standard deviations.

The scatterplot in figure 5.03 shows a significant correlation between refractive error and axial length for the right eyes of both the Caucasian ($r^2 = 0.72$, $p < 0.001$) and Chinese ($r^2 = 0.51$, $p < 0.001$) subjects.

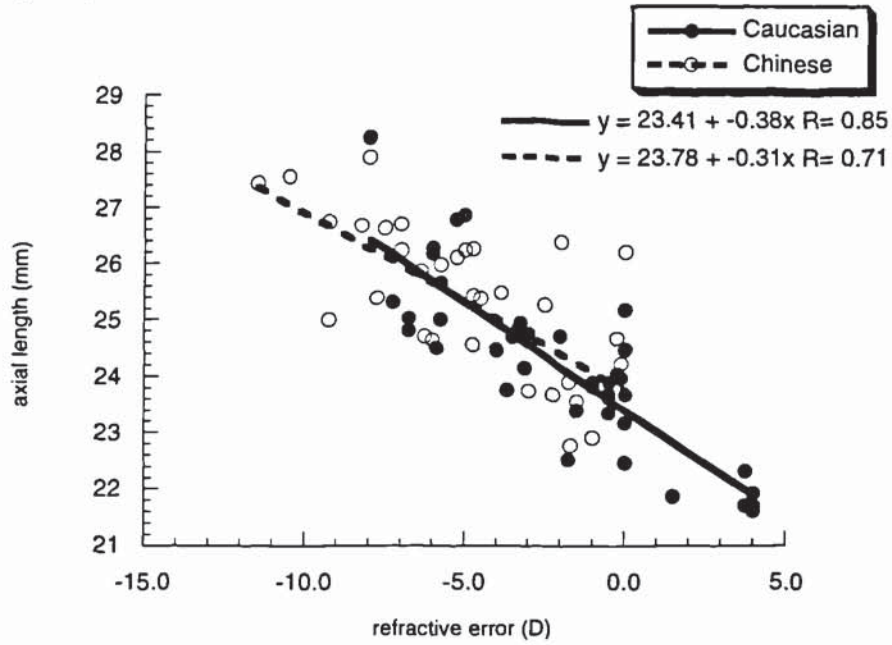



Figure 5.03 Shows axial length plotted against refractive error for the right eyes of both the Caucasian and Chinese subjects.

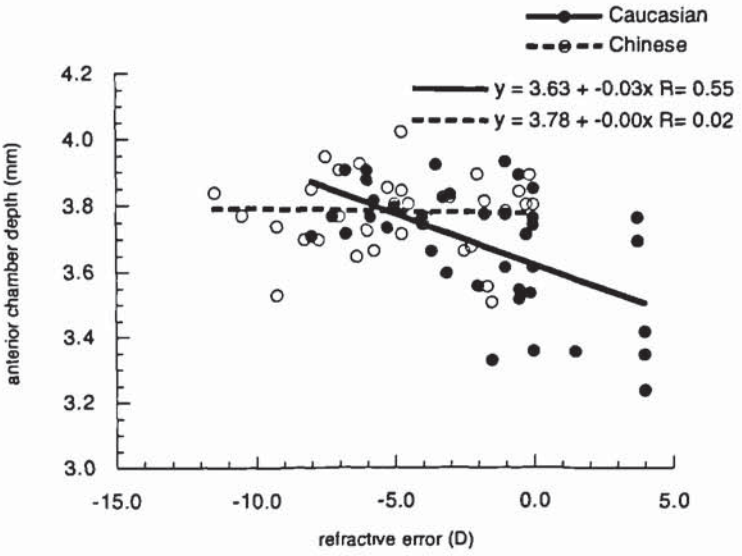
Figure 5.04 shows anterior chamber depth, lens thickness and vitreous chamber depth plotted against refractive error for the right eyes of both the Caucasian and Chinese subjects.

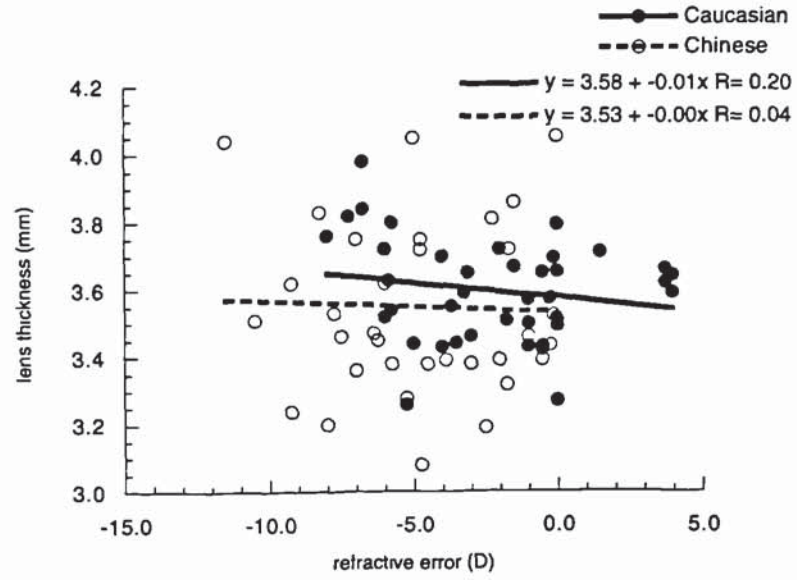
A weak correlation was found between anterior chamber depth and refractive error for the Caucasian subjects ($r^2 = 0.30$, $p < 0.001$) but no correlation was evident for the Chinese subjects ($r^2 = 0.0005$, $p > 0.50$), (see figure 5.4a). Figure 5.4b indicated that no correlations were found for lens thickness and refractive error for either the Caucasian subjects ($r^2 = 0.04$, $p > 0.50$) or the Chinese subjects ($r^2 = 0.002$, $p > 0.50$). As expected correlations were evident between vitreous

chamber depth and refractive error for both the Caucasians ($r^2 = 0.65$, $p < 0.001$) and Chinese ($r^2 = 0.51$, $p < 0.001$). This relationship is shown in figure 5.04c.

The differences in corneal curvature with refractive error have been assessed in Chapter 6.

Figure 5.04 Ocular components plotted against refractive error for both Caucasian and Chinese subjects. Figure 5.04a shows the anterior chamber depth against refractive error. Figure 5.04b shows the lens thickness against refractive error. Figure 5.04c shows vitreous chamber depth against refractive error.



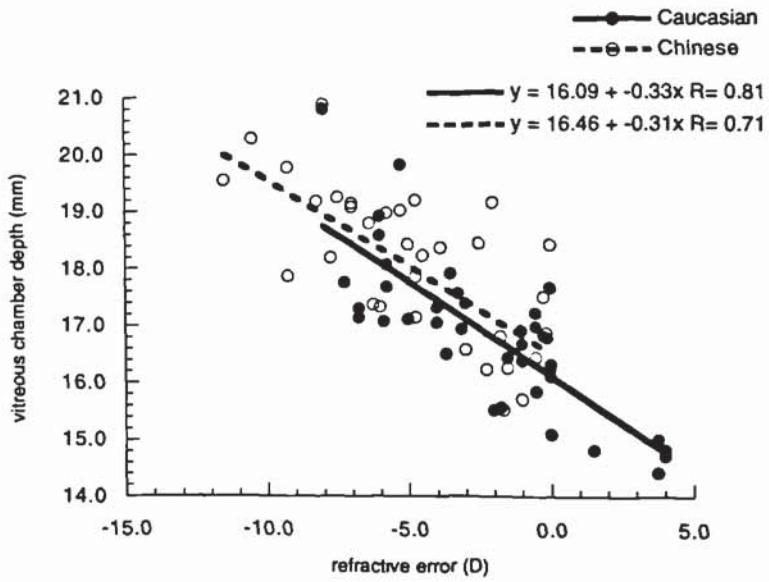
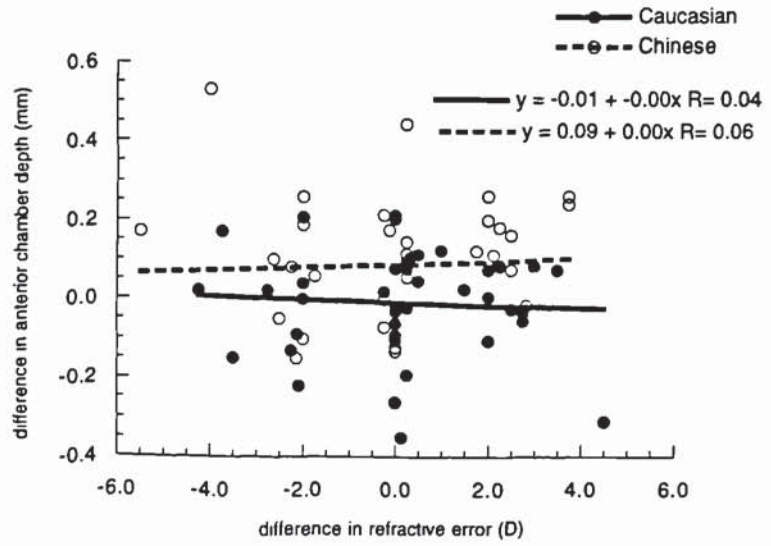
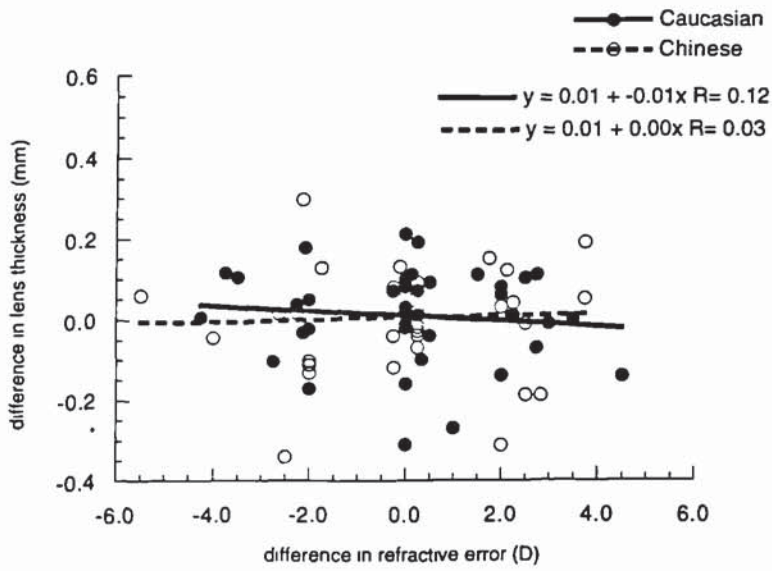
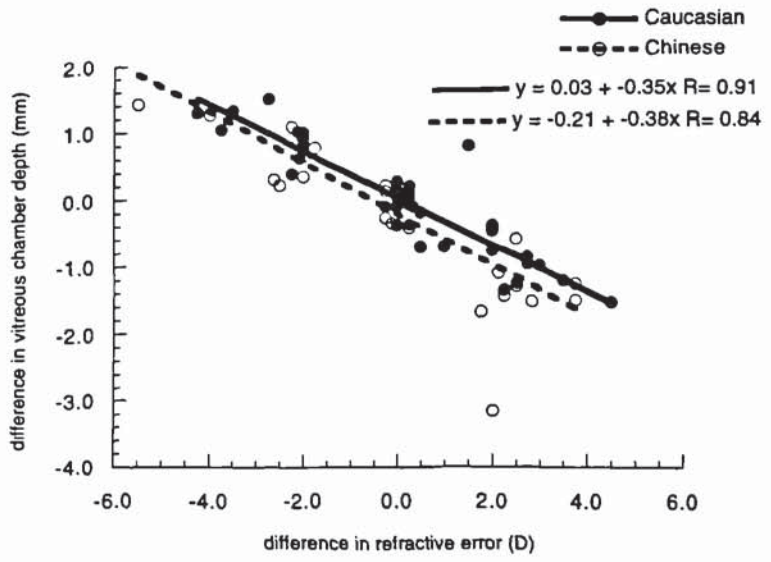



Figure 5.05 Interocular differences in ocular components plotted against inter-eye differences in refractive error for both Caucasian and Chinese subjects. Figure 5.05a shows the anterior chamber depth against difference in refractive error. Figure 5.05b shows the lens thickness against difference in refractive error. Figure 5.05c shows vitreous chamber depth against difference in refractive error.



*Interocular differences in biometric parameters*

Figure 5.05 shows the relationships between interocular differences in refractive error and inter-eye discrepancies in anterior chamber depth, lens thickness and vitreous chamber depth. No correlations were found between interocular differences in anterior chamber depth and refractive error for either the Caucasian ($r^2$ = 0.002, p >0.50) or Chinese subjects ($r^2$ = 0.004, p > 0.50). Similar results were found for interocular differences in lens thickness compared to inter-eye differences in refractive error for the Caucasian ($r^2$ = 0.01, p > 0.50) and Chinese subjects ($r^2$ = 0.001, p > 0.50). As evident in figure 5.5c there was a correlation between interocular differences in vitreous chamber depth and refractive error for both the Caucasian ($r^2$ = 0.83, p < 0.001) and Chinese subjects ($r^2$ = 0.71, p < 0.001). As expected significant correlations were found between interocular difference in refractive error and inter-eye difference in axial length ($r^2$ = 0.87, p < 0.001) for the Caucasian subjects and ($r^2$ = 0.67, p < 0.001) for the Chinese.

*Ocular component analysis by vergence contribution*

In order to allow comparison of the contribution of the individual ocular components to the total refractive system, the ocular components have been assessed in terms of ocular vergence (Leary, 1981; Erickson, 1984). The vergence contribution of the ocular components has been assessed using a computer programme based on Erickson's method (1984). However the current programme assesses the lens contribution in terms of Bennett's equivalent lens (1988). The computer programme used is shown in Appendix 4.

Table 5.2 shows the inter-eye differences in vergence contributions in dioptres and percent of the ocular components for both Caucasian anisometropes and isometropes. The results represent the more myopic eye minus the least myopic eye. Data for Chinese eyes is shown in Table 5.3. The mean interocular difference in refractive error for the Caucasian subjects was 2.70 ± 0.80 D for the anisometropes and 0.15 ± 0.18 D for the isometropes. The Chinese subjects had a mean interocular difference in refractive error of 2.85 ± 0.95D for the anisometropes and 0.19 ± 0.13D for the isometropic subjects.

Table 5.2 Interocular component differences in vergence contributions for Caucasian subjects.

| | anisometropes | | isometropes | |
|---|---|---|---|---|
| | V (D) | % | V (D) | % |
| cornea | 0.05 ± 0.28 | -0.42 ± 1.41 | 0.06 ± 0.26 | 0.02 ± 0.67 |
| separation | 1.23 ± 0.41 | 1.58 ± 0.55 | 0.13 ± 0.27 | 0.08 ± 0.37 |
| equiv. lens | -0.06 ± 1.65 | -0.94 ± 1.60 | -0.10 ± 0.84 | -0.09 ± 0.85 |
| vitreous | -3.66 ± 2.00 | | -0.12 ± 0.86 | |

V, vergence contribution; %, percentage contribution; separation, distance between cornea and equivalent lens; equiv. lens, equivalent lens; ± one standard deviation.

Table 5.3 Interocular component differences in vergence contributions for Chinese subjects.

| | anisometropes | | isometropes | |
|---|---|---|---|---|
| | V (D) | % | V (D) | % |
| cornea | -0.09 ± 0.30 | -0.91 ± 1.23 | 0.06 ± 0.34 | -0.11 ± 0.57 |
| separation | 1.18 ± 0.42 | 1.41 ± 0.69 | 0.17 ± 0.40 | 0.14 ± 0.52 |
| equiv. lens | 0.26 ± 2.50 | -0.76 ± 1.43 | 0.02 ± 0.75 | -0.07 ± 0.88 |
| vitreous | -3.15 ± 2.07 | | -0.64 ± 1.12 | |

V, vergence contribution; %, percentage contribution; separation, distance between cornea and equivalent lens; equiv. lens, equivalent lens; ± one standard deviation.

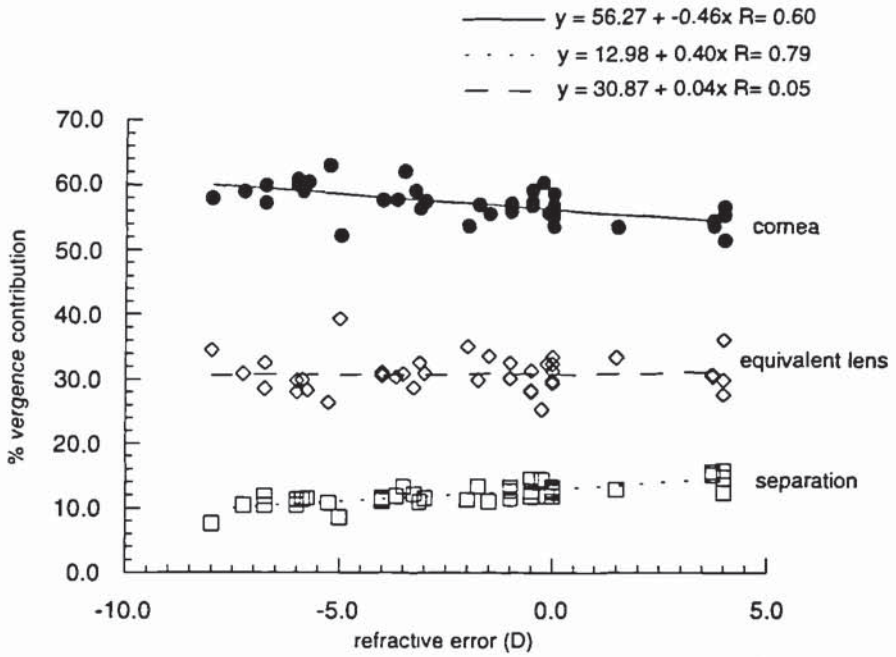



Figure 5.06 Shows the percentage vergence contribution of the cornea, equivalent lens and the separation between the cornea and equivalent lens plotted against refractive error for the Caucasian subjects.

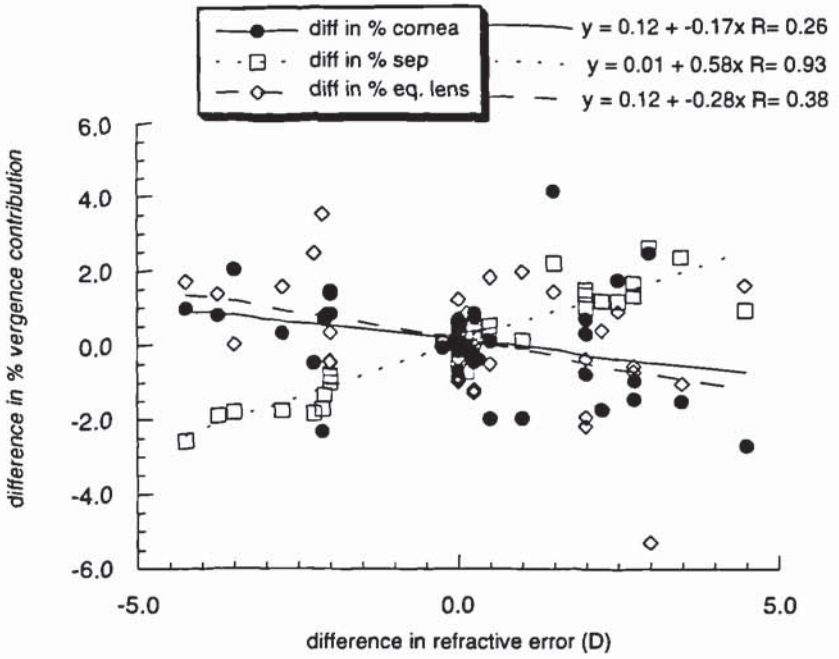



Figure 5.07 Shows the interocular difference in percentage vergence contribution of the cornea, equivalent lens and separation between cornea and equivalent lens plotted against inter-eye difference in refractive error. This data is for the Caucasian subjects.

As evident in figure 5.06 a correlation was found between refractive error and vergence contribution of cornea ($r^2 = 0.36$, $p < 0.001$) and separation of the cornea and equivalent lens ($r^2 = 0.62$, $p < 0.001$) for the Caucasian subjects. No correlation was found between refractive error and equivalent lens ($r^2 = 0.003$, $p > 0.50$). Figure 5.07 depicts a relationship between interocular difference in refractive error and inter-eye difference in separation of cornea and equivalent lens ($r^2 = 0.86$, $p < 0.001$). A weak correlation was observed between interocular difference in refractive error and equivalent lens ($r^2 = 0.14$, $p < 0.05$) but no correlation was evident for inter-eye difference in cornea ($r^2 = 0.07$, $p > 0.50$) .

The data for the Chinese subjects is shown in figures 5.08 and 5.09 A correlation was found between refractive error and vergence contribution of the separation between the cornea and equivalent lens ($r^2 = 0.73$, $p < 0.001$). A weak correlation was observed for refractive error and vergence contributions of the cornea ($r^2 = 0.12$, $p < 0.1$) and no correlation was evident for the vergence contribution of the equivalent lens ($r^2 = 0.08$, $p > 0.50$).

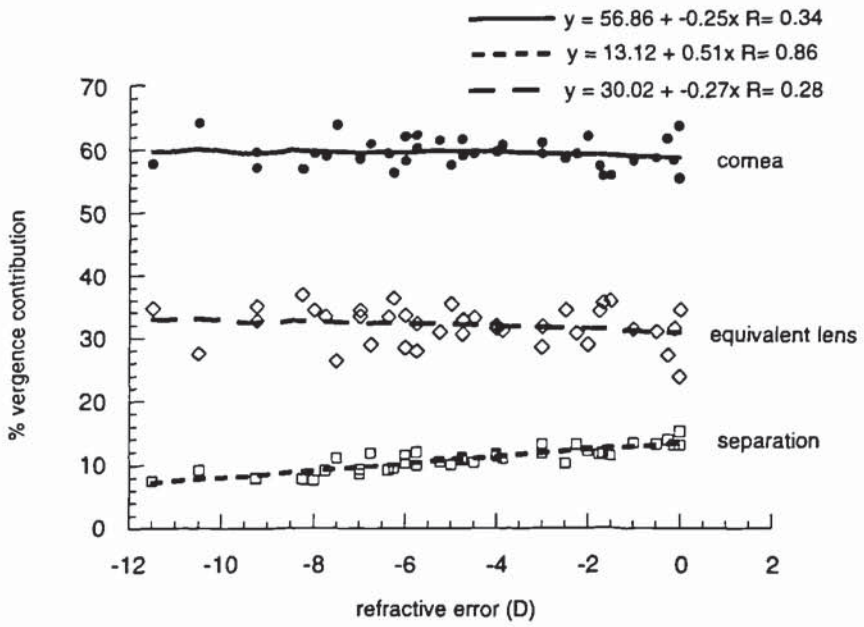



Figure 5.08 Shows the percentage vergence contribution of the cornea, equivalent lens and the separation between the cornea and equivalent lens plotted against refractive error.

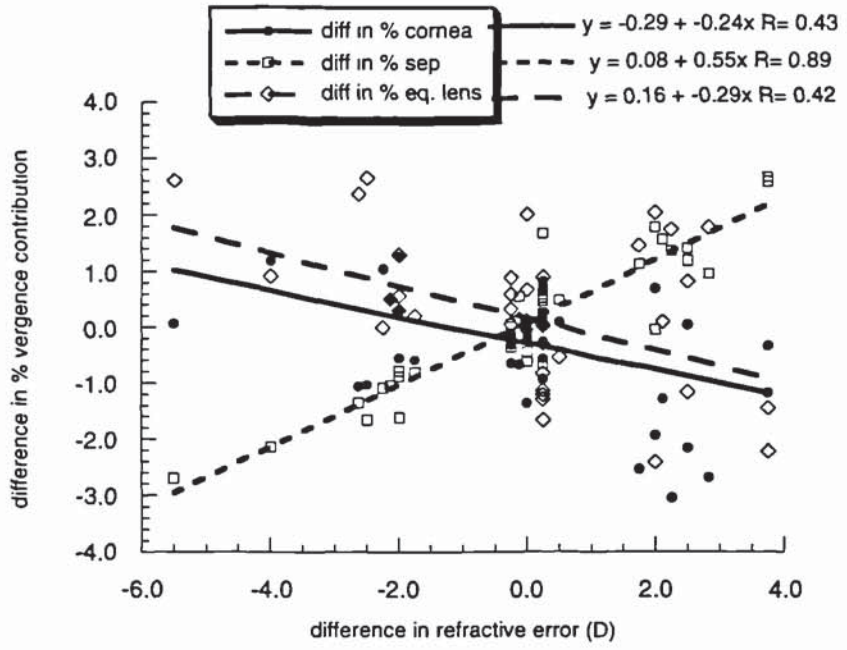



Figure 5.09 Shows the interocular difference in percentage vergence contribution of the cornea, equivalent lens and the separation between the cornea and equivalent lens plotted against inter-eye difference in refractive error.

The data on ocular component analysis by vergence contribution indicates that the interocular differences in anisometropia result mainly from differences in vitreous chamber depth and not from anterior segment differences. It is evident that the effect of the vitreous chamber depth causes a dampening effect on the other ocular components especially that of the cornea and equivalent lens separation.

## 5.4 Retinal contour in anisometropia

The possibility of determining the shape of the retinal surface by measurement of peripheral refraction was discussed by Ferree and Rand (1933). The inter-individual variation in type of peripheral astigmatism has been suggested to be attributed to retinal shape differences (see § 3.2). Dunne (1995) has developed a computing method to determine retinal contour from peripheral refraction and biometry measurements (see § 3.3).

### 5.4.1 *Peripheral refraction*

Peripheral refraction data for the right eye of three subjects is shown in skiagram form in figures 5.10, 5.11 and 5.12.

Figure 5.10 shows that the sagittal refractive error becomes progressively more hyperopic in the periphery and the tangential refractive error more myopic. The result is that the peripheral astigmatism increases with increasing eccentricity and is of the order of 6D at an eccentricity of 35°. The peripheral refraction data is typical of the 'type A' image shells described by Ferree, Rand and Hardy (1931) and 'type IV' image shells depicted by Rempt, Hoogerheide and Hoogenboom (1971).

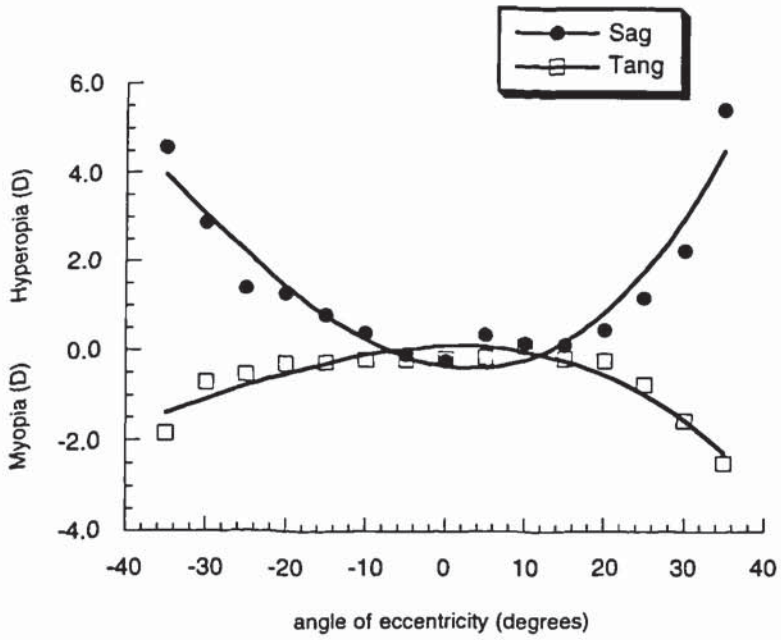



Figure 5.10 Shows a type A (type IV) skiagram.

In figure 5.11 it is evident that both the sagittal and tangential image shells become progressively more hyperopic in the periphery. This type of skiagram exhibits low levels of peripheral astigmatism of the order of 1 to 2 D, at an eccentricity of 35°. The peripheral refraction data in figure 5.12 is typical of the 'type B' image shells described by Ferree, Rand and Hardy (1931) and 'type I' image shells depicted by Rempt, Hoogerheide and Hoogenboom (1971).

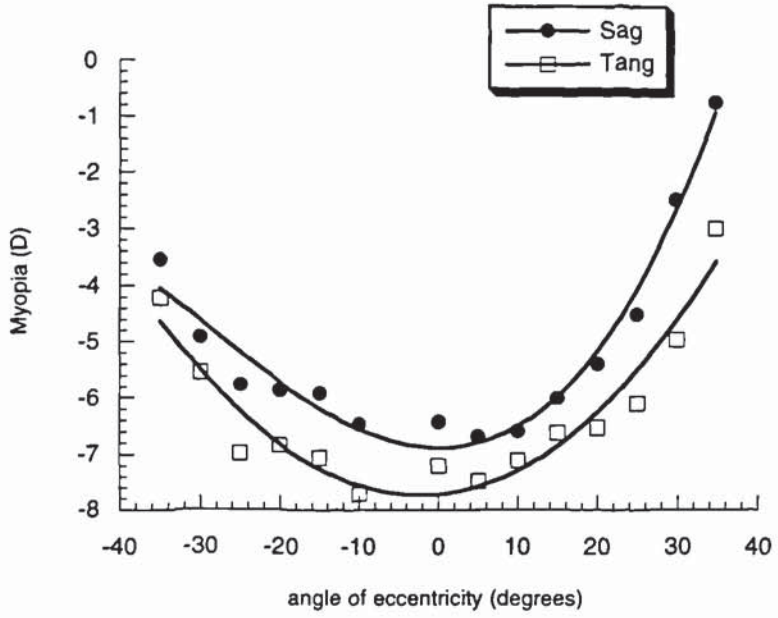



Figure 5.11 Shows a type B (type I) skiagram.

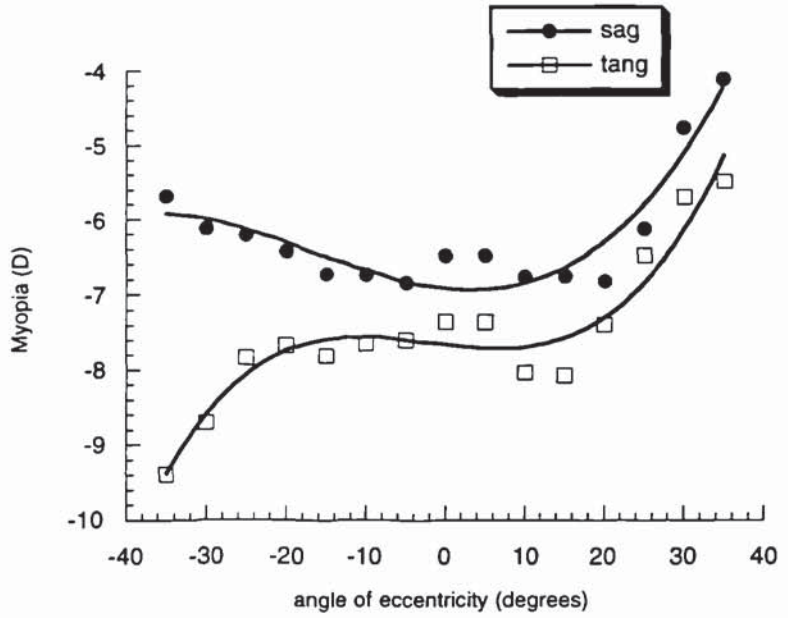



Figure 5.12 Shows a type C (type III) skiagram.

Figure 5.12 shows asymmetrical peripheral refraction data. In the nasal meridian the sagittal image shell becomes progressively more hyperopic in the periphery whereas the tangential image shell becomes more myopic. However in the temporal meridian both the sagittal and tangential image shells become more hyperopic. This type of peripheral refraction data is typical of the 'type C' image shells described by Ferree, Rand and Hardy (1931) and 'type III' image shells depicted by

Rempt, Hoogerheide and Hoogenboom (1971). The peripheral refraction data for all subjects is given in Appendix 5.

Table 5.4 shows the correlation between the different types of skiagrams and central refraction for all Caucasian eyes. Similar data is shown for the Chinese subjects in table 5.5.

Table 5.4 Relationship between type of skiagram and central refraction for the Caucasian subjects.

| Central | Types of Skiagrams* | | | | |
|---|---|---|---|---|---|
| Refraction | I | II | III | IV | V |
| > 0.50 D | — | — | 1 | 10 | 1 |
| 0 to 0.50 D | — | 2 | — | 12 | 2 |
| > 0 to -3 D | 7 | 2 | 1 | 7 | 1 |
| > -3 to -6 D | 18 | — | 1 | 5 | — |
| > -6 D | 9 | — | 1 | — | — |

*Types of skiagrams after Rempt, Hoogerheide and Hoogenboom (1971).

Table 5.5 Relationship between type of skiagram and central refraction for the Chinese subjects.

| Central | Types of Skiagrams* | | | | |
|---|---|---|---|---|---|
| Refraction | I | II | III | IV | V |
| 0 to 0.50 D | — | 2 | — | 4 | — |
| > 0 to -3 D | 4 | 2 | 1 | 9 | 1 |
| > -3 to -6 D | 21 | — | 2 | 4 | — |
| > -6 D | 29 | — | 1 | — | — |

*Types of skiagrams after Rempt, Hoogerheide and Hoogenboom (1971).

### 5.4.2 *Retinal contours*

Table 5.6 Relationship between interocular difference in refractive error and type of retinal contour.

| | Type of retinal contour | | | | |
|---|---|---|---|---|---|
| Subjects | type A | type B | type $C_N$ | type $C_T$ | type D |
| Cauc aniso | 14 | 0 | 3 | 3 | 0 |
| Chin aniso | 13 | 0 | 3 | 2 | 2 |
| Cauc iso | 0 | 0 | 0 | 0 | 20 |
| Chin iso | 0 | 0 | 0 | 0 | 20 |

Cauc, Caucasian; aniso, anisometropes; Chin, Chinese; iso, isometropes; type $C_N$ refers to type C with intersection of the peripheral retinal contours nasally; type $C_T$ refers to type C with intersection of peripheral retinal contours temporally.

*Repeatability of the computational technique*

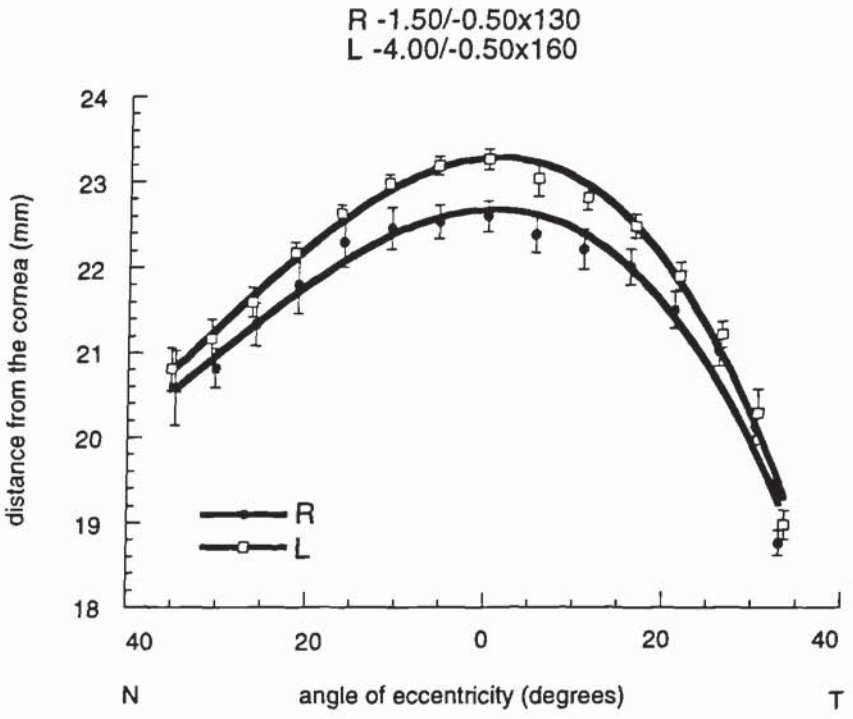



Figure 5.13 Shows the mean retinal contours for a 2.5D anisomyope derived from 10 separate measurement cycles. Error bars represent standard deviations.

Figure 5.13 shows the computed retinal contours for both the right and left eyes of a 2.5D anisomyope. The error bars represent standard deviations based on 10 derivations of retinal contour. The retinal contour is sampled out to 35° from the fovea in both the nasal and temporal meridia. The equator has been shown to be at approximately 60° from the fovea (Le Grand, 1967). Data illustrated in figure 5.13 shows an axial length difference of 0.70 mm. From figure 5.13 it is evident that the retinal contours intersect both nasally and temporally in the periphery which corresponds to approximately 35-40° of eccentricity from the fovea. There is asymmetry of the nasal retina compared to the temporal retina which may be reflecting slight asymmetry in peripheral refraction.

*Graphical representation of the different retinal contour types*

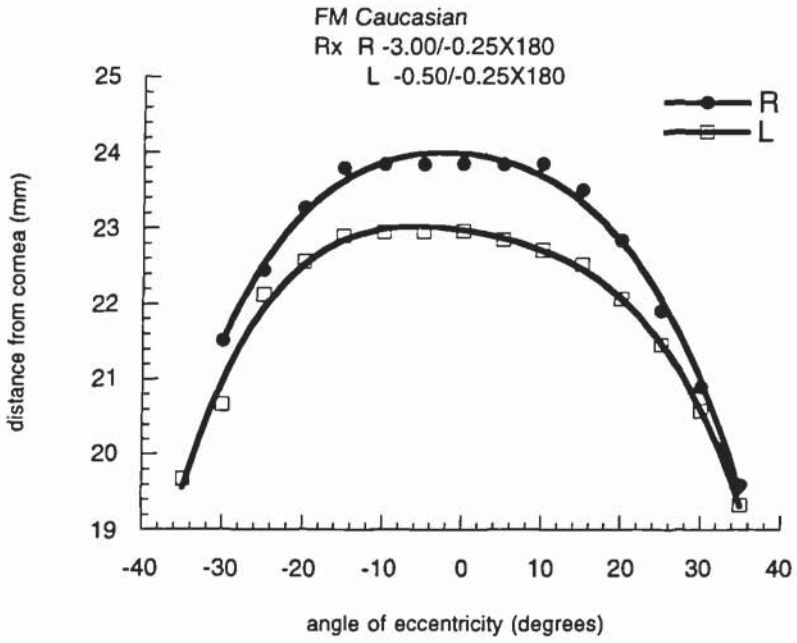



Figure 5.14 Shows a type A retinal contour profile.

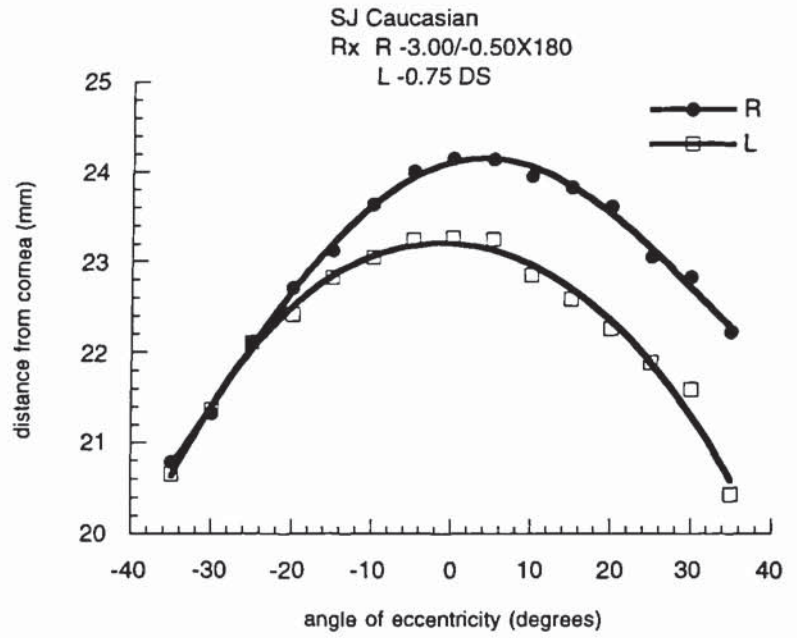



Figure 5.15 Shows a type C retinal contour profile.

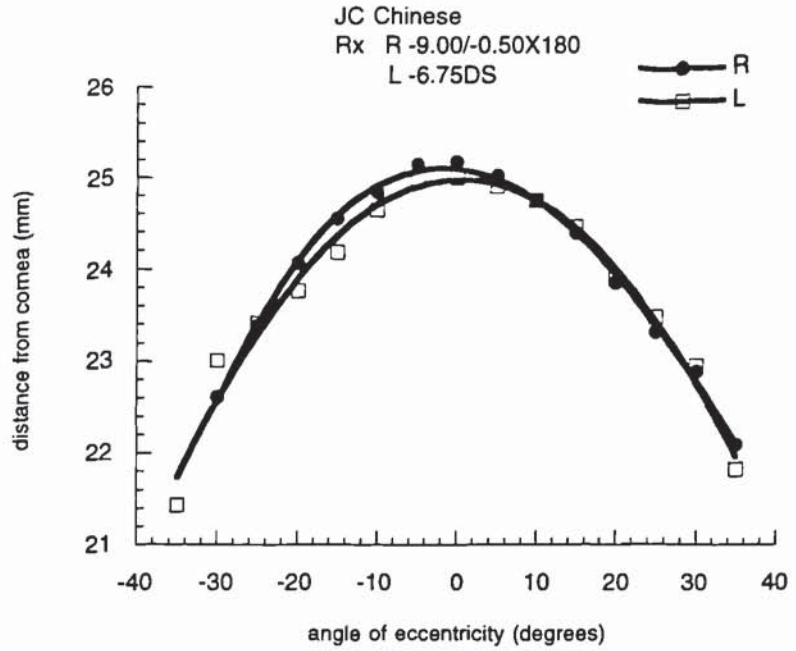



Figure 5.16 Shows a type D retinal contour profile.

The majority of the anisometropic subjects, 70% of the Caucasians and 65% of the Chinese, had type A retinal contours (see figure 5.14). None of the theoretical type B retinal contours were found in either the Caucasian or Chinese groups. Type C retinal contours (nasal type shown in figure 5.15) were found in 6 Caucasian and 5 Chinese anisometropes. All isometropic subjects and 2 of the Chinese anisometropic subjects were found to have type D retinal contours (see figure 5.16).

## 5.5 *Discussion*

*Biometric measurements of ocular components*

The mean values for anterior chamber depth, lens thickness and corneal curvature recorded in the present study are similar to those found in previous studies (see § 1.2). The predominance of myopic subjects in the present study has resulted in greater than normal mean values being found for the ocular components of axial length and vitreous chamber depth. The data for the Chinese subjects has a greater mean myopic refractive error and consequently a longer mean axial length and vitreous chamber depth. The anterior chamber depth and lens thickness is similar size in both the Caucasian and Chinese subjects. Corneal curvature data is discussed in Chapter 6.

Biometric data show that the differences between anisometropic eyes can be attributed to an elongation of the vitreous chamber of the more myopic eye. In figure 5.13 the discrepancy in axial length between the 2 eyes of a 2.5D anisomyope is 0.70 mm. This correlates with previous work

which has shown that an increase in axial length of 1 mm will produce approximately 2 to 3D of myopia (Erickson, 1991; Grosvenor, 1994).

*Ocular component analysis by vergence contribution*

The results presented in this thesis on the ocular component analysis by vergence contribution follow the predictions made by Erickson (1984). He suggested that for longer eyes the surface powers played an increasingly important role in determining refractive error. However, for shorter eyes the axial separations between the ocular components were more important. It is evident that including the effect of the vitreous chamber depth causes a dampening effect on the other ocular components.

*Peripheral refraction*

It is well documented that the astigmatic interval increases significantly in the periphery with the degree to which this occurs showing considerable individual variability (Ferree, Rand and Hardy, 1931; Rempt, Hoogerheide and Hoogenboom, 1971). Figure 5.10 showed the peripheral refraction image shells for an emmetrope. This subject displayed marked peripheral astigmatism typical of the most common type found by Ferree, Rand and Hardy (1931). The majority of subjects in the present study, with this type of marked peripheral astigmatism (type A/type IV) were emmetropic.

The present study showed a higher prevalence of type B (type I) skiagrams. Agreeing with earlier work by Rempt, Hoogerheide and Hoogenboom (1971) on type of skiagram and central refractive error, who found that type B (type I) skiagrams usually occurred in connection with myopic central refractive errors. As the majority of subjects in the present study were myopic, a high prevalence of type B (type I) skiagrams would be expected. Similarly to previous studies (Ferree, Rand and Hardy, 1931; Rempt, Hoogerheide and Hoogenboom, 1971), the present study found a few cases with asymmetrical peripheral refraction.

Both the Caucasian and Chinese subjects show a similar prevalence of types of skiagrams, with a predominance of type B/type I for myopic eyes and a predominance of type A/type IV for emmetropic eyes.

*Repeatability of the computational technique*

The finding that retinal contour derived from each measurement cycle is similar and that the respective errors are small indicates that the computing technique for determination of retinal contour is repeatable. The distinct separation of the retinal contours in the presence of low variance for the 2.5D anisomyope, demonstrated that the inherent variability of the computing scheme is not sufficient to mask the true disparity in retinal contour.

The repeatability of the retinal contour parameters are reliant on the repeatability of the Canon autorefractor, keratometry and A-scan ultrasonography. Zadnik, Mutti and Adams (1992) have

assessed the repeatability of ocular component measurements. They found that cycloplegic autorefraction measurement were the most reliable with 95% limits of agreement of ±0.32D. Corneal curvature measures had a reliability of ±0.87D, anterior chamber depth ±0.29 mm, lens thickness ±0.20 mm and vitreous chamber depth ±0.37 mm.

*Retinal contour*

The majority of the anisometropic subjects, 70% of the Caucasians and 65% of the Chinese, had type A retinal contours. Retinal contours of type A display axial elongation only of the vitreous chamber in the more myopic eye, with intersection of the two retinal contours in both the nasal and temporal peripheral loci. This finding supports the traditional belief that the myopic eye is elongated in shape.

Interestingly no overall expansion of the globe was found (type B) as some of the myopia research on animals has recorded overall expansion of the globe in the more myopic eye .

Asymmetrical retinal contours were found in a few subjects (type C). These asymmetrical retinal contours did not correlate with asymmetries in peripheral refraction or any deviations from the norm in the biometric data.

In the Chinese group, 2 anisomyopic subjects had similar retinal contours in both eyes. Comparison of the interocular difference in percentage vergence contribution with the mean for all Chinese subjects, reveals that both the equivalent lens and the axial separation of the cornea and equivalent lens differed considerably from the mean. The interocular difference in percentage vergence contribution of the equivalent lens, for both subjects, falls outside the 95% confidence intervals.

The preponderance of type A retinal contours in anisometropes is supported by research investigating the elasticity of the sclera. Battaglioli and Kamm (1984) found that the sclera was not so resistant to change in its radial dimension (thickness) but quite resistant to circumferential stretch. They noted that the collagen fibres run primarily in the circumferential direction and are able to resist changes in globe circumference better than changes in the radial dimension. The elasticity of the human sclera has been found to be more extensible posteriorly than anteriorly possibly arising from the different developmental time of the sclera; the posterior sclera develops last onotgenetically and matures only after completion of ocular growth (Curtin, 1969).

Van Alphen increased the pressure in enucleated human eyes to assess changes with increased IOP. The sclera from behind the equator was removed and a saline infusion was introduced into the eyes. The eyes were found to increase axially, from the region of the equator, rather than display overall radial expansion.

These investigations suggest that eyes stretch in connection with myopia development and that stretch is in the axial dimension only.

*Different methods for determination of eye shape*

Cheng *et al.* (1992) examined the shape of the myopic eye using magnetic resonance imaging (MRI). They imaged 7 myopic, 8 emmetropic and 7 hyperopic eyes in the axial and coronal planes. Myopic eyes were found to have a greater anterior-posterior dimension than emmetropic or hyperopic eyes. However they found variations in myopic eye dimensions in the equatorial and vertical diameters; 2 myopic eyes had identical axial and equatorial diameters, 4 had a longer equatorial diameter and 1 a longer axial diameter. Two of the myopic eyes were found to be asymmetrical in shape. Myopic eyes were also found to have a reduction in both scleral and choroidal thickness compared to emmetropic and hyperopic eyes. MRI images are obtained by taking images at different slices through the eye and measurements of ocular dimensions are taken at the maximum diameters of the globe. The judgement of this maximum diameter is examiner dependent and may result in an error in choosing the slice to measure. Image resolution obtained with standard diagnostic MRI is 0.33 mm which corresponds to a dioptric value of approximately 1D.

Eye shape has also been measured using laser Doppler interferometry by Schmid *et al.* (1994). They measured optical length in six eyes at different eccentricities out to a maximum of 20° nasally and temporally. They found considerable inter-individual variation in the retinal contours and suggested that a new classification of myopia may result from such measurements. Laser Doppler interferometry although highly accurate is not a commercially available technique.

## 5.6 *Verification of computational retinal contour technique*

### 5.6.1 *Introduction*

Much of the research in this thesis concerns the utility of the computational retinal contour technique (Dunne, 1995) described earlier in this chapter. The technique has been used to determine posterior eye shape for both eyes of 80 subjects with a range of refractive error. The method calculates retinal contour from ray tracing, established schematic eye parameters, and biometric and peripheral refraction data that have been measured for each individual eye. The computational technique is an indirect method for determination of retinal contours. Consequently actual direct measurements of retinal contours are required to assess the validity of the computational method.

*Methods of in vivo imaging of the eye*

Two techniques capable of *in vivo* imaging of the eye are magnetic resonance imaging (Strenk, Semmlow and Mezrich, 1994) and laser Doppler interferometry (Schmid *et al.*, 1996). These methods are not easily accessible and at present laser Doppler interferometers are not commercially available.

*Magnetic resonance imaging*

Magnetic resonance imaging (MRI) is used clinically to identify and examine internal ocular pathology. It has also been used in research to examine age-related changes in lens size and shape (Strenk, Semmlow and Mezrich, 1994) and differences in eye size of the myopic eye (Cheng *et al.*, 1992).

MRI involves imaging the eye in slices and consequently assumptions are made as to the orientation of the exact slice of the eye the image represents. The resolution of standard diagnostic MRI has been reported to be approximately 0.33 mm (Semmlow, Menditto and Mezrich, 1991). This resolution is not accurate enough for eye dimensions where a 1 mm difference in axial length of an eye equates to 2-3D of refractive error. The MRI software was modified by Semmlow, Menditto and Mezrich (1991) and use of a special small surface coil enabled them to theoretically achieve a resolution of 0.156 mm.

*Laser Doppler interferometry*

Laser Doppler interferometry was first described by Hitzenberger (1991) as a new method to determine axial length of the human eye *in vivo*. The technique is based on the principles of interferometry combined with the laser Doppler method. A beam from a laser diode (wavelength 780 nm, coherence length ~ 0.13 mm) is delivered to the eye through a Michelson interferometer (Schmid *et al.*, 1994). The light is partially reflected at the cornea and from the various layers of the retina. One of the interferometer mirrors is moved at a constant speed of 2 $mms^{-1}$ to change the

path length between the two plates in the interferometer, which results in a Doppler shift in the reflected light. Concentric interference fringes are produced in front of the eye when the mirror is adjusted so that the path length between the two interferometer plates is equal to the optical path difference between the cornea and the retina. A photodector measures the light intensity during the movement of the mirror. The light intensity is recorded by a computer as a function of the mirror position.

Laser Doppler interferometry is capable of measuring axial length along the anterioposterior axis of the eye and in peripheral regions of the posterior pole of the eye (Fercher, Hitzenberger and Juchem, 1991; Schmid *et al.*, 1994). LDI measurements are in optical length compared to standard ocular biometric measurements, e.g. ultrasound, which are measured in geometrical length.
The precision of measuring optical length of the eye from the cornea to the retina is between 10 and 25 μm (Fercher, Hitzenberger and Juchem, 1991; Hitzenberger, 1991). This measurement accuracy has been calculated to correspond to approximately 8 to 20 μm for geometric length. In comparison conventional ultrasound devices have a precision of approximately 100 μm in measuring axial length of the eye.

Schmid *et al.* (1996) have built a modified version of Hitzenberger's LDI. Their version has several advantages including an objective method to determine the peak locations of the intraocular surfaces (and hence intraocular distances), a fixation target for the eye under examination and an improved focusing system.

### 5.6.2 *Methods*

The LDI measurements were taken at the Scheie Eye Institute, University of Pennsylvania, Philadelphia, USA in collaboration with Gregor Schmid, Alan Laties and George Papastergiou, during 18-20 May 1996.

Data on the length of the eye at the fovea and at different off-axis eccentricities was obtained from both eyes of 3 subjects. One subject was a 3.75D anisohyperope, the other 2 subjects had 1 and 1.5D respectively of anisometropia. Retinal contours for both eyes of the 3 subjects were also determined using the computational technique described earlier in this chapter.

LDI measurements of the length of the eye were taken in 5° intervals along the horizontal meridian from 30° nasal to 30° temporal. A minimum of 7 measurements was obtained at each location. The subject viewed a fixation light which was attached to a vernier scale, the fixation light could then be moved accurately to correspond to the different eccentricities at which measurements were to be obtained. Recordings were obtained under cycloplegia with 1%

tropicamide and 2.5% epinephrine. The method is non-invasive and no contact between the eye and sensor is required.

In order to compare the LDI data and the computed retinal contours, the computed data was converted from geometrical to optical length. The conversion was carried out using a computer program (see Appendix 7). The program uses individual measured biometric parameters, computed retinal co-ordinates (methods for determining these parameters are described earlier in this chapter) and refractive indices, of the ocular components and media, for red laser light to convert the computed geometric data to optical lengths.

Any discrepancies in the retinal contour induced by converting from geometric to optical length using a spherical corneal surface in the conversion programme have been assessed. Apical radii and asphericity (*p*-values) have been calculated for the nasal and temporal semi-meridians. These parameters have been derived using a computer programme devised by Lam and Douthwaite (1994) and from corneal topography data described later in Chapter 6. The asphericity was calculated for the corneal zone between the centre and a horizontal distance of 4 mm both nasally and temporally. This corneal zone was chosen as 3.96 mm was found to be the mean maximum height that a ray strikes the corneal surface in the ray-tracing computer program to convert geometric lengths into optical lengths.

### 5.6.3 *Results*

Biometric parameters for the three subjects are shown in table 5.7.

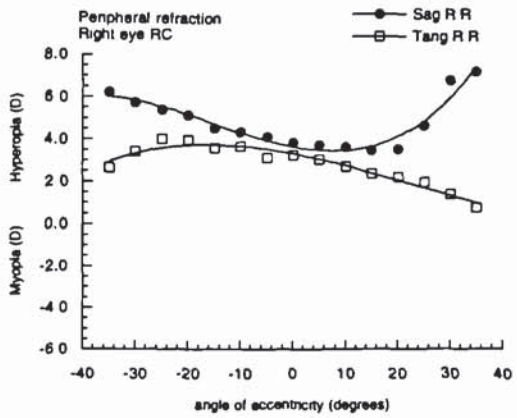
Table 5.7 Shows the biometric parameters for both eyes of the three subjects

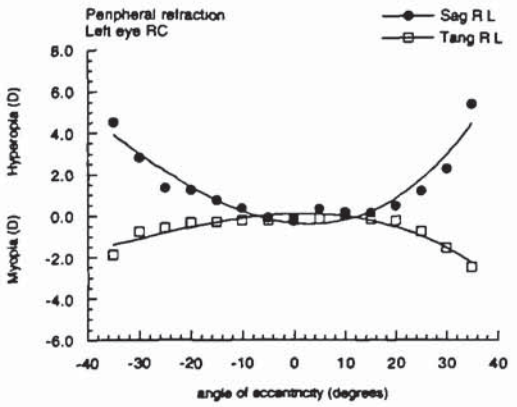
| | RC | | LD | | NL | |
|---|---|---|---|---|---|---|
| | R | L | R | L | R | L |
| Rx (D) | 3.75 | 0 | -0.50 | -1.50 | -2.50 | -4.00 |
| CR (mm) | 7.73 | 7.73 | 7.90 | 8.00 | 7.15 | 7.19 |
| ACD (mm) | 3.57 | 3.82 | 3.69 | 3.85 | 3.72 | 3.9 |
| LT (mm) | 3.73 | 3.59 | 3.25 | 3.25 | 3.51 | 3.54 |
| VCD (mm) | 14.42 | 15.35 | 16.88 | 17.57 | 15.66 | 16.04 |

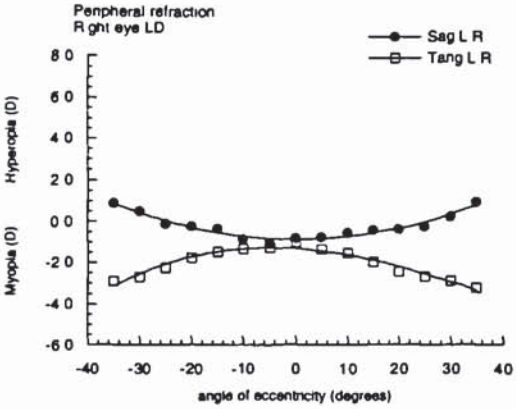
Rx, refractive error; CR, corneal radius; ACD, anterior chamber depth; LT, lens thickness; VCD, vitreous chamber depth.

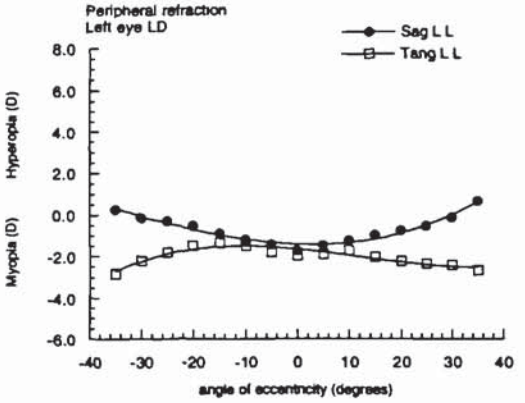
Peripheral refraction data in the form of skiagrams (see § 3.1.1) for the 3 subjects are shown in figure 5.17.

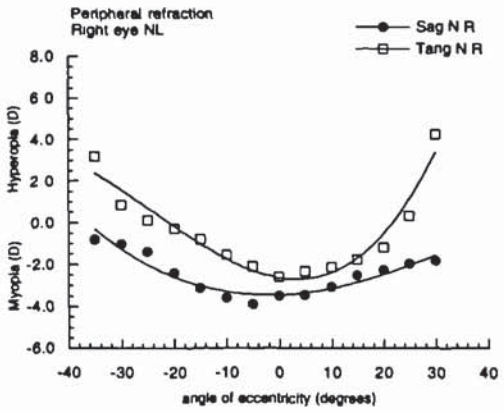
Figure 5.17 Peripheral refraction skiagrams for both eyes of the three subjects.

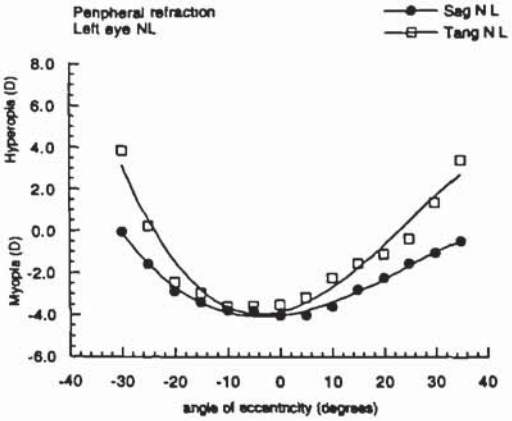


The LDI results for all six eyes are shown in graphical form in figure 5.18. From the graphs it is evident that LDI is capable of demonstrating the inter-individual differences in retinal contour that are also depicted by the computed technique.

Visual inspection of the results suggests that the two techniques produce similar retinal contours for an individual eye. A discrepancy in posterior dimensions of the eye as measured by the two methods is evident from figure 5.18.

Figure 5.19 shows the variance in the difference in eye dimensions at each measured location and the mean difference in eye dimensions. No systematic trend is observed in the data for subjects LD and NL, suggesting that the variances result from individual variance. However subject RC shows an asymmetrical trend which is mirror-imaged in the data from the left eye.

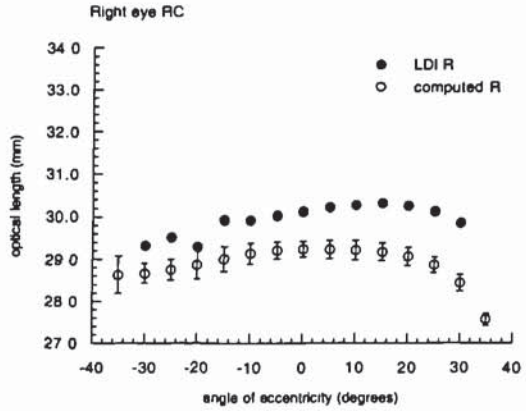
Table 5.8 shows the differences in retinal contour at each eccentricity when the asphericity of the cornea is taken into account when converting geometrical length to optical length. It is evident that the computed retinal contours are not significantly different when an aspheric corneal surface is used compared to a spherical corneal surface.

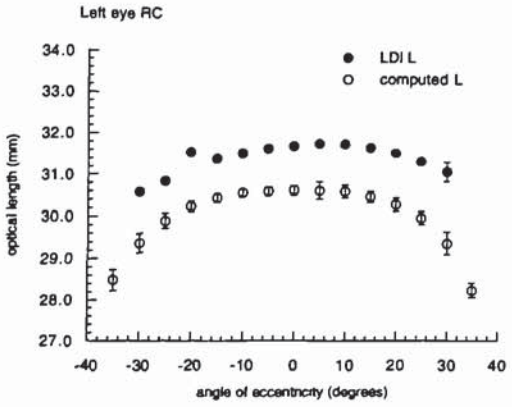
Table 5.8 Mean difference in the spherical and aspheric data in converting geometric to optical length.

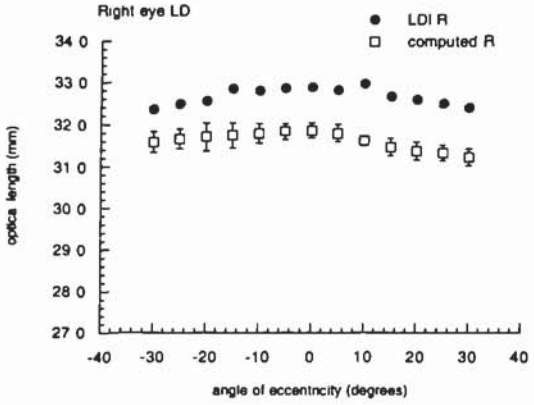
| | mean difference in spherical and aspheric data for all subjects | |
|---|---|---|
| eccentricity (degrees) | nasal meridian (mm) | temporal meridian (mm) |
| 0 | 0.00 ± 0 | 0.00 ± 0 |
| 5 | 0.00 ± 0 | 0.00 ± 0 |
| 10 | 0.00 ± 0 | 0.00 ± 0 |
| 15 | 0.01 ± 0 | 0.01 ± 0.005 |
| 20 | 0.02 ± 0.005 | 0.03 ± 0.01 |
| 25 | 0.03 ± 0.01 | 0.05 ± 0.01 |
| 30 | 0.04 ± 0.015 | 0.06 ± 0.02 |
| 35 | 0.07 ± 0.02 | 0.09 ± 0.03 |

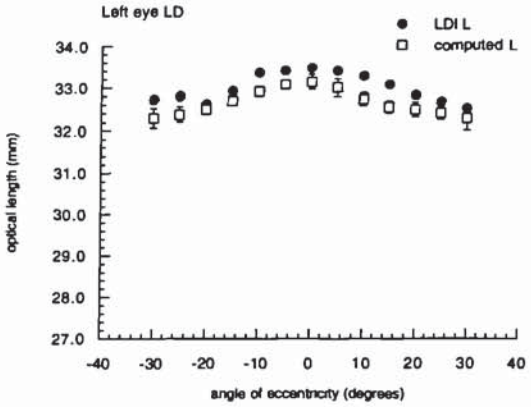
± one standard deviation.

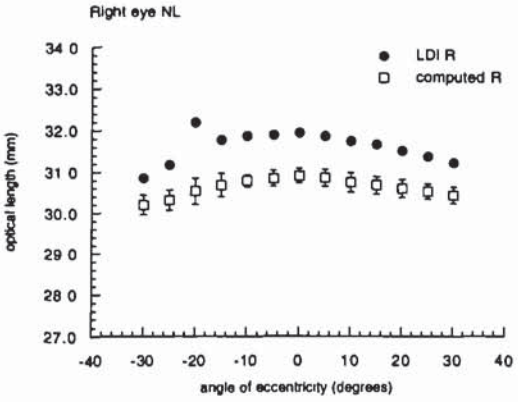
Figure 5.18 Retinal contours measured by both LDI and the computational technique for both eyes of three subjects.



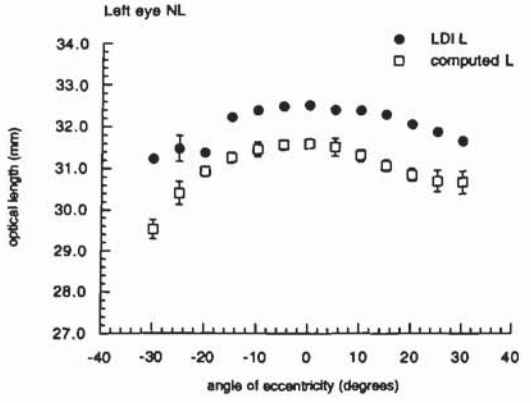
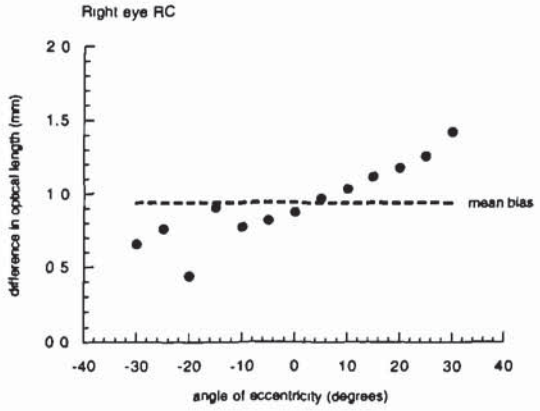
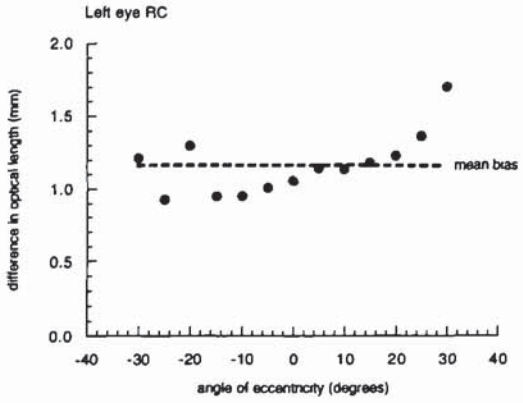
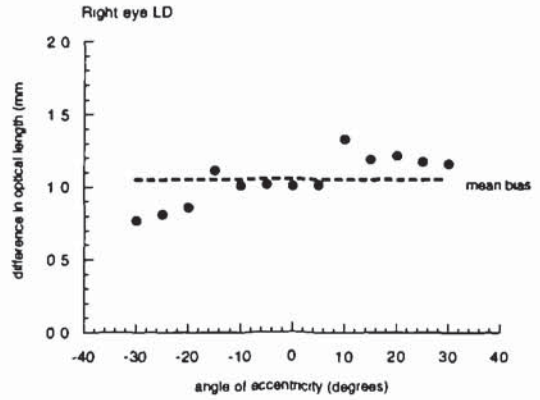
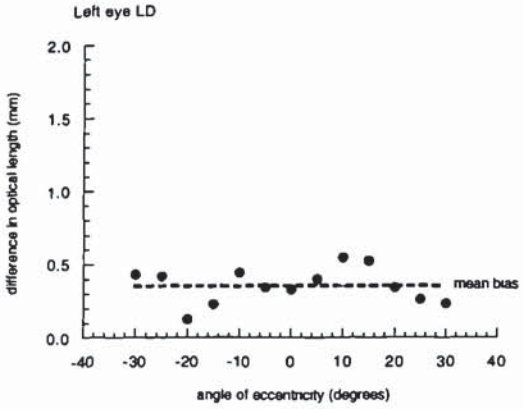



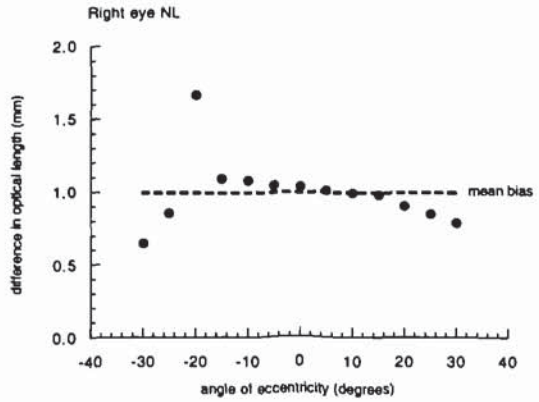
Figure 5.19 Variance between the two methods for measuring retinal contour for both eyes of the three subjects.

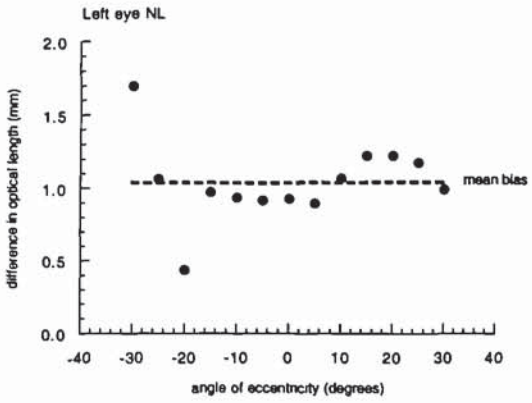


### 5.6.4 *Discussion*

LDI is an *in vivo* technique capable of determining the optical path length of the eye. The technique is repeatable, with an accuracy of ±20 μm (Schmid *et al.*, 1996). LDI has proven to be capable of demonstrating inter-individual differences in retinal contour. Comparison of LDI retinal contours and those obtained by computation give good agreement. The computed retinal contours are systematically shorter in length than the LDI contours. This discrepancy in measurement may arise from the different layers of the retina from which the measurements are taken. The computed retinal contours include data from ultrasonography and infra-red autorefraction. Ultrasonography measures to the vitreo-retinal boundary and infra-red light is also believed to be reflected from the vitreo-retinal boundary (Glickstein and Millodot, 1970).

LDI measurements are believed to result from light reflected from the retinal pigment epithelium. The LDI interference signal has a number of components corresponding to reflections from different layers. The signal obtained in the majority of subjects is from the retinal pigment epithelium. A second signal that is recorded intermittently is from the inner limiting membrane (Schmid *et al.*,1994). Theoretically it is possible to determine the retinal thickness from the difference in length between the signal from the inner limiting membrane and the retinal pigment epithelium. In the subjects in the present study, signals from the inner limiting membrane were not obtained at the fovea and were only seen at certain off-axis locations.

Peripheral refraction data for the three subjects show considerable inter-individual variability. Subject RC has marked peripheral astigmatism which is also asymmetric. This asymmetry in peripheral refraction is reflected in the retinal contour. The computational retinal contour technique is designed to compensate for marked peripheral astigmatism. However, it appears that the computational programme is unable to cope with the amount of astigmatism displayed be subject RC. This is suggested by the asymmetrical findings in the comparsion of the mean differences in the LDI and computational methods. However only 8 of the 80 subjects had marked peripheral astigmatism similar to that of subject RC.

The majority of the asymmetry in peripheral refraction for subject RC is depicted in the tangential image shell indicating that the asymmetry arises from the optical system. Asymmetries in the sagittal image shell are indicative of asymmetries in retinal contour (Rempt, Hoodgerheide and Hoogenboom, 1971).

Subjects LD and NL have less peripheral astigmatism. Comparison of mean differences in the LDI and computational methods shows no systematic trend suggesting that the retinal contour programme can account for the levels of peripheral astigmatism measured in subjects LD and NL, at least up to ± 30°.

## 5.7 *Summary*

The thesis uses a new computational technique to determine retinal contour shape. The method is based on ray-tracing formulae, biometric measurements and peripheral refraction data for each specific eye measured. The technique has been applied to anisometropic subjects to assess any discrepancies in retinal contour shape with respect to refractive error.

Biometric measurements obtained in the thesis have confirmed previous studies on anisometropia in that the anterior segments of the eye were similar in anisometropes with a significant amount of interocular difference in refractive error. The anomaly in anisometropia has been shown to arise from differences in vitreous chamber depth.

Peripheral refraction measurements have demonstrated inter-individual variation which correlate with the degree of central ametropia. The majority of myopes exhibited low amounts of peripheral astigmatism compared to emmetropes with high degrees of peripheral astigmatism

The principal finding of the thesis is that the main structural correlate of myopia is an increase in axial rather than equatorial dimensions of the posterior globe.

The correlation of the computational technique with direct *in vivo* measurements of retinal contour are essential to assess the validation of the computing scheme. Comparison with laser Doppler interferometry reveals good agreement and suggests that the computational technique is a feasible method for determination of retinal contour.

The computational method described in the thesis is a more accessible method for determination of eye shape than current imaging techniques such as magnetic resonance imaging or laser Doppler interferometry.

# CHAPTER 6

# CORNEAL TOPOGRAPHY IN AMETROPIA

## 6.1 *Introduction*

The cornea is the major refracting surface of the eye, contributing approximately two-thirds of the total dioptric power of the eye. Small changes in corneal topography will therefore result in significant changes in ocular power. Traditionally corneal curvature measurements have been obtained using keratometers. The principle behind keratometry is based on measuring the size of an image reflected from the cornea of an object of known size and position. From this data the radius of curvature can be calculated. These measurements are limited to two points on the central cornea approximately 3 mm apart. The general assumption is that the corneal surface between these two measurement mires is spherical. As the peripheral cornea is aspheric in nature, keratometry measurements are not accurate at locations remote from the optical axis.

*Methods of assessing corneal curvature*

In addition to keratometry, keratoscopy and rasterstereography are other methods of assessing corneal curvature (Fowler and Dave, 1994). The first keratoscope, the Placido disc consisted of a pattern of alternating black and white concentric rings. Corneal curvature was investigated by examining the reflection of these rings by the cornea. Improvements in design of the keratoscope have enabled an area of up to 10 mm of corneal surface to be measured. The more recent development of computer-assisted photokeratoscopy have computers to analyse the photographed keratoscopy data. These instruments are generally known as corneal topography systems. Examples of commercially available systems are the EyeSys 2000 Corneal Analysis System (EyeSys Laboratories, Houston, TX, USA) and the TMS-1 (Computer Anatomy Inc., New York NY, USA). Corneal topography systems are able to generate corneal curvature measurements over both central and peripheral areas of the cornea.

Rasterstereography is the technique of projecting a known pattern onto an object and recording the distortion when viewed from an oblique angle (Belin *et al.*, 1995). Measurements are made on a real image compared to the virtual image that is produced with keratometry and keratoscopy.

*Methods of quantifying corneal curvature*

Keratometry measurements are usually expressed in mm as radii of curvature. These results can be converted to dioptric power values by assuming that the cornea is a single surface and has a refractive index of 1.336.

The video image obtained by corneal topography systems is processed by a set of algorithms that are able to map the corneal surface in various ways. Dioptric power maps of the corneal surface are usually generated for clinical use. A colour coding scheme is applied to the power maps whereby different powers are represented by different colours (e.g. blues for lower powers and reds for higher). Other measurements include simulated K readings, location of the major astigmatic meridians and actual dioptric power measurements at each point.

Several algorithms exist which provide further quantitative information regarding the anterior corneal surface. The most commonly used model for describing the cornea is an ellipse. There are two different types of ellipse, those that display a flatter peripheral curvature than the apical radius and those with a steeper peripheral curvature. A general equation to describe a conic section has been modified by Bennett (1966),

$$y^2 = 2r_o x - px^2$$

where $r_o$ is the radius of curvature at the apex and $p$ is an index of peripheral flattening called the $p$-value. Other researchers have referred to $p$ as the shape factor to account for conditions where the peripheral cornea does not flatten with regard to $r_o$ (Guillon, Lydon and Wilson, 1986). The shape factor represents the level of asphericity and has the following values: $p < 0$ hyperbola; $p = 0$ parabola; $0 < p < 1$ oblate (flattening) ellipse; $p = 1$ sphere; $p > 1$ prolate (steepening) ellipse.

Corneal asphericity has also been defined by its eccentricity ($e$). The formula,

$$p = 1 - e^2$$

relates the eccentricity value to the shape factor.

*Variations in corneal curvature*

Research has indicated that adult values of corneal curvature are reached by age of 3 and remain relatively stable throughout life (see § 1.2). This finding is different to the other ocular components which change throughout childhood and stabilise at 15 to 18 years of age (see § 1.2). The average adult corneal curvature is approximately 7.86 mm with a range of 7.0 to 8.80 mm (Stenström, 1946).

Racial differences in corneal power are believed to exist with Chinese populations having steeper central corneal curvatures and a lower rate of peripheral flattening than Caucasian populations (Lam and Douthwaite, 1996; Lam and Loran, 1991).

*Purpose of present study*

Anisometropia of 2D or more is generally assumed to be axial in origin (Sorsby, Leary and Sheridan, 1962) (see § 2.2.1). However, as the cornea is the major ocular refracting surface, interocular differences in corneal power may account for, or contribute to, refractive differences in anisometropia. This hypothesis is addressed by assessing the differences in corneal topography between right and left eyes in anisometropes. Racial differences in the distribution of refractive error exist with Chinese populations have a much higher prevalence of myopia (see § 2.1.2). Corneal curvature data obtained from Caucasian subjects and from age-matched Chinese

subjects are compared to investigate whether the racial discrepancies in refractive error are also depicted in corneal topography. The corneal curvature is assessed by both conventional keratometry and by corneal topography.

## 6.2 *Methods*

*Subjects*

The study consisted 36 Caucasian and 23 Chinese subjects. The 36 Caucasian subjects were divided into 2 sub-groups; 18 anisometropes with 2D or more interocular difference in refractive error and 18 isometropes with 0.50D or less inter-eye refractive difference. The Chinese subjects also consisted 2 groups; 18 anisometropes and 5 isometropes. The data on the Caucasian subjects was obtained at Aston University, Birmingham, UK, whereas the measurements on the Chinese subjects were collected at Queensland University of Technology, Brisbane, Australia (see § 4.1).

None of the subjects had any current or past corneal pathology. The anisometropia was not secondary to any ocular pathology. Corrected visual acuity was at least 6/6 in each eye. If the subject wore contact lenses these were not worn on the day of testing.

*Experimental procedure*

Keratometry measurements on the Caucasian subjects were obtained with a Zeiss keratometer. A Bausch and Lomb keratometer was utilised to measure the corneal curvatures of the Chinese subjects. Prior to obtaining keratometer measurements for each subject, the eye piece was focused according to the manufacturer's instructions.

The keratometers were calibrated with steel balls whose diameters were measured with electronic callipers, capable of measuring to ± 0.001 mm. The range of diameters of the steel balls was 14.2 to 16.8 mm. The calibration of the keratometers was checked periodically.

Three measurements of corneal curvature and axis were made along both the steepest meridian and the flattest meridian for both eyes of all subjects.

Corneal topography data on the Caucasian subjects was obtained with an EyeSys 2000 Corneal Analysis System (EyeSys Laboratories, Houston, TX, USA). The corneal topography of the Chinese subjects was assessed with a Topographic Modelling System, TMS-1 (Computed Anatomy Inc., New York, NY, USA).

The calibration of the EyeSys system was checked periodically using the EyeSys calibration spheres. They ranged in power from 37.50D to 55.06D.

Each subject was instructed to place his/her chin on the chinrest and the forehead against the brow bar of the instrument, and asked to fixate a small light in the centre of the instrument. The subject was encouraged to blink freely while the corneal topography system was aligned, then instructed not to blink during the time required to capture the image. Both corneal topography

systems have an auto-alignment system whereby any changes in eye position, during image capture, are sensed and corrected for by re-alignment. The procedure was repeated until five good quality images were obtained for each eye. Images were considered to be of good quality if they were in focus, centred, with no dry spots, or excessive shadows from the lashes or the nose.

Refractive error was assessed by retinoscopy and a subjective examination for both eyes of each subject. The refractive error data is expressed in terms of spherical equivalent.

### 6.3 *Results*

Analysis of corneal topography by apical radii and *p*-values are based on rotationally symmetrical measurements and do not investigate the potential for asymmetric changes in corneal topography associated with different refractive errors. To assess any asymmetry in corneal topography the data has also been analysed by comparing the rate of change in peripheral radii at different distances from the centre of the cornea, for both the nasal and temporal meridians. The Caucasian and Chinese data were evaluated separately to allow comparisons between racial groups. Measurements from right and left eyes were also analysed separately to eliminate the effect of inter-eye correlation that may occur between a pair of eyes (Ray and O'Day, 1985).

*Precision of corneal topography*

The precision of the corneal topography measurements was investigated by taking 5 videokeratographs for each eye of each Caucasian subject.

Average standard deviation for all Caucasian right eyes was

| | |
|---|---|
| for central 1 mm zone | ± 0.042 mm (n=36) |
| for a 4 mm annulus | ± 0.023 mm (n=36) |
| for a 8 mm annulus | ± 0.055 mm (n=29) |

This suggests a reasonable precision of the repeated measurements taken using the corneal topographic system (equates to ≤ 0.50D for central and 4 mm annulus and ≤ 0.75D for 8 mm annulus). Similar standard deviations were found for the left eyes.

*Central corneal curvature*

Mean, standard deviation and range values for keratometry and corneal topography are given in Table 6.1. The corneal topography measurements are for the central 1 mm of the cornea. Data are reported for both eyes of the Caucasian and Chinese subjects (see Appendix 8).

Table 6.1 Central corneal curvature parameters for Caucasian and Chinese subjects.

| | Caucasian | | Chinese | |
|---|---|---|---|---|
| | right | left | right | left |
| K mean | 7.84 ± 0.23 | 7.81 ± 0.25 | 7.80 ± 0.26 | 7.81 ± 0.27 |
| K range | 7.29 - 8.77 | 7.27 - 8.69 | 7.42 - 8.34 | 7.41 - 8.35 |
| CT mean | 7.86 ± 0.33 | 7.87 ± 0.34 | 7.67 ± 0.23 | 7.67 ±0.23 |
| CT range | 7.20 - 8.73 | 7.23 - 8.77 | 7.20 - 8.20 | 7.23 - 8.30 |

K, keratometry; CT, corneal topography; all measurements are in mm; ± one standard deviations.

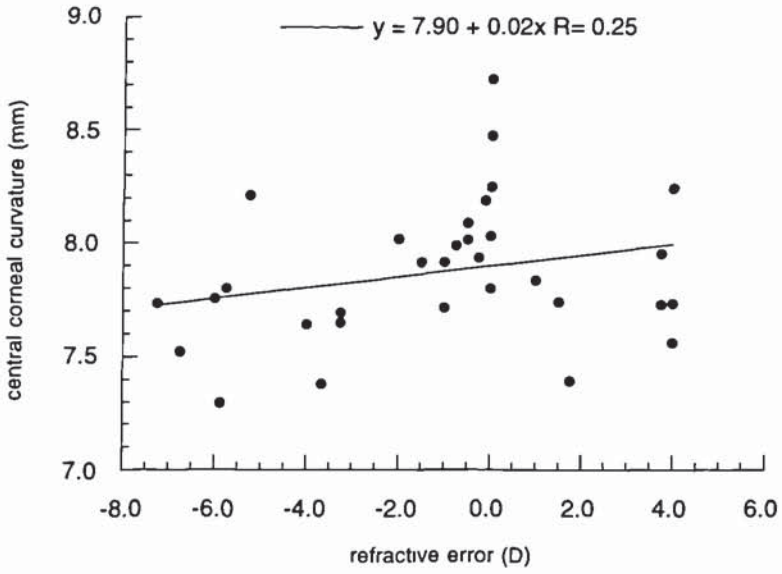



Figure 6.1 Central corneal curvature plotted against refractive error for the right eyes of the Caucasian subjects.

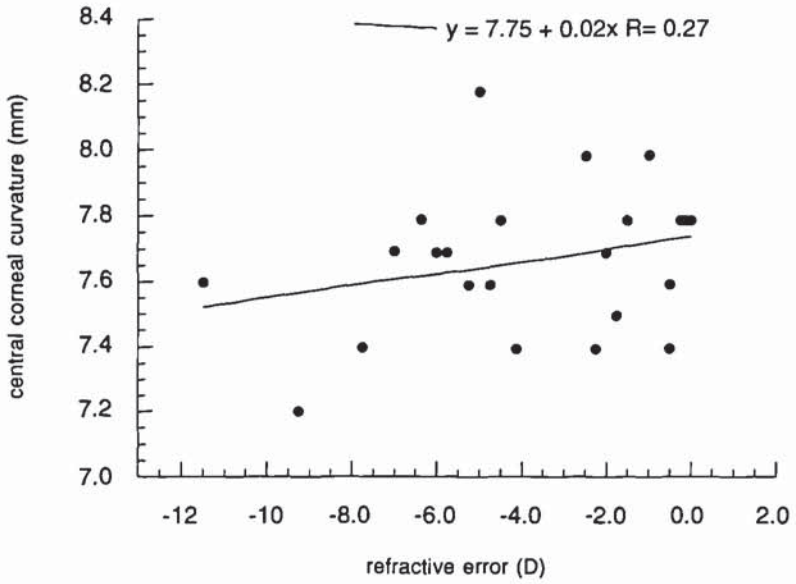



Figure 6.2 Central corneal curvature plotted against refractive error for the right eyes of the Chinese subjects.

A very weak correlation between refractive error and central corneal curvature is evident for both the Caucasian ($r^2 = 0.06, p < 0.20$) and Chinese subjects ($r^2 = 0.07, p < 0.20$).

A similar correlation between central corneal curvature and refractive error was found for the left eyes of both the Caucasian ($r^2 = 0.07, p < 0.20$) and Chinese subjects ($r^2 = 0.07, p < 0.20$).

*Peripheral corneal curvature*

The shape factor, which indicates the rate at which the curvature of the peripheral cornea departs from the central, has a mean value of 0.77 ± 0.07 (range 0.46 - 0.89) for all Caucasian right eyes and a mean of 0.75 ± 0.10 (range 0.41 - 0.88) for left eyes. The algorithms for the TMS-1 corneal topography system calculate the corneal surface in terms of polynomial functions. Therefore *p*-values have not been derived for the Chinese subjects. The data for both the Caucasian and Chinese subjects has been evaluated in terms of rate of change in curvature from the central cornea to the periphery (see figures 6.3 and 6.4). Corneal curvature values for the peripheral cornea at 2 mm and 4 mm from the centre of the cornea have been calculated for both the nasal and temporal meridians for all subjects (table 6.2).

*Table 6.2 Corneal curvature parameters at 2 mm and 4 mm from the centre of the cornea for both nasal and temporal meridians for Caucasian and Chinese subjects.*

| | Caucasian | | Chinese | |
|---|---|---|---|---|
| | right | left | right | left |
| mean 2 mm nasal | 7.93 ± 0.33 | 7.91 ± 0.35 | 7.86 ± 0.22 | 7.90 ± 0.23 |
| range 2 mm nasal | 7.36 - 8.83 | 7.33 - 8.81 | 7.51 - 8.32 | 7.52 - 8.50 |
| mean 2 mm temp | 7.90 ± 0.33 | 7.91 ± 0.33 | 7.81 ± 0.23 | 7.81 ± 0.24 |
| range 2 mm temp | 7.26 - 8.75 | 7.37 - 8.79 | 7.42 - 8.44 | 7.33 - 8.47 |
| mean 4 mm nasal | 8.22 ± 0.31 | 8.13 ± 0.38 | 8.17 ± 0.26 | 8.19 ± 0.27 |
| range 4 mm nasal | 7.65 - 8.72 | 7.48 - 9.12 | 7.70 - 8.62 | 7.71 - 8.70 |
| mean 4 mm temp | 8.05 ± 0.34 | 8.11 ± 0.35 | 7.94 ± 0.24 | 7.90 ± 0.30 |
| range 4 mm temp | 7.65 - 8.86 | 7.47 - 8.90 | 7.54 - 8.65 | 7.47- 8.64 |

all measurements are in mm; ± one standard deviation.

Corneal curvature showed the expected trend; an increase in corneal curvature from central to peripheral cornea, indicating that the cornea flattened peripherally. The data indicates that the cornea is asymmetrical in shape, flattening more on the nasal side. This asymmetry is found in both the Caucasian and Chinese subjects (Table 6.2).

The rate of change in corneal curvature from the centre of the cornea to 4 mm in the periphery for both the Caucasian and Chinese subjects is shown in figures 6.3 and 6.4. The graphs depict the data for the temporal cornea only.

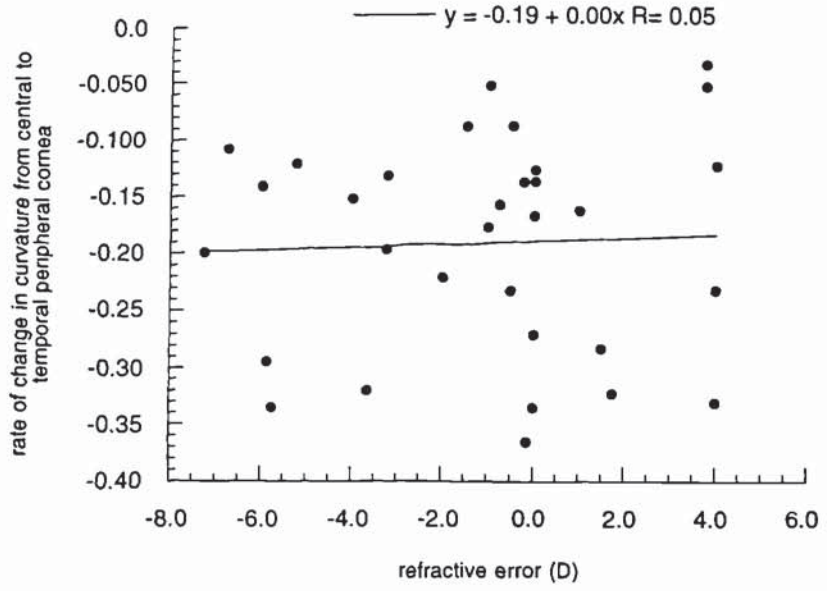



Figure 6.3 Rate of change in curvature from the central cornea to 4 mm in the temporal periphery plotted against refractive error for right Caucasian eyes.

No correlation was found between refractive error and rate of change of peripheral curvature (see figure 6.3) for the Caucasian subjects ($r^2$ = 0.003,p > 0.50). Similar results were found for both nasal and temporal meridians and for right and left eyes.

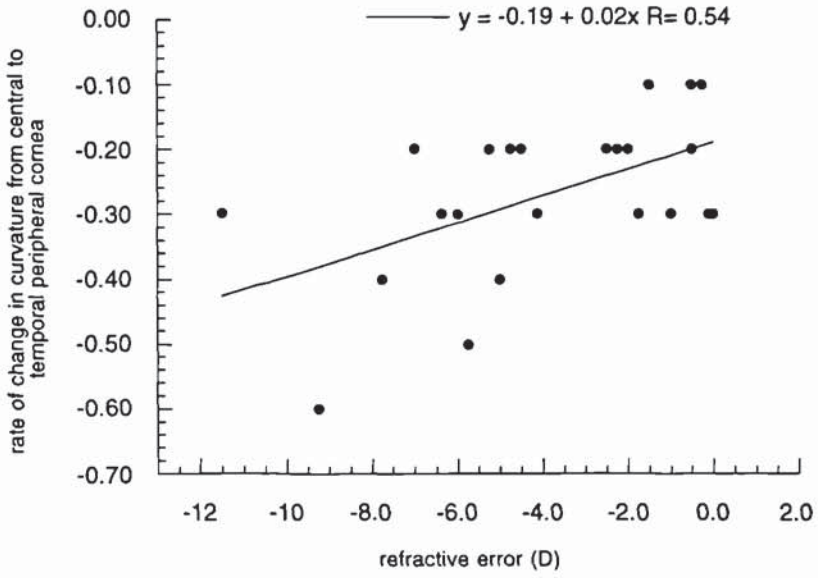



Figure 6.4 Rate of change in curvature from the central cornea to 4 mm in the temporal periphery plotted against refractive error for right Chinese eyes.

A weak correlation ($r^2$ = 0.29, p < 0.10) was found between refractive error and rate of change of peripheral curvature for the Chinese subjects (see figure 6.4). This finding was also evident for the nasal meridian and for the left eyes.

All the individual corneal topography results indicate that the cornea flattens peripherally for both the Caucasian and Chinese groups. No cases of peripheral corneal steepening were encountered.

*Interocular comparisons in corneal topography*

Corneal topography has been compared in right and left eye pairs to assess any contribution of the cornea to the refractive error difference that exists in anisometropia (see figures 6.5, 6.6, 6.7 and 6.8).

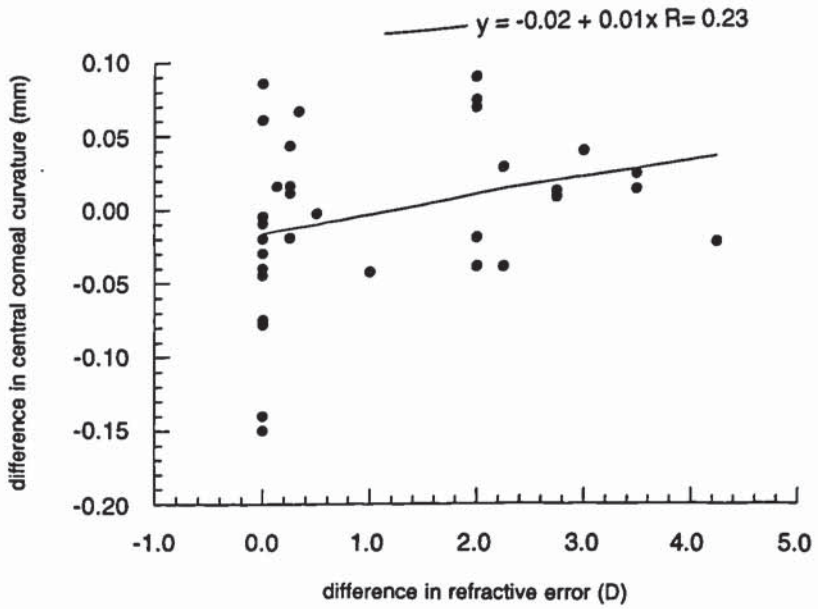



Figure 6.5 Interocular difference in central corneal curvatures plotted against the difference in refractive error for the Caucasian subjects.

No correlation between interocular difference in refractive error and central corneal curvature was found for both the Caucasian subjects ($r^2 = 0.05$, $p > 0.50$) and the Chinese subjects ($r^2 = 0.01$, $p > 0.50$) (see figures 6.5 and 6.6).

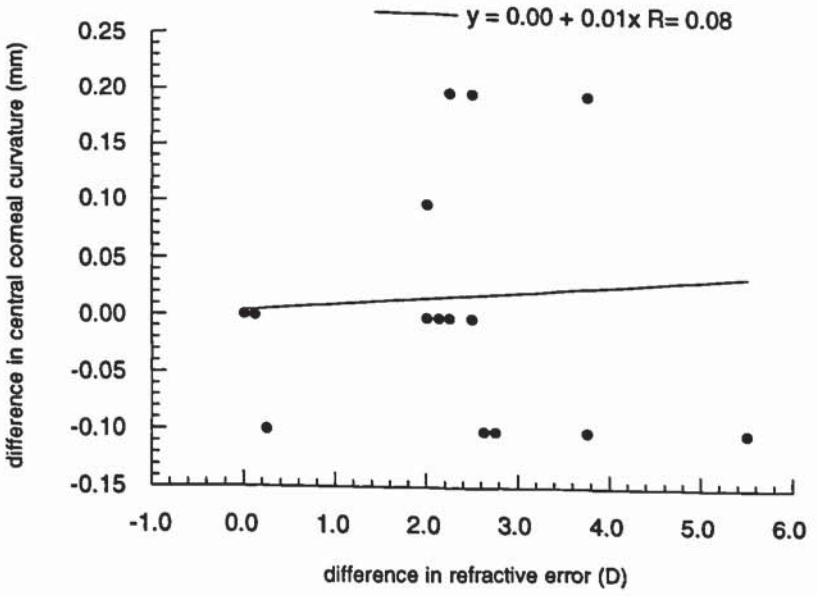



Figure 6.6 Interocular difference in central corneal curvature plotted against the difference in refractive error for the Chinese subjects.

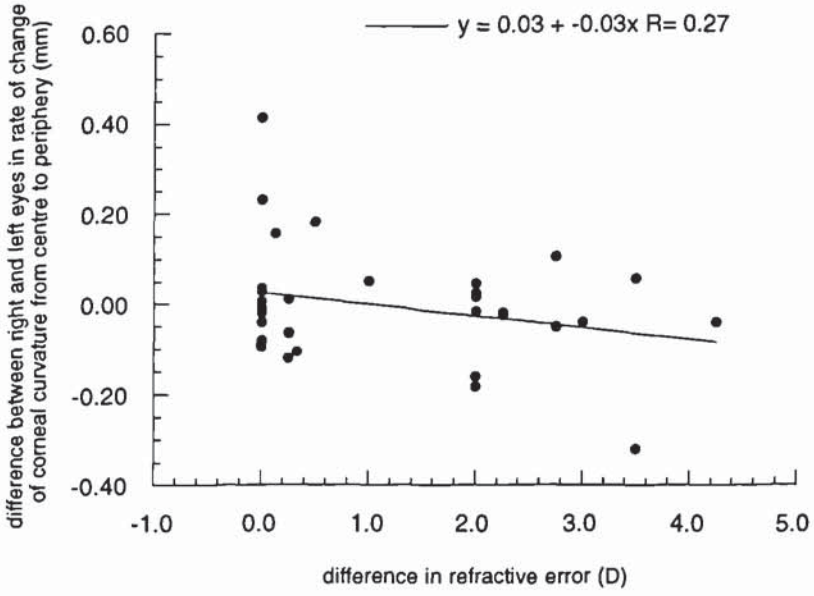



Figure 6.7 Difference in rate of change of curvature from central to peripheral temporal cornea in a pair of eyes plotted against difference in refractive error for Caucasian subjects.

Interocular difference in rate of change of corneal curvature from the centre to 4 mm in the temporal periphery showed no correlation with inter-eye difference in refractive error for either Caucasian ($r^2 = 0.07$, $p > 0.50$) or Chinese ($r^2 = 0.05$, $p > 0.50$) subjects (see figures 6.7 and 6.8). A similar finding was evident for the nasal meridians.

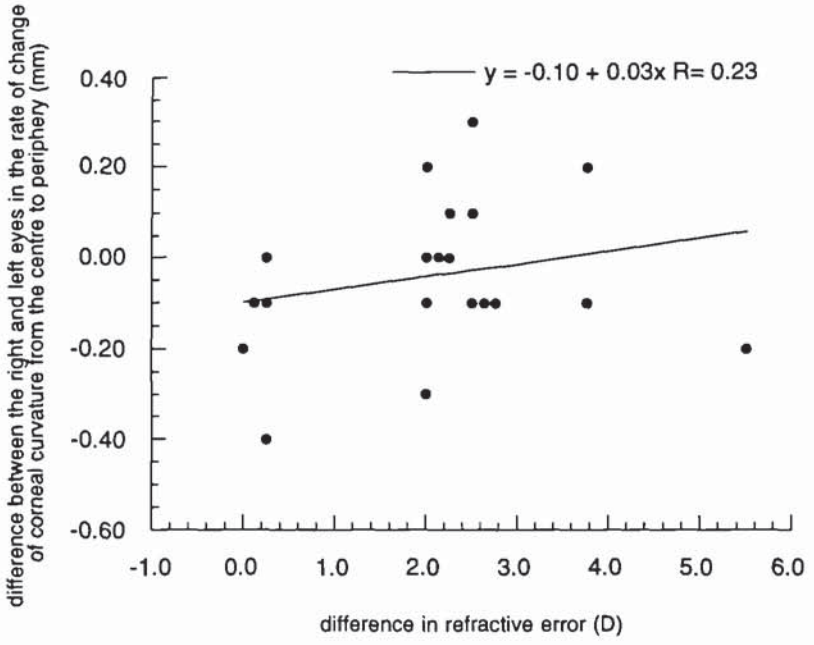



Figure 6.8 Difference in rate of change of curvature from central to peripheral temporal cornea in a pair of eyes plotted against difference in refractive error for Chinese subjects.

None of the changes in corneal refractive power associated with anisometropia approached significance for either the Caucasian or Chinese subjects.

## 6.4 *Discussion*

*Central corneal curvature*

The mean keratometric value of the Caucasian sample of 7.84 ± 0.23 mm is similar to that found in previous work on normal Caucasian populations (Guillon, Lydon and Wilson, 1986; Kiely,Smith and Carney, 1982). The Chinese subjects had a mean keratometry reading of 7.80 ± 0.26 mm, which is very similar to the Caucasian data. Other researchers have found a mean corneal radius of 7.70 ± 0.27 for a group of Hong Kong Chinese subjects (Goh, and Lam, 1994; Lam and Douthwaite, 1996).

Central corneal measurements with the corneal topography systems were found to be 7.86 ±0.33 mm for the right eyes of the Caucasian subjects and 7.67 ± 0.23 mm for the Chinese subjects. There is a discrepancy in the central corneal measurements by the two methods for the Chinese subjects compared to the Caucasian data. This may be due to instrument differences; the EyeSys gives curvatures at 16 positions along each of the 360 semi-meridians, whereas the TMS-1 instrument gives curvatures at 25 points along each of the 256 semi-meridians. The set-up procedures of different keratometers may also contribute to the discrepancy.

*Peripheral corneal curvature*

The averaged *p*-value of the Caucasian sample was 0.77 ± 0.07 mm. This is similar to the findings of Kiely, Smith and Carney (1982) (*p*-value = 0.74) on a Caucasian sample. A greater *p*-value in Chinese subjects has been reported by Lam and Douthwaite (1996) (*p*-value = 0.80). However, Guillon, Lydon and Wilson (1986) have recorded a similar value in a Caucasian sample (*p*-value = 0.82).

Interindividual variation in *p*-values is evident with a large range of 0.46 to 0.89. This agrees with previous findings by Kiely, Smith and Carney (1982). Correcting their data to *p*-values, they obtained a range of 0.24 to 1.47. A similar range of 0.21 to 1.20 was found by Guillon, Lydon and Wilson (1986). Interestingly these researchers found a number of cases where the cornea did not flatten peripherally but remained unchanged or steepened. This finding was not evident in the present study where all corneas depicted corneal flattening in the periphery, denoted by a *p*-value of $0<p<1$.

Chinese eyes have been reported to have a mean *p*-value of 0.8 - 0.9 horizontally (Lam and Loran, 1991; Lam and Douthwaite, 1996).

The variation in corneal topography with refractive error has been investigated by Sheridan and Douthwaite (1989), Carney and Henderson (1993) and Carney, Mainstone and Henderson (1997).

By analysing previously published results on central and peripheral corneal curvature, Sheridan and Douthwaite (1989) suggested that different refractive groups had similar *p*-values but different apical radii. They found myopes to have significantly steeper apical radii than emmetropes, whose central corneas were steeper than hyperopes.

Carney and Henderson (1993) measured the corneal topography of 40 emmetropes and 80 myopes with a range in refractive error up to -9D. They found no systematic variations in corneal topography for myopia up to -4D. However, higher levels of myopia were associated with steeper apical radii and reduced peripheral flattening. A similar finding has been reported by Carney, Mainstone and Henderson (1997). Corneal topography was measured in 30 emmetropes and 85 myopes divided into low, medium and high degrees of myopia. They found a low but statistically significant positive correlation between corneal asphericity and refractive error. Myopic eyes were also associated with steeper central corneas. These findings were mainly evident in the high myopic group i.e. myopia greater than -4D.

The results in the present study indicate a weak relationship between central corneal curvature and refractive error with the myopes having a steeper corneal radius than emmetropes and hyperopes. No relationship between myopia and reduced peripheral flattening was found for the Caucasian subjects. However, the Chinese subjects showed a reduction in rate of peripheral flattening. This discrepancy in the two findings may be accounted for by the different distributions of refractive error in the studies and the different sample sizes.

The corneal curvature in the Chinese subjects has been found to be steeper than that for the Caucasian subjects. This may reflect the greater proportion of high myopia in the Chinese group than in the Caucasian group. Other factors contributing to this discrepancy may be racial differences or differences in the instruments used to measure the corneal curvature.

*Interocular differences in corneal topography*

Research has indicated that the majority of corneal growth occurs pre-natally (Scammon and Wilmer, 1950) and nearly all post-natal growth has been found to occur within the first few years of life (Sorsby, Benjamin and Sheridan, 1961). In a cross-sectional study Zadnik *et al.* (1993) found that the corneal power varied non-systematically within 0.75D in 530 children between the ages of 6 and 12 years. Mean corneal power was 43.75D at 6 years of age and 43.91D at 12 years of age.

A longitudinal study of ocular changes in 67 full-term subjects from age 10 to 18 years was conducted by Fledelius (1982). He reported that there was no significant change in corneal radius over this period. The average value of corneal radius for the 36 male subjects was found to be 7.93 ± 0.27 mm for the 10 year olds and 7.95 ± 0.27 mm for the 18 year olds. At both ages the range of corneal radius was 7.5 to 8.5 mm.

The investigations suggest that adult values of corneal radius are reached by the age of 3 and remain relatively stable throughout life (see § 1.2). In contrast to the stability of corneal curvature throughout childhood, refractive error changes significantly during this period (see § 1.3). Unlike

corneal curvature, anisometropia has been found to be transient throughout childhood only attaining a degree of permanency by the second decade of life (Laird, 1991). These findings would suggest that an interocular difference in corneal curvature in anisometropia is unlikely.

All studies comparing the contribution of corneal curvature to anisometropia have concluded that the cornea does not appear to contribute significantly to anisometropia. Waardenburg (1930) found that only rarely do the powers of the two corneae show a difference in excess of 1D even with substantial degrees of anisometropia. In Sorsby, Leary and Richards' (1962) investigations, similar results were found. They noted that the range of differences in corneal power did not extend beyond 2D for 68 subjects with a range of 2 to 15D anisometropia. The difference in corneal power between a pair of eyes was sufficient to account for the anisometropia in 3 cases - all of a low order. In another 10 cases the cornea contributed to reduce the anisometropia. Otsuka, Sugata and Araki (1981) assessed the aetiology of myopia by comparing the refractive components in right and left eyes. They noted that low, medium and high anisometropes all had a significant correlation between degree of ametropia and axial length. They found no statistical significance in corneal power between a pair of eyes including high anisometropes. In another study on the refractive components of iso- and anisometropes, Fledelius(1981b) found similar results to Otsuka, Sugata and Araki in that corneal power did not contribute to the anisometropia.
In the present study both central and peripheral corneal curvature have been found to be similar in a pair of eyes for both anisometropes and the isometropic group.
This finding supports the earlier research on central corneal curvature and anisometropia suggesting that corneal curvature contributes little to the interocular refractive difference found in anisometropia.

*Asymmetries in corneal curvature*

A study of normal corneas has shown that many display substantial asymmetries, with the nasal peripheral cornea being the flattest and the inferior cornea flatter than the superior (Mandell, 1992). Table 6.2 confirms the assumption that corneal topography in the horizontal meridian is asymmetrical in nature with the cornea flattening more on the nasal side. This was evident for both the Caucasian and Chinese subjects. The variations in inter-eye peripheral refraction cannot be significantly affected by the refractive properties of the cornea. However, the asymmetry in peripheral refraction data may arise from the asymmetries in corneal topography.

## 6.5 *Summary*

The investigations into corneal topography and refractive error have indicated a slight correlation between myopia and steeper central corneal radii for both Caucasian and Chinese subjects, thus confirming previous research. However, no such correlation was evident for peripheral curvature changes in Caucasian eyes; no systematic variation between rate of peripheral flattening and degree of ametropia was found. In contrast, Chinese subjects had a weak correlation between ametropia and rate of peripheral flattening; the more myopic eyes demonstrating less peripheral flattening. The discrepancies in the results may arise from inherent racial differences, sample size differences or variations in the degree of subject's myopia.

Importantly, there was no relationship between degree of anisometropia and interocular difference in corneal curvature for both the central and peripheral cornea for both the Caucasian and Chinese subjects. These findings agree with earlier work and suggest that corneal curvature contributes little to the inter-eye refractive error difference in anisometropia.

# CHAPTER 7

# ACCOMMODATION IN ANISOMETROPIA AND ISOMETROPIA

## 7.1 *Introduction*

Near work has been implicated in the aetiology of myopia (Rosenfield, 1994) (see § 1.4.2). The contribution of accommodation to myopia development has been investigated by various researchers. They have attempted to correlate differences in accommodation with refractive error to ascertain whether there is a link between the development of myopia and sustained near work. McBrien and Millodot (1986a) have demonstrated that myopes have a poorer than normal amplitude of accommodation. Higher accommodative response gradients have been reported for emmetropes compared to myopes (McBrien and Millodot, 1986; Gwiazda *et al.*, 1993). Yet it is unclear whether the accommodative lag in myopes is the cause or the result of their refractive error.

Van Alphen (1986) suggested that the axial elongation in myopia may arise from an eye unable to resist potential stretching forces. These stretching forces may be proportional to the tone in the ciliary muscle. The ciliary muscle tone may be measured clinically as accommodation under open-loop conditions. However, the degree to which measures of tonic accommodation actually reflect choroidal tonus has yet to be resolved (Gilmartin, in preparation). He suggested that it is inherent ciliary muscle tonus that determines scleral stretch rather than stimulus-evoked contraction of the ciliary muscle. Studies investigating a correlation between refractive error and open-loop or tonic accommodation have revealed conflicting results (Bullimore and Gilmartin, 1987; McBrien and Adams, 1997).

The central drive from accommodation has to be the same in a pair of eyes i.e. is consensual. The purpose of the present study is to ascertain whether biometric factors affecting the accommodative plant may distribute the central accommodative gain unequally between the two eyes. If the peripheral accommodation response varies with refractive error, then anisometropes might be expected to demonstrate interocular differences in accommodation response. The present study, prompted by the McBrien and Millodot (1986a) paper, has addressed the above hypothesis by comparing the amplitude of accommodation, stimulus-response curves and tonic accommodation for subjects with a range of refractive error which includes anisometropia.

The amplitude of accommodation is the maximum amount of accommodation that one eye can exert. The accommodative amplitude is age-related and has been found to decline from approximately 14D at 10 years of age to 1.5D by the age of 50 (Bennett and Rabetts, 1989; Charman, 1989).

The steady-state accommodation response has traditionally been assessed by comparing the accommodative response to a known dioptric stimulus. The accommodative mechanism is able to operate over a relatively wide range, in young eyes, which is represented by the stimulus-response function. The accommodation stimulus-response relationship typically shows departure from the one-to-one slope (Morgan, 1944). For distant objects the accommodation response shows a 'lead' of accommodation. The lead magnitude decreases to zero at an intermediate stimulus vergence (about 1 to 2D). At high stimulus vergences, the error in the accommodation response again increases and shows a 'lag' in accommodation.

The central portion of the stimulus-response function between stimulus levels of about 1D and 6D is quasi-linear and its gradient is a measure of the gain of the accommodative system. The linear regression slope of this curve has been used as a measure of ability to accommodate to a known stimulus.

Chauhan and Charman (1995) have questioned the feasibility of using the linear regression parameter as a measure of accommodative ability. They have derived a new parameter, the accommodative error index, to combine the three regression line parameters of $m$, its slope, $c$, the intercept on the $y$-axis, and $r^2$, the Pearson correlation coefficient. The accommodative error index is the mean of the magnitude of the response error divided by the correlation coefficient. The accommodative error index is calculated from the area between the best fit curve, to the accommodation stimulus-response data, and the unit ratio.

In the present study the comparisons in the stimulus-response functions have been made using the accommodative error index parameter after Chauhan and Charman (1995). The interocular differences in accommodative response in both anisometropes and isometropes have been correlated with the inter-eye difference in refractive error to assess any discrepancies in the accommodation response found with different refractive errors. Comparisons of accommodation response between a pair of eyes in one individual reduce the effects of intersubject variability.

## 7.2 *Methods*

*Subjects*

The accommodation response was measured in 40 Caucasian subjects. These subjects consisted 20 anisometropes with a minimum interocular refractive error difference of 2D and 20 isometropes with a maximum inter-eye difference in refraction of 0.50D. The isometropic group matched the anisometropes for age and range of refractive error. All subjects had less than 1.00D astigmatism.

Refractive error was assessed by cycloplegic retinoscopy. Monocular visual acuities (corrected or uncorrected) were 6/6 or better. None of the subjects had any form of visual abnormality. All refractive errors were corrected using ultra-thin *Acuvue* (Johnson & Johnson, Vistakon, UK) soft contact lenses. The subjects were allowed 30 min to adapt to their soft contact lenses prior to the

accommodation measurements. The emmetropic subjects did not wear contact lenses during the experimental procedure (Edwards, 1994).

*Measurement of amplitude of accommodation*

Two techniques were used to assess the amplitude of accommodation, the push-up and push-down methods (Rosenfield and Cohen, 1995). All accommodation measurements for each subject were obtained at the same session.

The subjects viewed a high contrast (90%), black-on-white nearpoint card, with 6/9 Snellen print. This nearpoint card was mounted at eye level on an optical bench with the subject positioned on a chinrest at one end of the optical bench. The amplitude of accommodation of the right eye was measured first. One eye was fully occluded while the accommodation in the contralateral eye was measured.

The subjects were instructed to view a single optotype within the smallest line of letters that could be resolved at a distance of 40 cm.

For the push-up procedure, the experimenter moved the target slowly towards the subject until they reported the first sustained blur. For the push-down measurements, the target was advanced approximately 1 D beyond the blur point found by the push-up method and then moved away from the subject until the target just became clear. For each measurement an average of five readings was taken.

*Factors influencing the accommodative response*

The characteristics of the target have been found to influence the accuracy of the accommodation response. The effect of target spatial frequency on the stimulus-response relationship has been investigated by Charman and Tucker (1977). They found that the magnitude of the accommodative lag was greatest for low spatial frequencies. The accuracy of the accommodation response was reported to be greater for Snellen letters, as a chart with different letter sizes contains a range of spatial frequencies, than for any specific spatial frequency. In the present study a Maltese cross stimulus target was used for the stimulus-response accommodation measurements. A Maltese cross, like Snellen letters, comprises a wide range of spatial frequencies.

As mentioned above target proximity may influence the accommodative response. Rosenfield and Gilmartin (1990) noted an increase in the accommodative response when the subjects viewed a 3 D target compared to a 0.2 D target under open-loop accommodation conditions. Target size is often used as a cue in determining apparent distance; a smaller object is perceived as being further away. A Badal system was used in the present study to minimise the influence of target size. The Badal system is designed so that the perceived angular size of the target is independent of the target position and the power scale is linear. The luminance of the target is also maintained at a constant level (Atchison *et al.*, 1995; Gallagher and Citek, 1995).

*Measurement of accommodative stimulus-response curve*

Accommodation was measured with an infra-red autorefractor, the Canon R-1 autorefractor (Canon Europa, UK) in its single-shot mode of operation (see § 4.2.1a). All measurements were referred to the corneal plane. Mean spheres were calculated for all accommodation measures. Accommodation was sampled and recorded successively at 1.5 sec intervals by an interface connection (designed and distributed by S. W. Spadafore, Franklin & Marshall College, P. O. Box 3003, Lancaster, PA 17604, USA) between the printer port of the autorefractor and a Macintosh Classic computer.

The stimulus target was presented in a Badal system. The lens used in the Badal system was a +5D aspheric lens with a diameter of 70 mm. The stimulus target was a high contrast (90%) black Maltese cross against an internally illuminated white background (38 $cdm^{-2}$). The room luminaces were mesopic, averaging 5 $cdm^{-2}$ which were necessary to maintain pupil sizes at greater than 2.8 mm throughout the testing (see § 4.2.1).

The subjects placed their chin on the chinrest and forehead against the brow bar of the instrument. The subjects were allowed to blink freely during the experimental procedure, any measurements that were taken during a blink were eliminated by the computer software. Any drying out of the contact lenses was observed as blurring of the first Purkinje image, of the two alignment lights, that was displayed on the video monitor of the Canon. If this occurred the subject was encouraged to blink several times until the Purkinje image became clear.

The stimulus target was presented at the different dioptric levels of 0, 1, 2, 3, 4, and 4.5D in a random order. The subjects were allowed to adapt to the new stimulus level for 1 minute before measurements were taken. They were instructed to keep the target as clear as possible. Fifteen measurements of accommodation were then taken at each stimulus level at 1.5s intervals. Measurements were made monocularly while the eye not fixing was occluded.

*Measurement of accommodation under 'stimulus free' conditions*

Tonic accommodation was measured using a 0.5 mm pinhole in a Kodak Wratten 87 filter, mounted in a trial frame. The Wratten filter transmits non-visible infrared light but not visible light. This allows the subject to see through the 0.5 mm pinhole while the accommodation measurements taken with the non-visible IR light from the Canon autorefractor are not interfered with. The filter was tilted approximately 15° to the vertical plane to obtain readings with the Canon. The subjects viewed a Maltese cross. Measurements were made monocularly with an occluder over the eye not being examined. A period of 3 mins was allowed before readings were taken to allow the subjects to adapt and to reduce any transient fluctuations that may occur. Twenty measurements of tonic accommodation were taken for each eye.

### 7.3 *Results*

The mean amplitude of accommodation responses for both push-up and push-down procedures for right and left eyes of all subjects are shown in Table 7.1. Data is also given for the mean accommodative error index and the mean level of tonic accommodation. The results for the right and left eyes are similar. Mean individual accommodation data is shown in Appendix 9.

Interocular differences in accommodation parameters have been calculated by most myopic eye minus least myopic eye.

Table 7.1 Mean accommodation responses for right and left eyes of all subjects.

| accomm response | right eye (D) | left eye (D) |
|---|---|---|
| mean push-up | 10.07 (± 0.75) | 10.12 (± 0.72) |
| mean push-down | 9.72 (± 0.68) | 9.84 (± 0.66) |
| mean accomm error index | 0.41 (± 0.27) | 0.45 (± 0.25) |
| mean TA | 1.00 (± 0.65) | 1.12 ( ± 0.69) |

accomm, accommodation; TA, tonic accommodation; figures in parentheses are standard deviations; all measurements are in dioptres

*Amplitude of accommodation*

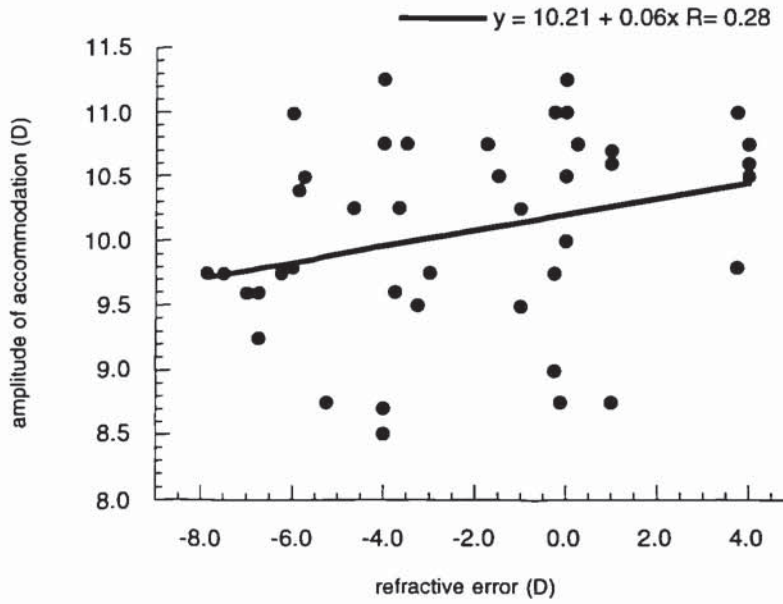



Figure 7.1 Shows the correlation between refractive error and push-up amplitude of accommodation for the right eyes of all subjects.

No correlation was found between refractive error and the push-up amplitude of accommodation ($r^2 = 0.079$, $p > 0.10$) (see figure 7.1). A similar finding was noted for the push-down amplitude of accommodation ($r^2 = 0.088$, $p = 0.50$).

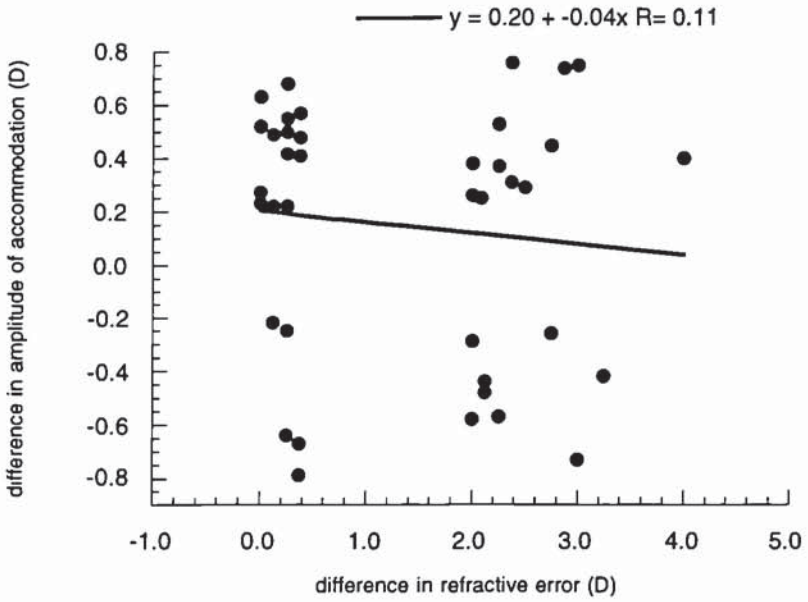



Figure 7.2 Shows the interocular difference in push-up amplitude of accommodation plotted against the difference in refractive error for all subjects.

From figure 7.2 it is evident that no correlation was found between interocular difference in push-up amplitude of accommodation and difference in refractive error ($r^2 = 0.011$, $p = 0.50$). A similar finding was observed for the push-down amplitude of accommodation ($r^2 = 0.027$, $p = 0.50$).

*Stimulus-response accommodation*

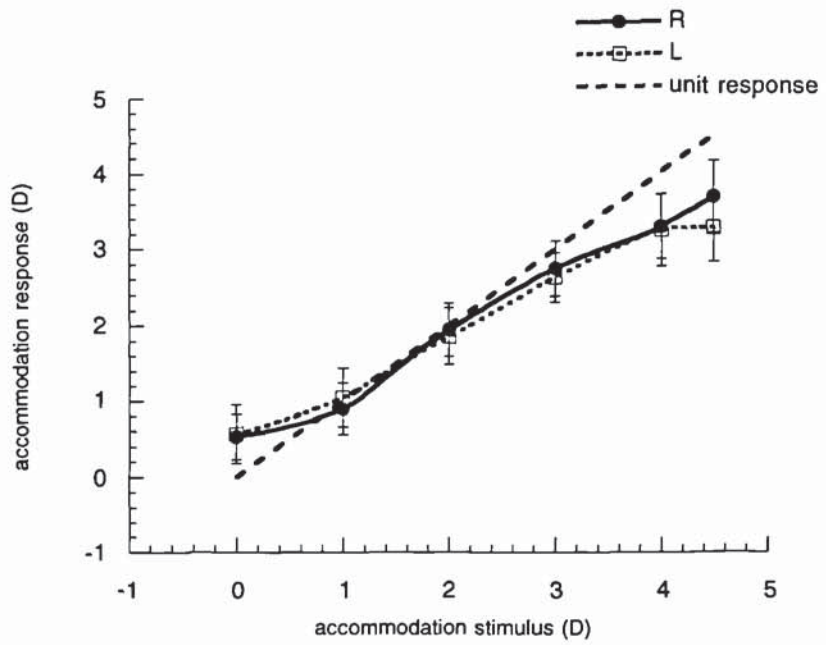



Figure 7.3 Represents an accommodation stimulus-response curve for subject FM, a 3 D anisomyope.

Figure 7.3 shows the typical stimulus-response curve with a lead of accommodation for low stimulus vergences and a lag of accommodation for high stimulus vergences. The data is for a 3 D anisomyope with a refractive error of R -0.25DS and L -3.25DS.

As depicted in figure 7.4, no correlation was found between accommodative error index and refractive error ($r^2 = 0.006$, $p = 0.50$) for all right eyes. A similar finding was recorded for all left eyes ($r^2 = 0.010$, $p = 0.50$).

Interocular comparisons of accommodative error index do not demonstrate a correlation with inter-eye differences in refractive error ($r^2 = 0.017$, $p > 0.50$) (see figure 7.5).

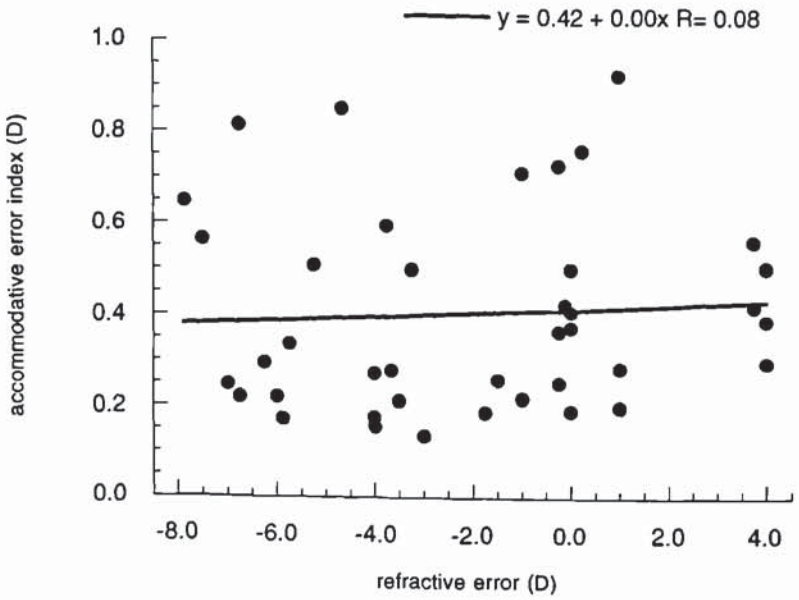



Figure 7.4 Shows the accommodative error index plotted against refractive error for the right eyes of all subjects.

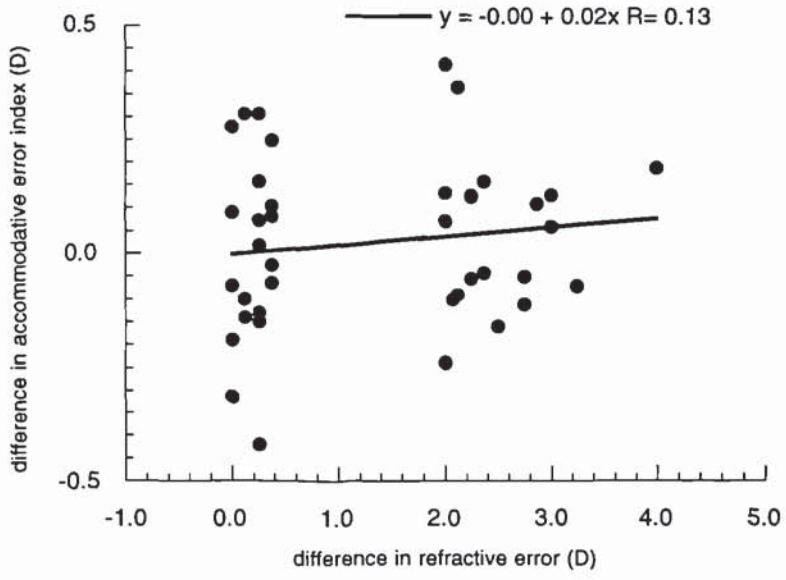



Figure 7.5 Shows the interocular difference in accommodative error index plotted against the inter-eye difference in refractive error.

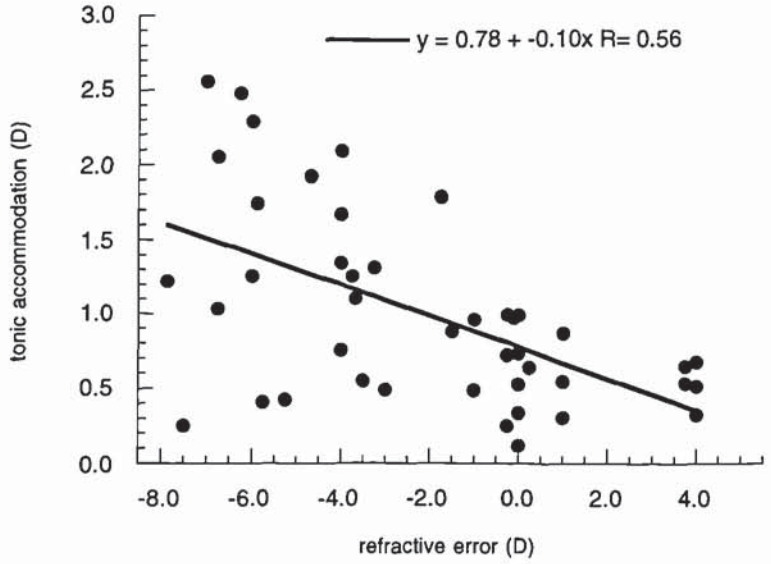



Figure 7.6 Shows the relationship between tonic accommodation and refractive error for the right eyes of all subjects.

A weak correlation was found between tonic accommodation and refractive error ($r^2 = 0.312$, $p < 0.10$) (see figure 7.6). However, no correlation between interocular difference in tonic accommodation and inter-eye difference in refractive error was found ($r^2 = 0.000$, $p > 0.50$) (see figure 7.7).

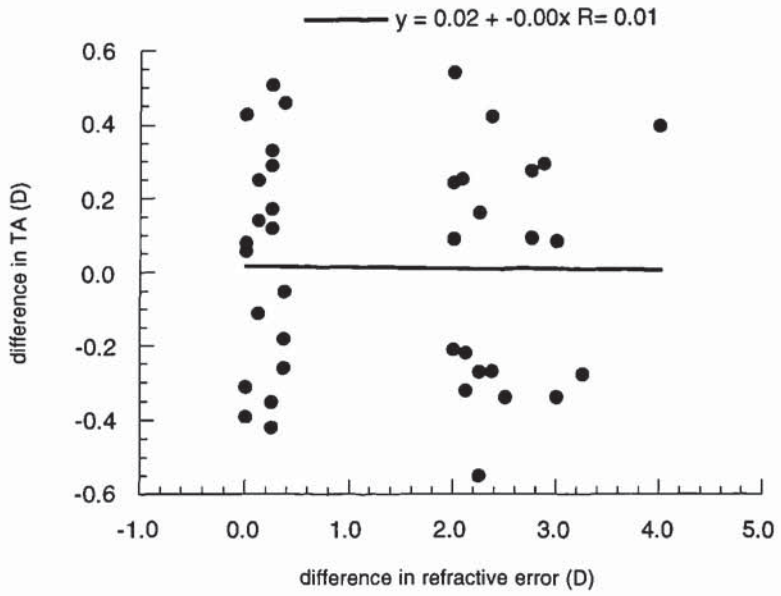



Figure 7.7 Shows the interocular difference in tonic accommodation plotted against the difference in refractive error.

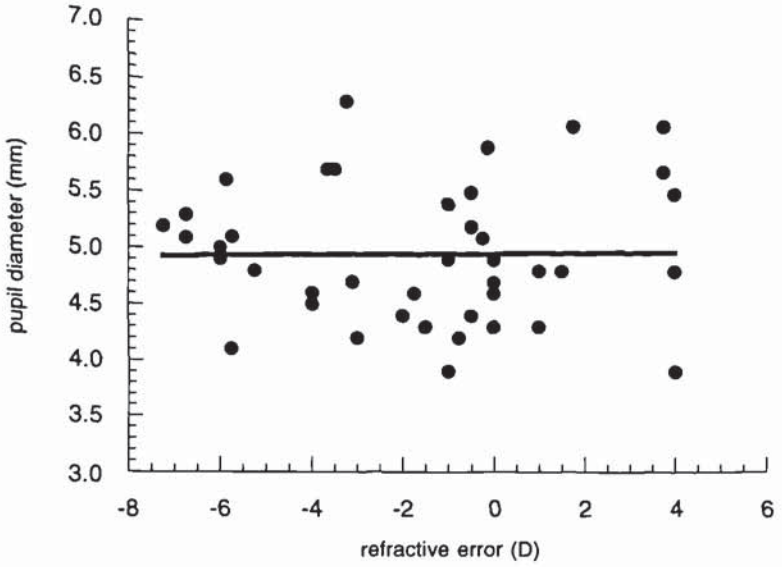



Figure 7.8 Shows the pupil diameter of the subjects plotted against refractive error. Pupil diameter was measured under closed-loop accommodation conditions while the subjects fixated the 0D stimulus target.

## 7.4 *Discussion*

*Amplitude of accommodation*

The mean values for the push-up amplitude of accommodation (10.07D for the right eye and 10.12D for the left eye) observed in the present study are similar to those found in the classic investigations of Donders (1864) and Duane (1912) for subjects of similar ages.

The push-up and push-down methods of measuring the amplitude of accommodation have been found to be repeatable by Rosenfield and Cohen (1995) with mean individual standard deviations of 0.73D and 0.71D respectively. The data recorded in the present study revealed similar standard deviations of 0.75D (push-up) and 0.68D (push-down) for amplitude of accommodation measurements. These findings suggest that the measurements recorded in this study are repeatable.

Higher values for amplitude of accommodation have been reported using the push-up method compared to the push-down procedure (Fitch, 1971; Hokoda and Ciuffreda, 1982). Although Fitch (1971) noted that for the age-group 25 to 40 years, the difference in values obtained by the 2 methods was small and not significant. This discrepancy in measurements between push-up and push-down procedures is also evident in the present study with a difference in accommodative power between the methods of 0.35D for the right eyes and 0.28D for the left eyes. The difference in measurements has been attributed to a greater proximally-induced accommodative response as the target approaches the subject (Rosenfield and Gilmartin, 1990).

*Stimulus-response accommodation*

The accommodation results reveal the typical stimulus-response curves that have been demonstrated by other researchers e.g. (McBrien and Millodot, 1986).

The position of the semi-silvered mirror limits the amount of accommodation at the higher end of accommodation stimulus-response that can be stimulated. The focal length of the lens used in the Badal system also restricts the amount of accommodation that can be stimulated. In the majority of subjects the stimulus-response curve did not asymptote as the greatest level of accommodation stimulated was not near the maximum amplitude of accommodation, which is approximately 10D for this age range.

The stimulus-response procedure revealed an increase in the error of the accommodation response as the target vergence increased. Ward and Charman (1985) have suggested that this may arise in part form the increased depth-of-focus associated with decreased pupil sizes. In the present study pupil diameters were kept to a maximum (approximately 5 mm) by using low room luminances as reliable measurements with a Canon autorefractor in its single-shot mode of operation are obtained only with pupil diameters greater than 2.8 mm.

*Tonic accommodation*

McBrien and Millodot (1986) reported that corrected hyperopes accommodated more than emmetropes to near targets. They hypothesised that these findings could result from a relatively weak sympathetic and strong parasympathetic accommodation input in myopes and the reverse in hyperopes. This theory is consistent with reports of different levels of tonic accommodation in different refractive groups (McBrien and Millodot 1987). The results of the present study demonstrate a weak correlation between refractive error and tonic accommodation with a higher level of tonic accommodation being associated with greater myopia. This finding is in conflict with data from previous studies which found a lower level of tonic accommodation with greater degrees of myopia (McBrien and Millodot, 1987). However, the data in this study appear to be more variable for the myopic subjects than for the emmetropes and hyperopes. Interestingly, no relationship was found between the interocular difference in tonic accommodation and inter-eye difference in refractive error. This finding suggests that the ciliary tone is similar in a pair of eyes and that there is no correlation between tonic accommodation and refractive error.

*Accommodation and refractive error*

A number of studies have shown that corrected myopic subjects tend to accommodate less to near targets than do emmetropic subjects (Gwiazda *et al.*, 1993; McBrien and Millodot, 1986).

The results of the present study do not reflect this finding; no correlations were found for either the push-up or push-down procedures and refractive error. More significantly no correlation was found between interocular difference in amplitude of accommodation and inter-eye difference in refractive error. One of the advantages of using the anisometropes is that in this procedure intersubject variability in assessing blur is not a consideration.

The accommodative error index represents the ability of an eye to accommodate to a known stimulus. No correlation between refractive error and accommodative error index was found. Nor was there a relationship between interocular difference in refractive error and inter-eye difference in accommodative error index. These findings do not agree with reports by Gwiazda *et al.* (1993 and1995) who found lower accommodative response gradients in myopic children compared to emmetropes. The children used in the study were relatively young and it is not known if they understood fully the nature of the task. The use of different parameters to assess the accommodation response may contribute to the discrepancies in the two sets of results.

### 7.5 *Summary*

Numerous investigations have reported accommodation to be influenced by a variety of factors including target characteristics, target proximity, ocular and cognitive factors. Several researchers have demonstrated a relationship between accommodation and refractive error; a reduced amplitude of accommodation has been observed in myopes compared to emmetropes and hyperopes. However, other investigators have disputed these findings of a relationship between refractive error and accommodation.

The present study has addressed the question of differences in accommodation response with refractive error. The study has compared the accommodative response in anisometropes, subjects with a significant interocular difference in refractive error. By using anisometropic subjects differences in accommodation with refractive error may be assessed without the consideration of inter-subject variation.

The findings of the study do not support the hypothesis that there is a link between accommodation and refractive error. Refractive error was not found to correlate with the amplitude of accommodation, the accommodative error index or tonic accommodation. More importantly no correlation between inter-eye differences in these parameters and interocular difference in refractive error was observed.

Accommodative function is independent of the biometric differences found in anisometropes. This finding therefore points to a posterior segment basis for the aetiology of anisometropia rather than an anterior component.

# CHAPTER 8

# THE EFFECT OF AMETROPIA ON MORPHOLOGY OF THE FUNDUS

## 8.1 *Introduction*

*Changes in fundus morphology in myopia*

Changes in fundus morphology, or structure, that occur with myopia development are well known (Curtin, 1985). The increased axial length in myopia is associated with scleral crescents, supertraction, generalised tessellation, pallor of the fundus, and posterior staphylomae. Myopic crescents have a predominantly temporal location and may increase in size with the progression of the myopic error. Scleral crescents are believed to result from a disparity in area between the sclera and the choroidal and retinal pigment layers. An exaggerated postnatal expansion of the globe, especially on the temporal side, has been suggested as causative of the retraction of the choroid from the optic nerve (Curtin and Karlin, 1971). The frequency of crescent formation has been found to increase with an increase in axial length (Curtin and Karlin, 1971; Hendicott and Lam, 1991). Hendicott and Lam (1991) assessed the relationship between myopic crescent, refractive error and axial length in 60 Chinese subjects. They found that the crescent diameter increased as axial length and degree of myopia increased when the data for all eyes were included. When they analysed the data from only eyes with crescents, no correlation between crescent diameter and axial length or refractive error was found.

Tessellation and pallor of the fundus are believed to arise from generalised thinning of the retinal pigment epithelium. These findings are not exclusive to myopic eyes and also occur in persons with fair complexions.

Posterior staphylomas are usually seen only in conjunction with high degrees of myopia; this type of myopia has been termed pathological myopia. Posterior staphylomae are a distention of the sclera and are associated with thinning of the posterior sclera. In addition to the myopic changes that occur with low and intermediate degrees of myopia, pathological myopia also demonstrates degenerative changes of the choroid and retinal pigment epithelium.

*Variability in optic disc size*

Optic disc size is known to vary considerably between individuals. Both histological studies (Quigley *et al.*, 1990) and retinal image analysis (Bengtsson, 1976; Jonas *et al.*, 1988; Miglior *et al.*, 1994) have shown substantial inter-individual variability in measurements of the optic disc diameter. Racial differences in optic nerve head parameters have also been demonstrated with blacks having a significantly larger disc area than age-matched white patients (Chi *et al.*, 1989; Varma *et al.*, 1994).

Quantification of optic disc morphology is recognised to be important in the diagnosis of anomalies and diseases of the optic nerve (Mullie and Sanders, 1985; Beck, Servais and Hayreh, 1987). The size of the optic disc may play a role in the pathogenesis of some disorders, whereas in other cases the disc appearance may arise from pathological changes.

*Methods for measuring optic disc size*

Current methods for *in vivo* measurement of optic disc size include planimetry (Jonas *et al.*, 1988), computerised image analysis from stereophotography such as the Topcon imagenet (Varma *et al.*, 1994) and the Rodenstock optic nerve head analyser (Bishop *et al.*, 1988), adaptation to indirect ophthalmoscopy (Jonas and Papastathopoulos, 1995; Spencer and Vernon, 1995), and scanning laser ophthalmoscopy (Burk *et al.*, 1993; Bhandari and Fitzke, 1994).

Scanning laser ophthalmoscopy has several advantages over the more conventional methods of fundus imaging. A high-quality image of the retina, using less than 1/1000 of the light required for conventional indirect ophthalmoscopy, is produced by scanning laser ophthalmoscopy. A three-dimensional image of the retina is generated which can be analysed using computer software (see § 4.3.2). The reproducibility of the results along with its ease of use, computer-aided analysis and storage of the data make the scanning laser ophthalmoscope more suitable for quantifying optic disc dimensions.

*Purpose of present study*

Eye shape with respect to different refractive errors has been investigated in Chapter 5. A computing scheme was utilised for the indirect determination of retinal contour in anisometropia. The principle finding was that the main structural correlate of myopia is an increase in axial rather than equatorial dimensions of the posterior globe. The present study examines evidence for a corollary: that retinal stretch occurs in central regions of the posterior pole with the development of myopia.

Pilot studies at Queensland University of Technology, Brisbane, using retinal photography have indicated that disc-to-fovea distance (DFD) increases with degree of myopia. The pilot study used conventional methods of fundus photography and planimetry to measure the optic disc size and DFD. In this study the computational facilities of retinal tomography have been utilised to measure posterior fundus dimensions for a range of refractive errors. Differences in vertical disc diameter (VDD) and DFD with refractive error have also been assessed in anisometropes by comparing right and left eyes. The discrepancies in VDD and DFD in anisometropes may provide an indication of the nature of retinal stretch in the development of myopia.

## 8.2 *Methods*

The study comprised 42 Caucasian students (age range 18 to 26 years) with a range in refractive error of -8D to +4D. The group included 10 myopes, 8 emmetropes, 6 hypermetropes and 18 anisometropes. The anisometropes all had an interocular difference in refractive error of 2D or more, spherical equivalent. All other subjects had less than 0.50D inter-eye difference in refraction. None of the subjects had any ocular or systemic diseases, cataracts, aphakia, pseudoaphakia or optic disc malformations. None of the subjects had strabismus, amblyopia or ametropia secondary to ocular pathology. Corrected visual acuity was 6/6 or better. Intraocular pressure was less than 21 mm Hg in all subjects, measured with Goldmann tonometry. Refractive error was assessed by retinoscopy followed by a subjective examination. Corneal curvatures were measured using a Zeiss keratometer. Axial length measurements were obtained with a Storz Omega ultrasound device. Specifications for these instruments are detailed in Chapter 4.

Topographic images were acquired using a confocal scanning diode laser ophthalmoscope, the Heidelberg Retina Tomograph (Heidelberg Instruments GmbH, Heidelberg, Germany). Technical details of the Heidelberg Retina Tomograph (HRT) have been described in Chapter 4. The device has a 670 nm wavelength diode laser which scans the optic disc over 1.6 seconds, taking 32 transverse optical section images at depths of 1.5 to 4.0 mm. The confocal optical system detects only reflected light from the actual focal plane. A topographic map is then computed showing the height of the retinal surface from the focal plane of the eye.

Refractive error and keratometry data were entered into the HRT database to correct for magnification differences (see § 4.3.2). Astigmatism over 0.75D was corrected using a full aperture trial lens.

The subject was positioned in a chinrest with a forehead bar and the eye not under examination fixated a distant cross. The image of the optic disc was generated on the video monitor and aligned using a joystick. The image was focused and recorded using the various settings on the control panel (see § 4.3.2).

The current software (version 1.11) available with the HRT includes quality control to improve the image taken until it is satisfactory for storage. Six images of the each eye were taken that passed quality control assessment; three of the optic disc with the 10 x 10 degree field size and three using the 20 x 20 degree field size to include the disc and macula regions.

*Repeatability*

The repeatability of the measurements obtained with the HRT were assessed. The experimental procedure was repeated on both eyes of one subject on 10 separate occasions. The tests were separated by a minimum time of 1 day and a maximum of 5 days. All the tests were performed by one experimenter.

*Magnification effects*

The effect on the results of magnification due to the different refractive errors was investigated. Images of the optic disc were taken from one subject with his refractive error corrected using contact lenses. A second set of optic disc images were obtained from the same subject with the refractive error uncorrected optically. In this case the refractive details were entered into the HRT database which is used by the software in compensating for magnification effects. The measurements of VDD obtained from these two methods were compared.

*Data analysis*

For each image a mean topographic image of the 32 transverse optical sections was obtained. Measurements were made on this mean using the HRT data analysis software.

The 'circle-draw' and 'cursor-location' modes of the HRT were used to measure in mm the VDD and DFD in both eyes of the subjects. The optic disc was defined as the area inside the white peripapillary scleral ring of Elschnig. The VDD was measured from the edge of the nerve fibre rim at 12 o'clock to the edge of the nerve fibre rim at 6 o'clock. The DFD was defined as the distance between the temporal disc margin and the foveola. A mean value was calculated from the three images that were taken for each parameter.

## 8.3 *Results*

Right and left eye results have been analysed separately to eliminate the effect of the inter-eye correlation that may occur between a pair of eyes (Ray and O'Day, 1985).

Inter-individual variation in optic disc size and DFD is evident. Table 8.1 shows the mean, standard deviation and range values for VDD, DFD, axial length and refractive error for both eyes of all subjects. Data for all eyes are shown in Appendix 10.

Table 8.1 Tabular results of the measured ocular parameters.

| parameter | right eye values (mm) | left eye values (mm) |
|---|---|---|
| VDD mean ± sd | 1.58 ± 0.20 | 1.57 ± 0.18 |
| VDD range | 1.25 - 1.98 | 1.24 - 1.95 |
| DFD mean ± sd | 3.75 ± 0.30 | 3.70 ±0.25 |
| DFD range | 3.27 - 4.69 | 3.17 - 4.59 |
| AL mean ± sd | 23.90 ± 1.30 | 23.92 ± 1.33 |
| AL range | 21.72 - 26.77 | 21.77 - 28.26 |
| Rx mean* ± sd | -1.57 ± 3.22 (D) | -1.66 ± 3.62 (D) |
| Rx range* | -7.25 - +4 (D) | -7.87 - +4 (D) |

VDD, vertical disc diameter; DFD, disc-to-fovea distance; Rx, refractive error; AL, axial length; sd, standard deviation; * values in Dioptres

The individual right eye results, presented in graphical form in Figures 8.1 and 8.2, show more myopic eyes to have a longer axial length and DFD and a larger VDD.

Statistical analysis revealed a significant correlation between axial length and degree of ametropia ($r^2$= 0.73, p<0.001) and DFD ($r^2$= 0.41, p<0.001) and a weak correlation with VDD ($r^2$= 0.26, p<0.05).

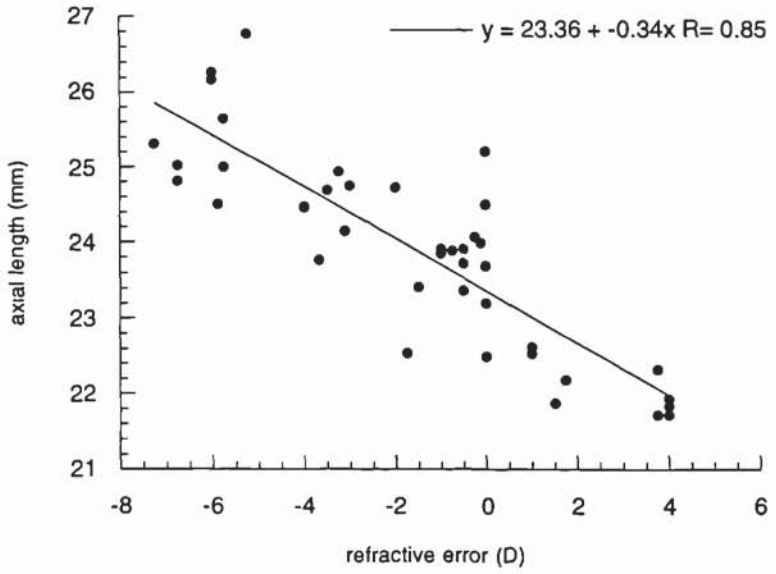



Figure 8.1 Mean spherical refractive error plotted against axial length for all right eyes.

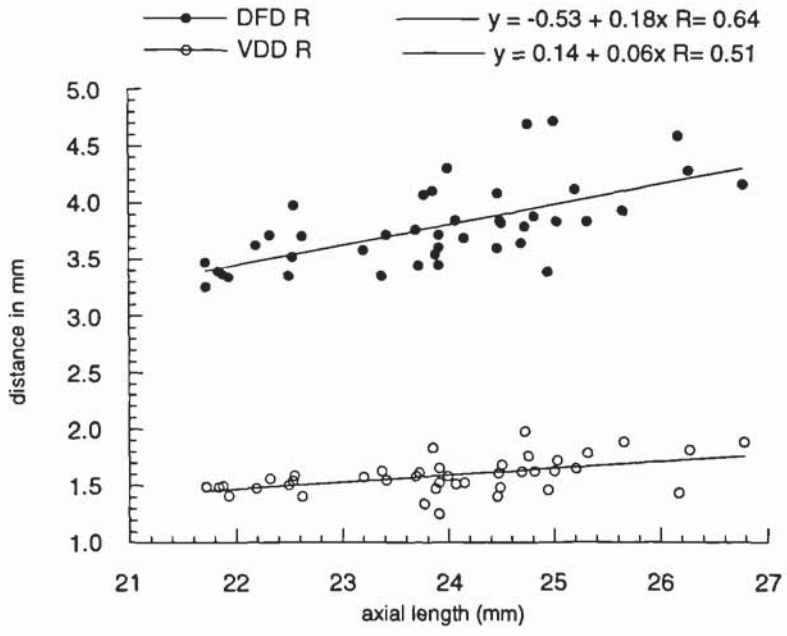



Figure 8.2 VDD and DFD plotted against axial length for all right eyes.

Similar correlations for all parameters were found for the left eyes. Significant correlations were found between axial length and degree of ametropia ($r^2$= 0.69, p<0.001) and DFD ($r^2$= 0.43, p<0.001) and a weak correlation with VDD ($r^2$= 0.25, p<0.05).

Importantly significant correlations were also evident for anisometropic eyes, such that the amount of anisometropia correlated with interocular differences in axial length ($r^2$= 0.74, p<0.001) and DFD ($r^2$= 0.73, p<0.001) but not for VDD ($r^2$= 0.09, p>0.05). Figures 8.3 and 8.4.

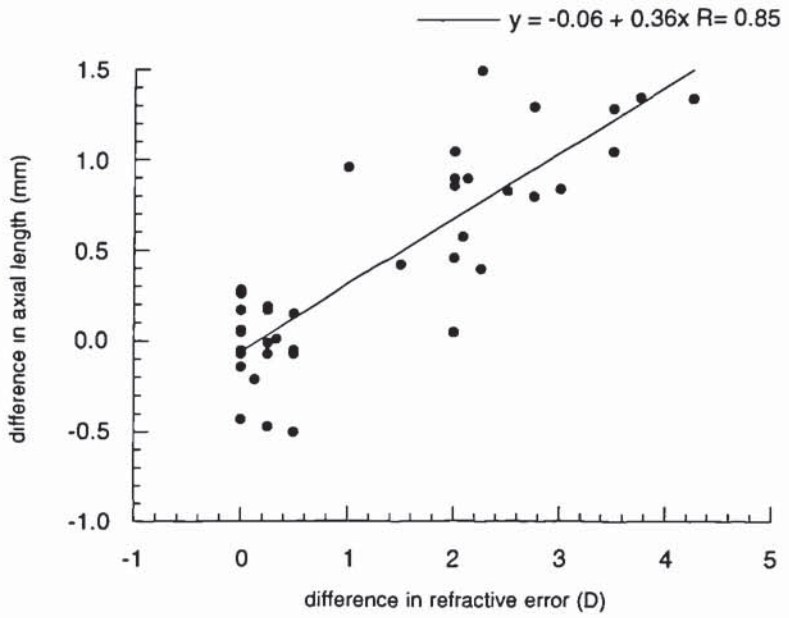



Figure 8.3 Interocular difference in axial length plotted against inter-eye difference in refractive error.

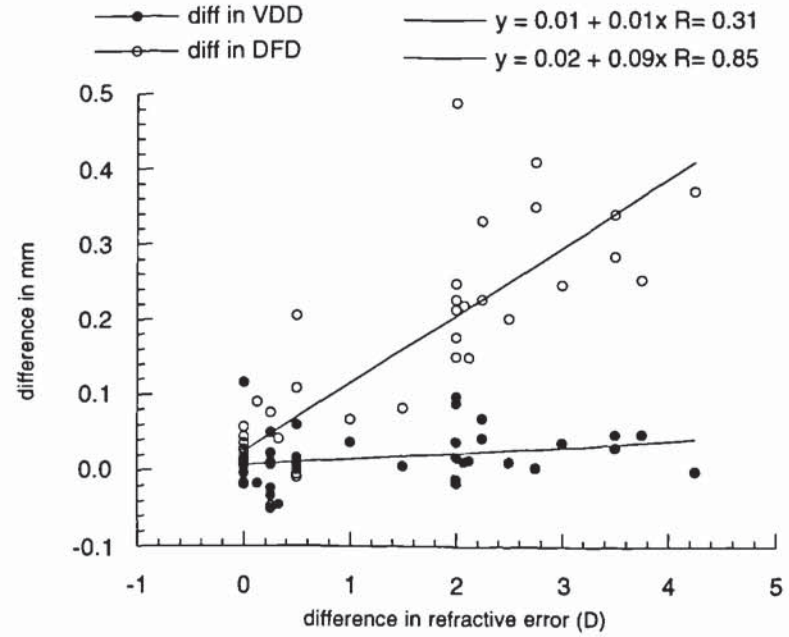



Figure 8.4 Interocular difference in VDD and DFD plotted against inter-eye difference in refractive error.

*Repeatability*

The subject in the repeatability study had an average-sized optic disc. The mean vertical optic disc diameter, standard deviation and coefficient of variation are shown in Table 8.2. The mean and standard deviation for all measurements was 1.538 ± 0.038 mm. The mean coefficient of variation for all 10 sets of measurements was 1.05% and varied between 0.53% and 1.42%.

Table 8.2 Mean VDD, standard deviation and coefficient of variation for 10 different measurement cycles for subject GH.

| | No. of experimental procedure | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Mean VDD* | 1.531 | 1.559 | 1.548 | 1.539 | 1.563 | 1.552 | 1.437 | 1.542 | 1.522 | 1.556 |
| sd* | ± 0.02 | ± 0.018 | ±0.022 | ±0.016 | ±0.009 | ±0.015 | ±0.018 | ±0.020 | ±0.008 | ±0.014 |
| CV** | 1.31 | 1.15 | 1.42 | 1.04 | 0.58 | 0.97 | 1.25 | 1.30 | 0.53 | 0.90 |

VDD, vertical disc diameter; sd, standard deviation; CV, coefficient of variation; *, measurements in mm; **, measurements in percentages

*Magnification effects*

Figure 8.5 is a difference versus the mean plot comparing the measurements of the VDD made with two different methods, i.e. with and without contact lenses, to determine magnification effect.

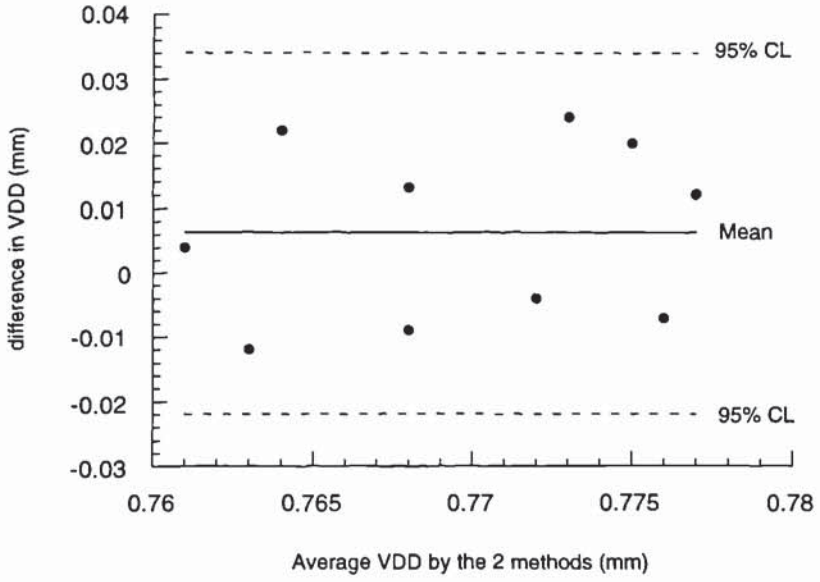



Figure 8.5 Difference against mean for VDD data by the 2 methods.
95% CL, 95% confidence limits

All results lie within 95% of the differences between the two methods of measuring.

## 8.4 *Discussion*

Information concerning the size of an optic nerve head can clearly only be obtained by measurements on an image of the optic disc rather than on the disc itself. The image is usually much larger than its object and variations in the size of the image may be caused by variations in the degree of magnification as well as in the inherent size of the object.

*Repeatability*

The results of this study suggest that the measurements of VDD and DFD are repeatable. Various studies have assessed the reproducibility of the HRT measurements of the optic nerve head with acceptable results (Caprioli *et al.*, 1986; Kruse *et al.*, 1989).

*Magnification effects*

The effect of magnification on the HRT images has not been evaluated for a range of refractive errors. Most research on optic disc size using the HRT have limited refractive errors to ± 3D (Spencer *et al.*, 1995). Magnification effects are corrected in the HRT using Littmann's formulae (1982) and individual schematic eyes. These individual schematic eyes are produced from the refraction and keratometry data that are entered into the database for each subject, and parameters taken from Gullstrands No. 1 schematic eye (see § 4.3.2). Ocular magnification as determined by Littmann does not vary markedly for the central 30° of the fundus (Jonas and Papastathopoulos, 1995). In the present study the size of the optic disc was compared in a -5D eye in which the refractive error was corrected by two different methods. Images were taken with the refractive error uncorrected optically but with the refractive data entered into the software database. A second set of images were obtained with the refractive error corrected with soft contact lenses. The results have been analysed as a difference versus the mean plot (Bland and Altman, 1986). The results lie within the 95% limits of agreement indicating that the measurements of VDD with the two methods are similar and that the effects of magnification are compensated by the HRT software.

*Optic disc size*

There are few reports on the absolute size of the optic disc evaluated for a range of refractive errors. These studies differ in methods, selection criteria, number of subjects examined and the optic disc parameters measured.

The mean vertical optic disc diameter in this study measured 1.58 ± 0.20 mm, with a high inter-individual variation, giving a range of 1.25 - 1.98 mm. Similar inter-individual size variation has already been reported by Bengtsson (1976) and Jonas (1988). Bengtsson, in a study of 2334

eyes using fundus photography, found a wide distribution of optic disc and cup diameters. The mean disc diameter (taken as an average of the horizontal and vertical diameters) was found to be 1.62 ± 0.17 mm. The disc diameters ranged from 1.10 to 2.35 mm. These values have been calculated from the published data in arbitrary units into mm;1 arbitrary unit corresponding to approximately 0.05 mm. Jonas *et al.* (1988) using planimetric methods assessed the variability of the dimensions of normal human optic discs by evaluating optic disc photographs from 88 eyes. High myopia (> -8D) was excluded along with optic nerve disease. Mean vertical disc diameter was found to be 1.97 ± 0.29 mm with a range of 1.08 to 2.76 mm.

The present study found a weak positive correlation between VDD and both axial length and refractive error. This finding is in agreement with previous studies on optic disc size and axial length. Miglior *et al.* (1994) assessed the correlations between optic disc area, axial length and refraction on 235 subjects using computer-aided morphometry. Male and female results were analysed separately. They found significant correlations between optic disc area and both axial length and refractive error for both male and female subjects. They also noted that disc area was greater in males and females, corresponding with the axial length difference observed between the two sexes. Similarly, Chihara and Chihara (1994) in a study of 210 Asian eyes using computerised planimetry found a positive relationship between axial length and the area of the optic disc.

Other studies have found poor correlations between optic disc size and axial length. Quigley *et al.* (1990) studied the size of the optic disc in post-mortem eyes from 60 adults. They found no correlation between vertical disc diameter and either axial length or refractive error. Bengtsson (1980) obtained measurements of optic disc diameter on 2274 eyes in 1287 subjects using fundus photography. The effect of refractive error on the magnification of the optic disc images was compensated for using a correcting factor (Bengtsson and Krakau, 1977). She found that the disc diameter (a mean of the horizontal and vertical disc diameters) was independent of the refractive error of the eye.
The correlation between optic disc size and refractive error in 1369 black patients and 1622 white patients was assessed by Varma *et al.* (1994). They found no correlation between refractive error and optic disc area for a range in refractive error of greater than -8D to greater than +8D.

The present study found similarities in the size of the VDD in the right and left eye pairs. Although a slight positive correlation was found between VDD and refractive error, symmetry in right and left eye pairs was evident in both the anisometropes and isometropic control group. Previous researchers have recorded similar findings. Bengtsson (1980a) compared the right and left eye optic disc diameters and found a similarity between them. She noted that the variance in right and left eye differences was less than half the variance observed for the optic disc diameters of all eyes. Varma *et al.* (1994) investigated the asymmetry in optic disc area in right and left eyes in the

same individual in 1369 black patients and 1622 white patients. In both races 99% of the subjects had less than 1 $mm^2$ of asymmetry between the eyes in disc area. The differences in optic disc size between right and left eyes were also evaluated by Jonas, Gusek and Naumann (1988). They examined 138 patients using fundus photography. Interocular differences of 0.50 $mm^2$ or less in optic disc area were found in 80% of the sample, with 27.5% having an inter-eye difference of 0.1 $mm^2$ or less. No mention is made of corresponding asymmetries in refractive error in any of these studies.

The use of different measuring techniques such as planimetry or optic disc analyser to trace the margin of the scleral ring or termination of Bruch's membrane may produce different results. Racial differences and varying male to female ratios in the study samples may also contribute to the discrepancies in the results.

As with other methods for measurement of the optic disc size, measurements with the HRT are reliant on the observer's interpretation of the optic disc boundary. However, the software with the HRT provides a useful guide on plotting the boundary of the optic disc. When the optic disc boundary or contour line is drawn on the HRT image, a plot of height along the contour line is produced. Typically this plot will be double humpbacked in shape for normal eyes. The two humpback peaks represent the superior and inferior areas of the disc where there is a higher concentration of nerve fibres compared to the nasal and temporal aspects of the disc. The double humpback plot is not produced if the contour line is plotted too far outside or inside the optic disc area.

It is unclear which factors determine optic disc, optic nerve and scleral canal dimensions. However the missing correlation between optic nerve head size and refraction in anisometropia may be explained by the fact that growth of the posterior scleral opening has finished at approximately the second year of life (Quigley, 1982). . This is in contrast to the growth of the total globe, especially in the anterior-posterior axis, which may last up to 15 to 20 years, at which point final refraction is reached (see § 1.2).

Various studies have shown the scanning laser ophthalmoscope image of the optic disc to be significantly smaller than conventional photographic images of the optic disc.
Spencer *et al.* (1995) compared the discrepancies in vertical disc diameter between planimetric and HRT measurements on 32 eyes. They found the HRT images to be significantly smaller than those from photographs. Errors in the compensation for magnification differences were cited as a possible source of the discrepancy in the two measurements. However as the majority of the eyes imaged in the study were within the range ± 3D, they concluded that other factors must also contribute to the difference in results. They suggested that the two methods may be measuring

different objects; the photographs measure the optic nerve head as it is recognised clinically whereas the HRT measures the scleral canal, detected by the laser as changes in reflectivity.
Similarly, Chihara, Takahashi and Chihara (1993) found a significantly smaller disc area with a scanning laser ophthalmoscope than with fundus photography. They considered that the discrepancies in size may result from images taken from different tomographic planes.

*Disc-to-fovea distance*

The DFD has been found to increase with degree of myopia. This relationship is also evident in the anisometropic group, where the degree of anisometropia and difference in axial length correspond to the inter-eye difference in DFD. The mean DFD in this study measured 3.79 ± 0.37 mm, with a range of 3.25 to 4.72 mm for all right eyes.
Chihara and Chihara (1994) measured the DFD in 210 Asian eyes. They found a mean DFD of 3.94 ± 0.48 mm. There greater DFD may correlate with the greater mean axial length of 24.68 ± 1.69 mm compared to a mean of 23.90 ± 1.30 mm found in this study. Chihara and Chihara found a positive correlation between axial length and DFD. They have not reported on any symmetry between right and left eye results.
The correlation between DFD and axial length and myopia have also been demonstrated in animal work. Research on myopia development in marmosets by Troilo (1996) has shown that unilateral form deprivation myopia results in asymmetrical DFDs; the more myopic eye having the greater DFD. The mean axial length expansion in the form-deprived eye was 10.6% and the corresponding increase in DFD was found to be approximately 10%. These expansion rates are similar to those found in the present study.

## 8.5 *Summary*

The present study has investigated the effect of ametropia on morphology of the fundus with reference to the vertical diameter of the optic disc and the distance between the disc and fovea. Measurements were obtained with a scanning laser ophthalmoscope, the Heidelberg Retina Tomograph, which enabled a computerised method of analysing the data to be employed. A weak correlation was found between VDD and refractive error. However, the DFD was found to increase significantly with the degree of myopia. Interocular differences in VDD and DFD were assessed in anisometropes and isometropes. Importantly there was no relationship between inter-eye difference in VDD and interocular difference in refractive error. A significant correlation was found between inter-eye difference in DFD and interocular difference in refractive error, with the more myopic eye having the longer DFD.
These findings are similar to a previous study where a longer DFD has been found with longer axial lengths. Reviewing the literature reveals equivocal results on VDD and ametropia. The results of the present study on the anisometropes suggest that VDD is not correlated with ametropia.

The results presented in the present study are consistent with the hypothesis that retinas stretch with the development of myopia. Whilst the present work cannot preclude a contribution to retinal stretch from equatorial regions, the combination of our biometric and retinal contour data (see Chapter 5) suggests that eye growth is confined to central posterior regions in myopia.

# CHAPTER 9

# OCULAR BLOOD FLOW IN AMETROPIA

## 9.1 *Introduction*

The flow of blood through the eye is essential for the maintenance of visual function and for the nourishment of eye tissues. The eye has a dual vascular system; the retinal vessels are distributed to the inner layers of the retina whereas the uveal blood vessels supply the choroid, ciliary body and iris (Bill, 1984). The retinal blood vessels are derived from the central retinal artery. The uvea is supplied by the ciliary arteries; the short posterior ciliary arteries form the posterior part of the choriocapillaris which is a continuous network of capillaries lying close to the retinal pigment epithelium. The anterior choriocapillaris receives blood from the long posterior ciliary arteries and the anterior ciliary arteries. Total ocular blood flow has been estimated to be approximately 1 ml per min (Williamson and Harris, 1994). Choroidal blood flow accounts for 90 - 95% of the total blood flow (Bill, 1984; Riva *et al.,* 1985; Langham, 1987), the remainder of the total blood flow is the retinal vascular circulation. Impaired vascular circulation is believed to be involved in pathology of the retina, the optic nerve head and the choroid (Langham and Krammer, 1990; Langham *et al.*, 1991).

*The ocular pulse*

The origin of the ocular pulse is well established (Bykne and Schéle, 1967). Each contraction of the heart causes an influx of blood into the eye via the ophthalmic artery. This bolus of blood spreads rapidly through the retinal and ciliary vascular network. The venous outflow of the eye is assumed to be a continuous flow. The relative rigidity of the sclera and the elastic vascular network produce a cyclic variation in intraocular pressure (IOP), the ocular pulse. The ocular pulse reflects the choroidal or uveal circulation. The increase in IOP is a function of the increase in intraocular volume. This relationship has been established by direct manometric studies on living human eyes (Langham, 1966 and 1987). The ocular pulse volume can be calculated from the ocular pulse pressure. The relationship between the change in volume of blood and the ocular pulse allows the estimation of the pulsatile choroidal blood flow. In the normal eye the ocular pulse has an amplitude of 2 - 3 mmHg and is synchronous with the cardiac cycle (Langham, 1975). The IOP and pulse are generally believed to be symmetrical in a pair of eyes, and loss of symmetry may be an indication of ocular or cerebrovascular disease (Perkins, 1981).

*Measurement of ocular blood flow*

Ocular blood flow can be assessed by several different techniques. These techniques fall into two categories; those which measure retinal blood flow and those which assess choroidal blood flow.

*Retinal blood flow*

Fluorescein angiography has been the main clinical method of investigating retinal blood flow. The time taken for a dye to pass through the circulation is measured by comparing the time delay between the passage of dye in a neighbouring arteriole and venule. This time delay is assumed to be related to the rate of blood flow. Disadvantages of this method include the use of a mydriatic drug and correction factors for magnification effects. Mydriatics may affect the ocular blood flow by their sympathomimetic or antimuscarinic actions. The diameter of the retinal blood vessels is required in calculating the blood flow. This measurement is affected by magnification effects arising from differences in refractive error.

Many laboratory studies have assessed human retinal blood flow with laser Doppler flowmetry (LDF) (Riva *et al.*, 1985). Frequency shifts in laser light reflected from the flow of erythrocytes are used as a measure of the velocity of blood in the retinal circulation. However, LDF has been reported to be sensitive to saccadic eye movements, which influence the measurements. This technique has also been applied to the assessment of choroidal (Riva *et al.*, 1994) and optic nerve head (Riva *et al.*, 1992) blood flow. The Heidelberg Retina Flowmeter (Heidelberg Engineering GmbH, Heidelberg, Germany) combines the technique of confocal laser scanning (see § 4.3.2) with laser Doppler flowmetry. An infrared laser scans the retina in 2-dimensions and the frequency of light reflected by moving erythrocytes is shifted due to the optical Doppler effect. A temporal variation in the intensity of the reflected light results from interference of the light reflected from stationary objects and that reflected from the moving red blood cells. The Heidelberg Retina Flowmeter assesses the temporal variation at each point in a 2-dimensional field by multiple scanning. The frequency shift is computed and used as a measure of the amount and velocity of retinal red blood cells.

*Choroidal blood flow*

The ocular blood flow (OBF) tonograph (OBF Labs, Cleverton, UK) is a non-invasive, objective method of measuring ocular blood flow (see § 4.5). The system allows continuous IOP measurement using a pneumatonometer described by Langham and To'mey (1978). An air flow circulates in the probe, the contact end of which is a distensible film. The film moves in response to the ocular pressure and consequently alters the flow of air in the probe. These changes in air flow are recorded and digitised by the computer software to generate pulses.

The OBF measures pulsatile choroidal blood flow. The pulsatile flow represents 75 to 85% of the total choroidal blood flow (Langham *et al.*, 1989; Riva *et al.*, 1994) and thus is a reliable parameter for evaluating choroidal circulation.

The accuracy of pneumatonometric IOP measurements compared with the Goldmann 'standard' has been previously established (Quigley and Langham, 1975; Jain and Marmion, 1976), with the IOP recorded with the pneumatic tonometer equivalent to the standardised Goldmann reading.

*Purpose of present study*

The ocular pulse has been found to be influenced by a variety of factors including posture (Trew and Smith, 1991a), glaucoma (Trew and Smith, 1991b), heart rate (Trew *et al.*, 1991), age (Ravalico *et al.*, 1996) and axial length (James *et al.*, 1991).

Various researchers have found IOP to vary with refractive error whilst other investigators have disputed this finding (see § 2.2.2). Similarly differences in the ocular pulse have been noted in different refractive groups (Perkins, 1981) and with different axial lengths (James *et al.*, 1991). There has been a suggestion that the variations in amplitude of the ocular pulse are related to the total intraocular volume of the eye rather than to the refractive error itself (Perkins, 1981). The present study looks at the variations in IOP and amplitude of the ocular pulse in relation to refractive error. Comparisons are also made between inter-eye pneumatonography data obtained from anisometropes. Anisometropic subjects have been used in this study as they offer an opportunity to investigate potential ocular differences in eyes with a significant difference in refractive error. By comparing right and left eyes in one individual, ocular differences may be assessed without consideration of intersubject variability in pneumatonographic parameters.

Ocular volume was calculated independently of the OBF measurements from the retinal contour equations described earlier in Chapter 5. The volume was compared with the tonography data to assess whether differences in ocular pulse volume could be related to ocular volume differences or to actual differences in choroidal blood flow.

## 9.2 *Methods*

*Subjects*

A total of 40 Caucasian subjects, 20 anisometropes and 20 isometropes, participated in this study. The anisometropic group all had a minimum inter-eye difference in refractive error of 2D, mean sphere. The isometropic group had an interocular refractive error difference of 0.50D or less. The isometropic control group matched the anisometropic group for age and range of refractive error. None of the subjects had any significant medical or ophthalmic history, nor were they receiving systemic or topical medication. If worn, contact lenses were not inserted on the day of the study.

*Experimental procedure*

IOP, pulse amplitude, pulse volume and pulsatile choroidal blood flow were measured with a pneumatonometer, the Ocular Blood Flow Tonograph (OBF Labs, UK). Measurements were made under topical anaesthesia with 0.4% benoxinate HCl (*Chauvin, Minims*).

The calibration of the system was checked before the pneumatonography parameters for each subject were determined.

The OBF sensor was mounted on the slit lamp with a new sterile tip for each subject. The subject was positioned with his chin on the chinrest and forehead against the brow bar of the slit lamp. On contact with the cornea a low air flow produces whistling noises in the probe's tip. This audible tone is accompanied by synthesised beeps and tones from the computer which indicate the progression of the test. During IOP testing a waveform of the ocular pulse is displayed on the system's LCD screen. The test time is a maximum of 20 seconds during which the system searches for five similar pulses. Failure of the system to detect five pulses results in an error warning and an option to repeat the testing procedure.

Measurements were obtained on both eyes of all subjects. The pneumatonometric measurements were taken first from the right eye, then from the left. The measurement procedure was repeated after a 10 minute break and the two sets of results were averaged.

Refractive error was obtained by retinoscopy and a subjective examination, and expressed as a spherical equivalent refraction (see § 5.2).

*Calculation of ocular volume*

Ocular volume measurements were calculated from the computed retinal contour equations described earlier in Chapter 5.

The co-ordinates for the nasal half of the retinal contour were mirrored in the anterior-posterior plane of the eye. This enabled an average retinal contour equation to be plotted to include both the temporal and nasal data. A second order polynomial was fitted to the data set. The averaged curve was rotated about the anterior-posterior axis of the eye to produce an ocular volume. This ocular volume represented the volume of the vitreous chamber between an arbitrary axial length value of 15 mm (which was constant for all eyes) and the real axial length of the eye. The volume values were calculated using the software Mathcad *Plus 6* for the Macintosh (MathSoft, Inc., Cambridge, MA). Appendix 12 shows the calculations used in deriving the ocular volume value. Calculations are based on the shell method of calculating volumes by integration (Thomas and Finney, 1996).

### 9.3 *Results*

The mean values and standard deviations of IOP, pulse amplitude, pulse volume and OBF are shown in Table 9.1. The results from the right and left eyes have been analysed separately to eliminate the effect of the inter-eye correlation that may occur between a pair of eyes (Ray and O'Day, 1985). Mean individual data is shown in Appendix 11.

Table 9.1 Mean and standard deviations for IOP, pulse amplitude, pulse volume and ocular blood flow measured with the OBF tonograph.

| parameter | right | left |
|---|---|---|
| mean IOP (mmHg) | 14.50 (± 2.30) | 14.71 (± 2.87) |
| mean PA (mmHg) | 2.35 (± 0.74) | 2.31 (± 0.67) |
| mean PV (µl) | 5.46 (± 1.28) | 5.37 (± 1.22) |
| mean OBF (µl per min) | 664.1 (± 193.5) | 658.3 ( ± 210.3) |

IOP, intraocular pressure; PA, pulse amplitude; PV, pulse volume; OBF, ocular blood flow; standard deviations are in parentheses.

*Variations in pneumatonographic data with refractive error*

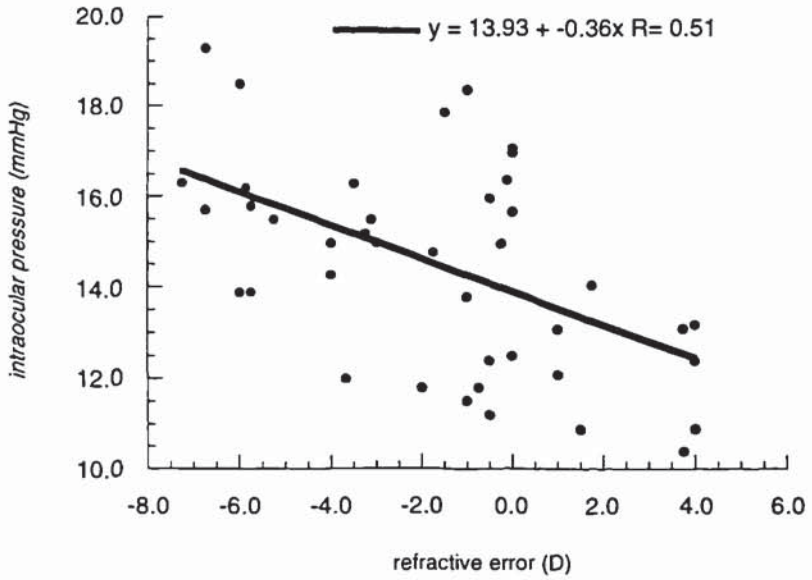



Figure 9.01 Shows intraocular pressure plotted against refractive error for all right eyes.

Figure 9.01 indicates that a weak correlation was found between intraocular pressure and refractive error for the right eyes ($r^2 = 0.26$, $p < 0.005$). A similar correlation was found for the left eyes ($r^2 = 0.22$, $p < 0.005$). As is evident in figure 9.02, pulse amplitude was found to correlate

with refractive error for the right eyes ($r^2$ = 0.40, $p < 0.001$). A similar finding was noted for the left eyes ($r^2$ = 0.36, $p < 0.001$).

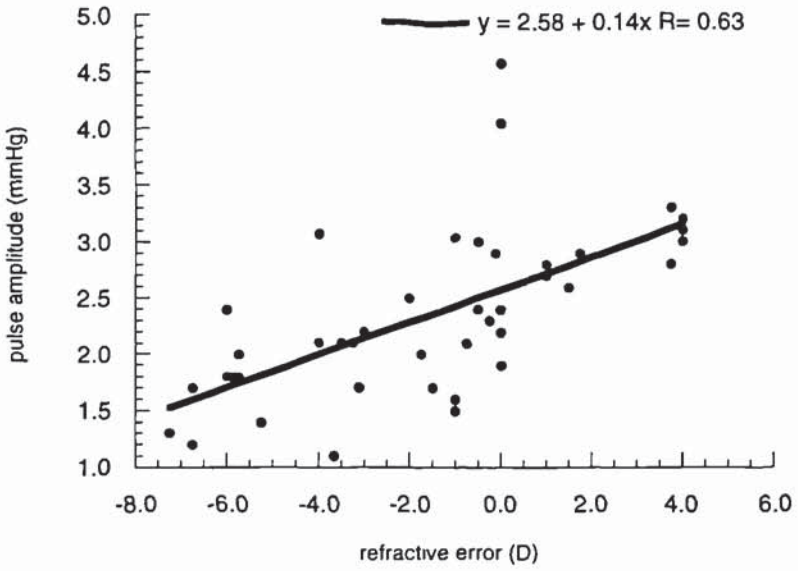



Figure 9.02 Shows pulse amplitude plotted against refractive error for all right eyes.

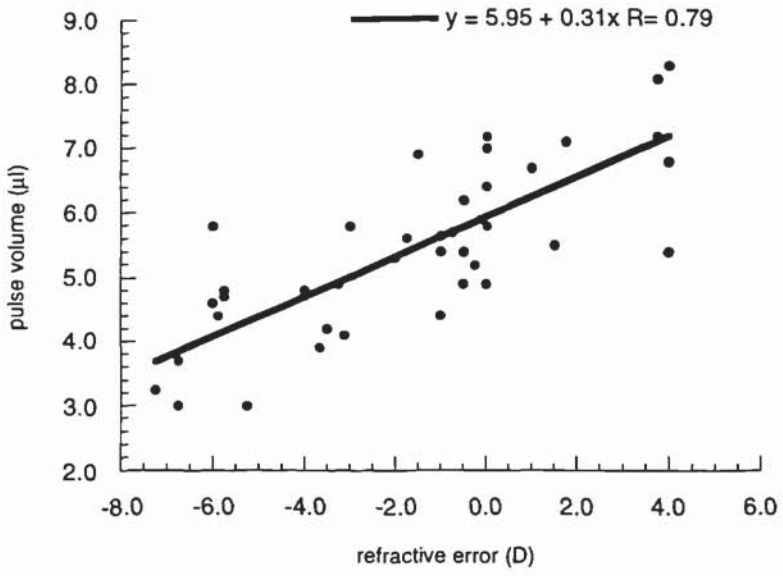



Figure 9.03 Shows pulse volume plotted against refractive error for all right eyes.

A positive correlation was found was pulse volume and refractive error (see figure 9.03) both for right ($r^2$ = 0.62, $p < 0.001$) and left ($r^2$ = 0.58, $p < 0.001$) eyes. A correlation was found for the pulsatile ocular blood flow and refractive error for the right eyes ($r^2$ = 0.35, $p < 0.001$) as shown in figure 9.04. A similar correlation was recorded for the left eyes ($r^2$ = 0.32, $p < 0.001$).

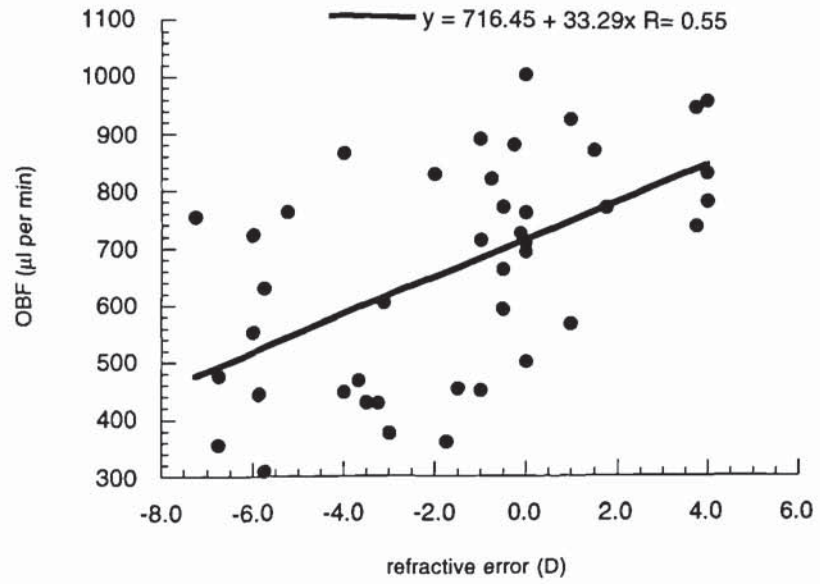



Figure 9.04 Shows ocular blood flow plotted against refractive error for the right eyes.

*Interocular differences in ocular blood flow*

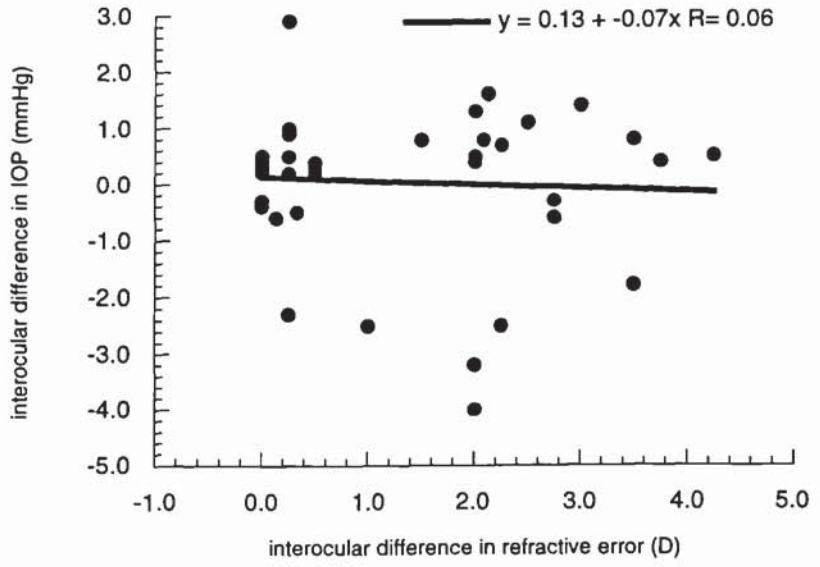



Figure 9.05 Shows the interocular difference in IOP plotted against the inter-eye difference in refractive error.

From figure 9.05 it is evident that no correlation was found between the interocular difference in IOP and the inter-eye discrepancy in refractive error ($r^2 = 0.003$, $p > 0.5$).

In contrast a correlation ($r^2 = 0.35$, $p < 0.001$) was found between interocular difference in pulse amplitude and interocular difference in refractive error (see figure 9.06).

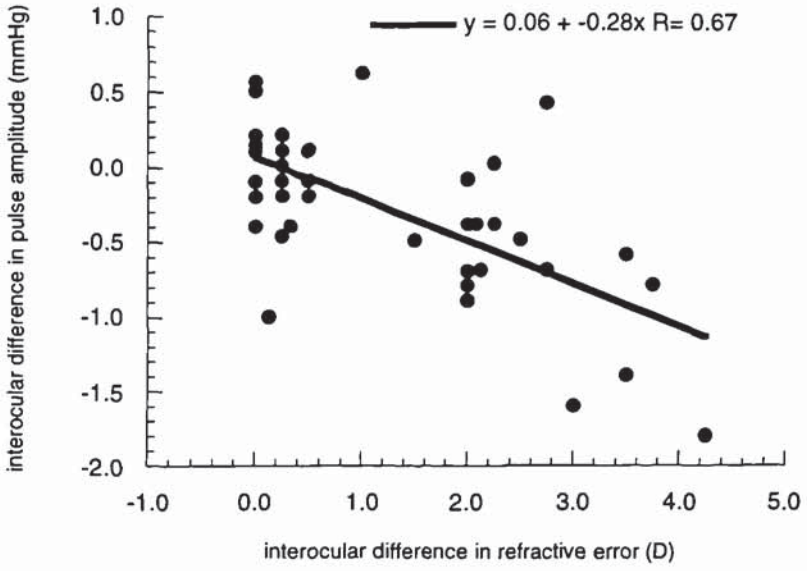



Figure 9.06 Shows the interocular differences in pulse amplitude plotted against inter-eye differences in refractive error.

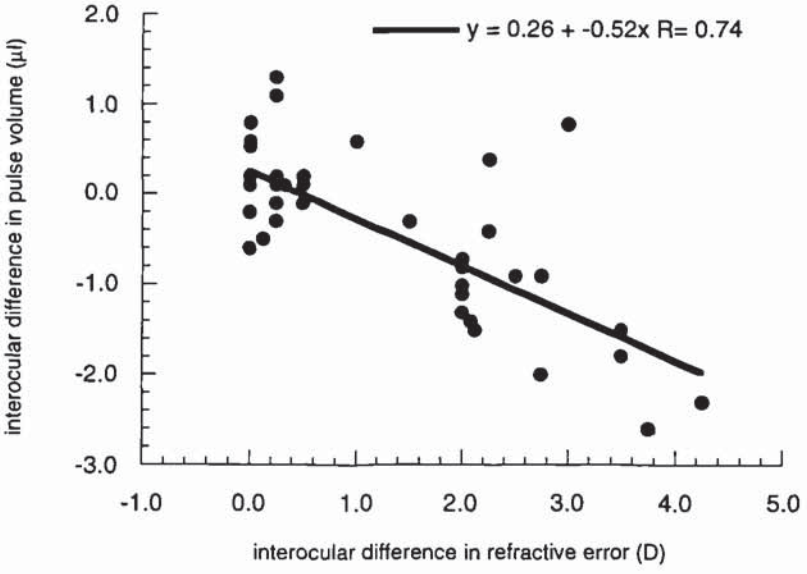



Figure 9.07 Shows the interocular differences in pulse volume plotted against the inter-eye difference in refractive error (D).

Correlations were found for inter-eye differences in refractive error and both the interocular differences in pulse volume ($r^2 = 0.55$, $p < 0.001$) and the interocular differences in OBF ($r^2 = 0.37$, $p < 0.001$). These correlations are shown in figures 9.07 and 9.08.

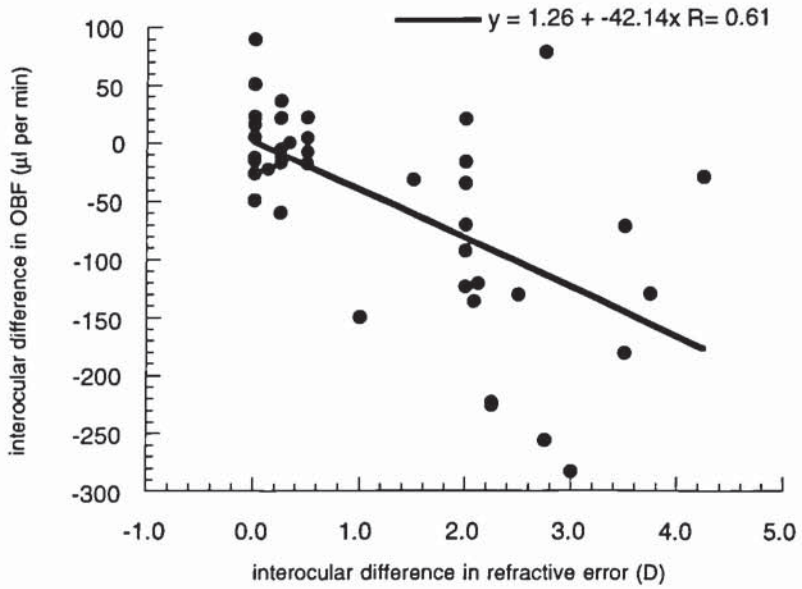



Figure 9.08 Shows the interocular difference in OBF plotted against the inter-eye difference in refractive error.

*Ocular volume*

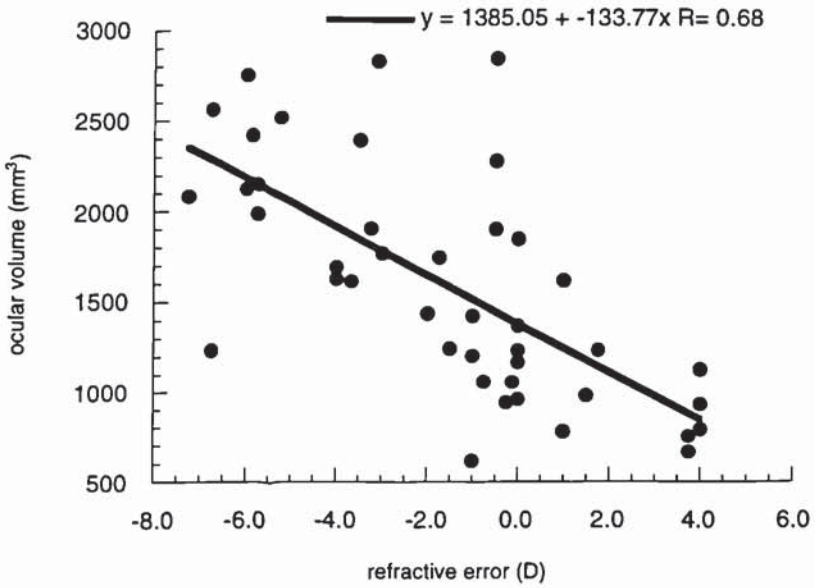



Figure 9.09 Shows the computed ocular volume of the posterior segment plotted against refractive error for the right eyes.

A correlation was found between computed ocular volume of the posterior segment of the eye and both refractive error ($r^2 = 0.46$, $p < 0.001$) and pulse volume ($r^2 = 0.44$, $p < 0.001$). The right eye correlations are shown in figures 9.09 and 9.10. Similar correlations were found for the left eyes; for refractive error ($r^2 = 0.31$, $p < 0.001$) and pulse volume ($r^2 = 0.34$, $p < 0.001$).

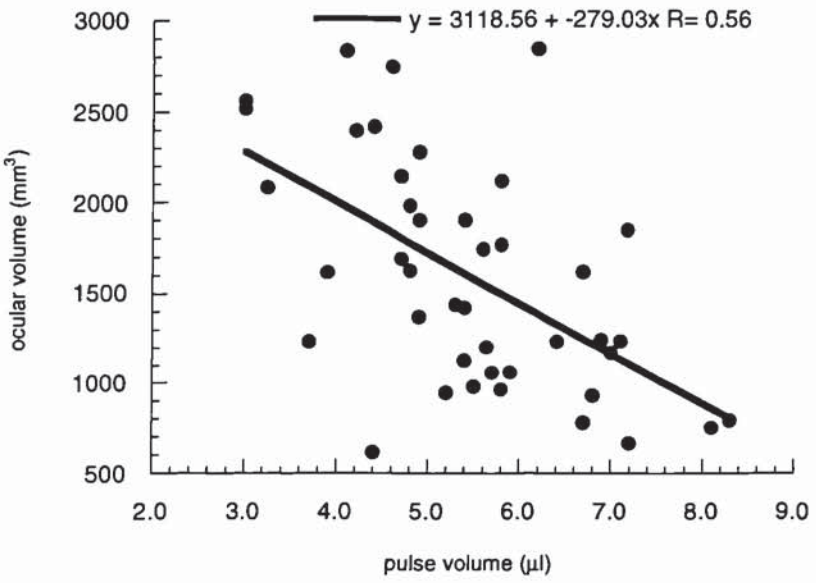



Figure 9.10 Shows the computed ocular volume of the posterior segment plotted against pulse volume for the right eyes.

*Interocular difference in ocular volumes*

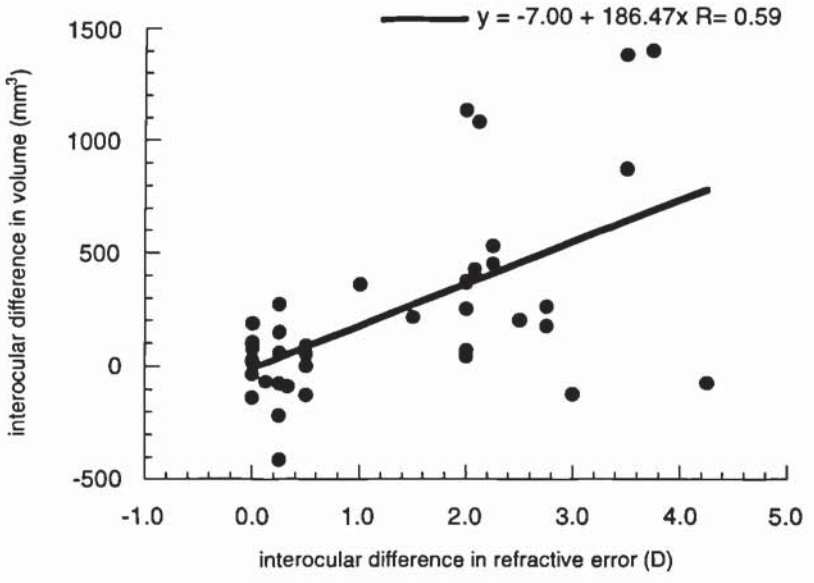



Figure 9.11 Shows the interocular difference in volumes plotted against the inter-eye difference in refractive error.

A weak correlation was found between interocular difference in volume of the posterior segment of the eye and inter-eye difference in refractive error ($r^2 = 0.35$, $p < 0.05$). This correlation is shown in figure 9.11.

### 9.4 *Discussion*

*Intraocular pressure*

The mean value of IOP in the present study was found to be 14.50 ± 2.30 mmHg. This value is similar to the mean IOP of a general population of 15 ± 3 mmHg (Klein *et al.*, 1992).

The present study found IOP to increase as the degree of myopia increased. Interestingly no correlation was found between interocular differences in IOP and inter-eye differences in refractive error. Various researchers have investigated the relationship between refractive error and IOP with equivocal results (see § 2.2.2). The finding in the present study agrees with a report by Bonomi, Mecca and Massa (1982) who studied the intraocular pressure in 137 anisometropes with unilateral high myopia (>-5D). The contralateral eye was hyperopic, emmetropic or had myopia less than 5D. They found no difference in intraocular pressure in a pair of eyes and concluded that high myopia is neither a cause nor a consequence of ocular hypertension. Bonomi, Mecca and Massa's findings conflict with the work of Tomlinson and Phillips (1970 and 1972) who found a statistically significant correlation between axial length and IOP, in that the eye with the longer axial length had the higher IOP. The age range of the 75 subjects was 18 to 27 years with a refractive error range of -7D to +4.75D. In a subsequent study they examined 13 anisometropic children aged 8-16 years from a school eye service clinic. Anisometropes were chosen to provide a control for the influence of sex, season, time of day and blood pressure. They found that the eye with the greater axial and vitreous length had the significantly higher ocular tension. Differences in methodology (e.g. Tomlinson and Phillips used Goldmann tonometry) may account for the discrepancies in IOP. The pneumatonography samples IOP continuously over a period of approximately 20 secs and thus the output value is a mean of several readings.

*Ocular blood flow*

The blood flow to the eye is pulsatile and induces variations in the ocular pressure, from which the mean pulsatile component has been estimated at approximately 724 µl per min (Langham *et al.*, 1989). The retinal circulation has been found to be 0.033 µl per min (Riva *et al.*, 1985). A study assessing normative values for choroidal OBF revealed an average value of 808 ± 344 µl per min for 664 subjects (Massey and O'Brien, 1996). Another study on 15 emmetropic subjects with an age range of 10 to 20 years, found a OBF of 819 ± 212 µl per min (Ravalico *et al.*, 1996). The data on OBF reported in this thesis have a lower mean value (664 ± 193 µl per min) than that found by previous researchers.

OBF, pulse amplitude and pulse volume have been found to vary with refractive error with myopes demonstrating a lower value than emmetropes or hyperopes. These findings are evident in the present study and have also been found by other researchers. Massey and O'Brien (1996)

found lower values of OBF in myopic eyes. A correlation has been reported between OBF and axial length, in that longer eyes have a lower OBF (James *et al.*, 1991). To'mey *et al.* (1981) examined ocular pulse amplitudes with a Langham pneumatonometer in 20 high myopic (>-5D) subjects. They compared the results with data from 20 subjects who were either emmetropic or had low refractive errors. Similarly to the results of the present study, they found that the high myopes had a significantly smaller mean pulse amplitude and a significantly higher mean intraocular pressure than the control group.

The lower mean value of OBF found in the present study may reflect a higher proportion of myopes in the study group. James *et al.* (1991) found a much lower mean OBF value of 444 ± 20 (SEM) µl per min for a group of 34 subjects with a mean refractive error of -1.15D and a mean age of 21.8 years. As no distribution of refractive error is given in the report, speculation may only be made to a greater proportion of high myopes in the study resulting in a low OBF value. They do report axial length data and from the graph it appears that 23% of the subjects had an axial length of 24.5 mm or greater, suggesting that these subjects were myopic. In the present study 39% of the subjects had an axial length of 24.5 mm or greater. The discrepancy in percentages of subjects with long axial lengths indicates that factors other than a high prevalence of myopic subjects may have contributed to the low OBF found by James *et al.* (1991).

The relationship between choroidal blood flow and the occurrence of myopia has been studied in animal models of myopia. Shih *et al.* (1993) induced unilateral myopia in chicks using opaque goggles. They found that choroidal blood flow was significantly reduced (40% of the control) in the myopic goggled eye compared to the contralateral control eye. The induced myopia was found to be axial in nature. Another study by Shih, Fitzgerald and Reiner (1993) investigated choroidal blood flow in chicks with unilateral corneal incisions. This second study was to ascertain whether the reduced choroidal blood flow in the chick myopic eyes observed in the first study, was secondary to the increased ocular temperature produced by the goggle. Similar results were noted with the corneal incised chicks. The deprived eye was more myopic and had a reduced choroidal blood flow (60% of the control) compared with the contralateral eye. They concluded that choroidal blood flow was reduced as a consequence of myopia development.

*Ocular volume*

Perkins (1981) found the amplitude of the ocular pulse to be significantly less in myopes than emmetropes and hyperopes and suggested that this is related to the total intraocular volume of the eye rather than to the refractive error itself. Ocular volume calculations based on retinal contour shape, reported in this thesis, have revealed a correlation between refractive error and ocular volume. A relationship has also been found between the calculated ocular volume and measured pulse volume. The volume changes are thought to result primarily from the expansion

of the choroidal vasculature during the ingress of blood with the systemic pulse (Hill, 1989,; Silver *et al.* 1989). These findings indicate that the reduction in pulse volume and hence in OBF that is observed in myopes may be related to a larger intraocular volume of the eye and not to actual changes in OBF.

*Factors influencing OBF*

To'mey *et al.* (1981) suggested that future work on OBF in different refractive groups should examine the effect of different corneal curvatures contributing to differences in area of applanation during tonometry. The contribution of corneal curvature to refractive error differences was examined in Chapter 6. The data indicate that corneal curvature is similar in a pair of eyes with significant differences in refractive error. This finding suggests that the area of applanation is the same in eyes with different refractive errors and thus would not contribute to apparent differences in OBF.

*Limitations of the OBF Tonograph*

Measurements recorded using the OBF tonograph reflect only the change in IOP produced by the entry of arterial blood into the ocular circulation at systole. However, Doppler ultrasound studies of the ophthalmic artery have shown diastolic blood flow which suggests the existence of a non-pulsatile component to the total ocular blood flow. The extent to which the observed changes in various ocular and systemic parameters affect non-pulsatile flow and, therefore, the total amount of blood passing through the eye remain unclear.

A variety of assumptions have been made in the estimation of the pulsatile component of total ocular blood flow from the variations that occur in the intraocular pressure with the systemic pulse. The calculations are based on a non-pulsatile outflow from the choroid, the assumption that the blood vessels do not collapse and that there is no retrograde blood flow.

## 9.5 *Summary*

Pulsatile choroidal blood flow is the largest component (approximately 80%) of the total ocular blood flow and has been found by previous researchers to be a reliable method of assessing ocular blood flow. The present study examined pulsatile choroidal blood flow, with an OBF Tonograph, in subjects with a range of refractive errors. In agreement with previous studies a correlation was found between refractive error and IOP, pulse amplitude, pulse volume, and OBF. Interocular differences in refractive error were found to correlate with inter-eye discrepancies in pulse amplitude, pulse volume and OBF. Interestingly no interocular differences were observed between refractive error and IOP.

The volume of the posterior segment of the eye was calculated from the retinal contour shape that was derived in Chapter 5. A relationship was evident between ocular volume and refractive error. A correlation was also found between the calculated ocular volume and the measured pulse volume. This relationship suggests that the differences in OBF with refractive error may result from differences in ocular volume rather than actual differences in OBF.

## CHAPTER 10

## GENERAL DISCUSSION

The thesis has investigated the biometric correlates in anisometropic eyes in order to provide a structural foundation for propositions concerning the development of ametropia. The paucity of information about the nature of myopic eye growth in humans reflects, in part, the lack of suitable and accessible *in vivo* techniques. A substantial proportion of the thesis has applied a new computational technique to derive retinal contour and thus eye shape using a population of anisometropes.

### 10.1 *Classification of anisometropia*

Anisometropia has traditionally been classified according to degree of interocular difference in refractive error and to the type of ametropia. If both eyes have different degrees of myopia or one eye myopic and the other emmetropic, they are referred to as anisomyopic. Anisohyperopia exists if both eyes are hyperopic or if one eye is hyperopic and the other emmetropic. Antimetropia is the term that denotes one myopic eye and the other hyperopic. There is no critical parameter which defines anisometropia. The thesis has adopted an interocular difference of 2D or more, spherical equivalent, to represent anisometropia. Inherent experimental errors may mask the true inter-eye variations in biometric parameters for a lower value of anisometropia.

A distinctive feature of the anisometropic population investigated in the thesis, is the absence of amblyopia. Anisometropia is commonly linked with amblyopia and strabismus, both in cause and effect relationships.
The anisometropes selected all have a relatively high degree of stereopsis which suggests an alternative system for classification of anisometropia based on degree of stereopsis.

Two anisometropic populations have been investigated: the first has been taken from a university population of Caucasian students, the subjects were principally anisomyopic but the group also included anisohyperopes and antimetropes; the second group consisted Chinese subjects who were all anisomyopic.

### 10.2 *Biometric correlates of anisometropia*

The majority of anisometropia is transient in childhood with the onset often in the second decade of life. It is interesting that both anisometropia and isometropia generally develop during a relatively slow phase of ocular growth, when the eye grows approximately 1 mm from the age of 3 to 15 years. This slow phase of growth coincides with the period of maximum body growth.

During emmetropisation, some process of correlation exists between the ocular components to integrate the changing curvatures of the cornea and crystalline lens surfaces with the changes in axial dimensions of the eye that occur through growth. However, the thesis, in agreement with previous studies, has shown that the biometric properties of the anterior segment components of the eye are similar in anisometropes, with the discrepancy in refractive error arising from differences in vitreous chamber length.

The corneal topography data revealed little inter-eye difference indicating that the anisometropia did not arise from differences in corneal power. This finding is not unexpected considering that the cornea has reached adult dimensions by the age of 3 and remains relatively stable throughout life.

### 10.3 *Growth of the eye*

The principal finding of the thesis was that the main structural correlate of myopia is an increase in axial rather than equatorial dimensions of the posterior globe. The finding has not been previously reported for *in vivo* work on humans. Investigations using animal models of myopia found both axial and equatorial expansion is some studies whereas other studies revealed axial expansion only. Stone *et al.* (1990), using evidence from muscarinic receptor antagonist experiments, have suggested that the axial and equatorial dimensions of the globe are regulated independently. Lin *et al.* (1996) have shown that excising the ciliary ganglion in chicks results in excessive growth in the equatorial dimensions of the globe with little increase in axial length. Whether the expansion of the globe is restricted by mechanical limitations of the ocular orbit is unknown.

*Elasticity of the sclera*

Expansion of the eye in an axial dimension only may result from differential properties of the sclera. Histological studies have indicated that highly myopic eyes have thinner than normal scleras (reviewed by Curtin, 1985). Magnetic resonance imaging of myopic, emmetropic and hyperopic eyes have revealed that the myopic eyes have a thinner sclera and choroid (Cheng *et al.*, 1992). The sclera has been found to be less resistant to change in its radial dimension (thickness) compared to its circumferential dimension (Battaglioli and Kamm, 1984). The collagen fibres run primarily in the circumferential direction and can resist changes in globe circumference better than changes in the radial dimension.

Curtin (1969) measured the elasticity of adult human scleral strips and found that the material was more extensible posteriorly than anteriorly. He stated that the posterior sclera develops last ontogenetically and that it matures only after completion of ocular growth of the eye about 14 years of age i.e. scleral elasticity and plasticity are related to age. These findings on differential elasticity properties of the sclera provide further support for the preponderance of the type A retinal contours in anisometropes i.e. the more myopic eye showing axial expansion only of the vitreous chamber compared to the contralateral eye (see § 5.4.2).

*Mechanical stress*

Mechanical stress on the posterior sclera induced by the extraocular muscles and the vitreous pressure has been proposed as a possible factor in the development of myopia (Greene, 1991). Greene considered the forces acting on the sclera in terms of engineering mechanical stresses. He calculated that the induced stress from the extraocular muscles was dependent upon the oblique tension, the width of the attachment line and the thickness of the posterior sclera. He stated that during convergence the rectus muscles increase the vitreous pressure of the eye by local indentation of the sclera. Extraocular muscle contraction was found to predominate over the ciliary muscle contraction in terms of mechanical stress. Greene concluded that if the sclera had a high propensity to creep then the effect of these forces could cause the sclera to stretch and hence produce myopia.

These proposals seem plausible and could account for equal amounts of myopia in a pair of eyes. How the anomaly of anisometropia could be explained by these theories remains unclear as the inter-eye variations in muscle tension, muscle width, scleral thickness are assumed to be negligible in an individual.

*Stretching in a myopic eye*

The fundus morphology data presented in chapter 8 shows that in anisometropes the disc-to-fovea distance is greater in the more myopic eye, whereas the optic disc size is similar in a pair of anisometropic eyes. However the lack of correlation between optic nerve head size and refraction in anisometropia may be explained by the fact that growth of the posterior scleral opening has finished at approximately the second year of life (Quigley *et al.*, 1982). This is in contrast to the growth of the total globe, especially in the anterior-posterior axis, which may last up to 15 to 20 years, at which point final refraction is reached (see § 1.2).

The investigations by Bradley *et al.* (1983) and Winn *et al.* (1988) on aniseikonia in anisometropes indicated that aniseikonia may result from non-optical factors. They found that correcting axial anisometropes with contact lenses produced less aniseikonia than corrections with spectacles. They suggested that the optical system may adapt to the difference in retinal image size by stretching of the retina so that the larger retinal image in the more myopic eye stimulates a similar number of receptors to the smaller retinal image in the less myopic eye.

A stretched myopic eye would be expected to have a thinner sclera. Phillips and McBrien (1995) investigated this hypothesis by examining the elastic properties of sclera in the development of form-deprived myopia in tree shrews. Monocular deprivation resulted in the tree shrews having a mean amount of anisomyopia of -5.60. The deprived eyes were found to be significantly longer in both axial and equatorial dimensions of the globe compared to the contralateral eyes. Compared to the contralateral control eye, a reduction in posterior scleral thickness, a lower failure load for both posterior and equatorial sclera, and an increased extensibility were found for the myopic

eyes. A finite element model of the tree shrew eye was developed to determine how much the observed difference in axial length between the deprived myopic eye and the contralateral eye could be accounted for by differential elastic expansion of the eye. Interestingly they found that the predicted axial expansion of the myopic eye was less than 20% of that observed. The model predicted a reduction in equatorial diameter of the myopic eye compared to the expansion observed in the myopic eye of the tree shrew. The finding that the model predicted less expansion than that observed, questions the assumption that in anisometropia the more myopic eye has merely stretched relative to the contralateral eye.

### 10.4 *Intraocular pressure*

One factor that has been suspected as important in the development of myopia is intraocular pressure (IOP). IOP has been postulated to act as a force on the sclera to stimulate excessive growth (Stuart-Black Kelly, 1981). The use of anti-glaucoma agents, such as beta-blockers, in children to lower the IOP have not however significantly reduced the progression of myopia e.g. (Jensen, 1988 and 1991). The thesis has found a similar IOP in both eyes of anisometropes. Thus, in anisometropes differences in IOP cannot account for the discrepancy in axial elongation. Whether differences in IOP occurred prior to the onset of anisometropia is unknown but considering that IOP is controlled centrally it would appear unlikely.

Van Alphen (1986) increased the pressure in enucleated human eyes (aged between 1 day and 68 years) to assess any changes with increased IOP. The sclera from behind the equator was removed and a saline infusion was introduced into the eyes. The eyes were found to increase axially rather than display overall radial expansion, with the stretch observed from in front of the equator. This type of expansion is similar to the that found from computed retinal contours, in the present thesis, in anisometropes.

### 10.5 *Choroidal blood flow*

Choroidal blood flow has been found to be significantly reduced in pathological myopia (Shih *et al.*, 1991) and in eyes with longer axial lengths (James *et al.*, 1991). The thesis investigated IOP, pulse amplitude and pulsatile choroidal blood flow in anisometropes. The choroidal blood flow was found to correlate with myopia, with a greater degree of myopia having a lower rate of blood flow. Interestingly anisometropes showed an interocular difference in blood flow which correlated with the degree of anisometropia (see § 9.3).

Several authors have suggested that fluctuations in choroidal blood flow serve, in part, to regulate ocular temperature (Bill, 1984; Parver, Auker and Carpenter, 1980). Parver, Auker and Carpenter suggested that the high rate of blood flow in the choroid acts as a 'heat sink' for the retina, dissipating heat through the blood stream. Impaired vascular circulation is believed to be

involved in pathology of the retina, the optic nerve head and the choroid (Langham and Krammer, 1990; Langham *et al.*, 1991).

Choroidal blood flow accounts for 90 - 95% of the total blood flow (Bill, 1984; Langham *et al.*, 1987), the remainder of the total blood flow is the retinal vascular circulation. The choroidal blood flow has a pulsatile component which represents 75 to 85% of the total choroidal blood flow (Langham *et al.*, 1989; Riva *et al.*, 1994).

The choroid has been shown to be thinner in myopic eyes compared to emmetropic eyes. Cheng *et al.* (1992) using magnetic resonance imaging showed significant thinning in both the choroid and sclera in the posterior part of the globe of myopic eyes compared to both emmetropic and hyperopic eyes. The thinning of the choroid and sclera was evident in all 7 myopic eyes which ranged in refractive error from -3 to -9.50D.
The inter-eye differences in choroidal thickness in anisometropes needs to be addressed. The choroidal accommodation experiments in chicks have demonstrated that monocular choroidal changes are possible. It may be that in humans, like the chick model of myopia, that short-term changes in the choroid occur before permanent scleral change.

It is feasible that the reduction in choroidal blood flow may result from a thinning choroid. The reduction of blood flow in humans with myopia has implications in the long-term health of the eye, especially in individuals whose myopia is progressing. Furthermore the reduction in choroidal blood flow is likely to render the myopic eye more vulnerable to other ocular pathologies such as macular degeneration, retinal detachment and glaucoma.

### 10.6 *Central versus peripheral form-deprivation in humans*

Human correlates of the high myopia produced in animals by form-deprivation are believed to exist in humans with eyelid and other ocular anomalies (see § 1.4.5). Form-deprivation in humans has mainly been found to correlate with axial elongation of the eye.
A paper by Hung *et al.* (1995) has raised some controversial issues concerning the correction of refractive errors in young children. Hung *et al.* imposed monocular defocus in monkey eyes using spherical lenses ranging in power from -6D to +6D. They found that the lenses induced anisometropia of at least 1D in all the monkeys (n = 10). They monitored, for each monkey, which eye was used for focusing and they found that the monkeys used their lens-covered eye for vision when positive lenses were fitted but used their uncovered eye when negative lenses were worn. By using this fixation strategy the monkey exerts the minimum amount of accommodative effort to obtain a clear retinal image. The non-fixating eye was rendered hyperopic for near distances. With positive lenses, the lens-covered eye was found to have a reduction in the rate of vitreous chamber elongation and an increase in hyperopia. Whereas with negative lenses, the lens-covered eye showed a relative increase in rate of axial growth and a corresponding myopic

refractive error. On removal of the lenses, Hung *et al.* found a the monkey eyes recovered in response to the induced anisometropia. They concluded that monkeys have a monocular emmetropisation mechanism which allows compensation for interocular differences in refractive error. They argued that full correction of refractive errors in very young children may impede the normal emmetropisation mechanism.

These findings support Medina's (1987) model of emmetropisation. Medina assumed a feedback control mechanism which implied that correcting myopia increased its progression. However, no data was presented to support the prediction.

The findings of Hung *et al.* and the suggestions by Medina question the correction of refractive errors, especially anisometropia, in very young children. However, the predictability of whether a high ametropic eye will emmetropise is unknown and the sensory effects of amblyopia and strabismus that are related to anisometropia, are more debilitating than the wearing of spectacles.

An interesting study by Nathan *et al.* (1985) examined the relationship between disease-associated vision deprivation and spherical refractive errors in 256 children aged 1-16 years. They found that diseases associated with the development of myopia correlated with peripheral or both peripheral and central visual impairment, such as nystagmus, aniridia, retinopathies and optic atrophy. However, diseases that affected only foveal vision, for example albinism and maculopathies, resulted in mild hypermetropia (+0.80D). Interestingly they found that hypermetropia was produced if the onset of visual impairment was in the first three years of life but was not congenital whereas myopia developed if the deprivation occurred at other ages except in cases where the macular function was specifically affected. It appears that there is no published research on animal models of myopia using annular occluders to differentiate between central and peripheral vision deprivation, to support the findings in humans.

If myopia can develop in an eye in the presence of a clear foveal image but with impaired peripheral vision, then the generally accepted views on myopia development may need to be reviewed. The studies by Ferree, Rand and Hardy (1931) and Rempt, Hoogerheide and Hoogenboom (1971) on peripheral refraction have revealed that emmetropic eyes usually have a marked degree of peripheral astigmatism (often of the order of 6D). However, myopic eyes have been found to exhibit low degrees of peripheral astigmatism (1-2D). Hoogerheide, Rempt and Hoogenboom (1971) stated that the type of skiagram is usually inborn and does not change much during a lifetime. If this is the case and emmetropic eyes result from eyes with marked peripheral astigmatism, then eyes with low degrees of peripheral astigmatism may in some way be deprived of a certain type of peripheral retinal image which may stimulate the development of myopia.

It is not known whether there is a genetic basis to the type of peripheral refraction exhibited in an individual or if peripheral refraction can be modified by the environment. Mutti *et al.* (1996) have recently incorporated peripheral refraction measurements at 40° in the nasal visual field into the Orinda longitudinal study of myopia. Peripheral refraction measurements have been made on

822 children in the first to eighth school grade. They found that emmetropes and hyperopes displayed relative myopia in the periphery which is consistent with an oblate retinal contour whereas myopes demonstrated relative hyperopia indicative of prolate retinal contour. These peripheral refraction findings are in agreement with those measured in the present thesis. They aim to correlate future changes in peripheral refraction with biometric parameters.

***Predictive factors for the development of myopia***

A suitable predictive factor for the development of myopia is an attractive proposition. Grosvenor (1988) has suggested the use of the axial length-to-corneal radius ratio as an indicator of myopia development. A ratio of greater than 3.0 has been implicated in the development of myopia. It may be that retinal contour shape is more important in myopia and thus an index, for example, of retinal contour to corneal curvature may provide further insight into predictive factors in myopia.

***Caucasian versus the Chinese eye***

The development of myopia is a fruitful area in an Asian population given the increased incidence of myopia and industrialisation of Asian and Far Eastern nations. The structural correlate of myopia, an increased vitreous chamber depth, has been found to be the same for both Caucasian and Chinese populations. Racial differences in corneal topography have been described in the literature (Lam and Loran, 1991), with Chinese eyes displaying slower rates of peripheral flattening compared to Caucasian eyes. However the results of the thesis do not support this finding. Discrepancies may arise from differences in refractive error in the two groups (the Chinese were all myopic or emmetropic whereas the Caucasian group included hyperopes) or from differences in methodology.

Whatever its aetiology, myopia is still progressing in Asian populations and its prevalence has reached approximately 70% (Lin *et al.*, 1996). Whether differences in environmental conditions, nutrition, or susceptibility to myopia can account for the large discrepancy in prevalence of myopia between the two races is unknown.

***Future work***

The paucity of information on peripheral refraction especially in both cross-sectional and longitudinal studies in infant populations, suggests that this area of research requires attention. The methods used in the thesis to obtain peripheral refraction data and consequently retinal contour data are easily applicable to studies on developmental work in children.

An interesting area of future study is that of a large longitudinal study on an infant population to measure retinal contour and corneal curvature. If the change in retinal contour through

development could be correlated with corneal curvature then some predictive factor for the development of myopia may be derived. Peripheral refraction measurements in infants may be more of a difficult task and cycloplegic retinoscopy may therefore be a more suitable method than using the Canon autorefractor. A longitudinal study both on the nature of peripheral refraction and retinal contour changes during growth in children may provide an indication of the aetiology in myopia development. New techniques such as laser Doppler interferometry would provide an *in vivo* method for determining retinal contour shape. Although not commercially-available at present it may become more accessible in the future.

Evidence has been presented that choroidal blood flow is reduced in myopia and has introduced new areas of research worthy of more attention for its predictive facility in the development of myopia. Longitudinal data on choroidal blood flow in persons in whom myopia is progressing would be of relevance to the cause and effect relationship between reduced choroidal blood flow and the development of myopia.

From the literature anisometropia has been shown to be transient in childhood. Infantile anisometropia that is persistent is believed to arise from interocular differences in axial length. It is unknown whether discrepancies in axial length do account for anisometropia in childhood, either of the persistent or transient type. A longitudinal study measuring axial length in infants would provide further insight into the development of ametropia.

To conclude, the thesis has confirmed previous studies in that anisomyopia has the same structural correlate as myopia and is therefore clearly a subtype of myopia. The specially designed computational program to determine retinal contours have provided new and interesting findings; that anisomyopia is associated with an elongation of the vitreous chamber in the axial dimension only. This elongation can be considered in terms of the retina stretching as the distance between the disc and the fovea was found to increase with increasing amounts of myopia. Differences in choroidal blood flow have suggested a new area requiring further research to ascertain whether choroidal changes occur prior or subsequent to the onset of myopia. Nevertheless, despite the new findings, the nature of anisomyopia is that of a subtype of myopia with a relatively low incidence and seems destined to remain an enigma.

## REFERENCES


Abdalla, M. I. and Hamdi, M. (1970) Applanation ocular tension in myopia and emmetropia. Br. J. Ophthalmol. 54, 122-125.

Abrahamsson, M., Fabian, G. and Sjöstrand, J. (1990) A longitudinal study of a population based sample of astigmatic children. II. The changeability of anisometropia. Acta Ophthalmol. 68, 435-440.

Abrahamsson, M. and Sjöstrand, J. (1994) Longitudinal studies of pat'ents with pronounced anisometropia at 1 year of age. Invest. Ophthalmol. Vis. Sci. 35, S1805.

Adams, D. W. and McBrien, N. A. (1993) A longitudinal study of the relationship between tonic accommodation (dark focus) and refractive error in adulthood. Invest. Ophthalmol. Vis. Sci. 34, S1308.

Almeder, L. M., Peck, L. B. and Howland, H. C. (1990) The preva ence of anisometropia in volunteer laboratory and screening studies. Invest. Ophthalmol. V s. Sc . 31, 2448-2455.

Atchison, D. A., Bradley, A., Thibos, L. N. and Smith, G. (1995) Useful variation of the Badal optometer. Optom. Vis. Sci. 72, 279-284.

Battaglioli, J. L. and Kamm, R. D. (1984) Measurements of the compressive properties of scleral tissue. Invest. Ophthalmol. Vis. Sci. 25, 59-65.

Beck, R. W., Servais, G. E. and Hayreh, S. S. (1981) Anterior ischaemic optic neuropathy. Ophthalmology, 94, 1503-1508.

Belin, M. W., Cambier, J. L., Nabors, J. R. and Ratliff, C. D. (1995) PAR Corneal Topography System (PAR CTS): The clincial application of close-range photogrammetry. Optom. Vis. Sci. 72, 828-837.

Bengtsson, B. (1972) Some factors affecting the distribution of intraocular pressures in a population. Acta Ophthalmol. 50, 33-45.

Bengtsson, B. (1976) The variation and covariance of cup and disc diameters. Acta Ophthalmo . 54, 801-818.

Bengtsson, B. (1980) The alteration and asymmetry of cup and disc diameters. Acta Ophthalmo . 58, 726-732.

Bengtsson, B. and Krakau, C. E. T. (1977) Some essential optical features of the Ze'ss fundus camera. Acta Ophthalmol. 55, 123-131.

Bennett, A. G. (1966) The calibration of keratometers. Optician 151, 317-322.

Bennett, A. G. (1988) A method of determining the equivalent powers of the eye and its crystalline lens without resort to phakometry. Ophthal. Physiol. Opt. 8, 53-59.

Bennett, A. G. and Rabbetts, R. B. (1989) Clinical Visual Optics. 2nd ed. Butterworths, London.

Bhandari, A. and Fitzke, F. (1994) Scanning laser ophthalmoscopy - an update. Optician 207, 15-17.

Bill, A. (1984) Circulation in the eye. In: Handbook of physiology: Section2: The cardiovascular system, ed. E. M. Renkin and C. C. Michel, American Physiological Society, Bethesda, Maryland.

Birch, E., Stager, D. and Everett, M. (1995) Natural history of infantile anisometropia. Invest. Ophthalmol. Vis. Sci. 36, S45.

Bishop, K. I., Werner, E. B., Krupin, T., Kozart, D. M., Beck, S. R., Nunan, F. A. and Wax, M. B. (1988) Variability and reproducibility of optic disc topographic measurements with the Rodenstock optic nerve head analyzer. Am. J. Ophthalmol. 106, 696-702.

Blaker, J. W. (1980) Toward an adaptive model of the human eye. J. Opt. Soc. Am. 70, 220-223.

Bland, J. M. and Altman, D. G. (1986) Statistical methods for assessing agreement between two methods of clinical measurement. The Lancet, Feb 8, 307-310.

Blum, H., Bettman, J. and Peters, H. B. (1959) Vision Screening for Elementary Schools: The Orinda Study. University of California Press, Berkley, CA.

Bonomi, L., Mecca, E. and Massa, F. (1982) Intraocular pressure in myopic anisometropia. Int. Ophthalmol. 5, 145-148.

Borish, I. M. (1970) Clinical Refraction. Vol. 1., 3rd ed. The Professional Press, Inc., Chicago.

Bradley, A., Rabin, J. and Freeman, R. D. (1983) Non-optical determinants of aniseikonia. Invest. Ophthalmol. Vis. Sci. 24, 507-512.

Brock, F. W. (1962) Factors in the management of amblyopic and strabismic patients. Optometric Weekly 53, 1617-1621.

Brooks, S. E., Johnson, D. and Fischer, N. (1996) Anisometropia and binocularity. Ophthalmology 103, 1139-1143.

Brown, N. (1974) The change in lens curvature with age. Exp. Eye Res. 19, 1759-1766.

Bruce, A., Hurst, M. A., Abbott, H. and Harrison, H. (1991) The incidence of refractive error and anomalies of binocular vision in infants. Br. Orthopt. J. 48, 32-35.

Bullimore, M. and Gilmartin, B. (1987) Aspects of tonic accommodation in emmetropia and late-onset myopia. Am. J. Optom. Physiol. Opt. 64, 499-503.

Burk, R. O. W., Rohrschneider, K. and Völcker, H. E. (1990) Three-dimensional optic disc analysis in glaucoma. Ophthalmol. 97, 142-147.

Burk, R. O. W., Rohrschneider, K., Takamoto, T., Völcker, H. E. and Schwartz, B. (1993) Laser scanning tomography and stereophotogrammetry in three-dimensional optic disc analysis. Graefe's Arch. Clin. Exp. Ophthalmol. 231, 193-198.

Bynke, H. G. and Schéle, B. (1967) On the origin of the ocular pressure pulse. Ophthalmology 153, 29-36.

Calossi, A. (1994) Increase of ocular axial length in infantile cataract. Optom. Vis. Sci. 71, 386-391.

Caprioli, J., Klingbeil, U., Sears, M. and Pope, B. (1986) Reproducibility of optic disc measurements with computerized analysis of stereoscopic video images. Arch. Ophthalmol. 104, 1035-1039.

Carney, L. G. and Henderson, B. (1993) Corneal topography as a function of refractive error. Invest. Ophthalmol. Vis. Sci. 34, S1217.

Carney, L. G., Mainstone, J. C. and Henderson, B. A. (1997) Corneal topography and myopia. Invest. Ophthalmol. Vis. Sci. 38, 311-320.

Charman, W. N. (1976) The Collins electronic refractionometer. Ophthal. Opt. 345-348.

Charman, W. N. (1983) The retinal image in the human eye. In: Progress in retinal research, ed. Osborne and Chandler, Pergamon Press, Oxford.

Charman, W. N. (1989) The path to presbyopia: straight or crooked? Ophthal. Physiol. Opt. 9, 424-430.

Charman, W. N. and Jennings, J. A. M. (1982) Ametropia and peripheral refraction. Am. J. Optom. Physiol. Opt. 59, 922-923.

Charman, W. N. and Tucker, J. (1977) Dependence of accommodation response on the spatial frequency spectrum of the observed object. Vision Res. 17, 129-139.

Chauhan, K. and Charman, W. N. (1995) Single figure indices for the steady-state accommodative response. Ophthal. Physiol. Opt. 15, 217-222.

Chen, C.-J., Cohen, B. H. and Diamond, E. L. (1985) Genetic and environmental effects on the development of myopia in Chinese twin children. Ophthal. Paediatr. Genet. 6, 113-119.

Cheng, H.-M., Singh, O. S., Kwong, K., Xiong, J., Woods, B. T. and Brady, T. J. (1992) Shape of the myopic eye as seen with high-resolution magnetic resonance imaging. Optom. Vis. Sci. 69, 698-701.

Chi, T., Stickler, D., Pitman, B., Tsai, C. and Hsieh, F. Y. (1989) Racial differences in optic nerve head parameters. Arch. Ophthalmol. 107, 836-839.

Chihara, E. and Chihara, K. (1994) Covariation of optic disc measurement and ocular parameters in the healthy eye. Graefe's Arch. Clin. Exp. Ophthalmol. 232, 265-271.

Chihara, E., Takahashi, F. and Chihara, K. (1993) Assessment of optic disc topography with scanning laser ophthalmoscope. Graefe's Arch. Clin. Exp. Ophthalmol. 231, 1-6.

Ciuffreda, K. J., Levi, D. M. and Semmlow, A. (1991) Amblyopia. Ist ed.Butterworth-Heinemann, Boston.

Cook, R. C. and Glassock, R. E. (1951) Refractive and ocular findings in the newborn. Am. J. Ophthalmol. 34, 1407-1413.

Cooper, J. and Feldman, J. (1978) Random-dot-stereogram performance by strabismic, amblyopic, and ocular-pathology patients in an operant-discrimination task. Am. J. Optom. Physiol. Opt. 55, 599-609.

Culham, L. E., Fitzke, F. W., Timberlake, G. T. and Marshall, J. (1992) Use of scrolled text in a scanning laser ophthalmoscope to assess reading performance at different retinal locations. Ophthal. Physiol. Opt. 12, 281-286.

Curtin, B. J. (1969) Physiopathic aspects of scleral stress-strain. Trans. Am. Ophthal. Soc. 67, 417-461.

Curtin, B. J. (1985) The Myopias: basic science and clinical management. Harper & Row, Philadelphia .

Curtin, B. J. and Karlin, D. B. (1971) Axial length measurements and fundus changes of the myopic eye. Am. J. Ophthalmol. 71, 42-53.

de Jong, P. T. V. M., Oostra, B. A. and de Faber, J.-T. H. N. (1993) High symmetrical anisometropia in monozygotic twins. Ophthal. Paediatr. Genet. 14, 29-32.

de Vries, J. (1985) Anisometropia in children: analysis of a hospital population. Br. J. Ophthalmol. 69, 504-507.

Dobson, V., Fulton, A. B., Manning, K., Salem, D. and Peterson, R. A. (1981) Cycloplegic refractions of premature infants. Am. J. Ophthalmol. 91, 490-495.

Donders, F. C. (1864) On the anomalies of accommodation and refraction of the eye. , (trans W.D. Moore), The New Sydenham Society, London.

Douthwaite, W. A. and Burek, H. (1995) The Bausch and Lomb keratometer does not measure the tangential radius of curvature. Ophthal. Physiol. Opt. 15, 187-193.

Drasdo, N. and Fowler, C. F. (1974) Non-linear projection of the retinal image in a wide-angle schematic eye. Br. J. Ophthal. 58, 709-714.

Duane, A. (1912) Normal values of the accommodation at all ages. J. Am. Med. Assoc. 59, 1010-1013.

Duke-Elder. (1970) Ophthalmic optics and refraction. Vol. V. System of Ophthalmology Kimpton, London.

Dunne, M. C. M. (1995) A computing scheme for determination of retinal contour from peripheral refraction, keratometry and A-scan ultrasonography. Ophthal. Physiol. Opt. 15, 133-143.

Dunne, M. C. M. and Barnes, D. A. (1987) Schematic modelling of peripheral astigmatism in real eyes. Ophthal. Physiol. Opt. 7, 235-239.

Dunne, M. C. M. and Barnes, D. A. (1990) Modelling oblique astigmatism in eyes with known peripheral refraction and optical dimensions. Ophthal. Physiol. Opt 10, 46-48.

Dunne, M. C. M., Barnes, D. A. and Clement, R. A. (1987) A model for retinal shape changes in ametropia. Ophthal. Physiol. Opt. 7, 159-160.

Edwards, N. R. (1994) Oculomotor responses in emmetropia and myopia. PhD Thesis, Aston University, UK.

Emsley, H. H. (1963) Visual Optics. 1, 5th ed. Hatton Press Ltd, London.

Erickson, P. (1984) Complete ocular component analysis by vergence contribution. Am. J. Optom. Physiol. Opt. 61, 469-472.

Erickson, P. (1991) Optical components contributing to refractive anomalies. In: Refractive Anomalies - Research and Clinical Implications, ed. T. Grosvenor and M. C. Flom. Butterworth-Heinemann, Boston.

Fercher, A. F., Hitzenberger, C. K. and Juchem, M. (1991) Measurement of intraocular distances using partially coherent laser light. J. Mod. Opt. 38, 1327-1333.

Fercher, A. F., Mengedoth, K. and Werner, W. (1988) Eye-length measurement by interferometry with partially coherent light. Opt. Lett. 13, 186-188.

Ferree, C. E. and Rand, G. (1933) Interpretation of refractive conditions in the peripheral field of vision. Arch. Ophthal., 925-938.

Ferree, C. E., Rand, G. and Hardy, C. (1931) Refraction for the peripheral field of vision. Arch. Ophthal. 5, 717-731.

Ferree, C. E., Rand, G. and Hardy, C. (1932) Refractive asymmetry in the temporal and nasal halves of the visual field. Am. J. Ophthalmol. 15, 513-522.

Fitch, R. C. (1971) Procedural effects on the manifest human amplitude of accommodation. Am. J. Optom. 48, 918-926.

Fledelius, H. C. (1981a) Changes in refraction and eye size during adolescence. In: Doc. Ophthal. Proc. Series, ed. H. C. Fledelius, P. H. Alsbirk and E. Goldschmidt. Dr W. Junk Publishers, The Hague.

Fledelius, H. C. (1981b) Refractive components in aniso- and isometropia. In: Doc. Ophthal. Proc. Series, ed. H. C. Fledelius, P. H. Alsbirk and E. Goldschmidt. Dr W. Junk Publishers, The Hague.

Fledelius, H. C. (1982) Ophthalmic changes from age of 10 to 18 years. A longitudinal study of sequels to low birth weight. III. Ultrasound oculometry and keratometry of anterior eye segment. Acta Ophthalmol. 60, 393-402.

Fledelius, H. C. (1983) Is myopia getting more frequent? A cross-sectional study of 1416 Danes aged 16 years +. Acta Ophthalmol. 61, 545-559.

Fledelius, H. C. (1984) Prevalence of astigmatism and anisometropia in adult Danes. Acta Ophthalmol. 62, 391-400.

Flom, M. C. and Bedell, H. E. (1985) Identifying amblyopia using associated conditions, acuity and nonacuity features. Am. J. Optom. Physiol. Opt. 62, 153-160.

Fowler, C. W. and Dave, T. N. (1994) Review of past and present techniques of measuring corneal topography. Ophthal. Physiol. Opt. 14, 49-58.

Friedman, Z., Neumann, E. and Abel-Peleg, B. (1985) Outcome of treatment of marked ametropia without strabismus following screening and diagnosis before the age of three. J. Ped. Ophthalmol. Strab. 22, 54-57.

Fukuda, M., Kuwayama, Y., Shiosoka, S., Inagaki, S., Ishimoto, I., Shimizu, Y., Takagi, H., Sakanada, M., Takatski, K., Senba, E. and Tohyama, M. (1981) Localization of vasoactive intestinal polypeptide and neurotensin immunoreactivities in the avian retina. Curr. Eye Res. 1, 115-118.

Fulton, A. B., Dobson, V., Salem, D., Mar, C., Petersen, R. A. and Hansen, R. M. (1980) Cycloplegic refractions in infants and young children. Am. J. Ophthalmol. 90, 239-247.

Fulton, A. B., Hansen, R. M. and Petersen, R. A. (1982) The relation of myopia and astigmatism in developing eyes. Ophthalmology 89, 298-302.

Gallagher, J. T. and Citek, K. (1995) A Badal optical stimulator for the Canon autoref R-1 optometer. Optom. Vis. Sci. 72, 276-278.

Garner, L. F., Kinnear, R. F., Klinger, J. D. and McKellar, M. J. (1985) Prevalence of myopia in school children in Vanuatu. Acta Ophthalmol. 63, 323-326.

Garner, L. F., Yap, M. K. H., Kinnear, R. F. and Firth, M. J. (1995) Ocular dimensions and refraction in Tibetan children. Optom. Vis. Sci. 72, 266-271.

Gee, S. S. and Tabbara, K. F. (1988) Increase in ocular axial length in patients with corneal opacification. Ophthalmology 95, 1276-1278.

Gilmartin, B. (In preparation) Autonomic correlates of near vision in emmetropia and myopia. In: Myopia and nearwork. ed. M. Rosenfield and B. Gilmartin, Butterworth-Heinemann, London.

Gilmartin, B., Gray, L. S. and Winn, B. (1991) The amelioration of myopia using biofeedback of accommodation: a review. Ophthal. Physiol. Opt. 11, 304-313.

Gilmartin, B. and Winfield, N. R. (1995) The effect of topical ß-adrenoceptor antagonists on accommodation in emmetropia and myopia. Vision Res. 35, 1305-1312.

Gimbel, H. V. (1973) The control of myopia with atropine. Canad. J. Ophthal. 8, 527-532.

Gimpel, G., Doughty, M. J. and Lyle, W. M. (1994) A large sample study of the effects of phenylephrine 2.5% eyedrops on the amplitude of accommodation in man. Ophthal. Physiol. Opt. 14, 123-128.

Glickstein, M. and Millodot, M. (1970) Retinoscopy and eye size. Science 168, 605-606.

Goh, W. S. H. and Lam, C. S. Y. (1994) Changes in refractive trends and optical components of Hong Kong Chinese aged 19-39 years. Ophthal. Physiol. Opt. 14, 378-382.

Goldschmidt, E. (1968) On the etiology of myopia. Acta Ophthalmol. (Suppl) 98.

Goldschmidt, E. (1969) Refraction in the newborn. Acta Ophthalmol. 47, 570-578.

Gomez, P. and Fern, K. (1991) Prevalence of anisometropia in a clinical population. Optom. Vis. Sci. 68, 198.

Goss, D. A. and Cox, V. D. (1985) Trends in the change of clincial refractive error in myopes. J. Am. Optom. Assoc. 56, 608-613.

Goss, D. A., Cox, V. D., Herrin-Lawson, G. A., Nielson, E. D. and Dolton, W. A. (1990) Refractive error, axial length and height as a function of age in young myopes. Optom. Vis. Sci. 67, 332-338.

Goss, D. A. and Erickson, P. (1990) Effects of changes in anterior chamber depth on refractive error of the human eye. Optom. Vis. Sci. 5, 197-201.

Goss, D. A. and Grosvenor, T. (1990) Rates of childhood myopia progression with bifocals as a function of nearpoint phoria: consistency of three studies. Optom. Vis. Sci. 67, 637-640.

Goss, D. A. and Jackson, T. W. (1993) Cross-sectional study of changes in ocular components in school children. App. Opt. 32, 4169-4173.

Goss, D. A. and Jackson, T. W. (1995) Clinical findings before the onset of myopia in youth. I. Ocular optical components. Optom. Vis. Sci. 72, 870-878.

Goss, D. A. and Jackson, T. W. (1996a) Clinical findings before the onset of myopia in youth: 2. Zone of clear single binocular vision. Optom. Vis. Sci. 73, 263-268.

Goss, D. A. and Jackson, T. W. (1996b) Clinical findings before the onset of myopia in youth: 3. Heterophoria. Optom. Vis. Sci. 73, 269-278.

Goss, D. A. and Jackson, T. W. (1996c) Clinical findings before the onset of myopia in youth: 4. Parental history of myopia. Optom. Vis. Sci. 73, 279-282.

Goss, D. A. and Wickham, M. G. (1995) Retinal image-mediated ocular growth as a mechanism for juvenile-onset myopia and for emmetropization. Doc. Ophthalmol. 90, 341-375.

Goss, D. A. and Winkler, R. L. (1983) Progression of myopia in youth: age of cessation. Am. J. Optom. Physiol. Opt. 60, 651-658.

Greene, P. R. (1991) Mechanical considerations in myopia. In: Refractive anomalies: research and clincial applications, ed. T. Grosvenor and M. C. Flom, Butterworth-Heinemann, London.

Grice, K. M., Del Bono, E. A., Haines, J. L., Wiggs, J. L. and Gwiazda, J. E. (1996) Genetic analysis of pedigrees affected by juvenile onset myopia. Invest. Ophthalmol. Vis. Sci. 37, S1002.

Grosvenor, T. (1987) A review and suggested classification of myopia on the basis of age-related prevalence and age of onset. Am. J. Optom. Physiol. Opt. 64, 545-554.

Grosvenor, T. (1988) High axial length/corneal radius ratio as a risk factor in the development of myopia. Am. J. Optom. Physiol. Opt. 65, 689-696.

Grosvenor, T. (1994) Refractive component changes in adult-onset myopia: evidence from five studies. Clin. Exp. Optom. 77, 196-205.

Grosvenor, T. and Scott, R. (1993) Three-year changes in refraction and its components in youth-onset and early adult-onset myopia. Optom. Vis. Sci. 68, 677-683.

Guillon, M., Lydon, D. P. M. and Wilson, C. (1986) Corneal topography: a clinical model. Ophthal. Physiol. Opt. 6, 47-56.

Gwiazda, J., Bauer, J., Thorn, F. and Held, R. (1995) A dynamic relationship between myopia and blur-driven accommodation in school-aged children. Vision Res. 35, 1299-1304.

Gwiazda, J., Thorn, F., Bauer, J. and Held, R. (1993) Emmetropisation and the progression of manifest refraction in children followed from infancy to puberty. Clin. Vis. Sci. 8, 337-344.

Gwiazda, J., Thorn, F., Bauer, J. and Held, R. (1993) Myopic children show insufficient accommodative response to blur. Invest. Ophthalmol. Vis. Sci. 34, 690-694.

Haim, M., Fledelius, H. C. and Skarsholm P. (1988) X-linked myopia in a Danish family. Acta Ophthalmol. 88, 450-456.

Hemenger, R. P., Garner, L. F. and Ooi, C. S. (1995) Change with age of the refractive index gradient of the human ocular lens. Invest. Ophthalmol. Vis. Sci. 36, 703-707.

Hendicott, P. and Lam, C. (1991) Myopic cresent, refractive error and axial length in Chinese eyes. Clin Expt Optom 74, 168-174.

Hendrickson, P. and Rosenblum, W. (1985) Accommodation demand and deprivation in kitten ocular development. Invest. Ophthalmol. Vis. Sci. 36, 343-349.

Hill, D. W. (1989) Ocular and retinal blood flow. Acta Ophthalmol. 67, 15-18.

Hirsch, M. J. (1964) Predictability of refraction at age 14 on the basis of testing at age 6 - interim report from the Ojai longitudinal study of reraction. Am. J. Optom. Arch. Am. Acad. Optom. 41, 567-573.

Hirsch, M. J. (1967) Anisometropia: A preliminary report of the Ojai longitudinal study. Am. J. Optom. Arch. Am. Acad. Optom. 44, 581-585.

Hitzenberger, C. K. (1991) Optical measurement of the axial eye length by laser Doppler interferometry. Invest. Ophthalmol. Vis. Sci. 32, 616-624.

Hokoda, S. C. and Ciuffreda, K. J. (1982) Measurement of accommodative amplitude in amblyopia. Ophthal. Physiol. Opt. 2, 205-212.

Honkanen, R. E., Howard, E. F. and Abdel-Latif, A. A. (1990) M3-muscarinic receptor subtype predominates in the bovine iris sphincter smooth muscle and ciliary processes. Invest. Ophthalmol. Vis. Sci. 31, 590-593.

Hoogerheide, J., Rempt, F. and Hoogenboom, W. P. H. (1971) Acquired myopia in young pilots. Ophthalmologica 163, 209-215.

Hoyt, C. S., Stone, R. D., Framer, C. and Billdon, F. A. (1981) Monocular axial myopia associated with neonatal eyelid closure in human infants. Am. J. Ophthalmol. 91, 197-200.

Hung, L.-F., Crawford, M. L. J. and Smith, E. L. (1995) Spectacle lenses alter eye growth and the refractive status of young monkeys. Nature Medicine 1, 761-765.

Hung, L.-F. and Smith, E. L. I. (1996) Extended-wear, soft, contact lenses produce hyperopia in young monkeys. Optom. Vis. Sci. 73, 579-584.

Inagaki, Y., Tanaka, M., Hirano, A., Magatani, H., Kato, K. and Nakajima, A. (1985) Rearranged automated keratometer for newborn infants and patients in the supine position. Am. J. Ophthalmol. 99, 664-666.

Ingram, R. M. (1979) Refraction of one year old children after atropine cycloplegia. Br. J. Ophthalmol. 63, 343-347.

Ingram, R. M. and Barr, A. (1979) Changes in refraction between the ages of 1 and 3 1/2 years. Br. J. Ophthalmol. 63, 339-342.

Ingram, R. M. and Walker, C. (1979) Refraction as a means of predicting a squint or amblyopia in preschool siblings of children known to have these defects. Br. J. Ophthalmol. 63, 238-242.

Ingram, R. M., Arnold, P. E., Dally, S. and Lucas, J. (1991) Emmetropisation, squint, and reduced visual acuity after treatment. Br. J. Ophthalmol. 75, 414-416.

Irving, E. L., Callender, M. G. and Sivak, J. G. (1995) Inducing ametropia in hatchling chicks by defocus - aperture effects and cylindrical lenses. Vision Res. 35, 1165-1174.

Iuvone, M., Tigges, M., Fernandes, A. and Tigges, J. (1989) Dopamine synthesis and metabolism in rhesus monkey retina: development, aging and the effects of monocular visual deprivation. Visual Neuroscience 2, 465-471.

Jackson, C. R. S. (1960) Hypermetropic anisometropia. Br. Orthopt. J. 21,106-110.

Jain, M. R. and Marmion, V. J. (1976) A clinical evaluation of the applanation pneumatonograph. Br. J. Ophthalmol. 60, 107-110.

James, C. B., Trew, D. R., Clark, K. and Smith, S., E. (1991) Factors influencing the ocular pulse - axial length. Graefe's Arch. Clin. Exp. Ophthalmol. 229, 341-344.

Jampolsky, A., Flom, B. C., Weymouth, F. W. and Moses, L. E. (1955) Unequal corrected visual acuity as related to anisometropia. Arch. Ophthalmol., 893-904.

Jensen, H. (1988) Timolol maleate in the control of myopia. A preliminary report. Acta Ophthalmol. Suppl. 185, 128-129.

Jensen, H. (1991) Myopia progression in young schoolchildren. A prospective study of myopia progression and the effect of a trial with bifocal lenses and beta blocker eye drops. In: Acta Ophthalmologica. Copenhagen, Scriptor.

Jensen, H. (1995) Myopia in teenagers. An eight-year follow-up study on myopia progression and risk factors. Acta Ophthalmol. Scand. 73, 389-393.

Johnson, G. J. (1988) Myopia in artic regions. Acta Ophthalmol. 66 (Suppl 185), 13-18.

Jonas, J. B., Gusek, G. C., Guggenmoos-Holzmann, I. and Naumann, G. O. H. (1988) Variability of the real dimensions of normal human optic discs. Graefe's Arch. Clin. Exp. Ophthalmol. 226, 332-336.

Jonas, J. B., Gusek, G. C. and Naumann, G. O. H. (1988) Optic disc, cup and neuroretinal rim size, configuration and correlations in normal eyes. Invest. Ophthalmol. Vis. Sci. 29, 1151-1158.

Jonas, J. B. and Papastathopoulos, K. (1995) Ophthalmoscopic measurement of the optic disc. Ophthalmology 102, 1102-1106.

Kehoe, J. C. (1942) The frequencey of vertical anisometropia. Am. J. Optom. Arch. Am. Acad. Optom. 19, 1-4.

Kiely, P. M., Smith, G. and Carney, L. G. (1982) The mean shape of the human cornea. Optica Acta 29, 1027-1040.

Kivlin, J. D. and Flynn, J. T. (1981) Therapy of anisometropic amblyopia. J. Pediatr. Ophthalmol. 18, 47-56.

Klein, B. E. K., Klein, R., Sponsel, W. E., Franke, T., Cantor, L. B., Martone, J. and Menage, M. J. (1992) Prevalence of glaucoma. The Beaver Dam eye study. Ophthalmol. 99, 1499-1504.

Knapp, H. (1869) The influences of spectacles on the optical constraints and visual acuteness of the eye. Arch. Opthtal. Opt. 1, 377.

Kooijman, A. C. (1983) Light distribution on the retina of a wide-angle theoretical eye. J. Opt. Soc. Am. 73, 1544-1550.

Koretz, J. F., Kaufman, P. L., Neider, M. W. and Goeckner, P. A. (1989) Accommodation and presbyopia in the human eye - aging of the anterior segment. *Vision Res.* 29, 1685-1692.

Krakau, C. E. T. (1992) Calculation of the pulsatile ocular blood flow. Invest. Ophthalmol. Vis. Sci. 33, 2754-2756.

Kruse, F. E., Burk, R. O. W., Völcker, H.-M., Zinser, G. and Harbarth, U. (1989) Reproducibility of topographic measurements of the optic nerve head with laser tomographic scanning. Ophthalmol. 96, 1320-1324.

Kutschke, P. J., Scott, W. E. and Keech, R. V. (1991) Anisometropic amblyopia. Ophthalmology 98, 258-263.

Laatikainen, L. and Erkkilä, H. (1980) Refractive errors and other findings in school children. Acta Ophthalmol. 58, 129-136.

Laird, I. K. (1991) Anisometropia. *In*: Refractive anomalies: research and clinical applications, ed. T. Grosvenor and M. C. Flom. London, Butterworth-Heinemann.

Lam, A. K. C. and Douthwaite, W. A. (1994) Derivation of corneal flattening factor, *p*-value. Ophthal. Physiol. Opt. 14, 423-427.

Lam, A. K. C. and Douthwaite, W. A. (1996) Application of a modified keratometer in the study of corneal topography on Chinese subjects. Ophthal. Physiol. Opt. 16, 130-134.

Lam, A. K. C. and Loran, D. F. C. (1991) Designing contact lenses for Oriental eyes. J. Br. Contact Lens Assoc. 14, 109-114.

Lam, C. S. Y. and Goh, W. S. H. (1991) The incidence of refractive errors among school children in Hong Kong and ots relationship with the optical components. Clin Exp Optom 74, pp. 97-103.

Langham, M. E. (1966). Monometric, pressure-cup, and tonographic procedures in the evaluation of intraocular dynamics. Paper read at Glaucoma Symposium, at Tuzing.

Langham, M. E. (1975) Vascular pathophysiology of the ocular postural response. A pneumatonometric study. Trans. Ophthal. Soc. U. K. 95, 281-287.

Langham, M. E. (1987). Ocular blood flow and visual loss in glaucomatous eyes. In: Glaucoma update III, ed. G. K. Krieglstein. Berlin, Springer-Verlag.

Langham, M. E., Farrell, R. A., O'Brien, V., Silver, D. M. and Schilder, P. (1989) Blood flow in the human eye. Acta Ophthalmol. 67, 9-13.

Langham, M. E., Grebe, R., Hopkins, S., Marcus, S. and Sebag, M. (1991) Choroidal blood flow in diabetic retinopathy. Exp. Eye Res. 52, 167-173.

Langham, M. E. and Kramer, T. (1990) Decreased choroidal blood flow associated with retinitis pigmentosa. Eye 4, 321-325 .

Langham, M. E. and To'mey, K. F. (1978) A clinical procedure for the measurement of the ocular pulse-pressure relationship and the ophthalmic arterial pressure. Exp. Eye Res. 27, 17-25.

Larsen, J. S. (1971a) The sagittal growth of the eye. I. Ultrasonic measurement of the depth of the anterior chamber form birth to puberty. Acta Ophthalmologica 49, 239-262.

Larsen, J. S. (1971b) The sagittal growth of the eye II. Ultrasonic measurement of the axial diameter of the lens and the anterior segment from birth to puberty. Acta Ophthalmol. 49, 427-440.

Larsen, J. S. (1971c) The sagittal growth of the eye III. Ultrasonic measurement of the posterior segment (axial length of the vitreous) from birth to puberty. Acta Ophthalmol 49, 441-453.

Larsen, J. S. (1971d) The sagittal growth of the eye IV. Ultrasonic measurement of the axial length of the eye from birth to puberty. Acta Ophthalmol. 49, 873-886.

Le Grand, Y. (1967) Form and space vision. (Trans by Millodot, M). Heath, G. G., Indiana University Press, Bloomington .

Leary, G. A. (1981) Ocular component analysis by vergence contribution to the back vertex power of the anterior segment. Am. J. Optom. Physiol. Opt 58, 899-909.

Leary, G. A. and Young, F. A. (1968) A set of equations for computing the components of ocular refraction. Am. J. Optom. A. A. A. O. 45, 743-759.

Leech, E. M., Cottrial, C. L. and McBrien, N. A. (1995) Pirenzepine prevents form deprivation myopia in a dose dependent manner. Ophthal. Physiol. Opt. 15, 351-356.

Leibowitz, H. W., Johnson, C. A. and Isabelle, E. (1972) Peripheral motion detection and refractive error. Science 177, 1207-1208.

Lepard, C. W. (1975) Comparative changes in the error of refraction between fixing and amblyopic eyes during growth and development. Am. J. Ophthalmol. 80, 485-490.

Lin, L. L.-K., Shih, Y.-F., Lee, Y.-C., Hung, P.-T. and Hou, P.-K. (1996a) Changes in ocular refraction and its components among medical students - a 5-year longitudinal study. Optom. Vis. Sci. 73, 495-498.

Lin, L. L.-K., Shih, Y.-F., Tsai, C.-B., Chen, C.-J., Lee, L.-A., Hung, P.-T. and Hou, P.-K. (1996b) Epidemiological study of ocular refractions among school-children. Invest. Ophthalmol. Vis. Sci. 37, S1002.

Lin, T., Zhu, X., Capehart, C. and Stone, R. A. (1996c) The ciliary ganglion and vitreous shape cavity. Curr. Eye Res. 15, 453-460.

Littmann, H. (1982) Zur Bestimmung der wahren Größe eines Objektes auf dem Hintergrund des lebenden Auges. Klin. Mbl. Augenheilk. 180, 286-289.

Lotmar, W. (1971) Theoretical eye model with aspherics. J. Opt. Soc. Am. 61, 1522-1529.

Lotmar, W. (1976) A theroetical model for the eye of newborn infants. Albrecht von Graefes Arch. Klin. Exp. Ophthalmol. 198, 179-185.

Lotmar, W. and Lotmar, T. (1974) Peripheral astigmatism in the human eye: Experimental data and theoretical model predictions. J. Opt. Soc. Am. 64, 510-513.

Lovasik, J. V. and Szymkiw, M. (1985) Effects of aniseikonia, anisometropia, accommodation, retinal illuminance, and pupil size on stereopsis. Invest. Ophthalmol. Vis. Sci. 26, 741-750.

Maddock, R. J., Millodot, M., Leat, S. and Johnson, C. A. (1981) Accommodation responses and refractive error. Invest. Ophthalmol. Vis. Sci. 20, 387-391.

Maguire, L. J., Singer, D. E. and Klyce, S. D. (1987) Graphic presentations of computer-analyzed keratoscope photographs. Arch. Ophthalmol. 105, .

Mandell, R. B. (1992) The enigma of the corneal contour. C. L. A. O. 20, 123-127.

Mäntyjärvi, M. (1983) Incidence of myopia in a population of Finish school children. Acta Ophthalmol. 61, 417-423.

Marran, L. and Schor, C. M. (1994) Retinal and extraretinal cues to nonconjugate accommodation. Invest. Ophthalmol. Vis. Sci. 35, S1736.

Marran, L. and Schor, C. M. (1995) Aniso-accommodation adapts to anisometropia. Invest. Ophthalmol. Vis. Sci. 36, S13.

Massey, A. D. and O'Brien, C. (1996) Pulsatile ocular blood flow: a population study of normals. Invest. Ophthalmol. Vis. Sci. 37, S31.

McBrien, N. A. and Adams, D. W. (1997) A longitudinal investigation of adult-onset and adult-progression of myopia in an occupational group. Invest. Ophthalmol. Vis. Sci. 38, 321-333.

McBrien, N. A. and Barnes, D. A. (1984) A review and evaluation of theories of refractive error development. Ophthal. Physiol. Opt. 4, 201-213.

McBrien, N. A. and Millodot, M. (1986a) Amplitude of accommodation and refractive error. Invest. Ophthalmol. Vis. Sci. 27, 1187-1190.

McBrien, N. A. and Millodot, M. (1986b) The effect of refractive error on the accommodative response gradient. Ophthal. Physiol. Opt. 6, 145-149.

McBrien, N. A. and Millodot, M. (1987) The relationship between tonic accommodation and refractive error. Invest Ophthalmol Vis Sci 28, 997-1004.

McKanna, J. A. and Casagrande, V. A. (1981) Atropine affects lid-suture myopia development. Experimental studies of chronic atropinization in tree shrews. In: Doc. Ophthal. Proc. Series, ed. H. C. Fledelius, P. H. Alsbirk and E. Goldschmidt. The Hague, Dr W. Junk Publishers.

Medina, A. (1987) A model for emmetropization. Acta Ophthalmol. 65, 565-571.

Miglior, S., Brigatti, L., Velati, P., Balestreri, C., Rossetti, L., Bujtar, E. and Orzalesi, N. (1994) Relationship between morphometric optic disc parameters, sex and axial length. Curr. Eye Res. 13, 119-124.

Millodot, M. (1981) Effect of ametropia on peripheral refraction. Am. J. Optom. Physiol. Opt. 58, 691-695.

Millodot, M. (1986) Dictionary of optometry. Butterworths, London .

Millodot, M. and Lamont, A. (1974) Refraction of the periphery of the eye. J. Opt. Soc. Am. 64, 110-111.

Mohindra, I. (1977) A non-cycloplegic refaction technique for infants and young children. J. Am. Optom. Assoc. 48, 518-523.

Mohindra, I. and Held, R. (1981) Refraction in humans from birth to five years. Doc. Ophthalmol. Proc. 28, 19-27.

Mordi, J., Tucker, J. and Charman, W. N. (1986) Effects of 0.1% cyclopentolate or 10% phenylephrine on pupil diameter and accommodation. Ophthal. Physiol. Opt. 6, 221-227.

Morgan, M. W. (1944) Accommodation and its relationship to convergence. Am. J. Optom. Arch. Am. Acad. Optom. 21, 183-195.

Mullie, M. A. and Sanders, M. D. (1985) Scleral canal size and optic nerve head drusen. Am. J. Ophthalmol. 99, 356-359.

Mutti, D. O., Friedmann, N. E., Sholtz, R. I. and Zadnik, K. (1996) Peripheral refraction and refractive error in schoolchildren. Optom. Vis. Sci. 73 S73.

Mutti, D. O. and Zadnik, K. (1995) The utility of three predictors of childhood myopia: a Bayesian analysis. Vision Res. 35, 1345-1352.

Nastri, G., Caccia Perugini, G., Savastano, S. and Polzella, A. (1984) The evolution of refraction in the fixing and the amblyopic eye. Doc. Ophthalmol. 56, 265-274.

Nathan, J., Kiely, P. A., Crewther, S. G. and Crewther, D. P. (1985) Disease-associated visual image degradation and spherical refractive errors in children. Am. J. Optom. Physiol. Opt. 62, 680-688.

Norton, T. T. and McBrien, N. A. (1992) Normal development of refractive state and ocular component dimensions in the tree shrew (*Tupaia belangeri*). Vision Res. 32, 833-842.

O'Leary, D. J. and Millodot, M. (1979) Eyelid closure causes myopia in humans. Experientia 35, 1478-1479.

Ong, J. and Burley, W. S. (1972) Effect of induced anisometropia on depth perception. Am. J. Optom. Arch. Am. Acad. Optom. 49, 333-335.

Otsuka, J., Sugata, T. and Araki, M. (1981) The aetiology of myopia as considered from the differences in the refractive components of the right and left eyes. In: Doc Ophthal Proc Series, ed. H. C. Fledelius, P. H. Alsbirk and E. Goldschmidt. The Hague, Dr W. Junk Publishers.

Parssinen, O. (1990) Anisometropia and changes in anisometropia in school myopia. Opt. Vis. Sci. 67, 256-259.

Parver, L. M., Auker, C. and Carpenter, D. O. (1980) Choroidal blood flow as a heat dissipating mechanism in the macula. Am. J. Ophthalmol. 89, 641-646.

Perkins, E. S. (1981) The ocular pulse. Curr. Eye Res. 1, 19-23.

Peters, H. B. (1969) The influence of anisometropia on stereosensitivity. Am. J. Optom. Arch. Am. Acad. Optom. 46, 120-123.

Phelps Brown, N. (1996) Amazing emmetropia. Optician 212, 28-32.

Phelps, W. L. and Muir, V. (1977) Anisometropia and strabismus. Am. Orthopt. J. 27, 131-133.

Phillips, C. I. (1959) Strabismus, anisometropia and amblyopia. Br. J. Ophthalmol. 43, 449-450.

Phillips, J. R. and McBrien, N. A. (1995) Form deprivation myopia: elastic properties of sclera. Ophthal. Physiol. Opt. 15, 357-362.

Pickett Seltner, R. L. and Stell, W. K. (1995) The effect of vasoactive intestinal peptide on development of form deprivation myopia in the chick: a pharmacological and immunocytochemical study. Vision Res. 35, 1265-1270.

Pomerantzeff, O., Fish, H., Govignon, J. and Schepens, C. L. (1972) Wide-angle optical model of the eye. Optica Acta 19, 387-388.

Pugh, J. R. and Winn, B. (1988) Modification of the Canon Auto Ref R1 for use as a continuously recording infra-red optometer. Ophthal. Physiol. Opt. 8, 460-464.

Quigley, H. A. (1982) Childhood glaucoma: results with trabeculotomy and study of reversible cupping. Ophthalmol. 89, 219-226.

Quigley, H. A., Brown, A. E., Morrison, J. D. and Drance, S. M. (1990) The size and shape of the optic disc in normal human eyes. Arch. Ophthalmol. 108, 51-57.

Quigley, H. A. and Langham, M. E. (1975) Comparative intraocular pressure measurements with the pneumatonograph and the Goldmann tonometer. Am. J. Ophthalmol. 80, 266-273.

Quinn, G. E., Berlin, J. A., Young, T. L., Ziylan, S. and Stone, R. A. (1995) Association of intraocular pressure and myopia in children. Ophthalmology 102, 180-185.

Ravalico, G., Toffoli, G., Pastori, G., Crocé, M. and Calderini, S. (1996) Age-related ocular blood flow changes. Invest. Ophthalmol. Vis. Sci. 37, 2645-2650.

Raviola, E. and Wiesel, T. N. (1985) An animal model of myopia. N. Engl. J. Med. 312, 1609-1615.

Raviola, E., Wiesel, T. N., Reichlin, S., Lam, K. S. L. and Chetri, A. (1991) Increase of retinal vasoactive intestinal polypeptide (VIP) after neonatal lid fusion in the rhesus macaque. Invest. Ophthalmol. Vis. Sci. 32, 1203.

Ray, W. A. and O'Day, D. M. (1985) Statistical analysis of multi-eye data in ophthalmic research. Invest. Ophthalmol. Vis. Sci. 26, 1186-1188.

Rempt, F., Hoogerheide, J. and Hoogenboom, W. P. H. (1971) Peripheral retinoscopy and the skiagram. Ophthalmologica 162, 1-10.

Riva, C. E., Cranstoun, S. D., Grunwald, J. E. and Petrig, B. L. (1994) Choroidal blood-flow in the foveal region of the human ocular fundus. Invest. Ophthalmol. Vis. Sci. 35, 4273-4281.

Riva, C. E., Grunwald, J. E., Sinclair, S. H. and Petrig, B. L. (1985) Blood velocity and volumetric flow rate in human retinal vessels. Invest. Ophthalmol. Vis. Sci. 26, 1124-1132.

Riva, C. E., Harino, S., Petrig, B. L. and Shonat, R. D. (1992) Laser Doppler flowmetry in the optic nerve. Exp. Eye Res. 55, 499-506.

Rohrer, B., Negishi, K., Tao, J. and Stell, W. K. (1993) A role for basic fibroblast growth factor (bFGF) in the visually guided regulation of eye growth in the chick. Invest. Ophthalmol. Vis. Sci. 34, S1209.

Rohrer, B., Spira, A. W. and Stell, W. K. (1993) Apomorphine blocks form-deprivation myopia in chickens by a dopamine D2-receptor mechanism acting in retina or pigmented epithelium. Visual Neuroscience 10, 447-453.

Rose, L. and Levinson, A. (1972) Anisometropia and aniseikonia. Am. J. Optom. Arch. Am. Acad. Optom. 49, 480-484.

Rosenfield, M. (1994) Accommodation and myopia are they really related? J. Behav. Optom. 5, 3-11.

Rosenfield, M. and Cohen, A. S. (1995) Push-up amplitude of accommodation and target size. Ophthal. Physiol. Opt. 15, 231-232.

Rosenfield, M. and Gilmartin, B. (1990) The effect of target proximity on open-loop accommodation. Optom. Vis. Sci. 67, 74-79.

Royston, J. M., Dunne, M. C. M. and Barnes, D. A. (1989) Calculation of crystalline lens radii without resort to phakometry. Ophthal Physiol Opt 9, 412-414.

Sanfilippo, S., Muchnick, R. S. and Schlossman, A. (1978) Preliminary observations on high anisometropia. Am. Orthoptic J. 28, 127-129.

Saunders, K. J., Woodhouse, J. M. and Westall, C. A. (1995) Emmetropisation in human infancy: rate of change is related to initial refractive error. Vision Res. 35, 1325-1328.

Scammon, R. E. and Wilmer, H. A. (1950) Growth of the components of the human eyeball II. Arch. Ophthalmol. 43, 620-637.

Schaeffel, F., Glasser, A. and Howland, H. C. (1988) Accommodation, refractive error, and eye growth in chickens. Vision Res. 28, 639-657.

Schaeffel, F., Hagel, G., Bartmann, M. and Kohler, K. (1994) 6-hydroxy dopamine does not affect lens-induced refractive errors but suppresses deprivation myopia. Vision Res. 34, 143-149.

Schapero, M. (1971) Amblyopia. Chilton Books, Philadelphia .

Schmid, G. F., Papastergiou, G. I., Nickla, D. L., Riva, C. E., Lin, T., Stone, R. A. and Laties, A. M. (1996) Validation of laser Doppler interferometric measurements *in vivo* of axial length and thickness of fundus layers in chicks. Curr. Eye Res. 15, 691-696.

Schmid, G. F., Petrig, B. L., Riva, C. E., Laties, A. M., Mendel, M. J. and Dunne, M. C. M. (1994) Eye-shape and diurnal variation by laser doppler interferometry. Paper read at Vision science and its applications, at Santa Fe, New Mexico.

Schmid, G. F., Petrig, B. L., Riva, C. E., Shin, K. H., Stone, R. A., Mendel, M. J. and Laties, A. M. (1996) Measurement by laser Doppler interferometry of intraocular distances in humans and chicks with a precision of better than ± 20 μm. App. Opt. 35, 3358-3361.

Semmlow, J. L., Menditto, S. A. and Mezrich, R. (1991) Magnetic resonance imaging of the presbyopic eye. In Presbyopia research, from molecular biology to visual adaptation, edited by G. Obrecht and L. W. Stark. New York, Plenum Press.

Sen, D. K. (1982) Results of treatment of anisohypermetropic amblyopia without strabismus. Br. J. Ophthalmol. 66, 680-684.

Shapiro, A., Yanko, L., Nawratzki, I. and Merin, S. (1980) Refractive power of premature children at infancy and early childhood. Am. J. Ophthalmol. 90, 234-238.

Sheridan, M. and Douthwaite, W. A. (1989) Corneal asphericity and refractive error. Ophthal. Physiol. Opt. 9, 235-238.

Shih, Y.-F., Fitzgerald, M. E. C., Norton, T. T., Gamlin, P. D. R., Hodos, W. and Reiner, A. (1993) Reduction on choroidal blood flow ocurs in chicks wearing goggles that induce eye growth toward myopia. Curr. Eye Res. 12, 219-227.

Shih, Y. F., Fitzgerald, M. E. C. and Reiner, A. (1993) Choroidal blood-flow is reduced in chicks with ocular enlargement induced by corneal incisions. Curr. Eye Res. 12, 229-237.

Shih, Y. F., Horng, I. H., Yang, C. H., Lin, L. L. K., Peng, Y. and Hung, P. T. (1991) Ocular pulse amplitude in myopia. J. Oc. Pharmacol. 7, 83-87.

Silver, D. M., Farrell, R. A., Langham, M. E., O'Brien, V. and Schilder, P. (1989) Estimation of pulsatile ocular blood flow from intraocular pressure. Acta Ophthalmol. 67, 25-29.

Simons, K. (1984) Effects on stereopsis of monocular versus binocular degradation of image contrast. Invest. Ophthalmol. Vis. Sci. 25, 987-989.

Smith, G. (1995) Schematic eyes: history, description and applications. Clin. Exp. Optom. 78, 176-189.

Sorsby, A., Benjamin, B., Davey, J. B., Sheridan, M. and Tanner, J. M. (1957) Emmetropia and its aberrations: Medical Research Council No. 293.

Sorsby, A., Benjamin, B. and Sheridan, M. (1961) Refraction and its components during the growth of the eye from the age of three: Medical Research Council No. 301.

Sorsby, A. and Leary, G. A. (1970) A longitudinal study of refraction and its components during growth: Medical Research Council No. 309.

Sorsby, A., Leary, G. A. and Richards, M. J. (1962) The optical components in anisometropia. Vision Research 2, 43-51.

Sorsby, A., Sheridan, M. and Leary, G. A. (1962) Refraction and its components in twins: Medical Research Council No. 303.

Spencer, A. F., Sadiq, S. A., Pawson, P. and Vernon, S. A. (1995) Vertical optic disk diameter: discrepancy between planimetric and SLO measurements. Invest. Ophthalmol. Vis. Sci. 36, 796-803.

Spencer, A. F. and Vernon, S. A. (1995) Optic disc measurement: a comparison of indirect ophthalmoscopic methods. Br. J. Ophthalmol. 79, 910-915.

Steele, C. F., Crabb, D. P. and Edgar, D. F. (1992) Effects of different ocular fixation conditions on A-scan ultrasound biometry measurements. Ophthal. Physiol. Opt. 12, 491-495.

Stenström, S. (1946) Untersuchungen über die Variation und Kovariation der optischen Elemente des menschlichen Auges. Acta Ophthalmol. Suppl. 26, .

Stevens, P. R. (1960) Anisometropia and amblyopia. Br. Orthopt. J. 17, pp. 66-73.

Stevenson, R. (1992) Corneal topographic modelling systems. Optician Nov. 6, 16-22.

Stone, R. A., Lin, T., Iuvone, P. M. and Laties, A. M. (1990) Postnatal control of ocular growth: dopaminergic mechanisms. In: Ciba Foundation Symposium 155. Chichester, Wiley.

Stone, R. A., Lin, T. and Laties, A. M. (1991) Muscarinic antagonist effects on experimental chick myopia. Exp. Eye Res. 52, 755-758.

Strenk, S. A., Semmlow, J. L. and Mezrich, R. S. (1994) Using magnetic resonance imaging to mathematically model the lens capsule. Invest. Ophthalmol. Vis. Sci. 35, S1948.

Stuart-Black Kelly, T. (1981) Myopia or expansion glaucoma. In: Doc. Ophthal. Proc. Series, ed. H. C. Fledelius, P. H. Alsbirk and E. Goldschmidt. The Hague, Dr W. Junk Publishers.

Tanlamai, T. and Goss, D. A. (1979) Prevalence of monocular amblyopia among anisometropes. Am. J. Optom. Physiol. Opt. 56, 704-715.

Thomas, G. B. and Finney, R. L. (1996) Calculus and analytic geometry. 9th ed.Addison-Wesley Publishing Company, Reading, MA .

Thompson, C. (1987) Objective and psychophysical studies of infant visual development. PhD Thesis, Aston University, UK.

To'mey, K. F., Faris, B. M., Jalkh, A. E. and Nasr, A. M. (1981) Ocular pulse in high myopia: a study of 40 eyes. Ann. Ophthalmol. 13, 569-571.

Tomlinson, A. and Phillips, C. I. (1970) Applanation tension and axial length of the eyeball. Br. J. Ophthalmol. 54, 548-553.

Tomlinson, A. and Phillips, C. I. (1972) Unequal axial length of eyeball and ocular tension. Acta Ophthalmol. 50, 872-876.

Trew, D. R., James, C. B., Thomas, S. H. L., Sutton, R. and Smith, S. E. (1991) Factors influencing the ocular pulse - the heart rate. Graefe's Arch. Clin. Exp. Ophthalmol. 229, 553-556.

Trew, D. R. and Smith, S. E. (1991a) Postural studies in pulsatile ocular blood flow: 1. Ocular hypertension and normotension. Br. J. Ophthalmol. 75, 66-70.

Trew, D. R. and Smith, S. E. (1991b) Postural studies in pulsatile ocular blood flow: 2. Chronic open angle glaucoma. Br. J. Ophthalmol. 75, 71-75.

Troilo, D. (1996) Effects of form deprivation myopia on retinal anatomy and cone distribution in the common marmoset. Invest. Ophthalmol. Vis. Sci. 37, S323.

Troilo, D., Gottlieb, M. D. and Wallman, J. (1987) Visual deprivation causes myopia in chicks with optic nerve section. Curr. Eye Res. 6, 993-999.

Tron, E. (1933) Ein Beitrag zur Frage der optischen Grundlagen der Aniso- und Isometropie. Von Graefe's Arch. Klin. Exp. Ophthalmol. 133, 211-230.

van Alphen, G. W. H. M. (1986) Choroidal stress and emmetropization. Vision Res. 26, 723-734.

Varma, R., Tielsch, J. M., Quigley, H. A., Hilton, S. C., Katz, J., Spaeth, G. L. and Sommer, A. (1994) Race-, age-, gender-, and refractive error-related differences in the normal optic disc. Arch. Ophthalmol. 112, 1068-1076.

von Noorden, G. K. (1967) Classification of amblyopia. Am. J. Ophthalmol. 63, 238-244.

von Noorden, G. K. and Lewis, R. A. (1987) Ocular axial length in unilateral congenital cataracts and blepharoptosis. Invest. Ophthalmol. Vis. Sci. 28, 750-752.

Waardenburg, P. J. (1930) Anisometropie und Hornhautbrechung. Klin. Mbl. Augenheikl. 84, 788-794.

Wallace, J. and Lovell, H. G. (1969) Glaucoma and intraocular pressure in Jamaica. Am. J. Ophthalmol. 67, 93-100.

Wallman, J., Gottlieb, M. D., Rajaram, V. and Fugate-Wentzek, L. A. (1987) Local retinal regions control local growth and myopia. Science 237, 73-77.

Wallman, J. and McFadden, S. (1995) Monkey eyes grow into focus. Nature Medicine 1, 737-739.

Wallman, J., Rosenthal, D., Adams, J. I., Trachtman, J. N. and Romagnano, L. (1981) Role of accommodation and developmental aspects of experimental myopia in chicks. In: Doc. Ophthal. Proc. Series, ed.H. C. Fledelius, P. H. Alsbirk and E. Goldschmidt. The Hague, Dr W. Junk Publishers.

Ward, P. A. and Charman, W. N. (1985) Effect of pupil size on steady-state accommodation. Vision Res. 25, 1317-1326.

Weale, R. A. (1982) A biography of the eye. H. K. Lewis & Co. Ltd, London.

Wiesel, T. N. and Raviola, E. (1977) Myopia and eye enlargement after neonatal lid fusion in monkeys. Nature 266, 66-68.

Wildsoet, C. F. (in press) Active emmetropization - evidence for its existence and ramifications for clincial practice. Ophthal. Physiol. Opt.

Wildsoet, C. F. and Wallman, J. (1995) Choroidal and scleral mechanisms of compensation for spectacle lenses in chicks. Vision Res. 35, 1175-1194.

Williamson, T. H. and Harris, A. (1994) Ocular blood flow measurement. Br. J. Ophthalmol. 78, 939-945.

Wilson, J. R. and Sherman, S. M. (1977) Differential effects of early monocular deprivation on the binocular and monocular segments of cat striate cortex. J. Neurophysiol. 40, 891.

Winkler, T. D. and Kame, R. T. (1995) Orthokeratology handbook. Butterworth-Heinemann, Boston .

Winn, B., Ackerley, R. G., Brown, C. A., Murray, F. K., Prais, J. and St. John, M. F. (1988) Reduced aniseikonia in axial anisometropia with contact lens correction. Ophthal. Physiol. Opt. 8, 341-344.

Winn, B., Pugh, J. R., Gilmartin, B. and Owens, H. (1989) The effect of pupil size on static and dynamic measurements of accommodation using an infra-red optometer. Ophthal. Physiol. Opt. 9, 277-283.

Winn, B., Pugh, J. R., Gilmartin, B. and Owens, H. (1990) Arterial pulse modulates steady-state ocular accommodation. Curr. Eye Res. 9, 971-975.

Wood, I. C. J., Mutti, D. O. and Zadnik, K. (1996) Crystalline lens parameters in infancy. Ophthal. Physiol. Opt. 16, 310-317.

Wood, I. J. C., Hodi, S. and Morgan, L. (1995) Longitudinal change of refractive error in infants during the first year of life. Eye 9, 551-557.

Woodruff, M. E. and Samek, M. J. (1977) A study of the prevalence of spherical equivalent refractive states and anisometropia in Amerind populations in Ontario. Can. J. Public Health 68, 414-424.

Young, T. (1801) Phil. Trans. R. Soc. Lond. 91.

Zadnik, K., Mutti, D. O. and Adams, A. J. (1992) The repeatability of measurement of the ocular components. Invest. Ophthalmol. Vis. Sci. 33, 2325-2333.

Zadnik, K., Mutti, D. O., Friedman, N. E. and Adams, A. J. (1993) Initial cross-sectional results from the Orinda longitudinal study of myopia. Optom. Vis. Sci. 70, 750-758.

Zonis, S. and Miller, B. (1974) Refractions in the Israeli newborn. J. Pediatr. Ophthalmol. 11, 77-81.

Zylbermann, R., Landau, D. and Berson, D. (1993) The influence of study habits on myopia in Jewish teenagers. J. Pediatr. Ophthalmol. Strabismus 30, 319-322.

# APPENDICES

## Appendix 1

### Biometric data

Biometric data for both eyes of the Caucasian subjects are shown below.

| subj. | age+sex (yrs) | Rx R (D) | Rx L (D) | ACD (mm) | ACD L (mm) | LT R (mm) | LT L (mm) | VCD R (mm) | VCD L (mm) | K R (mm) | K L (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| GH | 20 m | -5.87 | -7.85 | 3.77 | 3.69 | 3.63 | 3.57 | 17.03 | 17.5 | 7.20 | 7.22 |
| SP | 20 f | -1.00 | +1.00 | 3.94 | 3.73 | 3.57 | 3.74 | 16.34 | 15.49 | 7.68 | 7.63 |
| GR | 19 m | -5.25 | -7.50 | 3.74 | 3.65 | 3.26 | 3.25 | 19.77 | 21.13 | 7.68 | 7.66 |
| KT | 26 f | -6.00 | -4.00 | 3.88 | 3.88 | 3.52 | 3.47 | 18.88 | 17.88 | 7.70 | 7.72 |
| RC | 26 m | +3.75 | 0.00 | 3.77 | 3.69 | 3.66 | 3.66 | 14.42 | 15.63 | 7.66 | 7.70 |
| RM | 18 f | -0.25 | -3.25 | 3.72 | 3.63 | 3.57 | 3.58 | 16.78 | 17.77 | 7.47 | 7.50 |
| AD | 22 m | -0.50 | +3.25 | 3.90 | 3.73 | 3.65 | 3.53 | 15.82 | 14.78 | 7.40 | 7.35 |
| JF | 19 m | -3.25 | -5.25 | 3.83 | 3.93 | 3.59 | 3.51 | 17.52 | 17.94 | 7.60 | 7.64 |
| MH | 25 m | +3.75 | +1.00 | 3.70 | 3.73 | 3.62 | 3.51 | 15.00 | 15.87 | 7.84 | 7.81 |
| TC | 22 f | -1.00 | -3.00 | 3.78 | 3.77 | 3.50 | 3.64 | 16.63 | 17.39 | 7.72 | 7.75 |
| MO | 24 m | -5.75 | -3.50 | 3.82 | 3.95 | 3.80 | 3.76 | 18.03 | 17.65 | 7.41 | 7.43 |
| NG | 20 m | +0.50 | +3.75 | 3.55 | 3.53 | 3.43 | 3.42 | 16.93 | 15.63 | 7.93 | 7.91 |
| NP | 21 f | -3.00 | -5.00 | 3.93 | 3.90 | 3.44 | 3.33 | 17.87 | 17.06 | 7.32 | 7.36 |
| AS | 22 f | -7.25 | -3.75 | 3.77 | 3.92 | 3.82 | 3.71 | 17.72 | 16.40 | 7.34 | 7.41 |
| KS | 18 f | -1.00 | +1.00 | 3.62 | 3.58 | 3.43 | 3.45 | 16.86 | 16.03 | 7.97 | 8.00 |
| ED | 23 f | -1.75 | -4.25 | 3.78 | 3.80 | 3.51 | 3.41 | 15.54 | 16.80 | 7.22 | 7.21 |
| KB | 18 f | -3.12 | -1.00 | 3.60 | 3.69 | 3.68 | 3.65 | 16.90 | 15.89 | 7.73 | 7.70 |
| GB | 19 m | -6.75 | -4.67 | 3.72 | 3.94 | 3.98 | 3.80 | 17.11 | 16.50 | 7.40 | 7.42 |
| JT | 23 m | +4.00 | -0.50 | 3.24 | 3.55 | 3.59 | 3.73 | 14.79 | 16.33 | 8.20 | 8.10 |
| FR | 24 m | -8.00 | -5.25 | 3.69 | 3.76 | 3.76 | 3.86 | 20.78 | 19.29 | 8.42 | 8.38 |
| AT | 23 f | 0.00 | -0.25 | 3.62 | 3.52 | 3.79 | 3.78 | 16.28 | 16.33 | 7.75 | 7.71 |
| HW | 20 f | -4.00 | -3.75 | 3.77 | 3.75 | 3.43 | 3.36 | 17.27 | 17.37 | 7.58 | 7.62 |
| PK | 25 m | -3.00 | -3.50 | 3.84 | 3.79 | 3.46 | 3.50 | 17.35 | 17.54 | 7.75 | 7.79 |
| EM | 25 m | -5.75 | -6.25 | 3.82 | 3.70 | 3.54 | 3.45 | 17.64 | 18.35 | 7.25 | 7.20 |
| SK | 24 m | -0.12 | -0.25 | 3.54 | 3.89 | 3.69 | 3.58 | 16.75 | 16.73 | 8.10 | 8.05 |
| ER | 24 f | -3.67 | -4.00 | 3.67 | 3.56 | 3.55 | 3.65 | 16.46 | 16.55 | 7.31 | 7.28 |
| MK | 20 f | -0.50 | -0.75 | 3.52 | 3.45 | 3.43 | 3.51 | 17.13 | 17.27 | 7.41 | 7.39 |
| RW | 20 f | -1.50 | -1.75 | 3.33 | 3.52 | 3.67 | 3.60 | 16.40 | 16.76 | 7.82 | 7.87 |
| EB | 24 f | 0.00 | 0.00 | 3.86 | 3.64 | 3.27 | 3.58 | 16.08 | 15.81 | 7.83 | 7.85 |
| KR | 21 f | 1.50 | -1.25 | 3.36 | 3.41 | 3.71 | 3.78 | 14.81 | 15.78 | 7.65 | 7.72 |
| GG | 19 m | 0.00 | 0.00 | 3.75 | 3.85 | 3.65 | 3.66 | 15.09 | 15.04 | 7.64 | 7.59 |
| JB | 18 m | -4.00 | -4.00 | 3.75 | 3.78 | 3.70 | 3.60 | 17.01 | 16.92 | 7.52 | 7.48 |

Caucasian biometric data continued.

| subj. | age+sex (yrs) | Rx R (D) | Rx L (D) | ACD (mm) | ACD L (mm) | LT R (mm) | LT L (mm) | VCD R (mm) | VCD L (mm) | K R (mm) | K L (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| JS | 23 f | -2.00 | -2.00 | 3.56 | 3.58 | 3.72 | 3.88 | 15.50 | 15.38 | 7.64 | 7.68 |
| RJ | 20 m | 0.00 | 0.00 | 3.77 | 3.69 | 3.49 | 3.47 | 16.21 | 16.14 | 7.82 | 7.85 |
| RB | 21 f | +4.00 | +4.00 | 3.35 | 3.41 | 3.59 | 3.51 | 14.82 | 14.93 | 7.64 | 7.69 |
| SL | 24 f | 0.00 | 0.00 | 3.36 | 3.62 | 3.51 | 3.30 | 17.62 | 18.00 | 8.05 | 8.08 |
| LW | 26 f | -6.75 | -7.00 | 3.91 | 3.93 | 3.84 | 3.65 | 17.27 | 17.16 | 7.12 | 7.12 |
| EM | 22 m | -6.00 | -6.25 | 3.91 | 3.83 | 3.72 | 3.71 | 18.54 | 18.33 | 7.50 | 7.50 |
| DT | 20 m | +4.00 | +4.00 | 3.42 | 3.51 | 3.64 | 3.61 | 14.71 | 14.68 | 7.44 | 7.48 |
| NB | 21 m | -5.00 | -5.00 | 3.80 | 3.59 | 3.44 | 3.46 | 17.08 | 16.94 | 8.20 | 8.23 |

R, right eye; L, left eye; Rx, mean spherical refractive error; ACD, anterior chamber depth; LT, lens thickness; VCD, vitreous chamber depth; K, mean keratometry reading.

Biometric data for both eyes of the Chinese subjects are shown below.

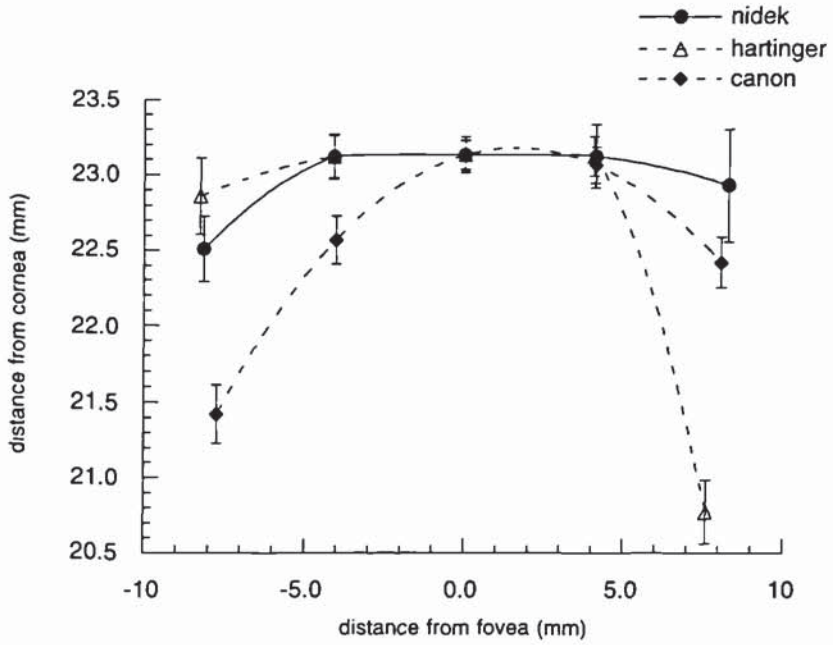
| subj. | age+sex (yrs) | Rx R (D) | Rx L (D) | ACD (mm) | ACD L (mm) | LT R (mm) | LT L (mm) | VCD R (mm) | VCD L (mm) | K R (mm) | K L (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| RL | 22 m | -1.67 | -4.50 | 3.56 | 3.57 | 3.72 | 3.91 | 15.50 | 17.03 | 7.63 | 7.65 |
| JK | 14 m | -2.50 | -0.50 | 3.67 | 3.41 | 3.19 | 3.29 | 18.40 | 18.06 | 8.30 | 8.33 |
| SH | 18 f | -4.75 | -0.75 | 4.03 | 3.50 | 3.08 | 3.12 | 19.15 | 17.89 | 7.90 | 8.02 |
| MH | 20 f | -5.25 | -9.00 | 3.86 | 3.61 | 3.28 | 3.09 | 18.96 | 20.22 | 7.81 | 7.76 |
| PL | 23 m | -7.00 | -4.37 | 3.77 | 3.67 | 3.36 | 3.34 | 19.10 | 18.81 | 7.96 | 8.00 |
| JT | 26 m | -4.50 | -6.25 | 3.81 | 3.68 | 3.38 | 3.23 | 18.18 | 19.85 | 7.90 | 7.95 |
| YH | 17 m | -6.37 | -0.87 | 3.65 | 3.48 | 3.47 | 3.41 | 18.75 | 17.32 | 7.84 | 7.88 |
| LC | 24 f | -6.00 | -3.75 | 3.73 | 3.65 | 3.62 | 3.60 | 17.29 | 16.12 | 7.52 | 7.45 |
| MH | 22 f | -3.87 | -5.87 | 3.77 | 3.56 | 3.39 | 3.36 | 18.32 | 18.70 | 7.85 | 7.86 |
| CL | 22 m | -2.00 | -5.75 | 3.90 | 3.63 | 3.39 | 3.34 | 19.11 | 20.62 | 8.20 | 8.13 |
| JH | 21 m | -1.00 | -3.25 | 3.79 | 3.60 | 3.46 | 3.42 | 15.68 | 17.12 | 7.41 | 7.39 |
| RL | 23 m | -0.50 | -3.00 | 3.85 | 3.68 | 3.39 | 3.58 | 16.40 | 17.71 | 7.70 | 7.72 |
| JF | 22 f | -11.50 | -9.37 | 3.84 | 3.99 | 4.04 | 3.74 | 19.56 | 18.75 | 7.69 | 7.68 |
| JY | 21 m | -1.75 | -3.75 | 3.82 | 3.55 | 3.32 | 3.63 | 16.78 | 19.94 | 7.91 | 7.90 |
| MW | 18 f | -2.25 | -0.25 | 3.68 | 3.78 | 3.81 | 3.92 | 16.20 | 15.28 | 7.43 | 7.41 |
| JC | 19 m | -9.25 | -6.75 | 3.53 | 3.58 | 3.62 | 3.96 | 17.85 | 17.65 | 7.42 | 7.50 |
| JP | 20 f | -5.37 | -7.87 | 3.67 | 3.55 | 3.38 | 3.26 | 18.92 | 20.02 | 7.85 | 7.81 |
| HM | 20 f | -4.75 | -3.00 | 3.85 | 3.79 | 3.75 | 3.62 | 17.82 | 17.05 | 7.82 | 7.76 |
| SH | 21 m | -8.00 | -10.50 | 3.85 | 3.77 | 3.20 | 3.21 | 20.86 | 21.47 | 8.30 | 8.20 |
| LY | 20 f | -7.50 | -5.50 | 3.95 | 3.76 | 3.46 | 3.59 | 19.22 | 18.58 | 7.28 | 7.32 |
| RL | 23 m | -5.00 | -5.00 | 3.81 | 3.93 | 4.05 | 3.96 | 18.37 | 18.74 | 8.24 | 8.35 |

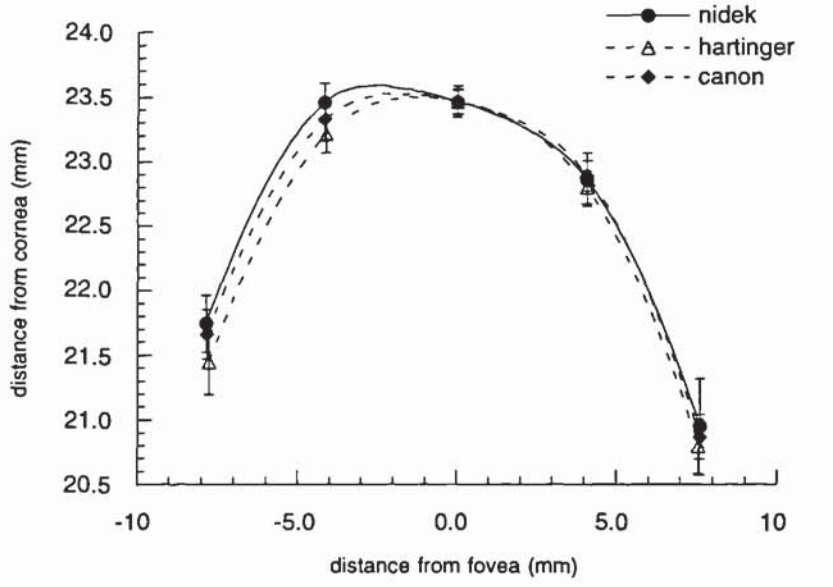
| subj. | age+sex (yrs) | Rx R (D) | Rx L (D) | ACD (mm) | ACD L (mm) | LT R (mm) | LT L (mm) | VCD R (mm) | VCD L (mm) | K R (mm) | K L (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| CC | 25 m | -7.00 | -7.25 | 3.91 | 3.85 | 3.75 | 3.77 | 19.03 | 18.97 | 7.95 | 7.92 |
| LW | 26 f | -8.25 | -8.00 | 3.70 | 3.70 | 3.83 | 3.87 | 19.16 | 19.43 | 8.13 | 8.16 |
| SW | 22 m | -1.50 | -1.50 | 3.51 | 3.64 | 3.86 | 3.79 | 16.21 | 16.28 | 7.97 | 8.00 |
| LC | 21 f | -5.75 | -6.00 | 3.82 | 3.70 | 3.54 | 3.45 | 17.64 | 18.05 | 7.18 | 7.22 |
| FC | 23 m | -4.00 | -4.00 | 3.75 | 3.78 | 3.70 | 3.60 | 17.01 | 16.92 | 7.52 | 7.48 |
| TP | 25 m | -6.25 | -6.50 | 3.93 | 3.95 | 3.45 | 3.43 | 17.33 | 17.36 | 7.75 | 7.81 |
| TW | 21 f | -3.00 | -3.25 | 3.83 | 3.38 | 3.38 | 3.41 | 16.54 | 16.96 | 7.20 | 7.35 |
| YC | 20 f | 0.00 | 0.00 | 3.75 | 3.85 | 3.65 | 3.66 | 15.09 | 15.04 | 7.64 | 7.59 |
| FH | 21 m | -3.00 | -3.50 | 3.84 | 3.79 | 3.46 | 3.50 | 17.35 | 17.54 | 7.75 | 7.79 |
| YW | 20 f | -4.00 | -3.75 | 3.77 | 3.75 | 3.43 | 3.36 | 17.27 | 17.37 | 7.58 | 7.62 |
| PC | 20 f | -6.75 | -7.00 | 3.91 | 3.93 | 3.84 | 3.65 | 17.17 | 17.16 | 7.12 | 7.12 |
| JP | 22 m | -6.00 | -6.25 | 3.91 | 3.83 | 3.72 | 3.71 | 18.54 | 18.33 | 7.50 | 7.50 |
| YF | 23 m | -4.75 | -4.50 | 3.72 | 3.79 | 3.72 | 3.64 | 17.11 | 16.99 | 7.55 | 7.49 |
| WP | 20 f | -9.25 | -9.50 | 3.74 | 3.65 | 3.24 | 3.25 | 19.76 | 20.12 | 7.69 | 7.66 |
| SY | 19 f | -10.5 | -10.75 | 3.77 | 3.69 | 3.51 | 3.55 | 20.28 | 20.25 | 7.24 | 7.29 |
| SL | 23 f | -7.75 | -8.00 | 3.70 | 3.55 | 3.53 | 3.60 | 18.17 | 18.23 | 7.52 | 7.49 |
| YP | 22 f | 0.00 | 0.00 | 3.81 | 3.93 | 4.01 | 3.96 | 18.37 | 18.77 | 8.02 | 7.98 |
| MC | 22 m | -0.12 | 0.00 | 3.90 | 3.72 | 3.52 | 3.39 | 16.83 | 17.18 | 8.00 | 8.05 |
| YH | 21 f | -0.25 | 0.00 | 3.81 | 3.59 | 3.43 | 3.55 | 17.46 | 17.26 | 7.79 | 7.71 |

## Appendix 2

### Pilot studies to determine a suitable instrument for peripheral refraction measurements

Peripheral refraction measurements were taken on 5 different subjects and repeated 5 times on each subject. The measurements were taken with a Canon R-1 infra-red autorefractor, a Hartinger coincidence optometer and a Nidek AR 800 autorefractor. Refraction data was obtained centrally,15° nasally, 30° nasally, 15° temporally and 30° temporally. Retinal contours were generated according to the methods described in chapter 5.
Examples of the data for one subject are shown below: the first figure represents the data non-cyclopleged and the second figure is the data under cycloplegia. Similar results were found with the other subjects.



## Appendix 3

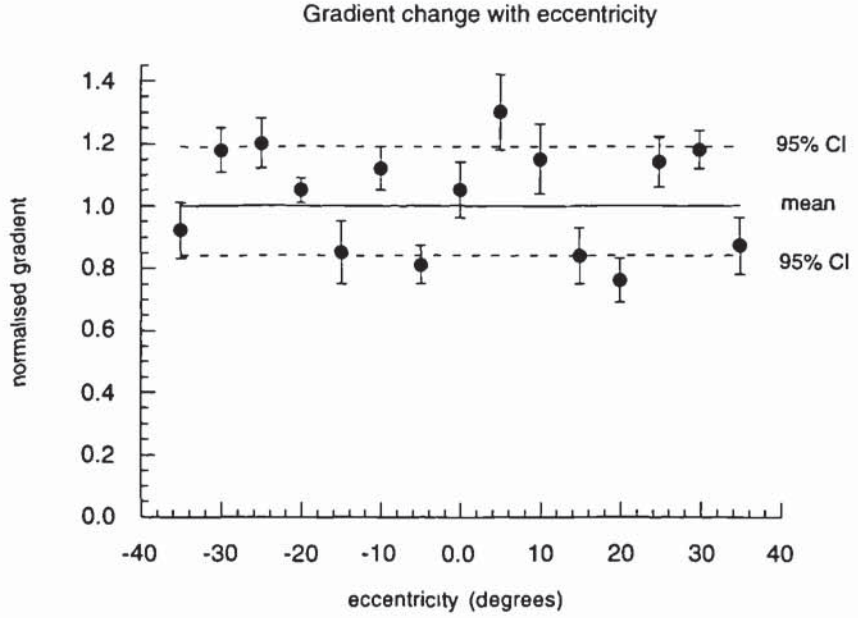
### The effect of eccentricity on measurements of refractive error using the Canon Autoref R-1

The mode of operation of the Canon is described in chapter 4.
The minimum amount of infra-red light required by the detection system of the optometer may be approached with large eccentricities, thus producing high cylinders at large eccentricites. This proposition was tested by analysing the output waveform from a single photodector. The qualitative effect of eccentricity on static measurements can be related to the normal mode of operation of the Canon by examining the profile of the sweep as eccentricity in increased.

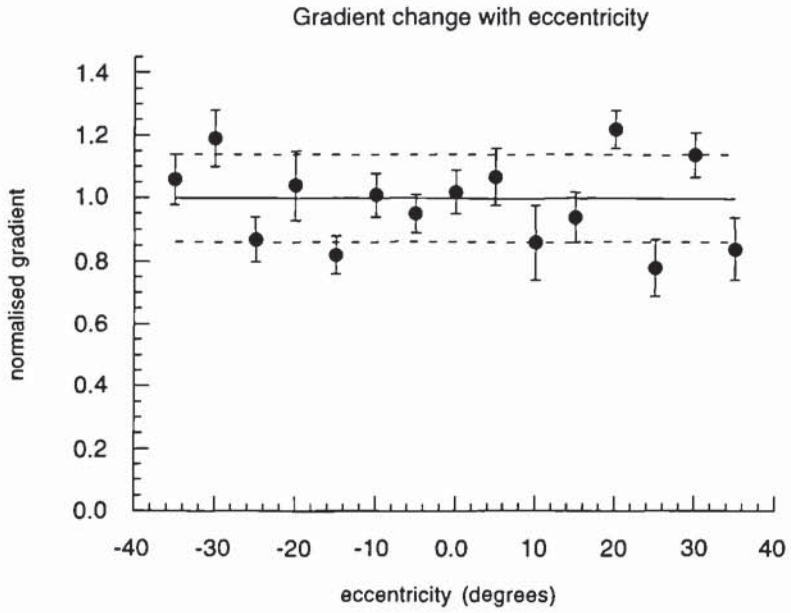
Measurements of refractive error were obtained with the Canon Autoref R-1 in its static mode of operation. The analogue output from a single photodetector was rectified, smoothed and fed into a digital storage oscilliocope (Gould 1604). The oscilloscope was connected to an on-line computer (Epson XT IBM-clone) through an IEEE-448 interface. In this mode of operation the output waveform is characterized by a peak position of optimal focus. Recorded traces were analysed using *Asystant* software. The effect of eccentricity was assessed by measurement of the gradient on both sides of the peak.
During recording note was also taken of the autorefraction measurements.

The gradients on each side of the peak (i.e. the sensitivities) were measured for each eccentricity and a graph of slope against eccentricity plotted. So that all graphs may be compared, the y-axes were scaled. The scaling process involved dividing all the y-values (in this case the measured slopes) by the mean of the y-values.

The data suggest that for eccentricities of up to and including 35 ° both nasally and temporally, the Canon output remains constant. An increase in eccentricity does not appear to cause a decrease in sensitivity.




Gradient change with eccentricity for subject RC with approximately 6D of peripheral astigmatism at an eccentricity of 35°.




Gradient change with eccentricity for subject LD with approximately 4D of peripheral astigmatism at an eccentricity of 35°.

## Appendix 4

### Calculation of vergence contribution of ocular components

```
REM use Bennett (1988) OPO 8 pp 53-59 - non-phakometric computing scheme
REM this also used in retinafit progam
REM carry out back vergence raytrace (Erickson)

CLS

REM non-phakometric computing scheme (Bennett, 1988)
    REM input biometric data
    REM fsp - resolved refractive error (D)
    INPUT "resolved refractive error (D)"; fsp
    REM v vertex distance (m)
    INPUT "vertex distance (mm)"; vd
    v = vd / 1000
    REM r1 - corneal radius (mm)
    INPUT "resolved K reading (mm)"; r1
    REM d1 - anterior chamber depth (m)
    INPUT "anterior chamber depth (mm)"; dd1
    d1 = dd1 / 1000
    REM d2 - lens thickness (m)
    INPUT "lens thickness (mm)"; dd2
    d2 = dd2 / 1000
    REM d3 - vitreous length (m)
    INPUT "vitreous length (mm)"; dd3
    d3 = dd3 / 1000
    REM n1 - refractive index air
    n1 = 1
    REM n2 - refractive index aqueous
    n2 = 1.3333
    REM n3 - refractive index lens
    n3 = 1.416
    REM n4 - refractive index of vitreous
    n4 = 1.3333
    REM f1 - corneal power
    f1 = (1000 * (n2 - n1)) / r1
    l1 = fsp / (1 - (v * fsp))
    l1a = l1 + f1
    el = .596 * d2
    ela = -.358 * d2
    w = d1 + el
    l2 = l1a / (1 - ((w / n2) * l1a))
    ll2a = -ela + d3
    l2a = n2 / ll2a
    fl = l2a - l2
    m = (w / n2) * f1 * fl
    N = f1 + fl
    fe = N - m

CLS
```

### REM calculation of vergence contribution of ocular components

```
PRINT : PRINT "vergence analysis (Erickson) : "
REM vergence contributions
REM use Erickson (1984) AJO&OPO 61 pp 469-472
REM present scheme differs in that non-phakometric data is analysed
REM therefore,it is only the contributions of the :
REM cornea, equivalent lens and their separations that are considered
```

```
REM Bennett's terminology converted to that of Erickson
REM Erickson traces wavefronts from retina to cornea
REM same vergences occur using Bennett's scheme which traces wavefronts
REM from far point, through cornea and lens, to retina
REM however, some signs need changeing

    REM starting from retina ...

    REM calculate vergences
    REM - vv - vergence after vitreous
    vv = -l2a
    REM - vl - vergence after equivalent lens
    vl = l2
    REM - vsep - vergence after travelling from lens to cornea
    vsep = l1a
    REM - vc - vergence after cornea
    vc = l1

    REM calculate component contributions
    PRINT : PRINT "component contributions : "
    REM - v1 - cornea
    v1 = f1: PRINT : PRINT "cornea ="; v1
    REM - v2 - separation between cornea and equivalent lens
    v2 = vl - vsep: PRINT "separation ="; v2
    REM - v3 - equivalent lens
    v3 = fl: PRINT "equivalent lens ="; v3
    PRINT "vitreous (does not contribute to total vergence) ="; vv

    REM calculate percent vergence contributions
    PRINT : PRINT "percent vergence contributions :"
    REM - vt - total vergence of eye
    vt = v1 + v2 + v3
    REM - pc1 - cornea
    pc1 = (100 * v1) / vt: PRINT : PRINT "cornea ="; pc1
    REM - pc2 - separation between cornea and equivalent lens
    pc2 = (100 * v2) / vt: PRINT "separation ="; pc2
    REM - pc3 - equivalent lens
    pc3 = (100 * v3) / vt: PRINT "equivalent lens ="; pc3

END
```

## Appendix 5

### Peripheral refraction

Peripheral refraction data for both eyes of all subjects. All data is in dioptres.

| ecc. | subject MC | | | | subject GH | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -5.68 | -9.39 | -7.04 | -11.60 | -4.00 | -4.94 | -6.02 | -6.87 |
| 30n | -6.31 | -8.71 | -7.84 | -11.40 | -4.60 | -5.24 | -6.54 | -7.32 |
| 25n | -6.22 | -7.84 | -7.77 | -10.51 | -5.10 | -5.37 | -6.97 | -7.41 |
| 20n | -6.44 | -7.68 | -8.02 | -10.37 | -5.30 | -5.74 | -7.22 | -7.77 |
| 15n | -6.72 | -7.81 | -8.22 | -10.44 | -5.35 | -5.34 | -7.28 | -7.43 |
| 10n | -6.73 | -7.64 | -8.29 | -10.29 | -5.37 | -6.16 | -7.39 | -8.15 |
| 5n | -6.82 | -7.58 | -8.52 | -10.54 | -5.62 | -6.14 | -7.64 | -8.23 |
| 0n | -6.47 | -7.34 | -8.27 | -10.42 | -5.67 | -6.20 | -7.87 | -8.45 |
| 5t | -6.57 | -7.34 | -8.62 | -11.17 | -5.70 | -6.69 | -7.68 | -8.54 |
| 10t | -6.74 | -8.02 | -8.88 | -11.92 | -5.75 | -6.16 | -7.65 | -8.23 |
| 15t | -6.76 | -8.06 | -8.90 | -12.33 | -5.65 | -6.18 | -7.54 | -8.15 |
| 20t | -6.81 | -8.18 | -9.29 | -13.14 | -5.35 | -5.80 | -7.34 | -7.36 |
| 25t | -6.11 | -6.96 | -8.90 | -12.01 | -4.88 | -5.24 | -6.76 | -7.02 |
| 30t | -4.76 | -5.49 | -8.16 | -11.07 | -3.80 | -4.78 | -6.75 | -6.65 |
| 35t | -4.11 | -6.48 | -8.14 | -11.12 | -2.00 | -4.64 | -5.12 | -5.21 |

| ecc. | subject SP | | | | subject GR | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.60 | -1.87 | 2.37 | -0.57 | -4.00 | -4.64 | -5.95 | -6.47 |
| 30n | 0.14 | -1.80 | -1.59 | -0.60 | -4.60 | -4.94 | -6.54 | -7.32 |
| 25n | -0.32 | -1.72 | 0.87 | -0.55 | -5.10 | -5.17 | -6.97 | -7.41 |
| 20n | -0.84 | -1.64 | 0.43 | -0.24 | -5.30 | -5.24 | -7.22 | -7.77 |
| 15n | -0.95 | -1.59 | 0.78 | 0.16 | -5.35 | -5.34 | -7.28 | -7.43 |
| 10n | -1.02 | -1.43 | 0.78 | 0.40 | -5.37 | -5.56 | -7.39 | -8.15 |
| 5n | -0.66 | -0.98 | 1.30 | 0.96 | -5.62 | -5.64 | -7.64 | -8.23 |
| 0n | -0.52 | -0.87 | 1.30 | 0.61 | -5.00 | -5.55 | -7.37 | -8.15 |
| 5t | -1.13 | -1.46 | 1.20 | 0.00 | -5.70 | -5.69 | -7.68 | -8.04 |
| 10t | -1.18 | -1.35 | 1.05 | -0.29 | -5.75 | -5.36 | -7.65 | -8.00 |
| 15t | -0.95 | -1.37 | 0.80 | -0.52 | -5.65 | -5.18 | -7.54 | -7.95 |
| 20t | -0.50 | -1.45 | 0.87 | -0.55 | -5.35 | -4.80 | -7.34 | -7.36 |
| 25t | 0.35 | -2.24 | 1.17 | -0.45 | -4.88 | -4.24 | -6.76 | -7.02 |
| 30t | 1.59 | -3.71 | 2.07 | -0.35 | -3.80 | -3.78 | -6.65 | -6.55 |
| 35t | 3.25 | -4.05 | 3.67 | -0.63 | -2.00 | -3.64 | -5.14 | -5.34 |

| ecc. | subject KT | | | | subject RC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -4.68 | -7.44 | -2.12 | -5.60 | 3.54 | -2.88 | 6.80 | 0.70 |
| 30n | -5.31 | -7.73 | -2.84 | -5.40 | 2.30 | -1.29 | 6.19 | 0.65 |
| 25n | -5.22 | -6.85 | -2.67 | -4.51 | 1.39 | -0.53 | 5.15 | 1.66 |
| 20n | -5.44 | -6.68 | -3.02 | -4.37 | 1.17 | -0.40 | 5.52 | 3.42 |
| 15n | -5.72 | -6.81 | -3.22 | -4.44 | 0.90 | -0.15 | 5.14 | 3.59 |
| 10n | -5.73 | -6.64 | -3.29 | -4.29 | 0.66 | 0.07 | 4.44 | 3.24 |
| 5n | -5.82 | -6.58 | -3.52 | -4.54 | 0.99 | 0.87 | 4.20 | 3.57 |
| 0n | -5.47 | -6.34 | -3.75 | -4.42 | 0.59 | 0.54 | 4.21 | 3.46 |
| 5t | -5.57 | -6.34 | -3.62 | -5.17 | 0.67 | 0.17 | 4.57 | 4.21 |
| 10t | -5.74 | -6.02 | -3.88 | -5.92 | 0.91 | 0.82 | 5.00 | 4.15 |
| 15t | -5.76 | -6.12 | -3.90 | -6.33 | 1.09 | 0.78 | 5.55 | 3.76 |
| 20t | -5.81 | -6.18 | -4.19 | -6.14 | 1.32 | 0.74 | 6.08 | 3.64 |
| 25t | -5.11 | -5.93 | -3.90 | -6.01 | 2.68 | 1.27 | 6.41 | 2.25 |
| 30t | -4.76 | -4.59 | -3.32 | -5.07 | 5.39 | 1.57 | 6.07 | 2.04 |
| 35t | -4.11 | -4.48 | -3.15 | -5.12 | 6.41 | -1.46 | 6.16 | 1.87 |

| ecc. | subject FM | | | | subject AD | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.60 | -1.87 | 2.15 | -0.72 | 1.00 | -2.94 | 4.02 | -2.87 |
| 30n | 0.14 | -1.80 | -1.59 | -0.63 | 1.60 | -1.24 | 4.54 | -2.32 |
| 25n | -0.32 | -1.72 | -2.87 | -0.55 | -0.10 | -1.37 | 4.97 | -1.41 |
| 20n | -0.84 | -1.64 | -2.43 | -0.24 | -0.30 | -1.74 | 3.22 | -1.77 |
| 15n | -0.95 | -1.59 | -3.85 | 0.16 | -0.35 | -1.34 | 3.28 | -1.43 |
| 10n | -1.02 | -1.13 | -3.78 | 0.40 | -0.37 | -0.16 | 3.39 | -1.15 |
| 5n | -0.66 | -0.48 | -3.30 | 0.96 | -0.62 | -0.14 | 3.64 | -0.23 |
| 0n | -0.12 | -0.37 | -3.10 | -0.61 | -0.37 | -0.20 | 3.37 | -0.45 |
| 5t | -0.13 | -0.46 | -3.20 | 0.00 | -0.70 | -0.69 | 3.68 | -0.54 |
| 10t | -0.88 | -0.85 | -3.05 | -0.29 | -0.75 | -0.16 | 3.65 | -0.23 |
| 15t | -0.95 | -1.37 | -3.80 | -0.52 | -0.65 | -0.18 | 3.54 | -0.15 |
| 20t | -0.50 | -1.46 | -3.87 | -0.56 | -0.35 | -1.80 | 3.34 | -0.36 |
| 25t | 0.35 | -2.24 | -3.17 | -0.63 | 1.88 | -1.24 | 4.76 | -0.02 |
| 30t | 1.62 | -3.67 | -4.04 | -0.75 | 2.80 | -2.78 | 4.75 | -1.65 |
| 35t | 3.25 | -4.12 | -4.57 | -0.87 | 3.00 | -2.64 | 5.12 | -2.21 |

| ecc. | subject JF | | | | subject MH | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -1.60 | -1.93 | -1.74 | -0.74 | 4.02 | -2.87 | 1.20 | -2.63 |
| 30n | -1.14 | -1.83 | -3.44 | -0.62 | 4.54 | -2.32 | 1.62 | -1.22 |
| 25n | -2.32 | -1.69 | -4.17 | -0.45 | 4.97 | -1.41 | -0.12 | -1.37 |
| 20n | -2.84 | -1.64 | -4.43 | -0.24 | 3.22 | -1.77 | -0.31 | -1.74 |
| 15n | -2.95 | -1.59 | -5.85 | 0.16 | 3.28 | -1.43 | -0.35 | -1.34 |
| 10n | -2.02 | -1.13 | -5.78 | 0.40 | 3.69 | -1.15 | -0.37 | -0.16 |
| 5n | -3.66 | -0.48 | -5.30 | 0.26 | 3.84 | -0.23 | -0.62 | -0.14 |
| 0n | -3.12 | -0.37 | -5.10 | -0.61 | 3.87 | -0.45 | -0.37 | -0.20 |
| 5t | -3.13 | -0.46 | -5.20 | 0.00 | 3.88 | -0.54 | -0.70 | -0.69 |
| 10t | -2.88 | -0.85 | -5.05 | -0.29 | 3.775 | -0.23 | -0.75 | -0.16 |
| 15t | -2.95 | -1.12 | -4.96 | -0.52 | 3.54 | -0.15 | -0.65 | -0.18 |
| 20t | -2.50 | -1.32 | -4.87 | -0.56 | 3.34 | -0.36 | -0.35 | -1.80 |
| 25t | -1.35 | -2.24 | -4.23 | -0.63 | 4.76 | -0.02 | 1.88 | -1.24 |
| 30t | 0.62 | -3.57 | -4.11 | -0.75 | 4.75 | -1.65 | 2.84 | -2.78 |
| 35t | 1.25 | -4.55 | -3.45 | -0.87 | 5.12 | -2.21 | 3.12 | -2.55 |

| ecc. | subject TC | | | | subject MO | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.60 | -1.87 | -1.55 | -1.85 | -4.00 | -4.64 | -1.63 | -1.73 |
| 30n | 0.14 | -1.80 | -1.14 | -1.73 | -4.60 | -4.83 | -1.14 | -1.71 |
| 25n | -0.32 | -1.77 | -2.32 | -1.69 | -5.10 | -5.27 | -2.32 | -1.59 |
| 20n | -0.84 | -1.71 | -2.84 | -1.64 | -5.30 | -5.32 | -2.84 | -1.58 |
| 15n | -0.95 | -1.59 | -2.95 | -1.59 | -5.35 | -5.44 | -2.95 | -1.47 |
| 10n | -1.02 | -1.43 | -2.02 | -1.23 | -5.37 | -5.74 | -2.02 | -1.16 |
| 5n | -0.66 | -0.98 | -3.66 | -0.48 | -5.62 | -5.85 | -3.66 | -0.37 |
| 0n | -0.52 | -0.87 | -3.00 | -0.15 | -5.00 | -5.95 | -3.12 | -0.39 |
| 5t | -1.13 | -1.46 | -3.13 | -0.46 | -5.70 | -5.87 | -3.13 | -0.56 |
| 10t | -1.18 | -1.35 | -2.88 | -0.76 | -5.75 | -5.36 | -2.88 | -0.85 |
| 15t | -0.95 | -1.37 | -2.95 | -1.08 | -5.65 | -5.18 | -2.95 | -1.12 |
| 20t | -0.50 | -1.45 | -2.50 | -1.32 | -5.35 | -4.80 | -2.50 | -1.35 |
| 25t | 0.35 | -2.24 | -1.35 | -2.24 | -4.88 | -4.24 | -1.35 | -2.32 |
| 30t | 1.59 | -3.71 | 0.62 | -3.57 | -3.80 | -3.78 | 0.62 | -3.61 |
| 35t | 3.25 | -4.05 | 1.25 | -4.35 | -2.00 | -3.64 | 1.25 | -4.59 |

| ecc. | subject NG | | | | subject NP | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.46 | -1.88 | 5.55 | 2.54 | -1.63 | -1.95 | -3.12 | -4.52 |
| 30n | 0.23 | -1.79 | 5.14 | 2.14 | -1.14 | -1.61 | -3.54 | -4.84 |
| 25n | -0.33 | -1.73 | 5.32 | 1.83 | -2.32 | -1.53 | -4.15 | -5.35 |
| 20n | -0.64 | -1.64 | 4.84 | 1.64 | -2.84 | -1.49 | -4.30 | -5.41 |
| 15n | -0.83 | -1.32 | 4.95 | 1.59 | -2.95 | -1.27 | -4.35 | -5.52 |
| 10n | -0.62 | -0.93 | 4.02 | 1.23 | -2.02 | -1.16 | -4.37 | -5.74 |
| 5n | -0.16 | -0.54 | 3.66 | 0.48 | -3.21 | -0.37 | -4.62 | -5.85 |
| 0n | 0.62 | -0.27 | 3.82 | 0.15 | -2.87 | -0.39 | -4.87 | -5.35 |
| 5t | -0.13 | -0.47 | 4.13 | 0.46 | -3.15 | -0.56 | -4.70 | -5.37 |
| 10t | -1.18 | -0.66 | 4.88 | 0.76 | -2.88 | -0.85 | -4.75 | -5.36 |
| 15t | -0.95 | -0.95 | 5.95 | 1.12 | -2.95 | -1.12 | -4.65 | -5.18 |
| 20t | -0.50 | -1.34 | 5.50 | 1.42 | -2.50 | -1.35 | -4.35 | -4.80 |
| 25t | 0.35 | -2.41 | 6.35 | 2.17 | -1.35 | -2.32 | -3.88 | -4.26 |
| 30t | 1.59 | -3.62 | 7.62 | 3.44 | 0.62 | -3.61 | -2.80 | -3.83 |
| 35t | 3.25 | -4.13 | 7.25 | 4.26 | 1.25 | -4.79 | -2.00 | -3.52 |

| ecc. | subject AS | | | | subject KS | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.46 | -1.88 | -1.25 | 2.54 | 0.66 | -1.94 | 2.37 | -0.75 |
| 30n | 0.23 | -1.79 | -1.34 | 2.14 | 0.14 | -1.87 | -1.59 | -0.60 |
| 25n | -0.33 | -1.73 | -1.47 | 1.83 | -0.32 | -1.65 | 0.87 | -0.55 |
| 20n | -0.64 | -1.64 | -2.85 | 1.64 | -0.84 | -1.58 | 0.43 | -0.24 |
| 15n | -0.83 | -1.32 | -2.95 | 1.59 | -0.95 | -1.49 | 0.78 | 0.16 |
| 10n | -0.62 | -0.93 | -3.02 | 1.23 | -1.02 | -1.43 | 0.78 | 0.40 |
| 5n | -0.16 | -0.54 | -3.66 | 0.48 | -0.66 | -0.98 | 1.30 | 0.96 |
| 0n | 0.62 | -0.27 | -3.55 | 0.55 | -0.62 | -0.87 | 1.30 | 0.61 |
| 5t | -0.13 | -0.47 | -3.13 | 0.46 | -1.13 | -1.46 | 1.20 | 0.00 |
| 10t | -1.18 | -0.66 | -3.88 | 0.76 | -1.18 | -1.35 | 1.05 | -0.29 |
| 15t | -0.95 | -0.95 | -3.95 | 1.12 | -0.95 | -1.37 | 0.80 | -0.52 |
| 20t | -0.50 | -1.34 | -3.50 | 1.42 | -0.50 | -1.45 | 0.87 | -0.55 |
| 25t | 0.35 | -2.41 | -2.35 | 2.17 | 0.35 | -2.24 | 1.17 | -0.45 |
| 30t | 1.59 | -3.62 | -1.62 | 3.44 | 1.59 | -3.71 | 2.07 | -0.35 |
| 35t | 3.25 | -4.13 | -1.25 | 4.26 | 3.25 | -4.05 | 3.67 | -0.63 |

| ecc. | subject ED | | | | subject KB | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -0.26 | -3.23 | -1.25 | -3.86 | 0.66 | -1.94 | 2.35 | -0.75 |
| 30n | -0.41 | -2.85 | -1.34 | -3.54 | 0.14 | -1.87 | 1.52 | -0.60 |
| 25n | -0.52 | -2.44 | -1.47 | -2.83 | -0.32 | -1.65 | 0.98 | -0.55 |
| 20n | -0.84 | -2.38 | -2.85 | -1.78 | -0.84 | -1.58 | 0.73 | -0.24 |
| 15n | -1.05 | -2.15 | -2.95 | -1.66 | -0.95 | -1.49 | 0.54 | -0.16 |
| 10n | -1.22 | -1.74 | -3.02 | -1.23 | -1.02 | -1.43 | -0.18 | -0.40 |
| 5n | -1.66 | -0.98 | -3.66 | -0.98 | -0.66 | -0.98 | -0.30 | -0.96 |
| 0n | -1.32 | -0.87 | -3.85 | -0.75 | -0.62 | -0.87 | -0.70 | -0.61 |
| 5t | -1.13 | -1.26 | -3.13 | -0.46 | -1.13 | -1.46 | 0.20 | -0.00 |
| 10t | -1.18 | -1.47 | -3.88 | -0.76 | -1.18 | -1.35 | 0.65 | -0.29 |
| 15t | -0.95 | -1.58 | -3.95 | -1.12 | -0.95 | -1.37 | 0.80 | -0.52 |
| 20t | -0.60 | -1.93 | -3.50 | -1.51 | -0.50 | -1.45 | 0.98 | -0.55 |
| 25t | -0.31 | -2.48 | -2.35 | -2.17 | 0.35 | -2.24 | 1.45 | -0.45 |
| 30t | -0.12 | -3.71 | -1.62 | -3.44 | 1.59 | -3.71 | 2.03 | -0.35 |
| 35t | 0.24 | -4.32 | -1.25 | -4.26 | 3.25 | -4.05 | 3.21 | -0.63 |

| ecc. | subject JT | | | | subject FR | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 6.64 | 1.87 | 0.66 | -2.53 | -5.76 | -6.54 | -3.02 | -3.87 |
| 30n | 5.72 | 2.32 | 0.14 | -2.28 | -6.15 | -6.82 | -3.54 | -4.32 |
| 25n | 5.24 | 2.41 | -0.32 | -1.85 | -6.45 | -7.11 | -3.97 | -4.41 |
| 20n | 4.62 | 2.77 | -0.84 | -1.64 | -6.84 | -7.32 | -4.22 | -4.77 |
| 15n | 4.28 | 3.43 | -0.95 | -1.45 | -7.06 | -7.55 | -4.28 | -4.43 |
| 10n | 4.39 | 4.15 | -0.62 | -1.31 | -7.26 | -7.86 | -4.39 | -5.15 |
| 5n | 4.64 | 4.23 | -0.46 | -0.28 | -7.44 | -8.09 | -4.64 | -5.23 |
| 0n | 4.37 | 4.45 | -0.22 | -0.57 | -7.65 | -8.42 | -4.87 | -5.45 |
| 5t | 4.38 | 4.54 | -0.73 | -1.26 | -7.43 | -8.22 | -4.68 | -5.54 |
| 10t | 4.45 | 4.23 | -1.06 | -1.37 | -7.25 | -7.96 | -4.65 | -5.23 |
| 15t | 4.52 | 4.15 | -0.95 | -1.44 | -7.04 | -7.46 | -4.54 | -5.15 |
| 20t | 4.61 | 3.76 | -0.50 | -1.67 | -6.87 | -7.28 | -4.34 | -5.36 |
| 25t | 5.29 | 3.02 | 0.35 | -2.24 | -6.53 | -6.94 | -3.76 | -5.02 |
| 30t | 5.75 | 2.72 | 1.59 | -3.75 | -6.21 | -6.41 | -3.75 | -4.65 |
| 35t | 6.12 | 2.16 | 3.25 | -4.37 | -5.88 | -6.19 | -2.12 | -4.21 |

| ecc. | subject AT | | | | subject HW | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 1.42 | -2.42 | 1.37 | -2.07 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 0.80 | -1.76 | 0.74 | -1.78 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 0.44 | -0.84 | 0.56 | -0.95 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 0.58 | -0.97 | 0.49 | -0.77 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 0.22 | -0.67 | 0.31 | -0.65 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 0.12 | -0.39 | 0.14 | -0.44 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 0.09 | -0.61 | 0.05 | -0.38 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 0.14 | -0.34 | 0.02 | -0.22 | -4.40 | -0.55 | -4.21 | -0.58 |
| 5t | 0.44 | -0.66 | 0.12 | -0.56 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 0.67 | -1.55 | 0.10 | -0.99 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 0.34 | -1.67 | 0.36 | -1.47 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 0.14 | -1.63 | 0.39 | -1.59 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 0.32 | -1.92 | 0.45 | -1.87 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 0.97 | -2.55 | 0.88 | -2.49 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 1.13 | -3.49 | 1.32 | -3.28 | -2.13 | -3.87 | -2.07 | -3.73 |

| ecc. | subject PK | | | | subject EM | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -1.63 | -1.95 | -1.78 | -2.34 | -4.00 | -4.64 | -3.78 | -4.64 |
| 30n | -1.14 | -1.61 | -1.33 | -1.85 | -4.60 | -4.83 | -4.23 | -4.94 |
| 25n | -2.32 | -1.53 | -2.51 | -1.66 | -5.10 | -5.27 | -4.97 | -5.17 |
| 20n | -2.84 | -1.49 | -2.71 | -1.37 | -5.30 | -5.32 | -5.22 | -5.24 |
| 15n | -2.95 | -1.27 | -2.85 | -1.24 | -5.35 | -5.44 | -5.29 | -5.34 |
| 10n | -3.02 | -1.16 | -3.04 | -0.87 | -5.37 | -5.74 | -5.36 | -5.56 |
| 5n | -3.21 | -0.37 | -3.11 | -0.44 | -5.62 | -5.85 | -5.41 | -5.64 |
| 0n | -2.87 | -0.39 | -3.14 | -0.57 | -5.00 | -5.95 | -5.50 | -5.89 |
| 5t | -3.15 | -0.56 | -3.35 | -0.76 | -5.70 | -5.87 | -5.48 | -5.69 |
| 10t | -2.88 | -0.85 | -2.76 | -0.98 | -5.75 | -5.36 | -5.55 | -5.27 |
| 15t | -2.95 | -1.12 | -2.65 | -1.24 | -5.65 | -5.18 | -5.42 | -5.02 |
| 20t | -2.50 | -1.35 | -2.53 | -1.76 | -5.35 | -4.80 | -5.32 | -4.73 |
| 25t | -1.35 | -2.32 | -1.45 | -2.41 | -4.88 | -4.24 | -4.76 | -4.15 |
| 30t | 0.62 | -3.61 | 0.24 | -3.73 | -3.80 | -3.78 | -3.65 | -3.67 |
| 35t | 1.25 | -4.79 | 1.02 | -5.04 | -2.00 | -3.64 | -1.98 | -3.25 |

| ecc. | subject SK | | | | subject ER | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 1.42 | -2.42 | 1.37 | -2.07 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 0.80 | -1.76 | 0.74 | -1.78 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 0.44 | -0.84 | 0.56 | -0.95 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 0.58 | -0.97 | 0.49 | -0.77 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 0.22 | -0.67 | 0.31 | -0.65 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 0.12 | -0.39 | 0.14 | -0.44 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 0.09 | -0.61 | 0.05 | -0.38 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 0.14 | -0.34 | 0.02 | -0.22 | -4.40 | -0.55 | -4.21 | -0.58 |
| 5t | 0.44 | -0.66 | 0.12 | -0.56 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 0.67 | -1.55 | 0.10 | -0.99 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 0.34 | -1.67 | 0.36 | -1.47 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 0.14 | -1.63 | 0.39 | -1.59 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 0.32 | -1.92 | 0.45 | -1.87 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 0.97 | -2.55 | 0.88 | -2.49 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 1.13 | -3.49 | 1.32 | -3.28 | -2.13 | -3.87 | -2.07 | -3.73 |

| ecc. | subject MK | | | | subject RW | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.66 | -2.53 | 1.37 | -2.07 | 0.54 | -4.37 | 1.89 | -4.43 |
| 30n | 0.14 | -2.28 | 1.14 | -1.78 | -0.06 | -3.89 | 1.12 | -3.85 |
| 25n | -0.32 | -1.85 | 1.26 | -0.95 | -0.47 | -3.25 | 0.44 | -3.33 |
| 20n | -0.84 | -1.64 | 0.89 | -0.77 | -0.69 | -2.76 | -0.62 | -2.59 |
| 15n | -0.95 | -1.45 | 0.71 | -0.65 | -0.84 | -2.26 | -0.74 | -2.34 |
| 10n | -0.62 | -1.31 | 0.64 | -0.44 | -1.33 | -1.54 | -1.27 | -1.51 |
| 5n | -0.46 | -0.28 | 0.55 | -0.38 | -1.44 | -0.72 | -1.53 | -0.66 |
| 0n | -0.22 | -0.57 | 0.52 | -0.42 | -1.40 | -0.25 | -1.21 | -0.58 |
| 5t | -0.73 | -1.26 | 0.52 | -0.56 | -1.32 | -0.76 | -1.38 | -0.77 |
| 10t | -1.06 | -1.37 | 0.60 | -0.99 | -0.93 | -1.44 | -0.87 | -1.36 |
| 15t | -0.95 | -1.44 | 0.76 | -1.47 | -0.76 | -1.89 | -0.66 | -1.79 |
| 20t | -0.50 | -1.67 | 0.89 | -1.59 | -0.23 | -2.37 | 0.14 | -2.41 |
| 25t | 0.35 | -2.24 | 0.95 | -1.87 | 0.95 | -2.77 | 0.89 | -2.68 |
| 30t | 1.59 | -3.75 | 1.08 | -2.49 | 1.64 | -3.43 | 1.61 | -3.38 |
| 35t | 3.25 | -4.37 | 1.32 | -3.28 | 1.73 | -3.87 | 2.07 | -3.73 |

| ecc. | subject EB | | | | subject KR | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.66 | -2.53 | 1.37 | -2.07 | 2.37 | -0.57 | 0.60 | -1.87 |
| 30n | 0.14 | -2.28 | 1.14 | -1.78 | -1.59 | -0.60 | 0.14 | -1.80 |
| 25n | -0.32 | -1.85 | 1.26 | -0.95 | 0.87 | -0.55 | -0.32 | -1.72 |
| 20n | -0.84 | -1.64 | 0.89 | -0.77 | 0.43 | -0.24 | -0.84 | -1.64 |
| 15n | -0.95 | -1.45 | 0.71 | -0.65 | 0.78 | 0.16 | -0.95 | -1.59 |
| 10n | -0.62 | -1.31 | 0.64 | -0.44 | 0.78 | 0.40 | -1.02 | -1.43 |
| 5n | -0.46 | -0.28 | 0.55 | -0.38 | 1.30 | 0.96 | -0.66 | -0.98 |
| 0n | -0.22 | -0.57 | 0.52 | -0.42 | 1.40 | 0.61 | -0.52 | -0.87 |
| 5t | -0.73 | -1.26 | 0.52 | -0.56 | 1.20 | 0.00 | -1.13 | -1.46 |
| 10t | -1.06 | -1.37 | 0.60 | -0.99 | 1.05 | -0.29 | -1.18 | -1.35 |
| 15t | -0.95 | -1.44 | 0.76 | -1.47 | 0.80 | -0.52 | -0.95 | -1.37 |
| 20t | -0.50 | -1.67 | 0.89 | -1.59 | 0.87 | -0.55 | -0.50 | -1.45 |
| 25t | 0.35 | -2.24 | 0.95 | -1.87 | 1.17 | -0.45 | 0.35 | -2.24 |
| 30t | 1.59 | -3.75 | 1.08 | -2.49 | 2.07 | -0.35 | 1.59 | -3.71 |
| 35t | 3.25 | -4.37 | 1.32 | -3.28 | 3.67 | -0.63 | 3.25 | -4.05 |

| ecc. | subject GG | | | | subject JB | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 1.42 | -2.42 | 1.37 | -2.07 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 0.80 | -1.76 | 0.74 | -1.78 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 0.44 | -0.84 | 0.56 | -0.95 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 0.58 | -0.97 | 0.49 | -0.77 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 0.22 | -0.67 | 0.31 | -0.65 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 0.12 | -0.39 | 0.14 | -0.44 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 0.09 | -0.61 | 0.05 | -0.38 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 0.14 | -0.34 | 0.02 | -0.22 | -4.40 | -0.55 | -4.21 | -0.58 |
| 5t | 0.44 | -0.66 | 0.12 | -0.56 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 0.67 | -1.55 | 0.10 | -0.99 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 0.34 | -1.67 | 0.36 | -1.47 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 0.14 | -1.63 | 0.39 | -1.59 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 0.32 | -1.92 | 0.45 | -1.87 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 0.97 | -2.55 | 0.88 | -2.49 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 1.13 | -3.49 | 1.32 | -3.28 | -2.13 | -3.87 | -2.07 | -3.73 |

| ecc. | subject JS | | | | subject RJ | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.54 | -4.37 | 0.89 | -4.43 | 1.42 | -2.42 | 1.37 | -2.07 |
| 30n | -0.06 | -3.89 | 0.12 | -3.85 | 0.80 | -1.76 | 0.74 | -1.78 |
| 25n | -0.47 | -3.25 | -0.44 | -3.33 | 0.44 | -0.84 | 0.56 | -0.95 |
| 20n | -0.69 | -2.76 | -0.62 | -2.59 | 0.58 | -0.97 | 0.49 | -0.77 |
| 15n | -0.84 | -2.26 | -0.74 | -2.34 | 0.22 | -0.67 | 0.31 | -0.65 |
| 10n | -1.43 | -1.54 | -1.27 | -1.51 | 0.12 | -0.39 | 0.14 | -0.44 |
| 5n | -1.64 | -0.72 | -1.53 | -0.66 | 0.09 | -0.61 | 0.05 | -0.38 |
| 0n | -1.90 | -0.25 | -1.71 | -0.58 | 0.14 | -0.34 | 0.02 | -0.22 |
| 5t | -1.74 | -0.76 | -1.58 | -0.77 | 0.44 | -0.66 | 0.12 | -0.56 |
| 10t | -1.37 | -1.44 | -0.87 | -1.36 | 0.67 | -1.55 | 0.10 | -0.99 |
| 15t | -0.76 | -1.89 | -0.66 | -1.79 | 0.34 | -1.67 | 0.36 | -1.47 |
| 20t | -0.23 | -2.37 | 0.14 | -2.41 | 0.14 | -1.63 | 0.39 | -1.59 |
| 25t | 0.95 | -2.77 | 0.89 | -2.68 | 0.32 | -1.92 | 0.45 | -1.87 |
| 30t | 1.64 | -3.43 | 1.61 | -3.38 | 0.97 | -2.55 | 0.88 | -2.49 |
| 35t | 1.73 | -3.87 | 2.07 | -3.73 | 1.13 | -3.49 | 1.32 | -3.28 |

| ecc. | subject RB | | | | subject SL | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 6.64 | 1.87 | 7.12 | 2.14 | 0.66 | -2.53 | 0.79 | -2.41 |
| 30n | 5.72 | 2.32 | 6.32 | 2.44 | 0.14 | -2.28 | 0.36 | -2.15 |
| 25n | 5.24 | 2.41 | 5.52 | 2.56 | -0.32 | -1.85 | -0.27 | -1.88 |
| 20n | 4.62 | 2.77 | 4.77 | 2.73 | -0.84 | -1.64 | -0.77 | -1.57 |
| 15n | 4.28 | 3.43 | 4.41 | 3.58 | -0.95 | -1.15 | -0.84 | -1.03 |
| 10n | 4.39 | 4.15 | 4.27 | 4.19 | -0.62 | -0.71 | -0.66 | -0.66 |
| 5n | 4.64 | 4.23 | 4.31 | 4.44 | -0.26 | -0.28 | -0.35 | -0.38 |
| 0n | 4.37 | 4.45 | 4.22 | 4.52 | 0.12 | -0.12 | 0.20 | -0.18 |
| 5t | 4.38 | 4.54 | 4.36 | 4.68 | -0.43 | -0.56 | -0.11 | -0.49 |
| 10t | 4.45 | 4.23 | 4.57 | 4.37 | -0.66 | -1.17 | -0.45 | -1.24 |
| 15t | 4.52 | 4.15 | 4.48 | 4.25 | -0.95 | -1.44 | -0.89 | -1.52 |
| 20t | 4.61 | 3.76 | 4.76 | 3.65 | -0.50 | -1.67 | -0.57 | -1.72 |
| 25t | 5.29 | 3.02 | 5.66 | 3.28 | 0.35 | -2.24 | 0.26 | -2.19 |
| 30t | 5.75 | 2.72 | 5.98 | 2.63 | 1.59 | -3.75 | 1.75 | -3.55 |
| 35t | 6.12 | 2.16 | 6.47 | 2.22 | 3.25 | -4.37 | 3.03 | -4.74 |

| ecc. | subject LW | | | | subject EM | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -5.00 | -3.64 | -4.78 | -5.64 | -4.66 | -2.53 | -4.79 | -2.41 |
| 30n | -5.60 | -4.83 | -5.23 | -5.94 | -5.14 | -2.28 | -4.96 | -2.15 |
| 25n | -6.10 | -5.27 | -5.97 | -6.17 | -5.32 | -1.85 | -5.27 | -1.88 |
| 20n | -6.30 | -5.32 | -6.22 | -6.24 | -5.84 | -1.64 | -5.77 | -1.57 |
| 15n | -6.35 | -5.44 | -6.29 | -6.34 | -5.95 | -1.15 | -5.84 | -1.03 |
| 10n | -6.37 | -5.74 | -6.36 | -6.56 | -6.62 | -0.71 | -6.66 | -0.66 |
| 5n | -6.62 | -5.85 | -6.41 | -6.64 | -6.26 | -0.28 | -6.35 | -0.38 |
| 0n | -6.30 | -6.95 | -6.50 | -6.89 | -6.12 | -0.12 | -6.20 | -0.18 |
| 5t | -6.70 | -5.87 | -6.48 | -6.69 | -6.43 | -0.56 | -6.11 | -0.49 |
| 10t | -6.75 | -5.36 | -6.55 | -6.27 | -6.66 | -1.17 | -6.45 | -1.24 |
| 15t | -6.65 | -5.18 | -6.42 | -6.02 | -5.95 | -1.44 | -5.89 | -1.52 |
| 20t | -6.35 | -4.80 | -6.32 | -5.73 | -5.50 | -1.67 | -5.57 | -1.72 |
| 25t | -5.88 | -3.24 | -5.76 | -5.15 | -5.35 | -2.24 | -5.26 | -2.19 |
| 30t | -4.80 | -2.78 | -4.65 | -3.67 | -4.59 | -3.75 | -4.75 | -3.55 |
| 35t | -4.00 | -2.64 | -3.98 | -2.25 | -4.25 | -4.37 | -4.03 | -4.74 |

| ecc. | subject DT | | | | subject NB | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 6.64 | 1.87 | 7.12 | 2.14 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 5.72 | 2.32 | 6.32 | 2.44 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 5.24 | 2.41 | 5.52 | 2.56 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 4.62 | 2.77 | 4.77 | 2.73 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 4.28 | 3.43 | 4.41 | 3.58 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 4.39 | 4.15 | 4.27 | 4.19 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 4.64 | 4.23 | 4.31 | 4.44 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 4.37 | 4.45 | 4.22 | 4.52 | -4.50 | -0.65 | -4.51 | -0.68 |
| 5t | 4.38 | 4.54 | 4.36 | 4.68 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 4.45 | 4.23 | 4.57 | 4.37 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 4.52 | 4.15 | 4.48 | 4.25 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 4.61 | 3.76 | 4.76 | 3.65 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 5.29 | 3.02 | 5.66 | 3.28 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 5.75 | 2.72 | 5.98 | 2.63 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 6.12 | 2.16 | 6.47 | 2.22 | -2.13 | -3.87 | -2.07 | -3.73 |

Peripheral refraction data for both eyes of the Chinese subjects.

| ecc. | subject RL | | | | subject JK | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -5.68 | -9.39 | -7.04 | -11.60 | -4.00 | -4.94 | -6.02 | -6.87 |
| 30n | -6.31 | -8.71 | -7.84 | -11.40 | -4.60 | -5.24 | -6.54 | -7.32 |
| 25n | -6.22 | -7.84 | -7.77 | -10.51 | -5.10 | -5.37 | -6.97 | -7.41 |
| 20n | -6.44 | -7.68 | -8.02 | -10.37 | -5.30 | -5.74 | -7.22 | -7.77 |
| 15n | -6.72 | -7.81 | -8.22 | -10.44 | -5.35 | -5.34 | -7.28 | -7.43 |
| 10n | -6.73 | -7.64 | -8.29 | -10.29 | -5.37 | -6.16 | -7.39 | -8.15 |
| 5n | -6.82 | -7.58 | -8.52 | -10.54 | -5.62 | -6.14 | -7.64 | -8.23 |
| 0n | -6.47 | -7.34 | -8.27 | -10.42 | -5.67 | -6.20 | -7.87 | -8.45 |
| 5t | -6.57 | -7.34 | -8.62 | -11.17 | -5.70 | -6.69 | -7.68 | -8.54 |
| 10t | -6.74 | -8.02 | -8.88 | -11.92 | -5.75 | -6.16 | -7.65 | -8.23 |
| 15t | -6.76 | -8.06 | -8.90 | -12.33 | -5.65 | -6.18 | -7.54 | -8.15 |
| 20t | -6.81 | -8.18 | -9.29 | -13.14 | -5.35 | -5.80 | -7.34 | -7.36 |
| 25t | -6.11 | -6.96 | -8.90 | -12.01 | -4.88 | -5.24 | -6.76 | -7.02 |
| 30t | -4.76 | -5.49 | -8.16 | -11.07 | -3.80 | -4.78 | -6.75 | -6.65 |
| 35t | -4.11 | -6.48 | -8.14 | -11.12 | -2.00 | -4.64 | -5.12 | -5.21 |

| ecc. | subject SH | | | | subject MH | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.60 | -1.87 | 2.37 | -0.57 | -4.00 | -4.64 | -5.95 | -6.47 |
| 30n | 0.14 | -1.80 | -1.59 | -0.60 | -4.60 | -4.94 | -6.54 | -7.32 |
| 25n | -0.32 | -1.72 | 0.87 | -0.55 | -5.10 | -5.17 | -6.97 | -7.41 |
| 20n | -0.84 | -1.64 | 0.43 | -0.24 | -5.30 | -5.24 | -7.22 | -7.77 |
| 15n | -0.95 | -1.59 | 0.78 | 0.16 | -5.35 | -5.34 | -7.28 | -7.43 |
| 10n | -1.02 | -1.43 | 0.78 | 0.40 | -5.37 | -5.56 | -7.39 | -8.15 |
| 5n | -0.66 | -0.98 | 1.30 | 0.96 | -5.62 | -5.64 | -7.64 | -8.23 |
| 0n | -0.52 | -0.87 | 1.30 | 0.61 | -5.00 | -5.55 | -7.37 | -8.15 |
| 5t | -1.13 | -1.46 | 1.20 | 0.00 | -5.70 | -5.69 | -7.68 | -8.04 |
| 10t | -1.18 | -1.35 | 1.05 | -0.29 | -5.75 | -5.36 | -7.65 | -8.00 |
| 15t | -0.95 | -1.37 | 0.80 | -0.52 | -5.65 | -5.18 | -7.54 | -7.95 |
| 20t | -0.50 | -1.45 | 0.87 | -0.55 | -5.35 | -4.80 | -7.34 | -7.36 |
| 25t | 0.35 | -2.24 | 1.17 | -0.45 | -4.88 | -4.24 | -6.76 | -7.02 |
| 30t | 1.59 | -3.71 | 2.07 | -0.35 | -3.80 | -3.78 | -6.65 | -6.55 |
| 35t | 3.25 | -4.05 | 3.67 | -0.63 | -2.00 | -3.64 | -5.14 | -5.34 |

| ecc. | subject PL | | | | subject JT | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -4.68 | -7.44 | -2.12 | -5.60 | 3.54 | -2.88 | 6.80 | 0.70 |
| 30n | -5.31 | -7.73 | -2.84 | -5.40 | 2.30 | -1.29 | 6.19 | 0.65 |
| 25n | -5.22 | -6.85 | -2.67 | -4.51 | 1.39 | -0.53 | 5.15 | 1.66 |
| 20n | -5.44 | -6.68 | -3.02 | -4.37 | 1.17 | -0.40 | 5.52 | 3.42 |
| 15n | -5.72 | -6.81 | -3.22 | -4.44 | 0.90 | -0.15 | 5.14 | 3.59 |
| 10n | -5.73 | -6.64 | -3.29 | -4.29 | 0.66 | 0.07 | 4.44 | 3.24 |
| 5n | -5.82 | -6.58 | -3.52 | -4.54 | 0.99 | 0.87 | 4.20 | 3.57 |
| 0n | -5.47 | -6.34 | -3.75 | -4.42 | 0.59 | 0.54 | 4.21 | 3.46 |
| 5t | -5.57 | -6.34 | -3.62 | -5.17 | 0.67 | 0.17 | 4.57 | 4.21 |
| 10t | -5.74 | -6.02 | -3.88 | -5.92 | 0.91 | 0.82 | 5.00 | 4.15 |
| 15t | -5.76 | -6.12 | -3.90 | -6.33 | 1.09 | 0.78 | 5.55 | 3.76 |
| 20t | -5.81 | -6.18 | -4.19 | -6.14 | 1.32 | 0.74 | 6.08 | 3.64 |
| 25t | -5.11 | -5.93 | -3.90 | -6.01 | 2.68 | 1.27 | 6.41 | 2.25 |
| 30t | -4.76 | -4.59 | -3.32 | -5.07 | 5.39 | 1.57 | 6.07 | 2.04 |
| 35t | -4.11 | -4.48 | -3.15 | -5.12 | 6.41 | -1.46 | 6.16 | 1.87 |

| ecc. | subject YH | | | | subject LC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.60 | -1.87 | 2.15 | -0.72 | 1.00 | -2.94 | 4.02 | -2.87 |
| 30n | 0.14 | -1.80 | -1.59 | -0.63 | 1.60 | -1.24 | 4.54 | -2.32 |
| 25n | -0.32 | -1.72 | -2.87 | -0.55 | -0.10 | -1.37 | 4.97 | -1.41 |
| 20n | -0.84 | -1.64 | -2.43 | -0.24 | -0.30 | -1.74 | 3.22 | -1.77 |
| 15n | -0.95 | -1.59 | -3.85 | 0.16 | -0.35 | -1.34 | 3.28 | -1.43 |
| 10n | -1.02 | -1.13 | -3.78 | 0.40 | -0.37 | -0.16 | 3.39 | -1.15 |
| 5n | -0.66 | -0.48 | -3.30 | 0.96 | -0.62 | -0.14 | 3.64 | -0.23 |
| 0n | -0.12 | -0.37 | -3.10 | -0.61 | -0.37 | -0.20 | 3.37 | -0.45 |
| 5t | -0.13 | -0.46 | -3.20 | 0.00 | -0.70 | -0.69 | 3.68 | -0.54 |
| 10t | -0.88 | -0.85 | -3.05 | -0.29 | -0.75 | -0.16 | 3.65 | -0.23 |
| 15t | -0.95 | -1.37 | -3.80 | -0.52 | -0.65 | -0.18 | 3.54 | -0.15 |
| 20t | -0.50 | -1.46 | -3.87 | -0.56 | -0.35 | -1.80 | 3.34 | -0.36 |
| 25t | 0.35 | -2.24 | -3.17 | -0.63 | 1.88 | -1.24 | 4.76 | -0.02 |
| 30t | 1.62 | -3.67 | -4.04 | -0.75 | 2.80 | -2.78 | 4.75 | -1.65 |
| 35t | 3.25 | -4.12 | -4.57 | -0.87 | 3.00 | -2.64 | 5.12 | -2.21 |

| ecc. | subject MH | | | | subject CL | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -1.60 | -1.93 | -1.74 | -0.74 | 4.02 | -2.87 | 1.20 | -2.63 |
| 30n | -1.14 | -1.83 | -3.44 | -0.62 | 4.54 | -2.32 | 1.62 | -1.22 |
| 25n | -2.32 | -1.69 | -4.17 | -0.45 | 4.97 | -1.41 | -0.12 | -1.37 |
| 20n | -2.84 | -1.64 | -4.43 | -0.24 | 3.22 | -1.77 | -0.31 | -1.74 |
| 15n | -2.95 | -1.59 | -5.85 | 0.16 | 3.28 | -1.43 | -0.35 | -1.34 |
| 10n | -2.02 | -1.13 | -5.78 | 0.40 | 3.69 | -1.15 | -0.37 | -0.16 |
| 5n | -3.66 | -0.48 | -5.30 | 0.26 | 3.84 | -0.23 | -0.62 | -0.14 |
| 0n | -3.12 | -0.37 | -5.10 | -0.61 | 3.87 | -0.45 | -0.37 | -0.20 |
| 5t | -3.13 | -0.46 | -5.20 | 0.00 | 3.88 | -0.54 | -0.70 | -0.69 |
| 10t | -2.88 | -0.85 | -5.05 | -0.29 | 3.775 | -0.23 | -0.75 | -0.16 |
| 15t | -2.95 | -1.12 | -4.96 | -0.52 | 3.54 | -0.15 | -0.65 | -0.18 |
| 20t | -2.50 | -1.32 | -4.87 | -0.56 | 3.34 | -0.36 | -0.35 | -1.80 |
| 25t | -1.35 | -2.24 | -4.23 | -0.63 | 4.76 | -0.02 | 1.88 | -1.24 |
| 30t | 0.62 | -3.57 | -4.11 | -0.75 | 4.75 | -1.65 | 2.84 | -2.78 |
| 35t | 1.25 | -4.55 | -3.45 | -0.87 | 5.12 | -2.21 | 3.12 | -2.55 |

| ecc. | subject JH | | | | subject RL | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.60 | -1.87 | -1.55 | -1.85 | -4.00 | -4.64 | -1.63 | -1.73 |
| 30n | 0.14 | -1.80 | -1.14 | -1.73 | -4.60 | -4.83 | -1.14 | -1.71 |
| 25n | -0.32 | -1.77 | -2.32 | -1.69 | -5.10 | -5.27 | -2.32 | -1.59 |
| 20n | -0.84 | -1.71 | -2.84 | -1.64 | -5.30 | -5.32 | -2.84 | -1.58 |
| 15n | -0.95 | -1.59 | -2.95 | -1.59 | -5.35 | -5.44 | -2.95 | -1.47 |
| 10n | -1.02 | -1.43 | -2.02 | -1.23 | -5.37 | -5.74 | -2.02 | -1.16 |
| 5n | -0.66 | -0.98 | -3.66 | -0.48 | -5.62 | -5.85 | -3.66 | -0.37 |
| 0n | -0.52 | -0.87 | -3.00 | -0.15 | -5.00 | -5.95 | -3.12 | -0.39 |
| 5t | -1.13 | -1.46 | -3.13 | -0.46 | -5.70 | -5.87 | -3.13 | -0.56 |
| 10t | -1.18 | -1.35 | -2.88 | -0.76 | -5.75 | -5.36 | -2.88 | -0.85 |
| 15t | -0.95 | -1.37 | -2.95 | -1.08 | -5.65 | -5.18 | -2.95 | -1.12 |
| 20t | -0.50 | -1.45 | -2.50 | -1.32 | -5.35 | -4.80 | -2.50 | -1.35 |
| 25t | 0.35 | -2.24 | -1.35 | -2.24 | -4.88 | -4.24 | -1.35 | -2.32 |
| 30t | 1.59 | -3.71 | 0.62 | -3.57 | -3.80 | -3.78 | 0.62 | -3.61 |
| 35t | 3.25 | -4.05 | 1.25 | -4.35 | -2.00 | -3.64 | 1.25 | -4.59 |

| ecc. | subject JF | | | | subject JY | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.46 | -1.88 | 5.55 | 2.54 | -1.63 | -1.95 | -3.12 | -4.52 |
| 30n | 0.23 | -1.79 | 5.14 | 2.14 | -1.14 | -1.61 | -3.54 | -4.84 |
| 25n | -0.33 | -1.73 | 5.32 | 1.83 | -2.32 | -1.53 | -4.15 | -5.35 |
| 20n | -0.64 | -1.64 | 4.84 | 1.64 | -2.84 | -1.49 | -4.30 | -5.41 |
| 15n | -0.83 | -1.32 | 4.95 | 1.59 | -2.95 | -1.27 | -4.35 | -5.52 |
| 10n | -0.62 | -0.93 | 4.02 | 1.23 | -2.02 | -1.16 | -4.37 | -5.74 |
| 5n | -0.16 | -0.54 | 3.66 | 0.48 | -3.21 | -0.37 | -4.62 | -5.85 |
| 0n | 0.62 | -0.27 | 3.82 | 0.15 | -2.87 | -0.39 | -4.87 | -5.35 |
| 5t | -0.13 | -0.47 | 4.13 | 0.46 | -3.15 | -0.56 | -4.70 | -5.37 |
| 10t | -1.18 | -0.66 | 4.88 | 0.76 | -2.88 | -0.85 | -4.75 | -5.36 |
| 15t | -0.95 | -0.95 | 5.95 | 1.12 | -2.95 | -1.12 | -4.65 | -5.18 |
| 20t | -0.50 | -1.34 | 5.50 | 1.42 | -2.50 | -1.35 | -4.35 | -4.80 |
| 25t | 0.35 | -2.41 | 6.35 | 2.17 | -1.35 | -2.32 | -3.88 | -4.26 |
| 30t | 1.59 | -3.62 | 7.62 | 3.44 | 0.62 | -3.61 | -2.80 | -3.83 |
| 35t | 3.25 | -4.13 | 7.25 | 4.26 | 1.25 | -4.79 | -2.00 | -3.52 |

| ecc. | subject MW | | | | subject JC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.46 | -1.88 | -1.25 | 2.54 | 0.66 | -1.94 | 2.37 | -0.75 |
| 30n | 0.23 | -1.79 | -1.34 | 2.14 | 0.14 | -1.87 | -1.59 | -0.60 |
| 25n | -0.33 | -1.73 | -1.47 | 1.83 | -0.32 | -1.65 | 0.87 | -0.55 |
| 20n | -0.64 | -1.64 | -2.85 | 1.64 | -0.84 | -1.58 | 0.43 | -0.24 |
| 15n | -0.83 | -1.32 | -2.95 | 1.59 | -0.95 | -1.49 | 0.78 | 0.16 |
| 10n | -0.62 | -0.93 | -3.02 | 1.23 | -1.02 | -1.43 | 0.78 | 0.40 |
| 5n | -0.16 | -0.54 | -3.66 | 0.48 | -0.66 | -0.98 | 1.30 | 0.96 |
| 0n | 0.62 | -0.27 | -3.55 | 0.55 | -0.62 | -0.87 | 1.30 | 0.61 |
| 5t | -0.13 | -0.47 | -3.13 | 0.46 | -1.13 | -1.46 | 1.20 | 0.00 |
| 10t | -1.18 | -0.66 | -3.88 | 0.76 | -1.18 | -1.35 | 1.05 | -0.29 |
| 15t | -0.95 | -0.95 | -3.95 | 1.12 | -0.95 | -1.37 | 0.80 | -0.52 |
| 20t | -0.50 | -1.34 | -3.50 | 1.42 | -0.50 | -1.45 | 0.87 | -0.55 |
| 25t | 0.35 | -2.41 | -2.35 | 2.17 | 0.35 | -2.24 | 1.17 | -0.45 |
| 30t | 1.59 | -3.62 | -1.62 | 3.44 | 1.59 | -3.71 | 2.07 | -0.35 |
| 35t | 3.25 | -4.13 | -1.25 | 4.26 | 3.25 | -4.05 | 3.67 | -0.63 |

| ecc. | subject JP | | | | subject HM | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -0.26 | -3.23 | -1.25 | -3.86 | 0.66 | -1.94 | 2.35 | -0.75 |
| 30n | -0.41 | -2.85 | -1.34 | -3.54 | 0.14 | -1.87 | 1.52 | -0.60 |
| 25n | -0.52 | -2.44 | -1.47 | -2.83 | -0.32 | -1.65 | 0.98 | -0.55 |
| 20n | -0.84 | -2.38 | -2.85 | -1.78 | -0.84 | -1.58 | 0.73 | -0.24 |
| 15n | -1.05 | -2.15 | -2.95 | -1.66 | -0.95 | -1.49 | 0.54 | -0.16 |
| 10n | -1.22 | -1.74 | -3.02 | -1.23 | -1.02 | -1.43 | -0.18 | -0.40 |
| 5n | -1.66 | -0.98 | -3.66 | -0.98 | -0.66 | -0.98 | -0.30 | -0.96 |
| 0n | -1.32 | -0.87 | -3.85 | -0.75 | -0.62 | -0.87 | -0.70 | -0.61 |
| 5t | -1.13 | -1.26 | -3.13 | -0.46 | -1.13 | -1.46 | 0.20 | -0.00 |
| 10t | -1.18 | -1.47 | -3.88 | -0.76 | -1.18 | -1.35 | 0.65 | -0.29 |
| 15t | -0.95 | -1.58 | -3.95 | -1.12 | -0.95 | -1.37 | 0.80 | -0.52 |
| 20t | -0.60 | -1.93 | -3.50 | -1.51 | -0.50 | -1.45 | 0.98 | -0.55 |
| 25t | -0.31 | -2.48 | -2.35 | -2.17 | 0.35 | -2.24 | 1.45 | -0.45 |
| 30t | -0.12 | -3.71 | -1.62 | -3.44 | 1.59 | -3.71 | 2.03 | -0.35 |
| 35t | 0.24 | -4.32 | -1.25 | -4.26 | 3.25 | -4.05 | 3.21 | -0.63 |

| ecc. | subject SH | | | | subject LY | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 6.64 | 1.87 | 0.66 | -2.53 | -5.76 | -6.54 | -3.02 | -3.87 |
| 30n | 5.72 | 2.32 | 0.14 | -2.28 | -6.15 | -6.82 | -3.54 | -4.32 |
| 25n | 5.24 | 2.41 | -0.32 | -1.85 | -6.45 | -7.11 | -3.97 | -4.41 |
| 20n | 4.62 | 2.77 | -0.84 | -1.64 | -6.84 | -7.32 | -4.22 | -4.77 |
| 15n | 4.28 | 3.43 | -0.95 | -1.45 | -7.06 | -7.55 | -4.28 | -4.43 |
| 10n | 4.39 | 4.15 | -0.62 | -1.31 | -7.26 | -7.86 | -4.39 | -5.15 |
| 5n | 4.64 | 4.23 | -0.46 | -0.28 | -7.44 | -8.09 | -4.64 | -5.23 |
| 0n | 4.37 | 4.45 | -0.22 | -0.57 | -7.65 | -8.42 | -4.87 | -5.45 |
| 5t | 4.38 | 4.54 | -0.73 | -1.26 | -7.43 | -8.22 | -4.68 | -5.54 |
| 10t | 4.45 | 4.23 | -1.06 | -1.37 | -7.25 | -7.96 | -4.65 | -5.23 |
| 15t | 4.52 | 4.15 | -0.95 | -1.44 | -7.04 | -7.46 | -4.54 | -5.15 |
| 20t | 4.61 | 3.76 | -0.50 | -1.67 | -6.87 | -7.28 | -4.34 | -5.36 |
| 25t | 5.29 | 3.02 | 0.35 | -2.24 | -6.53 | -6.94 | -3.76 | -5.02 |
| 30t | 5.75 | 2.72 | 1.59 | -3.75 | -6.21 | -6.41 | -3.75 | -4.65 |
| 35t | 6.12 | 2.16 | 3.25 | -4.37 | -5.88 | -6.19 | -2.12 | -4.21 |

| ecc. | subject RL | | | | subject SL | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 1.42 | -2.42 | 1.37 | -2.07 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 0.80 | -1.76 | 0.74 | -1.78 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 0.44 | -0.84 | 0.56 | -0.95 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 0.58 | -0.97 | 0.49 | -0.77 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 0.22 | -0.67 | 0.31 | -0.65 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 0.12 | -0.39 | 0.14 | -0.44 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 0.09 | -0.61 | 0.05 | -0.38 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 0.14 | -0.34 | 0.02 | -0.22 | -4.40 | -0.55 | -4.21 | -0.58 |
| 5t | 0.44 | -0.66 | 0.12 | -0.56 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 0.67 | -1.55 | 0.10 | -0.99 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 0.34 | -1.67 | 0.36 | -1.47 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 0.14 | -1.63 | 0.39 | -1.59 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 0.32 | -1.92 | 0.45 | -1.87 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 0.97 | -2.55 | 0.88 | -2.49 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 1.13 | -3.49 | 1.32 | -3.28 | -2.13 | -3.87 | -2.07 | -3.73 |

| ecc. | subject YP | | | | subject MC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -1.63 | -1.95 | -1.78 | -2.34 | -4.00 | -4.64 | -3.78 | -4.64 |
| 30n | -1.14 | -1.61 | -1.33 | -1.85 | -4.60 | -4.83 | -4.23 | -4.94 |
| 25n | -2.32 | -1.53 | -2.51 | -1.66 | -5.10 | -5.27 | -4.97 | -5.17 |
| 20n | -2.84 | -1.49 | -2.71 | -1.37 | -5.30 | -5.32 | -5.22 | -5.24 |
| 15n | -2.95 | -1.27 | -2.85 | -1.24 | -5.35 | -5.44 | -5.29 | -5.34 |
| 10n | -3.02 | -1.16 | -3.04 | -0.87 | -5.37 | -5.74 | -5.36 | -5.56 |
| 5n | -3.21 | -0.37 | -3.11 | -0.44 | -5.62 | -5.85 | -5.41 | -5.64 |
| 0n | -2.87 | -0.39 | -3.14 | -0.57 | -5.00 | -5.95 | -5.50 | -5.89 |
| 5t | -3.15 | -0.56 | -3.35 | -0.76 | -5.70 | -5.87 | -5.48 | -5.69 |
| 10t | -2.88 | -0.85 | -2.76 | -0.98 | -5.75 | -5.36 | -5.55 | -5.27 |
| 15t | -2.95 | -1.12 | -2.65 | -1.24 | -5.65 | -5.18 | -5.42 | -5.02 |
| 20t | -2.50 | -1.35 | -2.53 | -1.76 | -5.35 | -4.80 | -5.32 | -4.73 |
| 25t | -1.35 | -2.32 | -1.45 | -2.41 | -4.88 | -4.24 | -4.76 | -4.15 |
| 30t | 0.62 | -3.61 | 0.24 | -3.73 | -3.80 | -3.78 | -3.65 | -3.67 |
| 35t | 1.25 | -4.79 | 1.02 | -5.04 | -2.00 | -3.64 | -1.98 | -3.25 |

| ecc. | subject YH | | | | subject CC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 1.42 | -2.42 | 1.37 | -2.07 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 0.80 | -1.76 | 0.74 | -1.78 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 0.44 | -0.84 | 0.56 | -0.95 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 0.58 | -0.97 | 0.49 | -0.77 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 0.22 | -0.67 | 0.31 | -0.65 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 0.12 | -0.39 | 0.14 | -0.44 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 0.09 | -0.61 | 0.05 | -0.38 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 0.14 | -0.34 | 0.02 | -0.22 | -4.40 | -0.55 | -4.21 | -0.58 |
| 5t | 0.44 | -0.66 | 0.12 | -0.56 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 0.67 | -1.55 | 0.10 | -0.99 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 0.34 | -1.67 | 0.36 | -1.47 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 0.14 | -1.63 | 0.39 | -1.59 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 0.32 | -1.92 | 0.45 | -1.87 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 0.97 | -2.55 | 0.88 | -2.49 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 1.13 | -3.49 | 1.32 | -3.28 | -2.13 | -3.87 | -2.07 | -3.73 |

| ecc. | subject LW | | | | subject SW | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.66 | -2.53 | 1.37 | -2.07 | 0.54 | -4.37 | 1.89 | -4.43 |
| 30n | 0.14 | -2.28 | 1.14 | -1.78 | -0.06 | -3.89 | 1.12 | -3.85 |
| 25n | -0.32 | -1.85 | 1.26 | -0.95 | -0.47 | -3.25 | 0.44 | -3.33 |
| 20n | -0.84 | -1.64 | 0.89 | -0.77 | -0.69 | -2.76 | -0.62 | -2.59 |
| 15n | -0.95 | -1.45 | 0.71 | -0.65 | -0.84 | -2.26 | -0.74 | -2.34 |
| 10n | -0.62 | -1.31 | 0.64 | -0.44 | -1.33 | -1.54 | -1.27 | -1.51 |
| 5n | -0.46 | -0.28 | 0.55 | -0.38 | -1.44 | -0.72 | -1.53 | -0.66 |
| 0n | -0.22 | -0.57 | 0.52 | -0.42 | -1.40 | -0.25 | -1.21 | -0.58 |
| 5t | -0.73 | -1.26 | 0.52 | -0.56 | -1.32 | -0.76 | -1.38 | -0.77 |
| 10t | -1.06 | -1.37 | 0.60 | -0.99 | -0.93 | -1.44 | -0.87 | -1.36 |
| 15t | -0.95 | -1.44 | 0.76 | -1.47 | -0.76 | -1.89 | -0.66 | -1.79 |
| 20t | -0.50 | -1.67 | 0.89 | -1.59 | -0.23 | -2.37 | 0.14 | -2.41 |
| 25t | 0.35 | -2.24 | 0.95 | -1.87 | 0.95 | -2.77 | 0.89 | -2.68 |
| 30t | 1.59 | -3.75 | 1.08 | -2.49 | 1.64 | -3.43 | 1.61 | -3.38 |
| 35t | 3.25 | -4.37 | 1.32 | -3.28 | 1.73 | -3.87 | 2.07 | -3.73 |

| ecc. | subject LC | | | | subject FC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.66 | -2.53 | 1.37 | -2.07 | 2.37 | -0.57 | 0.60 | -1.87 |
| 30n | 0.14 | -2.28 | 1.14 | -1.78 | -1.59 | -0.60 | 0.14 | -1.80 |
| 25n | -0.32 | -1.85 | 1.26 | -0.95 | 0.87 | -0.55 | -0.32 | -1.72 |
| 20n | -0.84 | -1.64 | 0.89 | -0.77 | 0.43 | -0.24 | -0.84 | -1.64 |
| 15n | -0.95 | -1.45 | 0.71 | -0.65 | 0.78 | 0.16 | -0.95 | -1.59 |
| 10n | -0.62 | -1.31 | 0.64 | -0.44 | 0.78 | 0.40 | -1.02 | -1.43 |
| 5n | -0.46 | -0.28 | 0.55 | -0.38 | 1.30 | 0.96 | -0.66 | -0.98 |
| 0n | -0.22 | -0.57 | 0.52 | -0.42 | 1.40 | 0.61 | -0.52 | -0.87 |
| 5t | -0.73 | -1.26 | 0.52 | -0.56 | 1.20 | 0.00 | -1.13 | -1.46 |
| 10t | -1.06 | -1.37 | 0.60 | -0.99 | 1.05 | -0.29 | -1.18 | -1.35 |
| 15t | -0.95 | -1.44 | 0.76 | -1.47 | 0.80 | -0.52 | -0.95 | -1.37 |
| 20t | -0.50 | -1.67 | 0.89 | -1.59 | 0.87 | -0.55 | -0.50 | -1.45 |
| 25t | 0.35 | -2.24 | 0.95 | -1.87 | 1.17 | -0.45 | 0.35 | -2.24 |
| 30t | 1.59 | -3.75 | 1.08 | -2.49 | 2.07 | -0.35 | 1.59 | -3.71 |
| 35t | 3.25 | -4.37 | 1.32 | -3.28 | 3.67 | -0.63 | 3.25 | -4.05 |

| ecc. | subject TP | | | | subject TW | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 1.42 | -2.42 | 1.37 | -2.07 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 0.80 | -1.76 | 0.74 | -1.78 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 0.44 | -0.84 | 0.56 | -0.95 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 0.58 | -0.97 | 0.49 | -0.77 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 0.22 | -0.67 | 0.31 | -0.65 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 0.12 | -0.39 | 0.14 | -0.44 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 0.09 | -0.61 | 0.05 | -0.38 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 0.14 | -0.34 | 0.02 | -0.22 | -4.40 | -0.55 | -4.21 | -0.58 |
| 5t | 0.44 | -0.66 | 0.12 | -0.56 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 0.67 | -1.55 | 0.10 | -0.99 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 0.34 | -1.67 | 0.36 | -1.47 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 0.14 | -1.63 | 0.39 | -1.59 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 0.32 | -1.92 | 0.45 | -1.87 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 0.97 | -2.55 | 0.88 | -2.49 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 1.13 | -3.49 | 1.32 | -3.28 | -2.13 | -3.87 | -2.07 | -3.73 |

| ecc. | subject YC | | | | subject FH | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 0.54 | -4.37 | 0.89 | -4.43 | 1.42 | -2.42 | 1.37 | -2.07 |
| 30n | -0.06 | -3.89 | 0.12 | -3.85 | 0.80 | -1.76 | 0.74 | -1.78 |
| 25n | -0.47 | -3.25 | -0.44 | -3.33 | 0.44 | -0.84 | 0.56 | -0.95 |
| 20n | -0.69 | -2.76 | -0.62 | -2.59 | 0.58 | -0.97 | 0.49 | -0.77 |
| 15n | -0.84 | -2.26 | -0.74 | -2.34 | 0.22 | -0.67 | 0.31 | -0.65 |
| 10n | -1.43 | -1.54 | -1.27 | -1.51 | 0.12 | -0.39 | 0.14 | -0.44 |
| 5n | -1.64 | -0.72 | -1.53 | -0.66 | 0.09 | -0.61 | 0.05 | -0.38 |
| 0n | -1.90 | -0.25 | -1.71 | -0.58 | 0.14 | -0.34 | 0.02 | -0.22 |
| 5t | -1.74 | -0.76 | -1.58 | -0.77 | 0.44 | -0.66 | 0.12 | -0.56 |
| 10t | -1.37 | -1.44 | -0.87 | -1.36 | 0.67 | -1.55 | 0.10 | -0.99 |
| 15t | -0.76 | -1.89 | -0.66 | -1.79 | 0.34 | -1.67 | 0.36 | -1.47 |
| 20t | -0.23 | -2.37 | 0.14 | -2.41 | 0.14 | -1.63 | 0.39 | -1.59 |
| 25t | 0.95 | -2.77 | 0.89 | -2.68 | 0.32 | -1.92 | 0.45 | -1.87 |
| 30t | 1.64 | -3.43 | 1.61 | -3.38 | 0.97 | -2.55 | 0.88 | -2.49 |
| 35t | 1.73 | -3.87 | 2.07 | -3.73 | 1.13 | -3.49 | 1.32 | -3.28 |

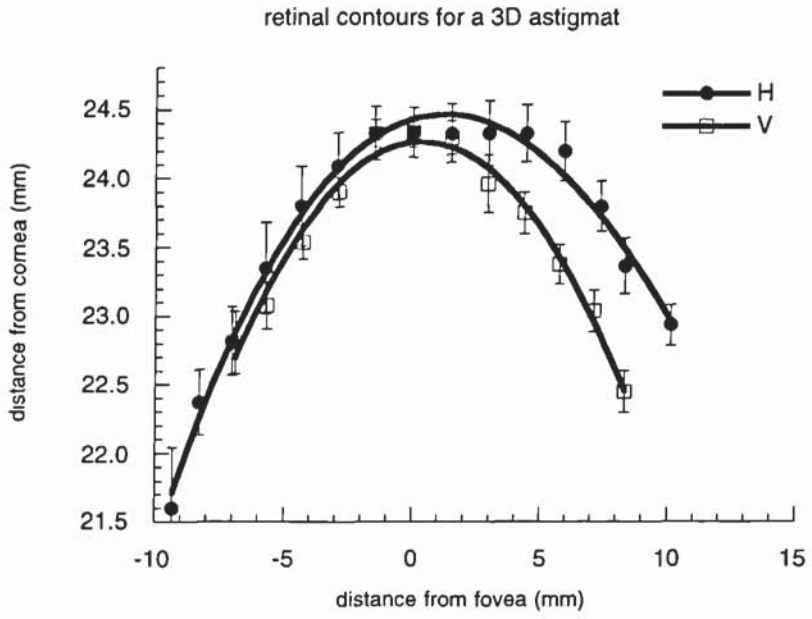
| ecc. | subject YW | | | | subject PC | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 6.64 | 1.87 | 7.12 | 2.14 | 0.66 | -2.53 | 0.79 | -2.41 |
| 30n | 5.72 | 2.32 | 6.32 | 2.44 | 0.14 | -2.28 | 0.36 | -2.15 |
| 25n | 5.24 | 2.41 | 5.52 | 2.56 | -0.32 | -1.85 | -0.27 | -1.88 |
| 20n | 4.62 | 2.77 | 4.77 | 2.73 | -0.84 | -1.64 | -0.77 | -1.57 |
| 15n | 4.28 | 3.43 | 4.41 | 3.58 | -0.95 | -1.15 | -0.84 | -1.03 |
| 10n | 4.39 | 4.15 | 4.27 | 4.19 | -0.62 | -0.71 | -0.66 | -0.66 |
| 5n | 4.64 | 4.23 | 4.31 | 4.44 | -0.26 | -0.28 | -0.35 | -0.38 |
| 0n | 4.37 | 4.45 | 4.22 | 4.52 | 0.12 | -0.12 | 0.20 | -0.18 |
| 5t | 4.38 | 4.54 | 4.36 | 4.68 | -0.43 | -0.56 | -0.11 | -0.49 |
| 10t | 4.45 | 4.23 | 4.57 | 4.37 | -0.66 | -1.17 | -0.45 | -1.24 |
| 15t | 4.52 | 4.15 | 4.48 | 4.25 | -0.95 | -1.44 | -0.89 | -1.52 |
| 20t | 4.61 | 3.76 | 4.76 | 3.65 | -0.50 | -1.67 | -0.57 | -1.72 |
| 25t | 5.29 | 3.02 | 5.66 | 3.28 | 0.35 | -2.24 | 0.26 | -2.19 |
| 30t | 5.75 | 2.72 | 5.98 | 2.63 | 1.59 | -3.75 | 1.75 | -3.55 |
| 35t | 6.12 | 2.16 | 6.47 | 2.22 | 3.25 | -4.37 | 3.03 | -4.74 |

| ecc. | subject JP | | | | subject YF | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | -5.00 | -3.64 | -4.78 | -5.64 | -4.66 | -2.53 | -4.79 | -2.41 |
| 30n | -5.60 | -4.83 | -5.23 | -5.94 | -5.14 | -2.28 | -4.96 | -2.15 |
| 25n | -6.10 | -5.27 | -5.97 | -6.17 | -5.32 | -1.85 | -5.27 | -1.88 |
| 20n | -6.30 | -5.32 | -6.22 | -6.24 | -5.84 | -1.64 | -5.77 | -1.57 |
| 15n | -6.35 | -5.44 | -6.29 | -6.34 | -5.95 | -1.15 | -5.84 | -1.03 |
| 10n | -6.37 | -5.74 | -6.36 | -6.56 | -6.62 | -0.71 | -6.66 | -0.66 |
| 5n | -6.62 | -5.85 | -6.41 | -6.64 | -6.26 | -0.28 | -6.35 | -0.38 |
| 0n | -6.30 | -6.95 | -6.50 | -6.89 | -6.12 | -0.12 | -6.20 | -0.18 |
| 5t | -6.70 | -5.87 | -6.48 | -6.69 | -6.43 | -0.56 | -6.11 | -0.49 |
| 10t | -6.75 | -5.36 | -6.55 | -6.27 | -6.66 | -1.17 | -6.45 | -1.24 |
| 15t | -6.65 | -5.18 | -6.42 | -6.02 | -5.95 | -1.44 | -5.89 | -1.52 |
| 20t | -6.35 | -4.80 | -6.32 | -5.73 | -5.50 | -1.67 | -5.57 | -1.72 |
| 25t | -5.88 | -3.24 | -5.76 | -5.15 | -5.35 | -2.24 | -5.26 | -2.19 |
| 30t | -4.80 | -2.78 | -4.65 | -3.67 | -4.59 | -3.75 | -4.75 | -3.55 |
| 35t | -4.00 | -2.64 | -3.98 | -2.25 | -4.25 | -4.37 | -4.03 | -4.74 |

| ecc. | subject YP | | | | subject SY | | | |
|---|---|---|---|---|---|---|---|---|
| (degrees) | sag r | tang r | sag l | tang l | sag r | tang r | sag l | tang l |
| 35n | 6.64 | 1.87 | 7.12 | 2.14 | -2.00 | -4.37 | -1.89 | -4.43 |
| 30n | 5.72 | 2.32 | 6.32 | 2.44 | -2.06 | -3.89 | -2.12 | -3.85 |
| 25n | 5.24 | 2.41 | 5.52 | 2.56 | -2.47 | -3.25 | -2.44 | -3.33 |
| 20n | 4.62 | 2.77 | 4.77 | 2.73 | -3.69 | -2.76 | -3.62 | -2.59 |
| 15n | 4.28 | 3.43 | 4.41 | 3.58 | -3.84 | -2.26 | -3.74 | -2.34 |
| 10n | 4.39 | 4.15 | 4.27 | 4.19 | -4.33 | -1.54 | -4.27 | -1.51 |
| 5n | 4.64 | 4.23 | 4.31 | 4.44 | -4.44 | -0.72 | -4.53 | -0.66 |
| 0n | 4.37 | 4.45 | 4.22 | 4.52 | -4.50 | -0.65 | -4.51 | -0.68 |
| 5t | 4.38 | 4.54 | 4.36 | 4.68 | -4.32 | -0.76 | -4.38 | -0.77 |
| 10t | 4.45 | 4.23 | 4.57 | 4.37 | -3.93 | -1.44 | -3.87 | -1.36 |
| 15t | 4.52 | 4.15 | 4.48 | 4.25 | -3.76 | -1.89 | -3.66 | -1.79 |
| 20t | 4.61 | 3.76 | 4.76 | 3.65 | -3.23 | -2.37 | -3.14 | -2.41 |
| 25t | 5.29 | 3.02 | 5.66 | 3.28 | -2.95 | -2.77 | -2.89 | -2.68 |
| 30t | 5.75 | 2.72 | 5.98 | 2.63 | -2.64 | -3.43 | -2.61 | -3.38 |
| 35t | 6.12 | 2.16 | 6.47 | 2.22 | -2.13 | -3.87 | -2.07 | -3.73 |

## Appendix 6

### Retinal contour in the horizontal and vertical meridia




Peripheral refraction was measured in both the horizontal and vertical meridia in 5° intervals to a maximum of 35° for 3 subjects. All subjects had at least 3D of astigmatism with orthogonal axis. The retinal contour data for one subject is shown above. The figure demonstrates that the equatorial and vertical diameters of the posterior segment of the globe are of different sizes. Similar results were found for the other two subjects.

## Appendix 7

### Conversion of geometrical length into optical length

```
REM - INCORPORATES ASPHERIC CORNEA
REM - INCORPORATE RETINAL COORDINATES DERIVED FROM PERIPHERAL REFRACTION
REM - PROGRAM AUTOMATICALLY FITS CURVE TO FIND R5 AND P5
REM - USES MEASURED PARAXIAL SCHEMATIC EYE PARAMETERS
REM - AUTOMATICALLY ADDS POST CORNEAL SURFACE
REM - USES REFRACTIVE INDICES FOR RED LASER LIGHT
REM - LIGHT AUTOMATICALLY ENTERS EYE PERPENDICULAR TO CORNEA (LDI)
REM - CALCULATES OPTICAL LENGTHS FOR DIRECT COMPARISON WITH LDI
REM - GIVES OUT CORNEAL INTERCEPT HEIGHTS
REM - ENTER BIOMETRIC PARAMETERS

PRINT " ** ENTER BIOMETRIC MEASUREMENTS ** "
PRINT :INPUT"MERIDIONAL REFRACTIVE ERROR (D)";L1

PRINT :PRINT "IMPORTANT NOTE :"
PRINT "IF ENTERING CORNEAL SEMI-MERIDIA"
PRINT "REMEMBER THAT ONE HALF OF CORNEA"
PRINT "FORMS IMAGES ON OPPOSITE HALF OF RETINA":PRINT

INPUT"MERIDIONAL APICAL RADIUS (MM) OF CORNEA"; R1
INPUT"MERIDIONAL CONIC CONSTANT OF CORNEA"; P1

REM - CALCULATE POSTERIOR CORNEAL SURFACE
REM - (GULLSTRAND)
REM - FIXED ANT:POST CORNEA SURFACE RADIUS; 7.7:6.8
R2=(6.8*R1)/7.7
REM - FIXED CORNEAL THICKNESS OF 0.5 MM (GULLSTRAND)
D1=.0005

INPUT"ANTERIOR CHAMBER DEPTH (MM)";DDD2
DD2=DDD2/1000
D2=DD2-D1
INPUT"LENS THICKNESS (MM)";DD3
D3=DD3/1000
INPUT"VITREOUS CHAMBER DEPTH (MM)";DD4
D4=DD4/1000

REM - ASSUMED REFRACTIVE INDICES (GULLSTRAND)
REM - FOR BIOMETRIC CALCULATIONS ONLY
REM - TAKEN FROM GULLSTRAND (NO1 & 2)
N1=1
N2=1.376
N3=1.336
N4=1.416
N5=1.336

REM - BENNETT (1988) COMPUTING SCHEME
F1=((N2-N1)*1000)/R1
L1B=L1+F1
L2= L1B/(1-((D1/N2)*L1B))
F2=((N3-N2)*1000)/R2
L2B=L2+F2
Q=.38
A=((N3/N4)*(1-Q))/(1-((D3/N4)*Q*21.93#))
EL=A*D3
B=(N3/N4)*Q
ELB=-B*D3
W=D2+EL
L3= L2B/(1-((W/N3)*L2B))
O =-ELB+D4
L3B=N5/O
FL=L3B-L3
F3=Q*FL
R3=((N4-N3)*1000)/F3
F4=-(F3*EL)/ELB
```

```
R4=((N5-N4)*1000)/F4

REM - INPUT RETINAL CONTOUR DATA
CLS
PRINT"INPUT RETINAL COORDINATES"
PRINT "DO EACH HALF OF RETINA SEPARATELY (+VE VALUES ONLY)"

PRINT :PRINT "IMPORTANT NOTE :"
PRINT "REMEMBER THAT ONE HALF OF RETINA"
PRINT "RECEIVES LIGHT FROM OPPOSITE HALF OF CORNEA":PRINT

PRINT :INPUT"HOW MANY X,Y SETS (MAX=9)";SET

REM ZERO ALL ELEMENTS
SUMX1=0:SUMX2=0:SUMY=0
SUMX1SQ=0:SUMX1X2=0:SUMX1Y=0
SUMX2SQ=0:SUMX2Y=0:SUMYSQ=0

FOR SETLOOP=1 TO SET

INPUT"X ";X
INPUT"Y ";Y
PRINT
X1=X
X2=X^2
Y=Y^2

REM CALCULATE INTERMEDIATES
X1SQ=X1^2
X1X2=X1*X2
X1Y=X1*Y
X2SQ=X2^2
X2Y=X2*Y
YSQ=Y^2

REM SUMMATE INTERMEDIATES
SUMX1=SUMX1+X1
SUMX2=SUMX2+X2
SUMY=SUMY+Y
SUMX1SQ=SUMX1SQ+X1SQ
SUMX1X2=SUMX1X2+X1X2
SUMX1Y=SUMX1Y+X1Y
SUMX2SQ=SUMX2SQ+X2SQ
SUMX2Y=SUMX2Y+X2Y
SUMYSQ=SUMYSQ+YSQ

NEXT SETLOOP

REM CALCULATE SUMS OF SQUARES
A=SUMX1SQ-((SUMX1^2)/SET)
B=SUMX1X2-((SUMX1*SUMX2)/SET)
C=SUMX2SQ-((SUMX2^2)/SET)
D=SUMX1Y-((SUMX1*SUMY)/SET)
E=SUMX2Y-((SUMX2*SUMY)/SET)

REM CALCULATE MEANS
YMEAN=SUMY/SET
X1MEAN=SUMX1/SET
X2MEAN=SUMX2/SET

REM CALCULATE COEFFICIENTS
B1=((C*D)-(B*E))/((A*C)-B^2)
B2=((A*E)-(B*D))/((A*C)-B^2)
A=YMEAN-(B1*X1MEAN)-(B2*X2MEAN)

REM CALCULATE RETINAL PARAMETERS
R5=B1/2
P5=-B2
PRINT "FITTED APICAL RADIUS (MM) =";R5
```

```
PRINT "FITTED CONIC CONSTANT =";P5
PRINT :INPUT"PRESS RETURN TO CONTINUE"; XYZ
R5=-R5

REM - CONVERT DISTANCES TO MILLIMETERS
D1=D1*1000
D2=D2*1000
D3=D3*1000
D4=D4*1000

REM - CONVERT INDICES TO THOSE APPROPRIATE FOR LASER LIGHT
REM - ASSUMED INDICES (FOR 780NM; calculated using eqns of Liou & Brennan)
N1=1
N2=1.3722
N3=1.3322
N4=1.4122
N5=1.3322

REM - CONVERT RADII TO CURVATURES
C1=1/R1
C2=1/R2
C3=1/R3
C4=1/R4
C5=1/R5

CLS
INPUT"ANGLE OF EYE ROTATION (LDI)";U
LOOPU:

REM - CARRY OUT LDI RAYTRACE

REM - OPENING-ENSURES RAY STRIKES ASPHERIC CORNEA NORMALLY (AS LDI)

REM - CALCULATION OF ASPHERIC CORNEAL SURFACE NORMAL

REM - DEGREES TO RADIANS CONVERSION FOR TRIG FUNCTIONS
RAD=180/3.1415926535897#

REM - CONIC EQUATIONS (SMITH, 1990, PP 445-446)

GAZE=-U
REM - CALCULATE GAZE FOR GIVEN Y INTERCEPT
  Y=.1
  LOOP:
  EXTRA=1-(P1*(C1^2)*(Y^2))

  REM - ERROR MESSAGE
  IF EXTRA<0 THEN PRINT "IMPORTANT NOTICE :"
  IF EXTRA<0 THEN PRINT"YOU WILL NEED TO ALTER THE GAIN ON FASTLOOP"
  IF EXTRA<0 GOTO END

  X=(C1*(Y^2))/(1+SQR(EXTRA))
  CALGAZE=ATN(-Y/(R1-(P1*X)))*RAD

REM - COMPARE REQUIRED AND CALCULATED GAZE
YDIFF=GAZE-CALGAZE
ABSYDIFF=SQR(YDIFF^2)
IF ABSYDIFF<.000001 THEN GOTO PRINTOUT

NUMBER =1

GOSUB FASTLOOP

PRINTOUT:
  y1=Y
  X1=(C1*(y1^2))/(1+SQR(1-(P1*(C1^2)*(y1^2))))
  SAGR1=SQR(y1^2+(R1-(P1*X1))^2)
  SINNORMANGLE=-y1/SAGR1
  NORMANGLE=ATN(-y1/(R1-(P1*X1)))*RAD
```

```
SINU=-SINNORMANGLE
COSU=COS(-NORMANGLE/57.29578#)
TANU=TAN(-NORMANGLE/57.29578#)
XA=Y/TANU
H=TANU*(100+X1+XA)
Q=(H*COSU)+(-100*SINU)

REM - REFRACTION AT FRONT CORNEA
C1=1/SAGR1
SINI=(Q*C1)-SINU
COSI=SQR(1-(SINI^2))
SINUPLUSI=(SINU*COSI)+(COSU*SINI)
COSUPLUSI=(COSU*COSI)-(SINU*SINI)
SINII=(N1*SINI)/N2
COSII=SQR(1-(SINII^2))
SINUU=(SINUPLUSI*COSII)-(COSUPLUSI*SINII)
COSUU=(COSUPLUSI*COSII)+(SINUPLUSI*SINII)
COSUU1=COSUU
QQ=(Q*(COSUU+COSII))/(COSU+COSI)

X1=(Q*SINUPLUSI)/(COSU+COSI)

REM - TRANSFER TO BACK CORNEA

Q=QQ-(D1*SINUU)
SINU=SINUU
COSU=COSUU

REM - REFRACTION AT BACK CORNEA

SINI=(Q*C2)-SINU
COSI=SQR(1-(SINI^2))
SINUPLUSI=(SINU*COSI)+(COSU*SINI)
COSUPLUSI=(COSU*COSI)-(SINU*SINI)
SINII=(N2*SINI)/N3
COSII=SQR(1-(SINII^2))
SINUU=(SINUPLUSI*COSII)-(COSUPLUSI*SINII)
COSUU=(COSUPLUSI*COSII)+(SINUPLUSI*SINII)
COSUU2=COSUU
QQ=(Q*(COSUU+COSII))/(COSU+COSI)

X2=(Q*SINUPLUSI)/(COSU+COSI)

REM - DISTANCE TRAVELLED BY RAY THRU CORNEA
DCN=(D1-X1+X2)/COSUU1

REM - TRANSFER TO FRONT LENS

Q=QQ-(D2*SINUU)
SINU=SINUU
COSU=COSUU

REM - REFRACTION AT FRONT LENS

SINI=(Q*C3)-SINU
COSI=SQR(1-(SINI^2))
SINUPLUSI=(SINU*COSI)+(COSU*SINI)
COSUPLUSI=(COSU*COSI)-(SINU*SINI)
SINII=(N3*SINI)/N4
COSII=SQR(1-(SINII^2))
SINUU=(SINUPLUSI*COSII)-(COSUPLUSI*SINII)
COSUU=(COSUPLUSI*COSII)+(SINUPLUSI*SINII)
COSUU3=COSUU
QQ=(Q*(COSUU+COSII))/(COSU+COSI)

X3=(Q*SINUPLUSI)/(COSU+COSI)

REM - DISTANCE TRAVELLED BY RAY THRU AQUEOUS
```

```
DAQ=(D2-X2+X3)/COSUU2

REM - TRANSFER TO BACK LENS

Q=QQ-(D3*SINUU)
SINU=SINUU
COSU=COSUU

REM - REFRACTION AT BACK LENS

SINI=(Q*C4)-SINU
COSI=SQR(1-(SINI^2))
SINUPLUSI=(SINU*COSI)+(COSU*SINI)
COSUPLUSI=(COSU*COSI)-(SINU*SINI)
SINII=(N4*SINI)/N5
COSII=SQR(1-(SINII^2))
SINUU=(SINUPLUSI*COSII)-(COSUPLUSI*SINII)
COSUU=(COSUPLUSI*COSII)+(SINUPLUSI*SINII)
COSUU4=COSUU
QQ=(Q*(COSUU+COSII))/(COSU+COSI)

X4=(Q*SINUPLUSI)/(COSU+COSI)
Y4=(Q*(1+COSUPLUSI))/(COSU+COSI)

REM - DISTANCE TRAVELLED BY RAY THRU LENS
DLN=(D3-X3+X4)/COSUU3

REM - TRANSFER TO RETINA

REM - CALCULATE INITIAL X5
Q=QQ-(D4*SINUU)
SINU=SINUU
COSU=COSUU
SINI=(Q*C5)-SINU
COSI=SQR(1-(SINI^2))
SINUPLUSI=(SINU*COSI)+(COSU*SINI)
X5=(Q*SINUPLUSI)/(COSU+COSI)

LOOPR5:

REM - EQUATION OF RAY
REM - FIND U
UR5=(ATN((SQR(1-COSU^2))/COSU))*57.29578#
REM - RAY
YRAY=Y4-(TAN(UR5/57.29578#)*((D4-X4)+X5))

REM - EQUATION OF ASPHERIC RETINAL SURFACE
INTERMEDIATE=SQR(((2*R5*X5)-(P5*(X5^2)))^2)
YSURF=-SQR(INTERMEDIATE)

REM - COMPARE Y FROM RAY AND RETINAL SURFACE
YDIFF=YRAY-YSURF
ABSYDIFF=SQR(YDIFF^2)
IF ABSYDIFF<.000001 THEN GOTO PRINTOUTR5

GOSUB FASTLOOPR5

PRINTOUTR5:
Y5=YSURF

REM - DISTANCE TRAVELLED BY RAY THRU VITREOUS
DVT=(D4-X4+X5)/COSUU4

REM - CALCULATE GEOMETRIC LENGTH
GL=DCN+DAQ+DLN+DVT

REM - CALCULATE OPTICAL LENGTH
OL=(DCN*N2)+(DAQ*N3)+(DLN*N4)+(DVT*N5)
```

```
REM - PRINTOUT
PRINT "corneal intersection height, y";y1
PRINT "OPTICAL LENGTH, GEOMETRIC LENGTH (MM) :"
PRINT OL,GL
PRINT "RETINAL COORDINATES (X,Y) :"
PRINT  X5, Y5
REM - NEXT ANGLE
PRINT :INPUT"NEXT ANGLE (ENTER ANGLE) OR FINISH (PRESS RETURN)";U
IF U>0 THEN GOTO LOOPU

END

REM - SUBROUTINE : FASTLOOP (RAY INTERCEPT WITH ASPHERIC CORNEA)
FASTLOOP:
DIFF(COUNT)=YDIFF
PARAMETER=Y
GAIN=.9
ACCURACY=.000001
INCREMENT=.0000001
IF COUNT=1 THEN GOSUB SPEEDUP
IF COUNT=2 THEN GOSUB SPEEDUP
GOSUB CONVERGE

REM - SUBROUTINE : SPEEDUP
SPEEDUP:
DELTAY=DIFF(COUNT-1)-DIFF(COUNT)
MULTIPLEPARAMETER=DIFF(1)/DELTAY
DELTAPARAMETER=(MULTIPLEPARAMETER*GAIN)*INCREMENT
RETURN

REM - SUBROUTINE : CONVERGE
CONVERGE:
IF COUNT=0 THEN DELTAPARAMETER=INCREMENT
COUNT=COUNT+1
IF COUNT>2 THEN COUNT=0
IF DIFF(COUNT)>ACCURACY THEN GOTO OPTION1
IF DIFF(COUNT)<-ACCURACY THEN GOTO OPTION2
OPTION1:
PARAMETER=PARAMETER+DELTAPARAMETER
IF NUMBER=1 THEN Y=PARAMETER
IF NUMBER=1 THEN GOTO LOOP
OPTION2:
PARAMETER=PARAMETER-DELTAPARAMETER:Y=PARAMETER
IF NUMBER=1 THEN Y=PARAMETER
IF NUMBER=1 THEN GOTO LOOP
RETURN

REM - SUBROUTINE : FASTLOOPR5 (RAY INTERCEPT WITH ASPHERIC RETINA)
FASTLOOPR5:
DIFFR5(COUNTR5)=YDIFF
PARAMETER=X5
GAIN=.9975
ACCURACY=.000001
INCREMENT=.0000001
IF COUNTR5=1 THEN GOSUB SPEEDUPR5
IF COUNTR5=2 THEN GOSUB SPEEDUPR5
GOSUB CONVERGER5
RETURN

REM - SUBROUTINE : SPEEDUPR5
SPEEDUPR5:
DELTAY=DIFFR5(COUNTR5-1)-DIFFR5(COUNTR5)
MULTIPLEPARAMETER=DIFFR5(1)/DELTAY
DELTAPARAMETER=(MULTIPLEPARAMETER*GAIN)*INCREMENT
RETURN

REM - SUBROUTINE : CONVERGER5
CONVERGER5:
IF COUNTR5=0 THEN DELTAPARAMETER=INCREMENT
```

```
COUNTR5=COUNTR5+1
IF COUNTR5>2 THEN COUNTR5=0
IF DIFFR5(COUNTR5)>ACCURACY THEN GOTO OPTION1R5
IF DIFFR5(COUNTR5)<-ACCURACY THEN GOTO OPTION2R5
OPTION1R5:
PARAMETER=PARAMETER+DELTAPARAMETER:X5=PARAMETER
GOTO LOOPR5
OPTION2R5:
PARAMETER=PARAMETER-DELTAPARAMETER:X5=PARAMETER
GOTO LOOPR5
RETURN
```

## Appendix 8

## Corneal topography

Corneal topography data for the Caucasian subjects.

| subject | *p* - value R | *p* - value L | apical radius R (mm) | apical radius L (mm) |
|---|---|---|---|---|
| JF | 0.81 | 0.84 | 7.69 | 7.74 |
| JT | 0.75 | 0.66 | 8.02 | 7.99 |
| KR | 0.75 | 0.76 | 7.74 | 7.74 |
| LW | 0.81 | 0.82 | 7.39 | 7.40 |
| RW | 0.87 | 0.86 | 7.52 | 7.48 |
| GR | 0.68 | 0.66 | 7.92 | 7.91 |
| KS | 0.81 | 0.80 | 8.21 | 8.26 |
| DT | 0.86 | 0.84 | 7.72 | 7.78 |
| RB | 0.70 | 0.60 | 8.24 | 8.26 |
| SK | 0.84 | 0.78 | 7.74 | 7.78 |
| AT | 0.71 | 0.74 | 8.20 | 8.27 |
| ER | 0.69 | 0.66 | 8.25 | 7.76 |
| JB | 0.75 | 0.84 | 7.56 | 8.18 |
| TC | 0.84 | 0.81 | 7.64 | 8.24 |
| MH | 0.81 | 0.83 | 7.92 | 7.57 |
| LD | 0.89 | 0.88 | 7.96 | 7.72 |
| AS | 0.81 | 0.76 | 8.09 | 7.84 |
| MO | 0.73 | 0.70 | 7.74 | 7.96 |
| GB | 0.69 | 0.66 | 7.80 | 8.14 |
| RM | 0.74 | 0.84 | 7.80 | 7.74 |
| KT | 0.83 | 0.79 | 7.93 | 7.82 |
| SL | 0.84 | 0.84 | 7.75 | 7.72 |
| SJ | 0.86 | 0.78 | 8.03 | 7.91 |
| MK | 0.71 | 0.75 | 8.08 | 7.92 |
| RJ | 0.79 | 0.66 | 7.99 | 8.04 |
| ED | 0.67 | 0.73 | 8.48 | 8.23 |
| NP | 0.82 | 0.77 | 7.84 | 7.93 |
| RC | 0.79 | 0.83 | 7.65 | 7.51 |
| SP | 0.83 | 0.77 | 7.73 | 7.87 |
| GH | 0.82 | 0.52 | 8.73 | 8.67 |
| EB | 0.66 | 0.41 | 7.29 | 7.32 |

Corneal topography data for the Caucasian subjects continued.

| subject | *p* - value R | *p* - value L | apical radius R (mm) | apical radius L (mm) |
|---|---|---|---|---|
| JS | 0.75 | 0.76 | 7.20 | 7.35 |
| HW | 0.79 | 0.68 | 8.02 | 7.98 |
| NG | 0.69 | 0.71 | 7.38 | 7.34 |
| PK | 0.72 | 0.75 | 7.70 | 7.69 |

Corneal topography data for the Chinese subjects

| subject | ap. radius R (mm) | ap. radius L (mm) | rate N flat R | rate T flat R | rate N flat L | rate T flat L |
|---|---|---|---|---|---|---|
| RL | 7.50 | 7.61 | 7.90 | 7.80 | 7.90 | 7.80 |
| JK | 8.00 | 8.10 | 8.30 | 8.20 | 8.20 | 8.60 |
| SH | 7.60 | 7.71 | 8.30 | 7.80 | 8.30 | 7.80 |
| MH | 7.70 | 7.59 | 8.40 | 7.90 | 8.10 | 7.90 |
| PL | 7.80 | 7.80 | 8.10 | 8.00 | 8.10 | 8.00 |
| JT | 7.80 | 7.77 | 8.20 | 8.10 | 8.40 | 8.20 |
| YH | 7.85 | 7.70 | 8.00 | 8.00 | 8.40 | 8.10 |
| LC | 7.73 | 7.40 | 7.90 | 7.70 | 7.80 | 7.60 |
| MH | 7.44 | 7.50 | 8.30 | 7.90 | 8.30 | 7.90 |
| CL | 7.71 | 7.80 | 8.60 | 8.30 | 8.40 | 8.20 |
| JH | 7.99 | 7.20 | 7.90 | 7.50 | 7.70 | 7.40 |
| RL | 7.41 | 7.58 | 7.90 | 7.80 | 7.80 | 7.70 |
| JF | 7.61 | 7.62 | 8.20 | 7.90 | 8.20 | 7.90 |
| JY | 7.59 | 7.69 | 8.30 | 7.90 | 8.40 | 8.00 |
| MW | 7,78 | 7.40 | 7.80 | 7.60 | 8.10 | 7.60 |
| JC | 7.40 | 7.40 | 7.90 | 7.80 | 7.70 | 7.77 |
| JP | 7.22 | 7.30 | 8.10 | 8.20 | 8.40 | 8.20 |
| HM | 7.70 | 7.60 | 8.10 | 7.80 | 8.10 | 7.90 |
| RL | 7.60 | 7.58 | 8.60 | 8.60 | 8.70 | 8.60 |
| SL | 8.21 | 8.30 | 7.70 | 7.80 | 7.60 | 7.50 |
| YP | 7.44 | 7.50 | 8.50 | 8.10 | 8.50 | 7.90 |
| MC | 7.81 | 7.80 | 8.50 | 8.10 | 8.40 | 8.20 |
| YH | 7.80 | 7.70 | 8.30 | 7.90 | 8.30 | 7.80 |

ap.radius, apical radius; rate N flat, rate of nasal flattening; rate T flat, rate of temporal flattening.

## Appendix 9

## Accommodation

Mean accommodation values for the Caucasian subjects.

| subject | R amp of acc (D) | R acc err ind. | R TA (D) | L amp of acc (D) | L acc err ind. | L TA (D) |
|---|---|---|---|---|---|---|
| GH | 10.50 | 0.41 | 0.53 | 10.00 | 0.54 | 0.76 |
| SP | 11.00 | 0.26 | 0.72 | 11.25 | 0.22 | 0.66 |
| GR | 9.75 | 0.37 | 0.99 | 9.25 | 0.44 | 1.12 |
| KT | 9.50 | 0.50 | 1.31 | 10.00 | 0.39 | 1.45 |
| RC | 9.25 | 0.81 | 1.03 | 9.75 | 0.77 | 0.89 |
| RM | 10.25 | 0.85 | 1.92 | 10.00 | 0.84 | 1.57 |
| AD | 10.50 | 0.34 | 0.41 | 11.00 | 0.58 | 0.65 |
| JF | 10.75 | 0.22 | 0.55 | 10.00 | 0.33 | 0.74 |
| MH | 9.75 | 0.14 | 0.49 | 10.00 | 0.28 | 0.72 |
| TC | 11.25 | 0.27 | 1.45 | 11.75 | 0.16 | 1.23 |
| MO | 9.50 | 0.72 | 0.49 | 9.75 | 0.69 | 0.62 |
| NG | 8.75 | 0.29 | 0.55 | 9.25 | 0.41 | 0.44 |
| NP | 8.75 | 0.43 | 0.97 | 8.50 | 0.28 | 1.17 |
| AS | 9.00 | 0.74 | 0.25 | 9.75 | 0.87 | 0.63 |
| KS | 10.00 | 0.51 | 0.99 | 10.50 | 0.66 | 0.67 |
| ED | 10.00 | 0.19 | 0.34 | 10.25 | 0.20 | 0.56 |
| KB | 11.00 | 0.22 | 1.25 | 11.55 | 0.65 | 1.74 |
| JT | 8.50 | 0.16 | 1.67 | 9.00 | 0.35 | 1.89 |
| FR | 11.00 | 0.57 | 0.54 | 11.25 | 0.41 | 0.47 |
| AT | 10.75 | 0.77 | 0.64 | 10.50 | 0.68 | 0.69 |
| HW | 10.50 | 0.26 | 0.88 | 10.50 | 0.42 | 0.88 |
| PK | 10.75 | 0.19 | 1.79 | 10.75 | 0.11 | 2.02 |
| EM | 9.60 | 0.22 | 2.05 | 10.20 | 0.18 | 2.15 |
| SK | 9.60 | 0.25 | 2.56 | 9.75 | 0.46 | 2.75 |
| ER | 10.40 | 0.17 | 1.74 | 10.40 | 0.27 | 1.79 |
| MK | 9.75 | 0.65 | 1.22 | 10.25 | 0.83 | 1.54 |
| RW | 9.80 | 0 43 | 0.65 | 9.60 | 0.25 | 0.77 |
| EB | 10.70 | 0 94 | 0.87 | 10.90 | 0.88 | 0.54 |
| KR | 8.70 | 0.18 | 1.34 | 8.70 | 0.26 | 1.72 |
| GG | 9.60 | 0.60 | 1.25 | 10.20 | 0.70 | 1.27 |
| JB | 10.25 | 0.28 | 1.10 | 10.60 | 0.38 | 1.32 |
| JS | 10.75 | 0.17 | 2.09 | 10.75 | 0.24 | 2.26 |
| RJ | 9 80 | 0 28 | 2 29 | 10.00 | 0.21 | 2.05 |

Mean accommodation data continued.

| subject | R amp of acc (D) | R acc err ind. | R TA (D) | L amp of acc (D) | L acc err ind. | L TA (D) |
|---|---|---|---|---|---|---|
| RB | 9.75 | 0.29 | 2.48 | 9.50 | 0.17 | 2.22 |
| SL | 8.75 | 0.51 | 0.43 | 8.60 | 0.62 | 0.63 |
| LW | 9.75 | 0.56 | 0.25 | 10.20 | 0.43 | 0.77 |
| EM | 10.25 | 0.22 | 0.96 | 10.40 | 0.29 | 1.28 |
| DT | 10.60 | 0.20 | 0.31 | 10.80 | 0.17 | 0.45 |
| NB | 11.25 | 0.18 | 1.21 | 11.25 | 0.35 | 1.07 |
| GB | 11.00 | 0.38 | 0.73 | 10.80 | 0.68 | 0.82 |
| SF | 10.75 | 0.51 | 1.52 | 10.50 | 0.79 | 1.75 |

## Appendix 10

## Fundus morphology

Mean fundus morphology data for the Caucasian subjects.

| subject | VDD R (mm) | VDD L (mm) | DFD R (mm) | DFD L (mm) |
|---|---|---|---|---|
| GH | 1.68 | 1.66 | 3.83 | 3.98 |
| SP | 1.83 | 1.79 | 4.11 | 3.87 |
| GR | 1.88 | 1.95 | 4.17 | 4.22 |
| KT | 1.81 | 1.90 | 4.29 | 4.04 |
| RC | 1.49 | 1.54 | 3.25 | 4.22 |
| RM | 1.51 | 1.47 | 3.85 | 3.40 |
| AT | 1.58 | 1.63 | 3.76 | 3.77 |
| HW | 1.60 | 1.65 | 4.09 | 4.13 |
| PK | 1.76 | 1.70 | 4.70 | 4.59 |
| EM | 1.62 | 1.62 | 4.72 | 4.73 |
| AD | 1.63 | 1.58 | 3.35 | 3.19 |
| JF | 1.46 | 1.56 | 3.39 | 3.88 |
| MH | 1.56 | 1.57 | 3.72 | 3.56 |
| SK | 1.58 | 1.60 | 4.30 | 4.21 |
| ER | 1.34 | 1.39 | 4.07 | 3.63 |
| MK | 1.61 | 1.57 | 3.44 | 3.51 |
| RW | 1.55 | 1.58 | 3.72 | 3.67 |
| EB | 1.57 | 1.56 | 3.58 | 3.56 |
| KR | 1.50 | 1.50 | 3.37 | 3.98 |
| GG | 1.51 | 1.52 | 3.35 | 3.31 |
| JB | 1.40 | 1.40 | 3.60 | 3.59 |
| JS | 1.98 | 1.86 | 3.80 | 3.76 |
| TC | 1.52 | 1.54 | 3.45 | 3.63 |
| MO | 1.88 | 1.84 | 3.93 | 3.40 |
| NG | 1.62 | 1.65 | 3.61 | 3.37 |
| RJ | 1.65 | 1.64 | 4.13 | 4.14 |
| SF | 1.47 | 1.49 | 3.54 | 3.53 |
| RB | 1.59 | 1.57 | 3.98 | 3.77 |
| NP | 1.47 | 1.47 | 3.63 | 3.63 |
| SL | 1.49 | 1.48 | 3.47 | 3.44 |
| DT | 1.62 | 1.62 | 3.65 | 3.73 |
| LW | 1.41 | 1.41 | 3.71 | 3.69 |
| AS | 1.48 | 1.49 | 3.84 | 3.82 |

VDD, vertical disc diameter; DFD, disc-to-fovea distance.

Mean fundus morphology data continued.

| subject | VDD R (mm) | VDD L (mm) | DFD R (mm) | DFD L (mm) |
|---|---|---|---|---|
| LD | 1.49 | 1.47 | 3.39 | 3.37 |
| EM | 1.72 | 1.69 | 3.84 | 3.83 |
| NB | 1.79 | 1.75 | 3.84 | 3.69 |
| ED | 1.44 | 1.46 | 4.59 | 3.81 |
| DT | 1.41 | 1.42 | 3.34 | 3.28 |
| KS | 1.25 | 1.26 | 3.72 | 3.41 |
| GB | 1.54 | 1.56 | 3.51 | 3.72 |

## Appendix 11

## Ocular blood flow

Mean puematonographic data for the Caucasian subjects.

| subject | IOP R (mmHg) | IOP L (mmHg) | PA R (mmHg) | PA L (mmHg) | PV R (µl) | PV L (µl) | OBF R (µl per min) | OBF L (µl per min) |
|---|---|---|---|---|---|---|---|---|
| MC | 16.2 | 17.5 | 1.8 | 1.6 | 4.4 | 4.1 | 444 | 408 |
| SP | 11.5 | 14.7 | 1.6 | 2.4 | 4.4 | 5.4 | 894 | 966 |
| GH | 15.5 | 13.0 | 1.4 | 1.4 | 3.0 | 3.4 | 761 | 535 |
| NC | 13.9 | 12.6 | 2.4 | 2.3 | 5.8 | 5.9 | 723 | 598 |
| RC | 10.4 | 11.2 | 2.8 | 2.4 | 7.2 | 6.1 | 740 | 667 |
| RM | 15.0 | 16.4 | 2.3 | 2.9 | 5.2 | 6.0 | 883 | 1166 |
| AS | 17.0 | 19.3 | 4.05 | 4.5 | 6.41 | 5.31 | 1009 | 1014 |
| HW | 14.3 | 13.3 | 2.1 | 1.9 | 4.8 | 4.6 | 447 | 507 |
| YN | 15.0 | 14.7 | 2.2 | 2.1 | 5.8 | 5.6 | 376 | 394 |
| SY | 15.8 | 15.6 | 1.8 | 2.0 | 4.8 | 4.9 | 309 | 317 |
| JT | 12.4 | 12.0 | 2.4 | 2.6 | 6.2 | 6.8 | 594 | 625 |
| AC | 15.2 | 15.7 | 2.1 | 1.7 | 4.9 | 4.6 | 429 | 411 |
| MH | 13.1 | 13.7 | 3.3 | 2.6 | 8.1 | 6.1 | 952 | 696 |
| SK | 16.4 | 15.8 | 2.9 | 1.9 | 5.9 | 5.4 | 727 | 705 |
| JB | 12.0 | 12.5 | 1.1 | 1.5 | 3.9 | 3.8 | 466 | 466 |
| LD | 16.0 | 18.5 | 3.0 | 2.4 | 4.9 | 4.3 | 665 | 815 |
| RW | 17.9 | 17.0 | 1.7 | 1.7 | 6.9 | 7.0 | 545 | 465 |
| GG | 17.0 | 16.8 | 4.55 | 4.01 | 7.18 | 6.59 | 764 | 748 |
| KR | 10.9 | 11.2 | 3.65 | 2.2 | 5.5 | 5.2 | 874 | 798 |
| SF | 17.1 | 16.8 | 2.4 | 2.8 | 7.0 | 7.6 | 711 | 688 |
| ER | 15.0 | 15.3 | 3.05 | 1.93 | 4.71 | 4.17 | 862 | 772 |
| EA | 11.8 | 11.4 | 2.5 | 2.3 | 5.3 | 5.5 | 829 | 841 |
| JF | 18.4 | 14.4 | 3.05 | 3.04 | 5.64 | 4.93 | 451 | 357 |
| MO | 13.9 | 13.2 | 2.0 | 2.1 | 4.7 | 5.1 | 629 | 853 |
| AD | 11.2 | 10.7 | 2.4 | 3.0 | 5.4 | 6.7 | 773 | 804 |
| RJ | 12.5 | 12.9 | 1.9 | 1.8 | 5.8 | 5.7 | 696 | 711 |
| MK | 11.8 | 11.3 | 2.1 | 2.3 | 5.7 | 5.6 | 823 | 849 |
| AH | 12.1 | 11.9 | 2.8 | 2.7 | 6.7 | 6.6 | 931 | 927 |
| JE | 14.1 | 13.7 | 2.9 | 3.0 | 7.1 | 7.2 | 774 | 752 |
| SE | 13.2 | 12.9 | 3.0 | 2.8 | 8.3 | 8.1 | 963 | 947 |

Mean pneumatonographic data continued.

| subject | IOP R (mmHg) | IOP L (mmHg) | PA R (mmHg) | PA L (mmHg) | PV R (µl) | PV L (µl) | OBF R (µl per min) | OBF L (µl per min) |
|---|---|---|---|---|---|---|---|---|
| IF | 16.3 | 17.1 | 2.1 | 1.6 | 4.2 | 3.9 | 429 | 396 |
| EB | 13.1 | 12.8 | 2.7 | 2.8 | 6.7 | 6.9 | 569 | 618 |
| SL | 15.7 | 15.3 | 2.2 | 1.7 | 4.9 | 4.1 | 502 | 451 |
| DT | 10.9 | 10.7 | 3.1 | 3.2 | 6.8 | 6.7 | 784 | 762 |
| LW | 19.3 | 16.4 | 1.7 | 1.6 | 3.0 | 3.3 | 477 | 494 |
| AS | 16.3 | 18.1 | 1.3 | 1.9 | 3.24 | 4.03 | 754 | 836 |
| EM | 18.5 | 18.0 | 1.8 | 2.0 | 4.6 | 3.3 | 553 | 417 |
| RS | 12.4 | 12.1 | 3.2 | 3.0 | 5.4 | 5.6 | 835 | 829 |
| KS | 13.8 | 13.4 | 1.5 | 1.9 | 5.4 | 6.2 | 716 | 697 |
| TC | 14.8 | 15.9 | 2.0 | 1.5 | 5.6 | 5.2 | 361 | 329 |
| SJ | 15.5 | 13.9 | 1.7 | 2.4 | 4.1 | 4.6 | 603 | 625 |

HRF data for one subject

| | nasal | superior | inferior | temporal |
|---|---|---|---|---|
| volume | 19.05 (15.45) | 11.21 (7.27) | 11.67 (6.98) | 13.46 (8.29) |
| flow | 365.38 (366.90) | 202.16 (176.08) | 255.64 ( 185.25) | 283.21 ( 228.02) |
| velocity | 1.27 (1.17) | 0.75 (0.63) | 0.94 ( 0.67) | 1.04 ( 0.82) |

all vaules are in arbitrary units. standard deviations are in parenthesis.

measurements were obtained at 20 pixels from the macula nasally, superiorly, inferiorly and temporally.

## Appendix 12

## Calculations for ocular volume

$y = ax^2 + bx + c$ *Retinal contour equation*

Section 1 Roots of the quadratic equation

$a := -0.051$

$b := 0.032$

$c := 22.11$

$$X_1 := \frac{-b + \sqrt{b^2 - 4 \cdot a \cdot c}}{2 \cdot a} \qquad X_2 := \frac{-b - \sqrt{b^2 - 4 \cdot a \cdot c}}{2 \cdot a}$$

$X_1 = -20.51$ $X_2 = 21.137$

Section 2 Intersection of retinal contour and transverse section of the eye at an axial length of h mm

$h := 15$

$$X_3 := \frac{-b + \sqrt{b^2 - 4 \cdot a \cdot (c - h)}}{2\ a} \qquad X_4 := \frac{-b - \sqrt{b^2 - 4 \cdot a \cdot (c - h)}}{2 \cdot a}$$

$X_3 = -11.498$ $X_4 = 12.125$

Section 3 Volume of vitreous chamber bounded by the transverse section of the eye at an axial length of h mm

$\alpha := 0$

$\beta := X_3$ The value of "x" at y = h

$\gamma := X_1$ The +ve root of the quadratic

$g(x) := a \cdot x^2 + b \cdot x + c$ Retinal contour equation

$V := 2 \cdot \pi \cdot \int_{\alpha}^{\beta} g(x) \cdot x \, dx$ Equation to calculate the volume of the eye

$F(x) := a \cdot x^3 + b \cdot x^2 + c \cdot x$ $F(x) = g(x) \cdot x$

$$\text{Volume} := \left[ \left( \int_{\alpha}^{\gamma} F(x) \, dx \right) \cdot \pi \cdot 2 \right] - \left[ \left( \int_{\beta}^{\gamma} F(x) \, dx \right) \cdot 2 \cdot \pi \right] - (\pi \cdot \beta^2 \cdot h)$$

$\text{Volume} = 1.451 \cdot 10^3 \ \text{mm}^3$

## Appendix 13

## Supporting publications

### Refereed published abstracts of conference proceedings

Logan, N.S., Gilmartin, B., Wildsoet, C.F., Dunne, M.C.M. and Malingré, R. (1995) Asymmetry of schematic retinal contour in anisomyopia. Invest. Ophthalmol. Vis. Sci., 36: S949

Logan, N.S. and Gilmartin, B. Optic disc size and disc-to-fovea distance in ametropia. Invest. Ophthalmol. Vis. Sci., 37: S476

### Published paper from conference transactions

Logan, N.S. and Gilmartin, B. Computation of retinal contour in anisomyopia. Ophthal. Physiol. Opt., 15: 363-366

### In preparation

Logan, N.S. and Gilmartin, B. Incidence and aetiology of anisomyopia. In: Myopia and nearwork. Eds. Rosenfield, M. and Gilmartin, B. Butterworths-Heinemann, London, UK