On and off-axis monochromatic aberrations and myopia in young children

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ON AND OFF-AXIS MONOCHROMATIC ABERRATIONS

AND MYOPIA IN YOUNG CHILDREN

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Purpose: To study "on" and "off-axis" wavefront aberration of eyes of children and to determine the relationship with refractive error development.

Methods: On and off-axis ocular aberrations of cyclopleged eyes of children (mostly 12 year olds) were measured and compared to data obtained from a group of mostly 6 year old children. Only data from the right eyes were analysed (pupil diameter=5 mm) and categorised into refractive error groups based on "M". Differences in "on" and "off-axis" aberrations between refractive and ethnic groups were analysed using univariate and multivariate analyses of variance with adjustment for multiple comparisons. Off-axis refraction was analysed using skiagrams and mean relative spherical equivalent.

Results: Data from 1,636 12 year old children (mean age 12.6 ± 0.4 years) was analysed. Lower order aberrations were the largest and higher order aberrations contributed to only 25% of the wavefront. There were no differences in the amount of total higher orders between refractive groups. Of the individual higher orders, spherical aberration was greater in hyperopic eyes (0.07 ± 0.06 µm) in comparison to emmetropic and myopic eyes (0.05 ± 0.04 µm and 0.05 ± 0.04 µm) ($p<0.001$). Myopic eyes had more positive values of Z(3,-1) ($p<0.05$). Similar results were obtained for the 1,364 6 year old children (mean age 6.7 ± 0.4 years). Despite East Asian children being more myopic than other ethnic groups ($p<0.01$), there were no differences in higher orders except for low hyperopic East Asian eyes presenting with higher levels of positive spherical aberrations ($p<0.001$). When compared to the fovea, off-axis myopic eyes had hyperopia (0.55 to 1.66 D) and emmetropes and hyperopes had myopia (0.10 to -2.00 D). Astigmatism and defocus were the dominant off-axis aberrations. The magnitude of higher order aberrations (mostly 3rd orders) increased with eccentricity but was similar across refractive error groups.

Conclusions: Myopic eyes do not have abnormal or excessive levels of on and off-axis higher order aberrations but had patterns of off-axis refraction that may be associated with progression. Considerable inter-subject variability in higher order aberrations was seen for all refractive groups. However, their magnitude was small and suggests that any impact on the optical quality of the eye is negligible.

ABBREVIATIONS

ACD	=	anterior chamber depth
AL	=	axial length
ANOVA	=	analysis of variance
B-F	=	Brown-Forsythe
CI	=	confidence interval
COAS	=	Complete Ophthalmic Analysis System
CR	=	coefficient of repeatability
D	=	dioptre
G-H	=	Games-Howell
HO	=	higher order
HOA	=	higher order aberration
LED	=	light-emitting diode
LO	=	lower order
LOA	=	lower order aberration
LSA	=	longitudinal spherical aberration
OR	=	odds ratio
PD	=	pupil diameter
RE	=	refractive error
RMS	=	root mean squared
SA	=	spherical aberration
SD	=	standard deviation
SE	=	spherical equivalent
VCD	=	vitreous chamber depth

CHAPTER 1: INTRODUCTION

1.1 INTRODUCTION

In the first few years of life the eye experiences a series of structural changes leading to the matching of the optical power of the eye with its axial length (AL) (or emmetropia) in a process commonly known as emmetropisation. In humans, emmetropisation has been reported to occur before the age of 6 years old, with the dispersion of refractions being the largest shortly after birth and smallest at 6 years old (Gwiazda *et al.* 1993A). The prevalence of emmetropia in newborns is low in comparison to older children. Gwiazda *et al.* (1993A), for example, found that while only 22% of children are emmetropic at infancy, 80% of children are emmetropic by the age of 6 years old. Hyperopia and astigmatism are the most common refractive errors (RE) in newborns and infants (Ehrlich *et al.* 1997; Gwiazda *et al.* 1993A; Gwiazda *et al.* 2000; Ingram 1979; Ingram and Barr 1979; Mutti *et al.* 2004A; Saunders *et al.* 1995). It has been estimated that approximately 88% of newborns have hyperopia of +1.00 dioptre (D) (Watanabe *et al.* 1999). However, after birth a rapid decrease of hyperopia occurs from 1 month to 48 months old (Mayer *et al.* 2001). Astigmatism >1.00 D (mostly "with-the-rule" and corneal in nature) is also common in infants (Howland and Sayles 1985; Shankar and Bobier 2004), having its greatest incidence at 3 months old, and decreasing rapidly during the first year of life to reach its lowest incidence between the ages of 3 to 10 years old (Atkinson *et al.* 1980; Gwiazda *et al.* 1993A; Gwiazda *et al.* 2000; Mohindra *et al.* 1978; Mutti *et al.* 2004A).

Myopia is noted in healthy infants (Watanabe *et al.* 1999), with a prevalence not higher than 3% (Mayer *et al.* 2001), although this prevalence is higher in premature infants ranging from 25 to 43% (Cook and Glasscock 1951; Goldschmidt 1969; Goss 1985; Grosvenor 1987).

Emmetropisation occurs more rapidly in the presence of high REs in infants (Ehrlich *et al.* 1997; Saunders *et al.* 1995). The reduction of the RE during emmetropisation in infants from 9 to 20 months old has been reported to depend directly upon its initial magnitude (at greater magnitudes of spherical and astigmatic RE, greater meridional emmetropisation is likely; Ehrlich *et al.* 1997). Recently (Mutti *et al.* 2004A) reported that astigmatism in infancy appears to be unrelated to emmetropisation of refractive spherical equivalent (SE) because emmetropisation of SE was faster (majority completed by 9 months) in comparison to 36 months for astigmatism.

Sir Stewart Duke-Elder noted "*it is an extraordinary fact that an approximation to emmetropia is maintained throughout infancy and childhood in spite of great alterations in the constituents of the refractive system*" (Duke-Elder and Abrams 1970).

During the first year of life, the cornea exhibits its fastest growth (Ronneburger *et al.* 2006) and also shows a rapid corneal flattening of approximately 1.5 mm (York and Mandell 1969) which translates into a rapid decrease of corneal power of approximately 5.00 D in the first 8 weeks of life (Inagaki 1986). Whilst this corneal flattening continues at a lower rate until the age of 6, the central corneal radii tend to become stabilised at approximately 1 year old, falling within the normal range for adults (York and Mandell 1969). After infancy and early childhood, the cornea seems to play little or no role in the process of emmetropisation (Grosvenor and Goss 1998).

From birth to 13 years old, the mean value of the anterior chamber depth (ACD) increases from 2.37 to 3.70 mm for boys and from 2.39 to 3.62 mm for girls, having then reached the same value as in young adults (Larsen 1971A). Several studies have reported that the main change that the crystalline lens experiences during infancy and childhood is a reduction of power of approximately 20 D (Garner *et al.* 1995; Larsen 1971B; Wood *et al.* 1996; Zadnik 1997). Two main mechanisms have been attributed to this reduction of power which ranges from 44.8 D in infancy to 25 D at age 6 (Wood *et al.* 1996): (a) a decrease in the equivalent refractive index of the crystalline lens (Wood *et al.* 1996); and (b) lens thinning (Larsen 1971B; Zadnik 1997). Wood *et al.* (1996) reported that the major contributor to this decrease is the equivalent index (14.8 D or 75%) and that only 4.9 D or 25% is due to changes in the radius of curvature. Larsen (1971B) reported that, during the first year and a half of life, the thickness of the crystalline lens decreases approximately 0.3 to 0.4 mm, with a further reduction of approximately 0.2 to 0.3 mm by puberty (11 to 13 years). This finding was later supported by Zadnik (1997) and Zadnik *et al.* (2003) who also found that a flattening of the lens surface occurs during infancy and childhood.

One of the most important changes that occur during ocular development is an increase of AL (mainly associated with an increase in the vitreous chamber depth (VCD); Garner *et al.* 1995). The mean value for the length of the VCD in newborns ranges between 10 and 11 mm, increasing by approximately 3.0 mm during the course of the first year and a half of life, 1.3 mm from ages 2 to 7 and by a further 1.1 mm until the age of 13. At this age, the mean value in the length of the vitreous chamber has then reached values as for young emmetropic adults (Larsen 1971C). Larsen (1971D) postulated that the growth of the eye can be divided into three growth phases: A rapid post-natal phase with an increase in length of 3.7 to 3.8 mm in the first year and a half of life, a slower infantile phase until the age of 5 with an increase in length of 1.1 to 1.2 mm and followed by a slow juvenile phase up to the age of 13 years, with an increase of 1.3 to 1.4 mm.

Although the concept of emmetropisation has been challenged by Hofstetter 1969 who stated that "*The so-called emmetropisation is merely an error of mathematical assumption that the radial dimensions of the eye (r) are inherently related to the refractive error, since the radial dimensions for the universal emmetropic eye drop out of the Gaussian formula. A special biological process does not have to be postulated to explain the leptokurtosis of refractive error distribution.*", others like Gilmartin (2004), support the existence of an inter-relationship between refractive components, such as the cornea and AL (Baldwin 1964), which act together as an emmetropisation mechanism, indicating the eye growth is a coordinated process rather than a haphazard collection of individually varying components. Furthermore, using mathematical models, it has been shown that, in order to obtain emmetropia and match the increase of AL from 22 to 26 mm, the back power of the anterior segment of the eye has to decrease from 88.39 to 72.13 D. Most of this compensation reduction is attributable to the lens (57%) followed by the cornea (36%) and the ACD (7%) (Dunne 1993).

1.2 MYOPIA

1.2.1 Definition

Over the years many definitions of myopia have been proposed based on optical or physical characteristics of the eye. Sir Stewart Duke-Elder in his book, System of Ophthalmology (Duke-Elder and Abrams 1970), provides the etymology of the word myopia: "*(μύω I close; ώψ the eye) (from the habit of short-sighted people develop of half closing the lids to gain the advantage of a stenopeic aperture)"* and defines myopia as *"that form of refractive error wherein parallel rays of light come into a focus in front of the sentient layer of the retina when the eye is at rest. Myopia occurs when parallel rays of light are not focused exactly upon the retina but in front of it with the eye in a state of rest. This is because the eye is relatively too long"*.

A simple definition of myopia from the optical point of view is provided by (Grosvenor and Goss 1999) as *"myopia is a refractive condition in which parallel rays are focused in front of the retina with accommodation at a zero level"*. This definition is further extended by Hofstetter *et al.* (2000): "*The refractive condition of the eye represented by the location of the conjugated focus of the retina at some finite point in front of the eye, when accommodation is said to be relaxed, or to the extent of that condition represented in the number of diopters of concave lens power required to compensate to the optical equivalent of emmetropia. The condition may also be represented as one in which parallel rays of light entering the eye, with accommodation relaxed, focus in front of the retina."*

1.2.2 Classification of Myopia

Over the years different classification systems of myopia have been proposed with most systems having the tendency to reflect ideas or theories regarding the aetiology or progression of the myopia. Reviews of the most representative classifications of myopia of the last 140 years can be found in Grosvenor (1987) and Edwards (1998). Myopia has been classified on the basis of its rate of progression, degree, age of onset, aetiology, biological variability, ocular accommodative state, relationship with degenerative ocular effects, physical ocular characteristics (such as axial or dioptric power), intraocular pressure, association with light conditions and statistical distribution of the RE. One method for classification of myopia that has been widely used in the myopia research community is based on the age-related prevalence and age-onset of myopia (Grosvenor 1987). The system consists of four categories (congenital myopia, youth-onset myopia, early adult-onset myopia and late adult-onset myopia). Congenital myopia is the myopia that persists during infancy and is present in the child when entering school. This type of myopia is usually high in magnitude and it is said to have a strong genetic aetiology. Young-onset myopia occurs during the age of 6 to the teenage years. The onset of this type of myopia is said to be strongly influenced by the environment and usually does not exceed 3.00 D. Early adult-onset myopia occurs primarily during the 2nd to the 4th decades of life. In most cases this kind of myopia will not exceed 3.00 D and will be relatively stable throughout life. Late-adult-onset myopia usually occurs after 40 years old and continually increases in the later years of life. This kind of myopia is often associated with physiological ocular changes that occur with aging (such as opacification of the crystalline lens).

1.2.3 Physical Characteristics of the Myopic Eye

The dioptric difference in RE between the myopic and emmetropic eye has been attributed primarily to the greater VCD in myopic eyes and secondarily to greater corneal power (Grosvenor and Goss 1999). However as Erickson (1984) pointed out, when describing RE, neither single components nor groups of components can be considered in isolation due to the marked interactions among these refractive parameters in determining ocular refraction. In this section, a review of the literature regarding the physical characteristics of the myopic eye is included.

Of the ocular structures that contribute to the refractive power of the eye, the cornea has been the subject of large debate, especially regarding the possible role that it might play in the onset or progression of myopia. Several studies have reported a steeper central or apical cornea in the myopic eyes in comparison to emmetropic eyes in both children and adults (Goss and Erickson 1987; Goss and Jackson 1995; Grosvenor and Goss 1998; Sheridan and Douthwaite 1989). Other studies also found that, as myopia increases, the periphery of the cornea flattens less rapidly (Carney *et al.* 1997; Horner *et al.* 2000); also, the corneas of myopic eyes tend to be significantly less prolate in shape than the corneas of hyperopes and emmetropes (Davis *et al.* 2005) but no correlation has been found between corneal asphericity and the corneal radius of curvature (Carney *et al.* 1997). In contrast, other studies did not find a difference in corneal curvature or a contribution of the cornea to the onset or progression of myopia (Baldwin 1964; Goss and Erickson 1987; Horner *et al.* 2000; Parssinen 1993; McBrien and Adams 1997; Zadnik *et al.* 2003), nor a difference in asphericity between myopic and emmetropic eyes (Sheridan and Douthwaite 1989). It is apparent that in children aged 6 to 15 years, corneal flattening of approximately 0.3 D over 3 years normally occurs irrespective of the refractive state of the eye (Friedman *et al.* 1996).

Although not statistically significant, a trend towards greater ACD and AL has been reported in eyes of children that became myopic in comparison to the eyes of children who remain emmetropic (Goss and Jackson 1995). Additionally, Davis *et al.* (2005) found that myopic eyes with less prolate corneas showed greater increase in ACD during a period of 5 years and the spherical RE was inversely related to ACD. In contrast, Horner *et al.* (2000) found a small increase in ACD consistent with the change in corneal asphericity but no significant correlation was found between the increase in the ACD and an increase in myopia.

With the introduction of a new video technique it has been possible to measure the thickness of the crystalline lens (Mutti *et al.* 1992) and to calculate its gradient index profile and equivalent index (Mutti *et al.* 1995). Together, these measurements have helped to understand the role that the crystalline lens plays in ocular development and myopia. As part of normal ocular development, the crystalline lens thins from 6 to 10 years old and then it maintains its thickness through to 14 years old (Zadnik *et al.* 1995). Thinner crystalline lenses have been found in myopic eyes of children (Zadnik *et al.* 1995; Carney *et al.* 1997; Zadnik *et al.* 2003), in eyes with deeper vitreous chambers (Mutti *et al.* 1998) and in adult-onset myopia (McBrien and Adams 1997) in comparison to emmetropic eyes. Mutti *et al.* (1998) have proposed a mechanism to explain this effect in which, as the equatorial diameter of the eye increases during growth, the crystalline lens thins, flattens and decreases its equivalent refractive index which leads to a decrease in lens power in coordination with the growth of the eye. Thinner crystalline lenses in myopic eyes compared to emmetropic and hyperopic eyes suggests that the lens may have difficulty satisfying the equatorial demands placed on it by the larger sizes of myopic or older eyes.

Another topic which is widely studied is the anatomical shape of the myopic eye. Debate is on as to whether the myopic eye elongates only in its axial diameter into a prolate shape or if it also elongates in its equatorial diameter into a larger spherical shape. A more extensive discussion of this topic is provided in subsection 1.5. Nevertheless, throughout the literature, a common consensus exists in associating the onset and progression of myopia principally as an increase of the AL of the eye (Atchison *et al.* 2004; Baldwin 1964; Chen *et al.* 1992; Cheng *et al.* 1992; Deller *et al.* 1947; Ferree 1933; Hyman *et al.* 2004; Logan *et al.* 1995A; Logan *et al.* 1995B; Meyer-Schwickerath and Gerke 1984; van Alphen 1961; Zadnik *et al.* 2003). This increase or elongation of the eye is due to an increase of the VCD both in children and in adults (Goss and Jackson 1995; Grosvenor and Goss 1998; McBrien and Adams 1997; Parssinen 1993; Zadnik *et al.* 2003). Scleral thinning or localised scleral ectasia is also associated with vitreous chamber elongation only in highly myopic eyes (Rada *et al.* 2006).

A concept developed in the late 80's, which received much attention for a few years and was used to describe the refractive state of the eye and to predict the onset of myopia is the axial length/corneal radius ratio (Goss and Jackson 1995; Grosvenor 1988; Grosvenor and Scott 1994; Scott and Grosvenor 1993). Using a structural model, Scott and Grosvenor (1993) found that the greatest correlation between ocular components was between corneal radius and VCD in both emmetropic and myopic eyes. Corneal radius and VCD were found to be the most important components in determining refractive state: steeper corneas and deeper vitreous chambers resulted in increasing amounts of myopia, whereas flatter corneas and shallower vitreous chambers resulted in decreasing amounts of myopia or emmetropia. An eye having a high axial length/corneal radius ratio was found to be at risk of developing myopia (Grosvenor 1988) and higher axial length/corneal radius ratios were found in children who developed myopia in comparison to those who remained emmetropic (Goss and Jackson 1995). The axial length/corneal radius ratio was later found to have only a moderate sensitivity and specificity in predicting the development of myopia (Zadnik *et al.* 1999).

In summary, the physical characteristics of the optical components of the eye that appear to best describe a myopic eye are: an enlarged AL (due primarily to an increase of the VCD and to a minor extent the ACD), a thin crystalline lens and a cornea which presents some degree of central steepness and a less prolate shape.

1.2.4 Prevalence

As discussed in Section 1.1, myopia is rare in healthy, full-term newborns and higher in premature babies (as the result of an underdeveloped eye). The prevalence of myopia in young children (age 6) is also low (less than 10%) but it seems to increase after starting school and continues to increase until middle age. A summary of studies which assessed the prevalence rates of myopia in children, teenagers and adults around the world is presented in Tables A1 to A3 in Appendix A.

As seen in Table A1, the prevalence of myopia in children aged 6 is non-existent or low in many countries around the globe such as:

- Nepal - 0% (Nepal *et al.* 2003)
- Rural Tibet - 2.9% (Garner *et al.* 1999)
- Australia - 2% (Junghans and Crewther 2003)
- USA - 3% (Zadnik 1997)
- South Africa - 3.2% (Naidoo *et al.* 2003)
- Chile - 3.4% (Maul *et al.* 2000)
- India - 3.19% (Dandona *et al.* 2002A) and 2.8 to 6.7% (Dandona *et al.* 2002B)
- Japan - 4.9% (Watanabe *et al.* 1999)
- Canada - 6% (Robinson 1999).

Studies that have assessed the prevalence of myopia in older children and teenagers confirm the increase in prevalence (see Tables A1 and A2):

- Australia - 6.5% (Junghans and Crewther 2003)
- Urban Tibet - 21.7% (Garner *et al.* 1999)
- Mexico - 44% (Villarreal *et al.* 2003)
- South Africa - 9.6% (Naidoo *et al.* 2003).

However, this trend is surpassed by far in many Asian countries where the prevalence rates of myopia in the world are quite high:

- China - 52.1% (Lam *et al.* 1999); 43.5% (Fan *et al.* 2004A); 78.4% (He *et al.* 2004)
- Hong Kong - 57% (Edwards 1999)
- Taiwan - 84% (Lin *et al.* 1999).

A strong suggestion that the environment has a direct influence in the development of myopia comes from comparisons of prevalence rates between ethnic groups from different geographical areas. In Singapore, Quek *et al.* (2004) determined the prevalence rates of myopia from a group of 946 teenagers (mean age 14.5 years) from three ethnic groups (Chinese, Malay and Indian). Overall the prevalence of myopia was as high as reported in other Asian countries, however, differences were found between ethnic groups. Chinese subjects had the highest rates (77.1%), followed by the Malay (69.4%) and Indian (65.8%) subjects, suggesting a predisposition of Chinese children to develop myopia. In addition, it is interesting to note that the prevalence of myopia in the Indian subjects (65.8%) in Singapore was very high in comparison to rates found for myopia (19.5%, 10.8%) in studies conducted in India (Dandona *et al.* 2002A, Murthy *et al.* 2002). Singapore is known for its highly demanding education system in which children are exposed to large amounts of reading. It is then possible that Indian children in Singapore exposed to such an environment may develop myopia faster than Indian children living in India.

Finally, the prevalence of myopia in adults aged 40 years and older (see Table A3) seems to remain high in some Asian countries:

- Singapore - 45.2% (Wong *et al.* 2000)
- Chinese - 82.2% (Wu *et al.* 2001)
- Malay - 65% (Wu *et al.* 2001)
- India - 68.7% (Wu *et al.* 2001)
- Taiwan - 26.5% (Cheng *et al.* 2003A)
- Indonesia - 39.7 to 61.6% (Saw *et al.* 2002A)

and also in some other countries such as:

- Norway - 30% (Midelfart *et al.* 2004)
- Denmark - 33.1% (Kessel *et al.* 2004)
- Barbados - 21.9% (Wu *et al.* 1999)
- Australia - 15% (Attebo *et al.* 1999).

It is clear the increase of prevalence rates of myopia in this age group has a different aetiology than in young children because it is directly related to physiological changes of the eye related to age (i.e. opacification of the ocular media, in particular the crystalline lens) (Attebo *et al.* 1999).

1.2.5 Associated Problems with Myopia

1.2.5.1 Economic Burden

The economic burden that RE (including myopia) imposes on our societies is very high. The cost of RE correction in the United States of America (USA) alone reached approximately $12.8 billion in 1990 (Congdon *et al.* 2003). Uncorrected RE was the cause of vision impairment in 61 to 81.7% of eyes in children from urban and rural populations in India respectively (Dandona *et al.* 2002B; Murthy *et al.* 2002). Together with age-related macular degeneration and glaucoma, myopia-related retinal disorders are included in the most common causes of visual impairment for persons 20 to 64 years in Copenhagen, Denmark (Buch *et al.* 2004). In an attempt to solve this problem, the World Health Organization, together with the Agency for Prevention of Blindness, launched the campaign VISION 2020-Right to Sight which aims to eliminate avoidable blindness, including RE, cataract, trachoma, onchocerciasis and vitamin A deficiency by the year 2020 (Frick and Foster 2003).

1.2.5.2 Pathological Ocular Changes Associated with Myopia

Some pathological ocular changes (principally of the anterior and posterior segments) are associated with myopia (mostly with high levels of myopia) which can contribute to the loss of vision. Myopic subjects have two- to three-fold more increased risk of glaucoma than non-myopic subjects (Mitchell *et al.* 1999). High myopia is associated with posterior subcapsular, cortical and nuclear cataract in Caucasians (Lim *et al.* 1999) and there is an increased risk of nuclear opacities with myopia in Blacks (relative risk 2.8) (Leske *et al.* 2002).

The myopic eye also presents several fundus changes (commonly known as myopic retinopathy) which include: crescent formation, chorioretinal atrophy, posterior staphyloma, lattice degeneration, pavingstone degeneration, white without pressure, pigmentary degeneration, posterior vitreous detachment, Fuchs spot and β-peripapillary atrophy (Curtin and Karlin 1971; Karlin and Curtin 1976; Kerkhoff *et al.* 2003; Pierro *et al.* 1992; Ruiz-Moreno *et al.* 2000; Vongphanit *et al.* 2002). Although the prevalence of myopic retinopathy is low (1.2%), it increases markedly with higher levels of myopia (>50%) (Vongphanit *et al.* 2002). Myopia is also moderately associated with uveitic and rhegmatogenous retinal detachment (Kerkhoff *et al.* 2003); retinal detachment is twice as likely to appear in people with myopia than in those without myopia (Vongphanit *et al.* 2002). These changes tend to indicate the involvement of biomechanical factors (Curtin and Karlin 1971) associated with the increment of

AL preferentially involving one or both temporal retinal quadrants (Karlin and Curtin 1976; Pierro *et al.* 1992).

There are also a range of eye diseases that are associated with peripheral or peripheral plus central impairment of vision which can lead to myopia (aniridia, brain damage, coloboma, glaucoma, nystagmus, optic nerve atrophy, optic nerve hypoplasia, retinitis pigmentosa, retinopathies, retinopathy of prematurity and toxoplasmosis) (Nathan *et al.* 1985). Some systemic disorders, including Sticklers syndrome, Weill-Marchesani syndrome and homocystinuria, have also been associated with high myopia (Logan *et al.* 2004A).

1.3 AETIOLOGY OF MYOPIA

Despite the extent and breadth of the knowledge of myopia, the most debated (and still unsolved) topic of myopia research is the aetiology of myopia. Multiple theories exist on the cause of myopia and the debate on whether heredity or environment causes myopia continues. While it has been proposed that different types of myopia may exist with each one having a different aetiology (genetically or environmentally determined) (Goldschmidt 1968), perhaps one of the best descriptions of this debate is provided by (Saw 2003) who states "*few researchers would question the argument that both environment and genetic factors contribute to the development of myopia. However, the exact nature of the environmental factors and the relative contributions of each environmental factor remain elusive*". She further adds "*it is possible that* *environmental factors may interact with genes to increase the risks of myopia*". A discussion of the nature and nurture theories is provided in the next subsection.

1.3.1 Nature

Studies investigating the relationship of heredity and myopia can be grouped into three main categories: genetics, twin studies and parent-offspring studies. Genetics primarily address the issue of genetic loci associated with myopia, twin studies investigate the genetic association of myopia in pairs of twins and parent-offspring studies analyse the odds ratios (OR) of a child becoming myope whether the parents are myopic or not.

Until now, five chromosomes have been mapped or identified in high myopia (>-6.00 D):

- chromosome 18p11.31 (MYP2) (Young *et al.* 1998)
- chromosome 12q21.23 (MYP3) (Young *et al.* 1998)
- chromosome 7q36 (Naiglin *et al.* 2002)
- transforming growth factor-β- induced factor (Lam *et al.* 2003)
- chromosome 17q21.22 (Paluru *et al.* 2003).

In a study involving 306 subjects of 51 families from the United Kingdom (UK) (Farbrother *et al.* 2004A), it was found that the MYP3 locus on 12q could be the cause of approximately 25% of apparent autosomal dominant high myopia, followed by MYP2 locus on 18p which accounted for fewer cases of high myopia than the MYP3 locus, while the locus on 17q appeared to be an infrequent cause of autosomal dominant high myopia. In another study, Farbrother *et al.* (2004B), after estimating the sibling recurrence risk and sibling recurrence risk ratio for high myopia in 296 high myopes, determined that the high penetrance autosomal dominant loci for high myopia accounted for only a minority of cases of high myopia and they suggested considering high myopia as a complex disease which results from the influence of susceptibility genes, environmental factors or both. After analysing 53 families from the Orinda longitudinal study of myopia (Mutti *et al.* 2002A), no confirmatory evidence of linkage between juvenile myopia and regions of chromosomes 12 and 18 previously associated with myopia >-6.00 D was found, thus, suggesting a different cause or heterogeneity in the aetiology of juvenile and pathological myopia.

Studies involving twins have been conducted mainly in adult populations (Dirani *et al.* 2006: Hammond *et al.* 2001; Lyhne *et al.* 2001; Wojciechowski *et al.* 2005) although there have also been studies conducted in children as reviewed by Guggenheim *et al.* (2000). After examining 506 pairs of twins (226 monozygotic, 280 dizygotic) with ages ranging from 49 to 79 years, Hammond *et al.* (2001) suggested that genetic effects are of major importance in myopia and hyperopia while astigmatism appears to be inherited. This study shows that genetic effects have the greatest contribution to the overall population variance of SE (85% heritability for SE). In another study (Lyhne *et al.* 2001) involving 114 20 to 45 year old pairs of twins (53 monozygotic and 61 dizygotic), a high heritability (0.89 to 0.94) was found for ocular refraction and its determiners (AL and corneal radius of curvature) suggesting that environment did not have a significant impact on RE. However, it was also found that some individuals might be genetically liable to develop myopia if exposed to certain environmental factors such as near work, education and urbanisation. Wojciechowski *et al.* (2005) found a heritability of RE of 62% in an elderly population. The risk of myopia was 1.90

to 2.52 higher in siblings of myopic participants than in the general population after adjusting for age, gender and race, therefore, these results seemed to confirm previous reports that non-pathological myopia is substantially determined by heredity.

In a more recent study which involved 612 pairs of twins (345 monozygotic and 267 dizygotic) aged 18 to 88 years (Dirani *et al.* 2006), it was determined that most of the variance in RE was explained by genetic influence. This influence was the result of the involvement of additive and dominant genetic effects translating to a high heritability (75% to 94%) of SE and AL. Despite such high heritability values of RE, this study also found that higher education levels were significantly associated with a more negative refraction, therefore, emphasising the importance of environment in RE development.

It was in the late 60's that Dennis L. Ditmars was interested in the question of whether heredity or environment were the cause of myopia. He measured the RE of 258 myopic children and also obtained the RE records from their parents. He found that 63% of the subjects had both parents hyperopic, 90% had only one parent hyperopic and only 8.5% had both parents myopic. These results led him to conclude that there was little hereditary influence to account for myopia (Ditmars 1967). A couple of years later, Hirsch and Ditmars (1969) re-analysed the data from Ditmars' study, grouping the myopic subjects by the degree of myopia in 1.00 D steps. They found that, in comparison to 55% of children with myopia of >-7.00 D who had both parents myopic, only 20% of children with myopia between -1.00 to -2.00 D had both parents myopic. These results suggest that heredity may play a role in the development of high myopia. Interestingly, the results also suggested that myopic parents may have hyperopic children, however, the degree of hyperopia of the children is limited to 2.00 D.

Gwiazda *et al.* (1993A) found that when both parents of children are myopic, 42% of the children are also myopic; when only one parent is myopic the incidence drops to 22.5% and when neither parent is myopic the incidence decreases to only 8%. In a similar fashion, Zadnik *et al.* (1994) concluded, after examining 716 children, that the onset of myopia in children is associated to parental history of myopia. They found that children of myopic parents have longer eyes even before they became myopic, and a higher prevalence of myopia in children of myopic parents (11.0% with two myopic parents, 5.0% with one myopic parent and 1.9% with no myopic parents). Also, Zadnik (1997) found that the risk of myopia in the offspring increased when the number of myopic parents increased. The OR of a child becoming myopic is 1.44 (95% Confidence Interval [CI], 0.66 to 3.14) when one parent is myopic and 5.62 (95% CI, 2.61 to 12.20) when both parents are myopic. Similarly, Saw *et al.* (2004) reported that myopia was associated with two myopic parents versus no myopic parents in univariate (OR 1.7, 95% CI 1.2 to 2.3) and multivariate models (OR 1.4, 95% CI 1.0 to 2.0) and also for one myopic parent versus no myopic parents in univariate (OR 1.5, 95% CI 1.1 to 2.0) and multivariate models (OR 1.4, 95% CI 1.1 to 1.9).

Mutti *et al.* (2002B) found that both heredity and near work are associated with myopia but heredity is by far a more important factor. Children with one or both myopic parents have a higher risk of developing myopia (6.3% no parent, 18.2% one parent, 32.9% both parents).

Recently Guggenheim *et al.* (2000) re-analysed the refractive data of 9,243 Danish children reported by Goldschmidt (1968) in which the prevalence of myopia (SE <-0.50 D) and high myopia (SE >-6.00 D) was 9.5% and 0.45%. It was estimated that the risk ratio for siblings for high myopia was approximately 20 in comparison to approximately 1.5 for low myopia suggesting that genetic factors play a significant role in the development of high myopia.

1.3.2 Nurture

Despite studies that have shown that heredity plays an important role in the genesis of myopia, it has also been suggested that myopic development follows a polygenic model with environmental influence (Pacella *et al.* 1999; Wu and Edwards 1999). Many investigators agree that myopia is not only the result of genes alone but also of the interaction of genetic predisposition with the environment (Chen *et al.* 1998; Edwards and Lam 2004; Mutti *et al.* 1996; Pacella *et al.* 1999; Robinson 1999; Saw *et al.* 2000A; Saw 2003; Thorn *et al.* 1998; Wu and Edwards 1999), with sustained work with high cognitive demand being the most likely environmental influences (Gilmartin 2004; Goss *et al.* 1988; Rose *et al.* 2002; Young 1955; Zadnik 1997).

While some forms of high myopia may be determined by monogenic inheritance, the fact that heritability of RE is higher in twin studies than in parent-offspring studies could be the result of the presence or absence of age-related changes in RE or by environment (Goss *et al.* 1988). One inconsistency of the theory of autosomal dominant mode of transmission of myopia is that there are also children with no myopic parents who actually become myopic by the age of 15 (Pacella *et al.* 1999). Wu and Edwards (1999) said that, while having myopic parents increases the OR for having myopia, suggesting a genetic influence, the odds of having myopia also increased in the offspring of non-myopic parents between 2nd and 3rd generations, suggesting an environmental influence. This may indicate that, while the environmental influence has increased over the years, the genetic input remained constant. Despite the indication that genetic inheritance plays an important role in the genesis of myopia, the increase in prevalence of myopia in some parts of the world, such as East Asia, is incompatible with rates of change in gene pools, suggesting that the current prevalence rates of myopia are the result of a strong environmental impact (Rose *et al.* 2002). Edwards and Lam (2004) hypothesised that the rapid increase of myopia prevalence in Chinese children in Hong Kong over a short period of time (one or two generations) strongly suggests that these children have a susceptibility to some environmental factors which result in excessive eye growth.

Mutti *et al.* (1996) point out that "*one of the weaknesses of family studies is that it is difficult to distinguish the contribution of familial genes from that of a shared environment*." It is then apparent that both nature and nurture play a role in the aetiology of myopia, although the predominant role appears to belong to positive parental history of myopia. There is also a constant relationship between the risk of myopia and near work and the risk of myopia increases with an increasing number of myopic parents (Zadnik 1997). It is possible that a significant gene-environment interaction exists which may vary the heritability of myopic parameters from population to population depending on the impact of environmental factors (Chen *et al.* 1998).

1.3.2.1 Environment (Near Work)

Two examples which perhaps best reflect the association of near work in the development of myopia are two studies conducted in Eskimo families in Alaska. Young *et al.* (1969) studied the transmission of REs within 41 Eskimo families in Alaska. They discovered that older subjects had virtually no myopia while younger subjects tended to show a relatively high incidence of myopia. A higher prevalence of myopia was found in subjects aged 25 years and below (43.4%) than in subjects older than 50 years (0.0%). Very low correlations were found between parent and sibling REs but high and significant correlations were found between siblings. They suggested that environmental factors (schooling, near work) play a greater role in the development of myopia among Eskimos than do hereditary factors. A few years later Young and Leary (1972) conducted a second study which involved 71 Eskimo families, 30 of them were 1st generation and 41 2nd generation. In those cases where the REs of the parents exceeded 3.00 D of hyperopia, there was increased likelihood that the children of such parents would be hyperopic to a level similar to the parents. It was also found that 53.1% of the children were more myopic than either parent, 14.7% were more hyperopic than either parent and 32.2% fell within 0.25 D of either parent. Also the depths of the vitreous chamber and ALs were considerably greater in the children than in the parents. The excessive deviation towards more myopia was suggested to be caused by some environmental factors rather than heredity factors.

It also appears that in cultures where children are encouraged to spend more time reading or performing near work tasks, there is a higher prevalence of myopia, suggesting an association of myopia with reading and close work. A low prevalence of myopia (5.8%) has been reported in rural Mongolian children aged between 7 and 17 years, where schooling is less intensive than other more industrialised countries (Morgan *et al.* 2006). In Nepal, Sherpa children with a rural lifestyle were found to have a lower prevalence (2.9%) of myopia in comparison to Tibetan children (21.7%) who undergo more rigorous schooling (Garner *et al.* 1999). In Jerusalem, Zylbermann *et al.* (1993) found a higher prevalence of myopia in Jewish boys attending Orthodox schools (81.3%) compared to boys attending general schools (27.4%) and in Jewish girls attending Orthodox schools (36.2%) compared to general schools (31.7%), which the investigators attributed to higher near work demands for children attending Orthodox schools compared to general schools. While a low prevalence of myopia was found in children from rural India (4.1%), myopia was found to be associated with increasing levels of schooling of the father (OR 1.48, 95% CI, 1.16 to 1.89) (Dandona *et al.* 2002B). Similar results have been reported by Murthy *et al.* (2002) who also found that the prevalence of myopia was low in children from an urban population of India (7.4%), while children of fathers with higher levels of education were more likely to have children with myopia (OR 1.69; 95% CI, 1.29 to 2.23). Saw *et al.* (2002B) reported that children aged 7 to 9 years who read more than two books per week were more likely to become myopic (OR 3.05, 95% CI 1.80 to 5.18). Also there was a higher prevalence of myopia in children whose parents had a higher education level. He *et al.* (2004) also found an association of myopia in children with higher parental education (OR 1.22; 95% CI 1.05 to 1.42).

Despite a report by Young (1955) who found no relationship between myopia and IQ, over the years it has been postulated that more highly educated people or people with higher IQs are more myopic than non-educated people or people with lower IQs. Myopic children have been found to have higher IQ scores (Grosvenor 1970; Hirsch 1959; Saw *et al.* 2004) and performed better at school than hyperopic children, independently from the amount of near work they performed (Saw *et al.* 2004). Similarly Mutti *et al.* (2002B) found myopic children scored higher than emmetropes and hyperopes in local percentiles of reading and in local Total Language tests, while also spending significantly more hours per week reading (studying and/or reading for pleasure) and less time in sports than hyperopes and emmetropes. Goldschmidt (1968) found a higher prevalence of myopia in Danish children from academic streams and low prevalence in special cases, such as intellectually handicapped children, while Ashton (1985) reported a significant association between school myopia and school grades.

There are also reports that a myopic shift or increase of prevalence and severity of myopia occurs in people attending University, especially those with high educational demands such as law (Zadnik and Mutti 1987), medical (Fledelius 1998; Midelfart *et al.* 1992) and engineering students (Kinge and Midelfart 1999). Also, in certain occupations which require higher demands of near work such as microscopists (Adams and McBrien 1992; McBrien and Adams 1997) or military conscripts (Wu *et al.* 2001), a higher prevalence or progression of myopia has been found. Saw *et al.* (1999) reported that women in Singapore who worked showed more myopia than women who did not work.

It is becoming more plausible that myopia has a genetic predisposition with environmental triggers, the interaction of which results in phenotypic plasticity (Foster 2004). It seems that near work is the strongest influence in this process, though recent reports failed to find a relationship between the progression of myopia with socio-economic status and near work activity in children (Saw *et al.* 2000B). As Saw (2003) states in her synopsis of the prevalence rates and environmental risk factors for myopia: "*Both genes and environment may be related to myopia. There are no conclusive studies at present, however, that identify the nature and extent of possible gene-environment interaction.*"

1.3.3 Animal Models of Myopia

In the last Century many studies have been conducted to understand the mechanisms of emmetropisation and myopia development using different animal models. The most important finding obtained from those studies is that the final refractive state and AL of the eye are not only predetermined by genetic factors but, as in the case of emmetropisation, it is the result of a vision-dependent mechanism. The existence of an active mechanism that matches the AL of the eye to its optical power has been observed in different animal species (chickens, guinea pigs, rats, rabbits, cats, mice, fishes, tree shrews and monkeys) (see Criswell and Goss 1983; Goss and Criswell 1981; Norton 1999; Norton and Siegwart 1995; Wildsoet 1997). From all the different animal models used, the monkey is considered the most suitable animal model for clinical or basic research, when then applying the experimental results to the human population (Harwerth and Smith 1985).

Myopia development has been observed in animals when the visual system has been severely disrupted (form-deprivation), for example, when performing lid suture in chickens (Yinon *et al.* 1980), marmosets (Troilo *et al.* 2000), mice (Tejedor and de la Villa 2003), tree-shrews (Marsh-Tootle and Norton 1989), monkeys (*Macaca mulatta, Macaca arctoides*) (Wiesel and Raviola 1977; Wiesel and Raviola 1979). Human eyes with ocular anomalies that disrupt vision and induce form-deprivation are seen to develop significant degrees of myopia; examples of such ocular anomalies are: congenital cataract, retrolental fibroplasia, congenital optic atrophy, juvenile macular dystrophy (Rabin *et al.* 1981), eyelid closure, blepharoptosis (Hoyt *et al.* 1981), corneal opacification (Gee and Tabbara 1988), corneal scars (Tabbara *et al.* 1999), traumatic cataract (Calossi 1994; Rasooly and BenEzra 1988) and vitreous haemorrhage (when the haemorrhage obscures the posterior segment) (Miller-Meeks *et al.* 1990).

Form-deprivation myopia has also been observed when using less invasive methods of vision disruption such as with translucent occluders/diffusers (complete/hemispherical) in chickens (Guo *et al.* 1996; Hodos and Kuenzel 1984; Napper *et al.* 1997; Troilo *et al.* 1987; Wallman *et al.* 1978; Wallman *et al.* 1987; Wildsoet and Schmid 2000), tree shrews (Norton 1990) and monkeys (Bradley *et al.* 1996; Smith EL III and Hung 2000; Smith EL III *et al.* 2005). The answer to this phenomenon is not clear yet. However, it is possible that by altering the integrity of the visual input, growth factors may no longer be able to modulate the eye's growth correctly, causing an abnormal elongation of the eyeball (Calossi 1994). In monkeys, chronic reduction of image contrast associated with optical diffusion causes axial myopia and the degree of such myopia varies directly with the degree of image degradation (Smith EL III and Hung 2000).

Another stimulus which also has an active effect in the emmetropisation process is defocus. It was first noted by Schaeffel *et al.* (1988) that, when raising chickens wearing negative lenses an increase axial growth (myopia) was observed, and that when raising chickens wearing positive lenses, reduced axial growth (hyperopia) occurred (mainly due to thickening of the choroid) (Diether and Schaeffel 1997). The development of different REs using positive, negative or cylindrical lenses (lens-induced) has also been reproduced in studies using other animal species such as chickens (Diether and Schaeffel 1997; Guo *et al.* 1996), cats (Smith EL III *et al.* 1980), tree shrews (Norton 1990) and monkeys (Hung *et al.* 1995; Kee *et al.* 2003; Kee *et al.* 2004A; Smith EL III *et al.* 1994; Smith EL III and Hung 1999).

While similar results have been observed across different species of animals, monkeys present some distinctive features, such as compensating ocular growth to positive and negative lenses but in smaller magnitude than other non-mammalian species (Hung *et al.* 1995; Smith EL III and Hung 1999). Also, high levels of negative defocus generates hyperopia rather than myopia in rhesus monkeys (Smith EL III *et al.* 1994). When binocular high powered lenses are used in monkeys, no effect in ocular growth is observed (Smith EL III and Hung 1999). Using contact lens diffusers also produces an opposite effect (hyperopia) on eye growth to that of severe pattern deprivation in rhesus monkeys (Bradley *et al.* 1996). It is possible that contact lens diffusers produced changes in refractive development that overshadowed the effects of form-deprivation through visual and non-visual mechanisms (Hung and Smith 1996). Recently Kee *et al.* (2003; 2004A) reported that astigmatic lenses can generate significant amounts of astigmatism in rhesus monkeys. In the presence of significant amounts of astigmatism, emmetropisation is directed toward one of the two focal planes (usually towards the least hyperopic meridian) and not the circle of least confusion.

Another interesting finding which supports the theory that emmetropisation is a visually-guided process is that, when the stimulus used to induce form-deprivation RE is removed from the eye, complete or partial recovery of the induced RE occurs in chickens (Wallman and Adams 1987; Wildsoet and Schmid 2000), tree shrews (Norton 1990) and monkeys (Kee *et al.* 2003; Smith EL III *et al.* 1994). In the case of chickens, removing the occluders from myopic eyes produces a rapid reduction of the degree of myopia with the eyes reaching the refractive state of normal eyes in approximately 2 weeks (Wallman and Adams 1987). However, this reduction is prevented when optically correcting the induced-myopia with lenses equivalent to the RE or when sectioning the optic nerve (Wildsoet and Schmid 2000). Tree shrews also exhibit recovery from experimentally-induced myopia after long periods of unrestricted binocular vision and, similar to chickens, the correction of optically-induced axial myopia prevents emmetropisation (Norton 1990). In monkeys, long periods of form-deprivation can be counterbalanced by short periods of unrestricted vision (1 hour reduces more than 50% degree of axial form-deprivation myopia, while 3 hours only reduces less than 10%) (Smith EL III *et al.* 2002).

Other manipulations which have also shown an effect in RE development in animals are elevation of temperature and intraocular pressure in rabbits (Mohan *et al.* 1977), while rearing chickens under continuous light or under low-intensity blue light also produces myopia (Guo *et al.* 1996; Napper *et al.* 1997).

1.4 ABERRATIONS AND MYOPIA

With all the evidence obtained from animal studies indicating that emmetropisation and RE are the result of a visually-guided control process, several studies have been conducted to identify the trigger stimulus for myopia development in humans. As myopia seems to be associated with near work, the logical step was to study accommodation, which is the ocular system that works during near visual activity.

Many distinct features of the accommodative system of the myopic eye of children and adults have been discovered. The myopic eye has reduced accommodation (lag of accommodation) in comparison to emmetropic or hyperopic eyes (Abbott *et al.* 1998; Gwiazda *et al.* 1993B; He *et al.* 2005; McBrien and Millodot 1986A) and this was observed prior to the onset (Gwiazda *et al.* 2005) and after the onset of myopia (Mutti *et al.* 2004B). Myopic eyes also have reduced accommodative speed (facility of accommodation) at far distances (O'Leary and Allen 2001; Pandian *et al.* 2006), larger amplitude of accommodation (McBrien and Millodot 1986B) and, therefore, higher accommodative convergence / accommodation ratios than emmetropes (Gwiazda *et al.* 1999; Gwiazda *et al.* 2005; Mutti *et al.* 2000A).

It appears that these deficiencies in the accommodative system of the myopic eye have their origin in a reduced sensitivity to blur (Rosenfield and Abraham-Cohen 1999). It has been observed that myopic children exhibit insufficient accommodative response to blur (Gwiazda *et al.* 1993B; He *et al.* 2005) and that myopes experience less visual acuity loss with negative defocus than with positive defocus (Radhakrishnan *et al.* 2004A). If insufficient accommodation is present in an emmetropic or optically-corrected ametropic eye, when reading, for example, the best focused image will lie behind the retina, and this perhaps could generate a myopic stimulus similar to that generated by negative lenses in animal models, resulting in elongation of the eye. Despite all the evidence showing that the myopic eye has an imperfect accommodative system, the exact mechanism of how or what causes it remains yet to be elucidated.

One possible answer to this dilemma is ocular monochromatic aberrations. Higher order aberrations (HOAs), such as spherical aberration (SA), affect the lead and lag of accommodation by increasing the depth of focus and tolerance to blur (Charman 2005; Collins *et al.* 2006) and they also provide an odd-error focus cue (even-order terms) (Wilson *et al.* 2002). It is possible that if, as suggested by Radhakrishnan *et al.* (2004B), myopic eyes have excessive amounts of aberrations (such as SA), a change in the position of intermediate spatial frequencies will occur, and, therefore, may affect the accommodative response (inducing lag of accommodation).

In addition to the possible effects on accommodative functions, ocular monochromatic aberrations have other potential effects on the development of the eye. Infantile astigmatism (lower order aberration [LOA]) is associated with myopia development in children (Fan *et al.* 2004B; Fulton *et al.* 1982; Gwiazda *et al.* 1993A; Gwiazda *et al.* 2000; Hirsch 1964). Despite one report which did not find a relationship between the degree and orientation of astigmatism and myopia progression in children (Parssinen 1991), it has been observed that in 3 year old children with astigmatism of >1.00 D, a progression of myopia occurs and in children with astigmatism of >3.00 D, higher degrees of myopia result by the age of 8 years (Fulton *et al.* 1982). Also, in a group of Chinese preschool children, the presence of astigmatism predisposed the eyes towards greater development of myopia and eyes with increased levels of astigmatism had greater myopic progression and AL growth (Fan *et al.* 2004B).

“Against-the-rule” astigmatism in 5 and 6 year old children is predictive of the later development of myopia at age 13 or 14 (Hirsch 1964). After tracking the RE of 72 children from early infancy until 9 to 16 years of age, Gwiazda *et al.* (1993A) found that children who have either "against-the-rule" astigmatism or no astigmatism during infancy and a negative SE are more likely to become myopic at school age than children with infantile "with-the-rule" astigmatism. Similarly, in adults, low myopes are more likely to have astigmatic axes "against-the-rule" (Farbrother *et al.* 2004C). One theory suggests that infantile astigmatism may disrupt emmetropisation by reducing the sensitivity of the child to focusing cues which may lead directly to underaccommodation and induce myopia (Gwiazda *et al.* 2000).

Other aberrations such as coma aberrations reduce retinal image quality (Howland and Howland 1977), and SA has an effect on the modulation transfer function with positive and negative defocus (Jansonius and Kooijman 1998). Wallman and Winawer (2004) suggest that aberrations may have an impact on the retinal image for different types of defocus (positive/negative) which can provide directional clues to the retina for growth.

It is possible that if the eye has different or abnormal levels of aberrations, the normal growth of the eye could be altered and RE will develop. Do myopic eyes have higher or abnormal levels of monochromatic aberrations than emmetropic eyes? Table 1.1 (*reproduced from Charman 2005),* provides a summary of some studies which have analysed the differences in higher order (HO) aberrations in adults and children.

Table 1.1: ***Summary of studies comparing the aberrations of myopic and emmetropic eyes: M, E and H represent myopes, emmetropes and hyperopes respectively. (Table reproduced from Charman 2005 with permission)***

Authors	No. of subjects	Ages	Pupil diam. (mm) used	Cycloplegia?	Type of aberrometer	Total higher-order aberration M > E?	Spherical aberration M > E?	Other comments
Applegate (1991a,b)	23	?	~7	Yes	X-cylinder (subjective)	Yes		
Collins *et al.* (1995)	21M, 16E	17–29	~4	None	X-cylinder (objective)	Possibly	No	Less fourth-order in measured myopes
He *et al.* (2002)	316	10–29	≥6.0	None	Psychophys. ray tracing	Yes	Yes	Measured at accomm. resting state
Marcos *et al.*	49M	Young	6.5	?	Laser ray tracing	Yes	No	
Porter *et al.* (2001)	109	21–65	5.0, 7.0	None	Hartmann–Shack	No	No	
Paquin *et al.* (2002)	27M, 7E	18–32	5, 9	Phenylephrine 2.5%/ tropicamide 1%	Hartmann–Shack	Yes	Yes	More coma in high myopes
Carkeet *et al.* (2002)	273	8–13	5.0	Three drops 1% cyclopentolate	Hartmann–Shack	No	No	
Cheng *et al.* (2003b)	200	26 ± 6	6.0	One drop 0.5% cyclopentolate	Hartmann–Shack	No	No	More aberration in astigmatic eyes
Radhakrishnan *et al.* (2004a,b)	8M, 8E	20–38	6.0	Two drops 1% cyclopentolate	Hartmann-Shack	No	Yes (but not sig.)	Asymmetry in blur effects on either side of focus in myopes
Llorente *et al.* (2004)	34M, 22H	23–40	6.5	One drop 1% tropicamide	Laser ray tracing			More aberration in hyperopic eyes

Few studies have found differences in monochromatic levels in myopic eyes in comparison to emmetropic eyes. Applegate (1991) found an increased mean squared error of the monochromatic wavefront with increased myopia. Collins *et al.* (1995) reported myopes have lower 4th order aberrations than emmetropes, however, it was noted that a high proportion of myopic subjects (36%) produced grids too highly distorted to permit analysis with confidence in comparison to 7% of emmetropes. Paquin *et al.* (2002) found aberrations increased when myopia increased for pupil diameters (PDs) of 5 and 9 mm and coma aberration was more frequent in high myopia. He *et al.* (2002) favoured the hypothesis of aberrations producing myopia after finding higher amounts of HOAs root mean squared (RMS) in myopic subjects than in emmetropes. Marcos *et al.* (2002) suggested that degraded retinal image quality occurs in high myopia. They found the total HO RMS (3rd and higher) increased significantly with myopia (slope = -0.085 μm/D, $p<0.001$). As myopia increased, corneal SA increased significantly ($p=0.001$) towards more positive values and internal SAs towards more negative values ($p=0.009$).

In contrast, other studies did not find any difference in the aberration patterns of myopic eyes in comparison to emmetropic eyes. After examining 200 eyes from 100 subjects (mean age 26.1 ± 5.6 years), SE (M) (9.50 to +5.50 D), Cheng *et al.* (2003B) found little evidence that aberrations (3rd and 4th orders, SA RMS) vary systematically with the degree of ametropia. Myopic eyes did not have significantly different amounts of monochromatic aberrations compared with emmetropes. Llorente *et al.* (2004) compared the aberration profiles and geometrical ocular properties (corneal curvature, corneal asphericity and AL) between a group of 24 myopic and 22 hyperopic eyes (mean age 30.5 and 30.3 respectively; range 26 to 39, 23 to 40), mean M (-3.3 ± 2.0 D and 3.0 ± 2.0 D), myopic and hyperopic eyes respectively). The only difference between RE groups was that myopes showed lower levels of positive SA than hyperopes (0.10 ± 0.13 μm and 0.22 ± 0.17 μm respectively). Radhakrishnan *et al.* (2004B) found higher levels of positive SA in a small group of myopes (n=8) in comparison to non-myopes (n=8) (though this difference was not-statistically significant).

As seen in Table 1.1, most studies conducted to assess ocular aberration differences between myopic and non-myopic eyes have been conducted in young adults and very few have been conducted in child populations. Carkeet *et al.* (2002) obtained ocular aberrations using a PD of 5 mm from a group of 217 Singaporean children (mean age 9.0 ± 0.84 years, range 7.9 to 12.7 years) from different ethnic backgrounds: Chinese (199), Malay (63) and Indian (11). Differences were found for astigmatism (Z(2,2)) between high myopes and low myopes or emmetropes. Low myopes had less SA than high myopes and emmetropes ($p<0.001$). An interesting finding from this study is that Malay subjects did not show differences for any HOAs but only for LOAs, indicating differences between races. Also Malay subjects had lower levels of coma and SA than Chinese subjects. He *et al.* (2002) obtained ocular aberrations from 170 children (83 emmetropic and 87 myopic), mean age (14.9 and 14.6; range 10 to 17 years, respectively) using a ray tracing technique and with natural pupils (usually >6 mm). Myopic subjects were found to have greater HO RMS than emmetropes. Recently, Kirwan *et al.* (2006) measured ocular aberrations (PD=6 mm) from 82 children, mean age 6.7 years (range 4 to 14 years) with a mean M 2.39 ± 3.35D (range -8.98 to +8.45 D). Myopes (mean M -3.8 ± 2.97 D) had higher levels of 3rd order aberrations (Z(3,-3), Z(3,-1), Z(3,3)) and some 4th order aberrations (Z(4,4) and Z(4,2)) than hyperopes (mean M +3.5 ± 1.9 D). No difference was found in the levels of SA between RE groups.

In summary, it remains inconclusive whether differences in the levels of on-axis ocular aberrations between RE groups exist or not. Whilst previous studies have assessed the distribution and individual variations in moderate to large populations (Castejon-Mochon *et al.* 2002; Howland 2002; Porter *et al.* 2001; Thibos *et al.* 2002A) these studies have been limited to adult populations only. Further studies are needed to determine the normal distribution of ocular aberrations in children and to identify the relationship between HOAs and a potential role in the ocular development and RE in children. It is also important to determine if ethnicity could play a role in the levels of ocular aberrations and, therefore, probably a role in the development of REs such as myopia.

1.5 OFF-AXIS ABERRATIONS AND MYOPIA

Another area which has been the subject of increased attention in the last few years, deals with the relationship between non-foveal (off-axis) RE and the development of foveal (on-axis) RE (especially myopia). Several studies have shown that myopic eyes are hyperopic in the periphery relative to the fovea while the reverse applies to hyperopic eyes, and emmetropic eyes were shown to have a tendency to have similar on and off-axis refraction (see Stone and Flitcroft 2004; Wallman and Winawer 2004) for extensive reviews in off-axis refraction and RE development).

The significance that the difference in refractive condition between the on and off-axis has in the development of myopia and in the development of a control method of myopia progression in humans has been noted by various investigators (Charman 2005; Charman 2006; Charman *et al.* 2006; Hoogerheide *et al.* 1971; Kee *et al.* 2004B; Schippert and Schaeffel 2006; Smith EL III *et al.* 2005; Smith EL III *et al.* 2006; Wallman and Winawer 2004). The hypothesis is that if peripheral hyperopic RE relative to the fovea is present in the eye, it will trigger a mechanism which will increase the AL of the eye in order to bring the peripheral retina in focus with the peripheral image. However, the consequence of this elongation will be the generation of myopic RE at the fovea. It has also been noted that when optically correcting myopic RE with negative lenses, while the image is in focus at the fovea, it creates hyperopic defocus at the periphery which could potentially trigger further axial elongation (Wallman and Winawer 2004). For this reason it has been proposed that any corrective method (spectacles, contact lenses or refractive surgery) aiming to control the progression of myopia should be designed to correct axial RE and make peripheral refraction emmetropic or even myopic (Charman 2006; Charman *et al.* 2006; Smith EL III *et al.* 2006; Wallman and Winawer 2004).

Much of the information on peripheral REs and myopia development comes from early studies by Ferree *et al.* (1931 1932) and Ferree (1933) and later by Rempt *et al.* (1971) and Hoogerheide *et al.* (1971). In 1931, Ferree *et al.* being interested in studying the refractive condition of the peripheral field, measured the off-axis (peripheral) refraction in 21 eyes (15 without cycloplegia, 6 with cycloplegia) in the horizontal retinal field up to 60 degrees temporally and nasally at intervals of 5 or 10 degrees using a modified Zeiss parallax refractometer. At each measured angle, the RE of both the horizontal (plane of incidence of the light) and the vertical meridian (plane located at 90 degrees from the horizontal meridian) was recorded and plotted in the form of curves (Figure 1.1).

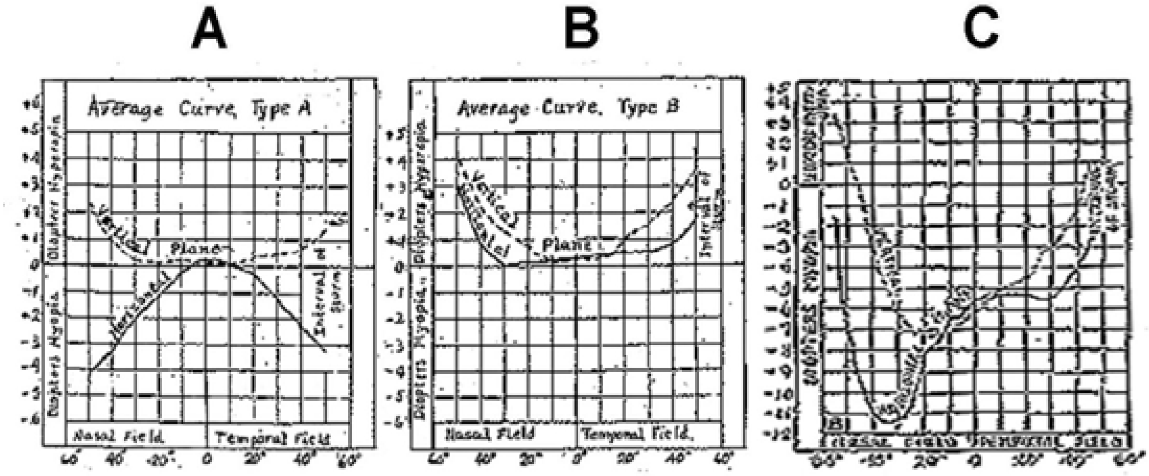

Figure 1.1: ***Diagrams showing the three types of peripheral refraction in the horizontal retinal field of 21 eyes found by Ferree et al. (A)Type A; (B) Type B; (C) Type C (reproduced and adapted from Ferree et al. 1931 and 1932)***

The results for the horizontal plane (also called tangential plane) were recorded as a continuous line and the vertical plane (also called sagittal plane) as a broken line. The degrees of eccentricity (visual field) from the on-axis refractive value (at 0 degrees) were plotted along the horizontal axis and the RE (D) was recorded along the vertical axis. The distance between the broken and continuous lines determined the amount of astigmatism (interval of Sturm). Some important points were noted by (Ferree *et al.* 1931) as to the interpretation of the curves:

1. The relationship of both curves to the baseline (on-axis refraction) indicated the type of astigmatism present at the peripheral field.

2. The vertical plane curve (broken line) gave information as to the shape of the eyeball.

3. The magnitude of the interval of Sturm gave information on the strength of the refractive system.

4. A comparison of the interval of Sturm between the nasal and temporal fields gave information on the asymmetry of the refraction for both halves.

5. Comparison of the shape of the curves provided information on the asymmetry of the refractive system or the shape of the eyeball.

6. Comparing the strength of the refractive system in the periphery in relation to the on-axis refraction provided information on the length of the eyeball.

Based on the pattern of peripheral refraction obtained from the 21 eyes measured by Ferree *et al.* (1931), the eyes were classified in three main types:

- Type A - as the periphery of the field is approached, the eye becomes more myopic in the horizontal meridian and more hyperopic in the vertical meridian, resulting in mixed astigmatism in the peripheral field of variable magnitude (Figure 1.1A). A feature of this pattern of peripheral refraction was that, in general, the defect in the vertical meridian was much smaller than the defect in the horizontal meridian.

- Type B - as the periphery of the field is approached, the eye becomes less myopic in the horizontal meridian and more hyperopic in the vertical meridian, resulting in compound hyperopic or myopic astigmatism (Figure 1.1B). The most relevant feature of these cases was the smallness of the interval of Sturm in the peripheral field.

- Type C - the pattern of peripheral refraction in this condition was a considerable difference (or asymmetry) in the nasal and temporal meridional quadrants (Figure 1.1C).

The main findings from the Ferree *et al.* (1931) study and from two later reports (Ferree *et al.* 1932; Ferree 1933) which re-analysed some of the data of the previous study were that (a) there is an asymmetry in the magnitude of off-axis astigmatism in the nasal and temporal retinal halves; (b) there is a shift in the astigmatic axis in the periphery in relation to the central refraction from “with-the-rule” to “against-the-rule” orientation; (c) asymmetry in peripheral RE can be indicative of decentration of the crystalline lens in reference to the antero-posterior plane of the eye or an asymmetry; and (d) different eyeball shapes and power strengths can occur in eyes regardless of the central RE.

Almost 40 years after Ferree’s studies, Rempt *et al.* (1971) also measured the off-axis refraction in the horizontal retinal plane (up to 60 degrees) in 442 pilots in training using retinoscopy. They plotted the results using diagrams similar to those by Ferree *et al.* but called them skiagrams. They renamed the Type A, B and C diagrams as Type IV, Type I and Type III, respectively (see Figure 1.2A) and also two new diagrams were created (Types II and V). In Type II, the Sagittal plane becomes more hyperopic in the periphery and the Tangential plane in the periphery remains the same, while in Type V the opposite occurs: the Sagittal plane remains the same in the periphery and the Tangential plane becomes more myopic.

The results of Rempt *et al.* (1971) confirmed previous findings in which there was an increase of astigmatism with the increase of eccentricity in the majority of cases and that peripheral refraction showed three distinct patterns: mixed astigmatism, hyperopic astigmatism and myopic astigmatism. A new finding in this study was that some associations between RE and off-axis refractions were determined such as (a) emmetropes and low hyperopes often showed peripheral mixed astigmatism and in some cases hyperopic astigmatism; while (b) myopes mostly showed peripheral hyperopic astigmatism and sometimes mixed astigmatism.

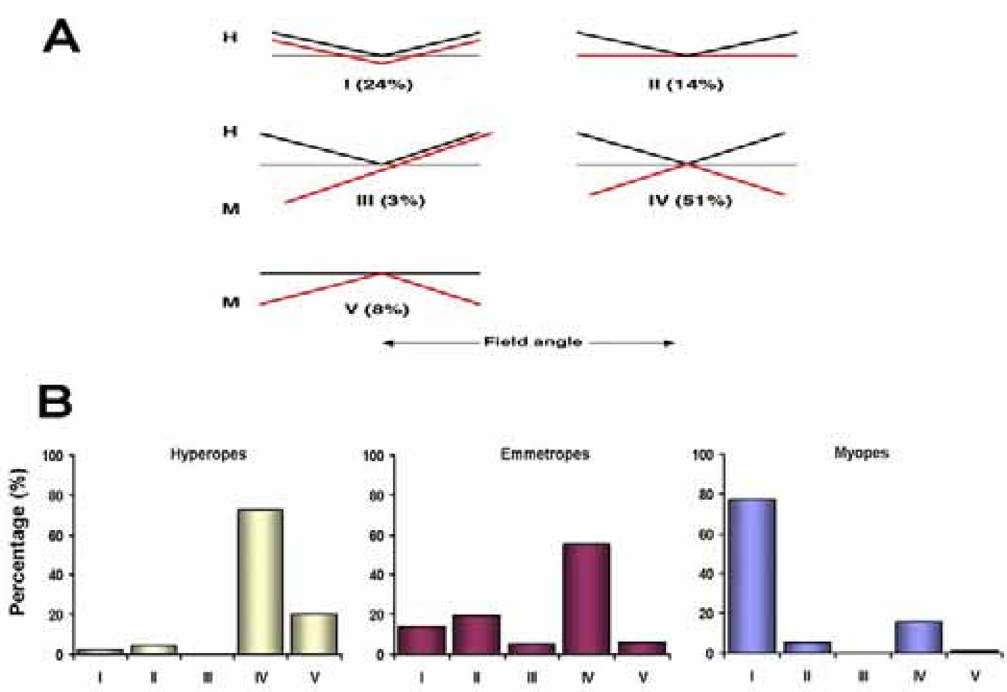

Figure 1.2: ***(A) Types of peripheral skiagrams described by Rempt et al. (1971) and their distribution from a group of 442 pilots in training (reproduced with permission from Charman and Jennings 2006); the black line indicates the sagittal plane and the red line indicates the tangential plane; (B) Distribution of types of skiagrams of the same subjects when grouped by central RE (Data obtained from Rempt et al. 1971)***

Some associations were found between the type of skiagram and RE (see Figure 1.2B). Based on the distribution of the skiagrams, Type IV was called the "normal" skiagram and was more prevalent in emmetropic and hyperopic eyes. Type I was found most frequently in myopic eyes, Type V was present almost exclusively in hyperopic eyes while Type III was present only in emmetropic eyes.

Hoogerheide *et al.* (1971) tracked the RE in 214 pilots from the group of 442 pilots in training measured by Rempt *et al.* (1971) to identify who became myopic and who remained emmetropic or hyperopic. They obtained the peripheral refraction patterns and grouped them based on the type of skiagram. They found the majority of emmetropic and hyperopic eyes with Type I skiagrams (compound hyperopic astigmatism) presented a shift towards myopia in their central refraction (45% and 77% respectively), while the majority of emmetropic and hyperopic eyes with skiagram Type IV (mixed astigmatism) did not show a myopic shift (66%).

While the results of Hoogerheide *et al.* (1971) and Rempt *et al.* (1971) suggest that (a) relative off-axis hyperopic RE is more common in myopic eyes and (b) emmetropic eyes or hyperopic eyes presenting relative off-axis hyperopic RE are at higher risk of becoming myopic, there is no explanation as to the reason for the existence of such patterns in myopic eyes and the influence on eye growth.

To understand the differences in off-axis refraction between RE groups it is necessary to look at the differences in ocular shape between RE groups. In the basic model of ametropia, RE occurs because of differences in AL while the optical elements of the eye remain the same (Charman and Jennings 1982); thus, as described in subsection 1.2.3, if myopic eyes have an enlarged AL (prolate shape), any ray or pencil of rays travelling along the visual axis of the eye will focus in front of the fovea but any other ray focusing from the periphery (off-axis) will focus on or behind the retina, while in the case of an emmetropic eye, all rays will focus on the retina. Several studies have been conducted to determine the ocular shape in different RE groups. Ocular shape and the conformation of the retina has been measured or estimated using different methods such as refraction (Chen *et al.* 1992; Dunne 1995; Ferree 1933; Logan *et al.* 2004B; Mutti *et al.* 2000B; Schmid 2003A/B; Walker and Mutti 2002), X-rays (Deller *et al.* 1947), ultrasound (Chen *et al.* 1992; Meyer-Schwickerath and Gerke 1984), scanning laser ophthalmoscope imaging (Chen *et al.* 1992), partial coherence interferometry (Drexler *et al.* 1998), and more recently using magnetic resonance imaging (Atchison *et al.* 2004;

Atchison *et al.* 2005A; Chau *et al.* 2004; Chen *et al.* 1992; Cheng *et al.* 1992) and optical low coherence reflectometry (Schmid 2003A; Schmid 2003B).

Throughout the literature there is evidence that myopic eyes have larger axial and equatorial dimensions than emmetropic or hyperopic eyes (Atchison *et al.* 2004; Chen *et al.* 1992; Deller *et al.* 1947; Logan *et al.* 1995A; Logan *et al.* 1995B). However, it is not completely clear if myopic eyes present an excessive growth only in the axial dimension (prolate shape) or also in the three dimensions (Atchison *et al.* 2004; Chau *et al.* 2004; Cheng *et al.* 1992). Nevertheless, it is possible to say that myopic eyes in general have a prolate shape and, as a consequence of this shape, they present off-axis hyperopic RE.

If hyperopic defocus in the peripheral retina is a stimulus for the eye to grow, how could the peripheral retina detect the differences in defocus and translate it into regulating eye growth? It is widely known that visual acuity declines with eccentricity from the fovea (Frisen and Glansholm 1975; Jennings and Charman 1978; Millodot *et al.* 1975; Navarro *et al.* 1993), and that the resolution of the peripheral retina to resolve complex targets like E letters is worse than for vertical sinusoidal gratings (Anderson and Thibos 1999). This reduction of visual acuity in the peripheral retina is mainly associated with two factors: One is by a reduction in optical quality with eccentricity (Navarro *et al.* 1993; Jennings and Charman 1997; Williams *et al.* 1996) associated to higher levels of oblique astigmatism (Frisen and Glansholm 1975) and a lesser degree to coma aberrations (Jennings and Charman 1981; Jennings and Charman 1997; Navarro *et al.* 1993; Williams *et al.* 1996) which, together with astigmatism, can substantially reduce aliasing by receptoral and post-receptoral spatial sampling (Williams *et al.* 1996).

The second factor is neural sampling. Despite the poor quality of the peripheral retina, the resolution acuity in the peripheral retina is not limited only by the off-axis dioptrics (Jennings and Charman 1978; Millodot *et al.* 1975) but by neural sampling density (Jennings and Charman 1981), in particular the sampling density of visual neurons (Ganglion cells) (Wang *et al.* 1997). While the optical correction of off-axis REs does not improve peripheral visual acuity (Millodot *et al.* 1975), off-axis corrections improve the thresholds of motion sensitivity (Leibowitz *et al.* 1972), peripheral contrast sensitivity (Gustafsson 2001; Gustafsson and Unsbo 2003) and the detection acuity of vertical sinusoidal gratings is nearly as good in the periphery as in the fovea when REs are corrected (Wang *et al.* 1997). Finally, it is also known that the post-retinal mechanisms are equally proficient at signalling contrast information in the fovea and in the peripheral retina up to 40 degrees (Banks *et al.* 1991).

As Wallman and Winawer (2004) noted in their review of homeostasis of eye growth and the question of myopia: "*Because the density of most neurons is greater in the central retinal one might think that the influence of the periphery would be modest; however the total area of the central retina is quite small (the area from 30 to 40 degrees from the fovea is six times as great as the area from the fovea to 10 degrees away; the area from 30 to 31 degrees from the fovea is 60 times the area of the 1 degree fovea). Consequently, the number of retinal neurons is relatively small*." They further add: "*…if there is spatial summation signals from the myopic center and from the hyperopic periphery, the periphery signal will dominate the emmetropisation, and the eye will continue to elongate until enough of the central retina is myopic that it balances the hyperopic periphery.*"

The centre of the fovea in the human retina is rods-free in a central area of approximately 260 μm, while the cone density in this area is the highest (140,000/mm^2). Beyond this area, the density of rods increases, reaching its maximum (160,000/mm^2) at approximately 20 degrees from the fovea and starts to slowly decrease when reaching the ora serrata (about 30,000/mm^2). The density of cones drops quickly with eccentricity to approximately 25,000/mm^2 at only 1.4 degrees from the centre of the fovea, and continues to progressively decrease with eccentricity to about 5,000/mm^2. At any eccentricity, the concentration of cones is higher at the nasal retina than in the temporal retina (Osterberg 1935 cited by Rodieck 1988).

So, if the peripheral retina has the capacity from the anatomical and functional point of view to regulate eye growth, what evidence exists to prove this is the case? The answer is found in studies from animal models of emmetropisation and eye growth. Using different animal models such as chickens (Diether and Schaeffel 1997; Hodos and Kuenzel 1984; Troilo *et al.* 1987; Wallman *et al.* 1978; Wallman *et al.* 1987; Wallman and I. Adams 1987), tree shrews (Norton 1990) and monkeys (Kee *et al.* 2004B; Smith EL III *et al.* 2005), it has been possible to determine that foveal defocus alone is not necessary to regulate eye growth and that the visual deprivation of the non-foveal retina also results in myopic RE even in cases where the optic nerve has been severely damaged.

When the visual field of chickens is restricted with translucent goggles to the front field only, extreme myopic error is induced, although complete translucent occluders still generate a greater myopic effect than frontal visual field goggles (Wallman *et al.* 1978; Wallman and Adams 1987). When peripheral vision is allowed with goggles covering only the frontal visual field, an increase in equatorial diameter, but not in axial diameter, occurs (Hodos and Kuenzel 1984). Similarly, when covering the nasal or temporal half of the visual field, deprived myopia is limited to the deprived part of the retina due to vitreous chamber enlargement, regardless of which half of the retina is visually deprived (Wallman *et al.* 1987). In another study (Diether and Schaeffel 1997), local and complete field response to negative and positive lenses covering either nasal, temporal or the full field of view in chickens was observed. It was also observed that the largest response was to positive lenses and this response was related to thickening of the choroid revealing the ability of the retina to recognise the direction of defocus.

Using a different setup, Troilo *et al.* (1987) conducted an experiment in which they sectioned the optic nerve of one eye of chickens and then partially restricted the visual field of the same eye. The result of this experiment was an enlargement of the VCD only in the deprived region of the eye. To the contrary, it was observed than when the optic nerve was sectioned and the eye remained non-deprived, severe hyperopia was generated. These results emphasised the importance of the peripheral retina in the development of myopia in chickens and perhaps also in humans as noted by Wallman *et al.*, (1987) who made reference to the study of Nathan *et al.* (1985) who observed that ocular diseases affecting the fovea and peripheral retina led to myopia in children with low vision, while those conditions principally affecting the foveal vision showed a trend to hyperopic RE.

Other studies using different animal models also obtained similar results. Norton (1990) induced myopia even when the efferent retinal activity was blocked by using sodium channel blocker tetrodoxin. As noted in subsection 1.3.3, monkeys are considered the most suitable animal model for clinical or basic research because the experimental results can be directly applied to the human population. Kee *et al.* (2004B) and Smith EL III *et al.* (2005) induced bilateral form-deprivation in 12 infant monkeys (*Macaca mulatta*) using diffusers with apertures that allowed 20 of 40 degrees of unrestricted vision. After 4 months of wearing the lenses, the macula of the treated eyes was ablated with Argon laser in one eye of seven monkeys and then the animals were allowed unrestricted vision (recovery). Myopia was induced in the majority (eight) of the treated monkeys and after the period of recovery it was observed that no intraocular difference in the recovery process occurred in the seven monkeys who had their fovea damaged by the laser.

Despite all the extensive work conducted into the understanding of the characteristics of off-axis refraction in animals and humans, the information available in the published literature regarding off-axis refraction in children has been limited until now. To date, only two studies (Mutti *et al.* 2000B; Schmid 2003A) have assessed the characteristics of off-axis RE in children. The first study published which measured peripheral refraction in children is the study by Mutti *et al.* (2000B). As part of the Orinda Longitudinal Study of Myopia, the off-axis refraction was obtained from 820 children up to 30 degrees in the nasal retina using an autorefractor. Using the off-axis refraction data, they compared the differences in relative off-axis refraction between RE groups and also described the ocular shape for the different RE groups. They found that myopic eyes had relative hyperopic RE while emmetropes and hyperopes, on average, had relative myopic RE (higher in hyperopes). They described the ocular shape of myopic eyes as prolate, while emmetropes and hyperopes had an oblate shape. Using logistic models, the shape of the myopic eyes was best characterised as an eye with an enlarged

VCD (as the strongest characteristic) with a prolate shape. One limitation of this study was that off-axis refraction was obtained only from one point, thus limiting the conclusions regarding eye shape and analysis of off-axis astigmatism asymmetry. In the study by Schmid (2003A), the primary aim was to determine the correlation between the variability of off-axis refraction from the four retinal quadrants (up to 15 degrees only) obtained with an autorefractor and the variability of retinal steepness as measured by an optical low coherence reflectometry in 63 children aged from 7 to 15 years with different RE. It was found that, on average, myopic eyes had less peripheral relative myopia and steeper retinas than emmetropes or hyperopes. However, at close inspection of these results, large standard deviations were found for all RE groups, which suggest that any eye could have a flat or steep retina and experience hyperopic or myopic relative peripheral RE, irrespectively of whether the eye was myopic, emmetropic or hyperopic. While measuring the four retinal quadrants, the study of Schmid provided a better understanding of the off-axis refraction of the overall retina, however, it was limited to the small angle measured and, as reported in the study, the reliability of the measurements obtained from the nasal retina were affected by the optic nerve.

In summary, there is evidence that certain patterns of off-axis refraction are present with different REs, and it is possible that certain patterns of off-axis refraction are associated to the development or progression of myopia. However, until now, information regarding the off-axis refractive status of eyes in children has been limited. Studies conducted in children have provided limited information of the optical characteristics of the off-axis RE at medium eccentricities and no study has previously assessed the characteristics of optical quality in terms of monochromatic aberrations in children. It is important to know if different patterns of off-axis HOAs are present with different REs, especially in myopia, as it is possible that off-axis REs may impact on ocular growth and/or the progression of myopia.

1.6 SUMMARY

Myopia is a significant health problem, the prevalence of which seems to have increased over the last few generations around the world affecting primarily young children during school years and more evidently in some countries of East Asia. At high levels, myopia is associated with retinal changes which lead to the loss of vision. While the cause of myopia is yet to be determined, it seems very likely that a combination of heredity and environment stimuli (near work being the most probable) has an association with the onset of myopia in children.

Conclusions drawn from the results of studies with different animal species are that both the emmetropisation process and development of RE can be controlled by local mechanisms at the retinal level which are triggered by image quality and optical defocus. It is possible that a similar mechanism occurs in humans, but the exact nature of it remains unclear. It is probable that imperfections in the optical system which cause an increase (or decrease) of ocular aberrations could act as the stimulus that triggers myopia-onset in children. It is also possible that the pattern of peripheral refraction or aberrations could be another causative factor for the eye to elongate and become myopic. Most studies until now have assessed these characteristics in adult populations and very little is known of these characteristics in children. It is important to conduct either longitudinal studies or studies on large cohorts of children to help in the understanding of such characteristics. Measuring and analysing the characteristics of on and off-axis aberrations in a large sample of children will offer invaluable information to researchers in the field of myopia.

1.7 PURPOSE OF RESEARCH

1.7.1 Hypotheses

1. Ocular monochromatic aberrations are normally distributed and highly correlated between eyes in 12 year old children.

2. In myopic eyes, abnormal amounts of HOAs exist in comparison to emmetropic and hyperopic eyes.

3. Inter-race differences exist in the patterns of ocular aberrations between RE groups in children - namely myopia, hyperopia and emmetropia.

4. Age differences exist in the patterns of ocular aberrations in children.

5. Differences in peripheral (off-axis) aberrations exist between RE groups in children.

1.7.2 Aims

The primary aims of this thesis were to determine the characteristics of on and off-axis optical quality in terms of monochromatic aberrations from a large sample of children and to determine the association of HOAs with RE, in particular with myopic RE.

The aims of the studies presented in the following chapters were:

- To determine the distribution and binocular correlation of LOAs and HOAs in a group of mostly 12 year old children and to determine their contribution to the refractive state of the eye (Chapter 4).
- To identify if inter-racial differences exist in the distribution of ocular aberrations in a group of mostly 12 year old children and to determine if these differences also exist in the patterns of ocular aberrations within different REs (Chapter 4).
- To determine the differences in the pattern of ocular aberrations and RMS in children from two distinct age groups (mostly 6 and 12 year olds) (Chapter 5).
- To determine the characteristics of off-axis peripheral refraction in a group of mostly 12 year old children and to determine if differences exist between different RE groups (Chapter 6).
- To determine the characteristics of off-axis HOAs in a group of mostly 12 year old children and to determine the characteristics of those aberrations in different RE groups (Chapter 6).

1.7.3 Study Design

A description of the instrument used in this study to measure the ocular aberrations can be found in Chapter 2. The repeatability of the instrument in measuring RE and HOAs in a model eye and in subjects was evaluated. A study that validated the ability of the instrument in measuring cycloplegic RE was conducted. The description of the method used to measure the peripheral aberrations in this study is also included. Chapter 3 describes the general methodology of this study, including the Sydney Myopia Study, subjects and the experimental procedures. Data analysis for these studies are presented in Chapters 4 to 6.

The studies presented in Chapters 4, 5 and 6 were based on the cross-sectional evaluation of a sample of 12 year old children from the Sydney Myopia Study. The aims of Chapter 4 were to describe the distribution of ocular aberrations in 12 year old children and to determine if there were differences in ocular aberrations between RE groups. It also aimed to identify if there were differences between ethnic groups.

The study presented in Chapter 5 was based on the cross-sectional evaluation of the sample of 12 year old children which was also evaluated in Chapters 4 and 6 and a sample of 6 year old children which was previously evaluated at the Sydney Myopia Study. The aims of Chapter 5 were to compare the aberration profiles between RE groups from these two samples. The aims of Chapter 6 were to determine the distribution of off-axis (peripheral) REs and their relationship with on-axis REs in 12 year old children. Additionally, Chapter 6 aimed to determine the distribution and characteristics of off-axis HOAs in 12 year old children and to determine if there were differences in off-axis HOAs between RE groups.

1.7.4 Expected Outcomes

At completion of this thesis, this study will produce normative data of the general characteristics of monochromatic aberrations in 12 year old children, to determine the associations that on and off-axis monochromatic aberrations have with RE and ethnicity. The results obtained from this study will help to understand the contribution that monochromatic aberrations have in RE, especially myopia, and the role that they might play in the emmetropisation and myopia development. Additionally, this study will provide normative data of monochromatic aberrations and off-axis (peripheral) aberrations in 12 year old children.

CHAPTER 2: METHOD DEVELOPMENT

2.1 ABERROMETRY

2.1.1 Introduction

In a perfect lens or "aberration-free" lens, the spherical wavefronts spreading out from a point object are focused as convergent spherical wavefronts, which are centred at the image point (Charman 1991). An eye focused at infinity is considered "aberration-free" when the ideal wavefront exiting the eye is a flat plane (Figure 2.1A), while in an aberrated eye the exit wavefront deviates from that plane (Figure 2.1B) (McRae *et al.* 2001).

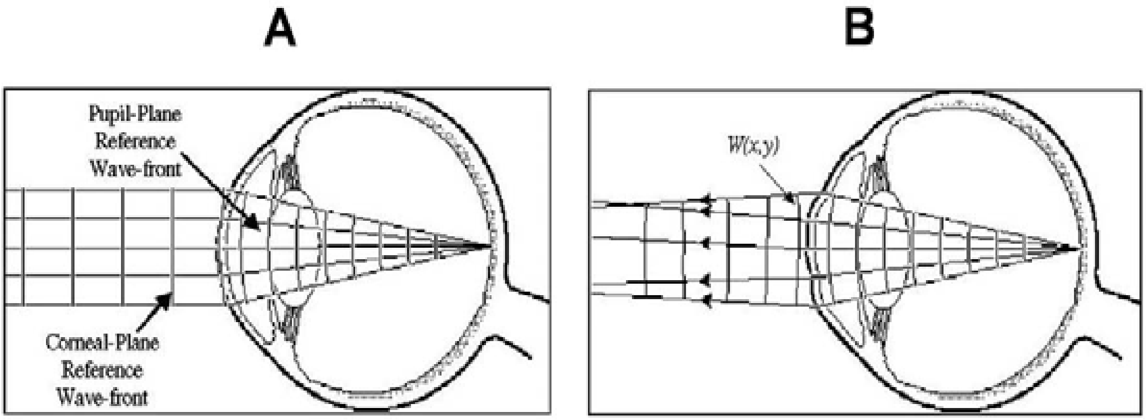

Figure 2.1: ***(A) Example of an "aberration-free" eye in which the pencils of light of the wavefront exiting the eye from the fovea form a flat plane. (B) Example of an aberrated eye in which the wavefront exiting the eye from the fovea are not parallel. (Diagrams reproduced from McRae et al. 2001)***

In the last few years several methods have been developed to measure the aberrations of the eye. Based on the optical principle they use, these methods can be classified as "into-the-eye" or "out-of-the-eye" aberrometry (Atchison 2005). In "into-the-eye" aberrometry, the image which is formed on the retina is analysed; while in "out-of-the-eye" aberrometry, a narrow beam which is projected into the eye and reflected from the retina is analysed.

The most common method used by commercial aberrometers is the Shack-Hartmann method, which was applied first to measure the wave aberrations in humans by Junzhong Liang around 1990 (Liang *et al.* 1994). In a Shack-Hartmann aberrometer, a narrow beam of light of approximately 1 mm is projected into the eye and the reflected light from the retina passes through an array of micro-lenses and focuses onto a CCD camera or Hartman screen (Figures 2.2A and B). Each of the micro-lenses in the array focuses a small sample of radiation corresponding to a small region of the pupil. The transverse ray aberration (local or partial derivatives) associated with each micro-lens can be determined from the departure of the centroid of its corresponding image from the ideal position (Atchison 2005).

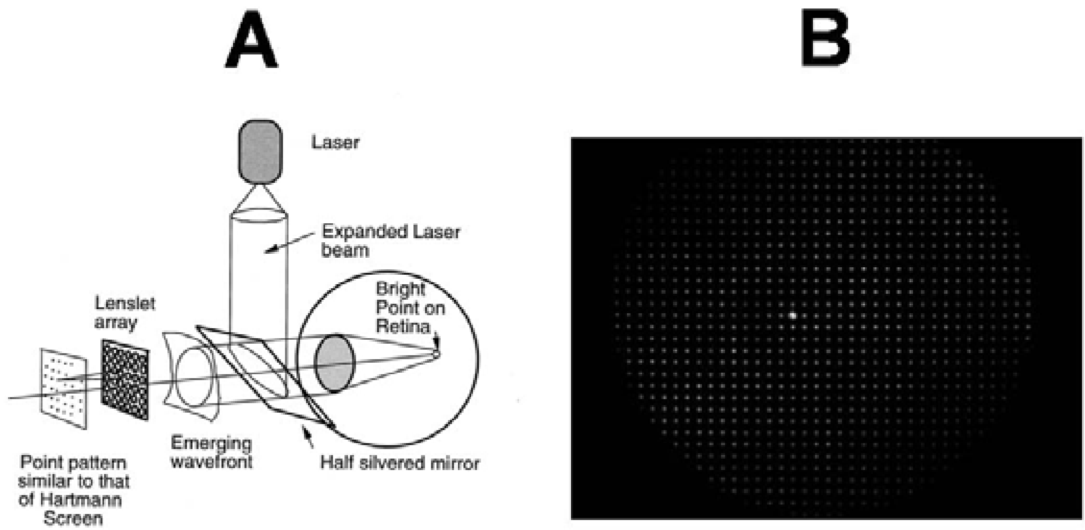

Figure 2.2: ***(A) Diagram of the optics of a Shack-Hartmann device (reproduced from McRae et al. 2001); (B) Array of spots obtained from a subject measured in the current study with the Complete Ophthalmic Analysis System G200 aberrometer***

Some advantages of Shack-Hartmann devices are the speed in measuring the wavefront (usually less than 1 second), the moderate to high sampling resolution of the aberration, high reliability and a moderate dynamic range. All these features are very important when measuring aberrations in children and, therefore, it was the instrument of choice for this study.

2.1.2 The Complete Ophthalmic Analysis System G200 Aberrometer

The Complete Ophthalmic Analysis System (COAS) G200 aberrometer is the first commercially introduced ophthalmic Shack-Hartmann aberrometer by Wavefront Sciences, Inc. (Albuquerque, NM, USA).

The COAS has an array of square lens-sets (44 x 33 lens-set array) that sample the aberration at intervals of 210 μm, allowing the sampling of approximately 600 sample points within a 6 mm diameter pupil. The COAS uses a 840 nm super luminescent diode as the light source for measurement. The results that the COAS provides are converted to a user-selected wavelength (550 nm).

The COAS can measure spherical REs in the range of -15.00 to +7.00 D and cylinders up to -6.00 D and PDs from 3.5 to 9.0 mm. The COAS provides sphero-cylindrical RE measurements (in steps of 0.01 D) at the corneal or spectacle plane. The wavefront error is reported as Zernike polynomials in Malacara or the Optical Society of America formats (Thibos *et al.* 2002B) (see Appendix C) from the second to the 12th order. Other results include the total and HOs RMS, and pupil size to the nearest 0.1 mm.

The COAS G200 calculates the RE from Zernike polynomials of the second order: Z(2,-2) and Z(2,2) for astigmatism and Z(2,0) for SE using a least-squares fitting of the wavefront (Thibos *et al.* 2004). This method has been found to be an inaccurate indicator in determining the SE of the RE as determined by subjective refraction in comparison to other methods such as paraxial curvature matching, which accurately predict subjective refraction (Cheng *et al.* 2004A). The COAS G200 offers an option similar to the paraxial curvature matching method called the "Seidel Sphere" (Salmon *et al.* 2003). In this option, the aberrometer incorporates the Z(4,0) term (primary SA) in the calculation of SE.

For this study, the analysis of aberrations was performed under cycloplegia for a 5 mm PD, the Zernike coefficients were reported using the Optical Society of America format and the Seidel Sphere option was chosen for the calculation of RE.

Whilst the COAS aberrometer has been found to be a reliable tool for measuring RE in young myopes (Salmon *et al.* 2003), and also to be an accurate instrument in the measurement of LOAs and HOAs in model eyes (Cheng *et al.* 2003C) and human eyes (Salmon and van de Pol 2005), there are no reports of the instrument being used in children or its reliability. Thus, the repeatability and accuracy of the instrument in measuring RE in children were assessed in this study.

2.1.3 Repeatability of the COAS G200 Aberrometer

The aims of this study were to determine the repeatability of the COAS aberrometer in measuring LOAs and HOAs in a model eye and in cyclopleged eyes of children.

2.1.3.1 Methods and Materials

Eighty-one (81) children from the Sydney Myopia Study were selected to assess the repeatability of the COAS. Subjects with a wide range of REs were selected for this study: mean right eye SE (±SD) -0.11 ± 1.98 D (range -6.22 to 5.05 D) and mean astigmatic error of -0.40 D (range -0.05 to -2.39 D). The mean age was 12.9 ± 0.4 years (range 12 to 13.8 years).

Two consecutive measurements were obtained from the right eye and then from the left eye with the patient remaining on the chin rest (mean time difference 10 ± 03 seconds). A few minutes later, after realignment of the instrument and repositioning of the patient on the instrument, a third measurement was also obtained (mean time difference 25 ± 15 minutes).

The COAS aberrometer is provided with a calibrating unit which, according to the manufacturer, has a spherical value of -5.00 DS. This model eye was for purposes of measuring the repeatability of the COAS in a model eye. Ten consecutive measurements were obtained after realignment between each reading.

Cycloplegia was induced using the protocol of the Sydney Myopia Study as described in Section 3.1.1.3. In both experiments, the PD used for analysis was set to 5 mm and RE was calculated using the Seidel sphere option.

To analyse the RE, the refractive data in S (Sphere), C (negative cylinder), α (axis in degrees) were converted into power vectors (Thibos *et al.* 1997) using the following equations:

$$M = S + C/2$$ **Equation 2.1**

$$J_0 = (-C/2)\cos(2\alpha)$$ **Equation 2.2**

$$J_{45} = (-C/2)\sin(2\alpha)$$ **Equation 2.3**

$$|P| = \sqrt{M^2 + J_0^2 + J_{45}^2}$$ **Equation 2.4**

The coefficient of repeatability (CR) for the LOs was obtained following two methods. For the first method, the CR was computed using the method suggested by Salmon *et al.*, (2003) and Salmon and van de Pol (2005). It was found that this method, as published, was missing a square-root operation (see point 5) which was included in the current calculations. When the square-root is omitted in the calculation, the variance is obtained and not the standard deviation, which is needed for the calculation of the CR. Personal communications with Dr Salmon, confirmed that the authors included this operation in their calculations, however, due to a typographical error, it was omitted in the text of their publications. Therefore, the method for calculating the CR in children was as follows:

1. Refractive data were converted to power vectors.
2. The mean of the three original power vectors was computed.
3. Three difference vectors were obtained (subtracting the mean from each of the three original power vectors).
4. The magnitude of each difference vector and the mean of the three magnitudes were computed to obtain the mean deviation for each eye.
5. The RMS deviation (standard deviation of the differences; Bland and Altman 1986) was obtained by squaring and adding up the mean deviations for 81 eyes, dividing by 81 and then taking the square-root.
6. The RMS deviation was multiplied by 1.96 to obtain the CR.

The second method consisted of the calculation of the 95% CIs (sum of the mean differences ± 1.96 * standard error) of the magnitude of the power vector

(P) from all subjects to obtain the CR (1.96 * standard deviation). This well-known method was used for comparison of the results obtained with the method from Salmon *et al.* (2003).

The method used to obtain the CR of the HOs (3rd to 6th orders) was computed as suggested by Salmon and van de Pol (2005) as follows:

1. From the three measurements obtained in the children, the standard deviation, the standard error ($\mathrm{SE} = \mathrm{SD}/\sqrt{3}$) and the 95% CI were computed.

2. The 95% CI were averaged across the 81 eyes.

3. The mean 95% CI for each coefficient was interpreted as the instrument noise.

In the experiment using the model eye, the same procedure was followed for computing both the LOs and HOs repeatability using the results from the 10 measurements.

2.1.3.2 Results

The mean results and CR obtained from the right and left eyes of the 81 children and the 10 readings of the model eye are presented in Appendix D.

The CR of LOs in children was 0.23 D (method 1) and 0.24 D (95% CI -0.03 to 0.03) (method 2) for the right eyes. For the left eyes, this coefficient was 0.23 D (method 1) and 0.19 D (95% CI -0.01 to 0.03) (method 2). For the model eye the CR of the LOs was found to be better than for children: 0.03 D (method 1) and SE=0.01 (95% CI 0.05 to 0.1) (method 2).

Figures 2.3 and 2.4 show the CR for the HOAs from the 81 children and the model eye respectively.

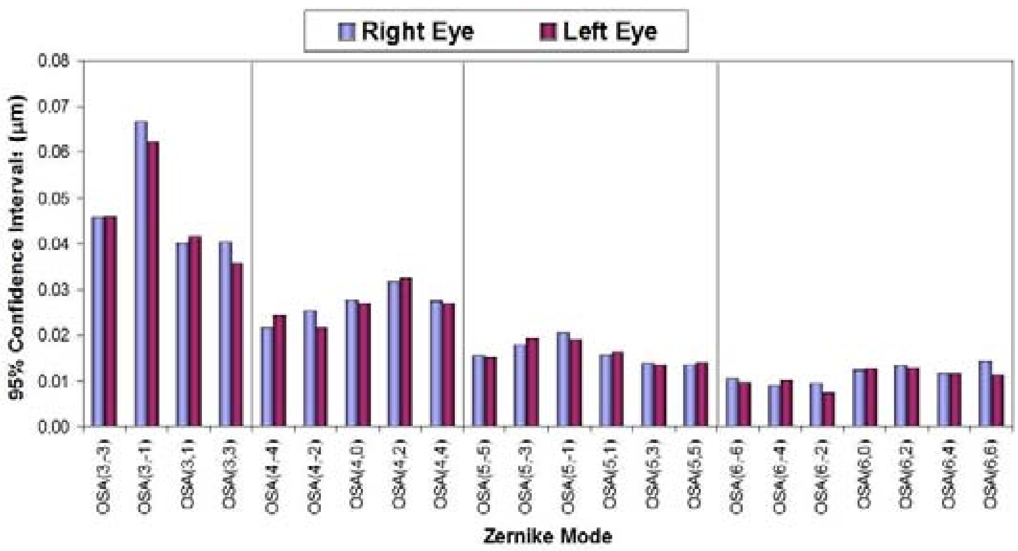

Figure 2.3: ***Repeatability of the COAS for measuring HOAs expressed as 95% CI for three readings from the right eyes (blue columns) and left eyes (purple columns) of 81 children***

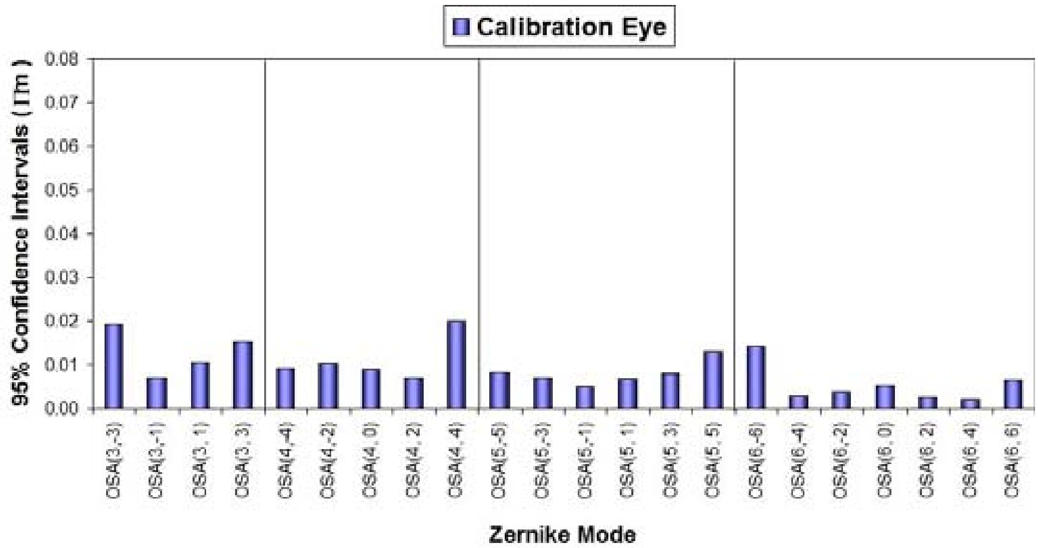

Figure 2.4: ***Repeatability of the COAS for measuring HOAs expressed as 95% CI for 10 readings from the model eye***

2.1.3.3 Discussion

This CR of LOs in children was very similar to that found by Salmon and van de Pol (2005), where a marginally better mean repeatability was found with the default sphere option of 0.17 D compared to the Seidel sphere option of 0.22 D. The repeatability of the COAS G200 in children was slightly lower than that specified by the manufacturer for sphere, cylinder and axis (±0.05 D) but similar to what can be expected from cycloplegic autorefraction (Zadnik *et al.* 1992).

A better CR of the HOs was found for the model eye than for children. This was expected because small fluctuations of wavefront aberrations can occur when measuring human eyes, caused by changes in the tear film or small movements that are not seen in the model eye. Nevertheless, because of the high repeatability found for the LO modes in children and its similarity to that obtained from an accurate autorefractor, during the whole study it was decided to obtain one measurement from each eye with the COAS G200.

2.1.4 Validation of COAS RE Measurements

The purpose of this study was to examine the reliability of cycloplegic RE measurement by the COAS G200, and its comparability to a known automatic refractor (Canon RK-F1, Canon Inc., Japan) in young children.

2.1.4.1 Methods

Cycloplegic refraction data was collected as part of the Sydney Myopia Study from a sample of Year 1 (mostly 6 year olds) and Year 7 (mostly 12 year olds) school children. Children in the Year 1 group (n=1,504) were measured during 2003-4 and children in the Year 7 group (n=890) were measured during 2004-5. All examinations took place at the schools during school hours.

Cycloplegia was achieved following the drops protocol of the Sydney Myopia Study described in subsection 3.1.1.2.

Autorefraction was performed 25 to 30 minutes after the last drop was instilled. Aberrometry was performed 5 to 10 minutes after autorefraction.

The mean of five readings taken with the autorefractor in automatic mode (K-R mode) was obtained from each eye for analysis.

Only one reading was obtained for analysis from both eyes with the COAS in autorefraction mode (Auto-acquire mode). The PD for analysis in the COAS was set to 5 mm and the Seidel Sphere option was chosen for the calculation of RE.

In a small number of cases, the PD obtained was less than 5 mm and these subjects were excluded from the analysis. All measurements were calculated at the corneal plane in the aberrometer and autorefractor.

The dioptric refractive data obtained with both instruments: S (Sphere), C (negative cylinder), α (axis in degrees) were converted into power vectors using equations 2.1 to 2.4.

The agreement between both instruments was evaluated using the method suggested by Bland and Altman (1986). The differences between instruments were tested with a two-tailed *t*-test for paired observations. Differences were considered to be statistically significant when $p < 0.05$.

For purposes of this study the Canon RK-F1 served as the gold standard and the coefficient of agreement between the COAS G200 and the Canon RK-F1 was defined and calculated as 1.96 times the standard deviation of the differences between the two instruments (Calver *et al.* 1999).

Data analysis was performed using SPSS (Version 12.0.1) statistical software.

Approval for the study was obtained from the University of Sydney Human Research Ethics Committee, and the New South Wales State Department of Education and Training, Australia. Informed written consent from at least one parent and verbal assent from each child were obtained.

2.1.4.2 Results

The mean ages (±SD) of the children in Year 1 and Year 7 were 6.7 ± 0.43 years (range 5.50 to 9.13 years) and 12.6 ± 0.45 years (range 11.06 to 14.44 years), respectively. Fifty-two percent (52%) of the Year 1 group and 57% of the Year 7 group were boys. The majority of children in both groups were Caucasian (55% Year 1, 49% Year 7) with the remaining children from diverse ethnic backgrounds (East Asian, Indian /Pakistani / Sri Lankan, Middle Eastern and others).

The mean vector components obtained with the Canon RK-F1 and the COAS G200 from both eyes of the Year 1 and Year 7 groups are presented in Tables 2.1 and 2.2, respectively. Since there was a high correlation between right and left eye SE in both the Year 1 and Year 7 groups for both the autorefractor (r=0.924, r=0.932, p<0.001) and the aberrometer (r=0.893, r=0.921, p<0.001), further analyses were limited to right eyes only.

Table 2.1: ***Mean cycloplegic refractive components of Year 1 children (n=1,504) obtained with the Canon RK-F1 autorefractor and the COAS G200 aberrometer***

Refractive Component	Canon RK-F1		COAS G200	
	Right Eye	Left Eye	Right Eye	Left Eye
	Mean ± SD (D)	Mean ± SD (D)	Mean ± SD (D)	Mean ± SD (D)
M	1.22 ± 0.70	1.28 ± 0.73	1.12 ± 0.80	1.15 ± 0.82
J_0	0.02 ± 0.22	0.04 ± 0.20	0.09 ± 0.24	0.11 ± 0.23
J_{45}	-0.02 ± 0.10	-0.03 ± 0.09	0.01 ± 0.13	-0.03 ± 0.11

Table 2.2: ***Mean cycloplegic refractive components of Year 7 children (n=890) groups obtained with the Canon RK-F1 autorefractor and the COAS G200 aberrometer***

Refractive Component	Canon RK-F1		COAS G200	
	Right Eye	Left Eye	Right Eye	Left Eye
	Mean ± SD (D)	Mean ± SD (D)	Mean ± SD (D)	Mean ± SD (D)
M	0.36 ± 1.45	0.43 ± 1.48	0.34 ± 1.50	0.37 ± 1.55
J_0	-0.04 ± 0.27	-0.02 ± 0.25	0.06 ± 0.27	0.09 ± 0.25
J_{45}	-0.03 ± 0.12	-0.03 ± 0.11	0.04 ± 0.14	-0.05 ± 0.13

In the Year 1 group, a two-tailed *t*-test indicated a significant difference ($p<0.001$) between the Canon RK-F1 and the COAS G200 for the three vectors (M, J_0 and J_{45}). The mean paired differences and 95% limits of agreement between the two instruments in the Year 1 group are summarised in Table 2.3. On average, the COAS G200 measured 0.10 D more myopia than the Canon RK-F1 in the Year 1 group.

The mean difference between the readings obtained in the Year 1 group with the Canon RK-F1 and the COAS G200 (M, J_0 and J_{45}, respectively), as a function of their mean, are plotted in Figures A to C in Appendix E. Positive values from the mean indicate that COAS G200 measured more minus than the Canon RK-F1 and negative values from the mean indicate that the COAS G200 measured more plus than the Canon RK-F1.

Table 2.3: ***Mean paired differences and limits of agreement between the Canon RK-F1 autorefractor and the COAS G200 aberrometer for each refractive component from right eyes of children in Year 1***

Refractive Component	Paired Differences		
	Mean ± SD (D)	**95% limits of agreement**	**Two-tailed *t*-test p-Values**
M	0.10 ± 0.33	-0.54 to +0.74	**<0.001**
J_0	-0.07 ± 0.14	-0.48 to +0.48	**<0.001**
J_{45}	-0.03 ± 0.12	-0.52 to +0.51	**<0.001**

A positive value in M indicates that the COAS G200 measured more myopia than the Canon RK-F1 autorefractor

For the Year 7 group, statistically significant differences were found for J_0 (two-tailed *t*-test, $p<0.001$) and for J_{45} (two-tailed *t*-test, $p<0.001$) only. Table 2.4 summarises the mean paired differences and the 95% limits of agreement, between the two instruments for the Year 7 group.

The coefficients of agreement found for the M, J_0, and J_{45} components between the Canon RK-F1 and the COAS G200 were 0.64, 0.28 and 0.23 D respectively in the Year 1 group. For the Year 7 group these coefficients of agreement were 0.54, 0.31 and 0.21 D respectively.

Table 2.4: ***Mean paired differences and limits of agreement between the Canon RK-F1 autorefractor and the COAS G200 aberrometer for each refractive component from right eyes of children in Year 7***

Refractive Component	Paired Differences		
	Mean ± SD (D)	**95% limits of agreement**	**Two-tailed *t*-test p-Values**
M	0.02 ± 0.28	-0.52 to +0.56	0.065
J_0	-0.10 ± 0.16	-0.41 to +0.21	**<0.001**
J_{45}	-0.07 ± 0.11	-0.28 to +0.14	**<0.001**

A positive value in M indicates that the COAS G200 measured more myopia than the Canon RK-F1 autorefractor.

The mean difference between readings obtained in the Year 7 group with the Canon RK-F1 and the COAS G200 (M, J_0 and J_{45}, respectively) as a function or their mean (Bland and Altman plot) are presented in Figures D to F in Appendix E. Positive values from the mean indicate that COAS G200 measured more minus than the Canon RK-F1 and negative values from the mean indicate that the COAS G200 measured more plus than the Canon RK-F1.

2.1.4.3 Discussion

Salmon *et al.* (2003) evaluated the accuracy of the COAS and an autorefractor (Nidek ARK-2000) when measuring myopic REs in adults and found that the mean difference of the power vector (in the current study |P|) between the COAS (PD 4 mm, non-Seidel sphere) and subjective refraction was 0.31 ± 0.04 D. In the current study, the mean difference of |P| between the Canon RK-F1 and the

COAS G200 was 0.05 ± 0.28 D (two-tailed *t*-test, $p<0.001$) for the Year 1 group and -0.03 ± 0.25 D (two-tailed *t*-test, $p=0.001$) for the Year 7 group.

In this study, a better agreement was found between the two instruments for M in the Year 7 group than in the Year 1 group. In the Year 1 group, there were a number of cases (n=25) in which the COAS G200 measured more than 1.00 D more myopia than the Canon RK-F1. Close inspection of the aberrometry data from these cases, including astigmatism, HOAs, RMS and PD, did not reveal any evident explanation for this clinically significant difference. This large difference in these subjects could be attributed to difference in pupil size, method of estimating RE, alignment and other fundamental differences between the two instruments. It could also be that partial cycloplegia allowed some accommodation that affected measurements with the COAS G200 only. Misalignment of the COAS G200 during measurement was ruled out as a possible cause because, as reported by Cheng *et al.* (2003A), small axial and lateral displacements with the COAS had little effect on measurement of myopic or hyperopic eyes.

The effect that these extreme cases may have had on the differences in vector components between the two instruments in the Year 1 group was examined. When these cases were removed from analysis, the mean paired difference for M was 0.08 ± 0.27 D and remained significant (two-tailed *t*-test, $p<0.001$). No change was found for the astigmatic components.

While the COAS in previous studies have presented some degree of error when compared to the subjective refraction (gold standard), the differences between the instrument and a Canon RK-F1 autorefractor proved to be minimal for measuring sphero-cylindrical errors. Because of the nature of the study, it was not possible to compare the accuracy of the COAS G200 to cycloplegic subjective refraction. The results obtained in this study from children under cycloplegia with the COAS G200 were comparable to those from a reliable autorefractor. It was determined that the COAS could be used as a reliable tool in the detection of REs in population-based studies of refraction in young children.

2.2 PERIPHERAL ABERROMETRY

2.2.1 Introduction

In recent years, peripheral (off-axis) aberrations have been extensively studied using different methods such as double-pass (Guirao and Artal 1999; Gustafsson *et al.* 2001; Seidemann *et al.* 2002), ray tracing (Navarro *et al.* 1998) and Shack-Hartmann (Atchison and Scott 2002; Atchison *et al.* 2003; Atchison 2004A; Lundström *et al.* 2005A; Ma *et al.* 2005). A considerable advantage of the Shack-Hartmann method in measuring off-axis aberrations in children over the other methods is that it takes less time to be performed which, in the case of subjective ray-tracing method, can take minutes. The Shack-Hartmann method has also been validated in measuring peripheral refractions (Atchison 2003).

Taking into consideration the advantages of the Shack-Hartmann method, it was decided to use the COAS aberrometer to measure the peripheral aberrations of the children who participated in the Sydney Myopia Study. At the time when the study commenced, no report existed of using a commercially-available aberrometer for measuring peripheral aberrations. Recently, the COAS aberrometer was used to measure off-axis RE from two myopic LASIK patients (Ma *et al.* 2005), therefore, the current study is the largest reported using a COAS aberrometer to measure off-axis aberrations in children.

2.2.2 The Peripheral Fixation Target

In most studies that measured off-axis aberrations, the experiments have been conducted in laboratories with spaces that allow placing peripheral targets on boards at different angles under well-controlled environments.

Because of the nature of the current study, such well-controlled conditions were not available, therefore presenting the fixation targets using a different approach was needed. An off-axis target device mounted on the measuring head of the COAS aberrometer (Figure 2.5) was built at the Vision Cooperative Research Centre (Vision CRC) to be used in this study. The off-axis fixation target device was designed to facilitate ipsilateral fixation at an angle of 30 degrees from the centre of the optical axis of the COAS G200 in the nasal, superior and temporal directions of both eyes. Given the close proximity of the device to the subject, high power focusing lenses were used in the fixation device to provide distant targets.

The targets used were simple crosses, illuminated from behind with a green light-emitting diode (LED). All three targets are mounted on a common block which could be moved along the optical axis of the device to provide focus adjustment. This adjustment was controlled via a single knob attached to a fine-pitch screw mechanism. In this arrangement, the focus of all three targets was synchronised. Between each target and the subject there was a focusing lens and a first surface mirror. The position of the lens and mirror was fixed, with some small adjustment provided for the initial calibration. The target device was connected to a switch control box which turned each target on or off according to the position needed.

Figure 2.5: ***The off-axis target device attached to the measuring head of the COAS G200***

When the fixation device was attached to the COAS aberrometer, the illumination LED's used by the COAS to illuminate the examined eye were covered, therefore, it was necessary to provide suitable "replacement" illumination with four small red LED's included in the fixation device. Replacing the internal illumination LED's of the COAS allowed for control of the illumination level, which was advantageous in assisting the examiner to achieve optimum focus of the instrument with both dark and light coloured irises in on and off-axis measurements.

A special calibration tool was fabricated for the initial adjustment (and periodic verification) of the angle subtended by the targets. The tool held a 20 cm long small diameter (4 mm) tube at a precise angle of 30 degrees. The tool fit snugly in the bore of the fixation device, holding it in a position which was representative of the visual axis of the subject. This tool could be rotated to the three positions: nasal, temporal and superior.

2.2.3 Peripheral Aberrations Software

The COAS was designed to provide measurements of on-axis aberrations of the eye. To calculate the aberrations of the eye, the COAS uses the line-of-sight (often considered to coincide with the visual axis of the eye) as the axis of reference. When measuring on or off-axis aberrations, the COAS fits an artificial pupil which is then used as the Zernike unit circle to compute the aberrations of the eye in the image of the artificial pupil captured. A problem which arises when measuring off-axis aberrations with the COAS is that the instrument computes the wavefront as if the instrument is still aligned with the line-of sight (or visual axis) of the eye (Figure 2.6A).

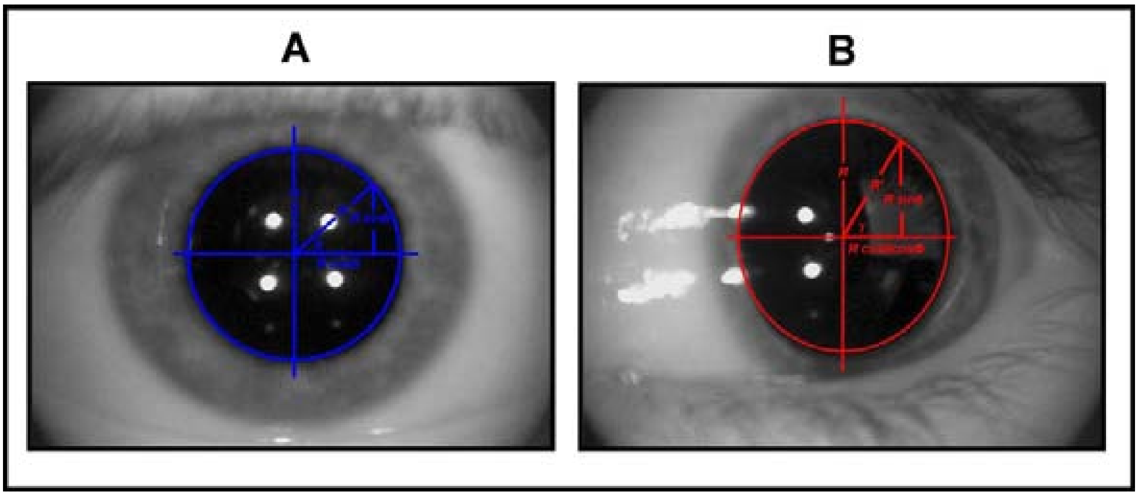

Figure 2.6: ***Differences in pupil dimensions when viewed with the COAS G200 on the visual axis (A) and 30 degrees temporal (B). Diagrams adapted from Atchison et al. 2003***

When an off-axis measurement is obtained with the COAS, the pupil is viewed through a horizontal angle ϕ (off-axis) (Figure 2.6B), and it becomes an ellipse with the x axis compressing by a factor of $1/\cos(\phi)$, and the semi-diameter R along any meridian θ changes to a new value R' along that meridian (Atchison *et al.* 2003). Because the Zernike system of aberrations is defined for circular pupils (not elliptical), a transformation of the wavefront is required. The Zernike coefficients for the elliptical pupil can be defined as a part of a circular pupil in which the major radius of the ellipse R equals the radius of the circle, whilst the minor radius of the ellipse equals a fraction of the circle radius (Lundstrom and Unsbo, 2007).

In order to obtain the transformed values of the wavefront, the program *"Wavefront Data Manipulator 1.3 for Windows 2000/XP"* was written in the Vision CRC using Lab Windows™/CVI Measurement Studio Version 8.0 software from National Instruments™ in collaboration with Drs Kodikullam and Chitralehka Avudainayagam from the School of Optometry and Vision Science, the University of New South Wales.

After reconstructing the wavefront from the off-axis aberrometry data (described as Zernike coefficients from 2nd to 6th orders) as calculated by the COAS, the program fits a new circular pupil into the wavefront which is perpendicular to the visual axis in accordance to the angle measured. Finally, using reverse decomposition, the program provides the new set of Zernike coefficients values for analysis. According to the standards recommended by the Optical Society of America (Thibos *et al.* 2002A) the angle used for computation of the off-axis aberrations in this study for the nasal, temporal and superior positions was 30 degrees. Following this approach, comparisons between on-axis aberrations (along the line-of-sight) and off-axis aberrations (along secondary lines-of-sight) could be made.

CHAPTER 3: METHODS AND MATERIALS

3.1 DATA COLLECTION

To evaluate the aims listed in Chapter 1, school children were evaluated in the Sydney Myopia Study. The study commenced in August 2003 examining children in Year 1 (mostly 6 year old children) and was completed in November 2005. Aberrometry was obtained from a total of 1,436 children in Year 1 (mostly 6 year old children) and 1,813 children in Year 7 (mostly 12 year old children). Off-axis aberrometry was obtained only from children in Year 7. A summary of the Sydney Myopia Study and the description of the procedures used in this study to measure the monochromatic ocular aberrations in children will be described in this chapter.

3.1.1 The Sydney Myopia Study

The Sydney Myopia Study is a population-based study of refraction and eye health of school children that was conducted in the Metropolitan region of Sydney, Australia. The city of Sydney was chosen because Sydney is the largest city of Australia and also because approximately 21% of its population is from diverse ethnic backgrounds.

The study methods have been described before (Ojaimi *et al.* 2005A). The study aimed to establish the prevalence of myopia and other eye diseases in a large representative sample of children attending primary and secondary schools across Sydney. It also aimed to examine the relationship between potential modifiable risks factors and myopia as well as to assess the interactions between environmental and genetic factors in myopia.

3.1.1.1 Examination Procedures

Figure 3.1 shows a flow diagram of the tests conducted at the Sydney Myopia Study.

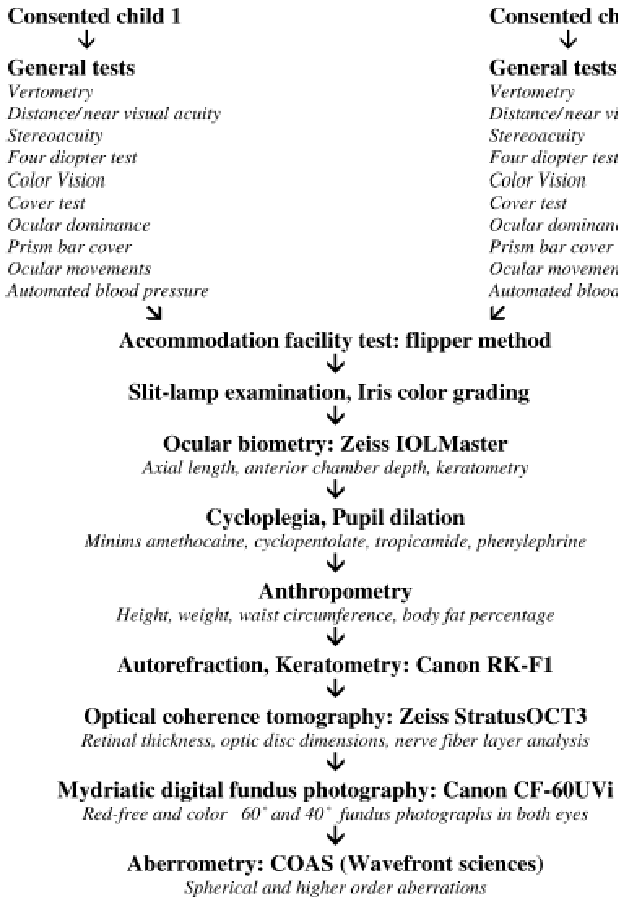

Figure 3.1: ***Flow diagram of the Sydney Myopia Study examination as published in Ojaimi et al. 2005A***

Combined, these procedures allowed information of the visual function, ocular dimensions, morphology and anthropometry of the child. Additional information such as socio-demographic information, ethnicity, medical and ocular history of eye disorders of the child and the parents was obtained via a 193-item questionnaire administered to the parents. Additional to aberrometry, other information reported in this thesis includes ethnicity of the child and cycloplegic autorefraction.

3.1.1.2 Cycloplegia

The protocol adopted in the Sydney Myopia Study to induce cycloplegia was as follows: First, one drop of 1% amethocaine hydrochloride (MINIMS™, Chauvin Pharmaceuticals Ltd., England) was instilled in both eyes to improve comfort and also to enhance the absorption of the subsequent drops (Mordi *et al.* 1986). Cycloplegia/mydriasis of each eye were then attained with two cycles of cyclopentolate 1% (1 drop) and tropicamide 1% (1 drop) instilled 5 minutes apart. Tropicamide 1% (Manny *et al.* 2001) and cyclopentolate 1% are both effective cycloplegic agents in school-age children after 30 minutes of instillation (Egashira *et al.* 1993) and when combined, they provide adequate effect for cycloplegic refractions 30 minutes after instillation, even in the dark irises of African-American children (Kleinstein *et al.* 1999).

Even though the cycloplegic effect was maximised using tropicamide 1% and cyclopentolate 1%, a small proportion of children were slow to dilate and, therefore, these children also received up to two drops of 2.5% phenylephrine. Autorefraction was performed 25 to 30 minutes after the last drop was instilled.

It is important to note that while, in the Study Methods, it was planned that ocular aberrometry should be conducted as the last test, this was not the case. In order to avoid potential recovery of ocular accommodation while measuring cycloplegic autorefraction and aberrometry, autorefraction was performed 25 to 30 minutes after cycloplegia was induced and aberrometry was performed 5 to 10 minutes after autorefraction.

3.2 ETHICS

The Sydney Myopia Study was approved by the Human Research Ethics Committee of the University of Sydney and the Department of Education and Training, New South Wales, Australia.

CHAPTER 4: OCULAR ABERRATION PROFILES IN 12 YEAR OLD CHILDREN

4.1 INTRODUCTION

Studies are needed to determine the normal distribution of ocular aberrations in children and to identify the relationship between HOAs and ocular development and REs in children. While several studies have been conducted in adults (Porter *et al.* 2001; Castejon-Mochon *et al.* 2002; Howland 2002; Thibos *et al.* 2002BA), the study of the characteristics of the ocular aberrations in children has been limited (Carkeet *et al.* 2002; Carkeet *et al.* 2003; He *et al.* 2002; Kirwan *et al.* 2006; Wang and Candy 2005). Results from these studies showed a small variation in the levels of HOAs between RE levels in children and also lower levels of positive SA in infant eyes in comparison to adults. However, no conclusive evidence for the role of ocular aberrations in the development of RE has been determined.

Reports in the literature show that the prevalence of RE in children varies between countries. It appears that the higher prevalence of myopia in young children reported in some Asian countries (Fan *et al.* 2004A) or the higher prevalence of hyperopia in Australian children (Junghans and Crewther 2005) could be the result of ethnic or environmental factors. It is possible that these differences in RE are also the result of inter-racial differences in the distribution or in the levels of HOAs, which could influence the development of emmetropia or ametropia. Ethnic background also appears to play a role in the amount of ocular aberrations in children (Carkeet *et al.* 2002). Comparing ocular aberration profiles between children from various ethnic backgrounds will help identify the relationship, between ocular on-axis aberrations and development of RE.

4.2 AIMS

The aims of this study were:

- to determine the distribution and characteristics of the ocular monochromatic aberrations in a large sample of 12 year old children;
- to evaluate the relationship between ocular monochromatic aberrations and RE, especially myopia;
- to determine if ethnic background plays a role in the distribution and characteristics of ocular aberrations and RE.

4.3 METHODS

4.3.1 Subjects

As described in Chapter 3, children in the 7th grade of school were recruited from 20 high schools which were randomly selected, using a cluster-sampling design, from the Sydney Metropolitan area. Measurements of ocular aberrations were conducted for both eyes of a total of 1,813 children in 7th grade at the schools during school hours in the period from November 2004 to November 2005.

4.3.2 Measurement of Ocular Aberrations

The measurement of the ocular aberrations was performed using the COAS G200 aberrometer under cycloplegia (subsection 3.1.1.2). Approximately 30 minutes after the last drop was instilled, one reading was obtained from each eye of the child and recorded for analysis. The PD for analysis was set at 5 mm to allow for a larger sampling area of the aberrations of the eye. In a small number of cases, the PD recorded was less than 5 mm and these subjects were excluded from the analysis.

The dioptric refractive data obtained with the COAS G200 aberrometer, in the format S/C x α, where S (Sphere), C (negative cylinder), α (axis in degrees), were converted into power vectors (subsection 2.1.3.1, equations 2.1 to 2.3). Based on the SE (M), subjects were assigned into various RE groups and subgroups. Table 4.1 shows the definition of the RE groups and subgroups used in this study.

Table 4.1: ***Definition of RE groups and subgroups (as M)***

Group	Subgroup	Definition (D)
Myopia		≤ -0.50
	Low	-0.50 < -3.00
	Moderate	-3.00 < -6.00
	High	> -6.00
Emmetropia	-	< 0.50 > -0.50
Hyperopia		≥ 0.50
	Low	0.50 < 3.00
	Moderate	3.00 < 6.00
	High	> 6.00

Infantile astigmatism is associated with increased astigmatism and myopia during childhood (Gwiazda *et al.* 2000) and "against-the-rule" astigmatism in 6 year old children is predictive of development of myopia at a later age (Hirsch 1964; Gwiazda *et al.* 2000; Fan *et al.* 2004B). It is evident that a relationship exists between RE and astigmatism and, whilst most of the astigmatism in preschool children is low and ranging between 0.50 to 1.00 D, the prevalence of astigmatism ≥ 1.00 D has been found to be 21% in preschool children.

In order to limit the influence of astigmatism as a confounding factor for myopia, the analysis of aberrations and RE groups was limited to those cases with small amounts of astigmatism; refractive data from eyes having a cylindrical component greater than or equal to ± 1.00 D were considered as astigmatic and, thus, excluded from analysis.

4.3.3 Aberrations

The aberration data is presented as Zernike polynomials coefficients in microns in Optical Society of America format (Appendix C). The analysis of the Zernike coefficients included those coefficients from the 2nd to the 6th order (Z(2,-2) to Z(6,6)).

The variance of the Zernike modes (RMS) was calculated and obtained from the COAS aberrometer for defocus Z(2,0), astigmatism Z(2,-2) and Z(2,2); coma Z(3,-1) and (Z(3,1); trefoil Z(3,-3) and Z(3,3); SA Z(4,0); quatrefoil Z(4,-4) Z(4,4); secondary astigmatism Z(4,-2) Z(4,2); HO RMS (coefficients from the 3rd to 6th orders) and Total RMS (RMS of all coefficients from Z(2,-2) to Z(6,6)).

4.3.4 Ethnicity

Ethnicity information was obtained with parent-administered questionnaires (subsection 3.1.1.1). Ethnicity of the child was determined through the ethnicity of the biological parents. Firstly, the parents were asked if they were the biological parents; they were then asked to provide their ethnic origin (mother and father separately) choosing one of the options provided: Caucasian, East Asian, Indian / Pakistani / Sri Lankan, Middle

Eastern, African, Indigenous Australian, South American, Malaysian / Polynesian. An extra option (Unsure) was provided for those cases where the parent(s) may not be the biological parent(s) or the parents did not have this information.

In this study, for those cases where the parents belonged to more than one ethnic group, the child was categorised as having mixed ethnicity and, for those cases where the ethnic background information could not be collected, were categorised as “Unknown”.

4.4 DATA ANALYSIS

Biometric data such as age, gender, power vectors, and Zernike coefficients were normally distributed and analysed using parametric tests. The statistical tests used to test for normality included the Kolmogorov-Smirnov and Shapiro-Wilk statistics with a Lilliefors significance of $p>0.05$ and by examination of box plots. Independent samples *t*-test was used to test for differences between age, gender, power vectors and RE groups.

The relationship between power vectors and Zernike coefficients between the right and left eyes was examined using Pearson’s bivariate correlation. Analysis of the distribution of LOAs and HOAs from right eyes was examined using Student t-test. Further relationships were tested in right eyes only using Pearson’s bivariate correlation; these included correlation of “M” and Zernike coefficients, correlation of “M” with the RMS of some Zernike coefficients (defocus, astigmatism, coma, trefoil, SA, quatrefoil, and secondary astigmatism). Finally, the correlation between M and HO

RMS (from 3rd to 6th order) and total aberrations RMS (2nd to 6th order) was also tested.

One-way Analysis of Variance (ANOVA) using the Brown-Forsythe (B-F) Statistic was used to test for differences between RE groups and subgroups in the refractive components and Zernike coefficients. Multiple comparisons between the groups and subgroups were performed using the Games-Howell (G-H) test. In addition, the distribution of refractive components and Zernike coefficients were analysed for each ethnic group. A one-way ANOVA test was conducted to look for differences in refractive components and Zernike coefficients for each ethnic group followed by the Games-Howell post-hoc test.

To analyse whether ethnicity had an effect on HOAs between RE groups, multivariate-adjusted analyses of variance were performed with the HOAs RMS as dependent variables and significance levels calculated using Pillai's trace. The analysis was extended to coma, trefoil, SA, tetrafoil, secondary astigmatism and HOAs RMS. Adjusted-multiple comparisons Bonferroni test was used to test for differences between ethnic groups.

The level of significance for all statistical analyses was set at $p<0.05$. Statistical analyses were performed using SPSS 12.0.1 Statistical Software (SPSS, Inc, Chicago, IL, USA).

4.5 RESULTS

4.5.1 Biometric Data

Of the 1,813 children measured with the COAS G200 aberrometer, nine subjects (0.5%) had a PD smaller than 5 mm in one or both eyes and 119 cases (6.5%) were astigmatic as described in Section 4.3.2 in the right eye or in both eyes. Finally, a further 48 cases were astigmatic in the left eyes only (2.8%) and were also excluded from analysis. For the purpose of this study, a total of 1,636 children were considered to meet the final criteria for analysis. Table 4.2 presents the biometric data for gender and age of the 1,636 children.

Table 4.2: ***Age distribution by gender among the 1,636 children***

Gender	n (%)	Mean ± SD (years)	95% CI for Mean		Range
			Lower Bound	Upper Bound	
Male	820 (50.1%)	12.7 ± 0.4	12.6	12.7	11.2 to 14.4
Female	816 (49.9%)	12.6 ± 0.4	12.6	12.6	11.1 to 14.2
All Cases	1636 (100%)	12.6 ± 0.4	12.6	12.7	11.1 to 14.4

Of the 1,636 children included in the analysis, 820 (50.1%) were males. The mean age of the children in the study was 12.6 ± 0.4 years with a range from 11.1 to 14.4 years. The mean age of the males was 12.7 ± 0.4 years; the mean difference in age between males and females (0.1 year) was statistically significant (Independent samples *t*-test, $p=0.046$).

Table 4.3 presents the refractive data from right and left eyes in power vectors and the Pearson's correlation coefficient.

Table 4.3: ***Correlation of refractive components between right and left eyes among the 1,636 children***

Refractive Component	Right Eye	Left Eye	Pearson Correlation (R)	p-Value (Two-tailed)
	Mean ± SD (D)	Mean ± SD (D)		
M	0.54 ± 1.16	0.56 ± 1.18	0.92	< 0.001
J_0	0.03 ± 0.16	0.05 ± 0.16	0.70	< 0.001
J_{45}	0.03 ± 0.10	-0.04 ± 0.10	-0.38	< 0.001

As seen from Table 4.3, the Pearson correlation between right and left eyes for M indicated a very strong correlation (r=0.92). Of the cylindrical components, a high correlation for J_0 (r=0.70) and a low inverse correlation for J_{45} (r= -0.38) were found. Given the high correlation between eyes for M, data from only the right eye were used for classification of RE groups for the remainder of the analysis. Figure 4.1 presents the histogram of the distribution of the RE based on M from the right eye of the 1,636 children.

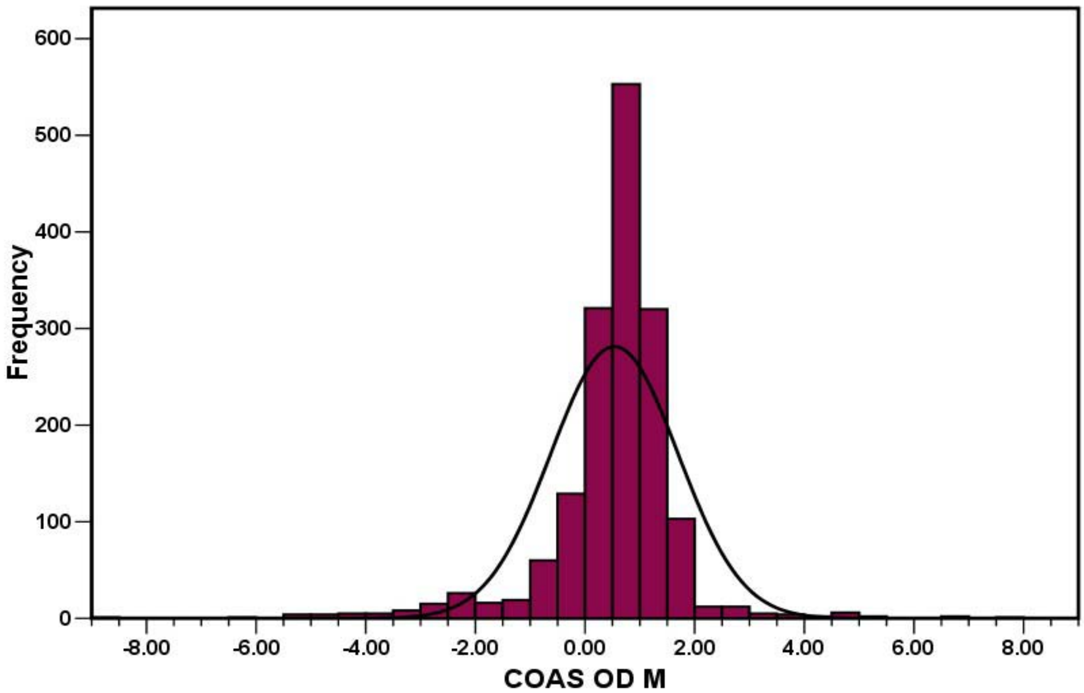

Figure 4.1: ***Distribution of SE (M) in dioptres from right eyes of 1,636 children***

RE in this sample of children presented a leptokurtic distribution (Kurtosis 9.757) and was slightly hyperopic (skewness -1.20) with a range from -8.58 to 7.69 D. Figure 4.2 plots the distribution of the astigmatic component in Cartesian form using power vectors (J_0, J_{45}) from the right eyes of the 1,636 children. In this plot, the positive x-axis values are equivalent to "with-the rule" astigmatism while the negative x-axis values represent "against-the-rule" astigmatism. In addition, positive y-axis values represent a cylinder axis at 45 degrees and negative y-axis values represent a cylinder axis at 135 degrees. Due to the exclusion of those cases with cylinders equal to and greater than 1.00 D from analysis, the cluster of points collapse around the origin with most of the values distributed around ±0.25 D.

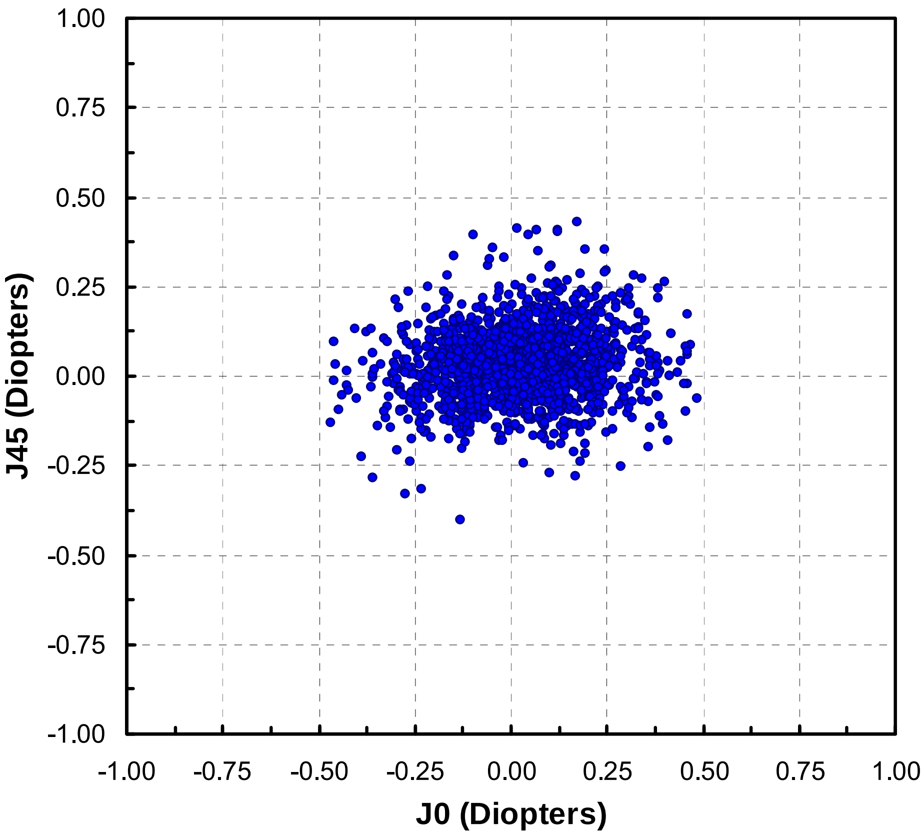

Figure 4.2: Distribution of astigmatism (J_0, J_{45}) in Cartesian form of the right eyes of 1,636 children

Table 4.4 presents the mean refractive components from the right eyes by gender.

Table 4.4: ***Refractive components from the right eyes of 1,636 children by gender***

Gender	M		J_0		J_{45}	
	Mean ± SD (D)	**Range**	**Mean ± SD (D)**	**Range**	**Mean ± SD (D)**	**Range**
Female	0.49 ± 1.24	-8.58 to 6.97	0.03 ± 0.16	-0.46 to 0.49	0.09 ± 0.10	-0.28 to 0.41
Male	0.57 ± 1.06	-5.10 to 7.69	0.02 ± 0.16	-0.47 to 0.46	0.03 ± 0.10	-0.40 to 0.43
All cases	0.53 ± 1.16	-8.58 to 7.69	0.03 ± 0.16	-0.47 to 0.49	0.03 ± 0.10	-0.40 to 0.43

Females were slightly less hyperopic than males but the mean difference did not reach significance (independent samples *t*-test, p=0.139). A small but significant difference was found for J_0 between genders (independent samples *t*-test, p=0.034). No difference was found for J_{45}.

4.5.2 Correlation of Ocular Aberrations Between Right and Left Eyes

In addition to M, J_0, and J_{45}, the correlation of the ocular aberrations between right and left eyes was analysed. Because bilateral symmetry between left and right eyes caused the Zernike coefficients for all those modes with odd symmetry about the y-axis to be of opposite sign, odd symmetric terms were inverted in sign in the left eyes to compensate for the enantiomorphism effect (Smolek *et al.* 2002; Thibos *et al.* 2002A). The results of the Pearson's correlation for the Zernike coefficients from 2nd to 6th order are presented in Table 4.5.

Table 4.5: ***Correlation of Zernike coefficients between right and left eyes among 1,636 children***

Order	Zernike Coefficient	Mean ± SD (μm)		Pearson Correlation (r)
		OD	OS	
2nd order	Z(2,-2)	-0.04 ± 0.13	-0.05 ± 0.13	0.38
	Z(2, 0)	-0.25 ± 1.02	-0.26 ± 1.04	**0.93**
	Z(2, 2)	-0.04 ± 0.20	-0.07 ± 0.20	**0.70**
3rd order	Z(3,-3)	-0.03 ± 0.07	-0.04 ± 0.07	**0.65**
	Z(3,-1)	0.00 ± 0.10	-0.00 ± 0.10	**0.67**
	Z(3, 1)	0.00 ± 0.06	0.00 ± 0.07	**0.57**
	Z(3, 3)	0.03 ± 0.06	0.00 ± 0.06	**0.54**
4th order	Z(4,-4)	0.01 ± 0.02	0.01 ± 0.02	0.21
	Z(4,-2)	-0.01 ± 0.03	-0.01 ± 0.03	-0.24
	Z(4, 0)	0.06 ± 0.06	0.06 ± 0.06	**0.78**
	Z(4, 2)	0.00 ± 0.03	-0.00 ± 0.03	0.44
	Z(4, 4)	0.01 ± 0.03	0.01 ± 0.03	0.34
5th order	Z(5,-5)	-0.00 ± 0.01	-0.00 ± 0.02	0.15
	Z(5,-3)	0.00 ± 0.01	0.00 ± 0.02	0.12
	Z(5,-1)	0.01 ± 0.02	0.01 ± 0.02	0.28
	Z(5, 1)	0.00 ± 0.02	0.00 ± 0.01	0.44
	Z(5, 3)	0.00 ± 0.01	0.00 ± 0.01	0.06*
	Z(5, 5)	0.00 ± 0.01	-0.00 ± 0.01	0.13
6th order	Z(6,-6)	-0.00 ± 0.01	-0.00 ± 0.01	0.06*
	Z(6,-4)	0.00 ± 0.01	0.00 ± 0.01	0.06*
	Z(6,-2)	-0.00 ± 0.01	-0.00 ± 0.01	0.13
	Z(6, 0)	-0.00 ± 0.01	-0.00 ± 0.01	0.40
	Z(6, 2)	-0.00 ± 0.01	-0.00 ± 0.01	0.07*
	Z(6, 4)	0.00 ± 0.01	0.00 ± 0.01	0.06*
	Z(6, 6)	-0.00 ± 0.01	-0.00 ± 0.01	0.08

All correlations are significant p<0.001, except those with an asterisk which are p<0.01

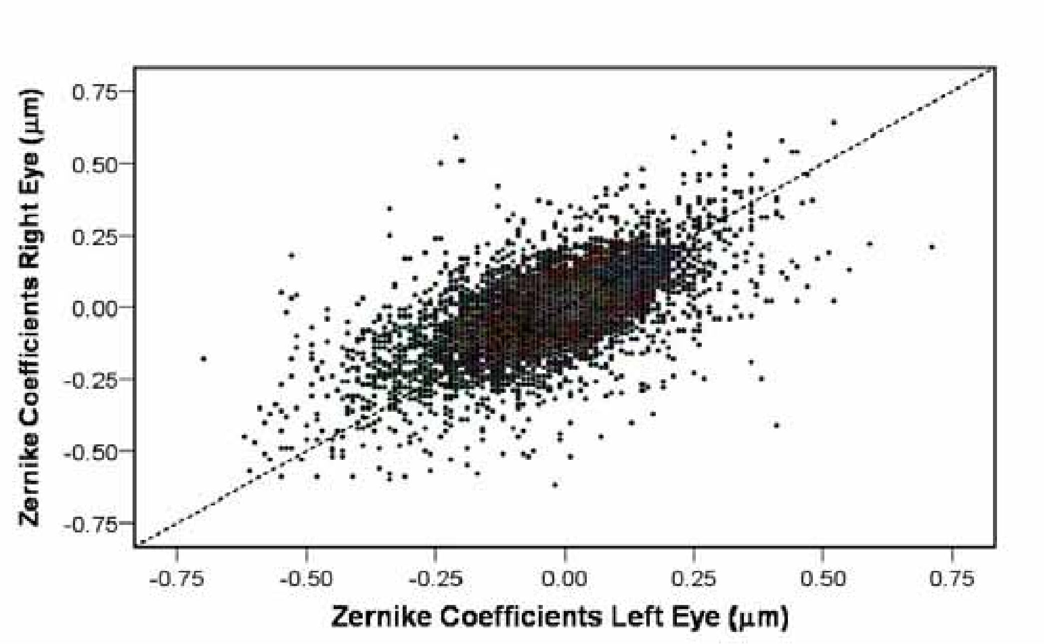

Figure 4.3: Correlation between astigmatism and HOs (3rd to 6th orders) Zernike coefficients from right and left eyes of 1,636 children (tilt and defocus are not included). The sign of odd symmetric terms in the left eyes have been changed to test for enantiomorphism

Defocus Z(2,0) presented the highest correlation of all Zernike coefficients ($r=0.93$, $p<0.001$), followed by primary SA Z(4,0) ($r=0.78$, $p<0.001$), "with-the-rule" / "against-the-rule" astigmatism Z(2,2) ($r=0.70$, $p<0.001$), vertical coma Z(3,-1) ($r=0.67$, $p<0.001$) and oblique trefoil Z(3,-3) ($r=0.65$, $p<0.001$). Third orders recorded moderate to high correlations. Whilst the other coefficients recorded significance, the correlations were low to negligible. The low correlation between coefficients in the HOs is associated with a reduction of the small mean values of each coefficient with values reaching zero.

As the data suggests, moderate mirror symmetry between eyes in the wave aberration was present for this study population and, therefore, it was decided to perform further analyses of the ocular aberrations from right eyes only.

4.5.3 Distribution of Ocular Monochromatic Aberrations in the Population

4.5.3.1 Mean Total Ocular Aberrations

The spread of ocular aberrations from Z(2,-2) to Z(6,6) for the right eyes of the entire study population is presented in Figure 4.4. It is seen that defocus Z(2,0) has the largest magnitude and also exhibits the largest variability in comparison to other aberrations.

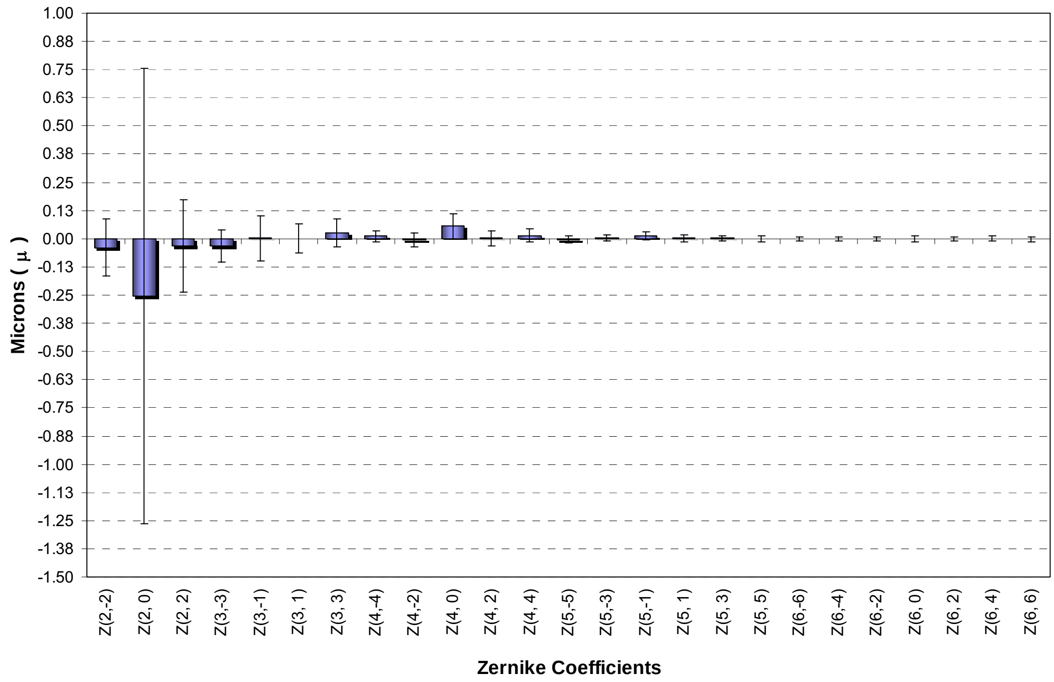

Figure 4.4: Mean spread of ocular aberrations Z(2,-2) to Z(6,6) in microns for a sample of right eyes of 1,636 children

The mean value calculated for a PD of 5 mm of Z(2,0) was -0.26 ± 1.00 µm. This was followed by primary SA Z(4,0) with a mean of 0.06 ± 0.06 µm. Second, 3rd and 4th order aberrations were found to be substantially larger than the 5th and 6th order aberrations. In addition, 3rd and 4th orders also presented with large variances. Of the HOAs, Z(4,0) presented with the highest value but accounts for only a 5th of the magnitude in comparison to defocus.

Due to the big differences present in the mean values between LOAs and HOAs, a plot of the spread of only the 2nd order aberrations (Z(2,-2), Z(2,0) and Z(2,2)) is presented in Figure 4.5 and a plot of the spread of the HO modes (Z(3,-3) to Z(6,6)) is presented in Figure 4.6.

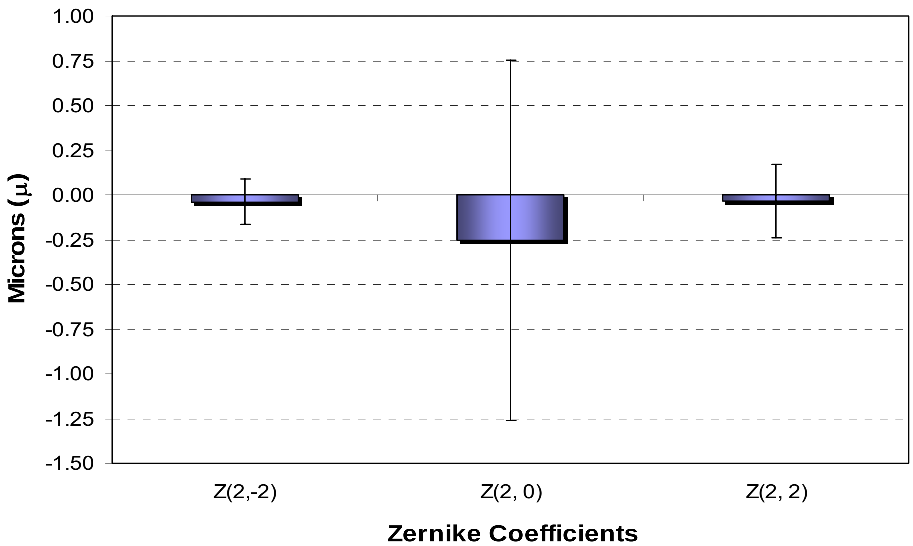

Figure 4.5: LOAs Z(2,-2), Z(2,0) and Z(2,2) in microns for a sample of right eyes of 1,636 children

Third order coefficients (Z(3,-3) to Z(3,3)) presented the highest variances from all HO coefficients. Fifth and 6th order mean values were very close to zero and their contribution to the total wavefront variance seemed to be very small to have any impact on degrading or improving the image quality in the eye.

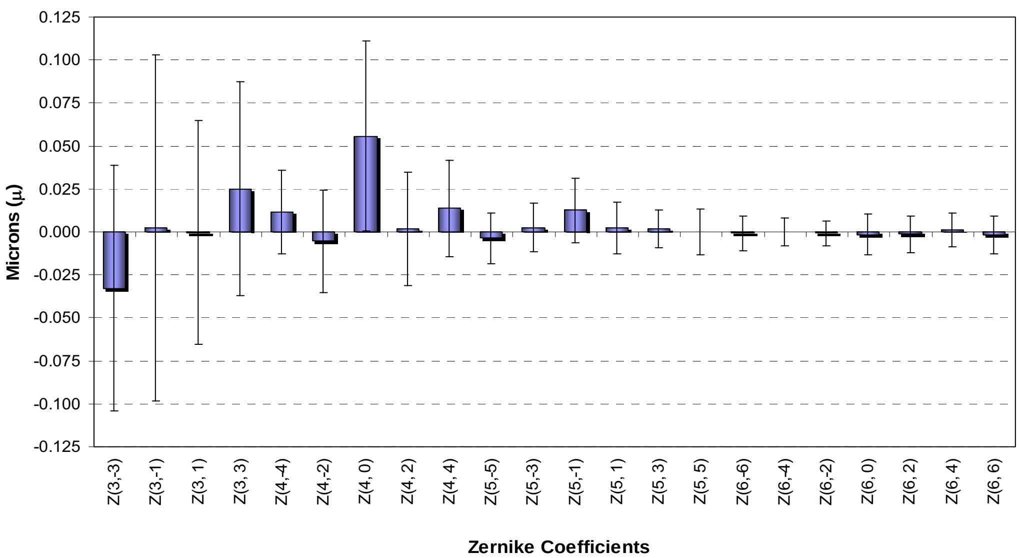

Figure 4.6: HO ocular aberrations Z(3,-3) to Z(6,6) in microns for a sample of right eyes of 1,636 children

Figure 4.7 presents the frequency histograms of Zernike coefficients from the 2nd to the 6th order of the uncorrected right eyes from 1,636 children. Because subjects were not optically corrected when aberrometry was obtained, Z(2,0) presents a negative shift equivalent to the RE of the population. Coefficients with an asterisk indicate that they were significantly deviated from zero (Student t-test, $p<0.01$).

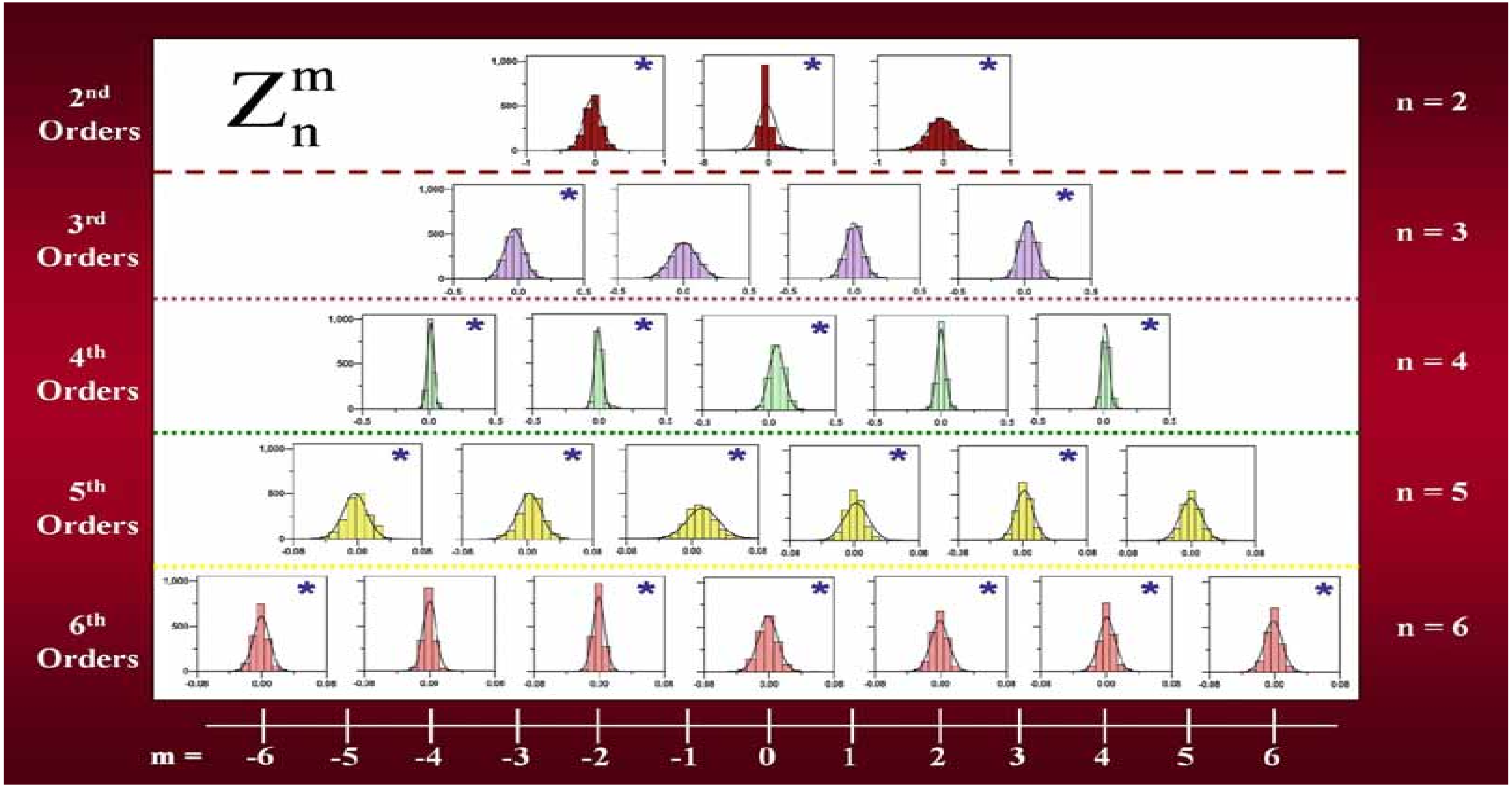

Figure 4.7: ***Frequency histograms of Zernike coefficients from 2nd through to 6th orders in microns from the right eyes of 1,636 children. Histograms are arranged in a pyramid where each column corresponds to a meridional frequency "m" and each row corresponds to a radial order "n". Solid curves represent the normal distribution for each coefficient. Asterisks indicate significantly different to zero (t-test, p<0.01).*** *Note differences in scales in the abscissas for different orders.*

4.5.3.2 Correlation Between M and Zernike Coefficients and RMS

The relationship between the SE (M) and the magnitude of the Zernike modes from 2nd to 6th order and RMS is presented below and summarised in Tables 4.6 and 4.7. The relationship between defocus mode Z(2,0), primary SA Z(4,0), total aberrations RMS and SA RMS were also analysed.

Table 4.6: ***Correlation of M and Zernike coefficients from 2nd to 6th order from the right eyes of 1,636 children***

Order	Zernike Coefficient	Pearson Correlation (r)*	p-Value (Two-tailed)
2nd order	Z(2,-2)	-0.04	0.151
	Z(2, 0)	-0.98	0.000
	Z(2, 2)	0.01	0.969
3rd order	Z(3,-3)	0.08	0.002
	Z(3,-1)	-0.12	0.000
	Z(3, 1)	-0.04	0.147
	Z(3, 3)	0.01	0.704
4th order	Z(4,-4)	-0.02	0.337
	Z(4,-2)	0.03	0.312
	Z(4, 0)	0.26	0.000
	Z(4, 2)	-0.04	0.147
	Z(4, 4)	0.05	0.030
5th order	Z(5,-5)	-0.01	0.973
	Z(5,-3)	-0.05	0.033
	Z(5,-1)	0.06	0.021
	Z(5, 1)	0.10	0.000
	Z(5, 3)	0.04	0.148
	Z(5, 5)	-0.06	0.019
6th order	Z(6,-6)	0.03	0.287
	Z(6,-4)	0.06	0.019
	Z(6,-2)	-0.01	0.883
	Z(6, 0)	-0.11	0.000
	Z(6, 2)	-0.04	0.087
	Z(6, 4)	0.03	0.262
	Z(6, 6)	0.02	0.511

** All correlations are significant $p<0.01$*

Table 4.7: ***Correlation of M and RMS of Zernike coefficients from the right eyes of 1,636 children***

	RMS	Pearson Correlation (r)	p-Value (Two-tailed)
M	Defocus	-0.19	**<0.001**
	Astigmatism	-0.09	**0.035**
	Coma	0.00	0.958
	Trefoil	-0.01	0.771
	Spherical aberration	0.23	**<0.001**
	Quatrefoil	0.00	0.948
	Secondary astigmatism	0.11	**<0.001**
	Higher order	0.10	**<0.001**
	Total aberrations	-0.20	**<0.001**

Figure 4.8 presents the scatter plot between M and defocus mode Z(2,0). Almost as expected, a quasi-linear high negative correlation between M and Z(2,0) was found (r= -0.979, p<0.001).

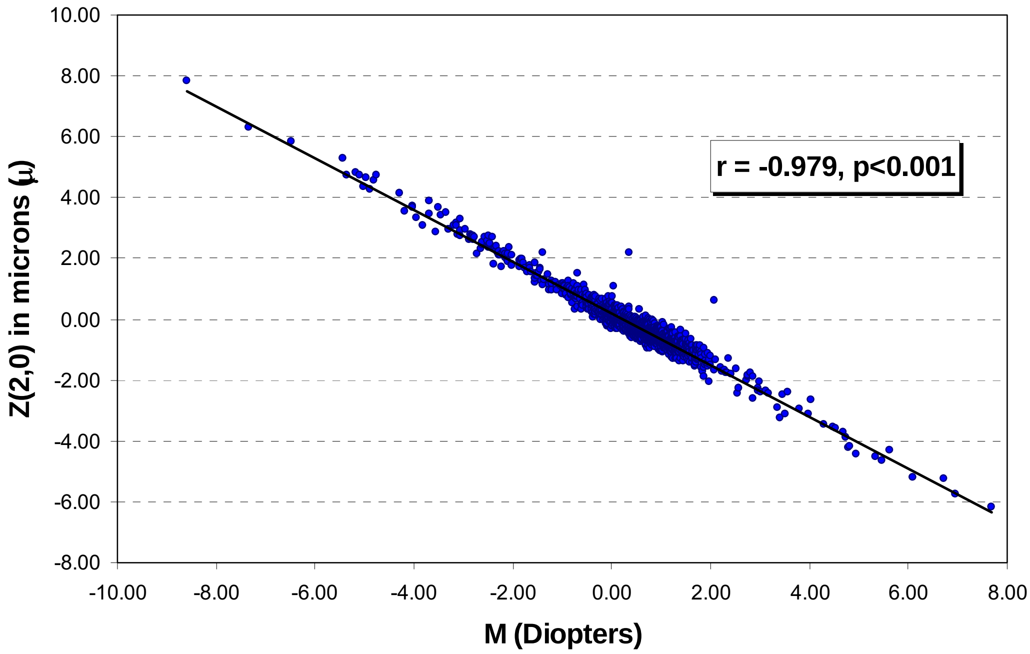

Figure 4.8: ***Correlation between M and defocus Z(2,0)***

A low correlation between M and primary SA Z(4,0) was found (r=0.257, p<0.001). Figure 4.9 shows the scatter plot between M and Z(4,0). Although it appears that the SA tends to be more positive with hyperopic RE than in myopic errors; the trend is not well-defined, presenting a large range in the distribution of primary SA.

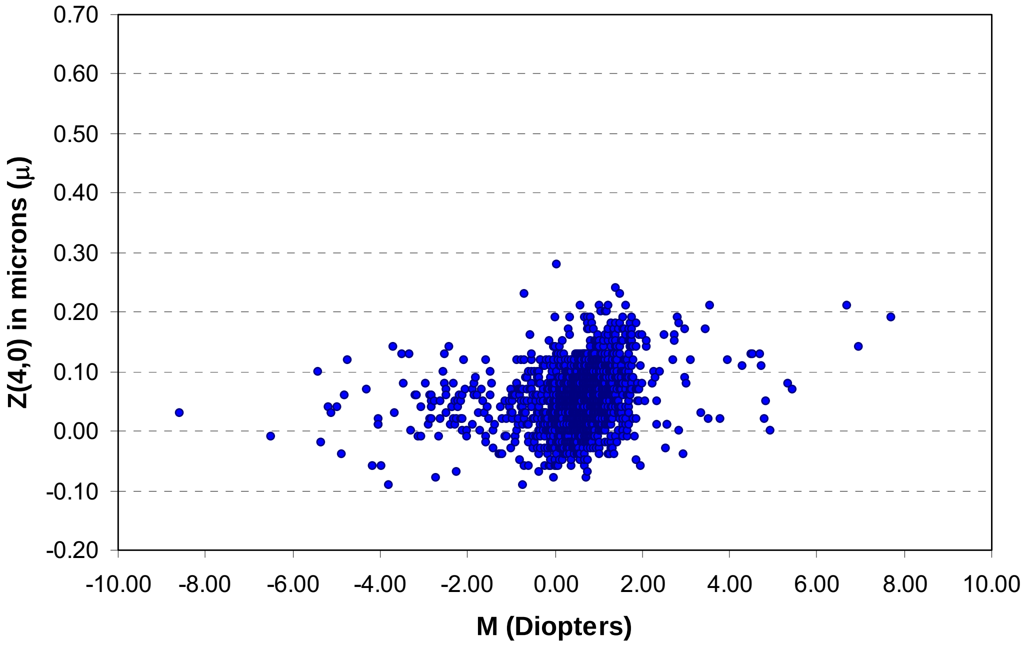

Figure 4.9*: Correlation between M and primary SA Z(4,0);. r=0.257, p<0.001*

As shown in subsection 4.5.3.1, SA Z(4,0) was the coefficient with greater contribution to the total ocular wavefront but also presented one of the highest variances of the HO modes. The correlation between M and the SA RMS was analysed and represented as scatter plot in Figure 4.10. A low correlation was found between M and SA RMS, suggesting that the amount of Z(4,0) is not related to the amount of M of the eye and it can be randomly distributed even in cases with the same M values.

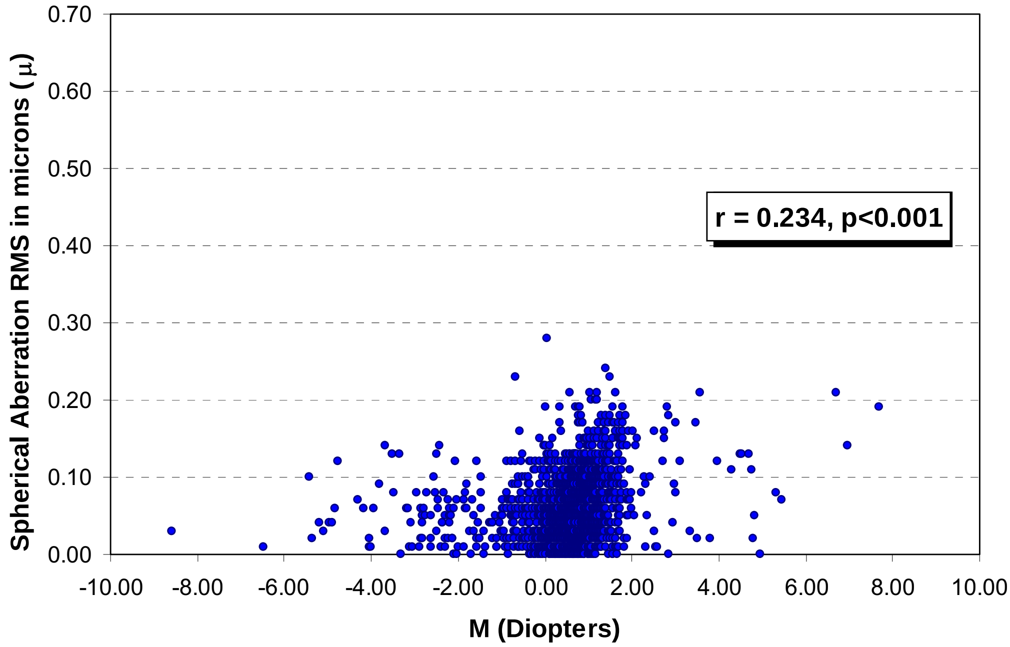

Figure 4.10: ***Correlation between M and SA RMS***

Figure 4.11 presents two scatters plot between M and total aberrations RMS (from Z(2,-2) to Z(6,6)). Scatter A presents the correlation between M and Total RMS when M ≤ 0.00 D, and scatter B shows the correlation between M and Total RMS when M >0.00 D. A better linear correlation existed between M and Total RMS, in the negative range of M values (n=315) than in the positive range (n=1,321).

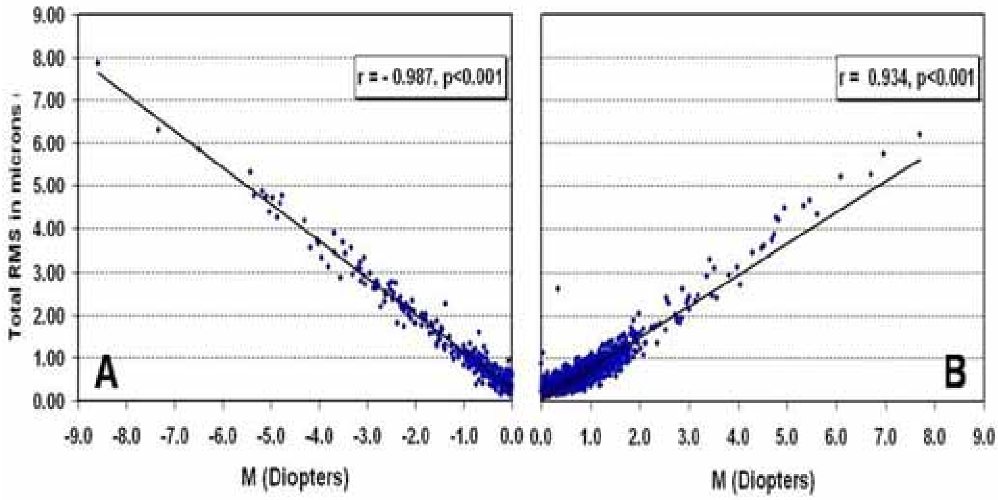

Figure 4.11: ***Correlation between M and total aberrations RMS: (A) Correlation when M ≤ 0.00 D; (B) Correlation when M ≥ 0.00 D***

4.5.4 Ocular Aberrations and RE Groups

The relationship between ocular aberrations and different RE groups was investigated. Aberrations from the 2nd, 3rd and 4th order were examined. No analysis was conducted for the 5th and 6th order because of their small contribution to the total ocular wavefront. Analysis of defocus, astigmatism, coma, trefoil, SA, HOs and total RMS was also conducted. For further reference of the ANOVA results and multiple comparison results for the refractive components between RE groups and subgroups, refer to Table F1 in Appendix F.

Table 4.8 presents the mean refractive components by RE groups. In this sample, no difference was found in the astigmatic components between RE groups - J_0 (B-F=2.805, p=0.062); J_{45} (B-F=2.332, p=0.098).

Table 4.8: ***Refractive components by RE groups among the 1,636 children***

RE group	n	M		J_0		J_{45}	
		Mean ± SD (D)	Range (D)	Mean ± SD (D)	Range (D)	Mean ± SD (D)	Range (D)
Myopes	165	-1.91 ± 1.38	-8.58 to -0.50	0.01 ± 0.19	-0.45 to 0.49	0.02 ± 0.11	-0.32 to 0.39
Emmetropes	449	0.14 ± 0.26	-0.49 to 0.49	0.04 ± 0.16	-0.47 to 0.47	0.03 ± 0.10	-0.40 to 0.41
Hyperopes	1,022	1.10 ± 0.68	0.50 to 7.69	0.02 ± 0.15	-0.46 to 0.46	0.03 ±0.09	-0.28 to 0.43

Figure 4.12 illustrates the distribution of RE based on the SE from the right eyes of 1,636 children. The predominant RE in this study population was hyperopia (63%) followed by emmetropia (27%) and myopia (10%).

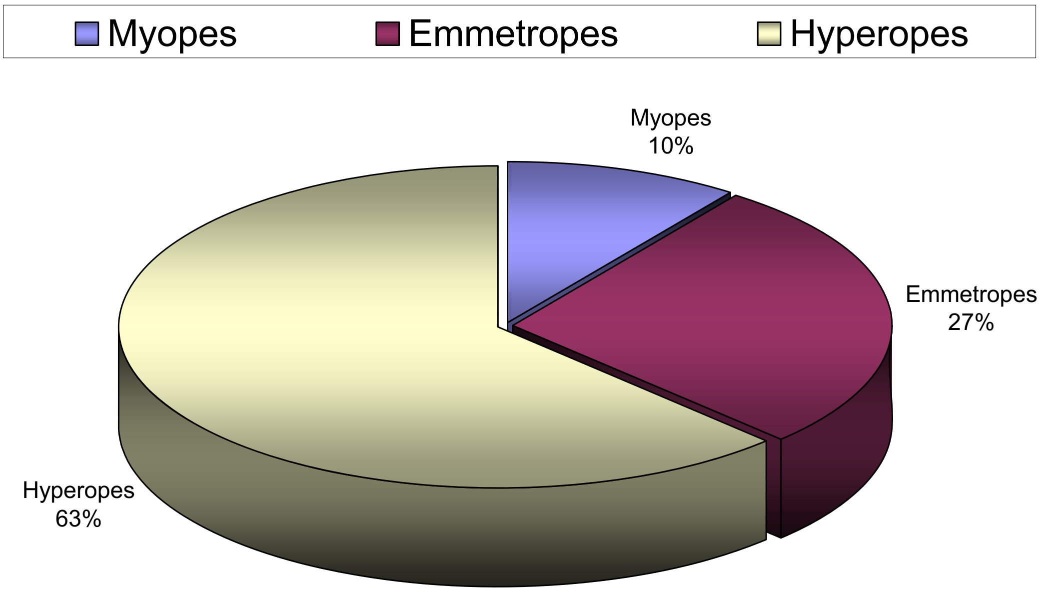

Figure 4.12: Distribution of RE groups among the sample of 1,636 children

Table 4.9 presents the age distribution for 1,636 children for the different RE groups. Myopic subjects were slightly older than the other RE groups; emmetropes - mean difference 0.03 years; hyperopes – mean difference 0.06 years; however these differences did not reach statistical significance (B-F=2.045, p=0.130).

Table 4.9: ***Age distribution by RE groups among the 1,636 children***

RE Group	n (%)	Mean ± SD (years)	95% CI for Mean		Range
			Lower Bound	Upper Bound	
Myopes	165 (10%)	12.68 ± 0.46	12.61	12.75	11.73 to 14.15
Emmetropes	449 (27%)	12.65 ± 0.43	12.61	12.69	11.29 to 13.88
Hyperopes	1,022 (63%)	12.62 ± 0.40	12.60	12.64	11.06 to 14.44
Total	1,636 (100%)	12.64 ± 0.42	12.61	12.66	11.06 to 14.44

When the distribution of RE groups was analysed by gender, it was found that the prevalence of myopia was slightly higher in females than in males and also that the mean M in the female myopic group was -0.30 D higher than in the male myopic group.

Independent samples *t*-tests between genders in the mean M for each RE group revealed differences between myopes (p=0.042), but not for emmetropes (p=0.496) and hyperopes (p=0.778). The distribution of the RE groups by gender and their mean M values are presented in Table 4.10.

Table 4.10: ***Distribution of RE groups and mean M by gender among the 1,636 children***

RE Group	Males			Females		
	n (%)	M		n (%)	M	
		Mean ± SD (D)	Range (D)		Mean ± SD (D)	Range (D)
Myopes	74 (9.0%)	-1.67 ± 1.15	-5.10 to -0.50	91 (11.2%)	-2.11 ± 1.51	-8.58 to 0.54
Emmetropes	236 (28.8%)	0.13 ± 0.26	-0.49 to 0.49	213 (26.1%)	0.15 ± 0.25	-0.49 to 0.49
Hyperopes	510 (62.2%)	1.10 ± 0.71	0.50 to 7.69	512 (62.7%)	1.10 ± 0.66	0.50 to 6.97
Total	820 (100%)	0.58 ± 1.14	-7.33 to 7.69	816 (100%)	0.48 ± 1.27	-8.58 to 7.69

Because of the greater range in RE for the myopic and hyperopic groups (-0.50 to -8.58 D and +0.50 to +7.69 D respectively) in comparison to the emmetropic group (-0.50 to +0.50 D), the Sydney Myopia Study adopted a new criteria of refraction parameters creating three subgroups for the myopic and emmetropic groups: low myopia / hyperopia (±0.50 to ± 2.99 D), moderate myopia / hyperopia (±3.00 to ± 5.99 D) and high myopia / hyperopia (±6.00 D or more). Table 4.11 summarises the distribution of RE subgroups and their mean M from the right eyes of the 1,636 children as in the Sydney Myopia Study classification.

Table 4.11: ***Distribution of RE subgroups and mean M as in the Sydney Myopia Study RE groups criteria among the right eyes of 1,636 children***

RE Group	n (%)	Mean ± SD (D)	Range
Moderate myopia	26 (1.6%)	-4.05 ± 0.78	-5.43 to -3.06
Low myopia	137 (8.4%)	-1.42 ± 0.76	-2.95 to -0.50
Emmetropia	449 (27.4%)	0.14 ± 0.26	-0.49 to 0.49
Low hyperopia	1,000 (61.1%)	1.03 ± 0.41	0.50 to 2.98
Moderate hyperopia	19 (1.2%)	4.15 ± 0.79	3.00 to 5.46
High hyperopia	3 (0.2%)	7.12 ± 0.51	6.71 to 7.69
All cases	1,636 (100%)	0.53 ± 1.21	-8.58 to 7.69

The majority of myopic and hyperopic cases were grouped in the lower and moderate subgroups, with the high subgroups having less than five cases in each group (<1% from the total population); for this reason, it was decided to concentrate the high and moderate subgroups into one subgroup - moderate to high myopia / hyperopia (see Table 4.12 and Figure 4.13). This final classification of RE will be used through the following sections of this thesis, following the general definition of RE groups with the purpose of identifying and comparing differences between RE groups when using different criteria.

Table 4.12: ***Distribution of M by RE groups for the right eyes of 1,636 children***

RE Group	n (%)	Mean ± SD (D)	95% CI for Mean		Range
			Lower Bound	Upper Bound	
Moderate to high myopia	28 (1.7%)	-4.30 ±1.29	-4.77	-3.86	-8.58 to -3.06
Low myopia	137 (8.4%)	-1.42 ± 0.75	-1.55	-1.27	-2.95 to -0.50
Emmetropia	449 (27.5%)	0.14 ± 0.26	0.12	0.16	-0.49 to 0.49
Low hyperopia	1,000 (61.1%)	1.03 ± 0.41	1.00	1.05	0.50 to 2.98
Moderate to high hyperopia	22 (1.3%)	4.56 ± 1.26	3.98	5.04	3.00 to 7.69
All cases	1,636 (100%)	0.53 ± 1.21	0.47	0.58	-8.58 to 7.69

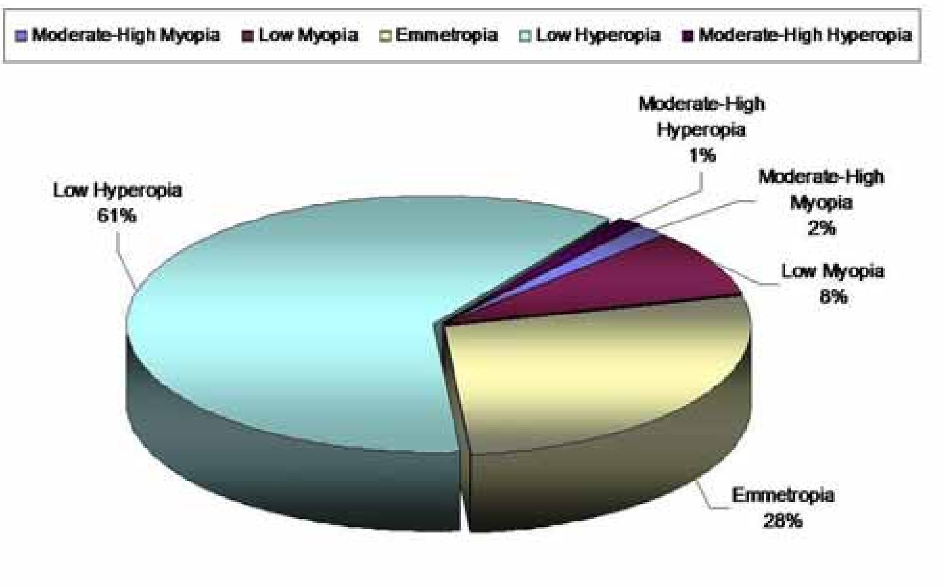

Figure 4.13: ***Distribution of RE subgroups for the sample of 1,636 right eyes***

4.5.4.1 Second Order Aberrations

Tables 4.13 to 4.14 detail the mean and standard deviation of 2nd order aberrations organised by RE groups and RE subgroups respectively. The distribution of 2nd order aberrations across RE groups and subgroups are presented in Figures 4.14 and 4.15. For further reference of the ANOVA results and multiple comparison results for the Zernike coefficients between RE groups and subgroups, refer to Table F2 and F3 in Appendix F.

Table 4.13: ***2nd aberrations in microns for general RE groups***

RE group	Mean ± SD (μm)		
	Z(2,-2)	Z(2, 0)	Z(2, 2)
Myopes	-0.02 ± 0.15	1.88 ± 1.24	0.00 ± 0.25
Emmetropes	-0.03 ± 0.13	0.02 ± 0.29	-0.05 ± 0.21
Hyperopes	-0.04 ± 0.12	-0.72 ± 0.59	-0.03 ± 0.19
All Cases	-0.04 ± 0.13	-0.26 ± 1.01	-0.03 ± 0.20

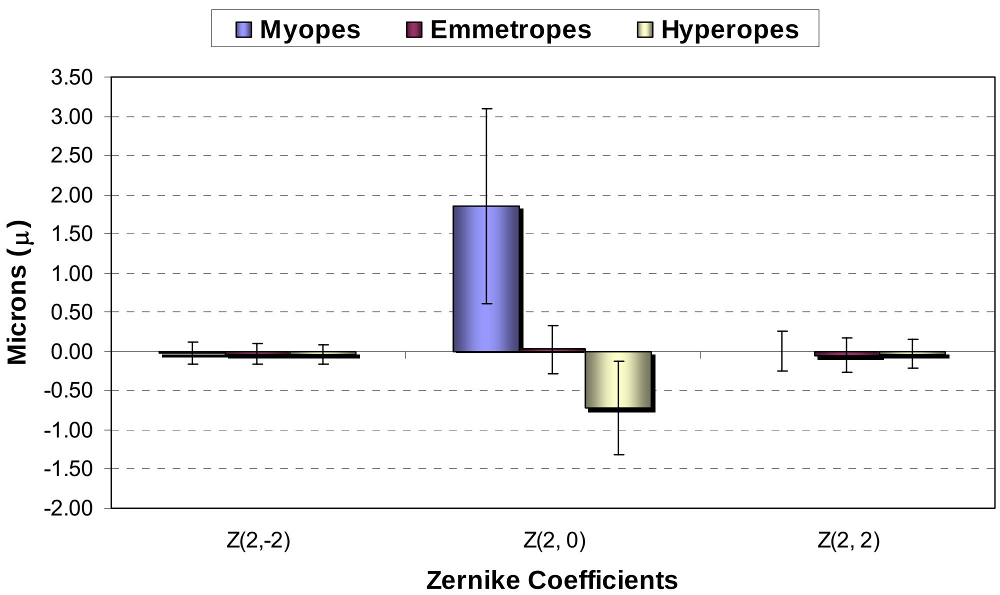

Figure 4.14***: 2nd order aberrations Z(2,-2), Z(2,0) and Z(2,2) in microns for general RE groups***

From the 2nd orders, significant differences between groups existed only for Z(2,0) (B-F=640.914, p<0.001). As expected, multiple comparisons revealed significant differences between all groups (p<0.001). Further analysis of RE subgroups confirmed that significant differences existed only for Z(2,0) between all RE subgroups (B-F=452.258, p<0.001), multiple comparisons (p<0.001).

Table 4.14: ***2nd order aberrations in microns for RE subgroups***

RE Group	**Mean ± SD (μm)**		
	Z(2,-2)	**Z(2, 0)**	**Z(2, 2)**
Moderate to high myopia	-0.08 ± 0.16	4.00 ± 1.10	-0.06 ± 0.22
Low myopia	-0.01 ± 0.14	1.44 ± 0.69	0.00 ± 0.25
Emmetropia	-0.03 ± 0.13	0.02 ± 0.29	-0.05 ± 0.21
Low hyperopia	-0.04 ± 0.12	-0.66 ± 0.37	-0.03 ± 0.19
Moderate to high hyperopia	-0.04 ± 0.17	-3.69 ± 1.13	-0.07 ± 0.24
All cases	-0.04 ± 0.13	-0.26 ± 1.00	-0.03 ± 0.20

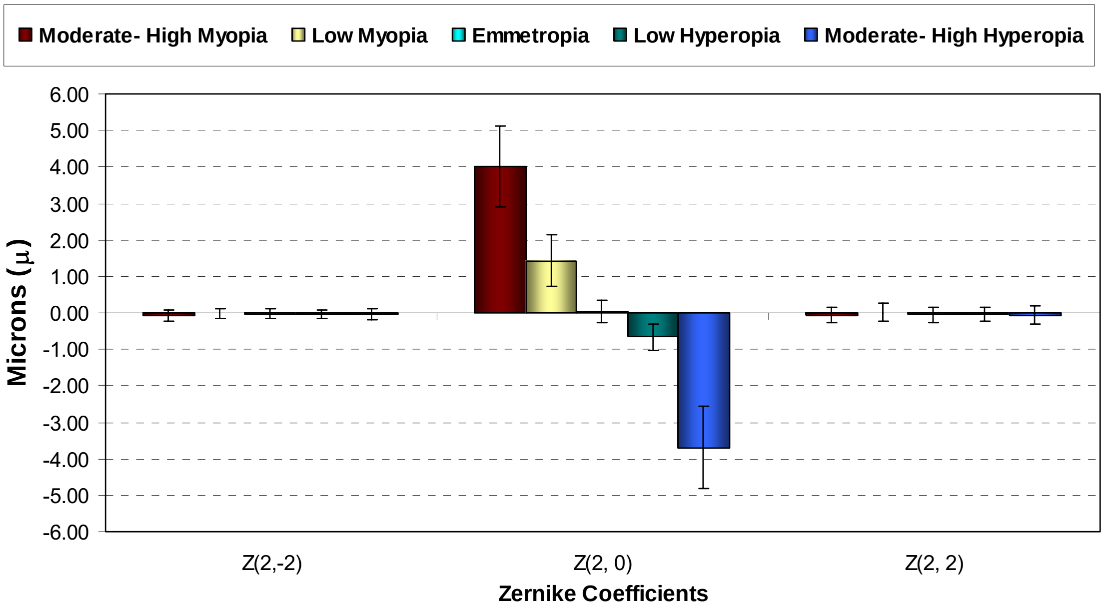

Figure 4.15: ***2nd order aberrations Z(2,-2), Z(2,0) and Z(2,2) in microns for RE subgroups***

4.5.4.2 Third Order Aberrations

Analysis of 3rd order aberrations revealed significant differences between RE groups for the coma terms Z(3,-1) (B-F=8.664, p<0.001) and Z(3,1) (B-F=4.906, p=0.008). Multiple comparisons showed that myopes had significantly more positive values for Z(3,-1) than emmetropes (p=0.001) and hyperopes (p<0.001). For Z(3,1), myopes also presented significantly more positive values than emmetropes (p=0.02) and hyperopes (p=0.007). No difference existed between emmetropes and hyperopes for any 3rd order term.

Table 4.15: ***3rd order aberrations in microns for general RE groups***

RE Group	Mean ± SD (μm)			
	Z(3,-3)	Z(3,-1)	Z(3, 1)	Z(3, 3)
Myopes	-0.04 ± 0.07	0.03 ± 0.11	0.01 ± 0.06	0.03 ± 0.06
Emmetropes	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.06	0.02 ± 0.06
Hyperopes	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.07	0.03 ± 0.06
All subjects	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.06	0.03 ± 0.06

When the RE subgroups were analysed, significant differences existed between subgroups for Z(3,-3) (B-F=4.573, p=0.002), Z(3,-1) (B-F=5.724, p<0.001) and Z(3,1) (B-F=2.935, p=0.024). Further analysis with multiple comparisons revealed moderate to high hyperopes to have significantly more positive values of Z(3,-3) than the other subgroups (p<0.05). moderate to high myopes had significantly more positive values of Z(3,-1) (p<0.05) than emmetropes and the two hyperopic subgroups but not with low myopes. Small significant differences existed for Z(3,1) between low myopes and emmetropes (p=0.017) and low hyperopes (p=0.005) with emmetropes and low hyperopes having slightly more negative mean values.

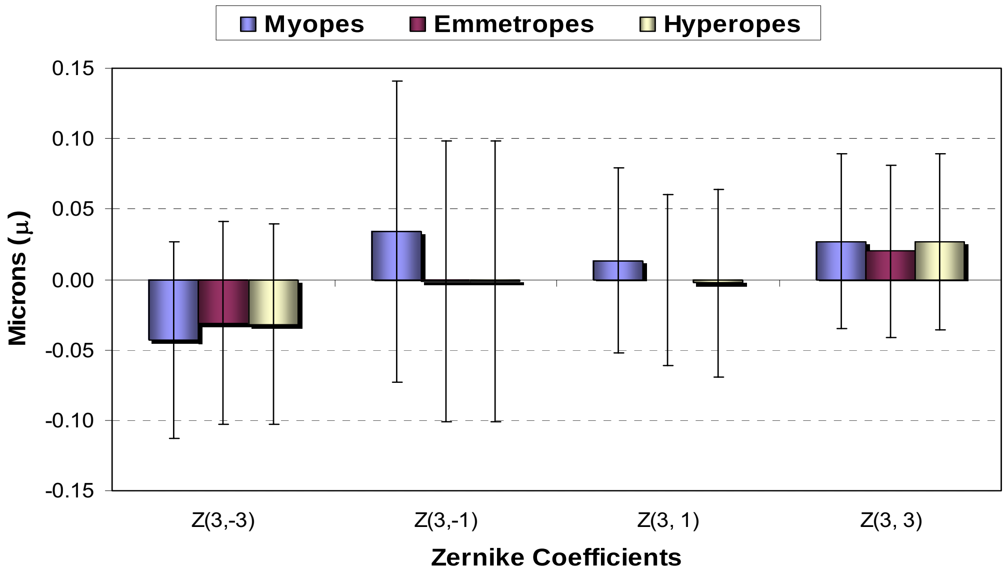

Figure 4.16: ***3rd order aberrations Z(2,-3) to Z(3,3) in microns for general RE groups***

Tables 4.15 to 4.16 present the mean and standard deviation of 3rd order aberrations organised by RE groups and RE subgroups respectively. The distribution of 3rd order aberrations across RE groups and subgroups are presented in Figures 4.16 and 4.17.

Table 4.16: ***3rd order aberrations in microns for RE subgroups***

RE Group	Mean ± SD (μm)			
	Z(3,-3)	Z(3, -1)	Z(3, 1)	Z(3, 3)
Moderate to high myopia	-0.04 ± 0.07	0.06 ± 0.08	-0.01 ± 0.06	0.04 ± 0.04
Low myopia	-0.04 ± 0.07	0.03 ± 0.11	0.02 ± 0.07	0.02 ± 0.07
Emmetropia	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.06	0.02 ± 0.06
Low hyperopia	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.07	0.03 ± 0.06
Moderate to high hyperopia	0.03 ± 0.07	-0.04 ± 0.12	-0.01 ± 0.09	0.03 ± 0.07
All cases	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.06	0.03 ± 0.06

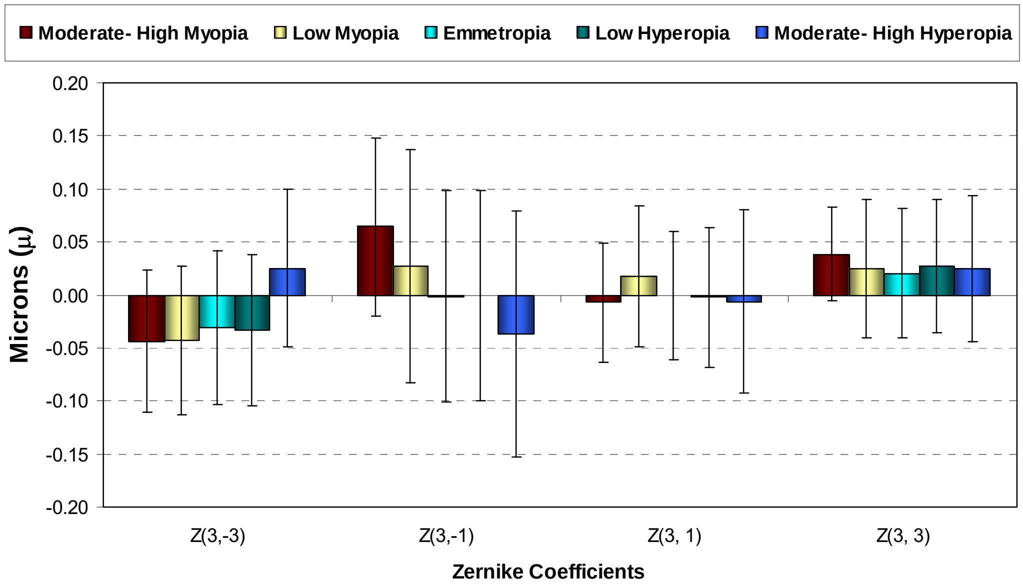

Figure 4.17: ***3rd order aberrations Z(2,-3) to Z(3,3) in microns for RE groups***

4.5.4.3 Fourth Order Aberrations

Tables 4.17 to 4.18 detail the mean and standard deviation of 4th order aberrations organised by RE groups and RE subgroups respectively. The distribution of primary SA Z(4,0) across RE groups and subgroups is shown in Figures 4.18 and 4.19.

Table 4.17: ***4th order aberrations in microns for general RE groups***

RE Group	Mean ± SD (µm)				
	Z(4,-4)	**Z(4,-2)**	**Z(4, 0)**	**Z(4, 2)**	**Z(4, 4)**
Myopes	0.01 ± 0.03	-0.01 ± 0.02	0.04 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
Emmetropes	0.01 ± 0.02	-0.01 ± 0.02	0.04 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
Hyperopes	0.01 ± 0.02	0.00 ± 0.03	0.07 ± 0.06	0.00 ± 0.03	0.01 ± 0.03
All Cases	0.01 ± 0.02	-0.01 ± 0.03	0.06 ± 0.06	0.00 ± 0.03	0.01 ± 0.03

Significant differences were found for Z(4,-2) (B-F=4.818, p=0.008) and for Z(4,0) (B-F=56.937, p<0.001) across the RE groups. Multiple comparisons revealed emmetropes being significantly different to hyperopes in Z(4,-2) (p=0.01); for Z(4,0) differences existed between hyperopes and myopes (p<0.001) and between hyperopes and emmetropes (p<0.001).

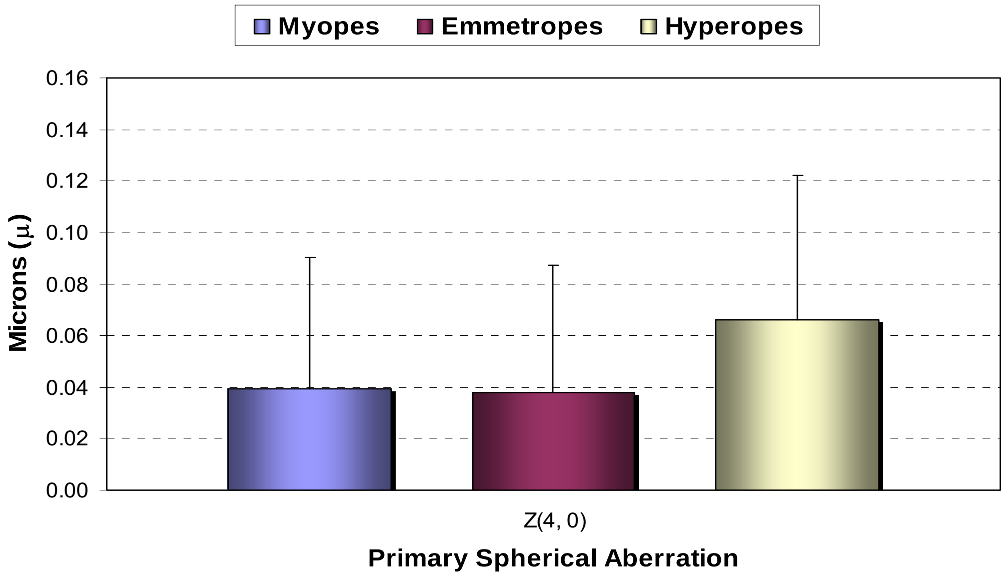

Figure 4.18: ***Primary SA Z(4,0) in microns for general RE groups***

Table 4.18: ***4th order aberrations in microns for RE subgroups***

RE Group	**Mean ± SD (μm)**				
	Z(4,-4)	**Z(4, -2)**	**Z(4, 0)**	**Z(4, 2)**	**Z(4, 4)**
Moderate to high myopia	0.02 ± 0.03	0.00 ± 0.02	0.03 ± 0.06	0.00 ± 0.03	0.01 ± 0.04
Low myopia	0.01 ± 0.03	-0.01 ± 0.02	0.04 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
Emmetropia	0.01 ± 0.02	-0.01 ± 0.02	0.04 ± 0.06	0.00 ± 0.03	0.01 ± 0.03
Low hyperopia	0.01 ± 0.02	0.00 ± 0.03	0.07 ± 0.06	0.00 ± 0.03	0.01 ± 0.03
Moderate to high hyperopia	0.01 ± 0.02	0.00 ± 0.04	0.11 ± 0.06	0.00 ± 0.04	0.03 ± 0.03
All cases	0.01 ± 0.02	-0.01 ± 0.03	0.06 ± 0.06	0.00 ± 0.03	0.01 ± 0.03

When the analysis was performed for the subgroups, Z(4,0) was the only coefficient to present with differences between subgroups (p<0.001). Moderate to high hyperopes and low hyperopes were significantly different to myopes (both moderate to high and low myopes) and emmetropes (p<0.001). No further differences existed between the remaining subgroups.

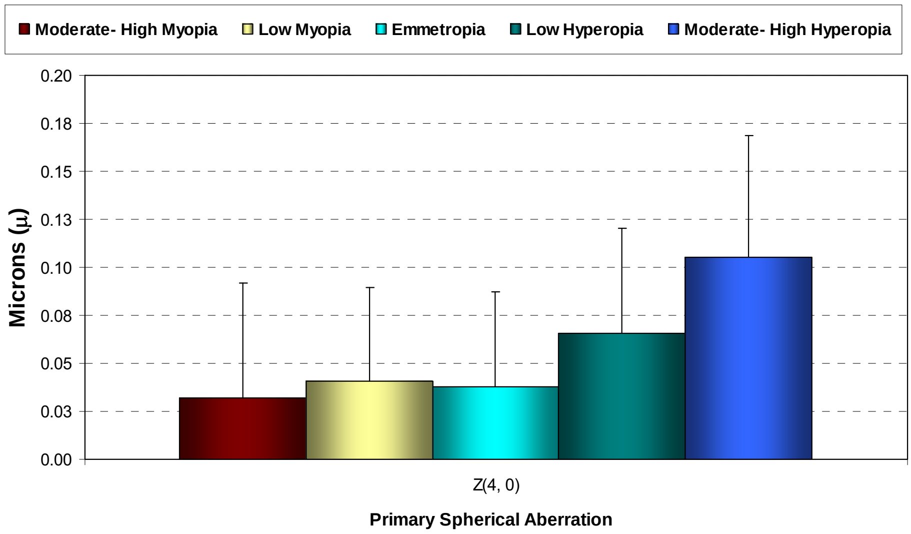

Figure 4.19: ***Primary SA Z(4,0) in microns for RE groups***

4.5.4.4 RMS of Aberrations

Table 4.19 presents the mean and standard deviation of the RMS for the different RE groups and subgroups. Defocus, astigmatism, coma, SA and total aberrations RMS were significantly different between the RE groups (ANOVA B-F<0.05) and no difference was found for HOs RMS. The distribution of the different RMS across RE groups and subgroups is shown in Figures 4.20 and 4.21. The results of the ANOVA and multiple comparisons for the RMS of the Zernike coefficients between RE groups and subgroups are presented in detail in Tables F4 and F5 in Appendix F.

Table 4.19: ***RMS of ocular aberrations in microns for general RE groups***

RE Group	Mean ± SD (µm)								
	Defocus	Astigmatism	Coma	Trefoil	Spherical Aberration	Quatrefoil	Secondary Astigmatism	Higher order	Total Aberrations
Myopes	1.88 ± 1.24	0.25 ± 0.14	0.11 ± 0.06	0.10 ± 0.05	0.05 ± 0.04	0.04 ± 0.02	0.03 ± 0.02	0.18 ± 0.06	1.92 ± 1.22
Emmetropes	0.23 ± 0.18	0.22 ± 0.13	0.10 ± 0.06	0.09 ± 0.05	0.05 ± 0.04	0.03 ± 0.02	0.03 ± 0.02	0.17 ± 0.06	0.40 ± 0.16
Hyperopes	0.73 ± 0.59	0.20 ± 0.12	0.10 ± 0.06	0.09 ± 0.05	0.07 ± 0.05	0.04 ± 0.02	0.04 ± 0.03	0.19 ± 0.07	0.81 ± 0.56
All cases	0.71 ± 0.76	0.21 ± 0.13	0.10 ± 0.06	0.09 ± 0.05	0.06 ± 0.05	0.04 ± 0.02	0.04 ± 0.02	0.18 ± 0.06	0.81 ± 0.73

Defocus RMS was different between all groups (p<0.001) and subgroups except between high to moderate myopes and high to moderate hyperopes (p>0.05). Differences in astigmatism RMS existed between all groups (p<0.05), and between low hyperopes and low myopes (p<0.001), and low hyperopes and emmetropes (p=0.045). Coma RMS was significantly different between hyperopic and myopic groups (p<0.05) and between low hyperopes and low myopic subgroups (p<0.036).

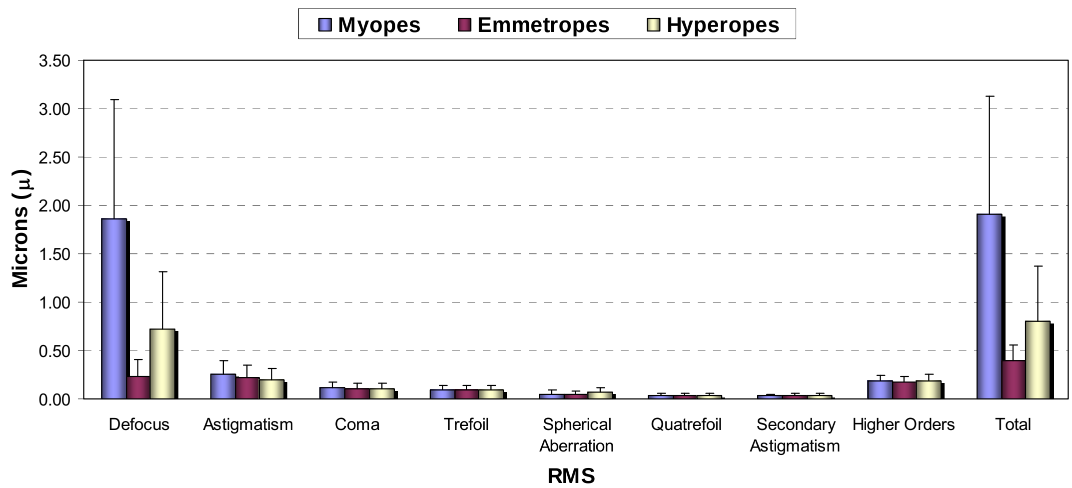

Figure 4.20: Ocular aberration profiles in RMS in microns for general RE groups

Whilst hyperopes were different to myopes and emmetropes for SA RMS (p<0.001), there was no difference between myopes and emmetropes (p=0.639). Comparisons between subgroups of SA RMS, revealed the moderate to high hyperopic group to be different to other subgroups (p<0.05) except the low hyperopic subgroup (p=0.107). The low hyperopic group was significantly different to the low myopic and emmetropic subgroups (p<0.001).

Table 4.20: ***RMS of ocular aberrations in microns for RE subgroups***

RE Group	Mean ± SD (μm)								
	Defocus	Astigmatism	Coma	Trefoil	SA	Quatrefoil	Secondary Astigmatism	Higher order	Total
Moderate to high myopia	4.01 ± 1.10	0.26 ± 0.14	0.11 ± 0.05	0.09 ± 0.04	0.05 ± 0.04	0.04 ± 0.02	0.04 ± 0.02	0.18 ± 0.06	4.02 ± 1.10
Low myopia	1.44 ± 0.69	0.25 ± 0.14	0.12 ± 0.07	0.10 ± 0.05	0.05 ± 0.04	0.04 ± 0.02	0.03 ± 0.02	0.19 ± 0.06	1.49 ± 0.67
Emmetropia	0.23 ± 0.18	0.22 ± 0.13	0.10 ± 0.06	0.09 ± 0.05	0.05 ± 0.04	0.03 ± 0.02	0.03 ± 0.02	0.17 ± 0.06	0.40 ± 0.19
Low hyperopia	0.66 ± 0.36	0.20 ± 0.192	0.10 ± 0.06	0.09 ± 0.05	0.07 ± 0.05	0.04 ± 0.02	0.04 ± 0.03	0.19 ± 0.07	0.74 ± 0.33
Moderate to high hyperopia	3.69 ± 1.13	0.27 ± 0.13	0.13 ± 0.06	0.10 ± 0.04	0.11 ± 0.06	0.04 ± 0.02	0.04 ± 0.03	0.23 ± 0.06	3.71 ± 1.12
All cases	0.71 ± 0.76	0.21 ± 0.13	0.10 ± 0.06	0.09 ± 0.05	0.06 ± 0.05	0.04 ± 0.02	0.04 ± 0.02	0.18 ± 0.06	0.81 ± 0.73

Similar to defocus RMS, differences between groups in total RMS existed between the three groups ($p<0.001$), and subgroups ($p<0.001$) except between moderate to high myopes and moderate to high hyperopes ($p>0.05$).

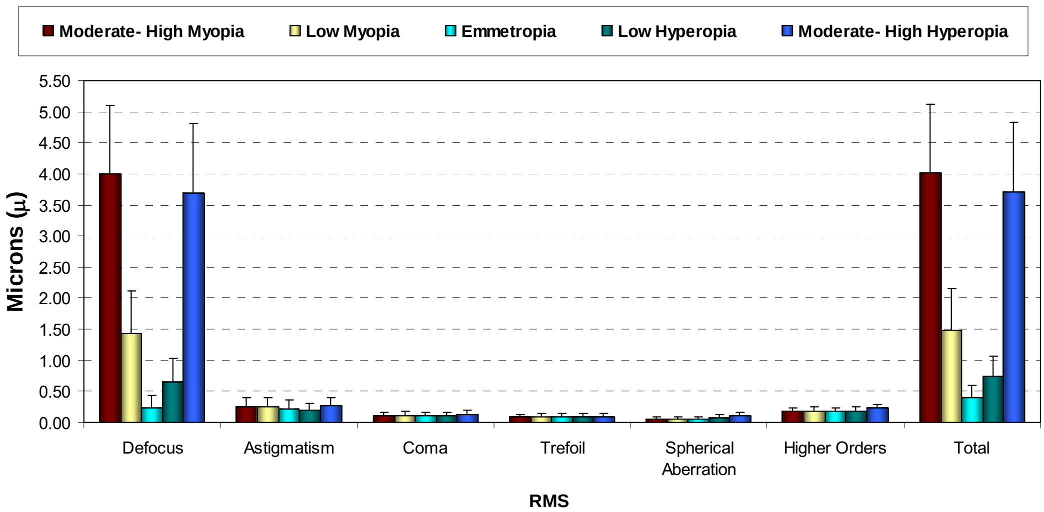

Figure 4.21: ***Ocular aberration profiles in RMS in microns by RE subgroups***

4.5.5 Monochromatic Aberrations and Ethnicity

For purposes of this thesis, the ethnic groups that were less than 5% of the whole study population were regrouped into a new group ("Others"). The final distribution of the various ethnic groups with percentages is presented in Figure 4.22.

The population in this study was predominantly Caucasian (41.4%), followed by those cases with Unknown ethnic background (21.1%), East Asian (12.4%), Mixed (9.3%), Middle Eastern (5.5%) and Indian / Pakistani / Sri Lankan groups (5.3%). Others group (5.0%) were Malaysian / Polynesian (2.9%), South American (0.8%), Unsure (0.7%), African (0.4%) and Indigenous Australian group (0.4%).

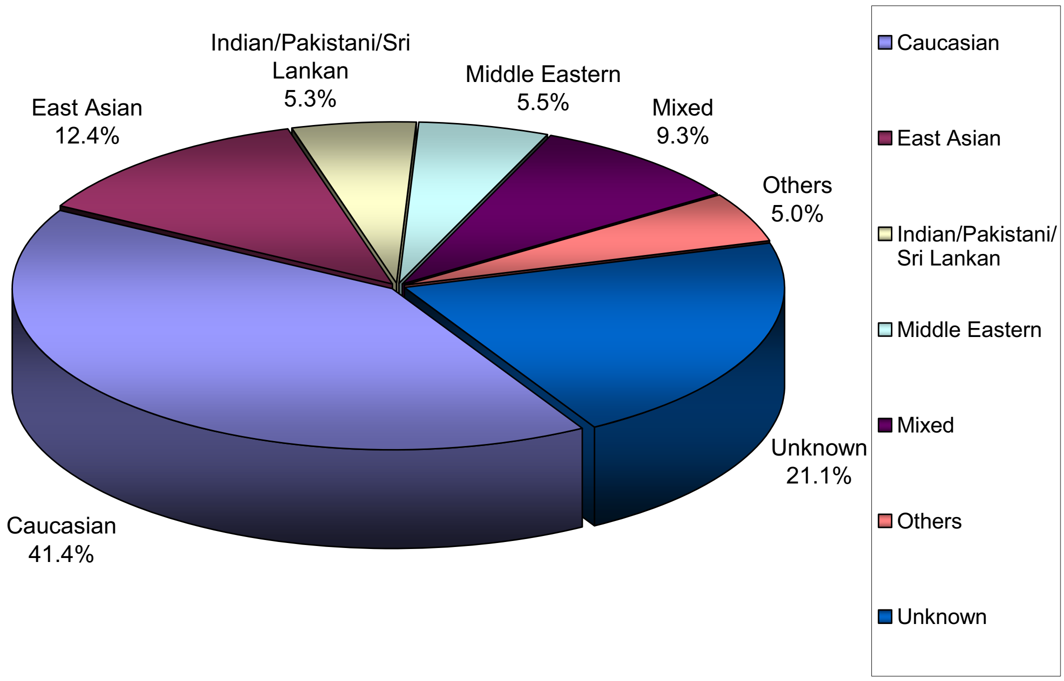

Figure 4.22: ***Distribution of ethnic groups***

4.5.5.1 Distribution of RE

Refractive data from the right eyes of the 1,636 children organised by ethnic background is presented in Table 4.21.

Significant differences were found in the mean M (B-F=41.038, p<0.001) and J_0 (B-F=4.662, p<0.001) between the ethnic groups. Caucasian children were significantly more hyperopic than the East Asian (p<0.001), Indian / Pakistani / Sri Lankan (p<0.001) and Mixed groups (p=0.02). Also, the East Asian and Indian /Pakistani / Sri Lankan groups were significantly more myopic than the other groups (p<0.001) but no difference existed between them (p=0.564). For the astigmatic component of the refraction, multiple comparisons for J_0 revealed the Caucasian group to be significantly different from the East Asian (p<0.001) and Others (p=0.010) groups. The results of the ANOVA and multiple comparisons for the refractive components between ethnic groups are presented in detail in Table F6 in Appendix F.

Table 4.21: ***Refractive components from the right eyes of 1,636 children by ethnic group***

Ethnic Group	n (%)	M		J_0		J_{45}	
		Mean ± SD (D)	Range (D)	Mean ± SD (D)	Range (D)	Mean ± SD (D)	Range (D)
Caucasian	678 (41.4%)	0.80 ± 0.93	-3.95 to 7.69	0.01± 0.15	-0.45 to 0.46	0.03 ± 0.10	-0.25 to 0.41
East Asian	203 (12.4%)	-0.45 ± 1.64	-8.58 to 2.07	0.07 ± 0.17	-0.46 to 0.41	0.03 ± 0.10	-0.32 to 0.36
Indian / Pakistani / Sri Lankan	86 (5.3%)	-0.14 ± 1.20	-3.81 to 1.44	0.02 ± 0.17	-0.47 to 0.46	0.03 ± 0.10	-0.40 to 0.41
Middle Eastern	90 (5.3%)	0.66 ± 0.72	-2.15 to 2.57	0.03 ± 0.15	-0.33 to 0.46	0.01 ± 0.10	-0.19 to 0.23
Mixed	152 (9.3%)	0.49 ± 1.14	-5.36 to 4.75	0.02 ± 0.16	-0.46 to 0.49	0.04 ± 0.10	-0.28 to 0.41
Others	82 (5.0%)	0.56 ± 0.85	-2.28 to 4.70	0.08 ± 0.17	-0.40 to 0.46	0.03 ± 0.10	-0.18 to 0.35
Unknown	345 (21.1%)	0.75 ± 0.85	-4.97 to 5.46	0.02 ± 0.16	-0.44 to 0.46	0.04 ± 0.10	-0.33 to 0.43
Total	1636 (100%)	0.53 ± 1.16	-8.58 to 7.69	0.03 ± 0.16	-0.47 to 0.49	0.03 ± 0.10	-0.40 to 0.43

Due to the lack of well-defined characteristics in terms of ethnic background for groups with mixed or unknown ethnicity, and the small number of cases in the Others group, further analyses were limited to 1,081 children from the first four ethnic groups: (a) Caucasian; (b) East Asian; (c) Indian / Pakistani / Sri Lankan and (d) Middle Eastern. Figure 4.23 presents the histograms of distribution of M for the four ethnic groups. Each histogram presents the distribution of M from the right eyes in 0.50 D steps and their frequency (number of cases).

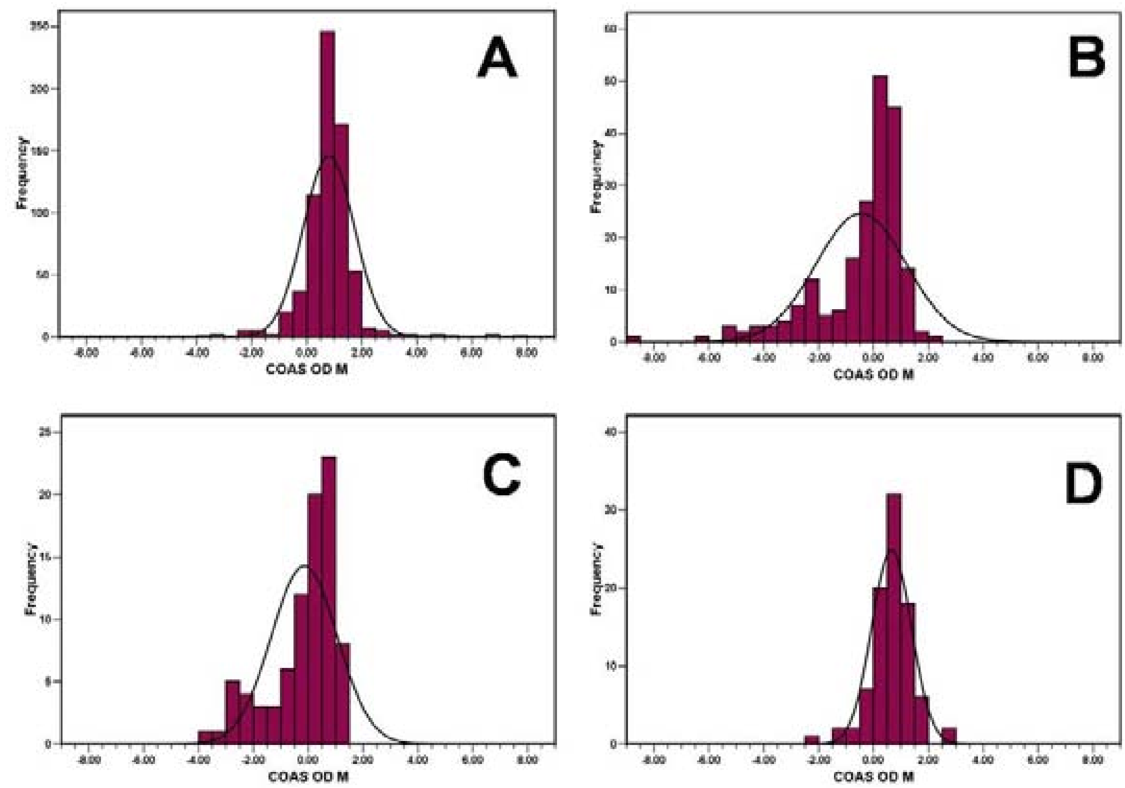

Figure 4.23: ***Distribution of M (D) from 1,081 right eyes by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D) Middle Eastern.*** **Note differences in scale in the ordinates of every graph.*

Differences were evident in the distribution of M between these groups, with the Caucasian (Skewness 1.184, Kurtosis 13.68) and Middle Eastern groups (Skewness -0.717, Kurtosis 2.814) being more hyperopic than the East Asian

(Skewness -1.775, Kurtosis 3.77) and Indian / Pakistani / Sri Lankan groups (Skewness -1.168, Kurtosis 0.610).

As shown in Figure 4.24, there were no differences in the distribution of the astigmatic component of the refraction between the four ethnic groups.

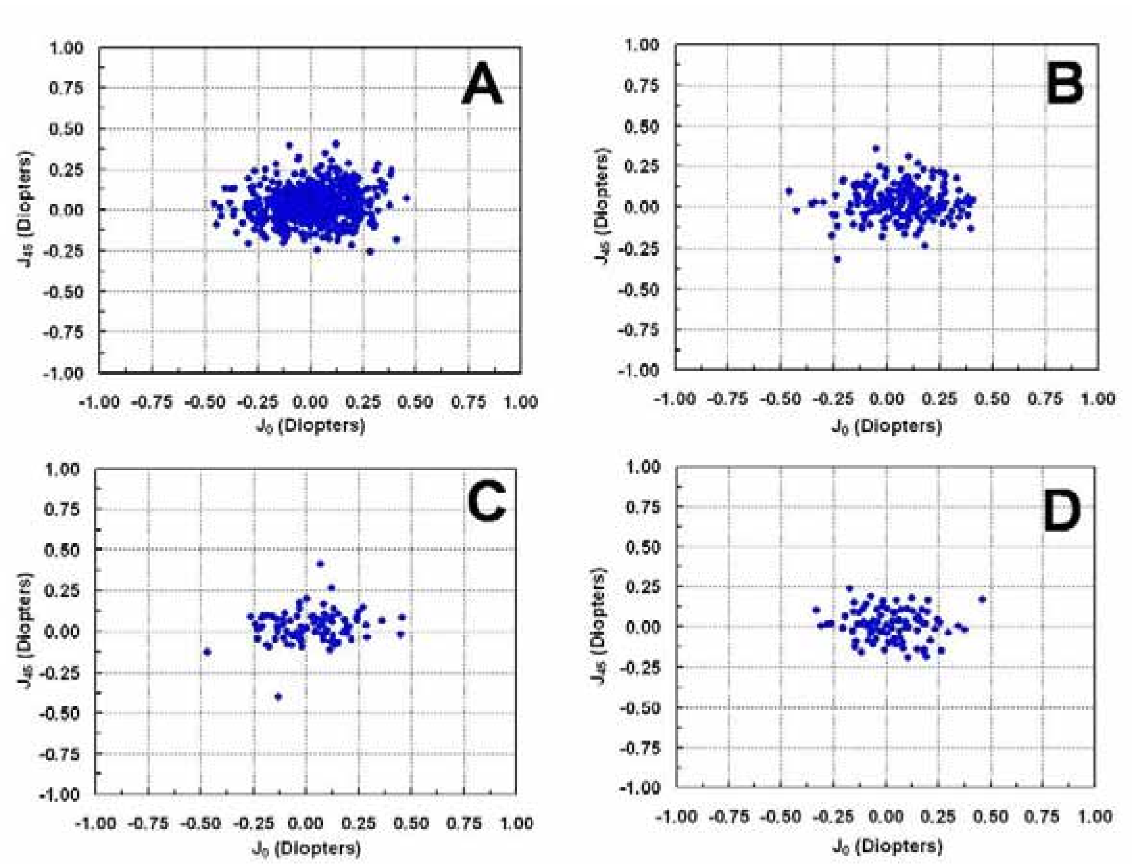

Figure 4.24: ***Distribution of astigmatism in Cartesian form of 1,081 right eyes by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D): Middle Eastern.***

4.5.5.2 Distribution of Monochromatic Aberrations

The distribution of monochromatic aberrations was analysed for each ethnic group and compared between groups. Schematic diagrams showing the spread of the ocular aberrations for the right eyes from Z(2,-2) to Z(6,6) and for only the higher modes in each group are presented in Figures 4.25 and 4.26 respectively.

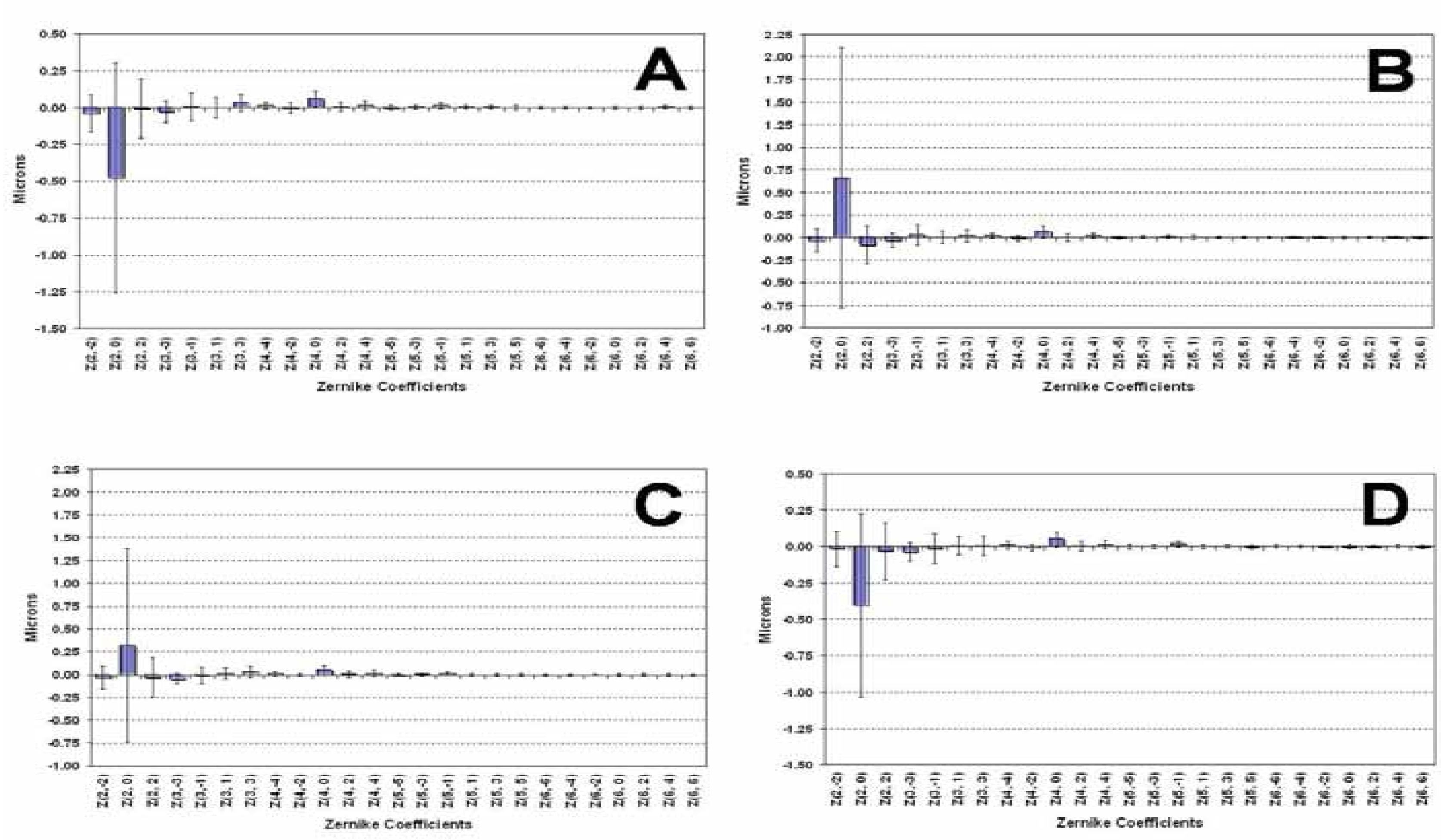

Figure 4.25: ***Mean spread of ocular aberrations Z(2,-2) to Z(6,6) in microns from the right eyes of 1,081 children by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D) Middle Eastern***

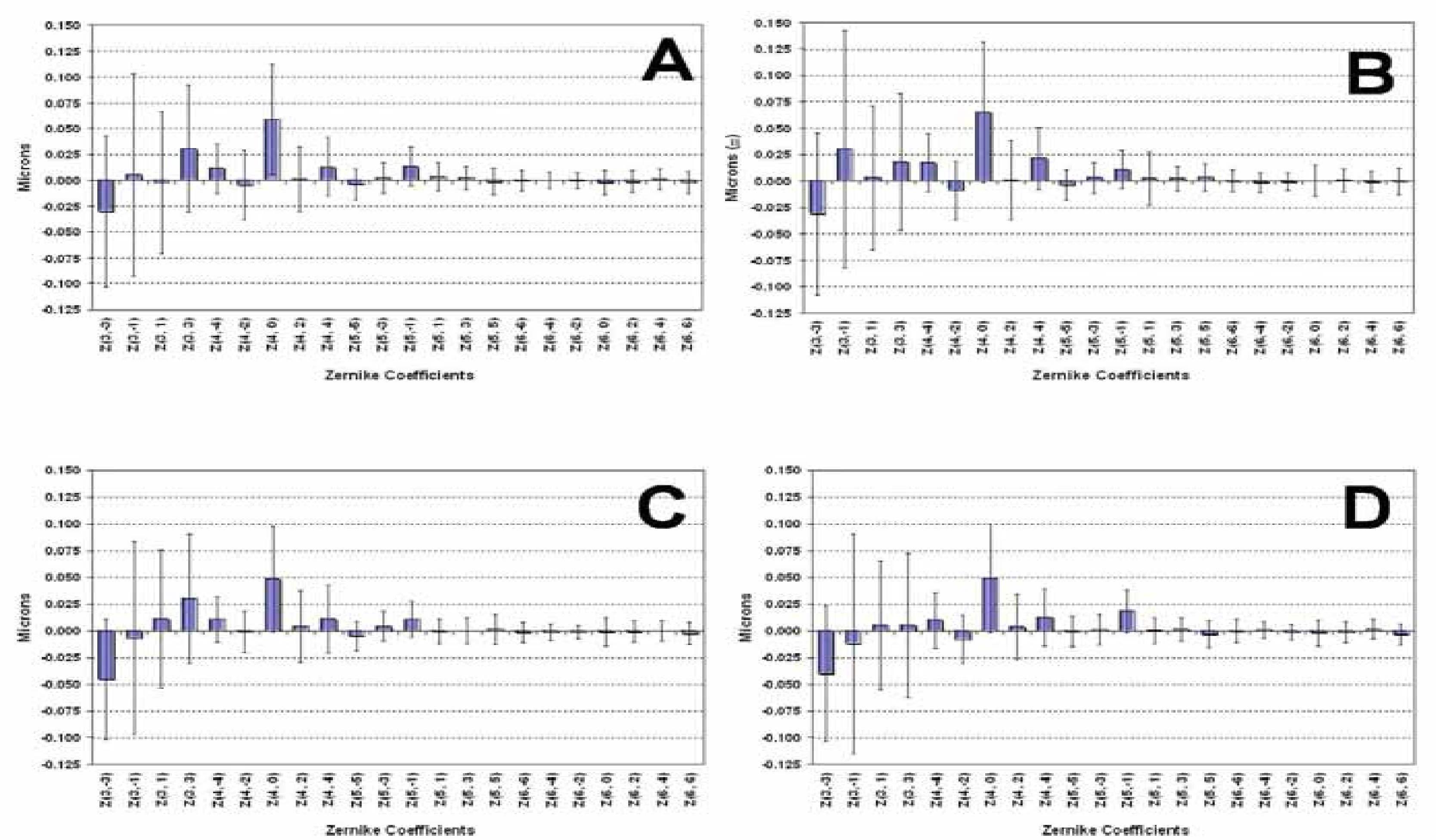

Figure 4.26: ***Mean spread of HOAs Z(3,-3) to Z(6,6) in microns from the right eyes of 1,081 children by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D) Middle Eastern***

Table 4.22 summarises the results of the Zernike coefficients from 2nd to 6th order for the four ethnic groups. For results of the ANOVA and multiple comparisons of the Zernike coefficients between the ethnic groups, refer to Table F7 in Appendix F.

Table 4.22*: Distribution of Zernike coefficients by ethnic group*

Order	Zernike coefficient	Caucasian	East Asian	Indian/ Pakistani/Sri Lankan	Middle Eastern
2nd order	Z(2,-2)	-0.04 ± 0.12	-0.04 ± 0.13	-0.03 ± 0.13	-0.01 ± 0.12
	Z(2, 0)*	**-0.48 ± 0.77†**	**0.66 ± 1.44†**	**0.32 ± 1.06 †**	**-0.40 ± 0.63†**
	Z(2, 2)*	**-0.01 ± 0.19†**	**-0.08 ± 0.21†**	-0.03 ± 0.21	-0.03 ± 0.20
3rd order	Z(3,-3)	-0.03 ± 0.07	-0.03 ± 0.08	-0.05 ± 0.06	-0.04 ± 0.06
	Z(3,-1)*	**0.00 ± 0.10†**	**0.03 ± 0.11†**	**-0.01 ± 0.09†**	**-0.01 ± 0.10†**
	Z(3, 1)	0.00 ± 0.07	0.00 ± 0.07	0.01 ± 0.06	0.01 ± 0.06
	Z(3, 3)*	**0.03 ± 0.06†**	**0.02 ± 0.06 †**	0.03 ± 0.06	**0.01 ± 0.07†**
4th order	Z(4,-4)*	**0.01 ± 0.02†**	**0.02 ± 0.03†**	0.01 ± 0.02	0.01 ± 0.03
	Z(4,-2)*	0.00 ± 0.03	**-0.01 ± 0.03 †**	**0.00 ± 0.02†**	-0.01 ± 0.02
	Z(4, 0)*	0.06 ± 0.05	0.07 ± 0.07	0.05 ± 0.05	0.05 ± 0.05
	Z(4, 2)	0.00 ± 0.03	0.00 ± 0.04	0.00 ± 0.03	0.00 ± 0.03
	Z(4, 4)*	**0.01 ± 0.03†**	**0.02 ± 0.03†**	**0.01 ± 0.03†**	**0.01 ± 0.03†**
5th order	Z(5,-5)	0.00 ± 0.01	0.00 ± 0.01	-0.01 ± 0.01	0.00 ± 0.01
	Z(5,-3)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(5,-1)*	0.01 ± 0.02	**0.01 ± 0.02†**	**0.01 ± 0.02†**	**0.02 ± 0.02†**
	Z(5, 1)	0.00 ± 0.01	0.00 ± 0.03	-0.00 ± 0.01	0.00 ± 0.01
	Z(5, 3)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(5, 5)*	**0.00 ± 0.01†**	**0.00 ± 0.01†**	0.00 ± 0.01	**0.00 ± 0.01†**
6th order	Z(6,-6)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(6,-4)*	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(6,-2)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(6, 0)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(6, 2)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(6, 4)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
	Z(6, 6)	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01

** denotes significant difference between groups as found by one way ANOVA analysis ($p<0.05$)*
† Indicates difference for the group by multiple comparisons $p<0.05$

From the 2nd order aberrations, differences existed as expected between the four groups for Z(2,0), with groups A and D being different to groups B and C ($p<0.001$). Differences in the Z(2,2) coefficient existed between groups A and B only ($p<0.001$).

For the HO modes (3rd to 6th orders), differences were found between all four groups for only Z(3,-1) and Z(4,4). Group B had higher levels of positive Z(3,-1) than the other three groups ($p<0.001$). Similarly, group B had higher levels of positive Z(4,4) than group A ($p<0.001$). Despite the small magnitude values of Z(4,4) in all groups, group D had statistically significant lower levels of Z(4,4) than groups B and C ($p<0.05$). From the 3rd orders, group A had higher levels of positive Z(3,3) than groups B and D ($p<0.05$). Further differences in other HOs modes were found only between two or three groups in seven coefficients: Z(4,-4), Z(4,-2), Z(4,4), Z(5,-1) and Z(5,5) (see Table 4.22).

4.5.5.3 RE Groups

The distribution of RE among the ethnic groups is presented in Table 4.23. The lowest prevalence of Myopic RE within each ethnic group was found in the Caucasian group (5.2%) and the highest was found in the East Asian group (31.0%). The highest prevalence of Emmetropia was found in the East Asian group (38.4%) followed by the Indian / Pakistani / Sri Lankan (37.2%), Middle Eastern (30.0%) and Caucasian (22.1%) groups. The highest prevalence of Hyperopia was found in the Caucasian group (72.7%) and the lowest was found in the East Asian group (30.5%).

Table 4.23: ***Distribution of RE groups among 1,081children by ethnic group.*** *Column % indicates the distribution of RE between the four ethnic groups. Row % indicates the distribution of RE within each ethnic group*

Ethnic Group	Myopes		Emmetropes		Hyperopes		***Total Row (%)***
	Column (%)	**Row (%)**	**Column (%)**	**Row (%)**	**Column (%)**	**Row (%)**	
Caucasian (n=678)	25.9	***5.2***	52.3	*22.1*	76.6	***72.7***	*100*
East Asian (n=203)	50.0	*31.0*	27.2	***38.4***	9.6	***30.5***	*100*
Indian / Pakistani / Sri Lankan (n=86)	18.3	***26.7***	11.1	***37.2***	4.8	*36.0*	*100*
Middle Eastern (n=90)	4.0	***5.6***	9.4	*30.0*	9.0	***64.4***	*100*
Total Column (%)	100	-	100	-	100	-	

The distribution of the mean M across the ethnic groups for each RE group is summarised in Table 4.24. For results of the ANOVA and multiple comparisons of the M between ethnic groups refer to Table F8 in Appendix F.

Significant differences in the mean M existed between ethnic groups in the Myopic (B-F=11.063, $p<0.001$) and Hyperopic (B-F=14.438, $p=0.001$) groups only. For the Myopic group, the mean M in the East Asian group was significantly higher than in the Caucasian ($p<0.001$) and Middle Eastern groups ($p=0.022$). No difference existed between the Indian / Pakistani / Sri Lankan group and the other three ethnic groups ($p>0.05$). For the Hyperopic group, Caucasians presented a higher mean M value than the East Asian ($p<0.001$) and Indian / Pakistani / Sri Lankan ($p<0.001$) groups. No further differences existed between ethnic groups across the Hyperopic group.

Table 4.24: ***Distribution mean M across ethnic groups among RE groups***

RE Group	Ethnic Background	n	Mean ± SD (D)	95% CI for Mean		Range
				Lower Bound	Upper Bound	
Myopes	Caucasian	35	-1.30 ± 0.91	-1.61	-0.98	-3.95 to -0.52
	East Asian	68	-2.42 ± 1.60	-2.83	-2.02	-8.58 to -0.52
	Indian / Pakistani / Sri Lankan	26	-1.85 ± 0.89	-2.23	-1.46	-3.81 to -0.60
	Middle Eastern	6	-1.19 ± 0.61	-1.95	-0.43	-2.15 to -0.59
	All Cases	126	-1.96 ± 1.38	-2.20	-1.71	-8.58 to -0.52
Emmetropes	Caucasian	151	0.17 ± 0.25	0.13	0.21	-0.50 to 0.50
	East Asian	79	0.10 ± 0.25	0.05	0.16	-0.48 to 0.49
	Indian / Pakistani / Sri Lankan	33	0.10 ± 0.27	0.00	0.20	-0.46 to 0.49
	Middle Eastern	28	0.17 ± 0.28	0.06	0.27	-0.36 to 0.49
	All Cases	287	0.14 ± 0.26	0.11	0.17	-0.50 to 0.50
Hyperopes	Caucasian	499	1.15 ± 0.74	1.08	1.21	0.50 to 7.69
	East Asian	64	0.85 ± 0.33	0.77	0.93	0.50 to 2.07
	Indian / Pakistani / Sri Lankan	31	0.87 ± 0.27	0.77	0.97	0.52 to 1.44
	Middle Eastern	61	1.05 ± 0.43	0.93	1.16	0.50 to 2.57
	All Cases	644	1.09 ± 0.68	1.04	1.15	0.50 to 7.69

RE subgroups were determined for each ethnic group as described in Section 4.7. The distribution of each RE subgroup based on the mean M for each ethnic group is presented in Table 4.25.

As there were very few to nil subjects in "Others", this group was excluded and further analyses of RE subgroups and ocular aberrations were limited to low myopic, emmetropic and low hyperopic groups independently for each ethnic group, leaving a total of 1,024 subjects in the next analyses.

Table 4.25: ***Distribution of mean M across RE subgroups among four ethnic groups***

Ethnic Background	RE Group	n (%)	Mean ± SD (D)	95% CI for Mean		Range
				Lower Bound	Upper Bound	
Caucasian	M-H myopia	3 (0.4%)	-3.49 ±0.41	-4.50	-2.48	-3.95 to -3.19
	Low myopia	32 (4.7%)	-1.09 ± 0.63	-1.32	-0.86	-2.47 to -0.52
	Emmetropia	150 (22.1%)	0.17 ± 0.25	0.13	0.21	-0.50 to 0.50
	Low hyperopia	482 (71.1%)	1.06 ± 0.41	1.02	1.09	0.50 to 2.98
	M-H hyperopia	11 (1.6%)	4.96 ± 1.56	3.84	5.82	3.01 to 7.69
	All cases	678 (100%)	0.80 ± 0.93	0.72	0.93	-3.95 to 7.69
East Asian	M-H myopia	17 (8.4%)	-4.49 ±1.42	-5.22	-3.76	-8.58 to -3.07
	Low myopia	46 (22.7%)	-1.66 ± 0.79	-1.89	-1.42	-2.95 to -0.52
	Emmetropia	79 (38.9%)	0.11 ± 0.25	0.50	0.17	-0.48 to 0.50
	Low hyperopia	61 (30.0%)	0.85 ± 0.33	0.77	0.93	0.50 to 2.07
	M-H hyperopia	-	-	-	-	-
	All cases	203 (100%)	-0.57 ± 1.88	-0.93	-0.21	-8.58 to 2.07
Indian/ Pakistani/ Sri Lankan	M-H myopia	2 (2.3%)	-3.43 ±0.53	-8.19	-1.33	-3.81 to -3.06
	Low myopia	21 (24.4%)	-1.70 ± 0.77	-2.05	-1.35	-2.85 to -0.60
	Emmetropia	32 (37.2%)	0.10 ± 0.27	0.00	0.20	-0.46 to 0.49
	Low hyperopia	31 (36.0%)	0.87 ± 0.27	0.77	0.97	0.52 to 1.44
	M-H hyperopia	-	-	-	-	-
	All cases	86 (100%)	-0.48 ± 1.56	-0.98	0.16	-3.81 to 1.44
Middle Eastern	M-H myopia	-	-	-	-	-
	Low myopia	5 (5.6%)	-1.19 ± 0.61	-1.95	-0.43	-2.15 to -0.59
	Emmetropia	27 (30.0%)	0.17 ± 0.26	0.06	0.27	-0.36 to 0.49
	Low hyperopia	58 (64.4%)	1.05 ± 0.43	0.93	1.16	0.50 to 2.57
	M-H hyperopia	-	-	-	-	-
	All cases	90 (100%)	0.69 ± 0.78	0.29	0.76	-2.15 to 2.57

4.5.5.4 Ocular Aberrations by RE (LOs)

Ocular aberrations were analysed by different RE subgroups for each ethnic group separately. Aberrations from the 2nd, 3rd and 4th orders were examined. No analysis was conducted for the 5th and 6th orders because of their small contribution to the total ocular wavefront. Analysis of defocus, astigmatism, coma, trefoil, SA, HOs and total RMS was also conducted.

Results of the ANOVA and multiple comparisons of the Zernike coefficients for each ethnic group are presented in Tables F9 to F12 in Appendix F.

Table 4.26 details the mean and standard deviation of 2nd order aberrations organised by RE subgroups for each ethnic group. The distribution of 2nd order aberrations across RE subgroups for each ethnic group is presented in Figure 4.27.

Table 4.26: ***2nd order aberrations in microns for RE groups by ethnic group***

Ethnic Background	RE Group	Mean ± SD (µm)		
		Z(2,-2)	Z(2, 0)	Z(2, 2)
Caucasian	Low myopia	-0.02 ± 0.14	1.11 ± 0.51	0.15 ± 0.21
	Emmetropia	-0.03 ± 0.13	-0.01 ± 0.27	-0.03 ± 0.20
	Low hyperopia	-0.04± 0.12	-0.68 ± 0.35	-0.02 ± 0.18
	All cases	-0.04 ± 0.12	-0.44 ± 0.56	-0.01 ± 0.19
East Asian	Low myopia	-0.03 ± 0.16	1.68 ± 0.72	-0.12 ± 0.21
	Emmetropia	-0.03 ± 0.12	0.13 ± 0.30	-0.10 ± 0.19
	Low hyperopia	-0.04± 0.12	-0.42 ± 0.32	-0.05 ± 0.23
	All cases	-0.03 ± 0.13	0.34 ± 0.92	-0.09 ± 0.21
Indian/ Pakistani/ Sri Lankan	Low myopia	-0.01 ± 0.11	1.75 ± 0.72	-0.01 ± 0.18
	Emmetropia	-0.03 ± 0.16	0.04 ± 0.26	-0.07 ± 0.25
	Low hyperopia	-0.05 ± 0.10	-0.53 ± 0.24	-0.02 ± 0.19
	All cases	-0.03 ± 0.13	0.26 ± 0.99	-0.04 ± 0.21
Middle Eastern	Low myopia	-0.06 ± 0.05	1.09 ± 0.63	0.30 ± 0.14
	Emmetropia	-0.02 ± 0.14	0.00 ± 0.29	-0.03 ± 0.18
	Low hyperopia	-0.01 ± 0.12	-0.72 ± 0.42	-0.06 ± 0.18
	All cases	-0.01 ± 0.12	-0.40 ±0.63	-0.03 ± 0.20

From the 2nd order aberrations, Z(2,0) was different between all RE subgroups for the four ethnic groups: Caucasian (B-F=149.324, $p<0.001$; G-H, $p<0.05$), East Asian (B-F=45.186, $p<0.001$; G-H, $p<0.001$), Indian / Pakistani / Sri Lankan (B-F=106.855, $p<0.001$; G-H, $p<0.05$), Middle Eastern (B-F=43.440, $p<0.001$;G-H, $p<0.05$).

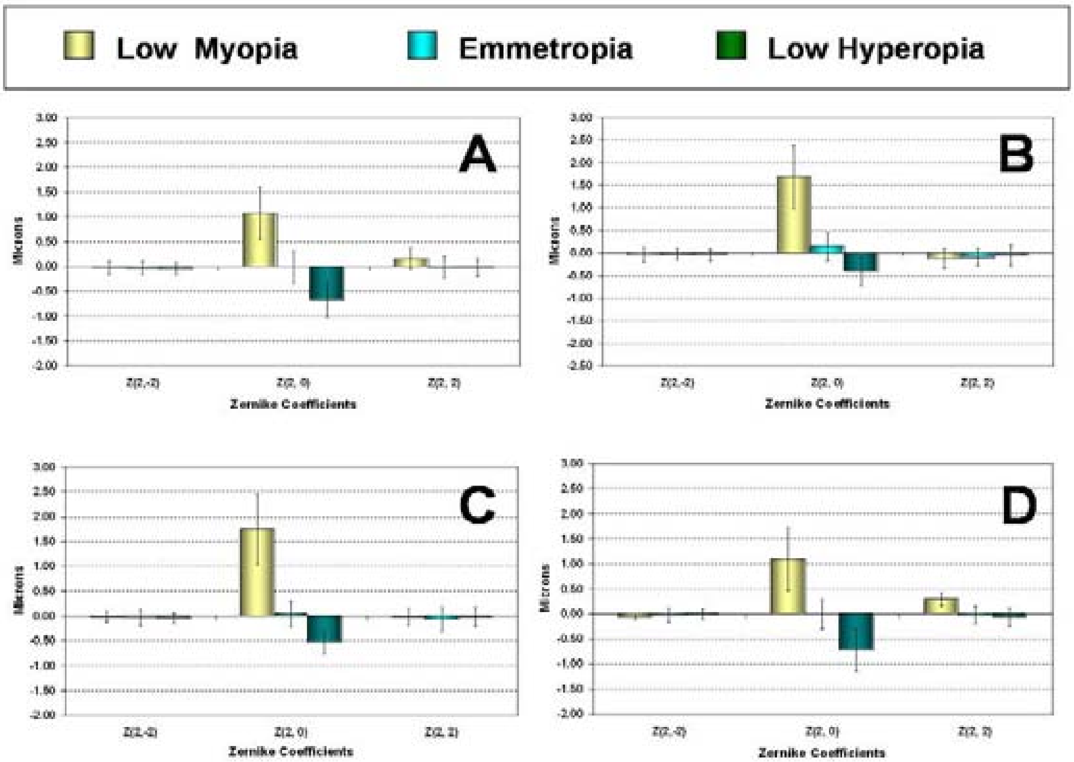

Figure 4.27: ***2nd order aberrations Z(2,-2), Z(2,0) and Z(2,2) in microns for RE groups by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D) Middle Eastern***

In the Caucasian and Middle Eastern groups, Z(2,2) was different between RE subgroups (B-F=5.614, p=0.001; B-F=11.614, p<0.001) respectively. Multiple comparisons in both groups revealed myopes had more positive levels of Z(2,2) than emmetropes (Caucasian, p=0.002; Middle Eastern, p=0.006) and low hyperopes (Caucasian, p=0.001; Middle Eastern, p=0.005). No further differences existed between RE groups for the other ethnic groups.

4.5.5.5 Ocular Aberrations by RE (HOs)

Third Orders

The mean and standard deviation of 3rd order aberrations organised by RE subgroups for each ethnic group is presented in Table 4.27. The distribution of 3rd order aberrations across RE subgroups for each ethnic group is presented in Figure 4.28.

Table 4.27: ***3rd order aberrations in microns for RE groups***

Ethnic Background	RE Group	Mean ± SD (μm)			
		Z(3,-3)	Z(3, -1)	Z(3, 1)	Z(3, 3)
Caucasian	Low myopia	-0.03 ± 0.09	0.02 ± 0.09	0.01 ± 0.07	0.03 ± 0.06
	Emmetropia	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.06	0.02 ± 0.06
	Low hyperopia	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.07	0.03 ± 0.06
	All cases	-0.03 ± 0.07	0.00 ± 0.10	0.00 ± 0.07	0.03 ± 0.06
East Asian	Low myopia	-0.05 ± 0.07	0.07 ± 0.12	0.03 ± 0.07	0.02 ± 0.08
	Emmetropia	-0.03 ± 0.08	0.02 ± 0.10	0.00 ± 0.06	0.02 ± 0.06
	Low hyperopia	-0.02 ± 0.08	0.00 ± 0.11	0.00 ± 0.07	0.01 ± 0.06
	All cases	-0.03 ± 0.08	0.02 ± 0.11	0.01 ± 0.07	0.02 ± 0.07
Indian/ Pakistani/ Sri Lankan	Low myopia	-0.05 ± 0.05	-0.02 ± 0.08	0.02 ± 0.07	0.03 ± 0.07
	Emmetropia	-0.04 ± 0.06	-0.01 ± 0.10	0.00 ± 0.06	0.03 ± 0.07
	Low hyperopia	-0.05 ± 0.06	0.00 ± 0.09	0.01 ± 0.07	0.03 ± 0.05
	All cases	-0.05 ± 0.06	-0.01 ± 0.09	0.01 ± 0.06	0.03 ± 0.06
Middle Eastern	Low myopia	-0.03 ± 0.05	0.01 ± 0.13	0.04 ± 0.03	0.00 ± 0.08
	Emmetropia	-0.05 ± 0.06	-0.02 ± 0.11	-0.01 ± 0.06	0.01 ± 0.07
	Low hyperopia	-0.04 ± 0.06	-0.01 ± 0.10	0.01 ± 0.06	0.00 ± 0.07
	All cases	-0.04 ± 0.06	-0.01 ± 0.10	0.01 ± 0.06	0.01 ± 0.07

From the four ethnic groups, differences in the 3rd order aberrations between RE subgroups were found only in the East Asian group for Z(3,-1) (B-F=5.069, p=0.007). This difference was present between myopes and the other two subgroups ($p<0.05$).

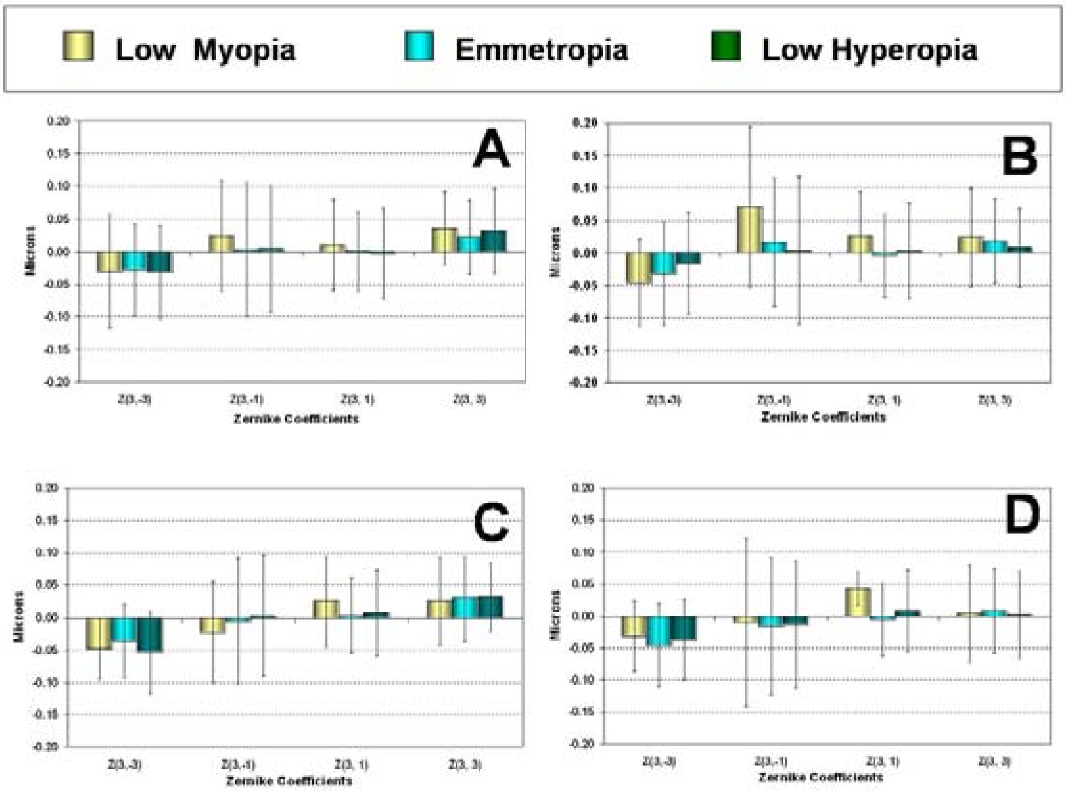

Figure 4.28: ***3rd order aberrations Z(2,-3) to Z(3,3) in microns for RE groups by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian/Pakistani/Sri Lankan, (D) Middle Eastern***

Fourth Orders

The mean and standard deviation of 4th order aberrations organised by RE subgroups for each ethnic group is presented in Table 4.28. The distribution of the primary SA across RE subgroups for each ethnic group is presented in Figure 4.29.

In the 4th order aberrations, primary SA Z(4,0) was found to be different between RE subgroups in the four ethnic groups: Caucasian (B-F=32.949, p<0.001); East Asian (B-F=5.770, p=0.004); Indian / Pakistani / Sri Lankan (B-F=3.580, p=0.33) and Middle Eastern (B-F=4.325, p=0.003).

Table 4.28: *4th order aberrations in microns for RE groups by ethnic group*

Ethnic Background	RE Group	Mean ± SD (µm)				
		Z(4,-4)	Z(4, -2)	Z(4, 0)	Z(4, 2)	Z(4, 4)
Caucasian	Low myopia	0.01 ± 0.02	-0.01 ± 0.03	0.04 ± 0.04	0.00 ± 0.03	0.01 ± 0.03
	Emmetropia	0.01 ± 0.02	-0.01 ± 0.02	0.03 ± 0.05	0.01 ± 0.03	0.01 ± 0.02
	Low hyperopia	0.01 ± 0.03	0.00 ± 0.04	0.07 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
	All cases	0.01 ± 0.02	0.00 ±0.03	0.06 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
East Asian	Low myopia	0.02 ± 0.03	-0.01 ± 0.02	0.05 ± 0.05	0.00 ± 0.02	0.02 ± 0.03
	Emmetropia	0.02 ± 0.03	-0.01 ± 0.02	0.06 ± 0.06	0.00 ± 0.03	0.02 ± 0.03
	Low hyperopia	0.02 ± 0.03	-0.01 ± 0.04	0.09 ± 0.09	0.01 ± 0.05	0.02 ± 0.03
	All cases	0.02 ± 0.03	-0.01 ±0.03	0.07 ± 0.07	0.00 ± 0.04	0.02 ± 0.03
Indian/ Pakistani/ Sri Lankan	Low myopia	0.01 ± 0.01	0.01 ± 0.01	0.05 ± 0.04	0.00 ± 0.03	0.01 ± 0.04
	Emmetropia	0.01 ± 0.02	0.00 ± 0.02	0.03 ± 0.05	0.00 ± 0.04	0.02 ± 0.03
	Low hyperopia	0.01 ± 0.02	0.00 ± 0.02	0.06 ± 0.05	0.01 ± 0.03	0.01 ± 0.03
	All cases	0.01 ± 0.02	0.00 ±0.02	0.05 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
Middle Eastern	Low myopia	0.01 ± 0.02	0.00 ± 0.01	0.00 ± 0.03	0.00 ± 0.02	0.00 ± 0.03
	Emmetropia	0.01 ± 0.03	-0.02 ± 0.02	0.04 ± 0.05	0.01 ± 0.03	0.01 ± 0.03
	Low hyperopia	0.01 ± 0.03	0.00 ± 0.02	0.06 ± 0.05	0.00 ± 0.03	0.01 ± 0.03
	All cases	0.01 ± 0.03	-0.01 ±0.02	0.05 ± 0.05	0.00 ± 0.03	0.01 ± 0.03

In the Caucasian group, hyperopes had significantly higher levels of Z(4,0) than Myopes ($p=0.002$) and Emmetropes ($p<0.001$). For the East Asian group, hyperopes had significantly higher levels of Z(4,0) than Myopes ($p=0.007$) only. In the Indian / Pakistani / Sri Lankan group, hyperopes had higher levels of Z(4,0) than Emmetropes ($p=0.037$) only and in the Middle Eastern group hyperopes had higher levels of Z(4,0) than Myopes ($p=0.01$) only.

In the Caucasian group, differences were also found for Z(4,2) (B-F=3.993, $p<0.001$) between Emmetropes and hyperopes ($p=0.018$). In the Middle Eastern group, analysis of variance revealed differences between the RE groups for

(4,-2) (B-F=3.318, p=0.045); however, multiple comparisons did not find any difference (p>0.05).

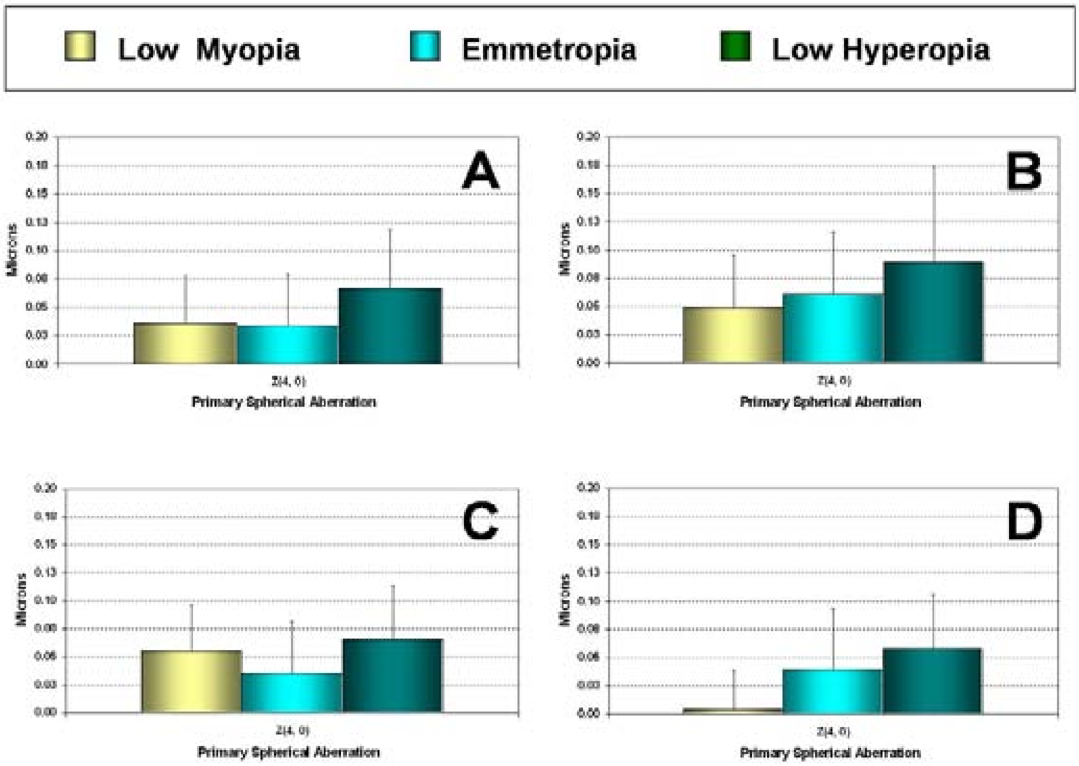

Figure 4.29: ***Primary SA Z(4,0) in microns for RE groups by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D) Middle Eastern***

RMS

Table 4.29 details the mean and standard deviation of the RMS organised by RE subgroups for each ethnic group. Differences in defocus RMS and Total Aberrations RMS were found in the four ethnic groups (B-F, p<0.05). Differences in SA RMS existed in the Caucasian (B-F=31.838, p<0.001), East Asian (B-F=5.044, p=0.008) and Middle Eastern groups (B-F=3.874, p=0.27). East Asians also had differences in coma RMS (B-F 3.891, p=0.023) and the Middle Eastern group had differences in secondary astigmatism RMS (B-F=3.803, p=0.029). Caucasians also presented differences for tetrafoil RMS

(B-F=3.969, p=0.021), secondary astigmatism RMS (B-F=7.970, p=0.001) and HO RMS (B-F=3.606, p=0.29). Results of the ANOVA and multiple comparisons of the RMS for each ethnic group are presented in Tables F13 to F16 in Appendix F.

Table 4.29: ***RMS of ocular aberrations in microns for RE groups***

Ethnic Background	RE Group	Mean RMS ± SD (μm)								
		Defocus	Astigmatism	Coma	Trefoil	SA	Tetrafoil	Second Astigmat	Higher order	Total
Caucasian	Low myopia	1.11 ± 0.51	0.25 ± 0.14	0.10 ± 0.06	0.10 ± 0.05	0.05 ± 0.03	0.03 ± 0.02	0.03 ± 0.02	0.17 ± 0.05	1.17 ± 0.49
	Emmetropia	0.21 ± 0.16	0.21 ± 0.13	0.11 ± 0.06	0.09 ± 0.05	0.05 ± 0.03	0.03 ± 0.02	0.03 ± 0.02	0.17 ± 0.06	0.38 ± 0.14
	Low hyperopia	0.68 ± 0.35	0.19 ± 0.11	0.10 ± 0.06	0.09 ± 0.05	0.07 ± 0.05	0.04 ± 0.02	0.04 ± 0.03	0.19 ± 0.06	0.75 ± 0.32
	All cases	0.59 ± 0.40	0.20 ± 0.12	0.16 ± 0.06	0.09 ± 0.05	0.06 ± 0.04	0.04 ± 0.02	0.04 ± 0.03	0.18 ± 0.06	0.69 ± 0.36
East Asian	Low myopia	1.68 ± 0.72	0.25 ± 0.15	0.14 ± 0.08	0.10 ± 0.05	0.06 ± 0.04	0.04 ± 0.03	0.03 ± 0.02	0.21 ± 0.07	1.73 ± 0.69
	Emmetropia	0.26 ± 0.21	0.22 ± 0.12	0.10 ± 0.06	0.09 ± 0.06	0.06 ± 0.05	0.04 ± 0.02	0.03 ± 0.02	0.18 ± 0.06	0.42 ± 0.18
	Low hyperopia	0.44 ± 0.29	0.23 ± 0.13	0.12 ± 0.07	0.09 ± 0.05	0.09 ± 0.08	0.04 ± 0.02	0.04 ± 0.05	0.21 ± 0.11	0.58 ± 0.26
	All cases	0.67 ± 0.72	0.23 ± 0.13	0.12 ± 0.07	0.09 ± 0.05	0.07 ± 0.06	0.04 ± 0.02	0.04 ± 0.03	0.20 ± 0.08	0.80 ± 0.67
Indian/ Pakistani/ Sri Lankan	Low myopia	1.75 ± 0.72	0.19 ± 0.08	0.10 ± 0.04	0.09 ± 0.03	0.06 ± 0.03	0.04 ± 0.02	0.03 ± 0.01	0.17 ± 0.04	1.77 ± 0.70
	Emmetropia	0.19 ± 0.19	0.26 ± 0.16	0.10 ± 0.05	0.09 ± 0.04	0.05 ± 0.03	0.04 ± 0.02	0.03 ± 0.03	0.17 ± 0.04	0.40 ± 0.18
	Low hyperopia	0.53 ± 0.24	0.19 ± 0.11	0.10 ± 0.06	0.09 ± 0.05	0.07 ± 0.04	0.04 ± 0.02	0.04 ± 0.02	0.18 ± 0.05	0.62 ± 0.18
	All cases	0.70 ± 0.74	0.22 ± 0.13	0.10 ± 0.05	0.09 ± 0.04	0.06 ± 0.04	0.04 ± 0.02	0.03 ± 0.02	0.17 ± 0.04	0.83 ± 0.67
Middle Eastern	Low myopia	1.09 ± 0.63	0.31 ± 0.13	0.12 ± 0.05	0.08 ± 0.03	0.03 ± 0.01	0.03 ± 0.00	0.02 ± 0.01	0.17 ± 0.03	1.16 ± 0.61
	Emmetropia	0.21 ± 0.19	0.21 ± 0.08	0.10 ± 0.07	0.09 ± 0.05	0.05 ± 0.04	0.04 ± 0.02	0.03 ± 0.02	0.18 ± 0.06	0.38 ± 0.15
	Low hyperopia	0.72 ± 0.42	0.19 ± 0.12	0.10 ± 0.06	0.09 ± 0.04	0.06 ± 0.04	0.03 ± 0.02	0.03 ± 0.02	0.18 ± 0.05	0.79 ± 0.39
	All cases	0.59 ± 0.46	0.20 ± 0.11	0.10 ± 0.06	0.09 ± 0.04	0.06 ± 0.04	0.04 ± 0.02	0.03 ± 0.02	0.18 ± 0.05	0.69 ± 0.41

Defocus RMS and Total Aberrations RMS were different between the three RE groups ($p<0.001$) in the Caucasian, East Asian and Indian / Pakistani / Sri Lankan groups. In the Middle Eastern group these differences existed only between Emmetropes and hyperopes ($p<0.001$). Coma RMS was different between low myopes and low hyperopes ($p=0.022$) in the East Asian group. SA RMS was different in the Caucasian group between low hyperopes and emmetropes ($p<0.001$) and low hyperopes and low myopes ($p=0.001$). Differences of SA RMS existed between low myopes and low hyperopes for the East Asians group ($p=0.017$) and the Middle Eastern group ($p=0.004$).

Secondary astigmatism RMS was different between low myopes and emmetropes ($p=0.0011$) and between low myopes and low hyperopes ($p=0.01$) for the Middle Eastern group and between emmetropes and low hyperopes ($p=0.001$) for the Caucasian group. Differences in tetrafoil RMS existed between emmetropes and low hyperopes ($p=0.025$) in the Caucasian group. Finally, for the Caucasian group, differences in HO RMS were found only between emmetropes and low hyperopes ($p=0.011$).

The distribution of RMS across RE subgroups for each ethnic group is presented in Figure 4.30.

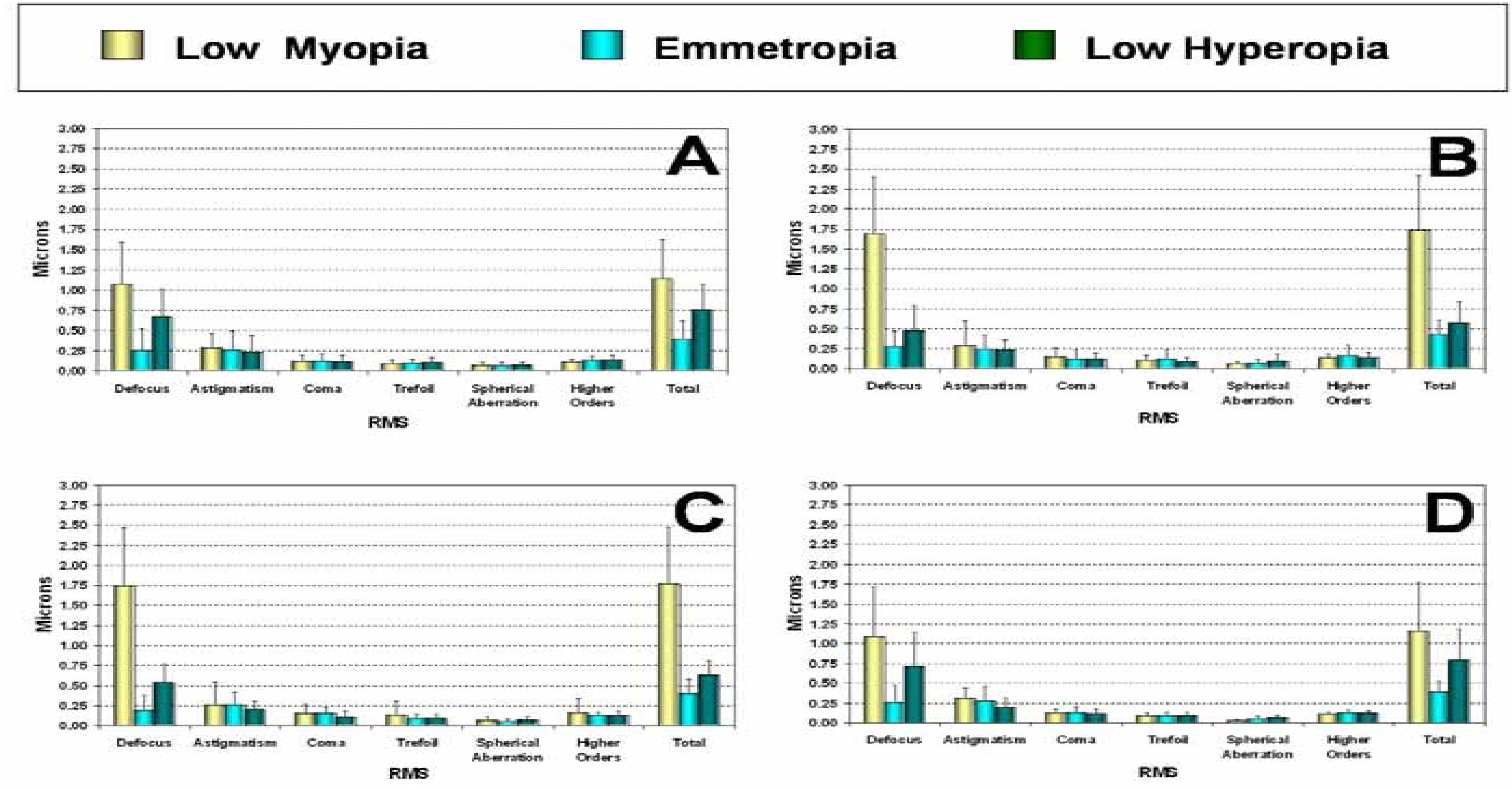

Figure 4.30: ***Ocular aberration profiles in RMS in microns for RE groups by ethnic group. (A) Caucasian, (B) East Asian, (C) Indian / Pakistani / Sri Lankan, (D) Middle Eastern***

HOAs RMS between Ethnic Groups

From subsection 4.5.5.3, it was evident that despite inter-racial differences in the mean M, differences in RMS between the three RE groups occurred in the 2nd orders (defocus RMS), with some variability of results in the HOs. In this subsection, the RMS of the 3rd, 4th and HOs was compared between ethnic groups within the three RE groups while adjusting for M. The results of the RMS of the HOAs of the low myopes, emmetropes and low hyperopes groups of each ethnic group are presented in Table 4.30.

Table 4.30: ***RMS of HOAs in microns for RE groups within ethnic groups***

RE Group	Ethnic Background	Mean RMS ± SD (μm)					
		Coma	Trefoil	SA	Tetrafoil	Second Astigmat	Higher order
Low myopia	Caucasian	0.10 ± 0.06	0.10 ± 0.05	0.05 ± 0.03	0.03 ± 0.02	0.03 ± 0.02	0.17 ± 0.05
	East Asian	0.14 ± 0.08	0.10 ± 0.05	0.06 ± 0.04	0.04 ± 0.03	0.03 ± 0.02	0.21 ± 0.07
	Indian/ Pakistani/ Sri Lankan	0.10 ± 0.04	0.09 ± 0.03	0.06 ± 0.03	0.04 ± 0.02	0.03 ± 0.01	0.17 ± 0.04
	Middle Eastern	0.12 ± 0.05	0.08 ± 0.03	0.03 ± 0.01	0.03 ± 0.00	0.02 ± 0.01	0.17 ± 0.03
Emmetropia	Caucasian	0.11 ± 0.06	0.09 ± 0.05	0.05 ± 0.03	0.03 ± 0.02	0.03 ± 0.02	0.17 ± 0.06
	East Asian	0.10 ± 0.06	0.09 ± 0.06	0.06 ± 0.05	0.04 ± 0.02	0.03 ± 0.02	0.18 ± 0.06
	Indian/ Pakistani/ Sri Lankan	0.10 ± 0.05	0.09 ± 0.04	0.05 ± 0.03	0.04 ± 0.02	0.03 ± 0.03	0.17 ± 0.04
	Middle Eastern	0.10 ± 0.07	0.09 ± 0.05	0.05 ± 0.04	0.04 ± 0.02	0.03 ± 0.02	0.18 ± 0.06
Low hyperopia	Caucasian	0.10 ± 0.06	0.09 ± 0.05	0.07 ± 0.05	0.04 ± 0.02	0.04 ± 0.03	0.19 ± 0.06
	East Asian	0.12 ± 0.07	0.09 ± 0.05	0.09 ± 0.08	0.04 ± 0.02	0.04 ± 0.05	0.21 ± 0.11
	Indian/ Pakistani/ Sri Lankan	0.10 ± 0.06	0.09 ± 0.05	0.07 ± 0.04	0.04 ± 0.02	0.04 ± 0.02	0.18 ± 0.05
	Middle Eastern	0.10 ± 0.06	0.09 ± 0.04	0.06 ± 0.04	0.03 ± 0.02	0.03 ± 0.02	0.10 ± 0.05

Multivariate analysis of coma, trefoil, SA, tetrafoil, secondary astigmatism and HO RMS, after adjusting for M, show an association of ethnicity with differences in RMS in the low hyperopic group only (Pillai's Trace 0.17, *F 1.1762*, p=0.056). Adjusted-multiple comparisons analysis showed low hyperopic East Asian children had higher levels of SA RMS and HO RMS than Caucasian (p<0.001, p=0.013) and Middle Eastern children (p=0.001, p=0.034). Also a slight difference was found between hyperopic East Asian and Caucasian children for quatrefoil (p=0.024). No further inter-race differences were found between RE groups.

4.6 DISCUSSION

4.6.1 Distribution of RE

In this study, RE and monochromatic aberration were obtained from 1,636 children with mean age (±SD) 12.6 ± 0.4 years (range 11.1 to 14.4 years). A similar proportion of boys (50%) and girls were measured. The distribution of RE, based on the SE from the right eye, was leptokurtic towards slight hyperopia (mean M +0.54 ± 1.16 D, range -8.58 to 7.69 D). There was a significant correlation of the mean M between right and left eyes (r=0.92, p<0.001). Similarly, the horizontal / vertical astigmatic component (J_0) was significantly high correlated between eyes (r=0.70, p<0.001), and a low but significant correlation existed for the oblique astigmatic component (J_{45}) (r=-0.38, p<0.001). Girls presented small but more positive values of mean J_0 than boys (p<0.034). Similar characteristics of astigmatism have been reported in adults who had higher correlation values for refractive and corneal J_0 than J_{45} (McKendrick and

Brennan 1996) and, in a group of 6 year old children, girls had slightly higher levels of refractive, corneal and internal astigmatism than boys (Huynh *et al.* 2006A).

4.6.2 Correlation of Monochromatic Aberrations Between Eyes

Despite large variability between individuals, right and left eyes tend to present similar levels of physical and optical characteristics in humans. Large differences of RE between eyes (anisometropia) are rare in non-strabismic children. Large cross-sectional studies in children younger than 10 years of age reported anisometropia based on the SE ≥1.00 D to range between 0% (Almeder *et al.* 1990), 1.6% (Huynh *et al.* 2006B) to 3.8% (Tong *et al.* 2004). The prevalence of aniso-astigmatism ≥1.00 D in children was also found to be 1.0% in 6 year old children (Huynh *et al.* 2006B). In the same way, studies in adults have found a high degree of mirror image symmetry (enantiomorphism) in corneal shape (Dingeldein and Klyce 1989), or a high correlation in corneal J_0 astigmatic power (McKendrick and Brennan 1996) between right and left eyes. These findings suggest the existence of a passive coordinated binocular eye-growth mechanism in humans.

Most studies have reported the degree of symmetry of monochromatic aberrations between right and left eyes to vary from none to variable mirror symmetry (Marcos and Burns 2000; Castejon-Mochon *et al.* 2002; Liang and Williams 1997; Porter *et al.* 2001). One study conducted in a group of 6 year old Chinese children reported significant correlations of aberrations from the 2nd to the 4th orders (Carkeet *et al.* 2003).

In the current study, the correlation between right and left eyes of Zernike coefficients from 2nd to 6th order was analysed. The highest correlations were found for defocus Z(2,0) (r=0.93), Z(4,0) (r=0.78) and Z(2,2) (r=0.70). The correlation for oblique astigmatism Z(2,-2) was moderate to low but significant (r=0.38, p<0.001). For HOs, after Z(4,0), 3rd order terms had the higher correlations. These results are in very close agreement to those reported from 109 young subjects (Porter *et al.* 2001) and from 34 children (Carkeet *et al.* 2003). In Porter *et al.* (2001) the highest correlations between eyes (5.7 mm PD) were found for Z(2,0) (r=0.98), Z(4,0) (r=0.82) and Z(2,2) (r=0.77), while in Carkeet *et al.* (2003) significantly high correlation values (5 mm PD) existed for Z(2,0) (r=0.97), Z(2,2) (r=0.83), Z(4,0) (r=0.80) and most 3rd order coefficients.

The results obtained in this study are also in agreement with those from Castejon-Mochon *et al.*, (2002), who showed that most 2nd and 3rd order terms showed a good correlation (p<0.05) between the right and left eyes (7 mm PD) of 35 young subjects (aged 20 to 30 years old). The authors reported that, for the astigmatic terms, while Z(2,2) had a high correlation (r=0.91), Z(2,-2) had a small correlation (r=-0.2) and after Z(4,0) (r=0.77), coma terms had the higher correlation values from the HOs.

In our present study, 80% of the coefficients were significantly correlated (p<0.001), although moderate to high correlations existed only for the 2nd, 3rd and 4th orders. This is also in agreement with Porter *et al.* (2001) who found that nearly 75% of the coefficients were significantly correlated between right and left eyes. While in Porter *et al.* (2001) reported mirror symmetry between right and left eyes was confirmed for odds terms except for Z(5,-1) and Z(5,1), in our present study, mirror symmetry was not found for Z(4,-2) (r=-0.24) and for 6th order terms Z(6,-6) (r=0.06), Z(6,-4) (r=0.06) and Z(6,-2) (r=0.13).

The high correlation values found for defocus (mainly related to AL), SA (the result of the balance between corneal and lenticular asphericity) (Artal *et al.* 2001; Artal *et al.* 2006; Millodot and Sivak 1979), and Z(2,2) (balance of corneal horizontal / vertical astigmatism and internal optics of the eye) (Kelly *et al.* 2004), support the existence of a passive coordinated binocular mechanism of eye growth in children. As a result, this reflects into a low prevalence of anisometropia and aniso-astigmatism in the current group. However, it has to be noted that cases with cylinders >1.00 D were excluded in the current study.

There was not a strong correlation of the oblique component of the astigmatism Z(2,-2). This could be due to the exclusion of those cases with cylinders >1.00 D from the analysis, reducing the mean astigmatism of the study population to less than 0.50 D. In this case, small variations of the astigmatic axis between eyes could have occurred. Similar findings of higher correlation values between right and left eyes for refractive and corneal J_0 than refractive and corneal J_{45} have been reported (McKendrick and Brennan 1996).

Whilst the correlation between Zernike coefficients of right and left eyes indicates the similarity of individual aberrations between eyes, it is not indicative of the symmetry in the pattern of optical quality within the pupil between eyes. Marcos and Burns (2000) found that, while the pattern of aberrations is not symmetrical between right and left eyes, there is a larger mirror symmetry tendency in cone directionality in the retina which it is not always aligned to the optically best pupillary region. In other words, it seems that, in the human eye, a system that coordinates the ocular optics and cone alignment towards developing an optimal optical system is non-existent.

4.6.3 Distribution of Monochromatic Aberrations

In agreement with previous studies in children (Carkeet *et al.* 2002; Castejon-Mochon *et al* 2002; Kirwan *et al.* 2006) and adults (Porter *et al.* 2001), the results from the current study show that children have low amounts of HOAs. From all the aberrations analysed, 2nd order aberrations (defocus and astigmatism) were dominant across the sample. Defocus Z(2,0) was the largest in magnitude and variance, followed by vertical/ horizontal Z(2,2) and oblique Z(2,-2) astigmatism. Of the HOAs, aberrations from the 3rd and 4th order had the largest contribution. SA Z(4,0) had the largest magnitude, followed by 3rd order aberrations which had the largest variability of the HO modes. The magnitude of the 5th and 6th orders was very small to be of any significance in degrading the optical quality of the eye.

Aberrations have been reported to vary with age (Brunette *et al.* 2003), however, the large inter-subject variability seen for all aberrations in this study cannot be attributed to age differences because the homogeneous distribution of age (11.1 to 14.4 years). In order to determine if the characteristics of aberrations and their variability change with age during childhood, the results from the present study will be compared with those from another cohort of younger children (mostly 6 year old children) in Chapter 5. Despite the large variability, most aberrations were normally distributed near to zero and from the HOs, Z(4,0) was biased towards positive values. These results are in agreement with those from adults (Cheng *et al.* 2004B; Salmon and van de Pol 2006) and with statistical models of the variation of the aberration in adults (Thibos *et al.* 2002B; Thibos *et al.* 2002C). These models showed that, while the aberration coefficients are significantly balanced around zero, due to random biological variability, any given individual is equally likely to have positive or negative aberrations.

The mean SA for the whole population in the current study was 0.06 ± 0.06 µm. Carkeet *et al.* (2002) also reported a positive mean value of Z(4,0) of 0.05 ± 0.04 µm from a group of 217 children (mean age 9.0 ± 0.84 years). In contrast, Kirwan *et al.* (2006) reported a mean negative value of Z(4,0) -0.12 ± 0.13 µm from a group of 82 children (mean age 6.7 years, range 4 to 14 years). Furthermore, they reported that negative SA was found in 84% of the eyes. The discrepancy in results between studies is not clear and could be possibly attributed to differences in corneal asphericity or to crystalline lens characteristics associated with age between the studied samples.

Similar to corneal astigmatism being compensated by lenticular astigmatism (Kelly *et al.* 2004), the positive corneal SA (Atchison and Smith 2000; Artal *et al.* 2001; Kelly *et al.* 2004; Kiely *et al.* 1982; Millodot and Sivak 1979; Smith *et al.* 2001) is compensated by internal negative SA (mainly associated to the crystalline lens) (Artal *et al.* 2001; Artal *et al.* 2006; Campbell and Hughes 1981; Glasser and Campbell 1998; Kelly *et al.* 2004; Roorda and Glasser 2004; Smith *et al.* 2001).

In young eyes, corneal aberrations are larger than ocular aberrations (Artal *et al.* 2001; Smith *et al.* 2001), while the opposite occurs in older eyes (Artal *et al.* 2001; Artal *et al.* 2002A). With age, the lenticular SA becomes less negative (Amano *et al.* 2004; Glasser and Campbell 1998) and the total ocular SA also becomes more positive (Amano *et al.* 2004; Guirao *et al.* 2000).

Furthermore, there are indications that SA is negative in children younger than 6 years of age (Jenkins 1963). It is possible that in the study by Kirwan *et al.* (2006), because of the younger age of the children measured, higher levels of negative internal SA or lower levels of positive corneal SA or a combination of both were present in those children in comparison to children from this study. Further discussions will be conducted in Chapter 5.

4.6.4 SA and SE (M)

A low but significant correlation between Z(4,0) and M was found ($r=0.257$, $p<0.001$). The low correlation was expected because Z(4,0) is primarily associated with corneal asphericity (Atchison and Smith 2000; Kiely *et al.* 1982) and the crystalline lens (Campbell and Hughes 1981; Glasser and Campbell 1998) and not to the AL, which is directly associated with RE. In the current study, the trend between SA and M was not clear; however, it seems to have a slight trend towards more positive values as positive M increases. This was also evident with the correlation of SA RMS and M ($r=0.234$, $p<0.001$).

One possible explanation for this association reflects an indirect association of corneal asphericity with RE. Whilst some studies have reported an association for corneal central curvature with AL and RE (Carney *et al.* 1997; Goss and Erickson 1987; Goss and Jackson 1995; Grosvenor 1988; Grosvenor and Goss 1998; Grosvenor and Scott 1994; Mainstone *et al.* 1998; Sheridan and Douthwaite 1989), other studies did not find an association between central (apical) curvature with RE (Davis *et al.* 2005), corneal asphericity (Carney *et al.* 1997; Davis *et al.* 2005; Mainstone *et al.* 1998) or SA (Kiely *et al.* 1982).

Some studies have observed that, in young myopic eyes, the cornea becomes more oblate with myopia progression (Carney *et al.* 1997; Horner *et al.* 2000), others have not observed significant changes in corneal curvature (Horner *et al.* 2000) or asphericity with myopia progression (Parssinen 1993). Carkeet *et al.* (2002) and Sheridan and Douthwaite (1989) did not find differences in corneal asphericity between RE groups, whilst Mainstone *et al.* (1998) did not find any association of corneal asphericity with hyperopic RE.

If an association of corneal asphericity with RE exists in which, for example, the peripheral cornea suffers changes of steepening to compensate for an increase of anterior chamber depth during the development of myopia, as suggested by Carney *et al.* (1997), then it is possible that such association was present in the children evaluated in the current study. Further longitudinal studies that measured these variables are needed to clarify this statement.

4.6.5 RE Distribution

In this study, the distribution of RE of 12 to 13 year old children, based on the mean M from the right eyes, was 63% hyperopic eyes, 27% emmetropic eyes and 10% myopic eyes. The prevalence rate of myopia found in this study, which was mostly less than 3.00 D in magnitude (78.8%), is similar to that reported in Australia for 12 year old school children: 8.3% (Junghans and Crewther 2003) and 14.7% (Junghans and

Crewther 2005). A similar rate of myopia has been reported in 12 year old children in the USA, 9.2% (Kleinstein *et al.* 2003) and 11.6% (Zadnik *et al.* 2003). Also, the prevalence found in the current study is lower than the rates found in other studies from around the world for a similar age group: Sweden - 39% (Villarreal *et al.* 2000), Mexico - 37% (Villarreal *et al.* 2003), Hong Kong - 20% (Edwards 1999) and Taiwan - 56% (Lin *et al.* 1999) and 36.7% (Lin *et al.* 2004).

A high prevalence of hyperopic eyes was found in this study. Most of the hyperopic cases (97.8%) were in the low range (+0.50 to +3.00 D). Hyperopia is a common RE in Australia, the prevalence of low to moderate hyperopia (0.75 to 1.25 D) in children aged 4 to 12 has been reported to be 32.3% (Junghans and Crewther 2003; Junghans and Crewther 2005). In a cohort of 6 year old children, Ojaimi *et al.* (2005B) reported the prevalence of hyperopia (SE>0.50 D) of 91% and a higher prevalence of hyperopia in children from a white European ethnic background (94.8%) in comparison to children from other ethnic backgrounds (84.1%). This higher prevalence of hyperopia in white children in comparison to other ethnic groups has also been reported in the USA (Kleinstein *et al.* 2003), and Dandona *et al.* (2002A) reported a prevalence of hyperopia of 62.2% in children younger than 15 years in India. In contrast, the prevalence of hyperopia was higher than found in other countries for a similar age group: China - 2.0% (He *et al.* 2004), India: New Delhi - 5.0% (Murthy *et al.* 2002) and Andhra Pradesh - 0.77% (Dandona *et al.* 2002B), Chile - 16.3% (Maul *et al.* 2000) and South Africa - 3.2% (Naidoo *et al.* 2003).

The reason for the low prevalence of myopia and high prevalence of hyperopia found in the current study is not clear. It could be attributed to several factors such as nutrition, environment, education, ethnicity or life style. The studied sample was obtained from diverse suburbs of the Sydney Metropolitan area which represent various socio-economic and ethnic strata samples. Such factors and their association with RE are being studied in the Sydney Myopia Study and, therefore, they will not be explored further in this thesis.

A higher proportion of females were myopic (11.2%) in comparison to males (9.0%). Myopic females were also on average -0.50 D higher myopic M than males (p=0.042). Females have been reported to have higher rates and degrees of myopia than males (Fan *et al.* 2004A; He *et al.* 2004; Lin *et al.* 1999; Villarreal *et al.* 2003; Zhao *et al.* 2002), while others have found an association of hyperopia with the female gender (Dandona *et al.* 2002A; Murthy *et al.* 2002; Naidoo *et al.* 2003) or no difference between gender as myopia progresses in young school children (Zadnik *et al.* 2003). The difference found in the current study could be indicative of a different myopisation process in females than in males, or perhaps a faster growth rate in females than in males who are already myopic. No further differences in age or gender were found between groups.

4.6.6 Monochromatic Aberrations and RE

In order to identify if the three RE groups had different patterns or higher levels of aberrations which could contribute to the progression of RE, the result of creating an increase of chronic blur other than defocus, individual lower and HOAs and their respective RMS were analysed between RE groups and subgroups.

From the 2nd orders, defocus Z(2,0) and defocus RMS showed the expected differences between RE groups as defocus is directly related to the mean M. Therefore no further analyses were conducted. The astigmatic modes Z(2,-2) and Z(2,2) did not present differences between any RE groups, however, when astigmatism RMS was analysed, higher levels were found in the myopic and moderate to high hyperopic groups while lower levels of astigmatism RMS were found in the low hyperopic and emmetropic groups. Carkeet *et al.* (2002) found a small difference in Z(2,2) between high myopes to low myopes and to emmetropes in a group of 9.0 ± 0.84 year olds, while other studies in children, as well as 5 to 7 week old infants did not report any difference (He *et al.* 2002; Kirwan *et al.* 2006; Martinez *et al.* 2006; Wang and Candy 2005). It is interesting to note that in the study of Wang and Candy (2005), the authors found similar levels of Z(2,-2) and Z(2,2) in infants as in adults. During infancy, it is expected to have higher levels of corneal astigmatism which rapidly decreases in the first months of life and then slowly changes during childhood (Ehrlich *et al.* 1997; Gwiazda *et al.* 1993A; Howland and Sayles 1985; Mayer *et al.* 2001; York and Mandell 1969). It is possible that the analysis of the aberrations based on a PD of 3 mm, or an error in the scaling factor that Wang and Candy used, may explain this discrepancy.

The role of astigmatism with the development of RE has been reported. Some studies have found an association of infantile astigmatism and development of myopia, especially in cases with higher astigmatism (Fan *et al.* 2004B), oblique astigmatism (Fulton *et al.* 1982) and with “against-the-rule” astigmatism (Hirsch 1964; Gwiazda *et al.* 1993A; Gwiazda *et al.* 2000). A positive correlation between astigmatism and hyperopic RE in a group of Navajo school children has also been reported (Garber 1985). However Parssinen (1991) found no correlation of astigmatism and myopic RE in children after a 3 year follow up. In the current study, such differences of astigmatism within RE groups could not be assessed due to the exclusion criteria of cases with cylinders ≥1.00 D, thus, limiting the amount of refractive astigmatism (J_0 and J_{45}) in all RE groups.

Of the HOAs, as shown in subsection 4.5.3.1., 5th and 6th order aberrations had a small contribution to the total wavefront variance. Therefore, the analysis of differences in HOs between RE groups was limited to 3rd and 4th orders only, with the exception of HO RMS, which incorporated terms from the 3rd to the 6th orders.

Of the 3rd orders, it was found that myopic eyes had higher positive levels of vertical coma Z(3,-1) and horizontal coma (Z(3,1) than emmetropes and hyperopes. The difference was more evident between the high myopic eyes than the emmetropic and hyperopic eyes. Myopes (especially low myopes) had slightly higher levels of coma RMS than hyperopes (low hyperopes) but no other difference was found between the other groups. These results are in agreement with those from Kirwan *et al.* (2006) who found higher levels of Z(3,-3), Z(3,-1) and Z(3,3) in myopes than in emmetropes, however, no other study has reported such differences in coma terms between RE groups (Carkeet *et al.* 2002; Collins *et al.* 1995; Cheng *et al.* 2003B).

Coma aberrations play a dominant role in reducing retinal image quality at all pupil sizes (Howland and Howland 1977), they increase with age (Amano *et al.* 2004; Brunette *et al.* 2003), they present a variable change with accommodation (Atchison *et al.* 1995; Cheng *et al.* 2004B; He *et al.* 2000) although they seem to not provide an odd-error cue to focus direction (Wilson *et al.* 2002; Lopez-Gil *et al.* 2007) and, together with SA, they are the most common type of aberrations found in myopes (Paquin *et al.* 2002). However, the importance of coma aberrations in the development of RE is not clear. In the current study, a large variability was seen for these aberrations for all RE groups. Coma aberrations are mainly the result of the interaction of decentration and tilt of the optical elements of the eye, i.e. the cornea, lens and pupil (Artal *et al.* 2001; Artal *et al.* 2006). A large amount of lateral corneal coma (51%) (Kelly *et al.* 2004), is cancelled by the internal optics of the eye (Artal *et al.* 2001). The compensation of corneal lateral coma by the lens depends linearly on the ϰ angle (kappa angle) (Artal *et al.* 2006), which is the angle formed by the pupillary axis and the line of sight (Atchison and Smith 2000). Because of the normal geometrical features of the hyperopic eye (shorter AL, larger ϰ angle) that lead to larger pupil decentration, hyperopic eyes compensate remarkably more lateral coma than myopic eyes (myopic eyes have longer ALs, and smaller ϰ angles) (Artal *et al.* 2006).

In the current study, a difference in lateral coma Z(3,1) was not found but it was evident that the myopic groups had more positive levels of vertical coma Z(3,-1) than emmetropes and hyperopes. The difference in coma between the three RE groups, as the result of their normal geometrical features, supports the presence of a passive mechanism of eye growth and aberrations compensations (genetically programmed) and not visually guided (active mechanism) (Artal *et al.* 2006; Kelly *et al.* 2004).

4.6.7 SA and RE

In the 4th orders, emmetropes had slightly more negative values (-0.01 ± 0.02 μm) of Z(4,-2) than hyperopes (0.00 ± 0.03 μm). While this difference was statistically significant (p=0.01), the mean values of Z(4,-2) were very close to zero to be of any significance to the differences in optical quality between the two groups. The only coefficient from the 4th orders that showed significant differences was SA Z(4,0).

Hyperopes had higher levels of positive SA (0.07 ± 0.06 μm) than emmetropes (0.04 ± 0.05 μm) and myopes (0.04 ± 0.05 μm). This difference was significant between hyperopes and the other two groups ($p<0.001$). The same difference occurred between RE subgroups, with the moderate to high hyperopes having the highest levels of positive SA (0.11 + 0.06 μm) compared to emmetropes, and low and moderate to high myopic subgroups ($p<0.001$). Moderate to high myopes had the lowest levels of positive SA from the sample (0.03 ± 0.06 μm).

There are inconsistencies in the literature as to whether differences exist in SA between RE groups and the effect of those differences in RE development. While some studies have found no difference between myopes and non-myopes (Cheng *et al.* 2003B; He *et al.* 2005; Kirwan *et al.* 2006), others have reported small differences: less SA in low myopes than high myopes or emmetropes (Carkeet *et al.* 2002), less levels of positive longitudinal spherical aberration (LSA) in myopes than in emmetropes (Collins *et al.* 1995) or slightly higher levels of SA in low myopes than emmetropes (Paquin *et al.* 2002). Finally, some studies have reported higher levels of positive SA in myopes than non-myopes (Radhakrishnan *et al.* 2004B), higher positive SA in hyperopes than in myopes (Llorente *et al.* 2004) and higher levels of 4th orders RMS in myopic adults than in emmetropic adults (He *et al.* 2002).

The results found in the current study are similar to those from Carkeet *et al.* (2002), Llorente *et al.* (2004) and Collins *et al.* (1995) with the hyperopic groups showing higher levels of positive SA and SA RMS than the emmetropic and myopic groups and no difference between the myopic and emmetropic groups. It has to be noted that the sample included in the current study is the largest ever reported in children.

The higher levels of positive SA found in myopes (0.40 ± 0.58 μm) in comparison to non-myopes (0.06 ± 0.23 μm) by Radhakrishnan *et al.* (2004B) could have been the result of the small sample size and also due to the fact that most of the myopic subjects included in their study (8 of the 12) had myopia levels >-3.00 D. In the current study, the mean SA found in the myopic subjects was only 10% of that reported from Radhakrishnan *et al.* (2004B). The differences between the data of the present study and that reported by He *et al.* (2002) could have been the result of a different method used to measure aberrations (psychophysical ray-tracing wavefront sensor; He *et al.* 2002) or the inclusion of two different samples (one from the USA and the other from China). Interestingly in another experiment involving different subjects, He *et al.* (2005) did not find differences in the amount of aberrations between myopes and emmetropes.

There is great interest in the field of myopia research to identify if HOAs contribute to the myopisation process in children through image degradation caused by high levels of these aberrations. Animal studies have provided evidence that support the concept of an active emmetropisation mechanism and development of RE (Wildsoet 1997; Wallman and Winawer 2004). Of all the HOAs, SA has been more widely studied because of the role it plays in the accommodative function and potentially in the development of myopia.

SA reduces the effect of defocus in large pupils and increases the depth of focus. In the case of positive blur, SA increases relative to the modulation transfer function for spatial frequencies of 4cd and over (especially at 0.5 and 1.0 D blur) and with negative blur, SA increases the relative modulation transfer function much more (Jansonius and Kooijman 1998). Lead and lag of accommodation have been found to be influenced by

HOAs (SAs and others), generating greater tolerance to induced defocus blur because of the higher depth of focus (Collins *et al.* 2006).

The direct effect that depth of focus has in the eye is to increase the lag of accommodation (lower accommodative response to the accommodative stimulus). Myopic eyes have larger depth of focus (Collins *et al.* 2006) and greater lags of accommodation than emmetropes (Gwiazda *et al.* 1993B; He *et al.* 2005). Myopes are less sensitive to blur (Rosenfield and Abraham-Cohen 1999), experience less acuity loss with negative lenses compared with positive lenses, with the magnitude of visual acuity loss being lower than that experienced by emmetropes (Radhakrishnan *et al.* 2004A). Myopic eyes accommodate less with negative lens-induced blur than positive lens-induced blur (Gwiazda *et al.* 1993B) and have less contrast sensitivity loss with negative defocus than with positive defocus, while non-myopic eyes experience the same reduction in contrast sensitivity to both conditions (Radhakrishnan *et al.* 2004B). Because of reduced accommodation, myopic children have been found to have elevated accommodative convergence / accommodation ratios (Gwiazda *et al.* 1999; Gwiazda *et al.* 2005), though this reduction of accommodation has not been found to be a risk factor of myopia development in emmetropic children (Gwiazda *et al.* 1995).

Mathematical models predict that a combination of poor accommodative function, high accommodative convergence / accommodation ratios, together with a decrease in illumination and increasing near work will cause myopia and the prescription of negative lenses under these conditions increments the progression of myopia (Blackie and Howland 1999; Flitcroft 1998). Gwiazda *et al.* (2005) reported that a group of emmetropic children who became myopic compared to those who remained emmetropic, presented elevated accommodative convergence / accommodation ratios at 1 and 2 years before the onset of myopia, and also the time of myopia onset and 1 year later. It was reported that the accommodative convergence / accommodation ratios in the children who became myopic were the result of significantly reduced accommodation. Furthermore, Mutti *et al.* (2000A), supported by findings of lens thinning in children (Mutti *et al.* 1998; Zadnik *et al.* 1995), suggested that the elevated accommodative convergence / accommodation ratios experienced in myopes could be the result of a pseudo-cycloplegic effect of a stretched lens (flat lens) caused by equatorial growth of the eye as a mechanism of reducing the lens power as the eye grows to maintain emmetropia.

Therefore, it could be hypothesised with higher levels of SA in myopes than in emmetropes, the accommodative lag increases contributing to the myopisation process. To date, only one study (He *et al.* 2005) has measured the association of wavefront and accommodative lag in myopes in comparison to emmetropes. The authors reported larger accommodative lag in myopes than in emmetropes for lens-induced and distance-induced examinations. Myopes also had smaller Strehl ratios (visual quality) than emmetropes ($p=0.055$). For similar levels of Strehl ratio, myopes exhibited higher accommodative lag than emmetropes, with Strehl ratio and accommodative lag presenting a significant correlation for myopes only (-0.45, $p<0.02$). The most interesting finding from the He *et al.* (2005) study was the correlation of greater lag of accommodation and reduced retinal image quality in myopic eyes but not in emmetropic eyes. Emmetropes could accommodate accurately, even with reduced retinal image quality, while myopes with similar levels of aberrations could not. This could indicate that, despite similar levels of SA being present in myopic and emmetropic eyes, the accommodative system of the myopic eye will be more affected than the emmetropic eye, thus, ruling out the possibility of an influence in the accommodative lag by the amount of SA.

The apparent lack of influence of SA in accommodative lag found in He *et al.* (2005) could be explained by geometrical models which predict that, even when SA changes towards more negative values with accommodation, the effect of SA on accommodation (increasing the lag) can be reduced by pupil miosis during accommodation (Charman 1999). More experiments are needed to confirm the role of SA on accommodation including larger samples. In Radhakrishnan *et al.* (2004B), the higher mean SA found in the myopic subjects could be the result of the high myopia or less prolate corneal shape that most of the subjects in that study had and might not be representative of the population. Also, the less sensitivity that myopes experience to blur, partially explaining why myopes have larger lags of accommodation, might not be associated to levels of SA. In Rosenfield and Abraham-Cohen (1999) the sensitivity to blur of the subject was measured through a 2 mm artificial pupil. This diameter is very close to the critical PD (0.76 mm - Thibos *et al.* 2002C; to 2.8 mm - Howland and Howland 1977), which is the largest PD considered diffraction-limited (where the wavefront RMS from a perfect sphero-cylinder is less than $\lambda/4$ and is also known as the Marechal's criterion) (Howland and Howland 1977). Some studies report critical PDs as large as 4 mm when there is a balance between defocus and SA (Thibos *et al.* 2002C).

In the current study, no difference in SA levels between myopic and emmetropic eyes was found. However, hyperopic eyes presented higher levels of positive SA and SA RMS than emmetropic and myopic eyes. These results could possibly be explained on the basis of the anatomical characteristics of the eyes such as corneal asphericity with different RE as discussed in subsection 4.6.4. Corneas that flatten less rapidly in the periphery (more spherical) have higher levels of positive SA than prolate corneas. Two studies have found the cornea to have a tendency for a less prolate shape with increasing amounts of myopic error (Carney *et al.* 1997; Horner *et al.* 2000). Davis *et al.* (2005), found myopic corneas in children were significantly less prolate in shape than those from emmetropic or hyperopic children. Carkeet *et al.* (2002) found no difference in corneal asphericity (Q) between RE groups in Singaporean children and Mainstone *et al.* (1998) did not find any association of corneal asphericity with hyperopic RE. Llorente *et al.* (2004) researched a group of adults (23 to 40 years) and found hyperopes had less prolate corneas than myopes but the differences were not significant ($p>0.5$). They also reported that myopes ($n=24$) and hyperopes ($n=22$) aged 23 to 40 years old, presented higher levels of positive total and corneal SA and both presented similar levels of internal aberrations.

It is possible that hyperopes in this sample had less prolate corneas than the other two groups while myopes and emmetropes had similar corneal shape and, as a result, hyperopic eyes presented higher levels of positive SA. Because a high proportion of myopic eyes found in this study (83%) had low levels of myopia (≥-3.00 D), it is possible that their corneas had not changed into a less prolate corneal shape yet as has been reported in older children or adults with higher levels of myopia (Carney *et al.* 1997; Horner *et al.* 2000). Perhaps there was no difference in corneal asphericity and corneal SA in the different RE groups at this age, and it is possible that the differences in SA were due to differences in internal aberrations, with hyperopes presenting lower levels of compensatory negative SA than the other RE groups.

At close inspection of the data, it was also noted that a small number of cases from the three RE groups presented negative SA, and that all RE subgroups, except moderate to high hyperopes, had a number of cases presenting negative SA. As previously discussed, possible explanations for eyes with higher negative SA are that they were the result of corneas with over-corrected (neutral or negative) SA due to higher Q values (more prolate shape) (Atchison and Smith 2000; Kiely *et al.* 1982), higher lenticular negative SA due to different gradient lenticular refractive index (Campbell and Hughes 1981), or that they were still exerting some amount of residual accommodation during measurement which increased the levels of negative SA (Artal *et al.* 2002B; Atchison *et al.* 1995; Cheng *et al.* 2004B; Glasser and Campbell 1998; He *et al.* 2003; Ninomiya *et al.* 2002).

Unfortunately in the Sydney Myopia Study, the measurement of the physical characteristics of both the cornea and crystalline lens were not including in the protocol, therefore, corneal asphericity, corneal aberrations, lens thickness and lens power could not be calculated, thus, limiting the conclusions that could be drawn from this study. On the other hand, the possibility that they were not completely cyclopleged is remote, because careful attention was paid during the drops protocol to observe full cycloplegic effect before the measurement of the ocular aberrations as described in subsection 3.1.1.2. To evaluate if negative SA in children is associated with age, a comparison of the distribution of negative SA of children from the present study with a younger cohort of children (mostly 6 year olds) will be conducted in Chapter 5.

4.6.8 Monochromatic Aberrations and Ethnicity

In order to determine the effect that ethnicity could have in the distribution and pattern of the ocular aberrations in the children examined in the current study, children were classified by the ethnicity of the biological parents obtained via questionnaires. Analyses of RE and ocular aberrations were conducted for children from Caucasian, East Asian, Indian / Pakistani / Sri Lankan and Middle Eastern ethnicity, which represented 64% of the whole study population. Of the four groups, Caucasian and Middle Eastern children presented with more leptokurtic and more hyperopic distribution of M, while East Asian and Indian / Pakistani / Sri Lankan children presented with a more negatively-skewed and more myopic distribution. While the East Asian children had significantly higher levels of mean J_0 and Caucasian children had lowest levels of the four groups, none of these differences were clinically significant, with the four groups showing a similar distribution of the astigmatic vector.

4.6.8.1 Distribution of LOAs and HOAs

As a consequence of the differences in distribution of the mean M between the four ethnic groups, differences in Z(2,0) were present between the two more hyperopic ethnic groups (Caucasian and Middle Eastern) and the two more myopic ethnic groups (East Asian, Indian / Pakistani / Sri Lankan). Also, similar characteristics, as for the general population, were observed in the distribution of the HOAs, with Z(4,0) presenting with the largest mean value (always positive) and 3rd order presenting with the largest variability. Coefficients from the 5th and 6th orders had small mean values near zero and, while some differences were found between ethnic groups, the magnitude of these coefficients was too small to affect the vision and, thus, were not further analysed.

When inter-race comparisons were performed for individual coefficients from the 3rd and 4th orders, the four groups had different mean levels of vertical coma Z(3,-1). East Asian children had higher positive mean levels of Z(3,-1) (0.03 ± 0.11 μm) than the other three groups. Similarly, Caucasian children had higher mean levels of horizontal trefoil Z(3,3) than the other groups except East Asians. Interestingly, Carkeet *et al.* (2002) also found higher levels of Z(3,-1) in Chinese children (0.07 ± 0.01 μm) than in Malay children (0.01 ± 0.01 μm). The authors could not find an explanation for this difference and suggested that small perturbations of the ocular surfaces or tear layer could have caused the difference. It is possible that as in Carkeet *et al.*'s study, such small disturbances of the ocular surfaces could have occurred and accounted for the differences found in the 3rd order terms, or that the differences were caused by the inter-racial difference in distribution of the mean M.

In the 4th orders, small inter-race differences were found for oblique quatrefoil Z(4,-4) and quatrefoil Z(4,4). The magnitude of these differences was too small to reveal any evident cause that could explain their origin. An interesting finding was that no difference existed in the mean SA Z(4,0) between the four ethnic groups regardless of the differences in distribution of the mean M. Only East Asian children had higher levels of positive SA than the other groups but this difference was not significant.

4.6.8.2 Inter-race Differences of RE and Aberrations

As described in subsection 4.7, the more prevalent RE was hyperopia (63%) followed by emmetropia (27%) and myopia (10%). However when the analysis of distribution of RE was performed within the four main ethnic groups, large differences were observed. East Asian children had the largest prevalence of myopia (31%) followed by Indian / Pakistani / Sri Lankan children (27%), while Caucasian children were predominantly hyperopic (73%) followed by Middle Eastern children (64%). Furthermore a large proportion of East Asian children (38%) and Indian / Pakistani / Sri Lankan children (37%) were emmetropic.

The high proportion of East Asian and Indian / Pakistani / Sri Lankan myopic children found in this study was lower than that reported in other Asian countries for a similar age group: China - 50% (He *et al.* 2004), Hong Kong - 54% (Fan *et al.* 2004C) and 55% (Edwards 1999), Taiwan - 56% (Lin *et al.* 1999), India: New Delhi - 10% (Murthy *et al.* 2002) and Andhra Pradesh - 5% (Dandona *et al.* 2002B) and higher than that reported in Australia - 8% (Junghans and Crewther 2003) and 15% (Junghans and Crewther 2005). When the mean M of the different RE groups was compared, East Asian children had higher levels of myopia (-2.42 ± 1.60 D, range -0.52 to -8.58 D) than the other three groups, while Caucasian children presented higher levels of hyperopia (1.15 ± 0.74 D, range 0.50 to 7.29 D) than the other three groups.

Almost 26% of the myopic East Asian children had myopia higher than -3.00 D, while only 8.5% of the myopic Caucasian children had myopia higher than -3.00 D. Moderate to high hyperopia was not present in East Asian, Indian / Pakistani / Sri Lankan and Middle Eastern children but it was present in 2.2% of Caucasian children. Such large inter-racial differences in the distribution of RE can be indicative of a nurture effect in RE development, or a combination of both nurture and nature effects. The interaction of such effects into the development of myopia are currently being analysed by the Sydney Myopia Study and will not be discussed in this thesis.

Analyses of LOAs and HOAs between RE groups within each main ethnic group were conducted, excluding moderate to high myopic and moderate to high hyperopic cases. This approach was undertaken as not all four ethnic groups had cases in those RE groups and, therefore, comparisons were made between low myopes, emmetropes and low hyperopes. For the LOs, as expected, differences were seen for Z(2,0), defocus RMS and total RMS between the three RE groups within the four ethnic groups. For the astigmatic terms, only myopic Caucasian and Middle Eastern children had higher positive levels of Z(2,2) than emmetropes and hyperopes. This indicated that myopic children had significantly more "against-the-rule" astigmatism than emmetropes and hyperopes. Previous studies have shown that "against-the-rule" astigmatism in infants (Gwiazda *et al.* 1993A) and in young children (5 to 6 years) (Hirsch 1964) is predictive of later development of myopia. Furthermore, infantile astigmatism has been suggested (Gwiazda *et al.* 2000) to disrupt the emmetropisation process and induce myopia by reducing the sensitivity to focusing cues. From the data collected in the present study, we are unable to determine if the myopic RE in these children will progress more rapidly or if these children had "against-the-rule" astigmatism since infancy. Similarly, we were unable to determine the structural origin of this "against-the-rule" in these children. The axis of corneal astigmatism in children is mostly "with-the-rule" and the internal "against-the-rule" astigmatism (Gwiazda *et al.* 2000; Huynh *et* *al.* 2006A). It is possible that these children have higher levels of internal astigmatism and, therefore, fail to compensate (overcompensating) for the corneal astigmatism (Kelly *et al.* 2004). Measurements of corneal and internal astigmatism could have revealed if this was the case.

Hyperopic eyes presented with higher levels of positive aberration Z(4,0) than myopic and emmetropic eyes in the four ethnic groups, although the difference was not always significant. Caucasian hyperopes had higher levels of Z(4,0) and SA RMS than emmetropes and myopes; East Asian and Middle Eastern hyperopes had higher levels of Z(4,0) and SA RMS than myopes only; Indian / Pakistani / Sri Lankan hyperopes had higher levels of Z(4,0) than emmetropes only. While myopic cases in the four ethnic groups presented some variation in the mean levels of Z(4,0) and SA RMS, no difference was found between myopes and emmetropes for any ethnic group, thus, ruling out the hypothesis of myopic eyes having higher levels of SA within different ethnic groups.

An interesting finding from visual inspection, as shown in Figure 4.29, was that, despite the similarities in the mean M of the RE groups, the mean values of Z(4,0) of the myopic, emmetropic and hyperopic groups in East Asian children were higher than those from the other three ethnic groups with the exception of the Indian / Pakistani / Sri Lankan myopic group.

When comparisons of the HO RMS between ethnic groups were made, differences were found only between the low hyperopic groups with East Asian children having significantly higher SA RMS and HO RMS than low hyperopic Caucasian and Middle Eastern children.

The explanation for these differences is not clear. It is possible that there are structural or ocular growth inter-race differences which reveal hyperopic East Asian children have higher levels of some HOAs. It is possible that the visual system of the hyperopic East Asian eye is more aberrated than in other ethnic groups. However, it is also possible that the visual cortical system of the East Asian eye is less sensitive to the higher levels of aberrations and not necessarily affected by the less optimal image quality that the optical system provides. A longitudinal study involving the same children examined in the current study could explain if such differences are just the result of the cross-sectional nature of the study. Also, comparisons with other populations of younger or older East Asian and Caucasian children would possibly determine if hyperopic East Asian eyes actually have higher levels of SAs or HOs than other ethnic groups. Importantly, no association of ethnicity and HOA RMS was found in the low myopic or emmetropic groups, suggesting that, therefore, factors other than monochromatic aberrations possibly contribute to the inter-racial differences found for the prevalence of myopia. As mentioned in subsection 4.6.7, the physical characteristics of the cornea and crystalline lens could not be measured in the current study, therefore, limiting the conclusions that can be made. Further studies which assess ocular aberrations should include these measurements in order to identify the structural origin of differences in ocular aberrations when considering ethnicity.

4.7 SUMMARY

In summary, in a group of 12 year old children, monochromatic aberrations (low and HOs) were normally distributed, with only a few coefficients not distributed near zero. A high correlation between right and left eyes were found for defocus, SA and horizontal / vertical astigmatism. Moderate correlations existed between terms of the 3rd order and Z(2,-2). Significant but low correlations were found for modes from 4th and 5th orders. The moderate correlation of aberrations found between eyes supports the presence of an active binocular coordinated mechanism of eye growth which involves the cornea, lens and AL but does not support the existence of perfect enantiomorphism for odd modes in 3rd, 4th and higher modes.

From the total variance of the wavefront, LOAs had the greatest contribution, with small contributions from aberrations beyond 4th orders, thus, ruling out the possibility of HOAs affecting image quality of the eye. A high variance was found for individual coefficients, especially in the 3rd and 4th orders.

Coma aberrations had the greatest variability and, from the HOAs, SA had the greatest magnitude and in most cases it had a positive value.

These results are in agreement with reports in the literature where HOAs were not found to be excessive with myopia.

The mean levels of HOAs obtained were lower than those reported from adults. Further longitudinal studies are needed to evaluate the changes that monochromatic aberrations suffer during childhood and identify if these changes are related specifically to corneal shape or internal optics changes.

East Asian children have more myopia, however, no differences were found for any of the HOAs between groups. While the results obtained in this study indicate that low hyperopic eyes of children from East Asian background were slightly more aberrated than low hyperopic eyes of Caucasian or Middle Eastern children, the effect of the elevated levels of aberrations in RE do not seem to be significant.

CHAPTER 5: COMPARISON OF THE PROFILE OF ON-AXIS ABERRATIONS BETWEEN 6 AND 12 YEAR OLD CHILDREN

5.1 INTRODUCTION

Chapter 4 detailed the distribution and characteristics of the ocular monochromatic aberrations and the relationship with RE and ethnicity as determined in a cohort of 1,636 children with ages ranging from 11 to 14 years of age (mean age 12.7 years).

Some differences in the distribution and levels of SA with RE were found when comparing the results obtained in Chapter 4 with those of other studies that have measured monochromatic ocular aberrations in children (Carkeet *et al.* 2002; Kirwan *et al.* 2006). The reason for the discrepancy in results between studies is not clear, however, possible explanations could be the difference in instruments and cycloplegic or PDs used for calculation of aberrations in the studies. Nevertheless, the difference in ages between the study samples seems to be a more reasonable explanation for the differences observed. Positive correlations of ocular coma-like and SAs with age have been reported in adults (Amano *et al.* 2004; Fujikado *et al.* 2004; McLellan *et al.* 2001). Also the relationship between monochromatic aberrations and age follows a quadratic model (Brunette *et al.* 2003) in which aberrations decrease progressively during childhood, adolescence and young adulthood. In late adulthood, aberrations increase again mainly due to changes in the internal optics of the eye (Amano *et al.* 2004; Artal *et al.* 2002A; Guirao *et al.* 1999) and at a lower level, due to the changes in corneal shape (Guirao *et al.* 2000).

These ocular changes could partially explain the lower levels of positive SA found in 5 to 7 week old infants in comparison to adults (Wang and Candy 2005), the high prevalence of negative SA reported in children younger than 6 years of age (Jenkins 1963), the higher levels of total aberrations found in emmetropic children in comparison to emmetropic adults (He *et al.* 2002) and the higher prevalence of children with negative SA (Kirwan *et al.* 2006). Despite the low magnitude that HOAs seem to have in human eyes, there is a great interest in the role that these HOAs might play in RE development. In particular, SA has been more widely studied because of the potential role it plays in the accommodative function and also because it can potentially control the development of REs (Collins and Wildsoet 2000).

Therefore, in order to determine if age is associated with a variation in the levels of monochromatic aberrations in children; the values of ocular monochromatic aberrations, in particular SA, obtained from a cohort of younger children (mostly 6 year old children) also examined at the Sydney Myopia Study were compared to the cohort of 12 year old children described in Chapter 4.

5.2 AIMS

To determine if there were any differences in the on-axis ocular aberration profiles between two different age groups of children (mostly 6 and 12 year old children).

5.3 METHODS

5.3.1 Subjects

On-axis ocular aberrations data obtained from both eyes of 1,436 children in the first grade of school (mostly 6 year olds) in the Sydney Myopia Study (Pandian 2007) were included in this analysis and compared to the on-axis aberration profile of the 12 year old children described in Chapter 4. Data for the 6 year old group was collected in exactly the same way as date for the 12 year old group and is described in Chapter 3.

5.3.2 Aberrations and RE Measurements

On-axis ocular aberrations and RE were measured and analysed in the 6 year old group using the same methods used for the cohort of 12 year old group as described in Chapter 4, subsections 4.3.2 and 4.3.3. Analysis of aberrations and RE groups was also limited to eyes with astigmatism <1.00 D.

In addition, to determine the contribution of individual Zernike coefficients and Zernike orders to the overall wavefront of the 6 and 12 year old groups, averages and percentage contributions of absolute Zernike coefficients and absolute Zernike orders RMS were calculated using the method described by Ramamirtham *et al.* (2006).

For individual Zernike coefficients:

1. Obtain the absolute values of each coefficient from the 2nd to the 6th orders.
2. Obtain the mean value of each coefficient for all subjects.
3. Add the mean values of all the coefficients to obtain the total absolute wavefront.

4. Obtain individual percentage values for each coefficient from the total wavefront.

For Zernike orders RMS:

1. Calculate the RMS for each order (2nd, 3rd, 4th, 5th and 6th) from the absolute Zernike coefficients.
2. Obtain the mean value for each order from all subjects.
3. Add the mean values of all orders RMS's to obtain the total absolute RMS.
4. Obtain individual percentage values of each order from the total absolute RMS.

To determine the distribution of primary SA in the different RE groups, eyes were assigned into three groups (negative, neutral and positive SA) where:

- Negative SA: Z(4,0) < 0.00 µm
- Neutral SA: Z(4,0) = 0.00 µm
- Positive SA: Z(4,0) > 0.00 µm

In order to determine the magnitude of Z(4,0) in terms of dioptres, SA was converted to LSA using the following equation (Carkeet *et al.* 2002):

$$LSA(D) = Z_4^0 \frac{24\sqrt{5}}{(y_{\max})^2}$$ **Equation 5. 5**

where Z(4,0) is in microns and $y_{\max}$ is the maximum pupil radius in mm.

5.4 DATA ANALYSIS

Biometric data such as age, power vectors, and Zernike coefficients were normally distributed and analysed using parametric tests in the 6 year old group. The statistical tests used to test for normality included the Kolmogorov-Smirnov and Shapiro-Wilk statistics with Lilliefors significance of $p < 0.05$ and by examination of boxplots.

The relationship between power vectors and Zernike coefficients between right and left eyes of the 6 year old group was examined using Pearson's bivariate correlation. Independent samples *t*-test was used to test for differences in power vectors within RE groups between age groups.

To analyse whether differences in LO and HO RMS within RE groups existed between age groups, multivariate-adjusted analyses of variance were performed. Defocus, astigmatism, coma, trefoil, SA, quatrefoil, secondary astigmatism, HOs and total aberrations RMS were the dependent variables and significance levels were calculated using Pillai's trace. Adjusted-multiple comparisons Bonferroni test was used to test for differences within RE groups between age groups.

The level of significance for all statistical analyses was set at $p<0.05$. Statistical analyses were performed using SPSS 14.0 Statistical Software (SPSS, Inc, Chicago, IL, USA).

5.5 RESULTS

5.5.1 Biometric Data of 6 Year Old Group

Whilst a total of 1,436 6 year old children were measured, only the data for 1,364 children met the inclusion criteria and were considered for this analysis. The mean age of the 6 year old group was 6.7 ± 0.4 years with a range from 5.5 to 8.8 years. Seven hundred and six (706; 51.8%) children were males with a mean age of 6.7 ± 0.4 years while 658 children were females with a mean age of 6.6 ± 0.4 years. The mean difference in age between the genders was statistically significant (Independent samples *t*-test, $p<0.001$). The mean refractive components in power vectors for both the right and left eyes and the Pearson's correlation coefficient are presented in Table 5.1.

Table 5.1: ***Correlation of refractive components between right and left eyes (n=1,364, 6 year old children)***

Refractive Component	Right Eye Mean ± SD (D)	Left Eye Mean ± SD (D)	Pearson Correlation (r)	p-Value (Two-tailed)
M	1.12 ± 0.72	1.14 ± 0.75	0.89	<0.001
J_0	0.06 ± 0.16	0.08 ± 0.16	0.70	<0.001
J_{45}	0.01 ± 0.10	-0.03 ± 0.10	-0.33	<0.001

A very strong correlation of M was found between right and left eyes (r=0.89). Of the cylindrical components, a high correlation for J_0 (r=0.70) and a low inverse correlation for J_{45} (r=-0.33) were found. RE in this sample of children based on M from the right eye (Figure 5.1) presented a leptokurtic distribution (Kurtosis 4.817) and was predominately hyperopic (Skewness 0.272) with a range from -3.34 to 5.25 D.

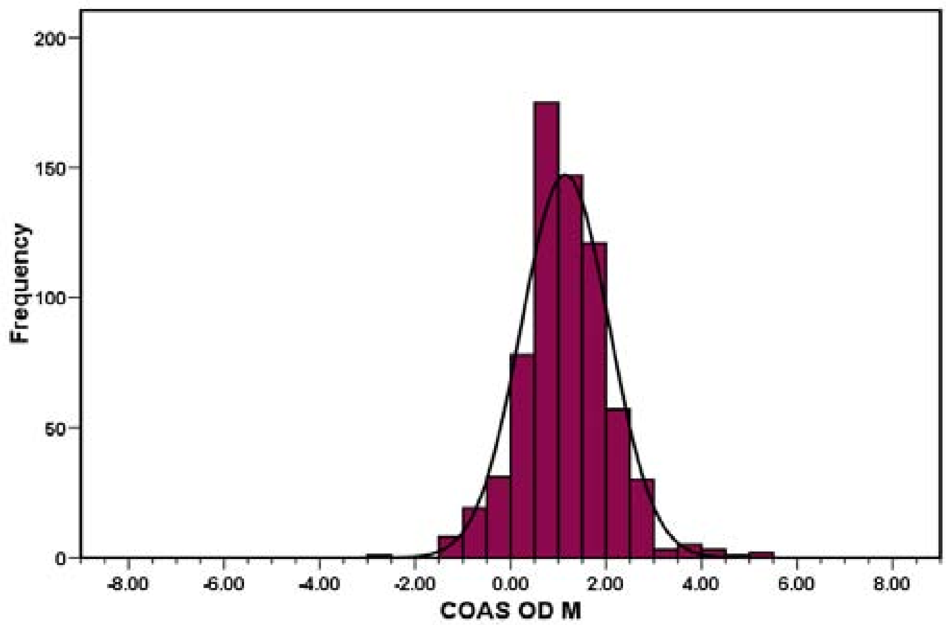

Figure 5.1*: Distribution of SE (M) in dioptres from right eyes of 1,364 6 year old children*

As seen in Figure 5.2, the distribution of the astigmatic component (J_0, J_{45}) from the right eyes of the 1,364 6 year old children was around ±0.50 D with the majority clustered around zero and a slight predominance of "with-the-rule" astigmatism.

When comparing the mean refractive components of the right eyes between this cohort of children and the cohort of 12 year old children described in Chapter 4 (Table 4.4), it was seen that this cohort was, on average, 0.60 D more hyperopic (independent samples *t*-test, $p<0.001$). The differences in the astigmatic components between cohorts were less than 0.05 D but reached statistical significance (independent samples *t*-test, $p<0.001$, for both J_0 and J_{45}). The mean J_0 astigmatism in the 6 year old cohort was slightly higher (0.03 D) than in the 12 year old cohort, whilst the mean J_{45} astigmatism in the 6 year old cohort was 0.02 D lower than in the 12 year old cohort.

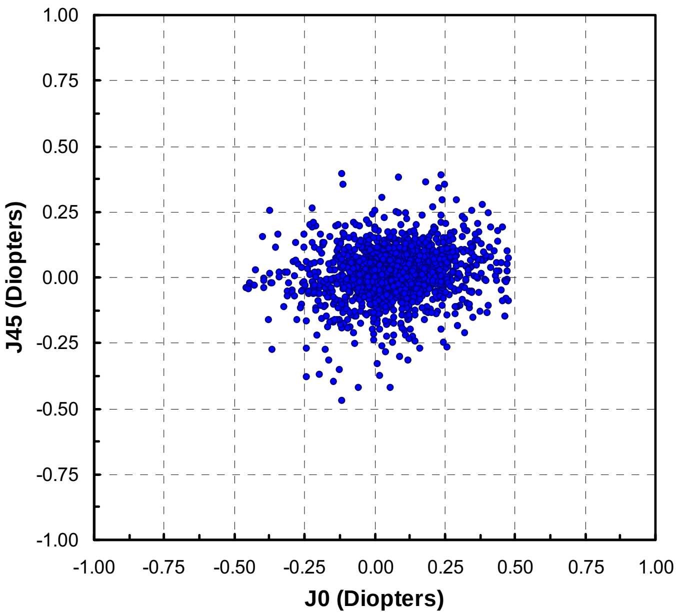

Figure 5.2: ***Distribution of astigmatism (J_0, J_{45}) in Cartesian form of the right eyes of 1,364 6 year old children***

5.5.2 Correlation of Ocular Aberrations Between Right and Left Eyes in 6 Year Old Children

The results of the Pearson's correlation for the Zernike coefficients from 2nd to 6th order are presented in Table 5.2. To compensate for the enantiomorphism effect (Smolek *et al.* 2002; Thibos *et al.* 2002A) the sign of the odd symmetric terms in the left eyes were inverted.

Of all Zernike coefficients, defocus presented the highest correlation (r=0.91, p<0.001), followed by primary SA Z(4,0) (r=0.73, p<0.001), "with-the-rule" / "against-the-rule" astigmatism Z(2,2) (r=0.70, p<0.001), vertical coma Z(3,-1) (r=0.63, p<0.001) and oblique trefoil Z(3,-3) (r=0.57, p<0.001). Third orders recorded moderate correlations, while the other HO coefficients presented low to negligible correlations. The low correlations between coefficients in the 4th, 5th and 6th orders are associated with the small mean values of each coefficient with values reaching zero.

Table 5.2: ***Correlation of Zernike coefficients between right and left eyes among 1,364 6 year old children.*** *All correlations are significant p<0.001. The sign of odd symmetric terms in the left eyes have been changed to test for enantiomorphism (Smolek et al. 2002)*

Order	Zernike Coefficient	Mean ± SD (μm)		Pearson Correlation (r)
		OD	OS	
2nd order	Z(2,-2)	-0.01 ± 0.13	-0.03 ± 0.12	0.33
	Z(2, 0)	-0.86 ± 0.62	-0.88 ± 0.64	**0.91**
	Z(2, 2)	-0.08 ± 0.21	-0.10 ± 0.21	**0.70**
3rd order	Z(3,-3)	0.00 ± 0.07	0.00 ± 0.07	**0.57**
	Z(3,-1)	-0.01 ± 0.10	-0.01 ± 0.10	**0.63**
	Z(3, 1)	0.01 ± 0.07	0.01 ± 0.06	0.46
	Z(3, 3)	0.01 ± 0.06	0.00 ± 0.06	**0.54**
4th order	Z(4,-4)	0.01 ± 0.03	0.01 ± 0.03	0.19
	Z(4,-2)	-0.01 ± 0.03	-0.01 ± 0.02	0.16
	Z(4, 0)	0.04 ± 0.06	0.04 ± 0.06	**0.73**
	Z(4, 2)	0.01 ± 0.03	0.01 ± 0.03	0.31
	Z(4, 4)	0.01 ± 0.03	0.01 ± 0.03	0.29
5th order	Z(5,-5)	-0.01 ± 0.02	0.00 ± 0.02	0.21
	Z(5,-3)	0.00 ± 0.02	0.00 ± 0.02	0.19
	Z(5,-1)	0.02 ± 0.02	0.02 ± 0.02	0.23
	Z(5, 1)	0.00 ± 0.01	0.01 ± 0.01	0.15
	Z(5, 3)	0.00 ± 0.01	0.00 ± 0.01	0.07
	Z(5, 5)	0.00 ± 0.02	0.00 ± 0.02	0.15
6th order	Z(6,-6)	0.00 ± 0.01	0.00 ± 0.01	0.11
	Z(6,-4)	0.00 ± 0.01	0.00 ± 0.01	0.04
	Z(6,-2)	0.00 ± 0.01	0.00 ± 0.01	0.08
	Z(6, 0)	-0.01 ± 0.01	-0.01 ± 0.01	0.21
	Z(6, 2)	0.00 ± 0.01	0.00 ± 0.01	0.10
	Z(6, 4)	0.00 ± 0.01	0.00 ± 0.01	0.08
	Z(6, 6)	0.00 ± 0.01	0.00 ± 0.01	0.16

5.5.3 Distribution of Ocular Aberrations in 6 Year Old Children

The spread of ocular aberrations calculated for a PD of 5 mm of Z(2,-2) to Z(6,6) for the right eyes of the 6 year old children group is presented in Figure 5.4. Due to the large differences present in the mean values between LOA and HOA, a plot of the spread of the HO modes (Z(3,-3) to Z(6,6)) is presented as an inset in Figure 5.3.

Defocus Z(2,0) was the dominant aberration and also exhibited the largest variability in comparison to other aberrations. The mean value of Z(2,0) was -0.86 ± 0.62 μm, followed by primary SA Z(4,0) with a mean of 0.04 ± 0.06 μm. Of the HOs, Z(4,0) had the highest value and the 3rd order coefficients presented with the largest variances. The mean values of 2nd, 3rd and 4th order aberrations were substantially larger than those of 5th and 6th order aberrations, which had mean values close to zero indicating a small contribution to the total wavefront of those coefficients. Most HO coefficients (n=22) had mean values greater than zero (*t*-test, $p<0.05$), except Z(3,-3) (*t*-test, p=0.074), Z(6,2) (*t*-test, p=0.111) and Z(6,6) (*t*-test, p=0.098).

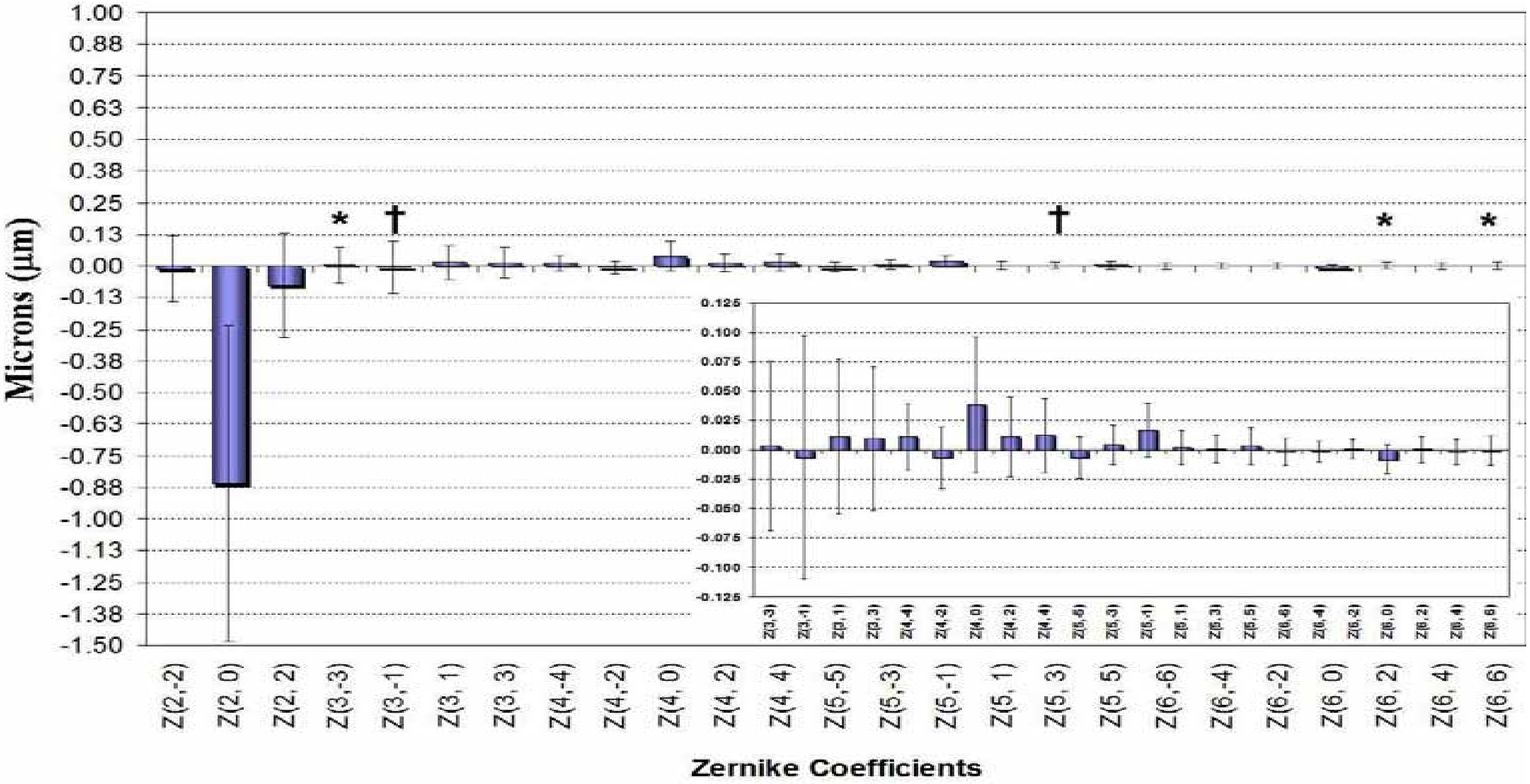

Figure 5.3: ***Mean spread of ocular aberrations Z(2,-2) to Z(6,6) in microns from right eyes of 1,364 6 year old children. HO terms Z(3,-3) to Z(6,6) are presented at a different scale in the inset.*** *Most coefficients were significantly different to zero (t-test, (p<0.001) except those with an asterisk * (t-test, p>0.05). Coefficients with a cross* † *were significantly different to zero (t-test, p<0.05)*

5.5.4 Contribution of Zernike Coefficients and Zernike Orders to the Overall Wavefront in 6 and 12 Year Old Children

To compare the magnitude of individual Zernike terms and orders between 6 and 12 year old children, the mean absolute values of the Zernike coefficients from the 2nd to the 6th orders and the RMS values from the 2nd, 3rd, 4th, 5th, 6th, HOs and total aberrations for a PD of 5 mm were obtained for both the groups. The comparison of the mean absolute Zernike coefficients and RMS values from the right eyes of both groups is shown in Table 5.3.

Statistically significant differences ($p<0.05$) were found for 17 of the 25 coefficients from the 2nd to the 6th orders (68%). As expected from comparisons of the refractive components, for the LOAs, eyes of 12 year old children showed greater levels of astigmatism Z(2,-2) and lower levels of Z(2,0) in comparison to the eyes of the 6 year old children ($p=0.001$, $p<0.001$), however, the eyes of the 12 year old children had a larger standard deviation. Of the 3rd orders, small differences were seen to exist for all modes but reached significance only for Z(3,-3) with higher levels present in 12 year old children ($p<0.001$). Similarly, for the 4th orders, small differences were found for all modes but reached significance only for Z(4,0) and Z(4,-4). Slightly higher levels of Z(4,0) ($p<0.001$) and lower levels of Z(4,-4) ($p<0.001$) were found in 12 year old children. Differences from the 5th and 6th orders were statistically significant for all coefficients except for Z(6,2) and Z(6,4). While the differences for the majority of the HOs (68.2%) were statistically significant, most of these differences were less than 0.01 μm. When comparing the RMS between 6 and 12 year old children, no differences were found for HO RMS ($p=0.182$) and 3rd orders RMS ($p=0.180$), however, differences in 4th, 5th and 6th orders RMS, while small in magnitude, were statistically significant ($p<0.01$). As expected, differences in 2nd and total aberrations RMS were also significant between groups ($p<0.001$).

Table 5.3*: Mean absolute Zernike coefficients and RMS values from the right eyes of 1,363 6 year old children and 1,608 12 year old children for a 5 mm PD*

Zernike Coefficient	6 year old group Mean ± SD	12 year old group Mean ± SD	p-Value (Two-tailed)
Z(2,-2)	0.099 ± 0.086	0.101 ± 0.090	***0.001***
Z(2, 0)	0.919 ± 0.537	0.707 ± 0.786	***0.000***
Z(2, 2)	0.172 ± 0.138	0.163 ± 0.127	0.426
Z(3,-3)	0.057 ± 0.044	0.062 ± 0.051	***0.000***
Z(3,-1)	0.081 ± 0.064	0.079 ± 0.065	0.815
Z(3, 1)	0.051 ± 0.043	0.050 ± 0.044	0.129
Z(3, 3)	0.049 ± 0.038	0.052 ± 0.040	0.585
Z(4,-4)	0.023 ± 0.020	0.021 ± 0.017	***0.000***
Z(4,-2)	0.021 ± 0.018	0.021 ± 0.022	0.882
Z(4, 0)	0.056 ± 0.042	0.063 ± 0.048	***0.000***
Z(4, 2)	0.027 ± 0.024	0.025 ± 0.023	0.192
Z(4, 4)	0.025 ± 0.023	0.024 ± 0.021	***0.039***
Z(5,-5)	0.014 ± 0.013	0.011 ± 0.010	***0.000***
Z(5,-3)	0.013 ± 0.012	0.011 ± 0.011	***0.000***
Z(5,-1)	0.022 ± 0.018	0.017 ± 0.015	***0.000***
Z(5, 1)	0.011 ± 0.010	0.010 ± 0.011	***0.000***
Z(5, 3)	0.008 ± 0.008	0.008 ± 0.008	***0.026***
Z(5, 5)	0.012 ± 0.011	0.010 ± 0.009	***0.000***
Z(6,-6)	0.008 ± 0.008	0.007 ± 0.007	***0.000***
Z(6,-4)	0.006 ± 0.007	0.005 ± 0.006	***0.010***
Z(6,-2)	0.005 ± 0.006	0.005 ± 0.006	***0.007***
Z(6, 0)	0.011 ± 0.009	0.008 ± 0.009	***0.000***
Z(6, 2)	0.007 ± 0.008	0.008 ± 0.008	0.704
Z(6, 4)	0.007 ± 0.008	0.007 ± 0.008	0.955
Z(6, 6)	0.009 ± 0.009	0.007 ± 0.008	***0.027***
RMS			
2nd order	0.966 ± 0.514	0.778 ± 0.760	***0.000***
3rd order	0.142 ± 0.064	0.145 ± 0.068	0.180
4th order	0.086 ± 0.039	0.091 ± 0.045	***0.001***
5th order	0.041 ± 0.019	0.035 ± 0.017	***0.000***
6th order	0.027 ± 0.013	0.024 ± 0.011	***0.000***
Higher order	0.179 ± 0.064	0.182 ± 0.063	0.182
Total aberrations	0.990 ± 0.504	0.814 ± 0.748	***0.000***

The average absolute Zernike coefficients in microns for individual modes (A) and order (B) for the right eyes of 1,634 6 year old and 1,636 12 year old children are presented in Figures 5.4 and 5.5 respectively.

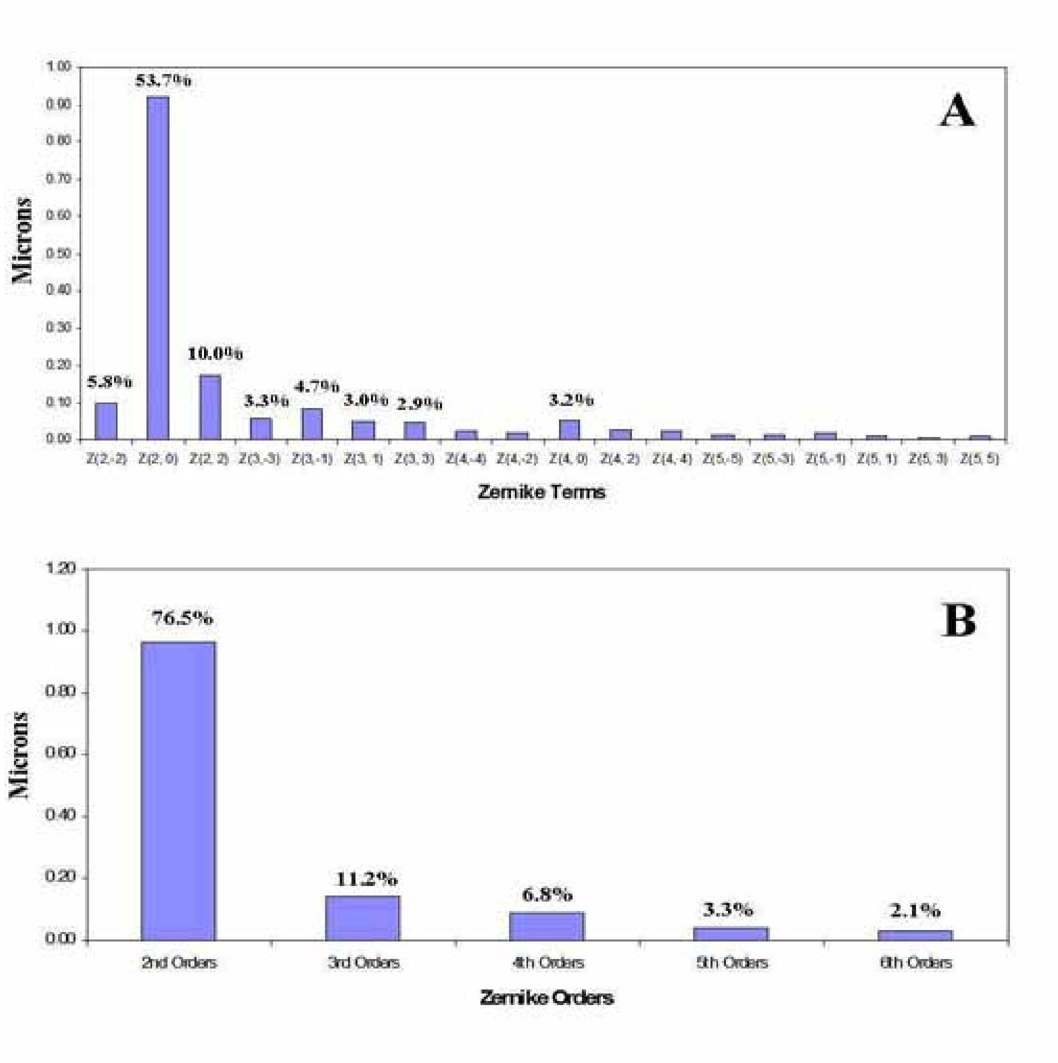

Figure 5.4: ***(after Ramamirtham et al. 2006): (A) Average absolute Zernike coefficients and percentage contributions of each of the Zernike terms from 2nd to 5th order to the overall wavefront aberrations in microns from right eyes of 1,364 6 year old children. (B) Average absolute Zernike orders RMS and percentage contribution of each Zernike orders RMS to the overall wavefront from 2nd to 6th order in microns from right eyes of 1,364 6 year old children***

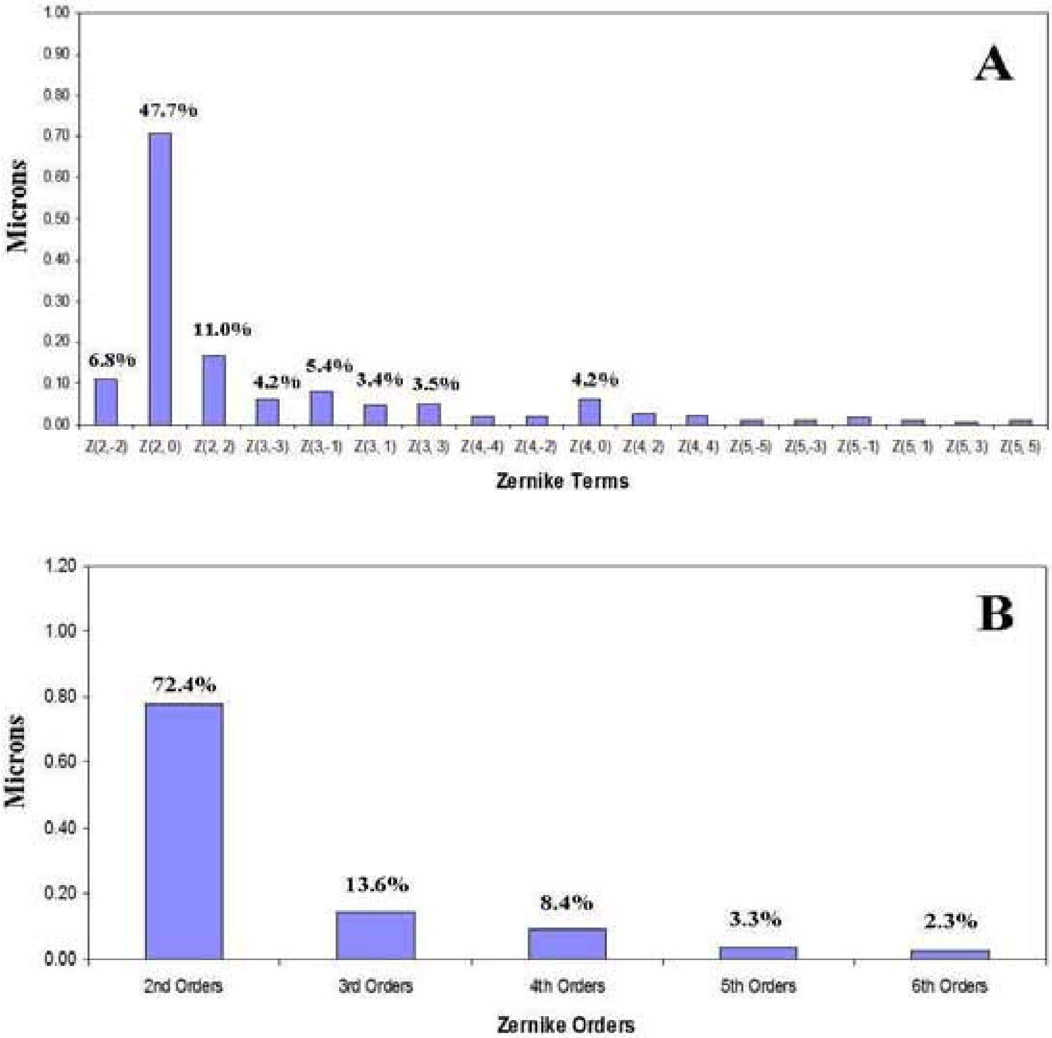

Figure 5.5: ***(after Ramamirtham et al. 2006): (A) Average absolute Zernike coefficients and percentage contributions of each of the Zernike terms from 2nd to 5th order to the overall wavefront aberrations in microns from right eyes of 1,636 12 year old children. (B) Average absolute Zernike orders RMS and percentage contribution of each Zernike orders RMS to the overall wavefront from 2nd to 6th order in microns from right eyes of 1,636 12 year old children***

The largest magnitudes of Zernike modes were in the 2nd orders Z(2,0), Z(2,-2) and Z(2,2) in both groups. Combined the 2nd order terms contributed to most of the overall wavefront, 76.5% (6 year old group), and 72.4% (12 year old group). When combined, the HO terms accounted for 23.5% (6 year old group) and 27.6% (12 year old group) of the total wavefront. Third and 4th order terms accounted for 11.2% and 6.8% (6 year old group), 13.6% and 8.4% (12 year old group) of the total wavefront respectively.

Combined, 3rd and 4th orders accounted for 76.9% (6 year old group) and 79.9% (12 year old group) of all HOAs.

The individual HO coefficients which had the largest contribution into the total wavefront were (in declining order):

- Z(3,-1) 4.7% (6 year old group), 5.4% (12 year old group);
- Z(3,-3) 3.3% (6 year old group), 4.2% (12 year old group);
- Z(4,0) 3.2% (6 year old group), 4.2% (12 year old group);
- Z(3,1) 3.0% (6 year old group), 3.4% (12 year old group);
- Z(3,3) 2.9% (6 year old group), 3.5% (12 year old group).

Contributions of the remaining coefficients were less than 2.0% in both groups.

Further analyses of ocular aberrations and RE in the 6 year old group were conducted in Pandian (2007) and, therefore, are not included in this thesis.

5.5.5 Comparison of Refractive Components Within RE Groups Between 6 and 12 Year Old Children

Based on the SE (M) from the right eyes, children were categorised into RE groups and subgroups as detailed in Table 4.1. The predominant RE in the 6 year old group was hyperopia (88%) followed by emmetropia (10%) and myopia (2%). The majority of myopic and hyperopic cases were grouped in the lower subgroups and only one case was categorised as a moderate to high myope. Therefore, to allow for comparisons with the 12 year old group, this case and the moderate to high myope subgroup were excluded from analysis, leaving a total of 1,363 6 year old children and 1,608 12 year old children. Table 5.4 presents the mean refractive components by RE groups of the 6 and 12 year old groups.

Table 5.4: ***Mean refractive components of RE groups from the right eye of 1,363 6 year old children and 1,608 12 year old children***

	6 year old group		**12 year old group**		**p-Value (Two-tailed)**
	n	**Mean ± SD**	**n**	**Mean ± SD**	
M (D)					
Low myopes	29	-0.94 ± 0.39	137	-1.42 ± 0.76	***<0.001***
Emmetropes	140	0.18 ± 0.25	450	0.14 ± 0.26	0.092
Low hyperopes	1,179	1.25 ± 0.50	999	1.03 ± 0.41	***<0.001***
Mod to high hyperopes	15	3.99 ± 0.69	22	4.56 ± 1.28	0.126
J_0 (D)					
Low myopes	29	-0.01 ± 0.17	137	-0.01 ± 0.20	0.892
Emmetropes	140	0.06 ± 0.19	450	0.04 ± 0.16	0.248
Low hyperopes	1,179	0.06 ± 0.16	999	0.02 ± 0.15	***<0.001***
Mod to high hyperopes	15	0.05 ± 0.18	22	0.05 ± 0.19	0.915
J_{45} (D)					
Low myopes	29	-0.07 ± 0.17	137	0.01 ± 0.11	***0.017***
Emmetropes	140	-0.01 ± 0.10	450	0.03 ± 0.10	***0.001***
Low hyperopes	1,179	0.01 ± 0.10	999	0.03 ± 0.10	***<0.001***
Mod to high hyperopes	15	0.03 ± 0.14	22	0.03 ± 0.13	0.953

Differences in the mean M were found between age groups for low myopes (independent samples *t*-test, $p<0.001$) and low hyperopes (independent samples *t*-test, $p<0.001$). Overall, 12 year old low myopes were more myopic than 6 year old myopes (-0.48 D). Conversely, 6 year old low hyperopes were more hyperopic than 12 year old low hyperopes (0.22 D). No difference was found in the mean M between age groups for emmetropes (independent samples *t*-test, $p=0.092$) and high hyperopes (independent samples *t*-test, $p=0.126$). In the astigmatic components, a small but statistically significant difference (0.04 D) was found in J_0 for low hyperopes between age groups (independent samples *t*-test, $p<0.001$). Small differences of less than 0.10 D were found in J_{45} between age groups for low myopes, emmetropes and low hyperopes (independent samples *t*-test; p=0.017, p=0.001 and p<0.001 respectively).

5.5.6 Distribution of SA in 6 and 12 Year Old Children

Table 5.5 presents the distribution of cases with negative, neutral or positive SA and the mean LSA by RE groups from 1,364 6 year old and 1,608 12 year old children.

Table 5.5: ***Average LSA (5 mm PD) for different RE groups based on distribution of SA from the right eyes of 1,364 6 year old and 1,608 12 year old children***

RE Groups	Spherical Aberration	6 year old group			12 year old group			p-Value (Two-tailed)
		n	(%)	LSA (D) Mean ± SD	n	(%)	LSA (D) Mean ± SD	
Low myopia	Negative	9	*31.0*	-0.44 ± 0.39	22	*16.1*	-0.28 ± 0.22	0.290
	Neutral	5	*17.2*	0.00 ± 0.00	5	*3.6*	0.00 ± 0.00	.
	Positive	15	*51.7*	0.35 ± 0.33	110	*80.3*	0.50 ± 0.32	0.100
	Total	29	*100*		137	*100*		.
Emmetropia	Negative	50	*35.7*	-0.36 ± 0.27	84	*18.7*	-0.26 ± 0.14	0.200
	Neutral	12	*8.6*	0.00 ± 0.00	32	*7.1*	0.00 ± 0.00	.
	Positive	78	*55.7*	0.39 ± 0.27	334	*74.2*	0.50 ± 0.33	***0.004***
	Total	140	*100*		450	*100*		
Low hyperopia	Negative	227	*19.3*	-0.34 ± 0.24	80	*8.0*	-0.22 ± 0.14	***0.000***
	Neutral	76	*6.4*	0.00 ± 0.00	37	*3.7*	0.00 ± 0.00	.
	Positive	876	*74.3*	0.57 ± 0.35	882	*88.3*	0.66 ± 0.42	***0.000***
	Total	1,179	*100*		999	*100*		
Moderation to high hyperopia	Negative	3	*20.0*	-0.31 ± 0.18	0	.	. .	.
	Neutral	1	*6.7*	0.00 ± 0.00	1	*4.5*	0.00 ± 0.00	.
	Positive	11	*73.3*	1.03 ± 0.62	21	*95.5*	0.94 ± 0.52	0.680
	Total	15	*100*		22	*100*		

Positive SA was present in more than 50% of cases of the three RE groups in both 6 and 12 year old children. From Table 5.5 it can be seen that, in comparison to 6 year old children, the percentage of eyes with positive SA was greater in 12 year old children. This was true for all the RE groups and was significant for emmetropes (p=0.004) and low hyperopes (p<0.001). It also appears that, with age, the amount of LSA becomes more positive and this appeared to be true for both the negative and positive SA groups. Despite the fact that, in both cohorts, the percentage of eyes with positive SA for the various RE groups appeared to be similar, statistical differences were found in both cohorts (χ^2=27.374, p<0.001; χ^2=48.598, p<0.001, for 6 and 12 year old groups respectively). In the 6 year old group, the percentage of eyes with positive SA in low hyperopes (74%) was significantly higher than in low myopes (52%) (χ^2=7.453, p=0.006) and also than in emmetropes (56%) (χ^2=21.598, p<0.001). Similarly in the 12 year group, the percentage of eyes with positive SA in low hyperopes (88%) was significantly higher than in low myopes (80%) (χ^2=6.959, p=0.008) or emmetropes (74%) (χ^2=45.489, p<0.001). The number of eyes with positive SA in moderate to high hyperopes (96%) was also significantly higher than in emmetropes (χ^2=5.072, Fisher's exact p=0.0174).

Comparisons of the mean M between SA groups within each RE group were also conducted. The results of the ANOVA are presented in Table 5.6. The data suggest that there was no difference in the M values for the various SA groups, except for the low hyperopic group in 6 year old children, where cases of positive SA also had more positive M values.

Table 5.6: ***Mean M by SA groups within RE groups from the right eyes of 1,364 6 year old and 1,608 12 year old children***

RE Groups	Spherical Aberration	6 year old group M (D) n	6 year old group M (D) Mean ± SD	6 year old group ANOVA (p-Value)	12 year old group M (D) n	12 year old group M (D) Mean ± SD	12 year old group ANOVA (p-Value)
Low myopia	Negative	9	-0.81 ± 0.22	0.276	22	-1.26 ± 0.63	0.328
	Neutral	5	-0.92 ± 0.22		5	-1.62 ± 0.51	
	Positive	15	-1.02 ± 0.49		110	-1.44 ± 0.79	
Emmetropia	Negative	50	0.18 ± 0.26	0.932	84	0.10 ± 0.28	0.248
	Neutral	12	0.21 ± 0.21		32	0.12 ± 0.26	
	Positive	78	0.18 ± 0.25		334	0.15 ± 0.25	
Low hyperopia	Negative	227	1.06 ± 0.43	***0.000***	80	0.93 ± 0.45	0.054
	Neutral	76	1.10 ± 0.41		37	0.95 ± 0.44	
	Positive	876	1.31 ± 0.50		882	1.04 ± 0.40	
Moderate to high hyperopia	Negative	3	3.82 ± 0.04	.	0		.
	Neutral	1	4.03 ± 0.00		1	4.95 ± 0.00	
	Positive	11	4.03 ± 0.81		21	4.54 ± 1.31	

5.5.7 Comparison of LO and HO RMS' Within RE Groups Between 6 and 12 Year Old Children

Whilst there were differences in the refractive components (M, J_0 and J_{45}) between the two cohorts (subsection 5.5.5), only the magnitude of the difference in M (0.60 D) was of clinical significance in comparison to the magnitude of the differences for the astigmatic components (<0.05 D). In this section, the RMS of the LOAs and HOAs (adjusted for M) was compared between the two cohorts. After adjusting for M, multivariate analysis of defocus, astigmatism, coma, trefoil, SA, tetrafoil, secondary astigmatism, HOs and total RMS, showed an association with age for low myopes (Pillai's Trace 0.132; F 2.628, p=0.007), emmetropes (Pillai's Trace 0.052; F 3.548, p<0.001) and low hyperopes (Pillai's Trace 0.117; F 31.826, p<0.001). No association was found for the moderate to high hyperopes (Pillai's Trace 0.318; F 1.345, p=0.263).

Differences between individual aberrations were computed using adjusted-multiple comparisons Bonferroni test and the results are presented in Table 5.7 and the distribution of LO and HO RMS across age groups for each RE group is presented in Figure 5.6. For clarity, SA RMS for each RE group is presented on a different scale in Figure 5.7.

An adjusted-multiple comparisons Bonferroni test showed 6 year old low myopes had lower levels of defocus RMS (p=0.001), SA RMS (p=0.022) and total aberrations RMS (p=0.004) than 12 year old low myopes.

Table 5.7: ***Mean RMS for RE groups from the right eyes of a group of 1,363 6 year old children and 1,608 12 year old children***

RE Group	RMS	6 year old Mean ± SD	12 year old Mean ± SD	p-Value (Bonferroni adjusted)
Low myopes	Defocus	0.87 ± 0.44	1.44 ± 0.69	***0.001***
	Astigmatism	0.28 ± 0.13	0.25 ± 0.14	0.417
	Coma	0.10 ± 0.07	0.12 ± 0.07	0.376
	Trefoil	0.08 ± 0.05	0.10 ± 0.05	0.160
	Spherical Aberration	0.04 ± 0.04	0.05 ± 0.04	***0.022***
	Quatrefoil	0.04 ± 0.02	0.04 ± 0.02	0.710
	Secondary Astigmatism	0.04 ± 0.02	0.03 ± 0.02	0.112
	Higher order	0.17 ± 0.07	0.19 ± 0.06	0.184
	Total Aberrations	0.96 ± 0.41	1.49 ± 0.67	***0.004***
Emmetropes	Defocus	0.26 ± 0.18	0.23 ± 0.18	***0.044***
	Astigmatism	0.24 ± 0.16	0.22 ± 0.13	0.118
	Coma	0.10 ± 0.06	0.10 ± 0.06	0.795
	Trefoil	0.08 ± 0.05	0.09 ± 0.05	0.533
	Spherical Aberration	0.04 ± 0.03	0.05 ± 0.04	***0.009***
	Quatrefoil	0.04 ± 0.03	0.03 ± 0.02	***0.030***
	Secondary Astigmatism	0.04 ± 0.03	0.03 ± 0.02	***0.022***
	Higher order	0.17 ± 0.07	0.17 ± 0.06	0.783
	Total Aberrations	0.43 ± 0.17	0.40 ± 0.16	***0.009***

Table 5.7: ***Mean RMS for RE groups from the right eyes of a group of 1,363 6 year old children and 1,608 12 year old children (cont.)***

RE Group	RMS	6 year old Mean ± SD	12 year old Mean ± SD	p-Value (Bonferroni adjusted)
Low hyperopes	Defocus	0.97 ± 0.44	0.66 ± 0.36	***<0.001***
	Astigmatism	0.21 ± 0.13	0.20 ± 0.12	***0.011***
	Coma	0.11 ± 0.06	0.10 ± 0.06	0.493
	Trefoil	0.08 ± 0.05	0.09 ± 0.05	***0.001***
	Spherical Aberration	0.06 ± 0.04	0.07 ± 0.05	***<0.001***
	Quatrefoil	0.04 ± 0.02	0.04 ± 0.02	0.125
	Secondary Astigmatism	0.04 ± 0.02	0.04 ± 0.03	0.108
	Higher order	0.18 ± 0.06	0.19 ± 0.07	***0.001***
	Total Aberrations	1.03 ± 0.41	0.74 ± 0.33	***<0.001***
Moderate to high hyperopes	Defocus	3.29 ± 0.57	3.69 ± 1.13	0.459
	Astigmatism	0.25 ± 0.15	0.27 ± 0.13	0.722
	Coma	0.15 ± 0.09	0.13 ± 0.06	0.412
	Trefoil	0.08 ± 0.04	0.10 ± 0.04	0.084
	Spherical Aberration	0.10 ± 0.07	0.11 ± 0.06	0.969
	Quatrefoil	0.05 ± 0.03	0.04 ± 0.02	0.533
	Secondary Astigmatism	0.04 ± 0.01	0.04 ± 0.03	0.319
	Higher order	0.23 ± 0.08	0.23 ± 0.06	0.719
	Total Aberrations	3.31 ± 0.57	3.71 ± 1.12	0.472

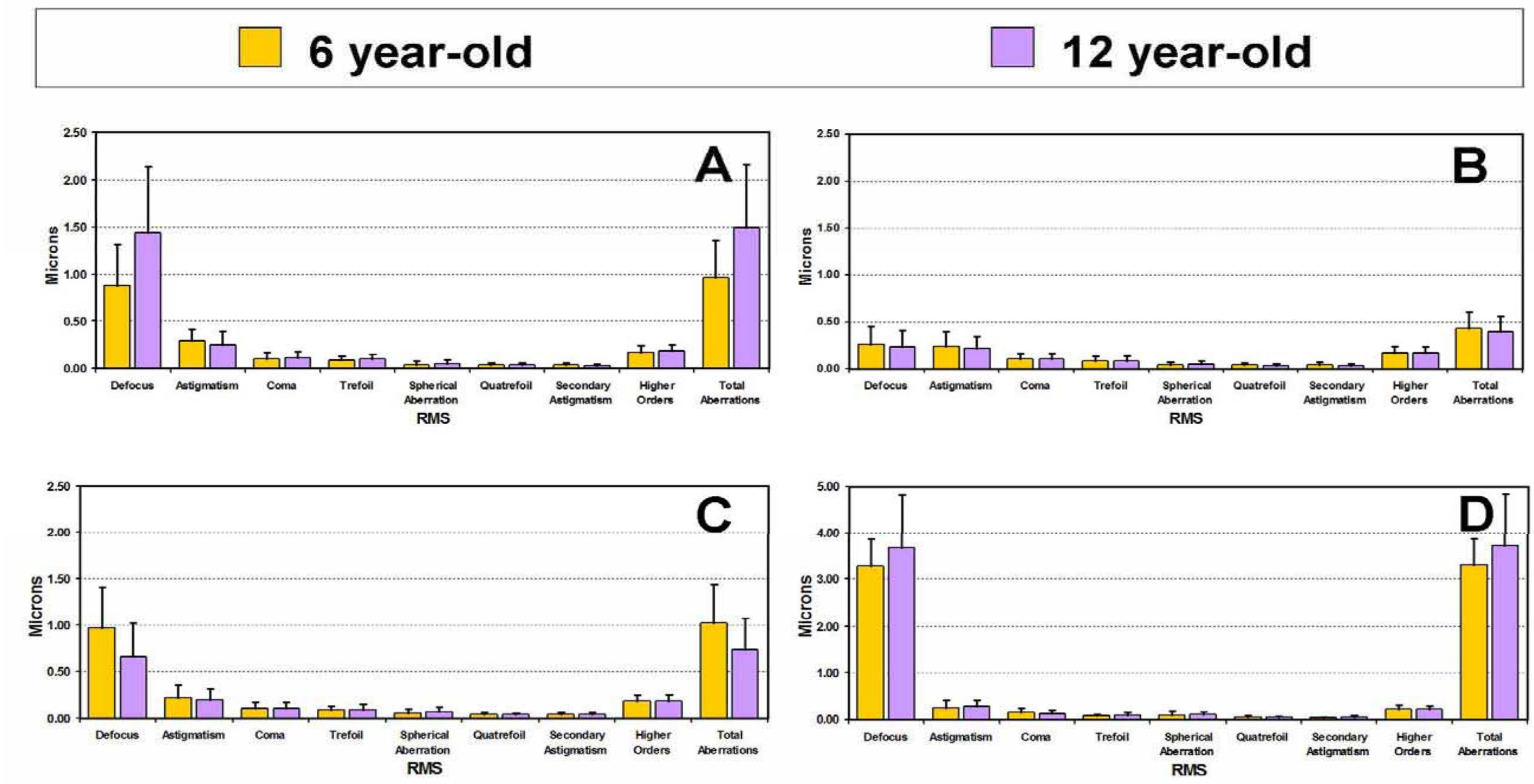

Figure 5.6: ***Ocular aberration profiles in RMS in microns from the right eyes of 1,363 6 and 1,608 12 year old children for different RE groups. (A) Low myopes, (B) Emmetropes, (C) Low hyperopes, (D) Moderate to high hyperopes.*** *Note difference in scale in the ordinates of group D*

Six year old emmetropes had higher levels of defocus RMS (p=0.044), quatrefoil RMS (p=0.03), secondary astigmatism RMS (p=0.022), SA RMS (p=0.009) and total RMS (p=0.009) than 12 year old emmetropes.

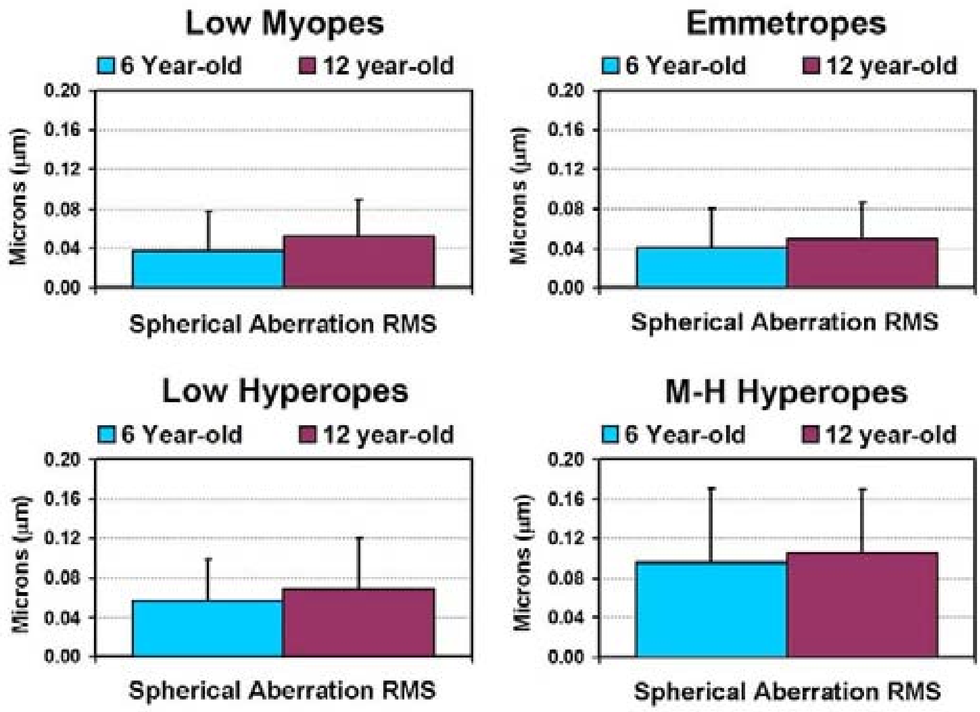

Figure 5.7: ***SA RMS from the right eyes of 1,363 6 year old and 1,608 12 year old children for different RE groups***

In comparison to 12 year old low hyperopes, 6 year old low hyperopes had higher levels of defocus RMS ($p<0.001$), astigmatism RMS (p=0.011) and total RMS ($p<0.001$). Also, 6 year old low hyperopes had lower levels of trefoil RMS (p=0.001), SA RMS ($p<0.001$) and HO RMS (p=0.001) than 12 year old low hyperopes.

Comparisons between age groups for the moderate to high hyperopic groups revealed no differences between any of the lower and HO RMS modes.

5.6 DISCUSSION

Studies reporting aberrations in humans have been conducted in small to medium populations involving mainly adults. This is the largest study to date that assessed ocular aberrations in a large sample of children (n=3,000).

One of the main reasons for choosing the ages of children evaluated in the current study was that the ages of both cohorts covered a key period in ocular growth and development of myopia. While the prevalence of myopia in 6 year old children is almost non-existent, in 12 year old children it can be as high as 84% in some Asian countries (Appendix A). In the current study, differences were found in the distribution of RE between cohorts, with the 6 year old cohort 0.60 D more hyperopic than the 12 year old cohort. The difference in “M” was also reflected in the distribution of REs. The prevalence of myopia in the 6 year old cohort was only 2% in comparison to 10% in the 12 year old cohort, and the prevalence of hyperopia in the 6 year old cohort was 88% in comparison to 63% in the 12 year old cohort. A lower prevalence of emmetropia was also observed in the 6 year old cohort (10%) in comparison to the 12 year old cohort (27%).

It was evident from these results that differences existed in the stages of the emmetropisation process between both cohorts. The current study was conducted in an attempt to determine if similar differences in the levels of HOAs would exist with age in these children.

5.6.1 Distribution of Ocular Aberrations in 6 Year Old Children

As observed in 12 year old children (Chapter 4) and in Carkeet *et al.* (2003), the majority of the LO and HO Zernike coefficients were significantly correlated between right and left eyes in this cohort of 6 year old children and supports existing literature that indicates a low prevalence of anisometropia in children (Almeder *et al.* 1990; Huynh *et al.* 2006B; Tong *et al.* 2004). However, the current study did not evaluate eyes with astigmatism ≥1.00 D. Of the HOAs, SA Z(4,0) presented with the largest correlation between eyes, followed by 3rd orders, while the correlation of other coefficients from the 4th, 5th and 6th orders between eyes remained small mainly due to the small mean values of these coefficients.

Small amounts of HOAs were found in 6 year old children, following the same trend as in 12 year old children and other studies in children (Carkeet *et al.* 2002; Castejon-Mochon *et al.* 2002). While small in magnitude, 19 of the 22 HO coefficients (86.4%) had mean values significantly different to zero while in the group of 12 year old children, 18 of the 22 HO coefficients (81%) were significantly different to zero. This result indicates that, during childhood, the eye is not completely free of HOAs but most aberrations are very low in magnitude.

5.6.2 Comparison of Ocular Aberrations Between 6 and 12 Year Old Children

In an attempt to look at the contribution or impact that ocular aberrations (especially HOAs) have on the optical quality of the eye regardless of their sign, individual, as well as aberrations grouped by order, were analysed based on their magnitude in 6 and 12 year old children. The major contribution to the total wavefront was with the 2nd orders contributing to nearly ¾ and the rest (¼) with HOAs. This was true for both cohorts. Of the HOs, the majority of the contributions were from 3rd and 4th orders, accounting for more than 75%. Small differences in the mean values of the 2nd orders were observed between cohorts with 12 year old children having lower levels of Z(2,0) and Z(2,-2) than 6 year old children.

The mean values of HO RMS observed in both cohorts are in close agreement with those found in other studies from children: +0.18 ± 0.06 µm (Carkeet *et al.* 2002), +0.2 ± 0.08 µm (Carkeet *et al.* 2003). From the 3rd orders, higher levels of Z(3,-3) were observed in 12 year old children, however, the levels of 3rd orders RMS were similar between cohorts. In comparison to 12 year old children, 6 year old children had lower levels of 4th orders RMS, mainly due to lower values of Z(4,0). The difference in Z(4,0) between cohorts is discussed in more detail in subsection 5.6.4.

One of the problems that exists when comparing aberrometry data across different studies has been the differences in PDs used to calculate the aberrometry data. This problem has been assessed recently by Salmon and van de Pol (2006). Aberrometry data from 1,433 subjects with different REs and ages (from 18 to 72 years) collected from 10 different laboratories were pooled and scaled to four different PDs (6, 5, 4 and 3 mm). The mean Zernike coefficients, distribution and absolute values for each coefficient and RMS values from both eyes were calculated for each PD. Aberrometry data for a PD of 5 mm was available for 2,560 eyes providing the largest aberrometry data pool for normal, healthy adult eyes ever reported. Interestingly, there was a remarkable similarity in the results obtained from this study with that reported using an adult population (Salmon and van de Pol 2006) (Table 5.8).

Table 5.8: ***Mean absolute Zernike coefficients and RMS values from the right eyes of 1,363 6 year old children, 1,608 12 year old children and 2,560 adult eyes for a 5 mm PD***

Zernike Coefficient	6 year old group			12 year old group			Adults PD=5 mm*		
	Mean	±	**SD**	**Mean**	±	**SD**	**Mean**	±	**SD**
Z(2,-2)	0.099	±	0.086	0.101	±	0.090		*NA*	
Z(2, 0)	0.919	±	0.537	0.707	±	0.786		*NA*	
Z(2, 2)	0.172	±	0.138	0.163	±	0.127		*NA*	
Z(3,-3)	0.057	±	0.044	0.062	±	0.051	0.069	±	0.056
Z(3,-1)	0.081	±	0.064	0.079	±	0.065	0.082	±	0.069
Z(3, 1)	0.051	±	0.043	0.050	±	0.044	0.056	±	0.047
Z(3, 3)	0.049	±	0.038	0.052	±	0.040	0.052	±	0.043
Z(4,-4)	0.023	±	0.020	0.021	±	0.017	0.023	±	0.020
Z(4,-2)	0.021	±	0.018	0.021	±	0.022	0.017	±	0.015
Z(4, 0)	0.056	±	0.042	0.063	±	0.048	0.064	±	0.049
Z(4, 2)	0.027	±	0.024	0.025	±	0.023	0.026	±	0.023
Z(4, 4)	0.025	±	0.023	0.024	±	0.021	0.025	±	0.022
Z(5,-5)	0.014	±	0.013	0.011	±	0.010	0.011	±	0.010
Z(5,-3)	0.013	±	0.012	0.011	±	0.011	0.010	±	0.009
Z(5,-1)	0.022	±	0.018	0.017	±	0.015	0.012	±	0.011
Z(5, 1)	0.011	±	0.010	0.010	±	0.011	0.009	±	0.008
Z(5, 3)	0.008	±	0.008	0.008	±	0.008	0.008	±	0.007
Z(5, 5)	0.012	±	0.011	0.010	±	0.009	0.010	±	0.009
Z(6,-6)	0.008	±	0.008	0.007	±	0.007	0.007	±	0.006
Z(6,-4)	0.006	±	0.007	0.005	±	0.006	0.005	±	0.005
Z(6,-2)	0.005	±	0.006	0.005	±	0.006	0.004	±	0.004
Z(6, 0)	0.011	±	0.009	0.008	±	0.009	0.008	±	0.007
Z(6, 2)	0.007	±	0.008	0.008	±	0.008	0.006	±	0.006
Z(6, 4)	0.007	±	0.008	0.007	±	0.008	0.006	±	0.006
Z(6, 6)	0.009	±	0.009	0.007	±	0.008	0.007	±	0.006
RMS									
2nd order	0.966	±	0.514	0.778	±	0.760		*NA*	
3rd order	0.142	±	0.064	0.145	±	0.068	0.153	±	0.153
4th order	0.086	±	0.039	0.091	±	0.045	0.090	±	0.090
5th order	0.041	±	0.019	0.035	±	0.017	0.030	±	0.030
6th order	0.027	±	0.013	0.024	±	0.011	0.020	±	0.020
HO RMS	0.179	±	0.064	0.182	±	0.063	0.186	±	0.186
Total RMS	0.990	±	0.504	0.814	±	0.748		*NA*	

** Data from adults obtained from Salmon and van de Pol 2006*

The mean values of 3rd, 4th, 5th, 6th and total HOs RMS did not differ by more than 0.1 µm, however, larger standard deviations existed in adults in some individual Zernike terms and RMS. Large standard deviation values in the results of Salmon and van de Pol (2006) are expected because they include large ranges of REs and ages in which, especially in older eyes, higher levels of HOAs, such as coma-like aberrations and SA, are present. It should also be recognised that, while the pupil size was equated to 5 mm, we expect some differences in the measured amounts of aberrations due to differences in the axial length (Wang and Candy, 2005) between the different age groups. However, we expect this effect to be small. Nevertheless, the similarity in the mean values of the majority of HOAs between children and adult populations evidences the robustness of the optical system of the human eye throughout life.

5.6.3 Differences of Ocular Aberrations and RE with Age

Despite the suggestion that elevated levels of optical aberrations could play a role in the development of myopia (Thorn *et al.* 1998) and earlier reports of different or higher levels of some HOAs in myopic eyes (Applegate 1991; Collins *et al.* 1995; He *et al.* 2002), most studies conducted in children and in adults, including this study, have found small or no differences in the levels of HOAs between myopic and emmetropic eyes (Carkeet *et al.* 2002; Cheng *et al.* 2003A; He *et al.* 2005; Martinez *et al.* 2006; Porter *et al.* 2001). Similarly the levels of HO RMS aberrations in myopic and emmetropic eyes were not different (p=0.946) in the 6 year old cohort (Pandian 2007) (see Appendix J).

This similarity of HOAs between RE groups and between children and adults suggests that the levels of HOAs would also remain constant regardless of the RE. However, He *et al.* (2002) found higher levels of aberrations RMS (excluding defocus and tilt) in emmetropic children than in emmetropic adults which led the investigators to suggest that emmetropic children with higher levels of aberrations would eventually shift to a state of myopia.

In the current study, differences were found for the LOs between 6 and 12 year old children in the levels of defocus RMS for low myopes, emmetropes and low hyperopes and also for astigmatism RMS for emmetropes. Some small differences between cohorts were also observed for the HOs. The levels of SA RMS were higher in 12 year old children for the myopic, emmetropic and low hyperopic groups. Trefoil RMS was also higher in 12 year old low hyperopes, while quatrefoil and secondary astigmatism were slightly lower in 12 year old emmetropes and in 6 year old emmetropes. Despite the differences in individual orders observed between RE groups, the mean levels of HO RMS were significantly different for low hyperopes only.

Direct comparisons of the results in this thesis with those from He *et al.* (2002) are difficult, firstly because of the age of the groups analysed, secondly because the analysis of aberrations in the He *et al.* (2002) study was performed for a PD of 6 mm and higher levels of aberrations were expected in their study (Atchison 2004B; Salmon and van de Pol 2006), thirdly because, in He *et al.* (2002), accommodation was not controlled with cycloplegia as in the current study and differences in aberrations with accommodation were also expected, and finally because He *et al.* (2002) included astigmatism in their analysis when describing aberrations. In regards to the inclusion of astigmatism when comparing aberrations, the amount of astigmatism of the different RE groups in both age groups was similar within RE groups, with the exception of low hyperopes. Therefore, it would not be expected to have an effect in the analyses if astigmatism had been included and this study did not provide evidence of abnormal levels of HO in young emmetropic children.

5.6.4 SA in 6 and 12 Year Old Children

SA Z(4,0) in the cohort of 6 year old children was, on average, positive although slightly lower (<0.01 µm) than in 12 year old children. The mean values of SA found in both cohorts are in close agreement with those reported from children with ages ranging from 6 to 9 years (Carkeet *et al.* 2002; Carkeet *et al.* 2003), adults (+0.06 ± 0.05 µm for 5 mm PD) (Salmon and van de Pol 2006) and are in contradiction with those reported by Kirwan *et al.* (2006) in children aged 4 to 14 years (-0.115 ± 0.126 µm for 6 mm PD). Approximately 79% of eyes from 6 year old children had SA values ≥0 µm, while 88% of eyes from 12 year old children had SA values ≥0 µm (in contrast to 85% of cases with negative SA reported by Kirwan *et al.* (2006). A better explanation for the difference of results could be the use of a different system by Kirwan *et al.* (2006) than the one recommended by the Optical Society of America (Appendix C) to report aberrations (perhaps Malacara).

The current study supports previous reports that showed a shift of negative SA in children younger than 6 years towards positive SA (Jenkins 1963). This shift, as Jenkins (1963) suggested, could be the result of ongoing changes of the optical elements (cornea and also the crystalline lens) that seem to occur during childhood.

It is evident that ocular SA is the result of the interaction between corneal and internal SA (Artal *et al.* 2001; Artal *et al.* 2006; Atchison and Smith 2000; Guirao *et al.* 2000; Kelly *et al.* 2004; Kiely *et al.* 1982; Millodot and Sivak 1979; Smith *et al.* 2001) and that the cornea suffers from under-corrected (positive) SA in the majority of cases as the result of its prolate shape (Artal *et al.* 2001; Artal *et al.* 2006; Atchison and Smith 2000; Guirao *et al.* 2000; Kelly *et al.* 2004; Kiely *et al.* 1982; Millodot and Sivak 1979; Smith *et al.* 2001). The prevalence of over-corrected (negative) corneal SA has been reported to be as low as 5 to 8.5% (Kiely *et al.* 1982; Carney *et al.* 1997).

Despite the large changes in size, shape, curvature and power that the cornea experiences during infancy until the age of 6 years (Friedman *et al.* 1996; Inagaki 1986; Ronneburger *et al.* 2006; York and Mandell 1969), there is no indication that changes in the curvature or asphericity of the cornea occur during childhood (Grosvenor and Goss 1998), at least in emmetropic eyes, until the 4th decade of life when the cornea starts to become more spherical (Guirao *et al.* 2000). Davis *et al.* (2005) found a prolate corneal shape in 99.7% of eyes of 643 children aged 6 to 15 years; which suggests that, in the majority of children, corneal SA is also positive. It is not clear if changes in asphericity occur with RE. Whilst some studies of young myopic eyes have observed that the cornea becomes more oblate with myopia progression (Carney *et al.* 1997; Horner *et al.* 2000), other studies did not find a difference in corneal asphericity between RE groups, in both adults and children (Carkeet *et al.* 2002; Mainstone *et al.* 1998; Parssinen 1993; Sheridan and Douthwaite 1989). Therefore, there is little evidence to suggest that positive corneal SA could explain the higher prevalence of negative ocular SA in 6 year old children in comparison to 12 year old children. A more plausible explanation lies in the crystalline lens.

Studies measuring the optical characteristics of the crystalline lens *in vitro* in young humans (Glasser and Campbell 1998), primates and pigs (Roorda and Glasser 2004) have shown that the crystalline lens has negative SA in its unaccommodated state and becomes more negative with accommodation. Interestingly, Glasser and Campbell, (1998) also found that, while the SA of crystalline lenses of young children is negative, in older crystalline lenses (older than 40 years), the SA is positive in its unaccommodated state. This finding could explain why some studies have found increasing positive internal SA in middle aged subjects (Amano *et al.* 2004; Guirao *et al.* 2000; Millodot and Sivak 1979; Salmon and Thibos 2002).

The origin of the SA of the crystalline lens is not completely clear, however, it has been suggested that the SA of the crystalline lens is directly associated with the gradient refractive index which peaks at the core and reduces towards the cortex (Campbell and Hughes 1981). During infancy and childhood, the crystalline lens experiences a reduction of its thickness (Larsen 1971B; Mutti *et al.* 1998; Zadnik 1997; Zadnik *et al.* 2003), a change in the radius of curvature of its surfaces (Wood *et al.* 1996) and a decrease of its refractive index (Mutti *et al.* 1995; Wood *et al.* 1996) resulting in the loss of approximately 20.00 D or power. During infancy alone, it has been estimated that 75% of the decrease in lens power is due to decreases in equivalent index (Wood *et al.* 1996). Mutti *et al.* (1995) calculated an equivalent refractive index of 1.427 for the crystalline lens during childhood which is higher than the refractive index of 1.416 calculated by the Gullstrand-Emsley model eye. Mutti *et al.* (1998) later suggested that, in order to maintain emmetropia during childhood while the AL of the eye increases, the crystalline lens continues experiencing a variation in its equatorial gradient index profile to reduce its power.

It is possible that, as a consequence of this reduction in equivalent refractive index of the crystalline lens during childhood, the negative SA of the lens also decreases. Furthermore, it is also possible that, during childhood, the changes in the curvature of the crystalline lens alone or in combination with the reduction of its equivalent refractive index could also result in a reduction of the negative SA of the lens. Indirectly, this process could explain why a greater proportion of 6 year old children (21%) had negative values of SA in comparison to 12 year old children (12%) and also explain the lower levels of positive SA found in 5 to 7 week old infants in comparison to adults (Wang and Candy 2005). Perhaps children with ocular negative SA have crystalline lenses with higher equivalent refractive index, which could indicate that the eye has not fully developed, or simply that its mechanism of compensation of corneal aberrations is faulty.

Unfortunately the characteristics of the crystalline lens or the cornea shape were not measured in the current study. It will be interesting if future studies could assess all these variables in children in order to extend our understanding of the ocular development during childhood.

To obtain a better understanding of the impact that SA has on the optical system of the eye, the values of Z(4,0) were converted into LSA. When describing SA in term of LSA, the difference in paraxial and marginal rays focusing in the eye is explained in terms of dioptres. So for those eyes with positive LSA, the marginal rays entering the eye focus in front of the paraxial rays (more myopic) and for eyes with negative LSA, the marginal rays entering the eye focus behind the paraxial rays (more hyperopic) (Bennett and Rabbetts 1998).

Collins and Wildsoet (2000) proposed an optical treatment method for RE onset or development based on the control of LSA and its potential relationship with the emmetropisation process. They also suggested that the negative defocus caused by negative SA promotes eye growth (myopisation) in a similar way as negative defocus produces myopia development (Diether and Schaeffel 1997; Guo *et al.* 1996; Hung *et al.* 1995; Kee *et al.* 2003; Kee *et al.* 2004A; Norton 1990; Schaeffel *et al.* 1988; Smith EL III *et al.* 1980; Smith EL III *et al.* 1994; Smith EL III and Hung 1999). Also suggested is that the typical positive LSA of the adult eye (approximately +0.50 D for a PD of 5 mm) would work as a stimulus to stop eye length growth. Finally, Collins and Wildsoet (2000) suggested that the presence of markedly positive LSA in juvenile emmetropic eyes may cause hyperopia onset, whilst those cases with negative LSA could be regarded as predictive of myopia development. Therefore, Collins and Wildsoet (2000) proposed an optical treatment method in which negative SA could be used to prevent the onset of, or reduce the progression of, hyperopia (by promoting eye growth) while positive SA (approximately +0.50 D) could be used to prevent the onset of, or progression of, myopia (by stopping eye growth).

Interestingly, the data from the current study suggests that a greater percentage of myopic eyes (69% of the myopic eyes in the 6 year old cohort and 84% in the 12 year old cohort) have positive or zero LSA rather than negative LSA. This was the case for emmetropic eyes as well, with only a small number of cases presenting with negative SA. These results then suggest that a majority of the myopic eyes from the current study will continue to remain stable as a result of positive SA and will not benefit from the treatment method proposed by Collins and Wildsoet (2000). Similarly, the majority of emmetropic eyes in the current study will remain emmetropic and will not need any preventive treatment. Such data on whether eyes with negative LSA will become myopic, while eyes with positive LSA will remain stable is not available at this time and can only be obtained in longitudinal studies. However, in this context it would be of interest to study the East Asian eyes in detail. As a significant number of East Asian children continue to become myopic with age (Edwards 1999; Lam *et al.* 1999), one would expect large number of eyes of these children to have negative LSA or significantly different amounts of LSA in comparison to Caucasian eyes. However, data from the current study showed that the levels of SA of myopic eyes in East Asian children were not different to those found in Caucasian children (see Chapter 4, subsection 4.5.5.5).

In addition, if negative LSA promotes eye growth, one may expect eyes with negative LSA to be more myopic in comparison to eyes with positive LSA. However, the results suggest that, for myopes and emmetropes, there was not statistical difference in the mean M. It therefore, appears that SA in isolation cannot explain the process of emmetropisation, however, to conclusively prove such a hypothesis, one would need to conduct longitudinal studies which include measurement of SA and RE.

5.7 SUMMARY

This study was aimed to compare the characteristics of ocular monochromatic aberrations of two large groups of children (n=3,000) examined at the Sydney Myopia Study, with ages ranging from 5 to 9 years and 11 to 14 years. It also aimed to look for differences in the levels of aberrations between young and older children when considering RE. To our knowledge this is the first study ever reporting the characteristics of ocular aberrations of such a large sample of children.

The main findings of this study were that the difference of the mean values of HOAs between young and older children, although statistically significant, were generally small in magnitude and comparable to those found in adults, suggesting that the optical quality of the eye reaches adult characteristics before 14 years of age.

Second order aberrations had the largest contribution to the total optical quality of the eye in both young and older children, while from the HOs, 3rd and 4th order aberrations contributed to almost 20% of the total wavefront. There was large variability in the levels of HOAs with the majority of HOs having means different to zero in both age groups. There were no differences in the amount of HO RMS within RE groups with age, although the mean values of SA RMS were higher in older children. The mean ocular SA was positive in the majority of 6 and 12 year old children and seems to become more positive with age. A small proportion of children from both age groups also presented negative values of SA, except in cases of children with hyperopia >3.00 D, as they presented positive values of SA. There was no difference in the levels of RE between cases with negative, neutral or positive SA.

The results found in this study provide further evidence that the onset of myopia in children is not related to abnormal levels of HOAs.

CHAPTER 6: OFF-AXIS (PERIPHERAL) REFRACTION AND ABERRATIONS IN 12 YEAR OLD CHILDREN

6.1 INTRODUCTION

Data from human studies suggest that the development and/or progression of REs such as myopia could be related to certain patterns of off-axis refraction. Also, other off-axis patterns of refraction appear to have a "protective" effect against the development of REs (Hoogerheide *et al.* 1971; Rempt *et al.* 1971).

More recently, studies conducted in animals, especially in primates (Kee *et al.* 2004B; Smith EL III *et al.* 2005) show that peripheral or off-axis defocus has an influence on eye growth and, as a consequence, development of RE. These studies thus emphasise the importance of off-axis optical quality in development and/or progression of REs.

Several studies have measured off-axis refraction and aberrations in adult populations (Tables B1 and B2 in Appendix B), however, there have been few studies on children (Mutti *et al.* 2000B; Schmid 2003B). These studies in children suffered from other limitations. Mutti *et al.* (2000B), addressed off-axis refraction only at a single point on the horizontal meridian (30 degrees eccentricity on the temporal retina). While Schmid (2003B) assessed all the four retinal quadrants, the angle measured was only 15 degrees from the fovea.

Measurement and analysis of the levels of LOAs and HOAs at various eccentricities on the retina, especially for the eyes of children, will help identify the patterns of peripheral REs and their role in the development and/or progression of myopia. In addition, the data has useful applications in the field of visual optics, such as the estimation of ocular shape, development of model eyes and development of methods of optical correction which could help control the progression of REs.

6.2 AIMS

- To determine the distribution of off-axis (peripheral) REs in a large sample of 12 year old children.
- To determine the relationship between off-axis and on-axis REs.
- To determine differences in the patterns for eye shape derived from off-axis REs between myopic, emmetropic and hyperopic eyes.
- To determine the distribution and characteristics of off-axis HOAs in various RE groups.

6.3 METHODS

6.3.1 Subjects

Measurements of off-axis refraction and monochromatic aberrations were conducted on the same sample of children (mostly 12 year old children) described in Chapter 4.

6.3.2 Off-Axis Refraction and HOA Measurements

In addition to on-axis measurements, off-axis refraction and aberrometry measurements were obtained under cycloplegia from 1,813 children using the COAS G200 aberrometer (Chapter 3, subsection 3.1.1.2). The method adopted to obtain the off-axis measurements was as follows:

- As described in Chapter 4, Section 4.3.2, approximately 30 minutes after the last cycloplegic drop was instilled, one on-axis aberrometry measurement was obtained for each eye and recorded. To avoid any double vision or confusion while looking at the target, the contralateral eye was covered with an eye-patch.
- Following measurement of on-axis aberrations, the subject was asked to rotate his/her eye towards the peripheral target located at 30 degrees eccentricity from the optical axis of the COAS G200 (Chapter 2, subsection 2.2.2) and was asked to fixate at the centre of the target (presented temporally for measurements of the temporal retina).
- One reading was obtained after re-alignment of the instrument onto the centre of the pupil of the subject.
- If the minimum PD was ≥ 5 mm, then the reading was recorded for analysis. If the minimum PD recorded was <5 mm, the measurement was discarded and another measurement taken.
- The procedure was repeated for the other retinal positions (superior and nasal) in the same eye and then repeated on the contralateral eye.
- Data recorded by the COAS G200 was exported using the method described in (Chapter 2, subsection 2.2.3) for analyses.

The Zernike coefficients obtained with a PD of 5 mm were converted to vector components using the following equations (Atchison 2004B):

$$M = \frac{-(4\sqrt{3Z_2^0}) - \sqrt{5Z_4^0})}{R^2}$$ **Equation 6. 1**

$$J_0 = \frac{-(2\sqrt{6Z_2^2})}{R^2}$$ **Equation 6. 2**

$$J_{45} = \frac{-(2\sqrt{6Z_2^{-2}})}{R^2}$$ **Equation 6. 3**

Where:

$R = \dfrac{Pupil \cdot Diameter}{2}$, and

Z_2^0, Z_2^2, Z_2^{-2} and Z_4^0 are Zernike coefficients

The tangential (along the measured meridian) and the sagittal (90 degrees from the tangential meridian) components of the refraction for both the horizontal and vertical (superior) retinal meridians were derived using the following equations (Atchison 2004B; Atchison *et al.* 2006A):

$$Tangential = M + J_0$$ **Equation 6. 4**

$$Sagittal = M - J_0$$ **Equation 6. 5**

It has to be noted that in both equations 6.4 and 6.5, oblique astigmatism (J_{45}) is not included. On and off-axis astigmatism was calculated using the following equation (Thibos *et al.* 1997):

$$J = \sqrt{J_0^{\ 2} + J_{45}^{\ 2}}$$ **Equation 6. 6**

In order to determine the patterns of off-axis refraction, cases were classified into types of skiagrams as described by Rempt *et al.* (1971). Off-axis refraction (tangential and sagittal components) from the horizontal retinal meridian was used for this analysis. To allow comparisons of off-axis refraction and aberrations between various RE groups, eyes were assigned to one of the five RE subgroups (Chapter 4, subsection 4.5.4, Table 4.12) based on the on-axis SE (M).

6.4 DATA ANALYSIS

The data from the right eyes were considered for the analysis. To analyse differences in off-axis astigmatism, refractive components, LO and HO RMS between the various RE groups and the effect of gender on these variables, Univariate-adjusted analyses of variance were performed. Astigmatism, power vectors (M, J_0, J_{45}), defocus RMS, astigmatism RMS, coma RMS, 3rd orders RMS, SA RMS, 4th orders RMS, and HO RMS were the dependent variables and significance levels were calculated using the *F* test. Adjusted-multiple comparisons test was used to test for differences between the various RE groups. The level of significance for all statistical analyses was set at $p<0.05$. Statistical analyses were performed using SPSS 14.0 Statistical Software (SPSS, Inc, Chicago, IL, USA).

6.5 RESULTS

As described in Chapter 4, 1,636 children complied with the selection criteria for on-axis aberrations measurements. Of these, off-axis measurements were not recorded for 33 cases (1.8%) in one or more positions and, therefore, were excluded from analysis. A total of 1,603 children met the final criteria for off-axis refraction and aberrations analysis.

6.5.1 Off-Axis Refraction

The tangential and sagittal components of the refraction were calculated for the central (on-axis), nasal, temporal and superior retinal positions (off-axis) in the right eyes of 1,603 children. The descriptive statistics of the tangential and sagittal components for the different RE groups are presented in Table 6.1. Mean values and standard deviations for the refractive components in the horizontal and superior retinal meridians are plotted in Figures 6.1 and 6.2 respectively.

Table 6.1: ***Descriptives of tangential and sagittal components from the Nasal, Central, Temporal and Superior retina for different RE groups from the right eyes of 1,603 12 year old children***

RE Groups	n	Tangential (D)				Sagittal (D)			
		Mean	SD	Min	Max	Mean	SD	Min	Max
Nasal									
M-H Myopia	28	-3.12	1.53	-7.87	-0.54	-2.90	1.88	-8.14	0.34
Low Myopia	136	-1.25	0.82	-3.55	0.82	-0.50	0.98	-3.51	1.63
Emmetropia	442	-0.39	0.55	-2.51	1.24	0.47	0.54	-2.09	2.04
Low Hyperopia	975	0.39	0.61	-1.37	3.35	1.32	0.62	-0.56	4.87
M-H Hyperopia	22	2.91	1.52	0.74	5.83	4.17	1.73	1.75	7.71
All Subjects	***1603***	***0.01***	***1.00***	***-7.87***	***5.83***	***0.90***	***1.10***	***-8.14***	***7.71***
Central									
M-H Myopia	28	-4.26	1.20	-8.71	-3.14	-4.35	1.25	-8.43	-2.96
Low Myopia	136	-1.43	0.75	-3.06	-0.11	-1.42	0.81	-3.14	-0.11
Emmetropia	442	0.18	0.31	-0.79	0.88	0.10	0.30	-0.88	0.86
Low Hyperopia	975	1.05	0.43	0.15	3.17	1.00	0.43	0.06	3.06
M-H Hyperopia	22	4.59	1.28	3.21	7.70	4.49	1.35	2.73	7.65
All Subjects	***1603***	***0.56***	***1.18***	***-8.71***	***7.70***	***0.50***	***1.18***	***-8.43***	***7.65***
Temporal									
M-H Myopia	28	-2.92	0.84	-5.25	-1.74	-2.36	1.32	-5.75	-0.47
Low Myopia	136	-1.40	0.74	-4.08	0.50	-0.14	0.94	-2.78	2.18
Emmetropia	442	-0.82	0.64	-4.21	0.85	0.72	0.62	-1.86	2.76
Low Hyperopia	975	-0.40	0.57	-2.37	1.90	1.46	0.67	-3.13	4.38
M-H Hyperopia	22	1.08	0.96	-0.65	3.51	3.78	1.36	1.82	6.63
All Subjects	***1603***	***-0.62***	***0.78***	***-5.25***	***3.51***	***1.09***	***1.03***	***-5.75***	***6.63***
Superior									
M-H Myopia	28	-3.78	1.33	-7.45	-1.40	-3.49	1.42	-8.05	-1.25
Low Myopia	136	-2.17	0.95	-4.82	0.42	-1.30	0.95	-3.51	0.70
Emmetropia	442	-1.35	0.82	-4.65	1.50	-0.03	0.71	-2.14	2.11
Low Hyperopia	975	-0.64	0.78	-4.10	3.07	0.92	0.78	-1.86	5.18
M-H Hyperopia	22	1.80	1.72	-0.57	5.45	4.20	1.73	1.70	6.81
All Subjects	***1603***	***-0.99***	***1.08***	***-7.45***	***5.45***	***0.44***	***1.26***	***-8.05***	***6.81***

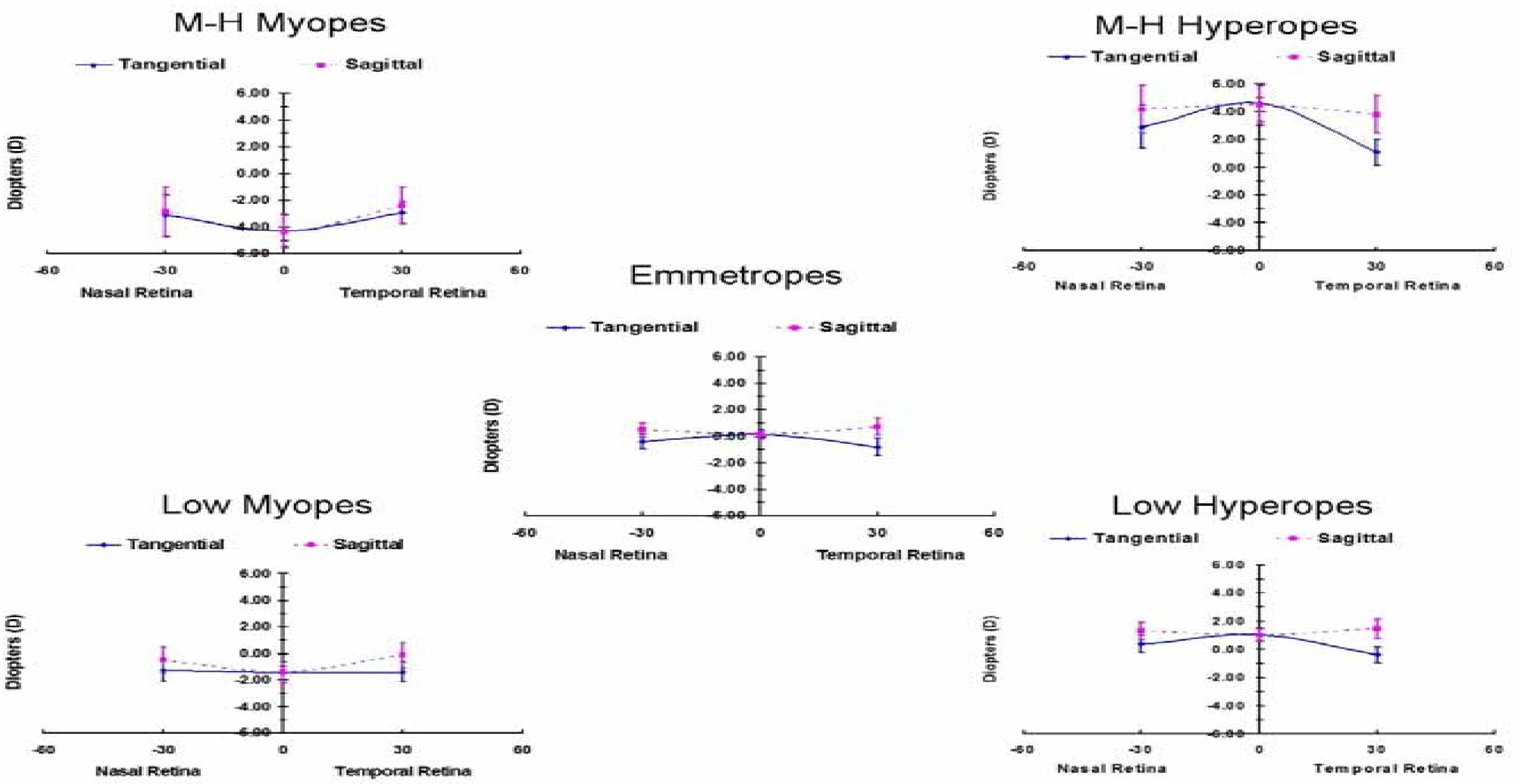

Figure 6.1: ***Mean off-axis refraction in dioptres of the horizontal retinal meridian (nasal, central and temporal retina) for different RE groups from the right eyes of 1,603 12 year old children. Each point represents the mean of all eyes from each group. The solid line represents the tangential (horizontal) meridian and the broken line indicates the sagittal (vertical) components***

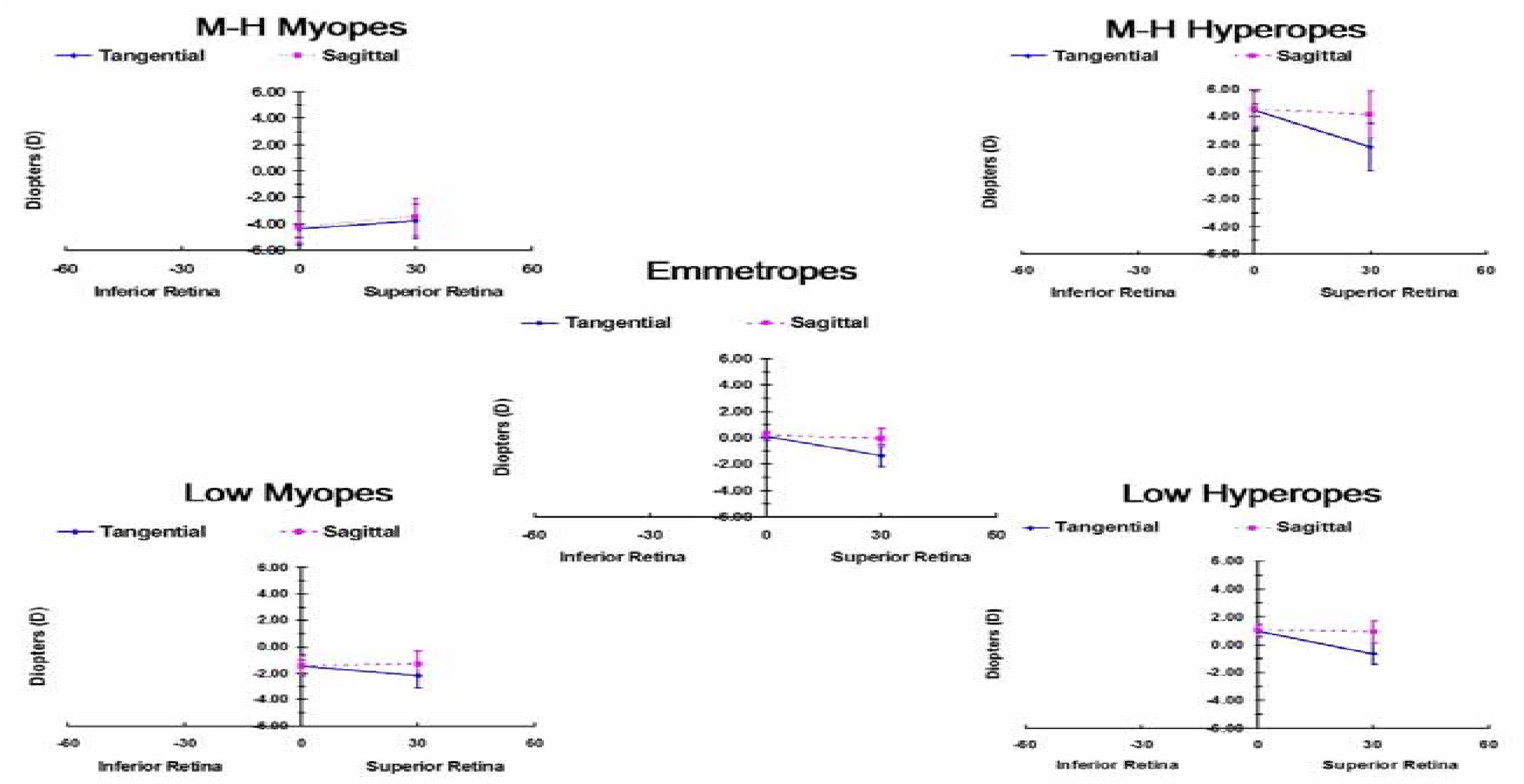

Figure 6.2: *Mean off-axis refraction in dioptres of the vertical retinal meridian (central and superior retina) for different RE groups from the right eyes of 1,603 12 year old children. Each point represents the mean of all eyes from each group. The solid line represents the tangential (horizontal) meridian and the broken line indicates the sagittal (vertical) components*

The type of astigmatism present at 30 degrees eccentricity was determined by comparing the position of the tangential and sagittal line foci to on-axis values. As seen in Figure 6.1, for the horizontal retina, different astigmatic patterns were observed in different RE groups. Moderate to high myopes exhibited compound myopic astigmatism in the periphery while moderate to high hyperopes presented compound hyperopic astigmatism. Low myopes had simple myopic astigmatism, while emmetropes and low hyperopes exhibited mixed astigmatism. Similar patterns were seen for the vertical retina (superior retina only, Figure 6.2). On average, moderate to high myopes had compound myopic astigmatism, moderate to high hyperopes had compound hyperopic astigmatism and emmetropes, low myopes and low hyperopes had simple hyperopic astigmatism.

The space between the sagittal and tangential lines describes the interval of Sturm (astigmatism) (Ferree 1933). Moderate to high myopes had less peripheral astigmatism in the horizontal and vertical meridians in comparison to other groups. Low myopes, emmetropes and low hyperopes had moderate peripheral astigmatism in both the horizontal and vertical meridians and moderate to high hyperopes had the highest amount of peripheral astigmatism in both meridians. Further analysis of peripheral astigmatism is presented in subsection 6.5.1.3. When comparing the magnitude of astigmatism in the nasal and temporal halves, an asymmetry was evident and was more pronounced for the moderate to high hyperopic eyes. In general, the temporal retina had higher levels of astigmatism than the nasal retina (0.50 D more). Asymmetry of the vertical retina could not be determined, as only the superior retina was measured in this study; however, the levels of astigmatism in the superior retina were similar in magnitude to the levels seen in the temporal retina.

The sagittal foci provide an estimate of the conformation and symmetry of the retina (Ferree *et al*. 1932; Ferree 1933). Horizontally, myopic eyes (moderate to high and low) had a prolate shape (difference between centre to periphery was on average -1.00 to -1.50 D) and in contrast moderate to high hyperopes had an oblate shape (difference between centre to periphery was on average 0.50 to 1.00 D). Using the same criteria, emmetropes and low hyperopes had a spherical to slight prolate shape (difference between centre to periphery -0.50 to -0.75 D). Vertically, moderate to high myopes also had a prolate shape whereas moderate to high hyperopes had an oblate shape. Further results regarding shape of the eye are given in subsection 6.5.1.3.

6.5.1.1 Skiagrams

The shape of the tangential and sagittal curves with eccentricity was used to classify the eyes into types of skiagrams as described by Rempt *et al.* (1971) (see Chapter 1, subsection 1.5). Only data from the horizontal retinal meridian (nasal and temporal retina) was used. While the majority of cases were classified into one of the five types described by Rempt *et al.* (1971), a small percentage of cases (1.5%) presented with a shape that was not previously described. These were classified into a new group called “Type VI”. They showed large asymmetry between the nasal and temporal retinal halves, and both the tangential and sagittal planes were either myopic or hyperopic in one quadrant in relation to the on-axis refraction and diagrammatically opposite in the other quadrant, resulting in a pattern of two parallel diagonal lines. Type VI cases resembled Type C skiagrams described by Ferree *et al.* (1932) wherein high asymmetry of the tangential and sagittal planes was observed between the nasal and temporal retinal halves (see Chapter 1, Figure 1.1C). The patterns of skiagrams for the entire population and for the different RE groups are presented in Table 6.2.

Table 6.2: ***Distribution of patterns of skiagrams for RE groups from the right eyes of 1,603 12 year old children. Types I – V as described by Rempt et al. (1971); Type VI (red text)***

RE Group	Type of Skiagrams												All Subjects
	Type I		Type II		Type III		Type IV		Type V		Type VI		
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
M-H Hyperopia	-	*0.0*	-	-	9	*40.9*	1	*4.5*	11	***50.0***	1	4.5	22
Low Hyperopia	4	*0.4*	-	-	290	*29.7*	579	***59.4***	91	*9.3*	11	1.1	975
Emmetropia	6	*1.4*	-	-	134	*30.3*	266	***60.2***	31	*7.0*	5	1.1	442
Low Myopia	56	***41.2***	-	-	39	*28.7*	31	*22.8*	3	*2.2*	7	5.1	136
M-H Myopia	26	***92.9***	-	-	2	*7.1*	-	-	-	-	-	0.0	28
All Subjects	**92**	**5.7**	**0**	**-**	**474**	**29.6**	**877**	**54.7**	**136**	**8.5**	**24**	**1.5**	**1,603**

When the population was considered as a whole, Type IV was the most frequently seen pattern (54.7% of cases) followed by Type III (29.6%). Type II was not seen in any of the eyes. Rather than using visual means, an automatic method of selection using logical conditions in Microsoft® Excel 2002 was used to classify a pattern into a skiagram type. In order for a pattern to be classified as Type II, the eye needs to have sagittal power of zero in both the nasal and temporal halves and the tangential power needs to be greater than zero in both halves. It is possible that adoption of this rule meant that there was not data that met the criteria. However, for classifying a pattern as Type V, a similar criterion was used (sagittal power equal to zero in both halves, while the tangential power was less than zero) and in this situation 1.5% of eyes met the criteria.

Interestingly, when considered on the basis of different RE groups, different patterns of skiagrams were observed (Figure 6.3). Moderate to high myopes had predominately Type I skiagrams (92.9%) and low myopes also had predominately Type I skiagrams (41.2%). However emmetropes and low hyperopes had predominately Type IV skiagrams (60.2% and 59.4%, respectively) and moderate to high hyperopes had predominately Type V and Type III skiagrams (50% and 40.9%). The least common type of skiagram in moderate to high myopic eyes and low myopic eyes was Type V (0.0% and 2.2% respectively), whilst the least common skiagram in emmetropic, low hyperopic and moderate to high hyperopic eyes was Type I (1.4%, 0.4% and 0.0% respectively).

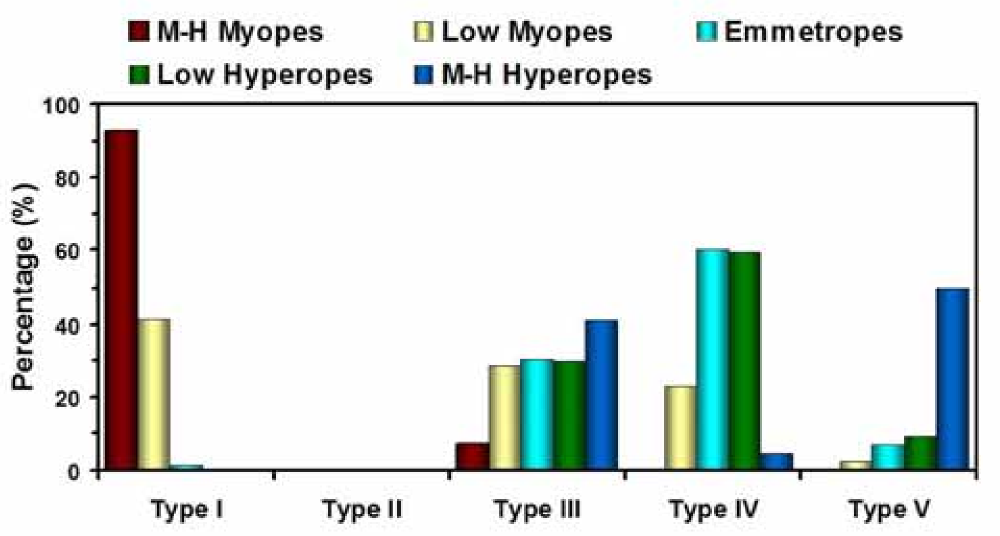

Figure 6.3: ***Distribution of types of skiagrams for different RE groups from the right eyes of 1,579 12 year old children. Bars indicate (%) of cases within each RE group. Cases presenting a Type VI skiagram have been omitted in this figure.***

6.5.1.2 Power Vectors (M)

Figures 6.4 and 6.5 present the M, J_0 and J_{45} vectors for various positions of eccentricity for the different RE groups in the horizontal and vertical retinal meridians. The on and off-axis M results from the right eyes of 1,603 12 year old children by RE groups are presented in Table 6.3.

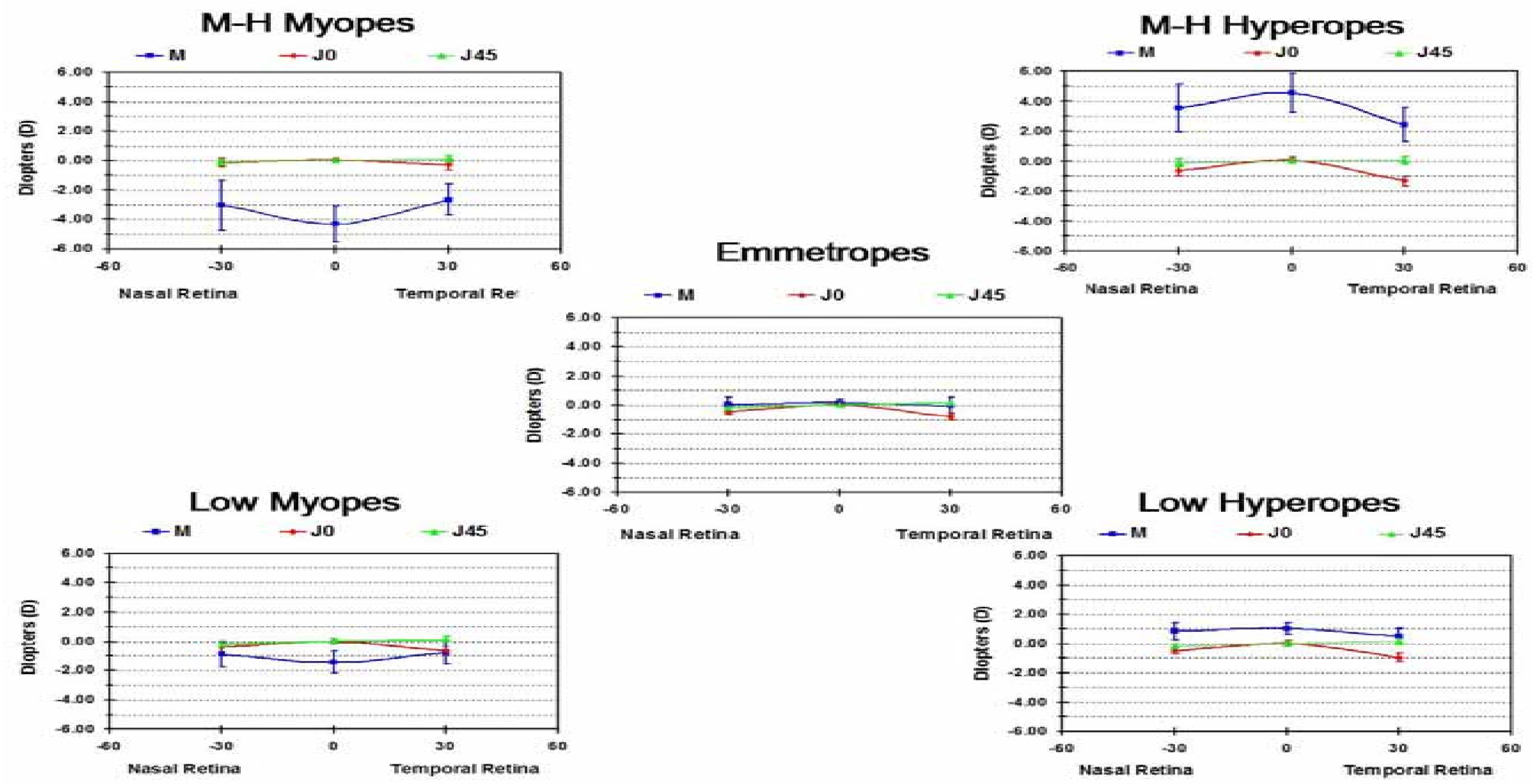

Figure 6.4: ***Off-axis refraction of the horizontal retinal meridian (nasal, central and temporal retina) for different RE groups from the right eyes of 1,603 12 year old children in power vectors (M, J_0 and J_{45})***

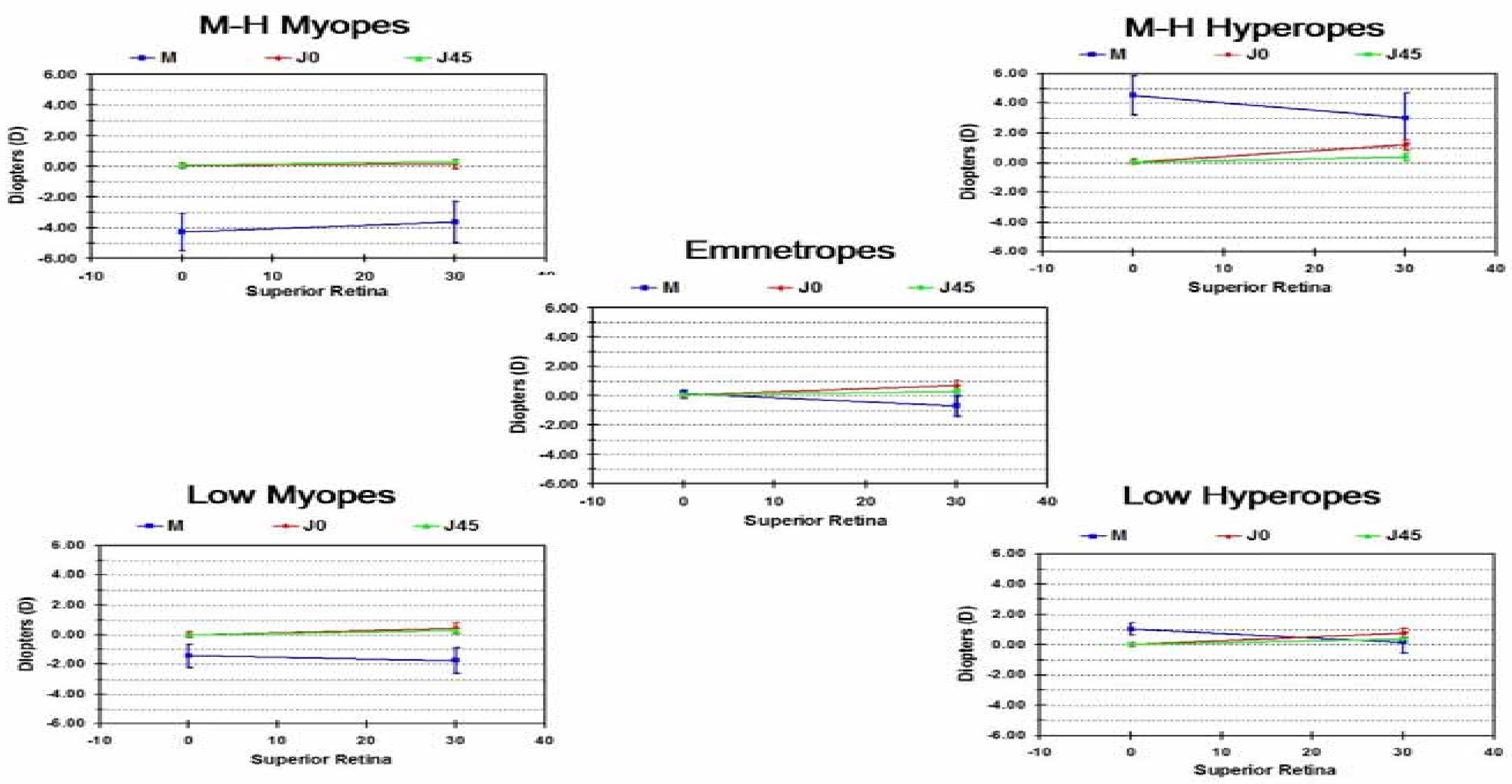

Figure 6.5: ***Off-axis refraction of the vertical retinal meridian (central and superior retina) for different RE groups from the right eyes of 1,603 12 year old children in power vectors (M, J_0 and J_{45})***

Table 6.3: ***Mean off-axis M component for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (D)					GLM (p-Value)	p-Value (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal M											
M-H Myopia	28	-3.01	1.69	-8.00	-0.10			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-0.87	0.86	-3.53	1.22		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.04	0.49	-1.68	1.45	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.86	0.58	-0.93	4.11		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	3.54	1.58	1.25	6.77		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.46	1.02	-8.00	6.77						
Central M											
M-H Myopia	28	-4.30	1.21	-8.57	-3.07			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-1.42	0.75	-2.94	-0.50		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.14	0.26	-0.49	0.49	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	1.03	0.41	0.50	2.98		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	4.54	1.30	3.01	7.68		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.53	1.17	-8.57	7.68						
Temporal M											
M-H Myopia	28	-2.64	1.05	-5.50	-1.11			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-0.77	0.79	-3.43	1.34		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	-0.05	0.58	-2.96	1.62	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.53	0.56	-2.25	3.10		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	2.43	1.13	0.71	5.07		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.23	0.86	-5.50	5.07						
Superior M											
M-H Myopia	28	-3.64	1.34	-7.75	-1.39			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-1.74	0.87	-3.98	0.10		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	-0.69	0.68	-3.39	1.30	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.14	0.71	-2.26	4.12		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	3.00	1.69	0.57	6.01		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	-0.27	1.12	-7.75	6.01						

The mean M values were significantly different for all on and off-axis positions between the RE groups (Gender-adjusted values General Linear Model [GLM] p=0.001; all differences significant, p<0.001). In addition, females had higher levels of M in the temporal retina (p=0.003), (estimated mean -0.14 D; 95% CI -0.22 to -0.7 D) than males (estimated mean -0.05 D; 95% CI -0.13 to 0.27 D), but no interaction was found between RE groups and gender (p=0.618).

A method used to determine the eyeball shape with mathematical models uses the mean SE (M vector) (Dunne 1995). To analyse whether differences in eye shape existed between the different RE groups, the algebraic difference between on and off-axis values was calculated (Mean relative off-axis M). A plot of the mean relative off-axis M values for the different RE groups in the horizontal and vertical retinal meridians is presented in Figure 6.6. The mean relative off-axis M values by RE groups and multiple comparisons are presented in Table 6.4.

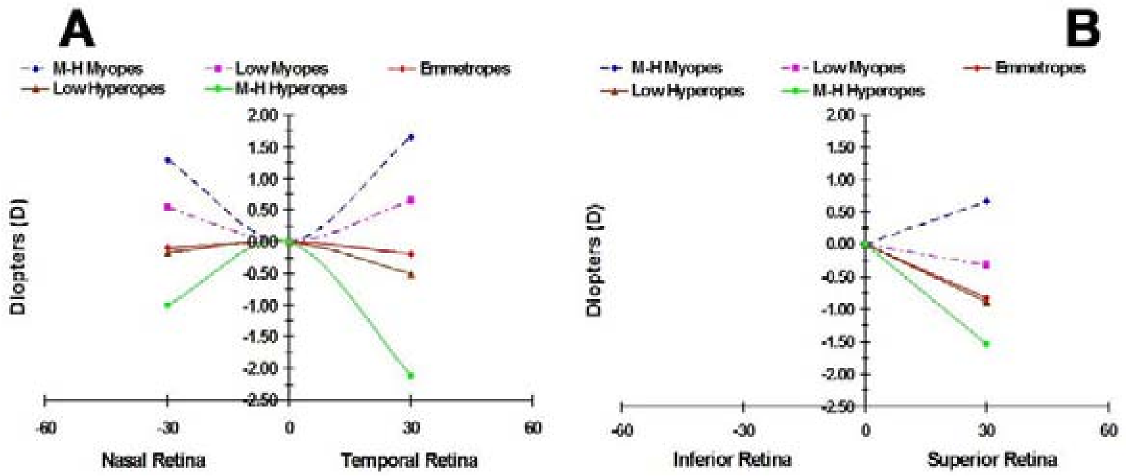

Figure 6.6: ***Mean relative off-axis M in dioptres from the right eyes of 1,603 12 year old children for RE groups and all subjects. Mean relative off-axis refraction at the nasal and temporal retina meridians (A) and superior retinal meridian (B)***

In the horizontal retinal meridian, myopic eyes were more hyperopic in the periphery (more prolate) than emmetropic and hyperopic eyes. Also hyperopic eyes were more myopic in the periphery (more oblate) than emmetropic and myopic eyes. In the superior retina, all RE groups except moderate to high myopes were myopic (oblate) in relation to the on-axis position. However, low myopes had the least myopic shift and moderate to high hyperopes had the greatest shift. Emmetropic eyes and low hyperopic eyes, on average, had closer values, which suggest that they have similar eyeball shapes. Whilst most RE groups had a quasi-symmetrical horizontal eyeball shapes, moderate to high hyperopes had an asymmetric retinal shape (Figure 6.6A).

Table 6.4: ***Mean relative off-axis M for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (D)					GLM (p value)	p-Value (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal mean relative M											
M-H Myopia	28	1.29	0.91	0.16	3.58	***0.001***		***0.003***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.55	0.81	-1.52	2.89		***0.003***		***0.000***	***0.000***	***0.000***
Emmetropia	442	-0.10	0.46	-1.63	1.32		***0.000***	***0.000***		0.063	***0.024***
Low Hyperopia	975	-0.17	0.46	-2.19	2.28		***0.000***	***0.000***	0.063		***0.041***
M-H Hyperopia	22	-1.00	1.27	-3.22	2.20		***0.000***	***0.000***	***0.024***	***0.041***	
All Subjects	1603	-0.07	0.60	-3.22	3.58						
Temporal mean relative M											
M-H Myopia	28	1.66	0.61	0.41	3.07	***0.001***		***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.65	0.70	-1.35	2.47		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	-0.19	0.56	-2.97	1.37		***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	-0.50	0.54	-4.33	1.17		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	-2.11	0.65	-4.09	-1.30		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	-0.30	0.73	-4.33	3.07						
Superior mean relative M											
M-H Myopia	28	0.67	0.66	-0.56	1.82	***0.001***		***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-0.32	0.83	-2.98	1.63		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	-0.83	0.65	-3.41	1.03		***0.000***	***0.000***		0.566	***0.017***
Low Hyperopia	975	-0.88	0.64	-3.16	2.70		***0.000***	***0.000***	0.566		***0.031***
M-H Hyperopia	22	-1.54	0.95	-2.98	0.67		***0.000***	***0.000***	***0.017***	***0.031***	
All Subjects	1603	-0.80	0.72	-3.41	2.70						

As expected, the gender-adjusted values of the mean relative nasal M were significantly different between most RE groups (GLM p=0.001; all differences significant, p<0.05), except between emmetropes and low hyperopes (p=0.063). Similarly, gender-adjusted values of the mean relative temporal M were significantly different between all RE groups (GLM p=0.001; all differences significant, p<0.001). Gender-adjusted values of the mean relative superior M were significantly different between RE groups (GLM p=0.001; all differences significant, p<0.05), except between emmetropes and low hyperopes (p=0.566).

6.5.1.3 Power Vectors (J_0 and J_{45})

The J_0 vector results for on and off-axis positions for the different RE groups are presented in Table 6.5. The mean values of J_0 increased for all the RE groups for all three off-axis positions. Additionally, in the horizontal retinal meridian, the mean on-axis J_0 values changed from positive (with-the-rule) on-axis astigmatism to negative (against-the-rule) off-axis astigmatism for all the RE groups. However, this shift was not observed for any of the RE groups in the superior retina (Figure 6.5).

Gender-adjusted multiple comparisons of the J_0 values revealed significant differences between all RE groups for the temporal and superior retinal positions (GLM p=0.001; all differences significant, p<0.001). However, for the nasal retina, gender-adjusted values of the J_0 vector were not significantly different between emmetropes, low hyperopes and moderate to high hyperopes (GLM p=0.001; p>0.05). It was also found that females had higher levels of J_0 in the superior retina (p=0.004), (estimated mean +0.67 D; 95% CI 0.63 to 0.71 D) than males (estimated mean +0.62 D; 95% CI 0.58 to 0.66 D), but no interaction was found between RE groups and gender (p=0.491).

Table 6.5: ***Mean off-axis J_0 component for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (D)					GLM (p-value)	p-Value (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal J_0											
M-H Myopia	28	-0.11	0.31	-0.74	0.59			***0.002***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-0.37	0.28	-0.92	0.68		***0.002***		0.166	***0.003***	***0.038***
Emmetropia	442	-0.43	0.24	-1.14	1.30	***0.001***	***0.000***	0.166		0.127	0.144
Low Hyperopia	975	-0.47	0.22	-1.29	0.68		***0.000***	***0.003***	0.127		0.275
M-H Hyperopia	22	-0.63	0.38	-1.13	0.67		***0.000***	***0.038***	0.144	0.275	
All Subjects	1603	-0.44	0.24	-1.29	1.30						
Central J_0											
M-H Myopia	28	0.05	0.18	-0.26	0.46			0.645	1.000	0.965	1.000
Low Myopia	136	-0.01	0.20	-0.45	0.49		0.645		0.125	0.449	0.669
Emmetropia	442	0.04	0.16	-0.47	0.47	***0.042***	1.000	0.125		0.481	0.997
Low Hyperopia	975	0.02	0.15	-0.46	0.46		0.965	0.449	0.481		0.951
M-H Hyperopia	22	0.05	0.19	-0.33	0.34		1.000	0.669	0.997	0.951	
All Subjects	1603	0.03	0.16	-0.47	0.49						
Temporal J_0											
M-H Myopia	28	-0.28	0.35	-0.80	0.41			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	-0.63	0.30	-1.32	0.19		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	-0.77	0.25	-1.53	0.13	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	-0.93	0.26	-1.61	1.10		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	-1.35	0.31	-1.99	-0.74		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	-0.86	0.30	-1.99	1.10						
Superior J_0											
M-H Myopia	28	0.14	0.30	-0.34	0.90			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.44	0.36	-0.72	1.36		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.66	0.35	-1.23	1.53	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.78	0.32	-0.24	2.19		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	1.20	0.34	0.56	1.90		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.71	0.36	-1.23	2.19						

Table 6.6 presents the mean values of the on and off-axis J_{45} vector for the different RE groups. Similar to J_0, the mean values of J_{45} were higher in the peripheral retina than the on-axis values. Higher values of the J_{45} vector were seen in the superior retina for all the different RE groups. Despite GLM analysis showing differences in the J_{45} vector between the different RE groups for the nasal (p=0.018), temporal (p=0.016) and superior (p=0.001) positions, multiple comparisons analysis revealed that significant differences existed only for low

hyperopes in comparison to emmetropes and low myopes for the superior retina only (p=0.001).

Table 6.6: ***Mean off-axis J_{45} component for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (D)					GLM (p value)	p-Value (G-H)				
	N	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal J_{45}											
M-H Myopia	28	-0.09	0.21	-0.48	0.37			0.101	0.066	0.084	0.978
Low Myopia	136	-0.20	0.22	-0.64	0.42		0.101		1.000	1.000	0.746
Emmetropia	442	-0.20	0.20	-0.71	0.55	***0.018***	0.066	1.000		0.986	0.703
Low Hyperopia	975	-0.19	0.19	-0.86	0.63		0.084	1.000	0.986		0.756
M-H Hyperopia	22	-0.13	0.26	-0.60	0.42		0.978	0.746	0.703	0.756	
All Subjects	1603	-0.19	0.20	-0.86	0.63						
Central J_{45}											
M-H Myopia	28	0.06	0.13	-0.12	0.39			0.250	0.507	0.754	0.905
Low Myopia	136	0.01	0.11	-0.32	0.35		0.250		0.654	0.098	0.944
Emmetropia	442	0.02	0.10	-0.40	0.41	***0.016***	0.507	0.654		0.372	0.999
Low Hyperopia	975	0.03	0.10	-0.28	0.43		0.754	0.098	0.372		1.000
M-H Hyperopia	22	0.03	0.13	-0.22	0.29		0.905	0.944	0.999	1.000	
All Subjects	1603	0.03	0.10	-0.40	0.43						
Temporal J_{45}											
M-H Myopia	28	0.12	0.22	-0.34	0.67			1.000	0.999	0.941	0.841
Low Myopia	136	0.12	0.20	-0.38	0.84		1.000		0.978	0.426	0.730
Emmetropia	442	0.13	0.21	-0.52	1.00	***0.049***	0.999	0.978		0.453	0.587
Low Hyperopia	975	0.15	0.21	-0.57	0.85		0.941	0.426	0.453		0.375
M-H Hyperopia	22	0.05	0.27	-0.67	0.41		0.841	0.730	0.587	0.375	
All Subjects	1603	0.14	0.21	-0.67	1.00						
Superior J_{45}											
M-H Myopia	28	0.31	0.19	0.05	0.87			0.913	1.000	0.887	0.927
Low Myopia	136	0.27	0.19	-0.27	0.72		0.913		0.550	***0.001***	0.533
Emmetropia	442	0.30	0.17	-0.25	0.80	***0.001***	1.000	0.550		***0.001***	0.807
Low Hyperopia	975	0.34	0.19	-0.42	1.03		0.887	***0.001***	***0.001***		0.997
M-H Hyperopia	22	0.36	0.25	-0.25	0.74		0.927	0.533	0.807	0.997	
All Subjects	1603	0.33	0.19	-0.42	1.03						

Differences between genders were found for J_{45}. Females had higher levels of J_{45} in the nasal retina (p<0.001), (estimated mean -0.18 D; 95% CI 0.21 to -0.16 D) than males (estimated mean -0.14 D; 95% CI -0.17 to -0.12 D), (and the interaction between RE groups and gender was significant [p=0.007]). Higher levels of nasal J_{45} were found in females than in males in the emmetropic (-0.23 ± 0.18 D vs -0.17 ± 0.22 D; p=0.005), low hyperopic (-0.22 ± 0.19 D vs -0.18 ± 0.19 D; p=0.005) and moderate to high hyperopic (-0.31 ± 0.15 D vs -0.23 ± 0.24 D; p=0.001) groups only. Females also had higher levels of J_{45} in the temporal (p<0.001) and superior retina (p=0.045) (temporal estimated mean +0.14 D; 95% CI 0.11 to 0.16 D; superior estimated mean +0.33 D; 95% CI 0.30 to 0.35 D) than males (temporal estimated mean +0.09 D; 95% CI 0.06 to 0.12 D; superior estimated mean +0.31 D; 95% CI 0.28 to 0.33 D), but no interactions were found between RE groups and gender (p=0.830, p=0.532 respectively).

To analyse the magnitude of astigmatism in the different RE groups, astigmatism (J) was calculated (equation 6.6). A plot of the mean astigmatism values for the different RE groups in the horizontal and vertical retinal meridians is presented in Figure 6.7. The mean astigmatism values by RE groups and multiple comparisons are also presented in Table 6.7.

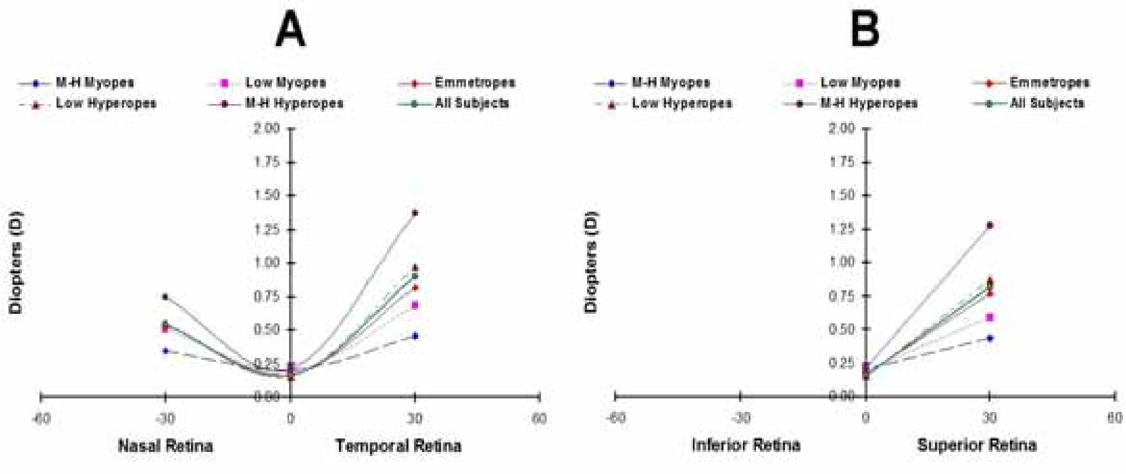

Figure 6.7: ***Mean astigmatism (J) in dioptres from the right eyes of 1,603 12 year old children for RE groups and all subjects. Astigmatism at the nasal and temporal retina (A) and superior retina (B)***

Table 6.7: ***Mean off-axis astigmatism (J) values (nasal, temporal and superior retina) for RE groups, GLM and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (D)					GLM (p-value)	p-Value (G-H)				
	N	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal Retina											
M-H Myopia	28	0.34	0.20	0.08	0.82			***0.004***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.50	0.22	0.05	0.99		***0.004***		0.442	0.160	***0.001***
Emmetropia	442	0.54	0.19	0.02	1.38	***0.001***	***0.000***	0.442		0.910	***0.004***
Low Hyperopia	975	0.55	0.19	0.02	1.34		***0.000***	0.160	0.910		***0.006***
M-H Hyperopia	22	0.75	0.24	0.32	1.28		***0.000***	***0.001***	***0.004***	***0.006***	
All Subjects	1603	0.54	0.20	0.02	1.38						
Temporal Retina											
M-H Myopia	28	0.46	0.23	0.06	0.82			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.69	0.27	0.02	1.32		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.81	0.24	0.02	1.54	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.97	0.23	0.17	1.64		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	1.37	0.32	0.78	1.99		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.90	0.27	0.02	1.99						
Superior Retina											
M-H Myopia	28	0.44	0.22	0.13	1.04			***0.019***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.59	0.29	0.04	1.39		***0.019***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.77	0.30	0.02	1.63	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.87	0.31	0.02	2.27		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	1.27	0.35	0.61	1.95		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.82	0.32	0.02	2.27						

Astigmatism in the three off-axis positions always increased in all RE groups. Moderate to high hyperopes had the highest magnitude of off-axis astigmatism from all the groups (nasal 0.75 D, temporal 1.37 D and superior 1.27 D), moderate to high myopes had the lowest magnitude from all groups (nasal 0.34 D, temporal 0.46 D and superior 0.44 D), while the magnitude of off-axis astigmatism in emmetropes was in the mid-point of these groups (nasal 0.54 D, temporal 0.81 D and superior 0.7 7D).

When the magnitude of off-axis astigmatism was compared between RE groups, differences were found for all three off-axis positions (Gender-adjusted GLM p=0.001) (Table 6.7).

In the nasal retina, moderate to high myopes and moderate to high hyperopes were significantly different to the other groups ($p<0.05$). Differences between low myopes, emmetropes and low hyperopes were not statistically significant ($p>0.05$). Gender-adjusted values of astigmatism in the temporal and superior retina were significantly different between all RE groups (GLM $p=0.001$; all differences significant, $p<0.001$, except in the superior retina between moderate to high myopes and low myopes $p=0.019$). Also, females had higher levels of astigmatism in the superior retina ($p=0.004$), (estimated mean +0.81 D; 95% CI 0.78 to 0.85 D) than males (estimated mean +0.76 D; 95% CI 0.73 to 0.81 D), but there was no interaction between gender and RE groups ($p=0.793$).

6.5.2 Off-Axis Aberrations

6.5.2.1 LOAs

The mean values of LO RMS (defocus and astigmatism) and HO RMS (3rd and 4th orders) for the horizontal and vertical retinal meridians for the different RE groups are plotted in Figures 6.8 and 6.9. Table 6.8 presents the mean values of defocus and astigmatism RMS from the nasal, temporal and superior retina for the different RE groups.

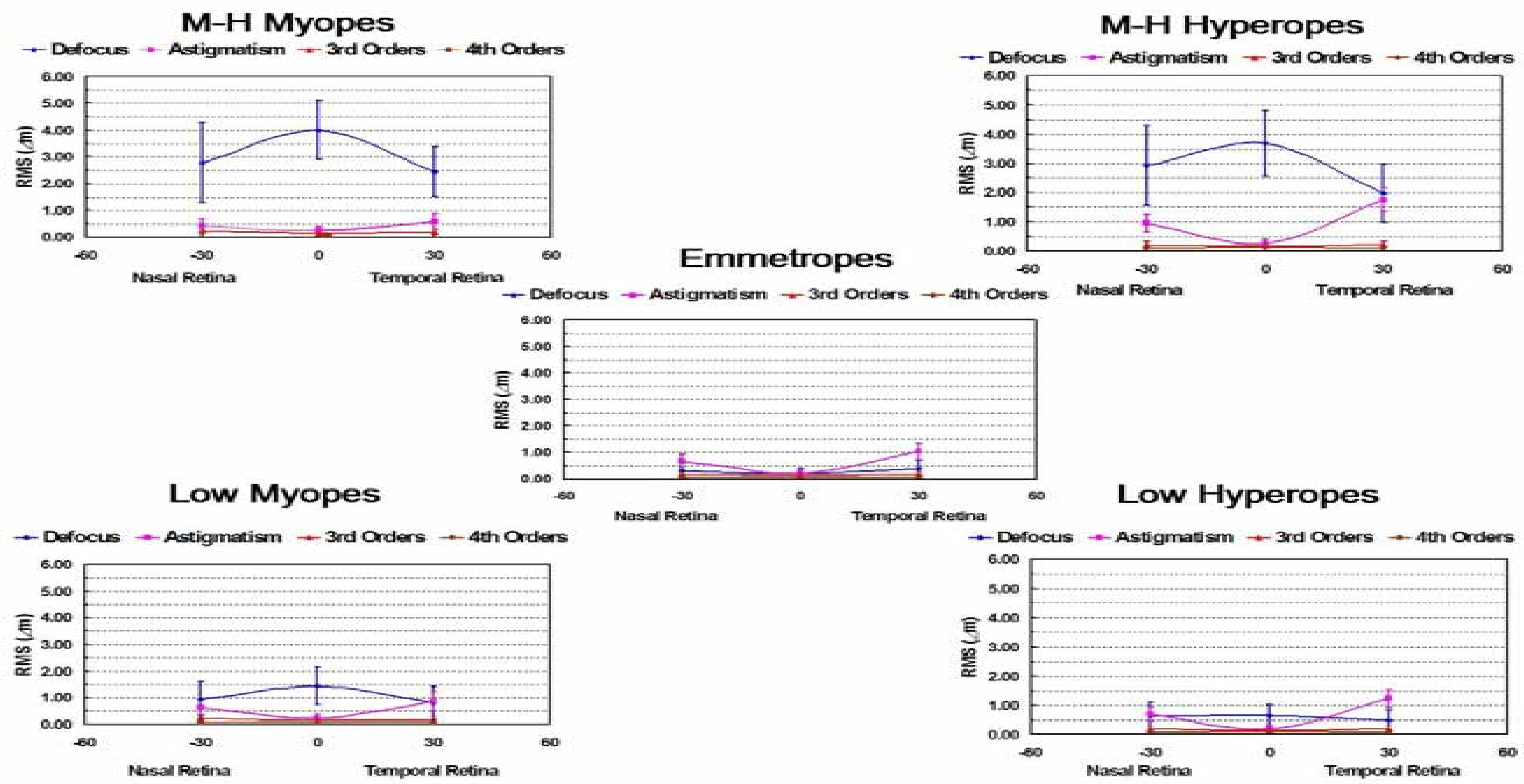

Figure 6.8: ***Off-axis defocus, astigmatism, 3rd and 4th orders RMS in microns the horizontal retinal meridian (nasal, central and temporal retina) from the right eyes of 1,603 12 year old children for different RE groups***

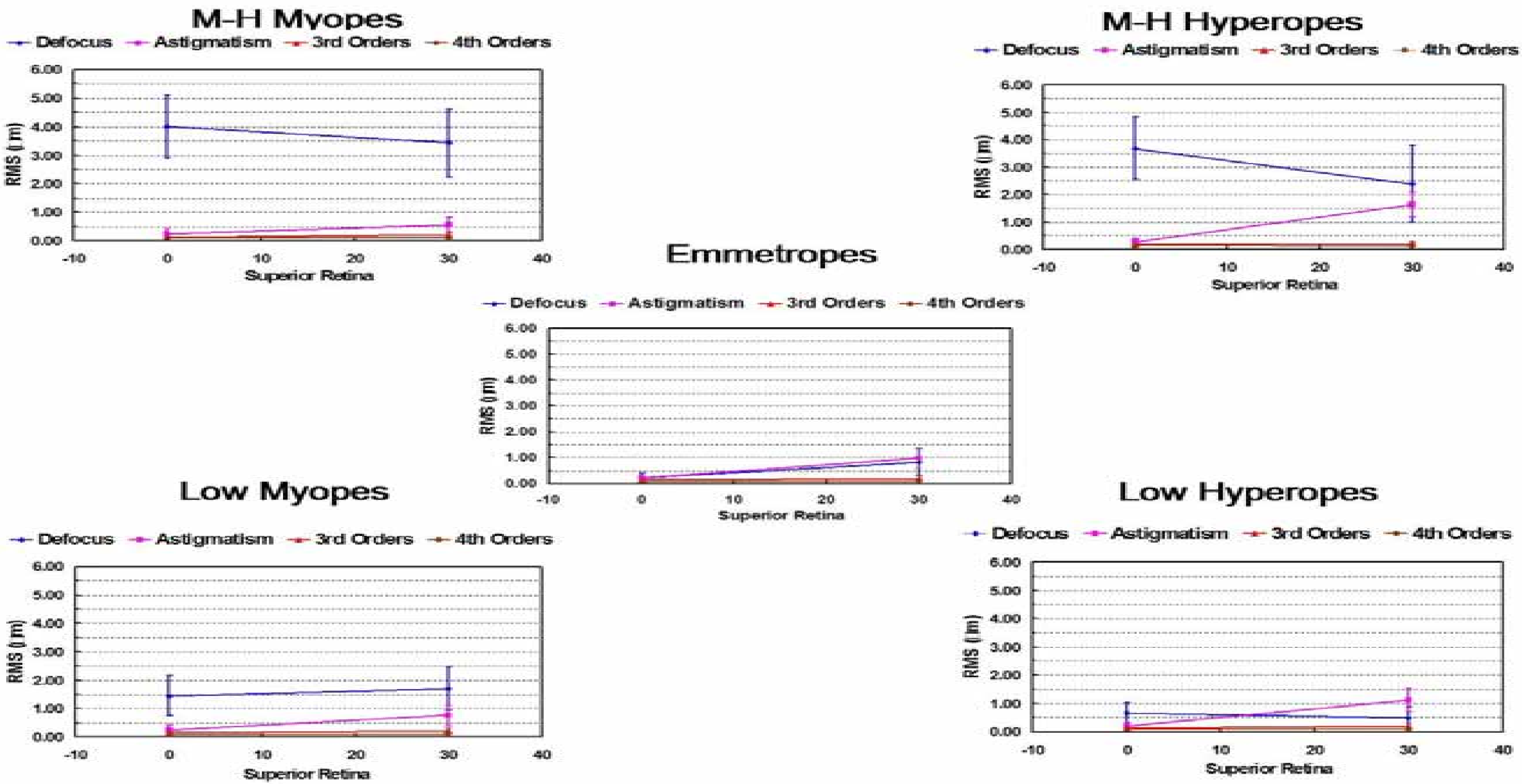

Figure 6.9: ***Off-axis defocus, astigmatism, 3rd and 4th orders RMS in microns of the vertical retinal meridian (central and superior retina) from the right eyes of 1,603 12 year old children for different RE groups***

Table 6.8: ***Mean off-axis defocus and astigmatism RMS for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (microns)					GLM (p-value)	p-Value (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal Defocus RMS											
M-H Myopia	28	2.79	1.50	0.09	7.26			***0.000***	***0.000***	***0.000***	0.997
Low Myopia	136	0.93	0.68	0.00	3.33		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.32	0.27	0.00	1.79	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.64	0.45	0.00	3.63		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	2.93	1.34	0.93	5.64		0.997	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.64	0.66	0.00	7.26						
Temporal Defocus RMS											
M-H Myopia	28	2.45	0.94	0.96	5.12			***0.000***	***0.000***	***0.000***	0.428
Low Myopia	136	0.83	0.62	0.01	3.33		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.38	0.32	0.00	2.32	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.48	0.38	0.00	4.12		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	1.98	0.99	0.56	4.07		0.428	***0.000***	***0.000***	***0.000***	
All Subjects	1603	0.54	0.53	0.00	5.12						
Superior Defocus RMS											
M-H Myopia	28	3.43	1.20	1.37	6.99			***0.000***	***0.000***	***0.000***	0.063
Low Myopia	136	1.71	0.76	0.22	3.86		***0.000***		***0.000***	***0.000***	0.212
Emmetropia	442	0.82	0.51	0.00	3.02	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	0.47	0.41	0.00	3.33		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	2.39	1.41	0.26	4.88		0.063	0.212	***0.000***	***0.000***	
All Subjects	1603	0.75	0.75	0.00	6.99						
Nasal Astigmatism RMS											
M-H Myopia	28	0.44	0.25	0.10	1.04			***0.004***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.64	0.28	0.06	1.26		***0.004***		0.442	0.160	***0.001***
Emmetropia	442	0.69	0.24	0.03	1.77	***0.001***	***0.000***	0.442		0.910	***0.004***
Low Hyperopia	975	0.70	0.25	0.03	1.71		***0.000***	0.160	0.910		***0.006***
M-H Hyperopia	22	0.96	0.30	0.41	1.63		***0.000***	***0.001***	***0.004***	***0.006***	
All Subjects	1603	0.69	0.25	0.03	1.77						
Temporal Astigmatism RMS											
M-H Myopia	28	0.58	0.30	0.07	1.05			***0.000***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.87	0.34	0.02	1.69		***0.000***		***0.000***	***0.000***	***0.000***
Emmetropia	442	1.04	0.31	0.02	1.97	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	1.24	0.30	0.21	2.10		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	1.75	0.40	1.00	2.54		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	1.15	0.35	0.02	2.54						
Superior Astigmatism RMS											
M-H Myopia	28	0.56	0.28	0.17	1.32			***0.019***	***0.000***	***0.000***	***0.000***
Low Myopia	136	0.75	0.37	0.05	1.77		***0.019***		***0.000***	***0.000***	***0.000***
Emmetropia	442	0.98	0.38	0.03	2.08	***0.001***	***0.000***	***0.000***		***0.000***	***0.000***
Low Hyperopia	975	1.12	0.40	0.03	2.89		***0.000***	***0.000***	***0.000***		***0.000***
M-H Hyperopia	22	1.62	0.44	0.78	2.49		***0.000***	***0.000***	***0.000***	***0.000***	
All Subjects	1603	1.05	0.41	0.03	2.89						

As expected, off-axis values of astigmatism RMS were higher than on-axis (for on-axis values see Chapter 4, Table 4.20). Third and 4th orders RMS also increased with eccentricity; however, their magnitude was small.

As expected, moderate to high myopes and moderate to high hyperopes had greater levels of defocus RMS for all off-axis positions. The gender-adjusted values of defocus RMS in the nasal and temporal retina were significantly different between RE groups (GLM $p=0.001$; all differences significant, $p<0.001$) except between moderate to high myopes and moderate to high hyperopes ($p>0.05$). In the superior retina, the values for defocus RMS were also significantly different, except between moderate to high hyperopes and low myopes ($p=0.212$) and between moderate to high hyperopes and moderate to high myopes ($p=0.063$). Off-axis astigmatism RMS values were higher in the hyperopic groups and lower in the emmetropic and myopic groups. Gender-adjusted values of astigmatism RMS in the temporal and superior retina were significantly different between all RE groups (GLM $p=0.001$; all differences significant, $p<0.001$) and in the nasal retina, differences were significant for some groups except between low myopes, emmetropes and low hyperopes ($p>0.05$). Females also had higher levels of astigmatism RMS in the superior retina ($p=0.004$), (estimated mean 1.03 μm; 95% CI 0.98 to 1.08 μm) than males (estimated mean 0.76 μm; 95% CI 0.93 to 1.03 μm), but no interaction was found between RE groups and gender ($p=0.793$).

6.5.2.2 HOAs

Figures 6.10 and 6.11 show the mean values of 3rd and 4th orders RMS across the horizontal and vertical meridians for all the RE groups. The mean values of coma RMS and 3rd orders RMS across the horizontal and superior retinal meridians for all the RE groups are presented in Table 6.9.

Table 6.9: ***Mean off-axis coma and 3rd orders RMS for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (microns)					GLM (p value)	p-Value (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal Coma RMS											
M-H Myopia	28	0.23	0.07	0.12	0.46			0.985	0.077	0.072	0.372
Low Myopia	136	0.22	0.10	0.04	0.55		0.985		***0.010***	***0.006***	0.469
Emmetropia	442	0.19	0.08	0.01	0.63	***0.001***	0.077	***0.010***		1.000	0.985
Low Hyperopia	975	0.19	0.08	0.02	0.58		0.072	***0.006***	1.000		0.984
M-H Hyperopia	22	0.18	0.11	0.01	0.45		0.372	0.469	0.985	0.984	
All Subjects	1603	0.19	0.08	0.01	0.63						
Temporal Coma RMS											
M-H Myopia	28	0.16	0.07	0.08	0.34			1.000	0.999	1.000	0.978
Low Myopia	136	0.16	0.10	0.00	0.69		1.000		1.000	0.999	0.922
Emmetropia	442	0.16	0.08	0.01	0.52	0.921	0.999	1.000		0.987	0.896
Low Hyperopia	975	0.16	0.09	0.01	1.43		1.000	0.999	0.987		0.937
M-H Hyperopia	22	0.18	0.08	0.04	0.42		0.978	0.922	0.896	0.937	
All Subjects	1603	0.16	0.09	0.00	1.43						
Superior Coma RMS											
M-H Myopia	28	0.18	0.08	0.06	0.33			0.996	1.000	0.884	0.965
Low Myopia	136	0.18	0.10	0.02	0.49		0.996		0.891	0.230	0.856
Emmetropia	442	0.17	0.09	0.01	0.49	0.123	1.000	0.891		0.302	0.968
Low Hyperopia	975	0.16	0.10	0.00	1.33		0.884	0.230	0.302		1.000
M-H Hyperopia	22	0.16	0.10	0.03	0.38		0.965	0.856	0.968	1.000	
All Subjects	1603	0.17	0.10	0.00	1.33						
Nasal 3rd Orders RMS											
M-H Myopia	28	0.24	0.07	0.14	0.46			0.998	0.232	0.303	0.821
Low Myopia	136	0.25	0.10	0.08	0.58		0.998		***0.002***	***0.003***	0.654
Emmetropia	442	0.21	0.08	0.04	0.63	***0.001***	0.232	***0.002***		0.975	1.000
Low Hyperopia	975	0.22	0.08	0.04	0.78		0.303	***0.003***	0.975		1.000
M-H Hyperopia	22	0.22	0.11	0.09	0.47		0.821	0.654	1.000	1.000	
All Subjects	1603	0.22	0.08	0.04	0.78						
Temporal 3rd Orders RMS											
M-H Myopia	28	0.20	0.09	0.11	0.42			1.000	1.000	1.000	0.743
Low Myopia	136	0.20	0.11	0.04	0.71		1.000		1.000	0.999	0.613
Emmetropia	442	0.20	0.09	0.02	0.56	0.668	1.000	1.000		0.978	0.525
Low Hyperopia	975	0.20	0.10	0.03	1.81		1.000	0.999	0.978		0.610
M-H Hyperopia	22	0.23	0.09	0.09	0.50		0.743	0.613	0.525	0.610	
All Subjects	1603	0.20	0.10	0.02	1.81						
Superior 3rd Orders RMS											
M-H Myopia	28	0.22	0.06	0.09	0.35			1.000	0.843	0.448	0.842
Low Myopia	136	0.22	0.10	0.04	0.54		1.000		0.627	0.136	0.793
Emmetropia	442	0.21	0.09	0.02	0.49	0.107	0.843	0.627		0.590	0.984
Low Hyperopia	975	0.20	0.10	0.02	1.50		0.448	0.136	0.590		1.000
M-H Hyperopia	22	0.20	0.09	0.08	0.41		0.842	0.793	0.984	1.000	
All Subjects	1603	0.20	0.10	0.02	1.50						

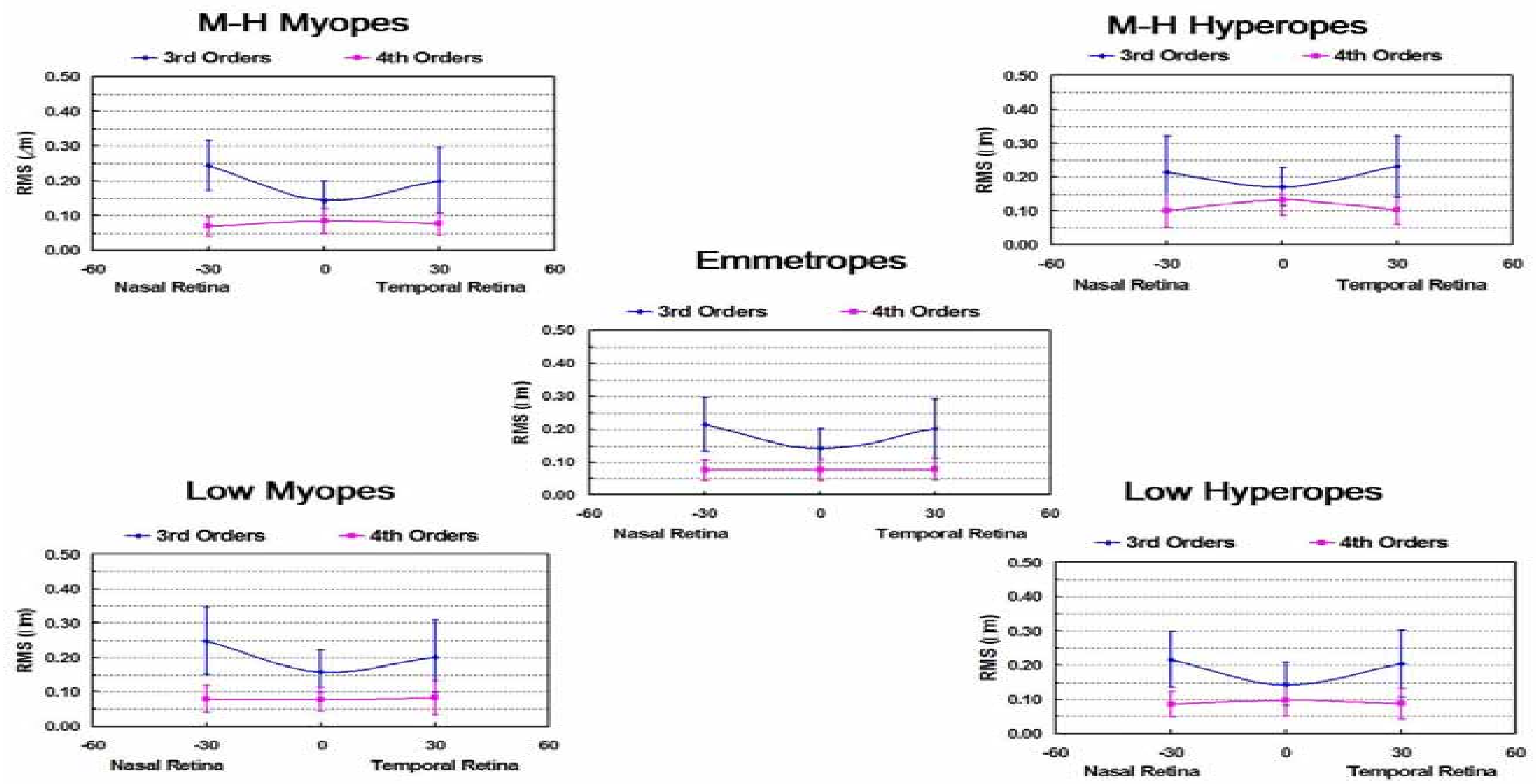

Figure 6.10: ***Off-axis 3rd and 4th orders RMS in microns of the horizontal retinal meridian (nasal, central and temporal retina) from the right eyes of 1,603 12 year old children for different RE groups***

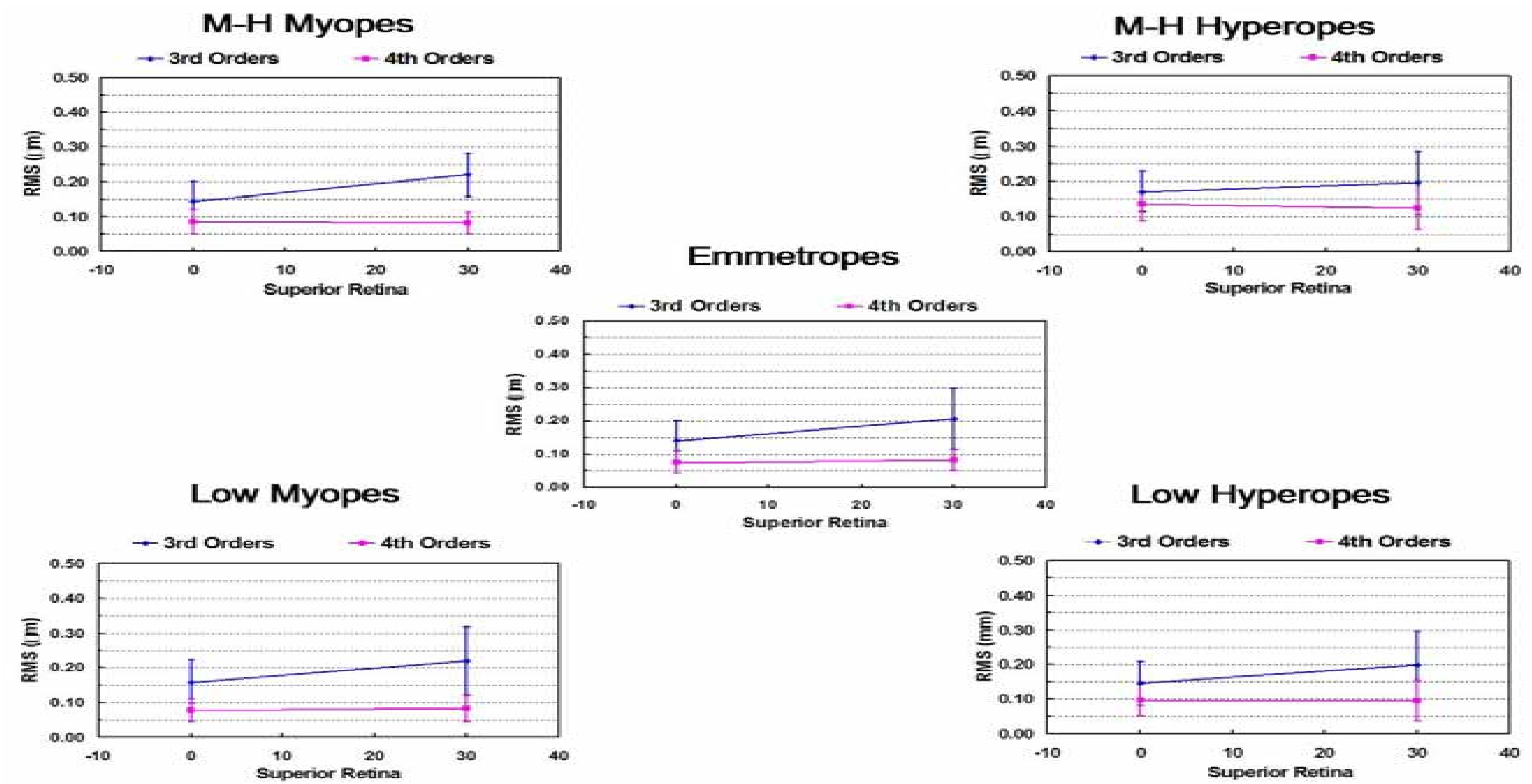

Figure 6.11:*Off-axis 3rd and 4th orders RMS in microns of the vertical retinal meridian (central and superior retina) from the right eyes of 1,603 12 year old children for different RE groups*

On average the mean values of off-axis coma RMS and 3rd orders RMS were two times higher than the on-axis mean values for all the RE groups (Chapter 4, Table 4.20). No differences were found between RE groups in the levels of coma RMS and 3rd orders RMS in the temporal and superior retina (Gender-adjusted GLM p=0.921 and p=0.123, respectively for coma RMS), (Gender-adjusted GLM p=0.668 and p=0.107, respectively for 3rd orders RMS). However, in the nasal retina, low myopes had significantly higher levels of coma and 3rd orders RMS than emmetropes (p=0.01 and p=0.002 respectively) and low hyperopes (p=0.006 and p=0.003 respectively). The only difference in off-axis coma and 3rd orders RMS between genders was found for the nasal retina. Females had lower levels of coma RMS in the nasal retina (p=0.011), (estimated mean 0.20 μm; 95% CI 0.19 to 0.21 μm) than males (estimated mean 0.21 μm; 95% CI 0.20 to 0.22 μm), but no interaction was found between RE groups and gender (p=0.09). Also, females had lower levels of 3rd orders RMS in the nasal retina (p=0.019), (estimated mean 0.22 μm; 95% CI 0.21 to 0.23 μm) than males (estimated mean 0.23 μm; 95% CI 0.22 to 0.24 μm), but no interaction was found between RE groups and gender (p=0.08).

The mean values of off-axis SA and 4th orders RMS for all the RE groups are presented in Table 6.10. In comparison to 3rd order, 4th orders RMS did not increase with eccentricity. Some differences in the mean values of SA and 4th orders RMS were found between RE groups (Table 6.10), however, the mean values of those aberrations were very small. Similar to on-axis aberrations (Chapter 4, Table 4.20), hyperopic eyes had higher levels of off-axis SA and 4th orders RMS than emmetropic and myopic eyes but the differences were not always statistically significant.

Table 6.10: ***Mean off-axis SA and 4th orders RMS for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (microns)					GLM (p-value)	p-Value (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal SA RMS											
M-H Myopia	28	0.03	0.03	0.00	0.11			0.490	0.466	***0.002***	***0.005***
Low Myopia	136	0.04	0.03	0.00	0.13		0.490		1.000	***0.000***	***0.026***
Emmetropia	442	0.04	0.03	0.00	0.14	***0.001***	0.466	1.000		***0.000***	***0.021***
Low Hyperopia	975	0.05	0.04	0.00	0.23		***0.002***	***0.000***	***0.000***		0.314
M-H Hyperopia	22	0.07	0.04	0.01	0.16		***0.005***	***0.026***	***0.021***	0.314	
All Subjects	1603	0.05	0.03	0.00	0.23						
Temporal SA RMS											
M-H Myopia	28	0.04	0.03	0.00	0.11			0.998	1.000	0.577	0.131
Low Myopia	136	0.04	0.03	0.00	0.17		0.998		0.995	0.221	0.120
Emmetropia	442	0.04	0.03	0.00	0.12	***0.001***	1.000	0.995		***0.000***	0.082
Low Hyperopia	975	0.04	0.04	0.00	0.54		0.577	0.221	***0.000***		0.345
M-H Hyperopia	22	0.06	0.04	0.00	0.13		0.131	0.120	0.082	0.345	
All Subjects	1603	0.04	0.03	0.00	0.54						
Superior SA RMS											
M-H Myopia	28	0.04	0.04	0.00	0.13			0.999	0.998	0.265	0.168
Low Myopia	136	0.05	0.03	0.00	0.18		0.999		1.000	***0.001***	0.159
Emmetropia	442	0.05	0.03	0.00	0.17	***0.001***	0.998	1.000		***0.000***	0.159
Low Hyperopia	975	0.06	0.05	0.00	0.76		0.265	***0.001***	***0.000***		0.522
M-H Hyperopia	22	0.08	0.07	0.00	0.29		0.168	0.159	0.159	0.522	
All Subjects	1603	0.05	0.04	0.00	0.76						
Nasal 4th Orders RMS											
M-H Myopia	28	0.07	0.03	0.02	0.14			0.369	0.727	***0.021***	0.082
Low Myopia	136	0.08	0.04	0.01	0.26		0.369		0.724	0.403	0.384
Emmetropia	442	0.08	0.03	0.01	0.21	***0.001***	0.727	0.724		***0.000***	0.178
Low Hyperopia	975	0.09	0.04	0.01	0.35		***0.021***	0.403	***0.000***		0.685
M-H Hyperopia	22	0.10	0.05	0.02	0.20		0.082	0.384	0.178	0.685	
All Subjects	1603	0.08	0.04	0.01	0.35						
Temporal 4th Orders RMS											
M-H Myopia	28	0.08	0.03	0.02	0.15			0.921	0.999	0.522	0.175
Low Myopia	136	0.08	0.05	0.02	0.49		0.921		0.865	0.934	0.367
Emmetropia	442	0.08	0.03	0.02	0.29	***0.004***	0.999	0.865		***0.002***	0.122
Low Hyperopia	975	0.09	0.04	0.02	0.87		0.522	0.934	***0.002***		0.496
M-H Hyperopia	22	0.10	0.04	0.04	0.17		0.175	0.367	0.122	0.496	
All Subjects	1603	0.08	0.04	0.02	0.87						
Superior 4th Orders RMS											
M-H Myopia	28	0.08	0.03	0.02	0.15			0.994	0.997	0.153	***0.030***
Low Myopia	136	0.08	0.04	0.02	0.29		0.994		1.000	***0.017***	***0.034***
Emmetropia	442	0.08	0.03	0.03	0.22	***0.001***	0.997	1.000		***0.000***	***0.027***
Low Hyperopia	975	0.10	0.06	0.01	1.19		0.153	***0.017***	***0.000***		0.191
M-H Hyperopia	22	0.12	0.06	0.05	0.32		***0.030***	***0.034***	***0.027***	0.191	
All Subjects	1603	0.09	0.05	0.01	1.19						

In Chapters 4 and 5, the magnitude of 5th and 6th order on-axis aberrations was very small in both cohorts of 12 year old and 6 year old children. Because of the small contribution of those orders into the optical quality of the eye, they were not analysed independently; instead, 3rd, 4th, 5th and 6th order aberrations were grouped as HO RMS. The mean values of the off-axis HO RMS for the different RE groups are presented in Table 6.11.

Table 6.11: ***Mean off-axis HO RMS for RE groups and multiple comparisons from the right eyes of 1,603 12 year old children***

RE Groups	All Subjects (microns)					GLM (p-value)	p-Values (G-H)				
	n	Mean	SD	Min	Max		M-H Myopia	Low Myopia	Emmetropia	Low Hyperopia	M-H Hyperopia
Nasal HO RMS											
M-H Myopia	28	0.26	0.07	0.15	0.48	***0.001***		0.956	0.481	0.772	0.998
Low Myopia	136	0.27	0.10	0.10	0.60		0.956		***0.002***	***0.016***	0.921
Emmetropia	442	0.24	0.08	0.09	0.64		0.481	***0.002***		0.518	0.960
Low Hyperopia	975	0.24	0.08	0.07	0.84		0.772	***0.016***	0.518		0.996
M-H Hyperopia	22	0.25	0.10	0.13	0.49		0.998	0.921	0.960	0.996	
All Subjects	1603	0.24	0.08	0.07	0.84						
Temporal HO RMS											
M-H Myopia	28	0.22	0.09	0.12	0.43	0.348		1.000	1.000	0.995	0.480
Low Myopia	136	0.23	0.11	0.08	0.94		1.000		0.998	0.999	0.401
Emmetropia	442	0.23	0.08	0.07	0.61		1.000	0.998		0.783	0.232
Low Hyperopia	975	0.23	0.10	0.06	2.06		0.995	0.999	0.783		0.371
M-H Hyperopia	22	0.26	0.08	0.17	0.50		0.480	0.401	0.232	0.371	
All Subjects	1603	0.23	0.10	0.06	2.06						
Superior HO RMS											
M-H Myopia	28	0.24	0.06	0.12	0.36	0.605		1.000	0.933	0.890	0.999
Low Myopia	136	0.24	0.10	0.08	0.59		1.000		0.723	0.609	1.000
Emmetropia	442	0.23	0.09	0.07	0.51		0.933	0.723		0.999	0.939
Low Hyperopia	975	0.23	0.11	0.07	1.87		0.890	0.609	0.999		0.917
M-H Hyperopia	22	0.25	0.09	0.12	0.50		0.999	1.000	0.939	0.917	
All Subjects	1603	0.23	0.10	0.07	1.87						

In comparison to on-axis HO RMS (Chapter 4, Table 4.20), off-axis HO RMS increased by approximately 50% for all RE groups. No differences in the levels of off-axis HO RMS were found between RE groups in the temporal and superior retina (Gender-adjusted GLM p=0.348 and p=0.605 respectively).

However, in the nasal retina, low myopes had statistically significantly higher levels of HO RMS than emmetropes (p=0.002) and low hyperopes (p=0.016). Finally, females had lower levels of HO RMS in the nasal retina (p=0.028), (estimated mean 0.25 μm; 95% CI 0.24 to 0.26 μm) than males (estimated mean 0.26 μm; 95% CI 0.25 to 0.27 μm), but no interaction was found between RE groups and gender (p=0.107).

6.6 DISCUSSION

Despite the study of the characteristics of off-axis refraction (principally off-axis astigmatism) of the human eye, dating back to the XVIII century (Ames and Proctor 1921), it was not until a few years ago that vision scientists became aware of the potential role that the peripheral retina could play in regulating eye growth and the development of RE. Furthermore, from the data obtained from studies conducted primarily in primates, it appears probable that the progression of REs in humans could be retarded or controlled by optically altering the characteristics of off-axis refraction (Wallman and Winawer 2004; Charman *et al.* 2006; Smith EL III *et al.* 2006).

Whilst various methods are available to determine the patterns of off-axis refraction (Table B1 in Appendix B), this study used the commercially-available Shack-Hartmann aberrometer because of its high accuracy and reliability in obtaining off-axis refraction (Lundström *et al*. 2005B) and because it also allowed measurements of off-axis HO aberrations. However, the current study still suffered from limitations: firstly off-axis measurements were limited to only three retinal quadrants (nasal, temporal and superior) and secondly, measurements were obtained from one single point (30 degrees) in each of the retinal quadrants. Aberrometry measurements of the inferior retina could not be obtained without manual retraction of the upper lid and it was considered that such an approach may impact on the results, due to possible mechanical forces on the eye and, hence, this position was not included in the study. It was also determined that the best angle to measure would be 30 degrees (which corresponds to the mid-point from the fovea to the equator [Lotmar 1971]) due to the following reasons:

1. choosing a larger angle such as 60 degrees or a smaller angle such as 10 degrees could not have allowed for identification of any differences between RE groups because, at those eccentricities, REs are similar between groups (Millodot 1981; Charman and Jennings 1982), and

2. previous studies have reported on angles at or close to the 30 degree angle chosen for the current study (Millodot 1981; Mutti *et al.* 2000B; Gustafsson *et al.* 2001; Atchison *et al.* 2006B).

6.6.1 Off-Axis Refraction

By using a similar approach as Ferree *et al.* (1931). Ferree *et al.* (1932), Ferree (1933), Hoogerheide *et al.* (1971) and Rempt *et al.* (1971). the characteristics of the off-axis refraction in this sample of 1,603 12 year old children were analysed. As with previous studies, off-axis refraction in the horizontal retinal meridian showed three distinct patterns: mixed astigmatism, myopic astigmatism and hyperopic astigmatism. On average, emmetropic and low hyperopic eyes showed mixed astigmatism in the periphery; myopic eyes had myopic astigmatism and moderate to high hyperopes showed hyperopic astigmatism. In the superior retina slight differences from the horizontal off-axis refraction patterns were observed. Emmetropic, low hyperopic, moderate to high hyperopic and low myopic eyes showed, on average, hyperopic astigmatism, whilst moderate to high myopic eyes showed myopic off-axis astigmatism. A more detailed discussion about off-axis astigmatism is presented in subsection 6.6.3.

One of the advantages of using skiagrams when analysing the characteristics of off-axis refraction is that they provide an easy to understand graphical description of the symmetry and power of the optical system in the periphery. Data from the horizontal meridian was used for the analysis. In this study, moderate to high hyperopic eyes were found to have the most asymmetrical refractive systems. It is possible that this was the result of differences in the magnitude of the angle alpha (Millodot 1981), eye rotation (Dunne 1993), tilt of the crystalline lens (Ferree *et al.* 1932; Dunne 1995; Atchison *et al.* 2006A) or a combination of these variables in the different RE groups. This could also explain the increased asymmetry in the small number of cases with Type VI skiagrams found in this study.

When eyes were grouped into types of skiagrams, some similarities were observed with previous results in adults (Rempt *et al.* 1971). Type I skiagram (both tangential and sagittal planes becoming less myopic in the periphery) was present almost exclusively in myopic eyes (93% moderate to high myopes, 41% low myopes), while Type V (both tangential and sagittal planes becoming less hyperopic in the periphery) skiagram was present almost exclusively in moderate to high hyperopic eyes (50%). Type IV skiagram (the tangential plane becoming more myopic and the sagittal plane becoming more hyperopic in the periphery), also called the “normal skiagram” by Rempt *et al.*

(1971), was present in the majority of emmetropic and low hyperopic eyes (60%). Interestingly, Type III skiagram (the sagittal plane becoming more hyperopic in the periphery while one half of the tangential becoming more hyperopic and the other half more myopic in the periphery) was present in all RE groups and not just in emmetropic eyes as reported by Rempt *et al*. (1971).

It should be noted that differences in the distribution of skiagrams observed between our study and that from Rempt et al. (1971) could have been the result of the differences in methods used to categorise skiagrams types in both studies. Whilst in Rempt et al. (1971) visual means were used (based on the overall shape of the skiagram), in our study we used computer-generated logical algorithms (using absolute values). In addition, although there was a small error associated with the refractive error measurements with the COAS (CR 0.23D [95% CI -0.03 to 0.03]), which our algorithm did not take in consideration. After considering the differences in methodology used in both studies, we decided to not include a tolerance value around zero power in the algorithm.

A different approach to describe the differences in off-axis refraction is by the analysis of the relative SE (in this study the "M relative"). Using this method, the resultant off-axis RE, after correction of the foveal RE, can be determined and, additionally, an estimate of the ocular shape can also be obtained (Dunne 1995). Based on the M relative, myopic eyes had, on average, peripheral hyperopic error ranging from 0.55 to 1.66 D in the horizontal retinal meridian, whereas emmetropic and hyperopic eyes had, on average, myopic RE from -0.10 to -2.00 D. Superiorly, myopic RE ranging from

-0.32 to -1.54 D was present in most RE groups except in moderate to high myopic eyes, which had hyperopic RE (0.67 D).

These results were in agreement with previous studies measuring off-axis refraction at 30 degrees (Love *et al.* 2000; Mutti *et al.* 2000B; Atchison *et al.* 2005B; Atchison *et al.* 2006B). Mutti *et al.* (2000B) reported relative peripheral hyperopia (0.80 ± 1.29 D) in myopic children at 30 degrees in the temporal retina, whilst relative peripheral myopia was present in emmetropic (-0.41 ± 0.75 D) and hyperopic eyes (-1.09 ± 1.02 D). Love *et al*. (2000) found relative peripheral hyperopia of 0.64 ± 1.12 D in the temporal retina and 0.52 ± 1.71 D in the nasal retina of 78% and 70% respectively of myopic subjects. On the other hand, 85% of emmetropic subjects showed relative myopia in both nasal (-0.89 ± 0.93 D) and temporal (-0.94 ± 1.09 D) retinal meridians. Using orthogonal polynomial regression analysis to compare the characteristics of off-axis refraction in different RE groups, Atchison *et al.* (2005B) and Atchison *et al.* (2006B) found relative hyperopic shifts in the horizontal retinal fields of myopic eyes, while relative myopic shifts were common in emmetropic eyes.

The major relevance of the results of off-axis refraction obtained in the current study lies in their potential association with the progression of REs. Different investigators agree that the consequence of optically correcting REs in children is a further progression of the RE by altering the emmetropisation process (Charman 2005; Hung *et al.* 1995; Ingram *et al.* 1991; McBrien *et al.* 1996; Medina 1987A; Medina 1987B; Wallman and Winawer 2004; Wildsoet and Schmid 2000). Through the decades, various treatment options such as: (a) bifocals or progressive lenses (Edwards *et al.* 2002; Gwiazda *et al.* 2003; Gwiazda *et al.* 2004; Leung and Brown 1999; Shih *et al.*

2001), (b) pharmacological (Chua *et al.* 2006; McBrien *et al.* 1993), (c) contact lenses (Cho *et al.* 2005; Fulk *et al.* 2003; Katz *et al.* 2003; Khoo *et al.* 1999; Santodomingo-Rubido *et al.* 2005; Walline *et al.* 2004) and (d) undercorrection (Adler and Millodot 2006; Chung *et al.* 2002; Ong *et al.* 1999; Tokoro and Kabe 1965) have been proposed to control the progression of myopia but none of them have been truly effective. Importantly, these approaches have concentrated exclusively on the characteristics of on-axis refraction and, until recently (Charman *et al.* 2006; Smith EL III *et al*. 2006), did not consider the patterns of off-axis refraction.

Our data and previously published reports (Atchison *et al.* 2006B; Hoogerheide *et al.* 1971; Millodot 1981; Mutti *et al.* 2000B; Rempt *et al*. 1971) show that, when axial RE is considered uncorrected, in general, myopic eyes have less myopic RE in the periphery relative to the fovea and hyperopic eyes have less hyperopic RE in the periphery relative to the fovea. When the axial myopic RE is then corrected optically with negative powered lenses, both the on and off-axis rays are shifted. On-axis, this brings the image onto the fovea, however, in the periphery, the retina becomes exposed to hyperopic defocus (peripheral rays focusing behind the retina). In contrast, when positive powered lenses are used to correct hyperopic RE, the image is brought to focus at the fovea, however, in the periphery, the retina experiences myopic defocus (peripheral rays focusing in front of the retina) (Wallman and Winawer 2004).

Animal models of emmetropisation have shown that eye growth is a visually-guided process and that it is able to discriminate between hyperopic and myopic defocus. Animal models have also shown the ability of the peripheral retina to modulate local and general axial eye growth (Bradley *et al*. 1996; Guo *et al*. 1996; Hodos and Kuenzel

1984; Kee *et al*. 2004B; Napper *et al*. 1997; Norton 1990; Smith and Hung 2000; Smith EL III *et al.* 2005; Troilo *et al*. 1987; Wallman *et al*. 1978; Wallman *et al*. 1987; Wildsoet and Schmid 2000). In addition, observation of eyes suffering from conditions affecting the peripheral retina show that these eyes tend to develop myopia (Nathan *et al.* 1985) (e.g. retinopathy of prematurity). These observations suggest that the peripheral retina possibly plays a role in the development of REs.

These findings have led investigators to suggest that the peripheral hyperopic defocus is responsible for triggering eye growth in an attempt to bring the peripheral retina in focus with the peripheral image. This process leads to axial elongation, thus, generating axial myopia (Charman 2005; Charman 2006; Charman *et al.* 2006; Kee *et al.* 2004B; Smith EL III *et al.* 2005; Smith EL III *et al.* 2006; Schippert and Schaeffel 2006; Wallman and Winawer 2004). For this reason it has been proposed that any optical treatment for myopia should be designed to correct axial RE and also make the peripheral refraction emmetropic or myopic (Charman 2006; Charman *et al.* 2006; Smith EL III *et al.* 2006; Wallman and Winawer 2004).

Based on the results of off-axis refraction observed in this study, it is to be expected that, if corrected with conventional negative powered lenses, most myopic eyes (65 to 85%) will continue to progress over time (those presenting with skiagrams Type I and Type III), due to hyperopic defocus in the horizontal and superior retinal peripheries. Sixty percent (60%) of emmetropic and low hyperopic eyes with Type III skiagram will also be at risk of developing myopia in the future if their peripheral hyperopic RE is left uncorrected. On the other hand, the majority of hyperopic eyes (70%), if corrected with conventional positive lenses, will remain hyperopic over time (those presenting with skiagrams Type IV and Type V) by suffering from myopic defocus in the horizontal and superior retinal meridians. Hoogerheide *et al.* (1971) reported that approximately 80% of eyes with Type I skiagram and 65% of eyes with Type III skiagram experienced a shift in their refraction towards myopia (less hyperopic), whereas the majority of eyes (80 to 100%) with Type II, IV and V did not experience a shift towards myopia.

Unfortunately, due to the cross-sectional nature of the current study, this hypothesis can not be proved. Longitudinal studies providing "tailored" optical corrections, for example, to myopic subjects based on their characteristics of on and off-axis refraction, will provide the answer.

6.6.2 Ocular Shape

Off-axis refraction has been used to estimate ocular shape because it has been found to provide valid retinal coordinates for field angles up to 40 degrees (Dunne 1995; Mutti *et al.* 2000B). In the current study, off-axis refraction was also used to describe ocular shape. At 30 degrees eccentricity, the relative myopia in emmetropic and hyperopic eyes in the horizontal and vertical retinal meridians indicated an oblate shape for these RE groups; whereas the relative hyperopia in myopic eyes in the horizontal and vertical retinal meridians indicated a prolate shape. There was a tendency for a more oblate shape (or less prolate shape) in the superior retina than in the horizontal retinal meridian for most RE groups with the exception of moderate to high hyperopes who had approximately the same shape.

A simple way to explain the differences in the patterns of off-axis refraction between RE groups is using the basic model of ametropia (Charman and Jennings 1982). In this model, the optical elements of the eye remain constant while REs are the result of differences in AL. Such differences translate to differences in eye shape between RE groups (prolate shape in myopic eyes, spherical shape in emmetropic eyes and oblate shape in hyperopic eyes). However, with the use of different technologies to measure the ocular and retinal shapes such as X-rays (Deller *et al.* 1947), ultrasound (Meyer-Schwickerath and Gerke 1984; Chen *et al.* 1992), scanning laser ophthalmoscope imaging (Chen *et al.* 1992), partial coherence interferometry (Drexler *et al.* 1998), magnetic resonance imaging (Chen *et al.* 1992; Cheng *et al.* 1992; Atchison *et al.* 2004; Chau *et al.* 2004; Atchison *et al.* 2005A) and optical low coherence reflectometry (Schmid 2003A; Schmid 2003B), the model has been challenged.

Atchison *et al.* (2004) found myopic eyes to be larger than emmetropic eyes in all dimensions, however, myopic eyes were found to elongate more in the axial than in the vertical dimension. Atchison *et al.* (2004) suggested anatomic constraints of the orbital walls as the cause for differences in shape between meridians. It is possible that those anatomic constraints could also explain the differences found in the present study; detailed information of the orbital walls is needed to confirm this statement.

The results of ocular shape obtained in the current study need to be interpreted cautiously. In order to accurately describe ocular shape, the ratio between the axial, horizontal and equatorial axes must be determined (Ferree 1933; Deller *et al.* 1947; Meyer-Schwickerath and Gerke 1984; Cheng *et al.* 1992; Atchison *et al.* 2004). Because the off-axis measurements obtained in the current did not reach the equator, it possible that an under or overestimation of ocular shapes could have resulted.

6.6.3 Off-Axis Astigmatism

The main characteristics of off-axis astigmatism are listed below:

1. It increases progressively with eccentricity (Rempt *et al.* 1971; Leibowitz *et al.* 1972; Millodot and Lamont 1974A; Millodot 1981; Millodot 1984; Smith *et al.* 1988; Dunne *et al.* 1993; Navarro *et al.* 1993; Artal *et al.* 1995; Williams *et al.* 1996; Jennings and Charman 1997; Navarro *et al.* 1998; Guirao and Artal 1999; Gustafsson *et al.* 2001; Atchison and Scott 2002; Atchison 2003; Atchison *et al.* 2003; Gustafsson and Unsbo 2003; Atchison 2004A; Lundström *et al.* 2005B; Ma *et al.* 2005; Atchison *et al.* 2006B).

2. Its magnitude is usually higher in the temporal retina than in the nasal retina (asymmetry) (Ames and Proctor 1921; Ferree *et al.* 1931; Rempt *et al.* 1971; Millodot 1981; Millodot 1984; Dunne *et al.* 1993; Gustafsson *et al.* 2001).

3. The asymmetry of off-axis astigmatism in the horizontal retinal meridians was originally suggested to be related to the angle alpha (Millodot 1981), however later it was found that there was no correlation between off-axis astigmatism and angle alpha (Dunne *et al.* 1993). More recently it has been suggested that it is the result of the combined effects of the cornea, crystalline lens and retina (Atchison *et al.* 2005B; Atchison *et al.* 2006B).

4. In the majority of cases it shifts in direction from on-axis "with-the-rule" astigmatism to "against-the rule" in the periphery (Ferree *et al.* 1931; Navarro *et al.* 1998) but also it can shift to an oblique direction (Gustafsson *et al.* 2001;

Atchison and Scott 2002; Atchison *et al.* 2003; Atchison 2004A; Ma *et al.* 2005; Atchison *et al.* 2006B; Charman and Jennings 2006).

5. It is caused by the corneal shape (Lotmar 1971; Millodot 1984; Atchison 2004A), the crystalline lens (asphericity of the lens curvatures and refractive index variations) (Millodot 1984; Dunne and Barnes 1987; Dunne and Barnes 1990; Smith and Lu 1991; Dunne 1995; Atchison 2004A) and ocular components misalignment (Dunne 1995).

6. It is not clear whether it increases or decreases with age. Millodot (1984) found higher off-axis astigmatism in "old" eyes (63 to 85 years of age) than in "young" eyes (31 to 34 years of age) and even less in aphakes, whilst Scialfa *et al.* (1989) found more in younger eyes than in older eyes. On the other hand, Atchison *et al.* (2005B) found no difference between younger and older subjects and Charman and Jennings (2006) did not find changes in peripheral refraction with age in adults during a period of 26 years.

7. It increases with accommodation but only at angles beyond 40 degrees (Smith *et al.* 1988).

8. It is the predominant aberration in the peripheral retina (Navarro *et al.* 1993) and its magnitude is relatively similar among subjects because the angular distance from the axis is the dominant factor in determining its magnitude (Guirao and Artal 1999).

9. Early reports found different patterns of off-axis astigmatism with on-axis REs (Ferree *et al.* 1931; Rempt *et al.* 1971), however, later reports did not find a tendency of off-astigmatism change with REs (Millodot 1981; Ma *et al.* 2005).

10. In the vertical retinal meridian, the oblique component of the astigmatism (J_{45}) is almost three times higher in magnitude than in the horizontal visual field, whilst J_0 is more asymmetric than along the horizontal retinal field (Atchison *et al.* 2006B).

11. Its major effects in the visual function of the peripheral retina are: decrease of visual acuity (Ames and Proctor 1921; Millodot *et al.* 1975), reduces the retinal image quality (Jennings and Charman 1978) and plays a major role in reducing the modulation transfer function (Navarro *et al.* 1993; Williams *et al.* 1996; Jennings and Charman 1997; Guirao and Artal 1999).

Despite off-axis astigmatism (or oblique astigmatism) being extensively studied for a long time (see Table B2 in Appendix B), very little is known about the characteristics of off-axis astigmatism in children. Although Mutti *et al.* (2000B) described the magnitude of off-axis astigmatism for the different RE groups, no further analysis was conducted. To date, this is the first study to describe the characteristics of off-axis astigmatism in the horizontal and vertical retinal meridians in children.

Off-axis astigmatism was analysed using two different methods. In the first method, off-axis astigmatism was described as the space between the sagittal and tangential lines (Ferree 1933). An advantage of this method is that it provides a simple graphical description of the characteristics of off-axis refraction. However, as noted in subsection 6.3.2, the equations used to obtain both the sagittal and tangential meridional components did not include the oblique component of the astigmatism (J_{45} vector) which could have led to an underestimation of the magnitude of off-axis astigmatism. Another limitation of using this method is that, while it provides the magnitude of the astigmatic error, it does not provide the direction of the axis of the astigmatism. For this reason a second analysis of off-axis astigmatism was conducted using power vectors (Thibos *et al*. 1997).

Many similarities in the characteristics of off-axis astigmatism with those from adults were found. For all the RE groups, the magnitude of off-axis astigmatism at the three angles was higher than on-axis astigmatism; also higher magnitudes of off-axis astigmatism were found in the temporal retina than in the nasal retina in all RE groups. Horizontally, for all the RE groups the mean value of J_0 shifted from positive "with-the-rule" on-axis to negative "against-the-rule" values off-axis; however, J_{45} also increased with eccentricity, indicating that the direction of off-axis astigmatism was not just "against-the-rule". Superiorly, both J_0 and J_{45} components increased towards more positive values and the magnitude of J_{45} was larger in the superior retina than in the horizontal meridian.

In contrast to studies that did not find differences in the amounts of off-axis astigmatism between RE groups, the magnitude of astigmatism was significantly different between all RE groups in the temporal and superior retina. The magnitude and asymmetry of off-axis astigmatism in the horizontal retinal meridian were larger in hyperopic eyes than in emmetropic and myopic eyes. Additionally, the magnitude of off-axis astigmatism in the superior retina was also higher in hyperopic eyes than in emmetropic and myopic eyes. It is not clear why, of all the RE groups, hyperopic eyes had the highest amounts of off-axis astigmatism. Perhaps this is indicative of a difference in structure or refractive gradient index in the crystalline lens as previously suggested in Chapter 5.

It is not clear whether variations in the magnitude of off-axis astigmatism occur with age. To evaluate this, the mean relative values of astigmatism (J) of the nasal and temporal retina were converted to conventional cylinder (Thibos *et al.* 1997) and plotted together with previous results from younger and older subjects (Millodot 1984) (Figure 6.12).

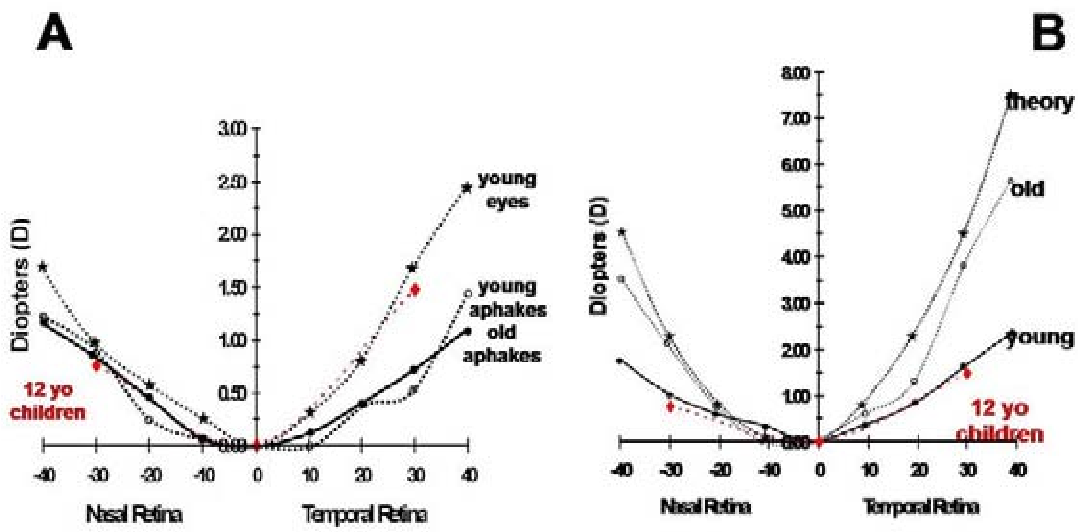

Figure 6.12: ***Comparison of mean off-axis astigmatism in conventional cylinder of 12 year old children measured in this study (red broken line) with (A) mean off-axis astigmatism of 62 young eyes, 2 young and 16 old aphakes; with (B) mean off-axis astigmatism of 63 young eyes, 10 old eyes and a theoretical eye as calculated by Le Grand using regular spherical surfaces and homogeneous indices of refraction. (Figures A and B reproduced from Millodot (1984) with permission).***

Despite differences in age and methods to measure off-axis refraction between studies, a remarkable similarity in the mean values of off-axis astigmatism of the 1,603 12 year old children with those from young adults was observed. This result highlights the similarity of characteristics of the optical system (cornea and crystalline lens) of children with young adults.

6.6.4 Off-Axis LOAs and HOAs

In the current study, both LO and HO off-axis aberrations (3rd and 4th order) were analysed. As with on-axis aberrations (Chapters 4 and 5), defocus and astigmatism were the dominant aberrations in the peripheral retina (both horizontally and superiorly), followed by 3rd orders and 4th orders. In most subjects, the mean off-axis values of astigmatism, coma, 3rd order, SA and 4th orders RMS were higher than on-axis, however, the magnitude of the HO modes was less than the magnitude of 2nd order aberrations. The mean values of off-axis astigmatism RMS were, on average, three to four times higher than on-axis. The mean values of off-axis coma RMS and off-axis 3rd orders RMS were approximately two times higher than on-axis. SA RMS increased slightly with eccentricity (around 20%), whereas the mean values of off-axis 4th orders RMS were approximately double than on-axis. In comparison to on-axis, the mean values of off-axis HO RMS were, on average, approximately 25% higher.

Small differences were found in the levels of coma RMS, third orders RMS and HO RMS between genders on the nasal retina. Females in the nasal retina had on average 0.01μm less coma RMS, third orders RMS and HO RMS than males. It is not clear why and whether these differences could have an impact into the development of refractive error. In addition, despite differences being statistically significant, they were was less than the coefficient of repeatability of the COAS for measurement of any of the 3rd orders individual modes in human eyes (Chapter 2, subsection 2.1.3.2). A small magnitude of the mean values of higher order aberrations together with a large sample size included in this study appear to be the best explanation for these differences.

Whilst direct comparisons of the current results with previous studies are difficult (due to differences in ages between the samples, methods used to measure the off-axis aberrations and in PDs used to calculate the aberrations), some general comparisons can be made. In agreement with Ma *et al.* (2005) who reported a low impact of 3rd and 4th order aberrations in the periphery in comparison to 2nd order aberrations, the magnitude of off-axis HO RMS in the horizontal and vertical retinal meridians (approximately 0.23 µm) was nearly 20 to 50% lower than the magnitudes of defocus and astigmatism RMS. In addition, the magnitude of 4th orders RMS was approximately 10 to 16% the magnitude of astigmatism or defocus RMS in all eccentricities.

Small differences were found in the levels of coma RMS in the nasal retina between the RE groups, however, in agreement with Navarro *et al.* (1998) and Guirao and Artal (1999), the magnitude of HO RMS and coma RMS was relatively similar among all subjects in the temporal and superior retina. Although the mean values of off-axis HO RMS were similar amongst all eyes, the mean values were nearly 1/3 lower than those reported by Navarro *et al*. (1998) (0.23 µm vs 0.75 µm for an angle of 30 degrees). The similarity in the magnitude of off-axis coma RMS between subjects was expected because the angular distance from the visual axis is the dominant factor determining the magnitude of these aberrations (Guirao and Artal 1999).

In contrast to Atchison and Scott (2002), who found the magnitude of 3rd order aberrations to increase five times in the temporal retina and three times in the nasal retina, the mean values of coma and 3rd orders RMS were always higher in the nasal retina than in temporal retina. In addition, despite the magnitude of on and off-axis SA RMS being similar among subjects, the mean values of 4th orders RMS increased by nearly 80% in the periphery. This increase could have been directly related to an increase in the magnitude of secondary astigmatism.

Although recently there has been an increase in the number of studies evaluating the characteristics of on-axis monochromatic aberrations in humans, only a small number of studies have analysed the characteristics of off-axis aberrations (Navarro *et al.* 1993; Williams *et al.* 1996; Navarro *et al.* 1998; Guirao and Artal 1999; Atchison and Scott 2002; Ma *et al.* 2005; Atchison 2006; Atchison *et al.* 2006A). Importantly, the majority of these studies have small samples sizes (<20 subjects) and included measurements on adults only. To date, there is no study that has reported the characteristics of off-axis HOAs in children. By studying the characteristics of off-axis aberrations, it will be possible to understand their potential role in eccentric or peripheral vision.

With eccentricity, there is a decrease of visual acuity (Leibowitz *et al.* 1972; Frisen and Glansholm 1975), motion detection (Leibowitz *et al.* 1972) and contrast detection (Wang *et al.* 1996). Studies have found a higher acuity for detection of sinusoidal gratings than for resolving gratings orientations (such as E letters) (Wang *et al.* 1997; Anderson and Thibos 1999). It also seems that there is a difference in visual acuity in different retinal areas (lower in the vertical retinal meridian than in the horizontal temporal retinal meridian) (Millodot and Lamont 1974B). This reduction of peripheral visual acuity is known to be caused by neural sampling and ocular dioptrics.

Resolution acuity is principally limited by neural sampling density (reduction of number of ganglion cells with eccentricity) (Artal *et al.* 1995; Wang *et al.* 1997). Different studies have found that, while there is slow decrease of optical quality with eccentricity, the decrease of visual acuity is more dramatic (Jennings and Charman 1978; Jennings and Charman 1981). Furthermore, it has also been found that no appreciable improvement of visual acuity occurs when optically correcting off-axis RE (Millodot *et al.* 1975).

On the other hand, there are suggestions that a reduction of optical quality due to aberrations (such as defocus, astigmatism and HOAs) also seems to contribute in the reduction of eccentric visual acuity (Frisen and Glansholm 1975; Jennings and Charman 1978; Navarro *et al.* 1998), motion perception (Leibowitz *et al.* 1972) and detection acuity (Wang *et al.* 1997). There are indications of reduction of the modulation transfer function, even when oblique astigmatism has been corrected, implying that other HOAs (mainly coma) (Guirao and Artal 1999), contribute to image degradation (Jennings and Charman 1981; Navarro *et al.* 1993; Williams *et al.* 1996; Jennings and Charman 1997). Recently it has also been reported that an increase of eccentric visual acuity and contrast sensitivity can be obtained by optically correcting 2nd order aberrations (Gustafsson 2001; Gustafsson and Unsbo 2003).

A limitation of the present study is that the effect of off-axis aberrations on the optical quality of the eye was not determined. Although the mean values of off-axis HOAs were small in comparison to defocus or astigmatism aberrations, it would have been interesting to evaluate the impact of these aberrations on the optical quality of the eye. The similarity in the mean values of off-axis and astigmatism (one of the most important aberrations in the peripheral retina) from this study versus data from young adults (Figure 6.12) suggests that the optical quality in the periphery of 12 year old children is similar to that in young adults. Although they increase in the peripheral retina, the magnitude of HOAs was too low to have a major effect on the optical quality in the peripheral retina. Similar to on-axis aberrations (Chapters 4 and 5), the mean levels of off-axis HOAs were similar among RE groups, with the exception of the nasal retina, in which low myopic eyes had higher levels of HO RMS than emmetropic or low hyperopic eyes.

6.7 SUMMARY

To date, this is the first study reporting the characteristics of off-axis, monochromatic ocular aberrations in children. The results support the presence of different patterns of peripheral refraction for different on-axis RE groups. The majority of myopic eyes showed patterns of peripheral refraction that have been associated with the development or progression of myopic RE; whereas the majority of hyperopic and emmetropic eyes showed patterns of peripheral refraction considered to have a protective effect against the development of myopia. Approximately 30% of emmetropic and hyperopic eyes also showed a peripheral refraction pattern associated with the development or progression of myopic RE.

Using the results of off-axis refraction, ocular shape was estimated for the different RE groups. In agreement with previous studies, myopic eyes appear to have prolate ocular shapes, whereas emmetropic and hyperopic eyes appear to have oblate ocular shapes.

Ocular shapes in the vertical meridian (superior retina only) showed less prolate (or more oblate) shape in all RE groups. The difference in shape between horizontal and vertical meridians appears to be associated with anatomical orbital constraints.

As previously reported, off-axis astigmatism was the main off-axis aberration in the periphery. Lower levels of off-axis astigmatism were observed in moderate to high myopic eyes; on the other hand moderate to high hyperopic eyes had higher levels of off-axis astigmatism than the other RE groups. The majority of emmetropic, low myopic and low hyperopic eyes presented mixed off-axis astigmatism (previously referred as “normal” astigmatism). The difference in levels of astigmatism between RE groups could be related to differences in the structure of the crystalline lens. As a whole population, the mean levels of off-axis astigmatism in the horizontal meridian appear to be in close agreement with those from young adults.

HOAs (principally 3rd order aberrations) also increased with eccentricity, however, their magnitudes were small in comparison to LOAs and, therefore, the role they may have in reducing the optical quality at the peripheral retina appears to be small.

CHAPTER 7: SUMMARY AND CONCLUSIONS

7.1 INTRODUCTION

Myopia is a significant health problem that affects nearly 50% of children aged 15 years and above in some countries in Asia (Edwards 1999; Lin *et al.* 1999; Fan *et al.* 2004C; He *et al.* 2004). High levels of myopia are associated with ocular complications such as: retinal detachment (Vongphanit *et al*. 2002; Kerkhoff *et al*. 2003), cataract (Lim *et al*. 1999; Leske *et al*. 2002) or glaucoma (Mitchell *et al.* 1999). Myopia imposes a very high economic burden on our societies (as one of the major causes of vision impairment in the world (Dandona *et al*. 2002B; Murthy *et al*. 2002; Buch *et al*. 2004), due to high costs associated with its management (Congdon *et al.* 2003).

Whilst different options have been used for the optical correction of myopia, an effective method to prevent or control the progression of myopia is yet to be found, principally because the aetiology of myopia still remains unclear. There are indications that myopia follows a model of interaction between genetic factors and environmental influences (especially continuous close work with high cognitive demands). Largely due to observations in different animal models, we now know that visual feedback plays an important role in guiding emmetropisation and myopia development. However, the nature of the stimuli causing retinal defocus and triggering axial growth remains unknown.

Based on observations from some animal studies and human adult populations, it has been suggested that excessive or abnormal levels of on-axis HOAs or certain patterns of off-axis aberrations may provide the stimuli for retinal defocus and, subsequently, ocular growth. Studying the characteristics of on and off-axis aberrations in children may provide information on whether these aberrations play a role in the development of REs such as myopia.

The main goal of this thesis was to investigate the characteristics of on and off-axis ocular aberrations from a large cohort (n=1,636) of Australian school children (mostly 12 year olds) and their relationship with RE. On and off-axis aberrations measurements were conducted as part of a population-based study of refraction and eye health (The Sydney Myopia Study) (Ojaimi *et al*. 2005A) during 2004-5 using a commercially-available aberrometer. The results were compared to another cohort of Australian schoolchildren (mostly 6 year olds, n=1,363). An off-axis target device was developed to be used with the aberrometer, allowing for the measurement of off-axis aberrations at an eccentricity of 30 degrees of the nasal, temporal and superior retina. In addition, a custom-made program was written to facilitate the analysis of the off-axis aberrations measurements.

7.2 OCULAR ABERRATIONS IN 12 YEAR OLD CHILDREN

This study showed that the on-axis LOAs and HOAs were normally distributed and that a considerable inter-subject variability for all aberrations existed across the 12 year old cohort. The 2nd order aberrations were the dominant aberrations and, importantly, the mean levels of HOAs were small in magnitude. Most aberrations were significantly correlated between right and left eyes, however, moderate to high correlations were found for 2nd and 3rd order aberrations only. Of the HOs, 3rd order aberrations had the greatest variability and SA had the greatest magnitude (in most cases it had a positive value). The magnitude of HOAs was too small to be of significance. Importantly, this study showed that eyes with myopia did not have greater levels of aberrations than emmetropes or hyperopes. Overall, the SA was positive and higher levels of positive SA were found in hyperopic children. There were no differences in the levels of SA between myopic and emmetropic children. Despite differences in the distribution of RE between ethnic groups, there were no differences in the levels of HOAs between ethnic groups.

7.3 COMPARISON OF THE PROFILE OF ON-AXIS ABERRATIONS BETWEEN 6 AND 12 YEAR OLD CHILDREN

This study compared the on-axis ocular aberrations between two cohorts (6 and 12 year old children) and showed that the mean values of HOAs were similar between both cohorts and comparable to the mean values found in adults. Second order aberrations were found to contribute almost 80% to the total wavefront of the eye and the remaining contribution was predominantly from 3rd and 4th orders. The levels of HOA RMS of the refractive groups were also similar between cohorts. While SA was positive in the majority of children, a small number of cases also presented with negative values. The levels of HO RMS aberrations in myopic and emmetropic eyes were not different in the 6 year old cohort. It should be noted that, in the present study, aberrations were calculated for a fixed pupil size (5 mm). We measured the pupil diameter for a group of

8 and 12 year old children* under photopic and mesopic conditions. The photopic PD was 3.6 ± 0.6 mm and 3.8 ± 0.7 mm for the 8 and 12 year old children respectively. The mesopic PD was 5.2 ± 0.8 mm and 5.9 ± 1.0 mm for the 8 and 12 year old children. The results suggest that pupil diameter was not significantly significant between both age groups and the 5 mm analysis diameter applies to real-life situations.

7.4 OFF-AXIS (PERIPHERAL) REFRACTION AND ABERRATIONS IN 12 YEAR OLD CHILDREN

The results of this study support the presence of different patterns of off-axis refraction in different refractive groups in a group of 12 year old children. Relative to the fovea, the majority of myopic eyes (80%), and approximately one third of emmetropic and hyperopic eyes, had peripheral hyperopic error. It has been suggested that this pattern is associated with the development or progression of myopia. In contrast, a large number of hyperopic eyes had patterns of off-axis refraction (mean relative myopic error) considered protective against the development of myopia. Additionally, myopic eyes appeared to have prolate ocular shapes, whilst emmetropic and hyperopic eyes had oblate ocular shapes. Second order aberrations were also the dominant monochromatic aberrations in the peripheral retina and, together with HOs (small magnitude), they increased in the periphery. The mean levels of off-axis astigmatism observed in the horizontal retinal meridian appear to be in close agreement with those from young adults. The impact of increased HOAs in the periphery on optical quality in children is unclear.

* Data was obtained from IER (data on file) and from personal communications with Dr Percy Lazon

7.5 CONCLUSIONS AND FUTURE DIRECTIONS

In summary, this is the first study to investigate the characteristics of on and off-axis aberrations and their association with myopia in a large sample of young children. The findings of this thesis suggest that, as in young adults, the eyes of a child are not free of on and off-axis HOAs, however, the mean values of these aberrations remain small. The similarity of HOAs between eyes supports the existence of a coordinated binocular passive mechanism of eye growth in children. Also importantly, myopic eyes do not have excessive levels of aberrations in comparison to emmetropes and hyperopes. The findings obtained in this thesis do not provide evidence to support the theory that higher levels of HOAs are associated with the development of myopia in children. On the other hand, the results of off-axis refraction observed in this study provide support to the theory that different patterns of off-axis refraction might have an influence in the development of REs.

Future studies investigating the characteristics of on or off-axis aberrations in children must include measurements of corneal optical characteristics (asphericity and aberrations) and also measurements of the crystalline lens (surface curvatures and thickness) to provide a better understanding of the relationship between corneal and internal aberrations that occur during ocular growth. Similarly, including an analysis of the optical quality of the eye (modulation transfer function, optical transfer function) could provide a better estimate of the contribution that HOAs have on the image quality of the eye. Also longitudinal studies that investigate the patterns of progression of on and off-axis REs in children will help to determine the effectiveness of correcting both on and off-axis RE.

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APPENDICES

APPENDIX A:

PREVALENCE OF MYOPIA TABLES

Table A1: Prevalence of myopia in children

Country	Year	Ethnicity	Study Design	(n)	Mean Age	Age (range)	Prevalence (Mean %)	Myopia cut-off	Method	References
Canada	1982	NS	Cross-Sectional	10,616	6	NS	6	-0.25 D	Non-cycloplegic retinoscopy	Robinson, 1999
Hong Kong	1991	Chinese	Longitudinal	123	7	NS	11.0	SE ≤ -0.50 D	Non-cycloplegic retinoscopy	Edwards, 1999
China	1991	Chinese	Longitudinal	142	NS	6	52.1	SE ≤ -0.50 D	Non-cycloplegic subrefraction	Lam *et al.* 1999
USA	1993	NS	Longitudinal	716	9.7	6	3.0	SE ≤ -0.50 D	Cycloplegic autorefraction	Zadnik, 1997
Australia	1994	NS	Retrospective	2,535	NS	4	2.0	SE ≤ -0.50 D	Non-cycloplegic retinoscopy	Junghans, Crewther 2003
Taiwan	1995	Chinese	Survey	11,178	NS	7	12.0	SE ≤ -0.25 D	Cycloplegic autorefraction	Lin *et al.* 1999
Japan	1995	Japanese	Longitudinal	350	NS	6 to 11	0.3 to 4.9	SE ≤ -1.00 D	Cycloplegic autorefraction	Watanabe *et al.* 1999
China	1995	Chinese	Cohort	255	4.96	3.42 to 7.25	4.6	SE ≤ -0.50 D	Cycloplegic autorefraction	Fan *et al.* 2004A
Hong Kong	1996	Chinese	Longitudinal	83	12	NS	57.0	SE ≤ -0.50 D	Subjective refraction	Edwards, 1999
USA	1997	Asians	Cohort/Long.	491	9.7	5 to 17	19.8	-0.50 D	Cycloplegic autorefraction	Kleinstein *et al.* 2003
USA	1997	Afro-American	Cohort/Long.	534	10.4	5 to 17	8.6	-0.50 D	Cycloplegic autorefraction	Kleinstein *et al.* 2003
USA	1997	Hispanic	Cohort/Long.	463	10.2	5 to 17	14.5	-0.50 D	Cycloplegic autorefraction	Kleinstein *et al.* 2003
USA	1997	Caucasian	Cohort/Long.	1,035	9.9	5 to 17	5.2	-0.50 D	Cycloplegic autorefraction	Kleinstein *et al.* 2003
Nepal	1998	Sherpa	Cross-Sectional	270	NS	7 to 12	2.9	SE ≤ -0.50 D	Non-cycloplegic retinoscopy	Garner *et al.* 1999
Nepal	1998	Tibet	Cross-Sectional	555	NS	7 to 12	21.7	SE ≤ -0.50 D	Cycloplegic autorefraction	Garner *et al.* 1999
Chile	1998	Hispanic	Cohort	5,303	NS	5	3.4	SE ≤ -0.50 D	Cycloplegic autorefraction	Maul *et al.* 2000
China	1998	Chinese	Longitudinal	7,560	9.33	5 to 16	36.7	SE ≤ -0.50 D	Cycloplegic autorefraction	Fan *et al.* 2004C
China	2000	Chinese	Cohort/Long.	108	NS	2 to 6	43.5	SE ≤ -0.50 D	Cycloplegic autorefraction	Fan *et al.* 2004A
India	2000	Indian	Cross-Sectional	9,882	NS	≤ 15	3.19	≤ -0.50 D	Cycloplegic refraction	Dandona *et al.* 2002A
India	2000	Indian	Cross-Sectional	6,447	NS	5 to 15	4.7 to 10.8	SE ≤ -0.50 D	Cycloplegic autorefraction	Murthy *et al.* 2002
India	2001	Indian	Cross-Sectional	3,976	NS	7 to 15	2.8 to 6.7	SE ≤ -0.50 D	Cycloplegic autorefraction	Dandona *et al.* 2002B
Nepal	2002	Nepal	Cross-Sectional	1,100	9.5	5 to 7	0	≤ -0.50 D	Cycloplegic refraction	Nepal *et al.* 2003
S. Africa	2002	African	Survey	4,190	NS	5	3.20	SE ≤ 0.50 D	Cycloplegic autorefraction	Naidoo *et al.* 2003
China	2002	Chinese	Cross-Sectional	4,364	NS	5 to 15	5.7 to 78.4	SE ≤ -0.50 D	Cycloplegic autorefraction	He *et al.* 2004

Table A2: Prevalence of myopia in teenagers

Country	Year	Ethnicity	Study Design	(n)	Mean Age	Age (Range)	Prevalence (Mean %)	Myopia cut-off	Method	References
China	1991	Chinese	Longitudinal	142	NS	17	63.3	SE ≤ -0.50D	Non-cycloplegic subjective refraction	Lam *et al.* 1999
USA	1993	NS	Longitudinal	716	9.7	14.9	≈28	SE ≤ -0.50D	Cycloplegic autorefraction	Zadnik, 1997
Australia	1994	NS	Retrospective	2535	NS	12	6.5	SE ≤ -0.50D	Non-cycloplegic retinoscopy	Junghans, Crewther 2003
Taiwan	1995	Polynesian/Chinese	Survey	11,178	NS	18	84	SE ≤ -0.25D	Cycloplegic autorefraction	Lin *et al.* 1999
China	1996	Chinese	Longitudinal	83	12	NS	57	SE ≤ -0.50D	Subjective refraction	Edwards, 1999
Chile	1998	Hispanic	Cohort	5,303	NS	15	≈17	SE ≤ -0.50D	Cycloplegic autorefraction	Maul *et al.* 2000
China	1998	Chinese	Longitudinal	7,560	9.33	16	36.7	SE ≤ -0.50D	Cycloplegic autorefraction	Fan *et al.* 2004A
Mexico	1999	Hispanic	Cross-Sectional	1,035	NS	12 to 13	44	SE ≤ -0.50D	Cycloplegic auto-refraction	Villarreal *et al.* 2003
India	2000	Indian	Cross-Sectional	9,882	NS	15 ≥	19.45	≤ -0.50D	Cycloplegic refraction	Dandona *et al.* 2002A
India	2000	Indian	Cross-Sectional	6,447	NS	15	10.8	SE ≤ -0.50D	Cycloplegic autorefraction	Murthy *et al.* 2002
Sweden	2000	Caucasian	Survey	1,045	NS	12 to 13	49.7	SE ≤ -0.50D	Cycloplegic autorefraction	Villarreal *et al.* 2000
Nepal	2002	Nepal	Cross-Sectional	1,100	9.5	14 to 16	31.46	≤ -0.50D	Cycloplegic refraction	Nepal *et al.* 2003
S. Africa	2002	African	Survey	4,190	NS	15	9.6	SE ≤ 0.50D	Cycloplegic autorefraction	Naidoo *et al.* 2003
China	2002	Chinese	Cross-Sectional	4,364	NS	15	78.4	SE ≤ -0.50D	Cycloplegic autorefraction	He *et al.* 2004
Singapore	2002	Chinese, Malay, Indian	Cross-Sectional	946	14.5	14 to 19	77.1, 69.4, 65.8	SE ≤ 0.50D	Non-cycloplegic autorefraction	Quek *et al.* 2004

Table A3: Prevalence of myopia in adults

Country	Year	Ethnicity	Study Design	(n)	Mean Age	Age (range)	Prevalence (Mean %)	Myopia cut-off	Method	References
Barbados	1992	Black	Cohort	4,036	57	40 to 80+	17 to 55.1 (21.9)	SE ≤ -0.50D	Non-cycloplegic autorefraction	Wu *et al.* 1999
Australia	1994	Caucasian	Cross-sectional	3,654	NS	49 to 97	15%	SE ≤ -0.50D	Non-cycloplegic autorefraction	Attebo *et al.* 1999
Norway	1995	Caucasian	Cohort/Long.	192	20.6	NS	65	SE ≤ -0.25D	Cycloplegic auto-refraction	Kinge, Midelfart 1999
Singapore	1996	Chinese, Malay, Indian	Survey / Cohort	15,086	19	16 to 25	82.2, 65.0, 68.7	SE ≤ -0.50D	Non-cycloplegic autorefraction	Wu *et al.* 2001
Norway	1996	Caucasian	Cross-sectional	1,248	NS	20 to 25	35	SE ≤ 0.50D	Non-cycloplegic autorefraction	Midelfart *et al.* 2004
Norway	1996	Caucasian	Cross-sectional	1,889	NS	40 to 45	30	SE ≤ 0.50D	Non-cycloplegic autorefraction	Midelfart *et al.* 2004
Singapore	1997	Chinese	Survey	1,113	58.8	40 to 81	45.2 to 31.7	SE ≤ -0.50D	Non-cycloplegic autorefraction	Wong *et al.* 2000
Mongolia	1997	Mongolian	Cross-sectional	1,617	NS	40 to 70+	11.8 to 39.2 (17.2)	SE ≤ -0.50D	Non-cycloplegic auto-refraction	Wickremasinghe *et al.* 2004
Bangladesh	2000	Bangladeshis	Survey	11,189	44	30 to 70+	17.5 to 65.5 (22.1)	SE ≤ -0.50D	Non-cycloplegic autorefraction	Bourne *et al.* 2004
Taiwan	2000	Chinese	Survey	1,108	72.2	65 to 80+	12.8 to 26.5 (18.3)	SE ≤ -0.50D	Non-cycloplegic autorefraction	Cheng *et al.* 2003
Finland	2000	Caucasian	Cohort	3,524	19.2	17 to 30	22.2	Wearing - lenses	Questionnaires	Vannas *et al.* 2003
Indonesia	2001	Indonesian	Survey	1,043	36.7	21 to 50+	61.6 to 39.7	SE ≤ -0.50D	Non-cycloplegic autorefraction	Saw *et al.* 2002A
Denmark	2001	Caucasian	Cross-sectional	499	46.8	30 to 60	33.1	SE ≤ -0.50D	Non-cycloplegic autorefraction	Kessel *et al.* 2004

APPENDIX B:

SUMMARY OF STUDIES, METHODS AND MAIN FINDINGS USED TO MEASURE PERIPHERAL REFRACTION AND ABERRATIONS

Table B1:
Summary of studies and methods used to measure peripheral refraction and aberrations

	Method	Authors
Peripheral Refraction	Ophthalmoscopy	Stammerhaus 1874 (reviewed in Ames and Proctor, 1921)
	Optometer	Dunne and Barnes, 1990
	Parallax Refractometer	Ames and Proctor, 1921; Ferree *et al.* 1931; Ferree *et al.* 1932; Lamont and Millodot, 1973; Millodot and Lamont 1974A; Dunne and Barnes, 1990; Dunne *et al.* 1993
	Skiascopic (retinoscopy)	Ames and Proctor, 1921; Hoogerheide *et al.* 1971; Rempt *et al.* 1971; Leibowitz *et al.* 1972; Lamont and Millodot, 1973; Millodot and Lamont, 1974A; Scialfa *et al.* 1989; Lundström *et al.* 2005A
	Double Pass	Jennings and Charman, 1978; Jennings and Charman, 1981; Navarro *et al.* 1993; Artal *et al.* 1995; Williams *et al.* 1996; Gustafsson *et al.* 2001
	Autorefraction	Millodot, 1981; Millodot, 1984; Smith *et al.* 1988; Dunne *et al.* 1993; Logan *et al.* 1995B; Love *et al.* 2000; Mutti *et al.* 2000B; Seidemann *et al.* 2002; Logan *et al.* 2004; Atchison *et al.* 2005A; Atchison *et al.* 2006B; Charman *et al.* 2006
	Subjective	Ames and Proctor, 1921; Lamont and Millodot, 1973; Millodot and Lamont 1974A; Dunne and Barnes, 1990; Dunne, 1993
	Photorefraction	Gustafsson 2001; Seidemann *et al.* 2002; Gustafsson and Unsbo 2003; Lundström *et al.* 2005B; Lundström *et al.* 2005A
	Aberrometry	Atchison 2003; Atchison *et al.* 2003; Lundström *et al.* 2005B; Lundström *et al.* 2005A; Ma *et al.* 2005
Peripheral Aberrations	Ray Tracing	Navarro *et al.* 1998
	Double Pass	Guirao and Artal, 1999; Gustafsson *et al.* 2001; Seidemann *et al.* 2002
	Shack-Hartmann	Atchison and Scott 2002; Lundström *et al.* 2004; Ma *et al.* 2005; Atchison *et al.* 2006A

Table B2:
Summary of most relevant studies in peripheral refraction and their main findings

Authors	No. of Subjects	Ages	Cycloplegia	Increased astigmatism with eccentricity	Asymmetry between nasal and temporal meridians	Other comments
Ames and Proctor, 1921	1	?	No	Yes	Yes	Asymmetry of nasal/temporal fields attributed to angle α
Ferree *et al.* 1931; Ferree *et al.* 1932; Ferree, 1933	21 eyes	?	Yes	Yes	Yes	Measurements up to 60° nasal/temporal retina Three patterns of peripheral astigmatism were found: Type A, B and C 1st study to report shift in astigmatic axis in the periphery from "with-the-rule" to "against-the-rule"
Rempt *et al.* 1971	884 eyes	?	No	Yes	Yes	Measurements up to 60° nasal/temporal retina Defined term peripheral skiagram (I, II, III, IV,IV) Identified differences in peripheral skiagrams with refractive error
Hoogerheide *et al.* 1971	214	young	?	Yes	-	Measurements up to 60° nasal/temporal retina Progression of myopia associated with Type 1 skiagram
Millodot and Lamont 1974A	3	?	No	Yes	-	Measurements up to 60° nasal retina only
Millodot, 1981	62 eyes	18 to 57	No	Yes in 91% of eyes (independent of on-axis refraction)	Yes (attributed to angle α)	Measurements up to 60° nasal/temporal retina Shift in axis of peripheral astigmatism to "against the rule" in 90% eyes
Millodot, 1984	18 aphakic eyes and 10 normal eyes	31 to 85	No	No (in 87% of young and old aphakes) Yes in normal eyes	Yes (in normal eyes more pronounced than in aphakes)	1st study to measure peripheral refraction in aphakic eyes (up to 40° nasal temporal retina) Lower amounts of peripheral astigmatism found in aphakic eyes
Smith *et al.* 1988	11	12 to 33	No	Yes	-	1st study to measure the effect of accommodation in peripheral refraction Measurements up to 60° nasal retina only Accommodation ↑ field of curvature and astigmatism for angles > 40°
Scialfa *et al.* 1989	20	22 to 69	No	Yes	-	Measurements up to 40° nasal retina only Higher levels of peripheral astigmatism in young eyes than in old eyes
Dunne *et al.* 1993	34	21.4 (mean)	No	Yes	Yes	Measurements up to 40° nasal/temporal retina Poor correlation between angle α and astigmatism minima)
Navarro *et al.* 1998	4	20 to 40	Yes	Yes	-	1st study to measure peripheral aberrations Measurements up to 40° nasal retina RMS increases linearly with eccentricity Major image degradation of peripheral image due to 2nd order aberrations

Authors	No. of Subjects	Ages	Cycloplegia	Increased astigmatism with eccentricity	Asymmetry between nasal and temporal meridians	Other comments
Guirao and Artal, 1999	4	25 to 35	No	Yes	-	Measurements up to 45° temporal meridian Coma is the main higher order aberration in the periphery after defocus and astigmatism are corrected
Mutti *et al.* 2000B	822	5 to 14	Yes	Yes	-	1st and only study measuring peripheral refraction in children Measurements @ 30° nasal retina only Myopic eyes are relatively hyperopic in the periphery Emmetropic and hyperopic eyes more myopic in the periphery
Gustafsson *et al.* 2001	20	20 to 45	No	Yes	Yes	Measurements up to 60° nasal/temporal retina Peripheral astigmatism is not always "against-the-rule" but in some cases is also oblique
Atchison and Scott, 2002; Atchison *et al.* 2003; Atchison 2004A	5	31 to 47	Yes	Yes	Yes	1st study to measure peripheral aberrations using a Shack-Hartmann aberrometer Increase of higher orders only 3rd orders; 4th and 5th orders no change with eccentricity Peripheral astigmatism not always "against-the-rule" Both corneal and internal aberrations ↑ with eccentricity
Seidemann *et al.* 2002	31	21 to 33	No	Yes	-	Measurements up to 45° temporal retina and up to 25° superior retina Increase of myopia in superior retina There is a trend towards more myopia when eyes are rotated by 40°
Ma *et al.* 2005; Atchison 2006	12	27 to 55	Yes	Yes	Yes	1st study measuring peripheral refraction in eyes with LASIK Myopic LASIK eyes present high myopia in the periphery ↑ Horizontal coma w/eccentricity 4th order aberrations show quadratic dependences with eccentricity
Atchison *et al.* 2005A	55 young 41 old	21 to 62	No	Yes	Yes	Measurements up to 35° temporal/nasal retina Peripheral refraction in emmetropic & low myopic eyes unaffected by age
Atchison *et al.* 2006B	116	18 to 35	No	Yes	Yes	Measurements up to ±35° horizontal and vertical meridians Differences in peripheral refraction in horizontal and vertical meridians
Charman and Jennings, 2006	2	32 and 40	No	Yes	Yes	1st longitudinal study to measure changes of peripheral refraction with age Changes in peripheral refraction with age across the horizontal meridian are small

APPENDIX C:

LISTING OF ZERNIKE POLYNOMIALS UP TO THE 7TH ORDER IN POLAR FORM

j = index	n = order	m = frequency	$Z_n^m(\rho,\theta)$
0	0	0	1
1	1	-1	$2\ \rho \sin\theta$
2	1	1	$2\ \rho \cos\theta$
3	2	-2	$\sqrt{6}\ \rho^2 \sin 2\theta$
4	2	0	$\sqrt{3}\ (2\rho^2-1)$
5	2	2	$\sqrt{6}\ \rho^2 \cos 2\theta$
6	3	-3	$\sqrt{8}\ \rho^3 \sin 3\theta$
7	3	-1	$\sqrt{8}\ (3\rho^3-2\rho) \sin\theta$
8	3	1	$\sqrt{8}\ (3\rho^3-2\rho) \cos\theta$
9	3	3	$\sqrt{8}\ \rho^3 \cos 3\theta$
10	4	-4	$\sqrt{10}\ \rho^4 \sin 4\theta$
11	4	-2	$\sqrt{10}\ (4\rho^4-3\rho^2) \sin 2\theta$
12	4	0	$\sqrt{5}\ (6\rho^4-6\rho^2+1)$
13	4	2	$\sqrt{10}\ (4\rho^4-3\rho^2) \cos 2\theta$
14	4	4	$\sqrt{10}\ \rho^4 \cos 4\theta$
15	5	-5	$\sqrt{12}\ \rho^5 \sin 5\theta$
16	5	-3	$\sqrt{12}\ (5\rho^5-4\rho^3) \sin 3\theta$
17	5	-1	$\sqrt{12}\ (10\rho^5-12\rho^3+3\rho) \sin\theta$
18	5	1	$\sqrt{12}\ (10\rho^5-12\rho^3+3\rho) \cos\theta$
19	5	3	$\sqrt{12}\ (5\rho^5-4\rho^3) \cos 3\theta$
20	5	5	$\sqrt{12}\ \rho^5 \cos 5\theta$
21	6	-6	$\sqrt{14}\ \rho^6 \sin 6\theta$
22	6	-4	$\sqrt{14}\ (6\rho^6-5\rho^4) \sin 4\theta$
23	6	-2	$\sqrt{14}\ (15\rho^6-20\rho^4+6\rho^2) \sin 2\theta$
24	6	0	$\sqrt{7}\ (20\rho^6-30\rho^4+12\rho^2-1)$
25	6	2	$\sqrt{14}\ (15\rho^6-20\rho^4+6\rho^2) \cos 2\theta$
26	6	4	$\sqrt{14}\ (6\rho^6-5\rho^4) \cos 4\theta$
27	6	6	$\sqrt{14}\ \rho^6 \cos 6\theta$
28	7	-7	$4\ \rho^7 \sin 7\theta$
29	7	-5	$4\ (7\rho^7-6\rho^5) \sin 5\theta$
30	7	-3	$4\ (21\rho^7-30\rho^5+10\rho^3) \sin 3\theta$
31	7	-1	$4\ (35\rho^7-60\rho^5+30\rho^3-4\rho) \sin\theta$
32	7	1	$4\ (35\rho^7-60\rho^5+30\rho^3-4\rho) \cos\theta$
33	7	3	$4\ (21\rho^7-30\rho^5+10\rho^3) \cos 3\theta$
34	7	5	$4\ (7\rho^7-6\rho^5) \cos 5\theta$
35	7	7	$4\ \rho^7 \cos 7\theta$

Zernike polynomials up to the 7th order in Polar representation according to the Optical Society of America-recommended standards (*Reprinted from Thibos et al. 2002A with permission from SLACK Incorporated).*

The Zernike polynomials are a set of functions that are independent of each other (orthogonal) over the unit circle used for describing the shape of a wavefront in the pupil of an optical system (Thibos *et al.* 2002A). The Zernike polynomials can be defined in polar or Cartesian form. When the polar form is used, the polynomials are defined in polar coordinates (ρ, θ) where ρ is the radial coordinate ranging from 0 to 1, and θ is the azimuthal component which has a range from 0 to 360° (2π).

Each Zernike polynomial Z_n^m is defined as:

$$Z_n^m(\rho,\theta) = \left\{ \frac{N_n^m R_n^{|m|}(\rho)\cos(m\theta), \text{for} \quad m \geq 0}{N_n^m R_n^{|m|}(\rho)\sin(m\theta), \text{for} \quad m < 0} \right\}$$

Where:

- N_n^m is the normalisation factor which is a function of ρ and given by:

  $N_n^m = \sqrt{n+1}$ for m =0 and,

  $N_n^m = \sqrt{2(n+1)}$ for $m \neq 0$ (Atchison 2004A).

- R_n^m is radial-dependent component which is a polynomial itself and defined as:

  $$R_n^{|m|}(\rho) = \sum_{s=0}^{(n-|m|)/2} \frac{(-1)^s (n-s)!}{s!\left[0.5(n+|m|)-s\right]!\left[0.5(n-|m|-s\right]!}\rho^{n-2s}$$

- |m| is the absolute value of m and is an azimuthal-dependent component (sinusoidal).

Zernike coefficients reported in this thesis are always described using the two index scheme.

APPENDIX D:

REPEATABILITY RESULTS OF THE COAS G200 FOR LOWER AND HIGHER ORDER ABERRATIONS

Repeatability of Lower Orders in Children

Right Eye (OD)

Table D1: Mean refractive components (D) from the right eyes of 81 children

Component	Mean (D)	Standard Deviation	Range (D)	
M	-0.11	1.98	-6.22	5.05
J_0	0.06	0.23	-0.93	0.89
J_{45}	0.00	0.13	-0.80	0.20
P	1.39	1.43	0.13	6.23

Table D2: Coefficient of Repeatability (D) of lower orders from the right eyes of 81 children

Mean Differences of P vector (D)		0.00
Standard Deviation of Mean Differences		0.12
Sum of Sq of Mean of P Vector Differences		1.09
RMS Deviation		0.12
Repeatability coefficient of P vector (D)		**0.23**
Standard Error		0.01
95% Confidence intervals	**Lower**	-0.026
	Upper	0.028
CR = 1.96 * SD of Mean Differences		**0.24**

Left Eye (OS)

Table D3: Mean refractive components (D) from the left eyes of 81 children

Component	Mean (D)	Standard Deviation	Range (D)	
M	-0.08	1.95	-6.12	6.42
J_0	0.08	0.24	-0.85	0.71
J_{45}	-0.02	0.11	-0.30	0.44
P	-0.08	1.95	-6.12	6.42

Table D4: Coefficient of Repeatability (D) of lower orders from the left eyes of 81 children

Mean Differences of P vector (D)		0.00
Standard Deviation of Mean Differences		0.10
Sum of Sq of Mean of P Vector Differences		1.10
RMS Deviation		0.12
Repeatability coefficient of P vector (D)		**0.23**
Standard Error		0.01
95% Confidence intervals	**Lower**	-0.013
	Upper	0.030
CR = 1.96 * SD of Mean Differences		**0.19**

Repeatability of Lower Orders in a Model Eye

Table D-5: Mean refractive components (D) from the Model Eye

Component	Mean (D)	Standard Deviation	Range (D)	
M	-5.11	0.08	-4.98	-5.21
J_0	-0.03	0.01	-0.01	-0.05
J_{45}	0.01	0.03	0.03	0.04
P	5.11	0.08	4.98	5.21

Table D-6: Coefficient of Repeatability (D) of lower orders from the Model Eye

Mean Differences of P vector (D)		0.07
Standard Deviation of Mean Differences		0.04
Sum of Sq of Mean of P Vector Differences		0.005
RMS Deviation		0.02
Repeatability coefficient of P vector (D)		**0.03**
Standard Error		**0.01**
95% Confidence intervals	**Lower**	0.05
	Upper	0.10

Repeatability of Higher Order Aberrations in Human Eyes

Right Eye (OD)

Table D7: Coefficient of Repeatability (microns) of higher order modes (3rd to 6th orders) from the right eyes of 81 children

Zernike Polynomial	Mean (μm)	SD	SE	95% Confidence Intervals
OSA(3,-3)	-0.036	0.029	0.016	**0.046**
OSA(3,-1)	0.014	0.042	0.024	**0.067**
OSA(3,1)	-0.004	0.025	0.014	**0.040**
OSA(3,3)	0.016	0.025	0.015	**0.040**
OSA(4,-4)	0.014	0.013	0.008	**0.022**
OSA(4,-2)	-0.016	0.016	0.009	**0.025**
OSA(4,0)	0.049	0.017	0.010	**0.028**
OSA(4,2)	-0.001	0.020	0.011	**0.032**
OSA(4,4)	0.017	0.017	0.010	**0.027**
OSA(5,-5)	-0.005	0.010	0.006	**0.015**
OSA(5,-3)	0.002	0.011	0.006	**0.018**
OSA(5,-1)	0.016	0.013	0.007	**0.021**
OSA(5,1)	0.003	0.010	0.006	**0.016**
OSA(5,3)	0.004	0.009	0.005	**0.014**
OSA(5,5)	0.001	0.008	0.005	**0.014**
OSA(6,-6)	0.002	0.006	0.004	**0.010**
OSA(6,-4)	-0.001	0.006	0.003	**0.009**
OSA(6,-2)	0.000	0.006	0.003	**0.009**
OSA(6,0)	-0.002	0.008	0.005	**0.013**
OSA(6,2)	0.000	0.008	0.005	**0.013**
OSA(6,4)	0.000	0.007	0.004	**0.011**
OSA(6,6)	0.000	0.009	0.005	**0.014**

Left Eye (OS)

Table D8: Coefficient of Repeatability (microns) of higher order modes (3rd to 6th orders) from the left eyes of 81 children

Zernike Polynomial	Mean (μm)	SD	SE	95% Confidence Intervals
OSA(3,-3)	-0.036	0.029	0.017	**0.046**
OSA(3,-1)	0.014	0.039	0.022	**0.062**
OSA(3,1)	0.007	0.026	0.015	**0.042**
OSA(3,3)	-0.006	0.022	0.013	**0.036**
OSA(4,-4)	-0.008	0.015	0.009	**0.024**
OSA(4,-2)	0.009	0.013	0.008	**0.022**
OSA(4,0)	0.054	0.017	0.010	**0.027**
OSA(4,2)	-0.008	0.020	0.012	**0.032**
OSA(4,4)	0.014	0.017	0.010	**0.027**
OSA(5,-5)	-0.001	0.009	0.005	**0.015**
OSA(5,-3)	0.004	0.012	0.007	**0.019**
OSA(5,-1)	0.014	0.012	0.007	**0.019**
OSA(5,1)	-0.004	0.010	0.006	**0.016**
OSA(5,3)	-0.003	0.008	0.005	**0.014**
OSA(5,5)	0.000	0.009	0.005	**0.014**
OSA(6,-6)	0.002	0.006	0.003	**0.010**
OSA(6,-4)	0.000	0.006	0.004	**0.010**
OSA(6,-2)	0.001	0.005	0.003	**0.007**
OSA(6,0)	-0.001	0.008	0.005	**0.013**
OSA(6,2)	-0.001	0.008	0.005	**0.013**
OSA(6,4)	0.001	0.007	0.004	**0.011**
OSA(6,6)	0.000	0.007	0.004	**0.011**

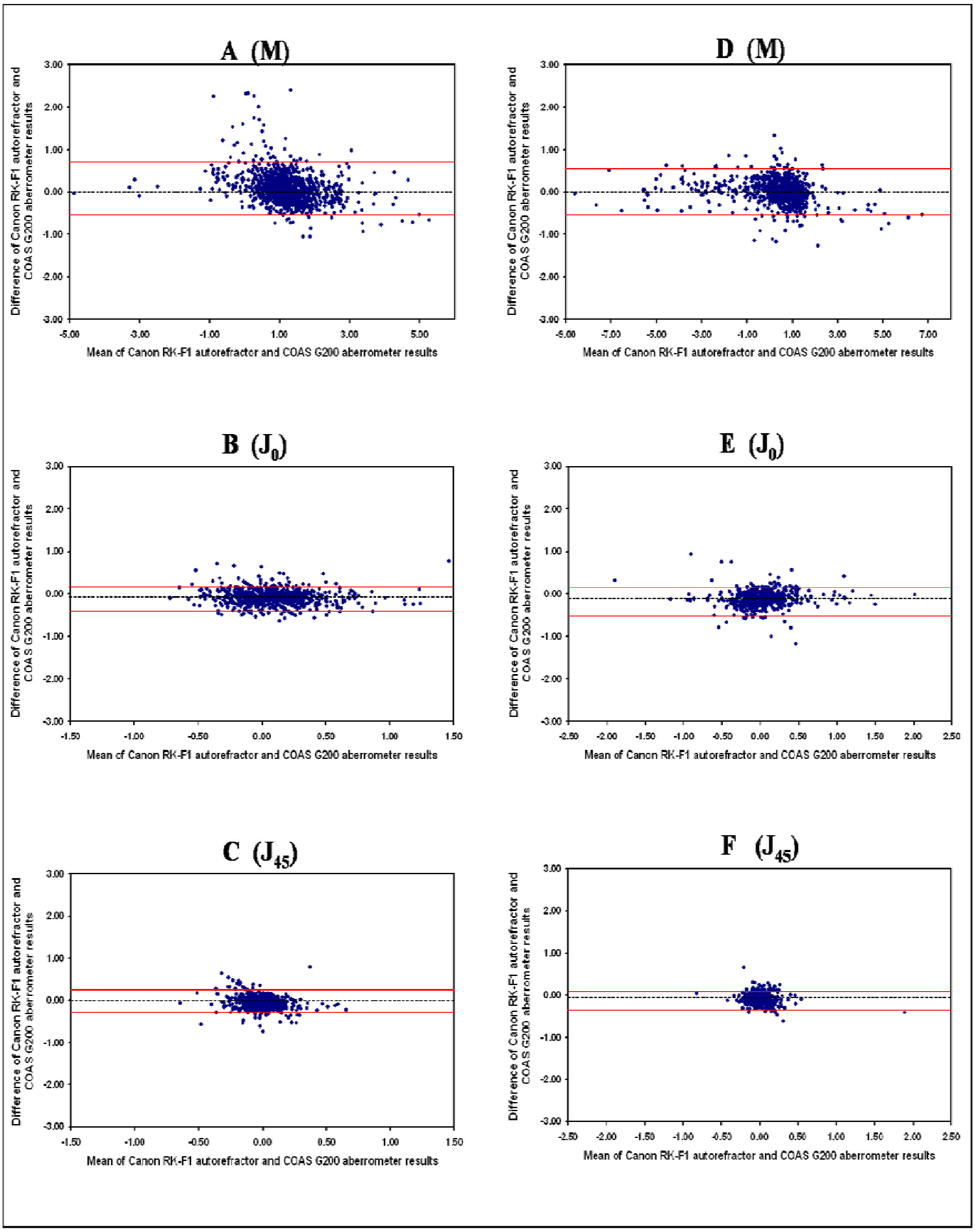
Repeatability of Higher Order Aberrations in a Model Eye

Table D9: Coefficient of Repeatability (microns) of higher order modes (3rd to 6th orders) from the model eye

Zernike Polynomial	Mean (μm)	SD	SE	95% Confidence Intervals
OSA(3,-3)	0.009	0.012	0.007	0.019
OSA(3,-1)	-0.084	0.004	0.003	0.007
OSA(3,1)	0.100	0.007	0.004	0.010
OSA(3,3)	0.007	0.010	0.005	0.015
OSA(4,-4)	0.007	0.006	0.003	0.009
OSA(4,-2)	0.022	0.006	0.004	0.010
OSA(4,0)	0.013	0.006	0.003	0.009
OSA(4,2)	-0.008	0.004	0.002	0.007
OSA(4,4)	-0.022	0.012	0.007	0.020
OSA(5,-5)	0.003	0.005	0.003	0.008
OSA(5,-3)	-0.001	0.004	0.003	0.007
OSA(5,-1)	0.002	0.003	0.002	0.005
OSA(5,1)	0.008	0.004	0.002	0.007
OSA(5,3)	0.005	0.005	0.003	0.008
OSA(5,5)	0.003	0.008	0.005	0.013
OSA(6,-6)	-0.002	0.009	0.005	0.014
OSA(6,-4)	-0.003	0.002	0.001	0.003
OSA(6,-2)	-0.003	0.002	0.001	0.004
OSA(6,0)	0.001	0.003	0.002	0.005
OSA(6,2)	-0.001	0.002	0.001	0.003
OSA(6,4)	0.001	0.001	0.001	0.002
OSA(6,6)	-0.004	0.004	0.002	0.007

APPENDIX E:

BLAND AND ALTMAN PLOTS OF MEAN DIFFERENCES OF CANON RK-F1 AND COAS G200 MEAUSUREMENTS OF REFRACTIVE COMPONENTS



Mean difference between Canon RK-F1 autorefractor and COAS G200 aberrometer results plotted as a function of their mean. The upper and lower solid lines indicate 95% limits of agreement, and the dashed line indicates the mean. Positive values from the mean indicate the aberrometer measured more minus than the autorefractor. Data are shown from the right eyes of 1,504 children in Year 1 (A, B, C) and 890 children in Year 7 (D, E, F). A and D: M vector; B & E: J_0 vector; C & F: J_{45} vector.

APPENDIX F:

REFRACTIVE COMPONENTS ANALYSES OF VARIANCE BROWN-FORSYTHE: GAMES-HOWELL POST-HOC MULTIPLE COMPARISONS TESTS FOR CHAPTER 4

Refractive components analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Refractive Error Group groups

Dependent Variable	(I) Refractive Error Group Groups	(J) Refractive Error Group Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
M	Myopes	Emmetropes	-2.05(*)	.108	.000	-2.30	-1.79
		Hyperopes	-3.01(*)	.109	.000	-3.27	-2.75
	Emmetropes	Myopes	2.05(*)	.108	.000	1.79	2.30
		Hyperopes	-.96(*)	.025	.000	-1.02	-.91
	Hyperopes	Myopes	3.01(*)	.109	.000	2.75	3.27
		Emmetropes	.96(*)	.025	.000	.91	1.02
J_0	Myopes	Emmetropes	-.04	.017	.078	-.08	.00
		Hyperopes	-.02	.016	.341	-.06	.02
	Emmetropes	Myopes	.04	.017	.078	.00	.08
		Hyperopes	.01	.009	.235	-.01	.04
	Hyperopes	Myopes	.02	.016	.341	-.02	.06
		Emmetropes	-.01	.009	.235	-.04	.01
J_{45}	Myopes	Emmetropes	-.01	.010	.859	-.03	.02
		Hyperopes	-.02	.009	.239	-.04	.01
	Emmetropes	Myopes	.01	.010	.859	-.02	.03
		Hyperopes	-.01	.006	.184	-.02	.00
	Hyperopes	Myopes	.02	.009	.239	-.01	.04
		Emmetropes	.01	.006	.184	.00	.02

** The mean difference is significant at the .05 level.*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Refractive Error Group groups

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(2,-2)	Myopes	Emmetropes	.007	.013	.850	-.023	.037
		Hyperopes	.020	.012	.231	-.009	.048
	Emmetropes	Myopes	-.007	.013	.850	-.037	.023
		Hyperopes	.013	.007	.183	-.004	.029
	Hyperopes	Myopes	-.020	.012	.231	-.048	.009
		Emmetropes	-.013	.007	.183	-.029	.004
Z(2, 0)	Myopes	Emmetropes	1.851(*)	.097	.000	1.621	2.081
		Hyperopes	2.598(*)	.098	.000	2.366	2.831
	Emmetropes	Myopes	-1.851(*)	.097	.000	-2.081	-1.621
		Hyperopes	.747(*)	.023	.000	.693	.801
	Hyperopes	Myopes	-2.598(*)	.098	.000	-2.831	-2.366
		Emmetropes	-.747(*)	.023	.000	-.801	-.693
Z(2, 2)	Myopes	Emmetropes	.047	.022	.077	-.004	.098
		Hyperopes	.028	.020	.340	-.019	.076
	Emmetropes	Myopes	-.047	.022	.077	-.098	.004
		Hyperopes	-.019	.012	.234	-.046	.008
	Hyperopes	Myopes	-.028	.020	.340	-.076	.019
		Emmetropes	.019	.012	.234	-.008	.046
Z(3,-3)	Myopes	Emmetropes	-.012	.006	.145	-.027	.003
		Hyperopes	-.011	.006	.141	-.025	.003
	Emmetropes	Myopes	.012	.006	.145	-.003	.027
		Hyperopes	.001	.004	.972	-.009	.010
	Hyperopes	Myopes	.011	.006	.141	-.003	.025
		Emmetropes	-.001	.004	.972	-.010	.009
Z(3,-1)	Myopes	Emmetropes	.035(*)	.010	.001	.013	.058
		Hyperopes	.035(*)	.009	.000	.014	.056
	Emmetropes	Myopes	-.035(*)	.010	.001	-.058	-.013
		Hyperopes	.000	.006	1.000	-.013	.013
	Hyperopes	Myopes	-.035(*)	.009	.000	-.056	-.014
		Emmetropes	.000	.006	1.000	-.013	.013
Z(3, 1)	Myopes	Emmetropes	.016(*)	.006	.022	.002	.029
		Hyperopes	.017(*)	.005	.007	.004	.030
	Emmetropes	Myopes	-.016(*)	.006	.022	-.029	-.002
		Hyperopes	.001	.004	.945	-.007	.009
	Hyperopes	Myopes	-.017(*)	.005	.007	-.030	-.004
		Emmetropes	-.001	.004	.945	-.009	.007
Z(3, 3)	Myopes	Emmetropes	.006	.006	.530	-.007	.019
		Hyperopes	.000	.005	1.000	-.012	.012
	Emmetropes	Myopes	-.006	.006	.530	-.019	.007
		Hyperopes	-.006	.003	.201	-.014	.002
	Hyperopes	Myopes	.000	.005	1.000	-.012	.012
		Emmetropes	.006	.003	.201	-.002	.014
Z(4,-4)	Myopes	Emmetropes	.002	.002	.633	-.003	.008
		Hyperopes	.003	.002	.436	-.003	.008
	Emmetropes	Myopes	-.002	.002	.633	-.008	.003
		Hyperopes	.001	.001	.878	-.002	.004
	Hyperopes	Myopes	-.003	.002	.436	-.008	.003
		Emmetropes	-.001	.001	.878	-.004	.002

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(4,-2)	Myopes	Emmetropes	.003	.002	.223	-.001	.008
		Hyperopes	-.001	.002	.883	-.006	.004
	Emmetropes	Myopes	-.003	.002	.223	-.008	.001
		Hyperopes	-.004(*)	.002	.010	-.008	-.001
	Hyperopes	Myopes	.001	.002	.883	-.004	.006
		Emmetropes	.004(*)	.002	.010	.001	.008
Z(4, 0)	Myopes	Emmetropes	.002	.005	.903	-.009	.013
		Hyperopes	-.026(*)	.004	.000	-.037	-.016
	Emmetropes	Myopes	-.002	.005	.903	-.013	.009
		Hyperopes	-.028(*)	.003	.000	-.035	-.022
	Hyperopes	Myopes	.026(*)	.004	.000	.016	.037
		Emmetropes	.028(*)	.003	.000	.022	.035
Z(4, 2)	Myopes	Emmetropes	.001	.003	.948	-.005	.007
		Hyperopes	.003	.002	.537	-.003	.008
	Emmetropes	Myopes	-.001	.003	.948	-.007	.005
		Hyperopes	.002	.002	.575	-.002	.006
	Hyperopes	Myopes	-.003	.002	.537	-.008	.003
		Emmetropes	-.002	.002	.575	-.006	.002
Z(4, 4)	Myopes	Emmetropes	-.001	.003	.905	-.007	.005
		Hyperopes	-.001	.002	.811	-.007	.004
	Emmetropes	Myopes	.001	.003	.905	-.005	.007
		Hyperopes	.000	.002	.965	-.004	.003
	Hyperopes	Myopes	.001	.002	.811	-.004	.007
		Emmetropes	.000	.002	.965	-.003	.004
Z(5,-5)	Myopes	Emmetropes	.002	.001	.347	-.001	.005
		Hyperopes	.001	.001	.518	-.001	.004
	Emmetropes	Myopes	-.002	.001	.347	-.005	.001
		Hyperopes	-.001	.001	.817	-.003	.001
	Hyperopes	Myopes	-.001	.001	.518	-.004	.001
		Emmetropes	.001	.001	.817	-.001	.003
Z(5,-3)	Myopes	Emmetropes	.001	.001	.796	-.002	.004
		Hyperopes	.001	.001	.569	-.002	.004
	Emmetropes	Myopes	-.001	.001	.796	-.004	.002
		Hyperopes	.000	.001	.897	-.002	.002
	Hyperopes	Myopes	-.001	.001	.569	-.004	.002
		Emmetropes	.000	.001	.897	-.002	.002
Z(5,-1)	Myopes	Emmetropes	-.004	.002	.074	-.008	.000
		Hyperopes	-.004(*)	.002	.022	-.008	.000
	Emmetropes	Myopes	.004	.002	.074	.000	.008
		Hyperopes	-.001	.001	.879	-.003	.002
	Hyperopes	Myopes	.004(*)	.002	.022	.000	.008
		Emmetropes	.001	.001	.879	-.002	.003
Z(5, 1)	Myopes	Emmetropes	-.002	.001	.305	-.004	.001
		Hyperopes	-.005(*)	.001	.000	-.007	-.002
	Emmetropes	Myopes	.002	.001	.305	-.001	.004
		Hyperopes	-.003(*)	.001	.001	-.005	-.001
	Hyperopes	Myopes	.005(*)	.001	.000	.002	.007
		Emmetropes	.003(*)	.001	.001	.001	.005
Z(5, 3)	Myopes	Emmetropes	-.001	.001	.671	-.003	.001
		Hyperopes	-.001	.001	.228	-.004	.001
	Emmetropes	Myopes	.001	.001	.671	-.001	.003
		Hyperopes	-.001	.001	.581	-.002	.001
	Hyperopes	Myopes	.001	.001	.228	-.001	.004
		Emmetropes	.001	.001	.581	-.001	.002

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(5, 5)	Myopes	Emmetropes	.001	.001	.908	-.002	.004
		Hyperopes	.002	.001	.148	-.001	.005
	Emmetropes	Myopes	-.001	.001	.908	-.004	.002
		Hyperopes	.002	.001	.061	.000	.003
	Hyperopes	Myopes	-.002	.001	.148	-.005	.001
		Emmetropes	-.002	.001	.061	-.003	.000
Z(6,-6)	Myopes	Emmetropes	-.001	.001	.473	-.003	.001
		Hyperopes	-.001	.001	.364	-.003	.001
	Emmetropes	Myopes	.001	.001	.473	-.001	.003
		Hyperopes	.000	.001	.995	-.001	.001
	Hyperopes	Myopes	.001	.001	.364	-.001	.003
		Emmetropes	.000	.001	.995	-.001	.001
Z(6,-4)	Myopes	Emmetropes	-.001	.001	.770	-.002	.001
		Hyperopes	-.001	.001	.112	-.003	.000
	Emmetropes	Myopes	.001	.001	.770	-.001	.002
		Hyperopes	-.001	.000	.121	-.002	.000
	Hyperopes	Myopes	.001	.001	.112	.000	.003
		Emmetropes	.001	.000	.121	.000	.002
Z(6,-2)	Myopes	Emmetropes	.000	.001	.992	-.002	.001
		Hyperopes	.000	.001	.827	-.001	.002
	Emmetropes	Myopes	.000	.001	.992	-.001	.002
		Hyperopes	.000	.000	.553	-.001	.001
	Hyperopes	Myopes	.000	.001	.827	-.002	.001
		Emmetropes	.000	.000	.553	-.001	.001
Z(6, 0)	Myopes	Emmetropes	.002	.001	.199	-.001	.004
		Hyperopes	.004(*)	.001	.000	.002	.007
	Emmetropes	Myopes	-.002	.001	.199	-.004	.001
		Hyperopes	.003(*)	.001	.000	.001	.004
	Hyperopes	Myopes	-.004(*)	.001	.000	-.007	-.002
		Emmetropes	-.003(*)	.001	.000	-.004	-.001
Z(6, 2)	Myopes	Emmetropes	.001	.001	.782	-.002	.003
		Hyperopes	.001	.001	.247	-.001	.003
	Emmetropes	Myopes	-.001	.001	.782	-.003	.002
		Hyperopes	.001	.001	.440	-.001	.002
	Hyperopes	Myopes	-.001	.001	.247	-.003	.001
		Emmetropes	-.001	.001	.440	-.002	.001
Z(6, 4)	Myopes	Emmetropes	-.001	.001	.648	-.003	.001
		Hyperopes	-.001	.001	.164	-.003	.000
	Emmetropes	Myopes	.001	.001	.648	-.001	.003
		Hyperopes	-.001	.001	.413	-.002	.001
	Hyperopes	Myopes	.001	.001	.164	.000	.003
		Emmetropes	.001	.001	.413	-.001	.002
Z(6, 6)	Myopes	Emmetropes	.000	.001	.998	-.002	.002
		Hyperopes	.001	.001	.576	-.001	.003
	Emmetropes	Myopes	.000	.001	.998	-.002	.002
		Hyperopes	.001	.001	.315	-.001	.002
	Hyperopes	Myopes	-.001	.001	.576	-.003	.001
		Emmetropes	-.001	.001	.315	-.002	.001

** The mean difference is significant at the .05 level.*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Refractive Error Group subgroups

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(2,-2)	M- H Myopes	Low Myopes	-.068	.033	.257	-.162	.026
		Emmetropes	-.049	.031	.528	-.139	.042
		Low Hyperopes	-.037	.031	.756	-.126	.053
		M- H Hyperopes	-.041	.047	.905	-.173	.092
	Low Myopes	M- H Myopes	.068	.033	.257	-.026	.162
		Emmetropes	.019	.013	.625	-.018	.056
		Low Hyperopes	.031	.013	.102	-.004	.066
		M- H Hyperopes	.027	.037	.948	-.082	.136
	Emmetropes	M- H Myopes	.049	.031	.528	-.042	.139
		Low Myopes	-.019	.013	.625	-.056	.018
		Low Hyperopes	.012	.007	.434	-.007	.032
		M- H Hyperopes	.008	.036	.999	-.098	.114
	Low Hyperopes	M- H Myopes	.037	.031	.756	-.053	.126
		Low Myopes	-.031	.013	.102	-.066	.004
		Emmetropes	-.012	.007	.434	-.032	.007
		M- H Hyperopes	-.004	.035	1.000	-.109	.101
	M- H Hyperopes	M- H Myopes	.041	.047	.905	-.092	.173
		Low Myopes	-.027	.037	.948	-.136	.082
		Emmetropes	-.008	.036	.999	-.114	.098
		Low Hyperopes	.004	.035	1.000	-.101	.109
Z(2, 0)	M- H Myopes	Low Myopes	2.568(*)	.216	.000	1.942	3.193
		Emmetropes	3.984(*)	.208	.000	3.375	4.592
		Low Hyperopes	4.666(*)	.208	.000	4.057	5.274
		M- H Hyperopes	7.695(*)	.318	.000	6.791	8.600
	Low Myopes	M- H Myopes	-2.568(*)	.216	.000	-3.193	-1.942
		Emmetropes	1.416(*)	.061	.000	1.248	1.584
		Low Hyperopes	2.098(*)	.060	.000	1.931	2.265
		M- H Hyperopes	5.128(*)	.248	.000	4.396	5.859
	Emmetropes	M- H Myopes	-3.984(*)	.208	.000	-4.592	-3.375
		Low Myopes	-1.416(*)	.061	.000	-1.584	-1.248
		Low Hyperopes	.682(*)	.018	.000	.633	.731
		M- H Hyperopes	3.712(*)	.241	.000	2.994	4.430
	Low Hyperopes	M- H Myopes	-4.666(*)	.208	.000	-5.274	-4.057
		Low Myopes	-2.098(*)	.060	.000	-2.265	-1.931
		Emmetropes	-.682(*)	.018	.000	-.731	-.633
		M- H Hyperopes	3.030(*)	.241	.000	2.312	3.747
	M- H Hyperopes	M- H Myopes	-7.695(*)	.318	.000	-8.600	-6.791
		Low Myopes	-5.128(*)	.248	.000	-5.859	-4.396
		Emmetropes	-3.712(*)	.241	.000	-4.430	-2.994
		Low Hyperopes	-3.030(*)	.241	.000	-3.747	-2.312
Z(2, 2)	M- H Myopes	Low Myopes	-.067	.048	.628	-.202	.069
		Emmetropes	-.008	.044	1.000	-.134	.118
		Low Hyperopes	-.028	.043	.964	-.153	.097
		M- H Hyperopes	.009	.067	1.000	-.180	.199
	Low Myopes	M- H Myopes	.067	.048	.628	-.069	.202
		Emmetropes	.059	.024	.099	-.006	.124
		Low Hyperopes	.039	.022	.412	-.023	.100
		M- H Hyperopes	.076	.056	.654	-.086	.238
	Emmetropes	M- H Myopes	.008	.044	1.000	-.118	.134
		Low Myopes	-.059	.024	.099	-.124	.006
		Low Hyperopes	-.020	.012	.419	-.052	.012
		M- H Hyperopes	.017	.052	.997	-.138	.172
	Low Hyperopes	M- H Myopes	.028	.043	.964	-.097	.153
		Low Myopes	-.039	.022	.412	-.100	.023
		Emmetropes	.020	.012	.419	-.012	.052
		M- H Hyperopes	.037	.052	.950	-.117	.191
	M- H Hyperopes	M- H Myopes	-.009	.067	1.000	-.199	.180
		Low Myopes	-.076	.056	.654	-.238	.086
		Emmetropes	-.017	.052	.997	-.172	.138
		Low Hyperopes	-.037	.052	.950	-.191	.117

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(3,-3)	M- H Myopes	Low Myopes	-.001	.014	1.000	-.041	.040
		Emmetropes	-.013	.013	.873	-.051	.026
		Low Hyperopes	-.010	.013	.927	-.048	.027
		M- H Hyperopes	-.069(*)	.020	.013	-.127	-.011
	Low Myopes	M- H Myopes	.001	.014	1.000	-.040	.041
		Emmetropes	-.012	.007	.416	-.031	.007
		Low Hyperopes	-.010	.006	.548	-.028	.008
		M- H Hyperopes	-.068(*)	.017	.004	-.118	-.018
	Emmetropes	M- H Myopes	.013	.013	.873	-.026	.051
		Low Myopes	.012	.007	.416	-.007	.031
		Low Hyperopes	.002	.004	.984	-.009	.013
		M- H Hyperopes	-.056(*)	.016	.017	-.104	-.008
	Low Hyperopes	M- H Myopes	.010	.013	.927	-.027	.048
		Low Myopes	.010	.006	.548	-.008	.028
		Emmetropes	-.002	.004	.984	-.013	.009
		M- H Hyperopes	-.058(*)	.016	.012	-.106	-.011
	M- H Hyperopes	M- H Myopes	.069(*)	.020	.013	.011	.127
		Low Myopes	.068(*)	.017	.004	.018	.118
		Emmetropes	.056(*)	.016	.017	.008	.104
		Low Hyperopes	.058(*)	.016	.012	.011	.106
Z(3,-1)	M- H Myopes	Low Myopes	.037	.019	.294	-.016	.089
		Emmetropes	.065(*)	.017	.004	.017	.113
		Low Hyperopes	.065(*)	.016	.003	.018	.112
		M- H Hyperopes	.101(*)	.029	.012	.017	.186
	Low Myopes	M- H Myopes	-.037	.019	.294	-.089	.016
		Emmetropes	.029	.011	.056	.000	.058
		Low Hyperopes	.028(*)	.010	.039	.001	.056
		M- H Hyperopes	.065	.027	.136	-.013	.142
	Emmetropes	M- H Myopes	-.065(*)	.017	.004	-.113	-.017
		Low Myopes	-.029	.011	.056	-.058	.000
		Low Hyperopes	.000	.006	1.000	-.016	.015
		M- H Hyperopes	.036	.025	.619	-.039	.111
	Low Hyperopes	M- H Myopes	-.065(*)	.016	.003	-.112	-.018
		Low Myopes	-.028(*)	.010	.039	-.056	-.001
		Emmetropes	.000	.006	1.000	-.015	.016
		M- H Hyperopes	.036	.025	.606	-.038	.110
	M- H Hyperopes	M- H Myopes	-.101(*)	.029	.012	-.186	-.017
		Low Myopes	-.065	.027	.136	-.142	.013
		Emmetropes	-.036	.025	.619	-.111	.039
		Low Hyperopes	-.036	.025	.606	-.110	.038
Z(3, 1)	M- H Myopes	Low Myopes	-.025	.012	.238	-.059	.009
		Emmetropes	-.006	.011	.986	-.037	.026
		Low Hyperopes	-.004	.011	.994	-.036	.027
		M- H Hyperopes	.000	.021	1.000	-.062	.061
	Low Myopes	M- H Myopes	.025	.012	.238	-.009	.059
		Emmetropes	.020(*)	.006	.017	.002	.037
		Low Hyperopes	.021(*)	.006	.005	.004	.037
		M- H Hyperopes	.025	.019	.698	-.032	.081
	Emmetropes	M- H Myopes	.006	.011	.986	-.026	.037
		Low Myopes	-.020(*)	.006	.017	-.037	-.002
		Low Hyperopes	.001	.004	.997	-.009	.011
		M- H Hyperopes	.005	.019	.999	-.050	.060
	Low Hyperopes	M- H Myopes	.004	.011	.994	-.027	.036
		Low Myopes	-.021(*)	.006	.005	-.037	-.004
		Emmetropes	-.001	.004	.997	-.011	.009
		M- H Hyperopes	.004	.019	1.000	-.051	.059
	M- H Hyperopes	M- H Myopes	.000	.021	1.000	-.061	.062
		Low Myopes	-.025	.019	.698	-.081	.032
		Emmetropes	-.005	.019	.999	-.060	.050
		Low Hyperopes	-.004	.019	1.000	-.059	.051

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(3, 3)	M- H Myopes	Low Myopes	.014	.010	.629	-.014	.043
		Emmetropes	.018	.009	.282	-.008	.043
		Low Hyperopes	.012	.009	.651	-.013	.037
		M- H Hyperopes	.014	.017	.928	-.035	.062
	Low Myopes	M- H Myopes	-.014	.010	.629	-.043	.014
		Emmetropes	.004	.006	.977	-.014	.021
		Low Hyperopes	-.002	.006	.995	-.019	.014
		M- H Hyperopes	-.001	.016	1.000	-.046	.045
	Emmetropes	M- H Myopes	-.018	.009	.282	-.043	.008
		Low Myopes	-.004	.006	.977	-.021	.014
		Low Hyperopes	-.006	.004	.420	-.016	.004
		M- H Hyperopes	-.004	.015	.998	-.049	.040
	Low Hyperopes	M- H Myopes	-.012	.009	.651	-.037	.013
		Low Myopes	.002	.006	.995	-.014	.019
		Emmetropes	.006	.004	.420	-.004	.016
		M- H Hyperopes	.002	.015	1.000	-.042	.046
	M- H Hyperopes	M- H Myopes	-.014	.017	.928	-.062	.035
		Low Myopes	.001	.016	1.000	-.045	.046
		Emmetropes	.004	.015	.998	-.040	.049
		Low Hyperopes	-.002	.015	1.000	-.046	.042
Z(4,-4)	M- H Myopes	Low Myopes	.003	.005	.984	-.012	.018
		Emmetropes	.005	.005	.887	-.010	.019
		Low Hyperopes	.005	.005	.819	-.009	.019
		M- H Hyperopes	.003	.007	.990	-.017	.023
	Low Myopes	M- H Myopes	-.003	.005	.984	-.018	.012
		Emmetropes	.002	.003	.968	-.005	.009
		Low Hyperopes	.002	.003	.880	-.005	.009
		M- H Hyperopes	.000	.006	1.000	-.016	.017
	Emmetropes	M- H Myopes	-.005	.005	.887	-.019	.010
		Low Myopes	-.002	.003	.968	-.009	.005
		Low Hyperopes	.001	.001	.984	-.003	.004
		M- H Hyperopes	-.001	.005	.999	-.017	.014
	Low Hyperopes	M- H Myopes	-.005	.005	.819	-.019	.009
		Low Myopes	-.002	.003	.880	-.009	.005
		Emmetropes	-.001	.001	.984	-.004	.003
		M- H Hyperopes	-.002	.005	.995	-.017	.013
	M- H Hyperopes	M- H Myopes	-.003	.007	.990	-.023	.017
		Low Myopes	.000	.006	1.000	-.017	.016
		Emmetropes	.001	.005	.999	-.014	.017
		Low Hyperopes	.002	.005	.995	-.013	.017
Z(4,-2)	M- H Myopes	Low Myopes	.001	.005	1.000	-.013	.014
		Emmetropes	.004	.004	.898	-.009	.017
		Low Hyperopes	.000	.004	1.000	-.013	.013
		M- H Hyperopes	-.008	.009	.901	-.035	.019
	Low Myopes	M- H Myopes	-.001	.005	1.000	-.014	.013
		Emmetropes	.003	.002	.554	-.003	.009
		Low Hyperopes	-.001	.002	.994	-.007	.005
		M- H Hyperopes	-.009	.009	.833	-.034	.016
	Emmetropes	M- H Myopes	-.004	.004	.898	-.017	.009
		Low Myopes	-.003	.002	.554	-.009	.003
		Low Hyperopes	-.004(*)	.002	.040	-.008	.000
		M- H Hyperopes	-.012	.008	.596	-.037	.013
	Low Hyperopes	M- H Myopes	.000	.004	1.000	-.013	.013
		Low Myopes	.001	.002	.994	-.005	.007
		Emmetropes	.004(*)	.002	.040	.000	.008
		M- H Hyperopes	-.008	.008	.873	-.033	.017
	M- H Hyperopes	M- H Myopes	.008	.009	.901	-.019	.035
		Low Myopes	.009	.009	.833	-.016	.034
		Emmetropes	.012	.008	.596	-.013	.037
		Low Hyperopes	.008	.008	.873	-.017	.033

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(4, 0)	M- H Myopes	Low Myopes	-.009	.012	.937	-.044	.025
		Emmetropes	-.006	.012	.986	-.039	.028
		Low Hyperopes	-.033	.011	.050	-.067	.000
		M- H Hyperopes	-.073(*)	.018	.001	-.123	-.023
	Low Myopes	M- H Myopes	.009	.012	.937	-.025	.044
		Emmetropes	.003	.005	.949	-.010	.017
		Low Hyperopes	-.024(*)	.005	.000	-.036	-.012
		M- H Hyperopes	-.064(*)	.014	.001	-.105	-.022
	Emmetropes	M- H Myopes	.006	.012	.986	-.028	.039
		Low Myopes	-.003	.005	.949	-.017	.010
		Low Hyperopes	-.027(*)	.003	.000	-.035	-.020
		M- H Hyperopes	-.067(*)	.014	.001	-.108	-.026
	Low Hyperopes	M- H Myopes	.033	.011	.050	.000	.067
		Low Myopes	.024(*)	.005	.000	.012	.036
		Emmetropes	.027(*)	.003	.000	.020	.035
		M- H Hyperopes	-.040	.014	.059	-.080	.001
	M- H Hyperopes	M- H Myopes	.073(*)	.018	.001	.023	.123
		Low Myopes	.064(*)	.014	.001	.022	.105
		Emmetropes	.067(*)	.014	.001	.026	.108
		Low Hyperopes	.040	.014	.059	-.001	.080
Z(4, 2)	M- H Myopes	Low Myopes	-.003	.007	.995	-.023	.017
		Emmetropes	-.001	.007	.999	-.021	.018
		Low Hyperopes	.000	.007	1.000	-.019	.020
		M- H Hyperopes	.001	.011	1.000	-.030	.032
	Low Myopes	M- H Myopes	.003	.007	.995	-.017	.023
		Emmetropes	.001	.003	.992	-.006	.009
		Low Hyperopes	.003	.003	.746	-.004	.010
		M- H Hyperopes	.004	.009	.994	-.023	.030
	Emmetropes	M- H Myopes	.001	.007	.999	-.018	.021
		Low Myopes	-.001	.003	.992	-.009	.006
		Low Hyperopes	.002	.002	.826	-.003	.007
		M- H Hyperopes	.002	.009	.999	-.023	.028
	Low Hyperopes	M- H Myopes	.000	.007	1.000	-.020	.019
		Low Myopes	-.003	.003	.746	-.010	.004
		Emmetropes	-.002	.002	.826	-.007	.003
		M- H Hyperopes	.001	.009	1.000	-.025	.026
	M- H Hyperopes	M- H Myopes	-.001	.011	1.000	-.032	.030
		Low Myopes	-.004	.009	.994	-.030	.023
		Emmetropes	-.002	.009	.999	-.028	.023
		Low Hyperopes	-.001	.009	1.000	-.026	.025
Z(4, 4)	M- H Myopes	Low Myopes	-.003	.007	.994	-.023	.018
		Emmetropes	-.004	.007	.984	-.023	.016
		Low Hyperopes	-.004	.007	.983	-.023	.016
		M- H Hyperopes	-.016	.009	.359	-.041	.009
	Low Myopes	M- H Myopes	.003	.007	.994	-.018	.023
		Emmetropes	-.001	.003	.999	-.008	.007
		Low Hyperopes	-.001	.003	.999	-.008	.006
		M- H Hyperopes	-.013	.006	.222	-.032	.005
	Emmetropes	M- H Myopes	.004	.007	.984	-.016	.023
		Low Myopes	.001	.003	.999	-.007	.008
		Low Hyperopes	.000	.002	1.000	-.004	.004
		M- H Hyperopes	-.013	.006	.226	-.030	.005
	Low Hyperopes	M- H Myopes	.004	.007	.983	-.016	.023
		Low Myopes	.001	.003	.999	-.006	.008
		Emmetropes	.000	.002	1.000	-.004	.004
		M- H Hyperopes	-.013	.006	.221	-.030	.005
	M- H Hyperopes	M- H Myopes	.016	.009	.359	-.009	.041
		Low Myopes	.013	.006	.222	-.005	.032
		Emmetropes	.013	.006	.226	-.005	.030
		Low Hyperopes	.013	.006	.221	-.005	.030

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(5,-5)	M- H Myopes	Low Myopes	.004	.003	.598	-.004	.012
		Emmetropes	.005	.003	.310	-.002	.013
		Low Hyperopes	.005	.003	.386	-.003	.012
		M- H Hyperopes	.004	.004	.910	-.009	.016
	Low Myopes	M- H Myopes	-.004	.003	.598	-.012	.004
		Emmetropes	.001	.001	.932	-.003	.005
		Low Hyperopes	.001	.001	.989	-.003	.004
		M- H Hyperopes	.000	.004	1.000	-.011	.011
	Emmetropes	M- H Myopes	-.005	.003	.310	-.013	.002
		Low Myopes	-.001	.001	.932	-.005	.003
		Low Hyperopes	.000	.001	.980	-.003	.002
		M- H Hyperopes	-.001	.004	.996	-.012	.010
	Low Hyperopes	M- H Myopes	-.005	.003	.386	-.012	.003
		Low Myopes	-.001	.001	.989	-.004	.003
		Emmetropes	.000	.001	.980	-.002	.003
		M- H Hyperopes	-.001	.004	.999	-.012	.010
	M- H Hyperopes	M- H Myopes	-.004	.004	.910	-.016	.009
		Low Myopes	.000	.004	1.000	-.011	.011
		Emmetropes	.001	.004	.996	-.010	.012
		Low Hyperopes	.001	.004	.999	-.010	.012
Z(5,-3)	M- H Myopes	Low Myopes	-.003	.002	.749	-.010	.004
		Emmetropes	-.002	.002	.948	-.008	.005
		Low Hyperopes	-.002	.002	.958	-.008	.005
		M- H Hyperopes	.008	.004	.305	-.004	.021
	Low Myopes	M- H Myopes	.003	.002	.749	-.004	.010
		Emmetropes	.001	.001	.871	-.002	.005
		Low Hyperopes	.001	.001	.785	-.002	.005
		M- H Hyperopes	.011	.004	.051	.000	.023
	Emmetropes	M- H Myopes	.002	.002	.948	-.005	.008
		Low Myopes	-.001	.001	.871	-.005	.002
		Low Hyperopes	.000	.001	1.000	-.002	.002
		M- H Hyperopes	.010	.004	.090	-.001	.021
	Low Hyperopes	M- H Myopes	.002	.002	.958	-.005	.008
		Low Myopes	-.001	.001	.785	-.005	.002
		Emmetropes	.000	.001	1.000	-.002	.002
		M- H Hyperopes	.010	.004	.094	-.001	.021
	M- H Hyperopes	M- H Myopes	-.008	.004	.305	-.021	.004
		Low Myopes	-.011	.004	.051	-.023	.000
		Emmetropes	-.010	.004	.090	-.021	.001
		Low Hyperopes	-.010	.004	.094	-.021	.001
Z(5,-1)	M- H Myopes	Low Myopes	-.001	.005	.998	-.014	.012
		Emmetropes	-.005	.004	.801	-.017	.008
		Low Hyperopes	-.005	.004	.731	-.018	.007
		M- H Hyperopes	-.008	.006	.669	-.024	.008
	Low Myopes	M- H Myopes	.001	.005	.998	-.012	.014
		Emmetropes	-.003	.002	.287	-.008	.001
		Low Hyperopes	-.004	.002	.120	-.008	.001
		M- H Hyperopes	-.006	.004	.555	-.018	.006
	Emmetropes	M- H Myopes	.005	.004	.801	-.008	.017
		Low Myopes	.003	.002	.287	-.001	.008
		Low Hyperopes	.000	.001	.990	-.003	.002
		M- H Hyperopes	-.003	.004	.949	-.014	.009
	Low Hyperopes	M- H Myopes	.005	.004	.731	-.007	.018
		Low Myopes	.004	.002	.120	-.001	.008
		Emmetropes	.000	.001	.990	-.002	.003
		M- H Hyperopes	-.002	.004	.973	-.014	.009
	M- H Hyperopes	M- H Myopes	.008	.006	.669	-.008	.024
		Low Myopes	.006	.004	.555	-.006	.018
		Emmetropes	.003	.004	.949	-.009	.014
		Low Hyperopes	.002	.004	.973	-.009	.014

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(5, 1)	M- H Myopes	Low Myopes	.000	.003	1.000	-.007	.008
		Emmetropes	-.001	.002	.975	-.008	.005
		Low Hyperopes	-.004	.002	.367	-.011	.002
		M- H Hyperopes	-.007	.004	.402	-.018	.004
	Low Myopes	M- H Myopes	.000	.003	1.000	-.008	.007
		Emmetropes	-.002	.001	.651	-.005	.002
		Low Hyperopes	-.005(*)	.001	.002	-.008	-.001
		M- H Hyperopes	-.007	.003	.232	-.017	.003
	Emmetropes	M- H Myopes	.001	.002	.975	-.005	.008
		Low Myopes	.002	.001	.651	-.002	.005
		Low Hyperopes	-.003(*)	.001	.002	-.005	-.001
		M- H Hyperopes	-.006	.003	.446	-.015	.004
	Low Hyperopes	M- H Myopes	.004	.002	.367	-.002	.011
		Low Myopes	.005(*)	.001	.002	.001	.008
		Emmetropes	.003(*)	.001	.002	.001	.005
		M- H Hyperopes	-.003	.003	.919	-.013	.007
	M- H Hyperopes	M- H Myopes	.007	.004	.402	-.004	.018
		Low Myopes	.007	.003	.232	-.003	.017
		Emmetropes	.006	.003	.446	-.004	.015
		Low Hyperopes	.003	.003	.919	-.007	.013
Z(5, 3)	M- H Myopes	Low Myopes	-.001	.002	.944	-.007	.004
		Emmetropes	-.002	.002	.768	-.007	.003
		Low Hyperopes	-.003	.002	.485	-.007	.002
		M- H Hyperopes	-.001	.003	.995	-.011	.008
	Low Myopes	M- H Myopes	.001	.002	.944	-.004	.007
		Emmetropes	-.001	.001	.984	-.004	.002
		Low Hyperopes	-.001	.001	.705	-.004	.001
		M- H Hyperopes	.000	.003	1.000	-.009	.009
	Emmetropes	M- H Myopes	.002	.002	.768	-.003	.007
		Low Myopes	.001	.001	.984	-.002	.004
		Low Hyperopes	-.001	.001	.807	-.002	.001
		M- H Hyperopes	.001	.003	.999	-.008	.010
	Low Hyperopes	M- H Myopes	.003	.002	.485	-.002	.007
		Low Myopes	.001	.001	.705	-.001	.004
		Emmetropes	.001	.001	.807	-.001	.002
		M- H Hyperopes	.001	.003	.989	-.007	.010
	M- H Hyperopes	M- H Myopes	.001	.003	.995	-.008	.011
		Low Myopes	.000	.003	1.000	-.009	.009
		Emmetropes	-.001	.003	.999	-.010	.008
		Low Hyperopes	-.001	.003	.989	-.010	.007
Z(5, 5)	M- H Myopes	Low Myopes	.006	.003	.334	-.003	.014
		Emmetropes	.005	.003	.364	-.003	.014
		Low Hyperopes	.007	.003	.108	-.001	.015
		M- H Hyperopes	.002	.004	.996	-.010	.013
	Low Myopes	M- H Myopes	-.006	.003	.334	-.014	.003
		Emmetropes	.000	.001	.997	-.004	.003
		Low Hyperopes	.001	.001	.808	-.002	.005
		M- H Hyperopes	-.004	.003	.699	-.014	.005
	Emmetropes	M- H Myopes	-.005	.003	.364	-.014	.003
		Low Myopes	.000	.001	.997	-.003	.004
		Low Hyperopes	.002	.001	.089	.000	.004
		M- H Hyperopes	-.004	.003	.749	-.013	.005
	Low Hyperopes	M- H Myopes	-.007	.003	.108	-.015	.001
		Low Myopes	-.001	.001	.808	-.005	.002
		Emmetropes	-.002	.001	.089	-.004	.000
		M- H Hyperopes	-.006	.003	.384	-.015	.004
	M- H Hyperopes	M- H Myopes	-.002	.004	.996	-.013	.010
		Low Myopes	.004	.003	.699	-.005	.014
		Emmetropes	.004	.003	.749	-.005	.013
		Low Hyperopes	.006	.003	.384	-.004	.015

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(6,-6)	M- H Myopes	Low Myopes	-.001	.002	.962	-.006	.004
		Emmetropes	-.002	.002	.762	-.007	.003
		Low Hyperopes	-.002	.002	.714	-.007	.003
		M- H Hyperopes	.000	.003	1.000	-.008	.007
	Low Myopes	M- H Myopes	.001	.002	.962	-.004	.006
		Emmetropes	-.001	.001	.910	-.003	.002
		Low Hyperopes	-.001	.001	.833	-.003	.001
		M- H Hyperopes	.001	.002	.993	-.006	.008
	Emmetropes	M- H Myopes	.002	.002	.762	-.003	.007
		Low Myopes	.001	.001	.910	-.002	.003
		Low Hyperopes	.000	.001	1.000	-.002	.001
		M- H Hyperopes	.002	.002	.934	-.005	.008
	Low Hyperopes	M- H Myopes	.002	.002	.714	-.003	.007
		Low Myopes	.001	.001	.833	-.001	.003
		Emmetropes	.000	.001	1.000	-.001	.002
		M- H Hyperopes	.002	.002	.917	-.005	.008
	M- H Hyperopes	M- H Myopes	.000	.003	1.000	-.007	.008
		Low Myopes	-.001	.002	.993	-.008	.006
		Emmetropes	-.002	.002	.934	-.008	.005
		Low Hyperopes	-.002	.002	.917	-.008	.005
Z(6,-4)	M- H Myopes	Low Myopes	-.003	.002	.605	-.008	.003
		Emmetropes	-.003	.002	.523	-.007	.002
		Low Hyperopes	-.004	.002	.226	-.008	.001
		M- H Hyperopes	-.001	.002	.971	-.008	.005
	Low Myopes	M- H Myopes	.003	.002	.605	-.003	.008
		Emmetropes	.000	.001	1.000	-.002	.002
		Low Hyperopes	-.001	.001	.662	-.003	.001
		M- H Hyperopes	.001	.002	.959	-.004	.006
	Emmetropes	M- H Myopes	.003	.002	.523	-.002	.007
		Low Myopes	.000	.001	1.000	-.002	.002
		Low Hyperopes	-.001	.000	.237	-.002	.000
		M- H Hyperopes	.001	.002	.936	-.003	.006
	Low Hyperopes	M- H Myopes	.004	.002	.226	-.001	.008
		Low Myopes	.001	.001	.662	-.001	.003
		Emmetropes	.001	.000	.237	.000	.002
		M- H Hyperopes	.002	.002	.655	-.003	.007
	M- H Hyperopes	M- H Myopes	.001	.002	.971	-.005	.008
		Low Myopes	-.001	.002	.959	-.006	.004
		Emmetropes	-.001	.002	.936	-.006	.003
		Low Hyperopes	-.002	.002	.655	-.007	.003
Z(6,-2)	M- H Myopes	Low Myopes	-.001	.002	.970	-.006	.004
		Emmetropes	-.001	.002	.976	-.006	.004
		Low Hyperopes	-.001	.002	.997	-.005	.004
		M- H Hyperopes	-.001	.003	.996	-.008	.006
	Low Myopes	M- H Myopes	.001	.002	.970	-.004	.006
		Emmetropes	.000	.001	1.000	-.002	.002
		Low Hyperopes	.001	.001	.904	-.001	.002
		M- H Hyperopes	.000	.002	1.000	-.006	.006
	Emmetropes	M- H Myopes	.001	.002	.976	-.004	.006
		Low Myopes	.000	.001	1.000	-.002	.002
		Low Hyperopes	.000	.000	.824	-.001	.002
		M- H Hyperopes	.000	.002	1.000	-.006	.006
	Low Hyperopes	M- H Myopes	.001	.002	.997	-.004	.005
		Low Myopes	-.001	.001	.904	-.002	.001
		Emmetropes	.000	.000	.824	-.002	.001
		M- H Hyperopes	.000	.002	.999	-.007	.006
	M- H Hyperopes	M- H Myopes	.001	.003	.996	-.006	.008
		Low Myopes	.000	.002	1.000	-.006	.006
		Emmetropes	.000	.002	1.000	-.006	.006
		Low Hyperopes	.000	.002	.999	-.006	.007

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(6, 0)	M- H Myopes	Low Myopes	.001	.002	.976	-.006	.009
		Emmetropes	.003	.002	.710	-.004	.010
		Low Hyperopes	.006	.002	.144	-.001	.012
		M- H Hyperopes	.004	.004	.792	-.006	.015
	Low Myopes	M- H Myopes	-.001	.002	.976	-.009	.006
		Emmetropes	.002	.001	.648	-.002	.005
		Low Hyperopes	.004(*)	.001	.001	.001	.007
		M- H Hyperopes	.003	.003	.901	-.006	.012
	Emmetropes	M- H Myopes	-.003	.002	.710	-.010	.004
		Low Myopes	-.002	.001	.648	-.005	.002
		Low Hyperopes	.003(*)	.001	.001	.001	.004
		M- H Hyperopes	.001	.003	.994	-.008	.010
	Low Hyperopes	M- H Myopes	-.006	.002	.144	-.012	.001
		Low Myopes	-.004(*)	.001	.001	-.007	-.001
		Emmetropes	-.003(*)	.001	.001	-.004	-.001
		M- H Hyperopes	-.001	.003	.991	-.010	.008
	M- H Hyperopes	M- H Myopes	-.004	.004	.792	-.015	.006
		Low Myopes	-.003	.003	.901	-.012	.006
		Emmetropes	-.001	.003	.994	-.010	.008
		Low Hyperopes	.001	.003	.991	-.008	.010
Z(6, 2)	M- H Myopes	Low Myopes	.001	.002	.983	-.005	.007
		Emmetropes	.002	.002	.934	-.004	.008
		Low Hyperopes	.002	.002	.785	-.004	.008
		M- H Hyperopes	.003	.003	.835	-.006	.013
	Low Myopes	M- H Myopes	-.001	.002	.983	-.007	.005
		Emmetropes	.000	.001	.991	-.002	.003
		Low Hyperopes	.001	.001	.729	-.001	.004
		M- H Hyperopes	.002	.003	.921	-.006	.010
	Emmetropes	M- H Myopes	-.002	.002	.934	-.008	.004
		Low Myopes	.000	.001	.991	-.003	.002
		Low Hyperopes	.001	.001	.788	-.001	.002
		M- H Hyperopes	.002	.003	.958	-.006	.010
	Low Hyperopes	M- H Myopes	-.002	.002	.785	-.008	.004
		Low Myopes	-.001	.001	.729	-.004	.001
		Emmetropes	-.001	.001	.788	-.002	.001
		M- H Hyperopes	.001	.003	.992	-.007	.009
	M- H Hyperopes	M- H Myopes	-.003	.003	.835	-.013	.006
		Low Myopes	-.002	.003	.921	-.010	.006
		Emmetropes	-.002	.003	.958	-.010	.006
		Low Hyperopes	-.001	.003	.992	-.009	.007
Z(6, 4)	M- H Myopes	Low Myopes	-.001	.002	.982	-.007	.005
		Emmetropes	-.002	.002	.904	-.007	.004
		Low Hyperopes	-.002	.002	.694	-.008	.003
		M- H Hyperopes	-.001	.003	.997	-.010	.008
	Low Myopes	M- H Myopes	.001	.002	.982	-.005	.007
		Emmetropes	-.001	.001	.974	-.003	.002
		Low Hyperopes	-.001	.001	.552	-.004	.001
		M- H Hyperopes	.000	.003	1.000	-.008	.008
	Emmetropes	M- H Myopes	.002	.002	.904	-.004	.007
		Low Myopes	.001	.001	.974	-.002	.003
		Low Hyperopes	-.001	.001	.640	-.002	.001
		M- H Hyperopes	.001	.003	.999	-.007	.008
	Low Hyperopes	M- H Myopes	.002	.002	.694	-.003	.008
		Low Myopes	.001	.001	.552	-.001	.004
		Emmetropes	.001	.001	.640	-.001	.002
		M- H Hyperopes	.001	.002	.983	-.006	.009
	M- H Hyperopes	M- H Myopes	.001	.003	.997	-.008	.010
		Low Myopes	.000	.003	1.000	-.008	.008
		Emmetropes	-.001	.003	.999	-.008	.007
		Low Hyperopes	-.001	.002	.983	-.009	.006

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(6, 6)	M- H Myopes	Low Myopes	-.001	.002	.990	-.008	.006
		Emmetropes	-.001	.002	.995	-.007	.006
		Low Hyperopes	.000	.002	1.000	-.006	.007
		M- H Hyperopes	-.002	.003	.964	-.011	.007
	Low Myopes	M- H Myopes	.001	.002	.990	-.006	.008
		Emmetropes	.000	.001	.999	-.003	.003
		Low Hyperopes	.001	.001	.773	-.002	.004
		M- H Hyperopes	-.001	.003	.994	-.008	.006
	Emmetropes	M- H Myopes	.001	.002	.995	-.006	.007
		Low Myopes	.000	.001	.999	-.003	.003
		Low Hyperopes	.001	.001	.540	-.001	.003
		M- H Hyperopes	-.001	.002	.984	-.008	.006
	Low Hyperopes	M- H Myopes	.000	.002	1.000	-.007	.006
		Low Myopes	-.001	.001	.773	-.004	.002
		Emmetropes	-.001	.001	.540	-.003	.001
		M- H Hyperopes	-.002	.002	.887	-.009	.005
	M- H Hyperopes	M- H Myopes	.002	.003	.964	-.007	.011
		Low Myopes	.001	.003	.994	-.006	.008
		Emmetropes	.001	.002	.984	-.006	.008
		Low Hyperopes	.002	.002	.887	-.005	.009

** The mean difference is significant at the .05 level.*

RMS of Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Refractive Error Group groups

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Defocus RMS	Myopes	Emmetropes	1.644(*)	.097	.000	1.415	1.873
		Hyperopes	1.150(*)	.098	.000	.918	1.382
	Emmetropes	Myopes	-1.644(*)	.097	.000	-1.873	-1.415
		Hyperopes	-.495(*)	.020	.000	-.542	-.447
	Hyperopes	Myopes	-1.150(*)	.098	.000	-1.382	-.918
		Emmetropes	.495(*)	.020	.000	.447	.542
Astigmatism RMS	Myopes	Emmetropes	.034(*)	.012	.018	.005	.064
		Hyperopes	.053(*)	.012	.000	.025	.080
	Emmetropes	Myopes	-.034(*)	.012	.018	-.064	-.005
		Hyperopes	.018(*)	.007	.030	.001	.035
	Hyperopes	Myopes	-.053(*)	.012	.000	-.080	-.025
		Emmetropes	-.018(*)	.007	.030	-.035	-.001
Coma RMS	Myopes	Emmetropes	.012	.006	.092	-.001	.025
		Hyperopes	.011	.005	.120	-.002	.023
	Emmetropes	Myopes	-.012	.006	.092	-.025	.001
		Hyperopes	-.001	.003	.913	-.009	.006
	Hyperopes	Myopes	-.011	.005	.120	-.023	.002
		Emmetropes	.001	.003	.913	-.006	.009
Trefoil RMS	Myopes	Emmetropes	.008	.004	.119	-.002	.019
		Hyperopes	.006	.004	.274	-.003	.015
	Emmetropes	Myopes	-.008	.004	.119	-.019	.002
		Hyperopes	-.002	.003	.662	-.009	.004
	Hyperopes	Myopes	-.006	.004	.274	-.015	.003
		Emmetropes	.002	.003	.662	-.004	.009
Spherical Aberration RMS	Myopes	Emmetropes	.003	.003	.639	-.005	.011
		Hyperopes	-.018(*)	.003	.000	-.026	-.010
	Emmetropes	Myopes	-.003	.003	.639	-.011	.005
		Hyperopes	-.021(*)	.002	.000	-.027	-.015
	Hyperopes	Myopes	.018(*)	.003	.000	.010	.026
		Emmetropes	.021(*)	.002	.000	.015	.027
Quatrefoil RMS	Myopes	Emmetropes	.004	.002	.152	-.001	.008
		Hyperopes	.001	.002	.713	-.003	.006
	Emmetropes	Myopes	-.004	.002	.152	-.008	.001
		Hyperopes	-.002	.001	.121	-.005	.000
	Hyperopes	Myopes	-.001	.002	.713	-.006	.003
		Emmetropes	.002	.001	.121	.000	.005
Secondary Astigmatism RMS	Myopes	Emmetropes	-.002	.002	.388	-.007	.002
		Hyperopes	-.008(*)	.002	.000	-.012	-.004
	Emmetropes	Myopes	.002	.002	.388	-.002	.007
		Hyperopes	-.006(*)	.001	.000	-.009	-.003
	Hyperopes	Myopes	.008(*)	.002	.000	.004	.012
		Emmetropes	.006(*)	.001	.000	.003	.009
Higher Orders RMS	Myopes	Emmetropes	.012	.005	.062	.000	.025
		Hyperopes	-.002	.005	.953	-.014	.011
	Emmetropes	Myopes	-.012	.005	.062	-.025	.000
		Hyperopes	-.014(*)	.003	.000	-.022	-.006
	Hyperopes	Myopes	.002	.005	.953	-.011	.014
		Emmetropes	.014(*)	.003	.000	.006	.022
Total Aberrations RMS	Myopes	Emmetropes	1.524(*)	.095	.000	1.299	1.749
		Hyperopes	1.115(*)	.096	.000	.887	1.342
	Emmetropes	Myopes	-1.524(*)	.095	.000	-1.749	-1.299
		Hyperopes	-.410(*)	.019	.000	-.455	-.365
	Hyperopes	Myopes	-1.115(*)	.096	.000	-1.342	-.887
		Emmetropes	.410(*)	.019	.000	.365	.455

** The mean difference is significant at the .05 level*

RMS of Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Refractive Error subgroups

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Defocus RMS	M-H Myopes	Low Myopes	2.568(*)	.216	.000	1.942	3.193
		Emmetropes	3.776(*)	.208	.000	3.168	4.385
		Low Hyperopes	3.346(*)	.208	.000	2.738	3.955
		M-H Hyperopes	.319	.318	.853	-.586	1.223
	Low Myopes	M-H Myopes	-2.568(*)	.216	.000	-3.193	-1.942
		Emmetropes	1.209(*)	.060	.000	1.043	1.374
		Low Hyperopes	.779(*)	.060	.000	.612	.945
		M-H Hyperopes	-2.249(*)	.248	.000	-2.980	-1.517
	Emmetropes	M-H Myopes	-3.776(*)	.208	.000	-4.385	-3.168
		Low Myopes	-1.209(*)	.060	.000	-1.374	-1.043
		Low Hyperopes	-.430(*)	.014	.000	-.469	-.391
		M-H Hyperopes	-3.458(*)	.241	.000	-4.175	-2.740
	Low Hyperopes	M-H Myopes	-3.346(*)	.208	.000	-3.955	-2.738
		Low Myopes	-.779(*)	.060	.000	-.945	-.612
		Emmetropes	.430(*)	.014	.000	.391	.469
		M-H Hyperopes	-3.027(*)	.241	.000	-3.745	-2.310
	M-H Hyperopes	M-H Myopes	-.319	.318	.853	-1.223	.586
		Low Myopes	2.249(*)	.248	.000	1.517	2.980
		Emmetropes	3.458(*)	.241	.000	2.740	4.175
		Low Hyperopes	3.027(*)	.241	.000	2.310	3.745
Astigmatism RMS	M-H Myopes	Low Myopes	.006	.028	1.000	-.075	.087
		Emmetropes	.039	.027	.583	-.038	.116
		Low Hyperopes	.059	.026	.184	-.017	.135
		M-H Hyperopes	-.010	.038	.999	-.118	.098
	Low Myopes	M-H Myopes	-.006	.028	1.000	-.087	.075
		Emmetropes	.033	.014	.106	-.004	.070
		Low Hyperopes	.053(*)	.013	.000	.018	.088
		M-H Hyperopes	-.016	.031	.983	-.105	.072
	Emmetropes	M-H Myopes	-.039	.027	.583	-.116	.038
		Low Myopes	-.033	.014	.106	-.070	.004
		Low Hyperopes	.020(*)	.007	.045	.000	.040
		M-H Hyperopes	-.049	.029	.440	-.134	.035
	Low Hyperopes	M-H Myopes	-.059	.026	.184	-.135	.017
		Low Myopes	-.053(*)	.013	.000	-.088	-.018
		Emmetropes	-.020(*)	.007	.045	-.040	.000
		M-H Hyperopes	-.069	.028	.139	-.153	.015
	M-H Hyperopes	M-H Myopes	.010	.038	.999	-.098	.118
		Low Myopes	.016	.031	.983	-.072	.105
		Emmetropes	.049	.029	.440	-.035	.134
		Low Hyperopes	.069	.028	.139	-.015	.153
Coma RMS	M-H Myopes	Low Myopes	-.009	.012	.938	-.042	.024
		Emmetropes	.004	.011	.994	-.026	.035
		Low Hyperopes	.004	.010	.996	-.026	.034
		M-H Hyperopes	-.026	.017	.550	-.075	.023
	Low Myopes	M-H Myopes	.009	.012	.938	-.024	.042
		Emmetropes	.013	.006	.211	-.004	.030
		Low Hyperopes	.013	.006	.206	-.004	.029
		M-H Hyperopes	-.017	.015	.776	-.060	.026
	Emmetropes	M-H Myopes	-.004	.011	.994	-.035	.026
		Low Myopes	-.013	.006	.211	-.030	.004
		Low Hyperopes	-.001	.003	1.000	-.010	.009
		M-H Hyperopes	-.030	.014	.222	-.072	.011
	Low Hyperopes	M-H Myopes	-.004	.010	.996	-.034	.026
		Low Myopes	-.013	.006	.206	-.029	.004
		Emmetropes	.001	.003	1.000	-.009	.010
		M-H Hyperopes	-.030	.014	.230	-.071	.011
	M-H Hyperopes	M-H Myopes	.026	.017	.550	-.023	.075
		Low Myopes	.017	.015	.776	-.026	.060
		Emmetropes	.030	.014	.222	-.011	.072
		Low Hyperopes	.030	.014	.230	-.011	.071

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Trefoil RMS	M-H Myopes	Low Myopes	-.010	.009	.832	-.036	.016
		Emmetropes	.001	.009	1.000	-.024	.025
		Low Hyperopes	-.002	.008	.999	-.026	.023
		M-H Hyperopes	-.009	.012	.927	-.043	.024
	Low Myopes	M-H Myopes	.010	.009	.832	-.016	.036
		Emmetropes	.010	.005	.174	-.002	.023
		Low Hyperopes	.008	.004	.365	-.004	.019
		M-H Hyperopes	.000	.009	1.000	-.027	.027
	Emmetropes	M-H Myopes	-.001	.009	1.000	-.025	.024
		Low Myopes	-.010	.005	.174	-.023	.002
		Low Hyperopes	-.002	.003	.910	-.010	.005
		M-H Hyperopes	-.010	.009	.773	-.036	.016
	Low Hyperopes	M-H Myopes	.002	.008	.999	-.023	.026
		Low Myopes	-.008	.004	.365	-.019	.004
		Emmetropes	.002	.003	.910	-.005	.010
		M-H Hyperopes	-.008	.009	.896	-.033	.018
	M-H Hyperopes	M-H Myopes	.009	.012	.927	-.024	.043
		Low Myopes	.000	.009	1.000	-.027	.027
		Emmetropes	.010	.009	.773	-.016	.036
		Low Hyperopes	.008	.009	.896	-.018	.033
Spherical Aberration RMS	M-H Myopes	Low Myopes	.001	.008	1.000	-.023	.025
		Emmetropes	.004	.008	.983	-.019	.027
		Low Hyperopes	-.016	.008	.278	-.039	.007
		M-H Hyperopes	-.051(*)	.016	.018	-.096	-.006
	Low Myopes	M-H Myopes	-.001	.008	1.000	-.025	.023
		Emmetropes	.003	.004	.939	-.007	.013
		Low Hyperopes	-.017(*)	.004	.000	-.027	-.008
		M-H Hyperopes	-.053(*)	.014	.007	-.094	-.012
	Emmetropes	M-H Myopes	-.004	.008	.983	-.027	.019
		Low Myopes	-.003	.004	.939	-.013	.007
		Low Hyperopes	-.020(*)	.002	.000	-.027	-.014
		M-H Hyperopes	-.056(*)	.014	.004	-.096	-.015
	Low Hyperopes	M-H Myopes	.016	.008	.278	-.007	.039
		Low Myopes	.017(*)	.004	.000	.008	.027
		Emmetropes	.020(*)	.002	.000	.014	.027
		M-H Hyperopes	-.035	.014	.107	-.076	.005
	M-H Hyperopes	M-H Myopes	.051(*)	.016	.018	.006	.096
		Low Myopes	.053(*)	.014	.007	.012	.094
		Emmetropes	.056(*)	.014	.004	.015	.096
		Low Hyperopes	.035	.014	.107	-.005	.076
Quatrefoil RMS	M-H Myopes	Low Myopes	.005	.005	.802	-.008	.018
		Emmetropes	.008	.004	.364	-.004	.020
		Low Hyperopes	.006	.004	.648	-.006	.018
		M-H Hyperopes	.002	.006	.999	-.016	.020
	Low Myopes	M-H Myopes	-.005	.005	.802	-.018	.008
		Emmetropes	.003	.002	.686	-.003	.009
		Low Hyperopes	.001	.002	.997	-.005	.006
		M-H Hyperopes	-.003	.005	.965	-.018	.012
	Emmetropes	M-H Myopes	-.008	.004	.364	-.020	.004
		Low Myopes	-.003	.002	.686	-.009	.003
		Low Hyperopes	-.002	.001	.342	-.005	.001
		M-H Hyperopes	-.006	.005	.720	-.021	.008
	Low Hyperopes	M-H Myopes	-.006	.004	.648	-.018	.006
		Low Myopes	-.001	.002	.997	-.006	.005
		Emmetropes	.002	.001	.342	-.001	.005
		M-H Hyperopes	-.004	.005	.915	-.018	.010
	M-H Hyperopes	M-H Myopes	-.002	.006	.999	-.020	.016
		Low Myopes	.003	.005	.965	-.012	.018
		Emmetropes	.006	.005	.720	-.008	.021
		Low Hyperopes	.004	.005	.915	-.010	.018

Dependent Variable	(I) Refractive Error Group	(J) Refractive Error Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Secondary Astigmatism RMS	M-H Myopes	Low Myopes	.005	.004	.807	-.008	.017
		Emmetropes	.002	.004	.995	-.011	.014
		Low Hyperopes	-.004	.004	.877	-.016	.008
		M-H Hyperopes	-.009	.008	.798	-.033	.014
	Low Myopes	M-H Myopes	-.005	.004	.807	-.017	.008
		Emmetropes	-.003	.002	.440	-.008	.002
		Low Hyperopes	-.009(*)	.002	.000	-.014	-.004
		M-H Hyperopes	-.014	.007	.340	-.035	.008
	Emmetropes	M-H Myopes	-.002	.004	.995	-.014	.011
		Low Myopes	.003	.002	.440	-.002	.008
		Low Hyperopes	-.005(*)	.001	.000	-.009	-.002
		M-H Hyperopes	-.011	.007	.578	-.032	.011
	Low Hyperopes	M-H Myopes	.004	.004	.877	-.008	.016
		Low Myopes	.009(*)	.002	.000	.004	.014
		Emmetropes	.005(*)	.001	.000	.002	.009
		M-H Hyperopes	-.005	.007	.948	-.026	.016
	M-H Hyperopes	M-H Myopes	.009	.008	.798	-.014	.033
		Low Myopes	.014	.007	.340	-.008	.035
		Emmetropes	.011	.007	.578	-.011	.032
		Low Hyperopes	.005	.007	.948	-.016	.026
Higher Orders RMS	M-H Myopes	Low Myopes	-.011	.012	.899	-.046	.024
		Emmetropes	.003	.011	.999	-.030	.036
		Low Hyperopes	-.010	.011	.911	-.043	.023
		M-H Hyperopes	-.052(*)	.017	.028	-.100	-.004
	Low Myopes	M-H Myopes	.011	.012	.899	-.024	.046
		Emmetropes	.014	.006	.115	-.002	.030
		Low Hyperopes	.001	.006	.999	-.014	.017
		M-H Hyperopes	-.041(*)	.014	.041	-.081	-.001
	Emmetropes	M-H Myopes	-.003	.011	.999	-.036	.030
		Low Myopes	-.014	.006	.115	-.030	.002
		Low Hyperopes	-.013(*)	.003	.001	-.022	-.004
		M-H Hyperopes	-.055(*)	.013	.003	-.094	-.017
	Low Hyperopes	M-H Myopes	.010	.011	.911	-.023	.043
		Low Myopes	-.001	.006	.999	-.017	.014
		Emmetropes	.013(*)	.003	.001	.004	.022
		M-H Hyperopes	-.042(*)	.013	.025	-.080	-.004
	M-H Hyperopes	M-H Myopes	.052(*)	.017	.028	.004	.100
		Low Myopes	.041(*)	.014	.041	.001	.081
		Emmetropes	.055(*)	.013	.003	.017	.094
		Low Hyperopes	.042(*)	.013	.025	.004	.080
Total Aberrations RMS	M-H Myopes	Low Myopes	2.531(*)	.216	.000	1.906	3.156
		Emmetropes	3.626(*)	.208	.000	3.018	4.234
		Low Hyperopes	3.280(*)	.208	.000	2.671	3.888
		M-H Hyperopes	.312	.317	.861	-.589	1.213
	Low Myopes	M-H Myopes	-2.531(*)	.216	.000	-3.156	-1.906
		Emmetropes	1.095(*)	.058	.000	.935	1.255
		Low Hyperopes	.748(*)	.058	.000	.587	.910
		M-H Hyperopes	-2.219(*)	.246	.000	-2.945	-1.494
	Emmetropes	M-H Myopes	-3.626(*)	.208	.000	-4.234	-3.018
		Low Myopes	-1.095(*)	.058	.000	-1.255	-.935
		Low Hyperopes	-.346(*)	.013	.000	-.381	-.311
		M-H Hyperopes	-3.314(*)	.239	.000	-4.026	-2.601
	Low Hyperopes	M-H Myopes	-3.280(*)	.208	.000	-3.888	-2.671
		Low Myopes	-.748(*)	.058	.000	-.910	-.587
		Emmetropes	.346(*)	.013	.000	.311	.381
		M-H Hyperopes	-2.968(*)	.239	.000	-3.680	-2.255
	M-H Hyperopes	M-H Myopes	-.312	.317	.861	-1.213	.589
		Low Myopes	2.219(*)	.246	.000	1.494	2.945
		Emmetropes	3.314(*)	.239	.000	2.601	4.026
		Low Hyperopes	2.968(*)	.239	.000	2.255	3.680

** The mean difference is significant at the .05 level*

Refractive components analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Ethnic groups

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
M	Caucasian	East Asian	1.255(*)	.121	.000	.896	1.613
		Indian/Pakistani/ Sri Lankan	.947(*)	.134	.000	.543	1.351
		Middle Eastern	.145	.084	.596	-.106	.397
		Mixed	.317(*)	.099	.026	.022	.613
		Others	.241	.100	.208	-.061	.543
		Unknown	.057	.065	.974	-.134	.249
	East Asian	Caucasian	-1.255(*)	.121	.000	-1.613	-.896
		Indian/Pakistani/ Sri Lankan	-.308	.173	.564	-.824	.208
		Middle Eastern	-1.109(*)	.138	.000	-1.519	-.700
		Mixed	-.937(*)	.148	.000	-1.376	-.499
		Others	-1.014(*)	.149	.000	-1.455	-.572
		Unknown	-1.197(*)	.127	.000	-1.575	-.820
	Indian/Pakistani/ Sri Lankan	Caucasian	-.947(*)	.134	.000	-1.351	-.543
		East Asian	.308	.173	.564	-.208	.824
		Middle Eastern	-.801(*)	.150	.000	-1.250	-.352
		Mixed	-.629(*)	.159	.002	-1.104	-.154
		Others	-.705(*)	.160	.000	-1.183	-.227
		Unknown	-.889(*)	.140	.000	-1.310	-.468
	Middle Eastern	Caucasian	-.145	.084	.596	-.397	.106
		East Asian	1.109(*)	.138	.000	.700	1.519
		Indian/Pakistani/ Sri Lankan	.801(*)	.150	.000	.352	1.250
		Mixed	.172	.120	.782	-.184	.529
		Others	.096	.121	.985	-.265	.457
		Unknown	-.088	.093	.965	-.366	.190
	Mixed	Caucasian	-.317(*)	.099	.026	-.613	-.022
		East Asian	.937(*)	.148	.000	.499	1.376
		Indian/Pakistani/ Sri Lankan	.629(*)	.159	.002	.154	1.104
		Middle Eastern	-.172	.120	.782	-.529	.184
		Others	-.076	.132	.997	-.469	.317
		Unknown	-.260	.107	.192	-.579	.059
	Others	Caucasian	-.241	.100	.208	-.543	.061
		East Asian	1.014(*)	.149	.000	.572	1.455
		Indian/Pakistani/ Sri Lankan	.705(*)	.160	.000	.227	1.183
		Middle Eastern	-.096	.121	.985	-.457	.265
		Mixed	.076	.132	.997	-.317	.469
		Unknown	-.184	.108	.620	-.508	.140
	Unknown	Caucasian	-.057	.065	.974	-.249	.134
		East Asian	1.197(*)	.127	.000	.820	1.575
		Indian/Pakistani/ Sri Lankan	.889(*)	.140	.000	.468	1.310
		Middle Eastern	.088	.093	.965	-.190	.366
		Mixed	.260	.107	.192	-.059	.579
		Others	.184	.108	.620	-.140	.508

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
J_0	Caucasian	East Asian	-.056(*)	.013	.000	-.095	-.018
		Indian/Pakistani/ Sri Lankan	-.014	.019	.991	-.071	.044
		Middle Eastern	-.015	.017	.977	-.066	.037
		Mixed	-.015	.014	.944	-.057	.027
		Others	-.068(*)	.019	.010	-.126	-.011
		Unknown	-.013	.010	.861	-.044	.018
	East Asian	Caucasian	.056(*)	.013	.000	.018	.095
		Indian/Pakistani/ Sri Lankan	.042	.022	.437	-.022	.107
		Middle Eastern	.041	.020	.378	-.018	.101
		Mixed	.041	.017	.210	-.010	.093
		Others	-.012	.022	.998	-.077	.052
		Unknown	.043	.015	.054	.000	.086
	Indian/Pakistani/ Sri Lankan	Caucasian	.014	.019	.991	-.044	.071
		East Asian	-.042	.022	.437	-.107	.022
		Middle Eastern	-.001	.024	1.000	-.074	.071
		Mixed	-.001	.022	1.000	-.067	.065
		Others	-.055	.026	.342	-.132	.022
		Unknown	.000	.020	1.000	-.060	.060
	Middle Eastern	Caucasian	.015	.017	.977	-.037	.066
		East Asian	-.041	.020	.378	-.101	.018
		Indian/Pakistani/ Sri Lankan	.001	.024	1.000	-.071	.074
		Mixed	.000	.021	1.000	-.061	.062
		Others	-.053	.024	.307	-.126	.019
		Unknown	.001	.018	1.000	-.053	.056
	Mixed	Caucasian	.015	.014	.944	-.027	.057
		East Asian	-.041	.017	.210	-.093	.010
		Indian/Pakistani/ Sri Lankan	.001	.022	1.000	-.065	.067
		Middle Eastern	.000	.021	1.000	-.062	.061
		Others	-.054	.022	.206	-.120	.013
		Unknown	.001	.016	1.000	-.045	.048
	Others	Caucasian	.068(*)	.019	.010	.011	.126
		East Asian	.012	.022	.998	-.052	.077
		Indian/Pakistani/ Sri Lankan	.055	.026	.342	-.022	.132
		Middle Eastern	.053	.024	.307	-.019	.126
		Mixed	.054	.022	.206	-.013	.120
		Unknown	.055	.020	.104	-.006	.116
	Unknown	Caucasian	.013	.010	.861	-.018	.044
		East Asian	-.043	.015	.054	-.086	.000
		Indian/Pakistani/ Sri Lankan	.000	.020	1.000	-.060	.060
		Middle Eastern	-.001	.018	1.000	-.056	.053
		Mixed	-.001	.016	1.000	-.048	.045
		Others	-.055	.020	.104	-.116	.006

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
J_{45}	Caucasian	East Asian	.002	.008	1.000	-.022	.026
		Indian/Pakistani/ Sri Lankan	.005	.011	.999	-.029	.039
		Middle Eastern	.020	.011	.520	-.012	.052
		Mixed	-.002	.009	1.000	-.028	.024
		Others	.005	.012	.999	-.030	.040
		Unknown	-.004	.007	.997	-.024	.016
	East Asian	Caucasian	-.002	.008	1.000	-.026	.022
		Indian/Pakistani/ Sri Lankan	.003	.013	1.000	-.035	.041
		Middle Eastern	.018	.012	.792	-.019	.054
		Mixed	-.004	.011	1.000	-.036	.027
		Others	.003	.013	1.000	-.036	.042
		Unknown	-.006	.009	.993	-.033	.021
	Indian/Pakistani/ Sri Lankan	Caucasian	-.005	.011	.999	-.039	.029
		East Asian	-.003	.013	1.000	-.041	.035
		Middle Eastern	.015	.015	.956	-.029	.058
		Mixed	-.007	.013	.998	-.047	.032
		Others	.000	.015	1.000	-.046	.045
		Unknown	-.009	.012	.988	-.045	.027
	Middle Eastern	Caucasian	-.020	.011	.520	-.052	.012
		East Asian	-.018	.012	.792	-.054	.019
		Indian/Pakistani/ Sri Lankan	-.015	.015	.956	-.058	.029
		Mixed	-.022	.013	.618	-.060	.016
		Others	-.015	.015	.956	-.059	.030
		Unknown	-.024	.012	.381	-.058	.011
	Mixed	Caucasian	.002	.009	1.000	-.024	.028
		East Asian	.004	.011	1.000	-.027	.036
		Indian/Pakistani/ Sri Lankan	.007	.013	.998	-.032	.047
		Middle Eastern	.022	.013	.618	-.016	.060
		Others	.007	.014	.998	-.033	.048
		Unknown	-.002	.010	1.000	-.031	.027
	Others	Caucasian	-.005	.012	.999	-.040	.030
		East Asian	-.003	.013	1.000	-.042	.036
		Indian/Pakistani/ Sri Lankan	.000	.015	1.000	-.045	.046
		Middle Eastern	.015	.015	.956	-.030	.059
		Mixed	-.007	.014	.998	-.048	.033
		Unknown	-.009	.012	.990	-.046	.028
	Unknown	Caucasian	.004	.007	.997	-.016	.024
		East Asian	.006	.009	.993	-.021	.033
		Indian/Pakistani/ Sri Lankan	.009	.012	.988	-.027	.045
		Middle Eastern	.024	.012	.381	-.011	.058
		Mixed	.002	.010	1.000	-.027	.031
		Others	.009	.012	.990	-.028	.046

** The mean difference is significant at the .05 level*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests across Ethnic groups

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Z(2,-2)	Caucasian	East Asian	-.004	.010	.986	-.030	.023
		Indian/Pakistani/ Sri Lankan	-.007	.014	.966	-.044	.031
		Middle Eastern	-.026	.014	.253	-.062	.010
	East Asian	Caucasian	.004	.010	.986	-.023	.030
		Indian/Pakistani/ Sri Lankan	-.003	.016	.997	-.046	.039
		Middle Eastern	-.022	.016	.505	-.063	.019
	Indian/Pakistani/ Sri Lankan	Caucasian	.007	.014	.966	-.031	.044
		East Asian	.003	.016	.997	-.039	.046
		Middle Eastern	-.019	.019	.747	-.067	.030
	Middle Eastern	Caucasian	.026	.014	.253	-.010	.062
		East Asian	.022	.016	.505	-.019	.063
		Indian/Pakistani/ Sri Lankan	.019	.019	.747	-.030	.067
Z(2, 0)	Caucasian	East Asian	-1.141(*)	.105	.000	-1.413	-.868
		Indian/Pakistani/ Sri Lankan	-.799(*)	.118	.000	-1.107	-.491
		Middle Eastern	-.076	.073	.725	-.265	.113
	East Asian	Caucasian	1.141(*)	.105	.000	.868	1.413
		Indian/Pakistani/ Sri Lankan	.342	.152	.116	-.053	.736
		Middle Eastern	1.065(*)	.121	.000	.753	1.377
	Indian/Pakistani/ Sri Lankan	Caucasian	.799(*)	.118	.000	.491	1.107
		East Asian	-.342	.152	.116	-.736	.053
		Middle Eastern	.723(*)	.132	.000	.380	1.067
	Middle Eastern	Caucasian	.076	.073	.725	-.113	.265
		East Asian	-1.065(*)	.121	.000	-1.377	-.753
		Indian/Pakistani/ Sri Lankan	-.723(*)	.132	.000	-1.067	-.380
Z(2, 2)	Caucasian	East Asian	.072(*)	.017	.000	.029	.114
		Indian/Pakistani/Sri Lankan	.017	.024	.889	-.046	.081
		Middle Eastern	.019	.022	.819	-.038	.076
	East Asian	Caucasian	-.072(*)	.017	.000	-.114	-.029
		Indian/Pakistani/ Sri Lankan	-.054	.027	.203	-.125	.017
		Middle Eastern	-.052	.025	.171	-.118	.014
	Indian/Pakistani/ Sri Lankan	Caucasian	-.017	.024	.889	-.081	.046
		East Asian	.054	.027	.203	-.017	.125
		Middle Eastern	.002	.031	1.000	-.079	.082
	Middle Eastern	Caucasian	-.019	.022	.819	-.076	.038
		East Asian	.052	.025	.171	-.014	.118
		Indian/Pakistani/ Sri Lankan	-.002	.031	1.000	-.082	.079
Z(3,-3)	Caucasian	East Asian	.001	.006	.999	-.015	.017
		Indian/Pakistani/ Sri Lankan	.015	.007	.112	-.002	.033
		Middle Eastern	.010	.007	.527	-.009	.029
	East Asian	Caucasian	-.001	.006	.999	-.017	.015
		Indian/Pakistani/ Sri Lankan	.014	.008	.293	-.007	.035
		Middle Eastern	.009	.009	.720	-.013	.031
	Indian/Pakistani/ Sri Lankan	Caucasian	-.015	.007	.112	-.033	.002
		East Asian	-.014	.008	.293	-.035	.007
		Middle Eastern	-.005	.009	.934	-.029	.018
	Middle Eastern	Caucasian	-.010	.007	.527	-.029	.009
		East Asian	-.009	.009	.720	-.031	.013
		Indian/Pakistani/ Sri Lankan	.005	.009	.934	-.018	.029

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(3,-1)	Caucasian	East Asian	-.025(*)	.009	.022	-.048	-.003
		Indian/Pakistani/ Sri Lankan	.011	.010	.695	-.016	.038
		Middle Eastern	.017	.011	.454	-.013	.047
	East Asian	Caucasian	.025(*)	.009	.022	.003	.048
		Indian/Pakistani/ Sri Lankan	.037(*)	.013	.020	.004	.069
		Middle Eastern	.042(*)	.013	.011	.007	.077
	Indian/Pakistani/ Sri Lankan	Caucasian	-.011	.010	.695	-.038	.016
		East Asian	-.037(*)	.013	.020	-.069	-.004
		Middle Eastern	.006	.015	.981	-.032	.043
	Middle Eastern	Caucasian	-.017	.011	.454	-.047	.013
		East Asian	-.042(*)	.013	.011	-.077	-.007
		Indian/Pakistani/ Sri Lankan	-.006	.015	.981	-.043	.032
Z(3, 1)	Caucasian	East Asian	-.005	.005	.788	-.019	.009
		Indian/Pakistani/ Sri Lankan	-.013	.007	.282	-.033	.006
		Middle Eastern	-.007	.007	.705	-.025	.011
	East Asian	Caucasian	.005	.005	.788	-.009	.019
		Indian/Pakistani/ Sri Lankan	-.008	.008	.763	-.030	.014
		Middle Eastern	-.002	.008	.991	-.023	.018
	Indian/Pakistani/ Sri Lankan	Caucasian	.013	.007	.282	-.006	.033
		East Asian	.008	.008	.763	-.014	.030
		Middle Eastern	.006	.009	.922	-.019	.030
	Middle Eastern	Caucasian	.007	.007	.705	-.011	.025
		East Asian	.002	.008	.991	-.018	.023
		Indian/Pakistani/ Sri Lankan	-.006	.009	.922	-.030	.019
Z(3, 3)	Caucasian	East Asian	.013	.005	.053	.000	.026
		Indian/Pakistani/ Sri Lankan	.001	.007	.999	-.017	.019
		Middle Eastern	.026(*)	.008	.005	.006	.045
	East Asian	Caucasian	-.013	.005	.053	-.026	.000
		Indian/Pakistani/ Sri Lankan	-.012	.008	.415	-.033	.008
		Middle Eastern	.013	.008	.445	-.009	.035
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.007	.999	-.019	.017
		East Asian	.012	.008	.415	-.008	.033
		Middle Eastern	.025	.010	.053	.000	.050
	Middle Eastern	Caucasian	-.026(*)	.008	.005	-.045	-.006
		East Asian	-.013	.008	.445	-.035	.009
		Indian/Pakistani/ Sri Lankan	-.025	.010	.053	-.050	.000
Z(4,-4)	Caucasian	East Asian	-.006(*)	.002	.033	-.011	.000
		Indian/Pakistani/Sri Lankan	.001	.002	.986	-.006	.007
		Middle Eastern	.002	.003	.928	-.006	.009
	East Asian	Caucasian	.006(*)	.002	.033	.000	.011
		Indian/Pakistani/ Sri Lankan	.007	.003	.120	-.001	.014
		Middle Eastern	.008	.003	.109	-.001	.016
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.002	.986	-.007	.006
		East Asian	-.007	.003	.120	-.014	.001
		Middle Eastern	.001	.004	.994	-.008	.010
	Middle Eastern	Caucasian	-.002	.003	.928	-.009	.006
		East Asian	-.008	.003	.109	-.016	.001
		Indian/Pakistani/ Sri Lankan	-.001	.004	.994	-.010	.008

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(4,-2)	Caucasian	East Asian	.004	.002	.219	-.002	.010
		Indian/Pakistani/ Sri Lankan	-.004	.002	.424	-.010	.003
		Middle Eastern	.003	.003	.605	-.004	.010
	East Asian	Caucasian	-.004	.002	.219	-.010	.002
		Indian/Pakistani/ Sri Lankan	-.008(*)	.003	.022	-.016	-.001
		Middle Eastern	-.001	.003	.982	-.009	.007
	Indian/Pakistani/ Sri Lankan	Caucasian	.004	.002	.424	-.003	.010
		East Asian	.008(*)	.003	.022	.001	.016
		Middle Eastern	.007	.003	.116	-.001	.015
	Middle Eastern	Caucasian	-.003	.003	.605	-.010	.004
		East Asian	.001	.003	.982	-.007	.009
		Indian/Pakistani/ Sri Lankan	-.007	.003	.116	-.015	.001
Z(4, 0)	Caucasian	East Asian	-.006	.005	.616	-.019	.007
		Indian/Pakistani/ Sri Lankan	.010	.006	.275	-.005	.025
		Middle Eastern	.010	.006	.336	-.005	.025
	East Asian	Caucasian	.006	.005	.616	-.007	.019
		Indian/Pakistani/ Sri Lankan	.017	.007	.094	-.002	.035
		Middle Eastern	.016	.007	.117	-.003	.034
	Indian/Pakistani/ Sri Lankan	Caucasian	-.010	.006	.275	-.025	.005
		East Asian	-.017	.007	.094	-.035	.002
		Middle Eastern	-.001	.008	1.000	-.020	.019
	Middle Eastern	Caucasian	-.010	.006	.336	-.025	.005
		East Asian	-.016	.007	.117	-.034	.003
		Indian/Pakistani/ Sri Lankan	.001	.008	1.000	-.019	.020
Z(4, 2)	Caucasian	East Asian	.000	.003	.999	-.007	.008
		Indian/Pakistani/ Sri Lankan	-.003	.004	.899	-.013	.007
		Middle Eastern	-.002	.003	.913	-.011	.007
	East Asian	Caucasian	.000	.003	.999	-.008	.007
		Indian/Pakistani/ Sri Lankan	-.003	.004	.909	-.015	.009
		Middle Eastern	-.003	.004	.924	-.013	.008
	Indian/Pakistani/ Sri Lankan	Caucasian	.003	.004	.899	-.007	.013
		East Asian	.003	.004	.909	-.009	.015
		Middle Eastern	.000	.005	1.000	-.012	.013
	Middle Eastern	Caucasian	.002	.003	.913	-.007	.011
		East Asian	.003	.004	.924	-.008	.013
		Indian/Pakistani/ Sri Lankan	.000	.005	1.000	-.013	.012
Z(4, 4)	Caucasian	East Asian	-.008(*)	.002	.002	-.014	-.002
		Indian/Pakistani/ Sri Lankan	.002	.004	.941	-.007	.011
		Middle Eastern	.001	.003	.997	-.007	.008
	East Asian	Caucasian	.008(*)	.002	.002	.002	.014
		Indian/Pakistani/ Sri Lankan	.010(*)	.004	.046	.000	.021
		Middle Eastern	.009(*)	.003	.047	.000	.018
	Indian/Pakistani/ Sri Lankan	Caucasian	-.002	.004	.941	-.011	.007
		East Asian	-.010(*)	.004	.046	-.021	.000
		Middle Eastern	-.001	.004	.989	-.013	.010
	Middle Eastern	Caucasian	-.001	.003	.997	-.008	.007
		East Asian	-.009(*)	.003	.047	-.018	.000
		Indian/Pakistani/Sri Lankan	.001	.004	.989	-.010	.013

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(5,-5)	Caucasian	East Asian	.000	.001	.992	-.003	.003
		Indian/Pakistani/ Sri Lankan	.001	.002	.903	-.003	.005
		Middle Eastern	-.003	.002	.192	-.007	.001
	East Asian	Caucasian	.000	.001	.992	-.003	.003
		Indian/Pakistani/ Sri Lankan	.001	.002	.856	-.003	.006
		Middle Eastern	-.003	.002	.370	-.008	.002
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.002	.903	-.005	.003
		East Asian	-.001	.002	.856	-.006	.003
		Middle Eastern	-.004	.002	.174	-.010	.001
	Middle Eastern	Caucasian	.003	.002	.192	-.001	.007
		East Asian	.003	.002	.370	-.002	.008
		Indian/Pakistani/ Sri Lankan	.004	.002	.174	-.001	.010
Z(5,-3)	Caucasian	East Asian	-.001	.001	.932	-.004	.002
		Indian/Pakistani/ Sri Lankan	-.002	.002	.702	-.006	.002
		Middle Eastern	.001	.002	.810	-.003	.006
	East Asian	Caucasian	.001	.001	.932	-.002	.004
		Indian/Pakistani/ Sri Lankan	-.001	.002	.939	-.006	.004
		Middle Eastern	.002	.002	.646	-.003	.007
	Indian/Pakistani/ Sri Lankan	Caucasian	.002	.002	.702	-.002	.006
		East Asian	.001	.002	.939	-.004	.006
		Middle Eastern	.003	.002	.447	-.002	.009
	Middle Eastern	Caucasian	-.001	.002	.810	-.006	.003
		East Asian	-.002	.002	.646	-.007	.003
		Indian/Pakistani/ Sri Lankan	-.003	.002	.447	-.009	.002
Z(5,-1)	Caucasian	East Asian	.003	.001	.320	-.001	.006
		Indian/Pakistani/ Sri Lankan	.003	.002	.591	-.003	.008
		Middle Eastern	-.005	.002	.099	-.011	.001
	East Asian	Caucasian	-.003	.001	.320	-.006	.001
		Indian/Pakistani/ Sri Lankan	.000	.002	1.000	-.006	.006
		Middle Eastern	-.008(*)	.002	.011	-.014	-.001
	Indian/Pakistani/ Sri Lankan	Caucasian	-.003	.002	.591	-.008	.003
		East Asian	.000	.002	1.000	-.006	.006
		Middle Eastern	-.008(*)	.003	.035	-.015	.000
	Middle Eastern	Caucasian	.005	.002	.099	-.001	.011
		East Asian	.008(*)	.002	.011	.001	.014
		Indian/Pakistani/ Sri Lankan	.008(*)	.003	.035	.000	.015
Z(5, 1)	Caucasian	East Asian	.001	.002	.923	-.004	.006
		Indian/Pakistani/ Sri Lankan	.004(*)	.001	.025	.000	.007
		Middle Eastern	.003	.001	.171	-.001	.007
	East Asian	Caucasian	-.001	.002	.923	-.006	.004
		Indian/Pakistani/ Sri Lankan	.003	.002	.585	-.003	.008
		Middle Eastern	.002	.002	.861	-.004	.007
	Indian/Pakistani/ Sri Lankan	Caucasian	-.004(*)	.001	.025	-.007	.000
		East Asian	-.003	.002	.585	-.008	.003
		Middle Eastern	-.001	.002	.941	-.006	.004
	Middle Eastern	Caucasian	-.003	.001	.171	-.007	.001
		East Asian	-.002	.002	.861	-.007	.004
		Indian/Pakistani/ Sri Lankan	.001	.002	.941	-.004	.006

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(5, 3)	Caucasian	East Asian	.000	.001	.995	-.002	.003
		Indian/Pakistani/ Sri Lankan	.002	.001	.444	-.002	.006
		Middle Eastern	.001	.001	.945	-.003	.004
	East Asian	Caucasian	.000	.001	.995	-.003	.002
		Indian/Pakistani/ Sri Lankan	.002	.002	.634	-.002	.006
		Middle Eastern	.000	.001	.987	-.003	.004
	Indian/Pakistani/ Sri Lankan	Caucasian	-.002	.001	.444	-.006	.002
		East Asian	-.002	.002	.634	-.006	.002
		Middle Eastern	-.001	.002	.872	-.006	.003
	Middle Eastern	Caucasian	-.001	.001	.945	-.004	.003
		East Asian	.000	.001	.987	-.004	.003
		Indian/Pakistani/ Sri Lankan	.001	.002	.872	-.003	.006
Z(5, 5)	Caucasian	East Asian	-.005(*)	.001	.000	-.008	-.002
		Indian/Pakistani/ Sri Lankan	-.003	.002	.244	-.007	.001
		Middle Eastern	.002	.001	.505	-.002	.006
	East Asian	Caucasian	.005(*)	.001	.000	.002	.008
		Indian/Pakistani/ Sri Lankan	.002	.002	.752	-.003	.006
		Middle Eastern	.007(*)	.002	.000	.003	.011
	Indian/Pakistani/ Sri Lankan	Caucasian	.003	.002	.244	-.001	.007
		East Asian	-.002	.002	.752	-.006	.003
		Middle Eastern	.005	.002	.067	.000	.010
	Middle Eastern	Caucasian	-.002	.001	.505	-.006	.002
		East Asian	-.007(*)	.002	.000	-.011	-.003
		Indian/Pakistani/ Sri Lankan	-.005	.002	.067	-.010	.000
Z(6,-6)	Caucasian	East Asian	.000	.001	.957	-.003	.002
		Indian/Pakistani/ Sri Lankan	.001	.001	.526	-.001	.004
		Middle Eastern	.000	.001	1.000	-.003	.003
	East Asian	Caucasian	.000	.001	.957	-.002	.003
		Indian/Pakistani/ Sri Lankan	.002	.001	.433	-.001	.005
		Middle Eastern	.000	.001	.987	-.003	.004
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.001	.526	-.004	.001
		East Asian	-.002	.001	.433	-.005	.001
		Middle Eastern	-.001	.002	.787	-.005	.003
	Middle Eastern	Caucasian	.000	.001	1.000	-.003	.003
		East Asian	.000	.001	.987	-.004	.003
		Indian/Pakistani/ Sri Lankan	.001	.002	.787	-.003	.005
Z(6,-4)	Caucasian	East Asian	.002	.001	.115	.000	.003
		Indian/Pakistani/ Sri Lankan	.001	.001	.403	-.001	.004
		Middle Eastern	-.001	.001	.786	-.003	.001
	East Asian	Caucasian	-.002	.001	.115	-.003	.000
		Indian/Pakistani/ Sri Lankan	.000	.001	.996	-.003	.003
		Middle Eastern	-.002	.001	.093	-.005	.000
	Indian/Pakistani/Sri Lankan	Caucasian	-.001	.001	.403	-.004	.001
		East Asian	.000	.001	.996	-.003	.003
		Middle Eastern	-.002	.001	.235	-.005	.001
	Middle Eastern	Caucasian	.001	.001	.786	-.001	.003
		East Asian	.002	.001	.093	.000	.005
		Indian/Pakistani/ Sri Lankan	.002	.001	.235	-.001	.005

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(6,-2)	Caucasian	East Asian	.000	.001	.957	-.001	.002
		Indian/Pakistani/ Sri Lankan	.001	.001	.654	-.001	.003
		Middle Eastern	.001	.001	.687	-.001	.003
	East Asian	Caucasian	.000	.001	.957	-.002	.001
		Indian/Pakistani/ Sri Lankan	.001	.001	.939	-.002	.003
		Middle Eastern	.001	.001	.935	-.002	.003
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.001	.654	-.003	.001
		East Asian	-.001	.001	.939	-.003	.002
		Middle Eastern	.000	.001	1.000	-.003	.003
	Middle Eastern	Caucasian	-.001	.001	.687	-.003	.001
		East Asian	-.001	.001	.935	-.003	.002
		Indian/Pakistani/ Sri Lankan	.000	.001	1.000	-.003	.003
Z(6, 0)	Caucasian	East Asian	-.002	.001	.143	-.005	.001
		Indian/Pakistani/Sri Lankan	-.002	.001	.722	-.005	.002
		Middle Eastern	.000	.001	.998	-.004	.003
	East Asian	Caucasian	.002	.001	.143	-.001	.005
		Indian/Pakistani/ Sri Lankan	.001	.002	.958	-.004	.005
		Middle Eastern	.002	.002	.562	-.002	.006
	Indian/Pakistani/ Sri Lankan	Caucasian	.002	.001	.722	-.002	.005
		East Asian	-.001	.002	.958	-.005	.004
		Middle Eastern	.001	.002	.907	-.004	.006
	Middle Eastern	Caucasian	.000	.001	.998	-.003	.004
		East Asian	-.002	.002	.562	-.006	.002
		Indian/Pakistani/ Sri Lankan	-.001	.002	.907	-.006	.004
Z(6, 2)	Caucasian	East Asian	-.002	.001	.067	-.004	.000
		Indian/Pakistani/ Sri Lankan	-.001	.001	.966	-.003	.002
		Middle Eastern	.000	.001	1.000	-.003	.003
	East Asian	Caucasian	.002	.001	.067	.000	.004
		Indian/Pakistani/ Sri Lankan	.002	.001	.617	-.002	.005
		Middle Eastern	.002	.001	.360	-.001	.005
	Indian/Pakistani/ Sri Lankan	Caucasian	.001	.001	.966	-.002	.003
		East Asian	-.002	.001	.617	-.005	.002
		Middle Eastern	.001	.001	.985	-.003	.004
	Middle Eastern	Caucasian	.000	.001	1.000	-.003	.003
		East Asian	-.002	.001	.360	-.005	.001
		Indian/Pakistani/ Sri Lankan	-.001	.001	.985	-.004	.003
Z(6, 4)	Caucasian	East Asian	.002	.001	.080	.000	.004
		Indian/Pakistani/Sri Lankan	.001	.001	.542	-.001	.004
		Middle Eastern	.000	.001	.999	-.003	.003
	East Asian	Caucasian	-.002	.001	.080	-.004	.000
		Indian/Pakistani/ Sri Lankan	.000	.001	.979	-.004	.003
		Middle Eastern	-.002	.001	.311	-.005	.001
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.001	.542	-.004	.001
		East Asian	.000	.001	.979	-.003	.004
		Middle Eastern	-.002	.001	.667	-.005	.002
	Middle Eastern	Caucasian	.000	.001	.999	-.003	.003
		East Asian	.002	.001	.311	-.001	.005
		Indian/Pakistani/ Sri Lankan	.002	.001	.667	-.002	.005

Dependent Variable	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z(6, 6)	Caucasian	East Asian	-.002	.001	.398	-.004	.001
		Indian/Pakistani/ Sri Lankan	.001	.001	.932	-.002	.004
		Middle Eastern	.002	.001	.505	-.001	.005
	East Asian	Caucasian	.002	.001	.398	-.001	.004
		Indian/Pakistani/ Sri Lankan	.002	.001	.395	-.001	.006
		Middle Eastern	.003	.001	.111	.000	.007
	Indian/Pakistani/ Sri Lankan	Caucasian	-.001	.001	.932	-.004	.002
		East Asian	-.002	.001	.395	-.006	.001
		Middle Eastern	.001	.002	.940	-.003	.005
	Middle Eastern	Caucasian	-.002	.001	.505	-.005	.001
		East Asian	-.003	.001	.111	-.007	.000
		Indian/Pakistani/ Sri Lankan	-.001	.002	.940	-.005	.003

** The mean difference is significant at the .05 level*

M vector analysis of variance Brown-Forsythe by Refractive Error Group: Games-Howell post-hoc multiple comparisons tests across Ethnic groups

Refractive Error Group	(I) Ethnic Group	(J) Ethnic Group	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Myopes	Caucasian	East Asian	1.13(*)	.25	.000	.46	1.79
		Indian/Pakistani/ Sri Lankan	.55	.24	.116	-.09	1.20
		Middle Eastern	-.11	.31	.986	-1.15	.94
	East Asian	Caucasian	-1.13(*)	.25	.000	-1.79	-.46
		Indian/Pakistani/ Sri Lankan	-.57	.27	.169	-1.30	.15
		Middle Eastern	-1.23(*)	.34	.022	-2.28	-.18
	Indian/Pakistani/ Sri Lankan	Caucasian	-.55	.24	.116	-1.20	.09
		East Asian	.57	.27	.169	-.15	1.30
		Middle Eastern	-.66	.33	.266	-1.71	.39
	Middle Eastern	Caucasian	.11	.31	.986	-.94	1.15
		East Asian	1.23(*)	.34	.022	.18	2.28
		Indian/Pakistani/ Sri Lankan	.66	.33	.266	-.39	1.71
Emmetropes	Caucasian	East Asian	.06	.04	.288	-.03	.15
		Indian/Pakistani/Sri Lankan	.07	.05	.584	-.07	.20
		Middle Eastern	.00	.05	1.000	-.15	.15
	East Asian	Caucasian	-.06	.04	.288	-.15	.03
		Indian/Pakistani/ Sri Lankan	.00	.06	1.000	-.14	.15
		Middle Eastern	-.06	.06	.711	-.22	.09
	Indian/Pakistani/ Sri Lankan	Caucasian	-.07	.05	.584	-.20	.07
		East Asian	.00	.06	1.000	-.15	.14
		Middle Eastern	-.07	.07	.782	-.25	.12
	Middle Eastern	Caucasian	.00	.05	1.000	-.15	.15
		East Asian	.06	.06	.711	-.09	.22
		Indian/Pakistani/ Sri Lankan	.07	.07	.782	-.12	.25
Hyperopes	Caucasian	East Asian	.30(*)	.05	.000	.16	.44
		Indian/Pakistani/Sri Lankan	.28(*)	.06	.000	.12	.43
		Middle Eastern	.10	.07	.434	-.07	.27
	East Asian	Caucasian	-.30(*)	.05	.000	-.44	-.16
		Indian/Pakistani/ Sri Lankan	-.02	.06	.990	-.19	.15
		Middle Eastern	-.20(*)	.07	.032	-.38	-.01
	Indian/Pakistani/ Sri Lankan	Caucasian	-.28(*)	.06	.000	-.43	-.12
		East Asian	.02	.06	.990	-.15	.19
		Middle Eastern	-.18	.07	.091	-.37	.02
	Middle Eastern	Caucasian	-.10	.07	.434	-.27	.07
		East Asian	.20(*)	.07	.032	.01	.38
		Indian/Pakistani/ Sri Lankan	.18	.07	.091	-.02	.37

** The mean difference is significant at the .05 level*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for Caucasian group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (2,-2)	Low Myopes	Emmetropes	.006	.026	.973	-.058	.070
		Low Hyperopes	.021	.025	.678	-.040	.082
	Emmetropes	Low Myopes	-.006	.026	.973	-.070	.058
		Low Hyperopes	.015	.012	.396	-.012	.043
	Low Hyperopes	Low Myopes	-.021	.025	.678	-.082	.040
		Emmetropes	-.015	.012	.396	-.043	.012
Z (2, 0)	Low Myopes	Emmetropes	1.122(*)	.093	.000	.894	1.351
		Low Hyperopes	1.785(*)	.092	.000	1.559	2.011
	Emmetropes	Low Myopes	-1.122(*)	.093	.000	-1.351	-.894
		Low Hyperopes	.662(*)	.027	.000	.599	.726
	Low Hyperopes	Low Myopes	-1.785(*)	.092	.000	-2.011	-1.559
		Emmetropes	-.662(*)	.027	.000	-.726	-.599
Z (2, 2)	Low Myopes	Emmetropes	.179(*)	.040	.000	.081	.276
		Low Hyperopes	.166(*)	.037	.000	.074	.258
	Emmetropes	Low Myopes	-.179(*)	.040	.000	-.276	-.081
		Low Hyperopes	-.013	.019	.777	-.056	.031
	Low Hyperopes	Low Myopes	-.166(*)	.037	.000	-.258	-.074
		Emmetropes	.013	.019	.777	-.031	.056
Z (3,-3)	Low Myopes	Emmetropes	-.001	.017	.999	-.042	.040
		Low Hyperopes	.002	.016	.988	-.037	.042
	Emmetropes	Low Myopes	.001	.017	.999	-.040	.042
		Low Hyperopes	.003	.007	.887	-.013	.019
	Low Hyperopes	Low Myopes	-.002	.016	.988	-.042	.037
		Emmetropes	-.003	.007	.887	-.019	.013
Z (3,-1)	Low Myopes	Emmetropes	.021	.018	.452	-.021	.064
		Low Hyperopes	.020	.016	.416	-.019	.060
	Emmetropes	Low Myopes	-.021	.018	.452	-.064	.021
		Low Hyperopes	-.001	.009	.996	-.023	.022
	Low Hyperopes	Low Myopes	-.020	.016	.416	-.060	.019
		Emmetropes	.001	.009	.996	-.022	.023
Z (3, 1)	Low Myopes	Emmetropes	.014	.013	.522	-.017	.045
		Low Hyperopes	.016	.012	.370	-.013	.046
	Emmetropes	Low Myopes	-.014	.013	.522	-.045	.017
		Low Hyperopes	.003	.006	.906	-.012	.017
	Low Hyperopes	Low Myopes	-.016	.012	.370	-.046	.013
		Emmetropes	-.003	.006	.906	-.017	.012
Z (3, 3)	Low Myopes	Emmetropes	.011	.011	.601	-.016	.038
		Low Hyperopes	.003	.011	.951	-.023	.029
	Emmetropes	Low Myopes	-.011	.011	.601	-.038	.016
		Low Hyperopes	-.008	.006	.350	-.021	.005
	Low Hyperopes	Low Myopes	-.003	.011	.951	-.029	.023
		Emmetropes	.008	.006	.350	-.005	.021
Z (4,-4)	Low Myopes	Emmetropes	-.001	.004	.990	-.011	.010
		Low Hyperopes	.000	.004	.999	-.010	.010
	Emmetropes	Low Myopes	.001	.004	.990	-.010	.011
		Low Hyperopes	.001	.002	.922	-.004	.005
	Low Hyperopes	Low Myopes	.000	.004	.999	-.010	.010
		Emmetropes	-.001	.002	.922	-.005	.004

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (4,-2)	Low Myopes	Emmetropes	-.002	.005	.868	-.014	.009
		Low Hyperopes	-.006	.005	.390	-.018	.005
	Emmetropes	Low Myopes	.002	.005	.868	-.009	.014
		Low Hyperopes	-.004	.003	.311	-.010	.002
	Low Hyperopes	Low Myopes	.006	.005	.390	-.005	.018
		Emmetropes	.004	.003	.311	-.002	.010
Z (4, 0)	Low Myopes	Emmetropes	.004	.008	.900	-.017	.024
		Low Hyperopes	-.029(*)	.008	.002	-.048	-.009
	Emmetropes	Low Myopes	-.004	.008	.900	-.024	.017
		Low Hyperopes	-.032(*)	.004	.000	-.043	-.022
	Low Hyperopes	Low Myopes	.029(*)	.008	.002	.009	.048
		Emmetropes	.032(*)	.004	.000	.022	.043
Z (4, 2)	Low Myopes	Emmetropes	-.004	.005	.740	-.017	.009
		Low Hyperopes	.003	.005	.774	-.009	.016
	Emmetropes	Low Myopes	.004	.005	.740	-.009	.017
		Low Hyperopes	.007(*)	.003	.018	.001	.014
	Low Hyperopes	Low Myopes	-.003	.005	.774	-.016	.009
		Emmetropes	-.007(*)	.003	.018	-.014	-.001
Z (4, 4)	Low Myopes	Emmetropes	-.002	.005	.928	-.014	.010
		Low Hyperopes	-.003	.005	.745	-.015	.008
	Emmetropes	Low Myopes	.002	.005	.928	-.010	.014
		Low Hyperopes	-.002	.002	.777	-.007	.004
	Low Hyperopes	Low Myopes	.003	.005	.745	-.008	.015
		Emmetropes	.002	.002	.777	-.004	.007
Z (5,-5)	Low Myopes	Emmetropes	.001	.002	.875	-.005	.007
		Low Hyperopes	.002	.002	.752	-.004	.007
	Emmetropes	Low Myopes	-.001	.002	.875	-.007	.005
		Low Hyperopes	.000	.001	.959	-.003	.004
	Low Hyperopes	Low Myopes	-.002	.002	.752	-.007	.004
		Emmetropes	.000	.001	.959	-.004	.003
Z (5,-3)	Low Myopes	Emmetropes	-.001	.003	.881	-.008	.006
		Low Hyperopes	-.001	.003	.957	-.007	.006
	Emmetropes	Low Myopes	.001	.003	.881	-.006	.008
		Low Hyperopes	.001	.001	.902	-.003	.004
	Low Hyperopes	Low Myopes	.001	.003	.957	-.006	.007
		Emmetropes	-.001	.001	.902	-.004	.003
Z (5,-1)	Low Myopes	Emmetropes	-.003	.003	.664	-.011	.005
		Low Hyperopes	-.002	.003	.771	-.010	.006
	Emmetropes	Low Myopes	.003	.003	.664	-.005	.011
		Low Hyperopes	.001	.002	.901	-.003	.005
	Low Hyperopes	Low Myopes	.002	.003	.771	-.006	.010
		Emmetropes	-.001	.002	.901	-.005	.003
Z (5, 1)	Low Myopes	Emmetropes	-.002	.003	.726	-.009	.005
		Low Hyperopes	-.006	.003	.093	-.012	.001
	Emmetropes	Low Myopes	.002	.003	.726	-.005	.009
		Low Hyperopes	-.004(*)	.001	.018	-.007	.000
	Low Hyperopes	Low Myopes	.006	.003	.093	-.001	.012
		Emmetropes	.004(*)	.001	.018	.000	.007
Z (5, 3)	Low Myopes	Emmetropes	-.003	.002	.214	-.007	.001
		Low Hyperopes	-.002	.001	.275	-.006	.001
	Emmetropes	Low Myopes	.003	.002	.214	-.001	.007
		Low Hyperopes	.000	.001	.878	-.002	.003
	Low Hyperopes	Low Myopes	.002	.001	.275	-.001	.006
		Emmetropes	.000	.001	.878	-.003	.002

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (5, 5)	Low Myopes	Emmetropes	.002	.003	.623	-.004	.009
		Low Hyperopes	.003	.002	.382	-.003	.009
	Emmetropes	Low Myopes	-.002	.003	.623	-.009	.004
		Low Hyperopes	.001	.001	.785	-.002	.004
	Low Hyperopes	Low Myopes	-.003	.002	.382	-.009	.003
		Emmetropes	-.001	.001	.785	-.004	.002
Z (6,-6)	Low Myopes	Emmetropes	.002	.002	.347	-.002	.006
		Low Hyperopes	.001	.002	.673	-.002	.005
	Emmetropes	Low Myopes	-.002	.002	.347	-.006	.002
		Low Hyperopes	-.001	.001	.509	-.003	.001
	Low Hyperopes	Low Myopes	-.001	.002	.673	-.005	.002
		Emmetropes	.001	.001	.509	-.001	.003
Z (6,-4)	Low Myopes	Emmetropes	.000	.001	.961	-.003	.004
		Low Hyperopes	-.001	.001	.870	-.004	.002
	Emmetropes	Low Myopes	.000	.001	.961	-.004	.003
		Low Hyperopes	-.001	.001	.397	-.003	.001
	Low Hyperopes	Low Myopes	.001	.001	.870	-.002	.004
		Emmetropes	.001	.001	.397	-.001	.003
Z (6,-2)	Low Myopes	Emmetropes	.001	.001	.889	-.002	.003
		Low Hyperopes	.000	.001	.988	-.003	.003
	Emmetropes	Low Myopes	-.001	.001	.889	-.003	.002
		Low Hyperopes	.000	.001	.827	-.002	.001
	Low Hyperopes	Low Myopes	.000	.001	.988	-.003	.003
		Emmetropes	.000	.001	.827	-.001	.002
Z (6, 0)	Low Myopes	Emmetropes	.003	.002	.305	-.002	.007
		Low Hyperopes	.005(*)	.002	.024	.001	.009
	Emmetropes	Low Myopes	-.003	.002	.305	-.007	.002
		Low Hyperopes	.002	.001	.154	-.001	.004
	Low Hyperopes	Low Myopes	-.005(*)	.002	.024	-.009	-.001
		Emmetropes	-.002	.001	.154	-.004	.001
Z (6, 2)	Low Myopes	Emmetropes	.004	.002	.149	-.001	.009
		Low Hyperopes	.003	.002	.375	-.002	.007
	Emmetropes	Low Myopes	-.004	.002	.149	-.009	.001
		Low Hyperopes	-.001	.001	.393	-.004	.001
	Low Hyperopes	Low Myopes	-.003	.002	.375	-.007	.002
		Emmetropes	.001	.001	.393	-.001	.004
Z (6, 4)	Low Myopes	Emmetropes	-.001	.002	.959	-.005	.004
		Low Hyperopes	.000	.002	.975	-.005	.004
	Emmetropes	Low Myopes	.001	.002	.959	-.004	.005
		Low Hyperopes	.000	.001	.987	-.002	.002
	Low Hyperopes	Low Myopes	.000	.002	.975	-.004	.005
		Emmetropes	.000	.001	.987	-.002	.002
Z (6, 6)	Low Myopes	Emmetropes	.002	.002	.623	-.003	.007
		Low Hyperopes	.002	.002	.638	-.003	.007
	Emmetropes	Low Myopes	-.002	.002	.623	-.007	.003
		Low Hyperopes	.000	.001	.982	-.003	.002
	Low Hyperopes	Low Myopes	-.002	.002	.638	-.007	.003
		Emmetropes	.000	.001	.982	-.002	.003

* *The mean difference is significant at the .05 level*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for East Asian group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (2,-2)	Low Myopes	Emmetropes	-.008	.028	.960	-.074	.059
		Low Hyperopes	.001	.028	1.000	-.067	.068
	Emmetropes	Low Myopes	.008	.028	.960	-.059	.074
		Low Hyperopes	.008	.020	.913	-.039	.056
	Low Hyperopes	Low Myopes	-.001	.028	1.000	-.068	.067
		Emmetropes	-.008	.020	.913	-.056	.039
Z (2, 0)	Low Myopes	Emmetropes	1.548(*)	.111	.000	1.281	1.816
		Low Hyperopes	2.104(*)	.113	.000	1.832	2.376
	Emmetropes	Low Myopes	-1.548(*)	.111	.000	-1.816	-1.281
		Low Hyperopes	.556(*)	.053	.000	.429	.682
	Low Hyperopes	Low Myopes	-2.104(*)	.113	.000	-2.376	-1.832
		Emmetropes	-.556(*)	.053	.000	-.682	-.429
Z (2, 2)	Low Myopes	Emmetropes	-.017	.038	.893	-.109	.074
		Low Hyperopes	-.069	.043	.257	-.172	.035
	Emmetropes	Low Myopes	.017	.038	.893	-.074	.109
		Low Hyperopes	-.051	.037	.353	-.140	.037
	Low Hyperopes	Low Myopes	.069	.043	.257	-.035	.172
		Emmetropes	.051	.037	.353	-.037	.140
Z (3,-3)	Low Myopes	Emmetropes	-.014	.013	.551	-.046	.018
		Low Hyperopes	-.031	.014	.084	-.064	.003
	Emmetropes	Low Myopes	.014	.013	.551	-.018	.046
		Low Hyperopes	-.017	.013	.433	-.049	.015
	Low Hyperopes	Low Myopes	.031	.014	.084	-.003	.064
		Emmetropes	.017	.013	.433	-.015	.049
Z (3,-1)	Low Myopes	Emmetropes	.052(*)	.022	.047	.001	.103
		Low Hyperopes	.069(*)	.023	.011	.013	.125
	Emmetropes	Low Myopes	-.052(*)	.022	.047	-.103	-.001
		Low Hyperopes	.017	.018	.625	-.026	.060
	Low Hyperopes	Low Myopes	-.069(*)	.023	.011	-.125	-.013
		Emmetropes	-.017	.018	.625	-.060	.026
Z (3, 1)	Low Myopes	Emmetropes	.029	.012	.056	-.001	.058
		Low Hyperopes	.024	.014	.203	-.009	.057
	Emmetropes	Low Myopes	-.029	.012	.056	-.058	.001
		Low Hyperopes	-.005	.012	.902	-.033	.023
	Low Hyperopes	Low Myopes	-.024	.014	.203	-.057	.009
		Emmetropes	.005	.012	.902	-.023	.033
Z (3, 3)	Low Myopes	Emmetropes	.006	.013	.894	-.026	.038
		Low Hyperopes	.016	.014	.482	-.017	.048
	Emmetropes	Low Myopes	-.006	.013	.894	-.038	.026
		Low Hyperopes	.010	.011	.631	-.015	.035
	Low Hyperopes	Low Myopes	-.016	.014	.482	-.048	.017
		Emmetropes	-.010	.011	.631	-.035	.015
Z (4,-4)	Low Myopes	Emmetropes	.005	.005	.616	-.008	.018
		Low Hyperopes	.005	.006	.613	-.008	.019
	Emmetropes	Low Myopes	-.005	.005	.616	-.018	.008
		Low Hyperopes	.000	.005	.995	-.010	.011
	Low Hyperopes	Low Myopes	-.005	.006	.613	-.019	.008
		Emmetropes	.000	.005	.995	-.011	.010

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (4,-2)	Low Myopes	Emmetropes	.006	.004	.287	-.004	.017
		Low Hyperopes	.001	.006	.991	-.013	.015
	Emmetropes	Low Myopes	-.006	.004	.287	-.017	.004
		Low Hyperopes	-.006	.005	.522	-.018	.007
	Low Hyperopes	Low Myopes	-.001	.006	.991	-.015	.013
		Emmetropes	.006	.005	.522	-.007	.018
Z (4, 0)	Low Myopes	Emmetropes	-.012	.009	.374	-.034	.009
		Low Hyperopes	-.040(*)	.013	.007	-.071	-.009
	Emmetropes	Low Myopes	.012	.009	.374	-.009	.034
		Low Hyperopes	-.028	.013	.073	-.058	.002
	Low Hyperopes	Low Myopes	.040(*)	.013	.007	.009	.071
		Emmetropes	.028	.013	.073	-.002	.058
Z (4, 2)	Low Myopes	Emmetropes	.004	.005	.698	-.008	.016
		Low Hyperopes	-.004	.008	.859	-.022	.014
	Emmetropes	Low Myopes	-.004	.005	.698	-.016	.008
		Low Hyperopes	-.008	.007	.536	-.026	.010
	Low Hyperopes	Low Myopes	.004	.008	.859	-.014	.022
		Emmetropes	.008	.007	.536	-.010	.026
Z (4, 4)	Low Myopes	Emmetropes	-.005	.005	.635	-.017	.007
		Low Hyperopes	-.003	.006	.812	-.017	.010
	Emmetropes	Low Myopes	.005	.005	.635	-.007	.017
		Low Hyperopes	.001	.005	.970	-.011	.013
	Low Hyperopes	Low Myopes	.003	.006	.812	-.010	.017
		Emmetropes	-.001	.005	.970	-.013	.011
Z (5,-5)	Low Myopes	Emmetropes	.001	.003	.864	-.005	.007
		Low Hyperopes	-.002	.003	.867	-.009	.006
	Emmetropes	Low Myopes	-.001	.003	.864	-.007	.005
		Low Hyperopes	-.003	.002	.454	-.008	.003
	Low Hyperopes	Low Myopes	.002	.003	.867	-.006	.009
		Emmetropes	.003	.002	.454	-.003	.008
Z (5,-3)	Low Myopes	Emmetropes	.003	.003	.434	-.003	.010
		Low Hyperopes	.004	.003	.305	-.003	.012
	Emmetropes	Low Myopes	-.003	.003	.434	-.010	.003
		Low Hyperopes	.001	.002	.890	-.005	.007
	Low Hyperopes	Low Myopes	-.004	.003	.305	-.012	.003
		Emmetropes	-.001	.002	.890	-.007	.005
Z (5,-1)	Low Myopes	Emmetropes	-.004	.003	.393	-.012	.004
		Low Hyperopes	-.007	.004	.172	-.015	.002
	Emmetropes	Low Myopes	.004	.003	.393	-.004	.012
		Low Hyperopes	-.002	.003	.749	-.010	.005
	Low Hyperopes	Low Myopes	.007	.004	.172	-.002	.015
		Emmetropes	.002	.003	.749	-.005	.010
Z (5, 1)	Low Myopes	Emmetropes	-.002	.002	.645	-.007	.003
		Low Hyperopes	-.008	.006	.348	-.021	.006
	Emmetropes	Low Myopes	.002	.002	.645	-.003	.007
		Low Hyperopes	-.006	.006	.527	-.019	.007
	Low Hyperopes	Low Myopes	.008	.006	.348	-.006	.021
		Emmetropes	.006	.006	.527	-.007	.019
Z (5, 3)	Low Myopes	Emmetropes	.003	.002	.403	-.002	.008
		Low Hyperopes	-.001	.002	.888	-.007	.005
	Emmetropes	Low Myopes	-.003	.002	.403	-.008	.002
		Low Hyperopes	-.004	.002	.121	-.009	.001
	Low Hyperopes	Low Myopes	.001	.002	.888	-.005	.007
		Emmetropes	.004	.002	.121	-.001	.009

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (5, 5)	Low Myopes	Emmetropes	-.002	.003	.652	-.008	.004
		Low Hyperopes	-.002	.003	.632	-.008	.004
	Emmetropes	Low Myopes	.002	.003	.652	-.004	.008
		Low Hyperopes	.000	.002	1.000	-.005	.005
	Low Hyperopes	Low Myopes	.002	.003	.632	-.004	.008
		Emmetropes	.000	.002	1.000	-.005	.005
Z (6,-6)	Low Myopes	Emmetropes	-.002	.002	.450	-.006	.002
		Low Hyperopes	-.004	.002	.170	-.008	.001
	Emmetropes	Low Myopes	.002	.002	.450	-.002	.006
		Low Hyperopes	-.002	.002	.704	-.006	.003
	Low Hyperopes	Low Myopes	.004	.002	.170	-.001	.008
		Emmetropes	.002	.002	.704	-.003	.006
Z (6,-4)	Low Myopes	Emmetropes	-.001	.002	.759	-.005	.003
		Low Hyperopes	-.001	.002	.783	-.006	.003
	Emmetropes	Low Myopes	.001	.002	.759	-.003	.005
		Low Hyperopes	.000	.002	.997	-.004	.004
	Low Hyperopes	Low Myopes	.001	.002	.783	-.003	.006
		Emmetropes	.000	.002	.997	-.004	.004
Z (6,-2)	Low Myopes	Emmetropes	.000	.001	.989	-.003	.003
		Low Hyperopes	.001	.002	.687	-.003	.005
	Emmetropes	Low Myopes	.000	.001	.989	-.003	.003
		Low Hyperopes	.002	.002	.577	-.002	.005
	Low Hyperopes	Low Myopes	-.001	.002	.687	-.005	.003
		Emmetropes	-.002	.002	.577	-.005	.002
Z (6, 0)	Low Myopes	Emmetropes	.003	.002	.247	-.002	.008
		Low Hyperopes	.002	.003	.818	-.006	.010
	Emmetropes	Low Myopes	-.003	.002	.247	-.008	.002
		Low Hyperopes	-.001	.003	.906	-.008	.006
	Low Hyperopes	Low Myopes	-.002	.003	.818	-.010	.006
		Emmetropes	.001	.003	.906	-.006	.008
Z (6, 2)	Low Myopes	Emmetropes	-.002	.002	.286	-.006	.001
		Low Hyperopes	.001	.002	.903	-.004	.006
	Emmetropes	Low Myopes	.002	.002	.286	-.001	.006
		Low Hyperopes	.003	.002	.202	-.001	.008
	Low Hyperopes	Low Myopes	-.001	.002	.903	-.006	.004
		Emmetropes	-.003	.002	.202	-.008	.001
Z (6, 4)	Low Myopes	Emmetropes	-.001	.002	.678	-.006	.003
		Low Hyperopes	-.003	.002	.357	-.008	.002
	Emmetropes	Low Myopes	.001	.002	.678	-.003	.006
		Low Hyperopes	-.001	.002	.663	-.006	.003
	Low Hyperopes	Low Myopes	.003	.002	.357	-.002	.008
		Emmetropes	.001	.002	.663	-.003	.006
Z (6, 6)	Low Myopes	Emmetropes	-.001	.002	.955	-.006	.005
		Low Hyperopes	.000	.003	.991	-.006	.006
	Emmetropes	Low Myopes	.001	.002	.955	-.005	.006
		Low Hyperopes	.001	.002	.895	-.004	.006
	Low Hyperopes	Low Myopes	.000	.003	.991	-.006	.006
		Emmetropes	-.001	.002	.895	-.006	.004

** The mean difference is significant at the .05 level*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for Indian/Pakistani/Sri Lankan group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (2,-2)	Low Myopes	Emmetropes	.019	.037	.866	-.070	.108
		Low Hyperopes	.033	.030	.501	-.038	.105
	Emmetropes	Low Myopes	-.019	.037	.866	-.108	.070
		Low Hyperopes	.015	.033	.899	-.066	.095
	Low Hyperopes	Low Myopes	-.033	.030	.501	-.105	.038
		Emmetropes	-.015	.033	.899	-.095	.066
Z (2, 0)	Low Myopes	Emmetropes	1.701(*)	.163	.000	1.293	2.109
		Low Hyperopes	2.277(*)	.162	.000	1.871	2.683
	Emmetropes	Low Myopes	-1.701(*)	.163	.000	-2.109	-1.293
		Low Hyperopes	.576(*)	.063	.000	.423	.728
	Low Hyperopes	Low Myopes	-2.277(*)	.162	.000	-2.683	-1.871
		Emmetropes	-.576(*)	.063	.000	-.728	-.423
Z (2, 2)	Low Myopes	Emmetropes	.058	.059	.586	-.083	.200
		Low Hyperopes	.010	.052	.979	-.117	.137
	Emmetropes	Low Myopes	-.058	.059	.586	-.200	.083
		Low Hyperopes	-.048	.056	.672	-.182	.087
	Low Hyperopes	Low Myopes	-.010	.052	.979	-.137	.117
		Emmetropes	.048	.056	.672	-.087	.182
Z (3,-3)	Low Myopes	Emmetropes	-.012	.014	.670	-.047	.022
		Low Hyperopes	.005	.015	.932	-.031	.042
	Emmetropes	Low Myopes	.012	.014	.670	-.022	.047
		Low Hyperopes	.018	.015	.485	-.019	.054
	Low Hyperopes	Low Myopes	-.005	.015	.932	-.042	.031
		Emmetropes	-.018	.015	.485	-.054	.019
Z (3,-1)	Low Myopes	Emmetropes	-.016	.024	.778	-.075	.042
		Low Hyperopes	-.025	.024	.544	-.083	.033
	Emmetropes	Low Myopes	.016	.024	.778	-.042	.075
		Low Hyperopes	-.009	.024	.928	-.067	.049
	Low Hyperopes	Low Myopes	.025	.024	.544	-.033	.083
		Emmetropes	.009	.024	.928	-.049	.067
Z (3, 1)	Low Myopes	Emmetropes	.021	.018	.480	-.023	.066
		Low Hyperopes	.018	.019	.623	-.029	.065
	Emmetropes	Low Myopes	-.021	.018	.480	-.066	.023
		Low Hyperopes	-.003	.016	.975	-.041	.034
	Low Hyperopes	Low Myopes	-.018	.019	.623	-.065	.029
		Emmetropes	.003	.016	.975	-.034	.041
Z (3, 3)	Low Myopes	Emmetropes	-.004	.019	.978	-.050	.042
		Low Hyperopes	-.006	.018	.943	-.049	.037
	Emmetropes	Low Myopes	.004	.019	.978	-.042	.050
		Low Hyperopes	-.002	.015	.991	-.038	.034
	Low Hyperopes	Low Myopes	.006	.018	.943	-.037	.049
		Emmetropes	.002	.015	.991	-.034	.038
Z (4,-4)	Low Myopes	Emmetropes	.004	.005	.687	-.008	.016
		Low Hyperopes	-.003	.005	.870	-.015	.010
	Emmetropes	Low Myopes	-.004	.005	.687	-.016	.008
		Low Hyperopes	-.007	.006	.507	-.021	.008
	Low Hyperopes	Low Myopes	.003	.005	.870	-.010	.015
		Emmetropes	.007	.006	.507	-.008	.021

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (4,-2)	Low Myopes	Emmetropes	.008	.004	.137	-.002	.018
		Low Hyperopes	.004	.005	.717	-.009	.017
	Emmetropes	Low Myopes	-.008	.004	.137	-.018	.002
		Low Hyperopes	-.004	.005	.695	-.016	.008
	Low Hyperopes	Low Myopes	-.004	.005	.717	-.017	.009
		Emmetropes	.004	.005	.695	-.008	.016
Z (4, 0)	Low Myopes	Emmetropes	.020	.012	.240	-.010	.050
		Low Hyperopes	-.010	.013	.705	-.041	.020
	Emmetropes	Low Myopes	-.020	.012	.240	-.050	.010
		Low Hyperopes	-.030(*)	.012	.037	-.059	-.001
	Low Hyperopes	Low Myopes	.010	.013	.705	-.020	.041
		Emmetropes	.030(*)	.012	.037	.001	.059
Z (4, 2)	Low Myopes	Emmetropes	.001	.009	.993	-.020	.022
		Low Hyperopes	-.004	.008	.883	-.024	.016
	Emmetropes	Low Myopes	-.001	.009	.993	-.022	.020
		Low Hyperopes	-.005	.009	.856	-.027	.017
	Low Hyperopes	Low Myopes	.004	.008	.883	-.016	.024
		Emmetropes	.005	.009	.856	-.017	.027
Z (4, 4)	Low Myopes	Emmetropes	-.007	.010	.775	-.030	.017
		Low Hyperopes	.004	.009	.908	-.019	.026
	Emmetropes	Low Myopes	.007	.010	.775	-.017	.030
		Low Hyperopes	.010	.008	.377	-.008	.029
	Low Hyperopes	Low Myopes	-.004	.009	.908	-.026	.019
		Emmetropes	-.010	.008	.377	-.029	.008
Z (5,-5)	Low Myopes	Emmetropes	.001	.004	.938	-.008	.011
		Low Hyperopes	.006	.004	.289	-.003	.015
	Emmetropes	Low Myopes	-.001	.004	.938	-.011	.008
		Low Hyperopes	.004	.003	.426	-.004	.013
	Low Hyperopes	Low Myopes	-.006	.004	.289	-.015	.003
		Emmetropes	-.004	.003	.426	-.013	.004
Z (5,-3)	Low Myopes	Emmetropes	.002	.004	.819	-.007	.011
		Low Hyperopes	-.005	.004	.407	-.015	.005
	Emmetropes	Low Myopes	-.002	.004	.819	-.011	.007
		Low Hyperopes	-.007	.004	.100	-.016	.001
	Low Hyperopes	Low Myopes	.005	.004	.407	-.005	.015
		Emmetropes	.007	.004	.100	-.001	.016
Z (5,-1)	Low Myopes	Emmetropes	-.003	.005	.779	-.014	.008
		Low Hyperopes	.005	.004	.442	-.005	.016
	Emmetropes	Low Myopes	.003	.005	.779	-.008	.014
		Low Hyperopes	.009	.004	.145	-.002	.019
	Low Hyperopes	Low Myopes	-.005	.004	.442	-.016	.005
		Emmetropes	-.009	.004	.145	-.019	.002
Z (5, 1)	Low Myopes	Emmetropes	.002	.004	.848	-.007	.011
		Low Hyperopes	.006	.004	.347	-.004	.015
	Emmetropes	Low Myopes	-.002	.004	.848	-.011	.007
		Low Hyperopes	.004	.003	.341	-.002	.010
	Low Hyperopes	Low Myopes	-.006	.004	.347	-.015	.004
		Emmetropes	-.004	.003	.341	-.010	.002
Z (5, 3)	Low Myopes	Emmetropes	-.002	.003	.798	-.011	.006
		Low Hyperopes	-.004	.003	.501	-.011	.004
	Emmetropes	Low Myopes	.002	.003	.798	-.006	.011
		Low Hyperopes	-.001	.003	.908	-.009	.006
	Low Hyperopes	Low Myopes	.004	.003	.501	-.004	.011
		Emmetropes	.001	.003	.908	-.006	.009

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (5, 5)	Low Myopes	Emmetropes	.002	.004	.923	-.008	.012
		Low Hyperopes	-.005	.004	.431	-.015	.005
	Emmetropes	Low Myopes	-.002	.004	.923	-.012	.008
		Low Hyperopes	-.007	.003	.111	-.015	.001
	Low Hyperopes	Low Myopes	.005	.004	.431	-.005	.015
		Emmetropes	.007	.003	.111	-.001	.015
Z (6,-6)	Low Myopes	Emmetropes	-.003	.003	.608	-.009	.004
		Low Hyperopes	.003	.003	.530	-.004	.010
	Emmetropes	Low Myopes	.003	.003	.608	-.004	.009
		Low Hyperopes	.005	.002	.050	.000	.011
	Low Hyperopes	Low Myopes	-.003	.003	.530	-.010	.004
		Emmetropes	-.005	.002	.050	-.011	.000
Z (6,-4)	Low Myopes	Emmetropes	.000	.002	.987	-.005	.005
		Low Hyperopes	.002	.002	.606	-.002	.006
	Emmetropes	Low Myopes	.000	.002	.987	-.005	.005
		Low Hyperopes	.002	.002	.630	-.003	.007
	Low Hyperopes	Low Myopes	-.002	.002	.606	-.006	.002
		Emmetropes	-.002	.002	.630	-.007	.003
Z (6,-2)	Low Myopes	Emmetropes	-.003	.002	.105	-.007	.001
		Low Hyperopes	-.001	.002	.923	-.004	.003
	Emmetropes	Low Myopes	.003	.002	.105	-.001	.007
		Low Hyperopes	.003	.002	.275	-.001	.007
	Low Hyperopes	Low Myopes	.001	.002	.923	-.003	.004
		Emmetropes	-.003	.002	.275	-.007	.001
Z (6, 0)	Low Myopes	Emmetropes	-.007	.003	.073	-.015	.001
		Low Hyperopes	.001	.003	.970	-.007	.008
	Emmetropes	Low Myopes	.007	.003	.073	-.001	.015
		Low Hyperopes	.008	.003	.057	.000	.016
	Low Hyperopes	Low Myopes	-.001	.003	.970	-.008	.007
		Emmetropes	-.008	.003	.057	-.016	.000
Z (6, 2)	Low Myopes	Emmetropes	.003	.003	.686	-.005	.010
		Low Hyperopes	.003	.003	.576	-.004	.009
	Emmetropes	Low Myopes	-.003	.003	.686	-.010	.005
		Low Hyperopes	.000	.002	1.000	-.006	.006
	Low Hyperopes	Low Myopes	-.003	.003	.576	-.009	.004
		Emmetropes	.000	.002	1.000	-.006	.006
Z (6, 4)	Low Myopes	Emmetropes	.002	.003	.804	-.005	.008
		Low Hyperopes	.000	.003	.998	-.006	.006
	Emmetropes	Low Myopes	-.002	.003	.804	-.008	.005
		Low Hyperopes	-.002	.002	.772	-.007	.004
	Low Hyperopes	Low Myopes	.000	.003	.998	-.006	.006
		Emmetropes	.002	.002	.772	-.004	.007
Z (6, 6)	Low Myopes	Emmetropes	.000	.003	.999	-.008	.008
		Low Hyperopes	.005	.003	.226	-.002	.012
	Emmetropes	Low Myopes	.000	.003	.999	-.008	.008
		Low Hyperopes	.005	.002	.106	-.001	.011
	Low Hyperopes	Low Myopes	-.005	.003	.226	-.012	.002
		Emmetropes	-.005	.002	.106	-.011	.001

** The mean difference is significant at the .05 level*

Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for Middle Eastern group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Z (2,-2)	Low Myopes	Emmetropes	-.041	.037	.517	-.135	.053
		Low Hyperopes	-.054	.029	.208	-.137	.029
	Emmetropes	Low Myopes	.041	.037	.517	-.053	.135
		Low Hyperopes	-.013	.031	.905	-.089	.063
	Low Hyperopes	Low Myopes	.054	.029	.208	-.029	.137
		Emmetropes	.013	.031	.905	-.063	.089
Z (2, 0)	Low Myopes	Emmetropes	1.091(*)	.286	.036	.106	2.076
		Low Hyperopes	1.814(*)	.286	.005	.829	2.800
	Emmetropes	Low Myopes	-1.091(*)	.286	.036	-2.076	-.106
		Low Hyperopes	.723(*)	.078	.000	.536	.910
	Low Hyperopes	Low Myopes	-1.814(*)	.286	.005	-2.800	-.829
		Emmetropes	-.723(*)	.078	.000	-.910	-.536
Z (2, 2)	Low Myopes	Emmetropes	.322(*)	.070	.006	.116	.528
		Low Hyperopes	.360(*)	.065	.005	.152	.567
	Emmetropes	Low Myopes	-.322(*)	.070	.006	-.528	-.116
		Low Hyperopes	.038	.042	.641	-.063	.138
	Low Hyperopes	Low Myopes	-.360(*)	.065	.005	-.567	-.152
		Emmetropes	-.038	.042	.641	-.138	.063
Z (3,-3)	Low Myopes	Emmetropes	.014	.027	.864	-.069	.097
		Low Hyperopes	.006	.026	.971	-.078	.090
	Emmetropes	Low Myopes	-.014	.027	.864	-.097	.069
		Low Hyperopes	-.008	.015	.844	-.045	.028
	Low Hyperopes	Low Myopes	-.006	.026	.971	-.090	.078
		Emmetropes	.008	.015	.844	-.028	.045
Z (3,-1)	Low Myopes	Emmetropes	.006	.062	.996	-.197	.209
		Low Hyperopes	.001	.060	1.000	-.206	.207
	Emmetropes	Low Myopes	-.006	.062	.996	-.209	.197
		Low Hyperopes	-.005	.024	.980	-.064	.054
	Low Hyperopes	Low Myopes	-.001	.060	1.000	-.207	.206
		Emmetropes	.005	.024	.980	-.054	.064
Z (3, 1)	Low Myopes	Emmetropes	.048(*)	.016	.030	.005	.091
		Low Hyperopes	.035	.015	.097	-.006	.076
	Emmetropes	Low Myopes	-.048(*)	.016	.030	-.091	-.005
		Low Hyperopes	-.013	.014	.605	-.046	.020
	Low Hyperopes	Low Myopes	-.035	.015	.097	-.076	.006
		Emmetropes	.013	.014	.605	-.020	.046
Z (3, 3)	Low Myopes	Emmetropes	-.004	.036	.993	-.121	.113
		Low Hyperopes	.000	.035	1.000	-.119	.119
	Emmetropes	Low Myopes	.004	.036	.993	-.113	.121
		Low Hyperopes	.004	.016	.958	-.033	.042
	Low Hyperopes	Low Myopes	.000	.035	1.000	-.119	.119
		Emmetropes	-.004	.016	.958	-.042	.033
Z (4,-4)	Low Myopes	Emmetropes	-.002	.012	.990	-.038	.035
		Low Hyperopes	-.002	.011	.983	-.039	.035
	Emmetropes	Low Myopes	.002	.012	.990	-.035	.038
		Low Hyperopes	.000	.006	.998	-.016	.015
	Low Hyperopes	Low Myopes	.002	.011	.983	-.035	.039
		Emmetropes	.000	.006	.998	-.015	.016

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (4,-2)	Low Myopes	Emmetropes	.013	.007	.151	-.004	.031
		Low Hyperopes	.003	.006	.877	-.014	.019
	Emmetropes	Low Myopes	-.013	.007	.151	-.031	.004
		Low Hyperopes	-.010	.005	.129	-.023	.002
	Low Hyperopes	Low Myopes	-.003	.006	.877	-.019	.014
		Emmetropes	.010	.005	.129	-.002	.023
Z (4, 0)	Low Myopes	Emmetropes	-.035	.019	.198	-.088	.017
		Low Hyperopes	-.054(*)	.017	.046	-.106	-.001
	Emmetropes	Low Myopes	.035	.019	.198	-.017	.088
		Low Hyperopes	-.018	.012	.288	-.048	.011
	Low Hyperopes	Low Myopes	.054(*)	.017	.046	.001	.106
		Emmetropes	.018	.012	.288	-.011	.048
Z (4, 2)	Low Myopes	Emmetropes	.001	.009	.997	-.023	.025
		Low Hyperopes	.000	.008	.999	-.023	.023
	Emmetropes	Low Myopes	-.001	.009	.997	-.025	.023
		Low Hyperopes	.000	.007	.999	-.017	.017
	Low Hyperopes	Low Myopes	.000	.008	.999	-.023	.023
		Emmetropes	.000	.007	.999	-.017	.017
Z (4, 4)	Low Myopes	Emmetropes	-.007	.013	.845	-.047	.032
		Low Hyperopes	-.013	.012	.582	-.053	.028
	Emmetropes	Low Myopes	.007	.013	.845	-.032	.047
		Low Hyperopes	-.005	.007	.699	-.022	.011
	Low Hyperopes	Low Myopes	.013	.012	.582	-.028	.053
		Emmetropes	.005	.007	.699	-.011	.022
Z (5,-5)	Low Myopes	Emmetropes	.006	.008	.694	-.017	.029
		Low Hyperopes	.007	.007	.581	-.016	.031
	Emmetropes	Low Myopes	-.006	.008	.694	-.029	.017
		Low Hyperopes	.001	.004	.962	-.008	.010
	Low Hyperopes	Low Myopes	-.007	.007	.581	-.031	.016
		Emmetropes	-.001	.004	.962	-.010	.008
Z (5,-3)	Low Myopes	Emmetropes	.002	.006	.953	-.015	.018
		Low Hyperopes	-.005	.005	.619	-.022	.012
	Emmetropes	Low Myopes	-.002	.006	.953	-.018	.015
		Low Hyperopes	-.007	.004	.140	-.015	.002
	Low Hyperopes	Low Myopes	.005	.005	.619	-.012	.022
		Emmetropes	.007	.004	.140	-.002	.015
Z (5,-1)	Low Myopes	Emmetropes	-.009	.007	.476	-.029	.011
		Low Hyperopes	-.006	.006	.657	-.026	.014
	Emmetropes	Low Myopes	.009	.007	.476	-.011	.029
		Low Hyperopes	.003	.005	.818	-.009	.015
	Low Hyperopes	Low Myopes	.006	.006	.657	-.014	.026
		Emmetropes	-.003	.005	.818	-.015	.009
Z (5, 1)	Low Myopes	Emmetropes	-.010	.004	.114	-.023	.003
		Low Hyperopes	-.008	.004	.187	-.021	.004
	Emmetropes	Low Myopes	.010	.004	.114	-.003	.023
		Low Hyperopes	.002	.003	.789	-.005	.009
	Low Hyperopes	Low Myopes	.008	.004	.187	-.004	.021
		Emmetropes	-.002	.003	.789	-.009	.005
Z (5, 3)	Low Myopes	Emmetropes	-.006	.005	.530	-.024	.011
		Low Hyperopes	-.006	.005	.587	-.023	.012
	Emmetropes	Low Myopes	.006	.005	.530	-.011	.024
		Low Hyperopes	.001	.002	.959	-.005	.007
	Low Hyperopes	Low Myopes	.006	.005	.587	-.012	.023
		Emmetropes	-.001	.002	.959	-.007	.005

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Z (5, 5)	Low Myopes	Emmetropes	-.001	.006	.994	-.021	.020
		Low Hyperopes	-.001	.006	.993	-.021	.020
	Emmetropes	Low Myopes	.001	.006	.994	-.020	.021
		Low Hyperopes	.000	.003	1.000	-.006	.006
	Low Hyperopes	Low Myopes	.001	.006	.993	-.020	.021
		Emmetropes	.000	.003	1.000	-.006	.006
Z (6,-6)	Low Myopes	Emmetropes	-.007	.005	.387	-.022	.008
		Low Hyperopes	-.011	.005	.129	-.027	.004
	Emmetropes	Low Myopes	.007	.005	.387	-.008	.022
		Low Hyperopes	-.004	.002	.195	-.010	.002
	Low Hyperopes	Low Myopes	.011	.005	.129	-.004	.027
		Emmetropes	.004	.002	.195	-.002	.010
Z (6,-4)	Low Myopes	Emmetropes	-.001	.005	.947	-.017	.014
		Low Hyperopes	-.001	.005	.993	-.016	.015
	Emmetropes	Low Myopes	.001	.005	.947	-.014	.017
		Low Hyperopes	.001	.002	.839	-.003	.005
	Low Hyperopes	Low Myopes	.001	.005	.993	-.015	.016
		Emmetropes	-.001	.002	.839	-.005	.003
Z (6,-2)	Low Myopes	Emmetropes	.003	.003	.393	-.004	.010
		Low Hyperopes	.004	.002	.283	-.003	.011
	Emmetropes	Low Myopes	-.003	.003	.393	-.010	.004
		Low Hyperopes	.000	.002	.990	-.004	.005
	Low Hyperopes	Low Myopes	-.004	.002	.283	-.011	.003
		Emmetropes	.000	.002	.990	-.005	.004
Z (6, 0)	Low Myopes	Emmetropes	.009	.006	.336	-.009	.028
		Low Hyperopes	.015	.006	.112	-.004	.034
	Emmetropes	Low Myopes	-.009	.006	.336	-.028	.009
		Low Hyperopes	.005	.003	.131	-.001	.012
	Low Hyperopes	Low Myopes	-.015	.006	.112	-.034	.004
		Emmetropes	-.005	.003	.131	-.012	.001
Z (6, 2)	Low Myopes	Emmetropes	.005	.004	.561	-.008	.017
		Low Hyperopes	.003	.004	.712	-.010	.016
	Emmetropes	Low Myopes	-.005	.004	.561	-.017	.008
		Low Hyperopes	-.001	.002	.838	-.007	.005
	Low Hyperopes	Low Myopes	-.003	.004	.712	-.016	.010
		Emmetropes	.001	.002	.838	-.005	.007
Z (6, 4)	Low Myopes	Emmetropes	.004	.004	.631	-.010	.018
		Low Hyperopes	.005	.004	.490	-.009	.019
	Emmetropes	Low Myopes	-.004	.004	.631	-.018	.010
		Low Hyperopes	.001	.002	.883	-.004	.006
	Low Hyperopes	Low Myopes	-.005	.004	.490	-.019	.009
		Emmetropes	-.001	.002	.883	-.006	.004
Z (6, 6)	Low Myopes	Emmetropes	.002	.004	.825	-.009	.013
		Low Hyperopes	.004	.003	.447	-.006	.015
	Emmetropes	Low Myopes	-.002	.004	.825	-.013	.009
		Low Hyperopes	.002	.002	.609	-.003	.008
	Low Hyperopes	Low Myopes	-.004	.003	.447	-.015	.006
		Emmetropes	-.002	.002	.609	-.008	.003

** The mean difference is significant at the .05 level*

RMS of Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for Caucasian group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Defocus RMS	Low Myopes	Emmetropes	.896(*)	.092	.000	.671	1.121
		Low Hyperopes	.432(*)	.092	.000	.206	.658
	Emmetropes	Low Myopes	-.896(*)	.092	.000	-1.121	-.671
		Low Hyperopes	-.464(*)	.021	.000	-.513	-.416
	Low Hyperopes	Low Myopes	-.432(*)	.092	.000	-.658	-.206
		Emmetropes	.464(*)	.021	.000	.416	.513
Astigmatism RMS	Low Myopes	Emmetropes	.044	.027	.241	-.021	.109
		Low Hyperopes	.061	.025	.056	-.001	.122
	Emmetropes	Low Myopes	-.044	.027	.241	-.109	.021
		Low Hyperopes	.017	.011	.313	-.010	.044
	Low Hyperopes	Low Myopes	-.061	.025	.056	-.122	.001
		Emmetropes	-.017	.011	.313	-.044	.010
Coma RMS	Low Myopes	Emmetropes	-.011	.011	.610	-.038	.016
		Low Hyperopes	-.006	.011	.855	-.032	.020
	Emmetropes	Low Myopes	.011	.011	.610	-.016	.038
		Low Hyperopes	.005	.005	.624	-.008	.018
	Low Hyperopes	Low Myopes	.006	.011	.855	-.020	.032
		Emmetropes	-.005	.005	.624	-.018	.008
Trefoil RMS	Low Myopes	Emmetropes	.018	.009	.142	-.005	.041
		Low Hyperopes	.011	.009	.435	-.011	.033
	Emmetropes	Low Myopes	-.018	.009	.142	-.041	.005
		Low Hyperopes	-.007	.005	.282	-.018	.004
	Low Hyperopes	Low Myopes	-.011	.009	.435	-.033	.011
		Emmetropes	.007	.005	.282	-.004	.018
Spherical Aberration RMS	Low Myopes	Emmetropes	.000	.007	1.000	-.016	.016
		Low Hyperopes	-.025(*)	.006	.001	-.041	-.009
	Emmetropes	Low Myopes	.000	.007	1.000	-.016	.016
		Low Hyperopes	-.025(*)	.003	.000	-.033	-.017
	Low Hyperopes	Low Myopes	.025(*)	.006	.001	.009	.041
		Emmetropes	.025(*)	.003	.000	.017	.033
Quatrefoil RMS	Low Myopes	Emmetropes	.001	.003	.933	-.007	.009
		Low Hyperopes	-.003	.003	.536	-.011	.004
	Emmetropes	Low Myopes	-.001	.003	.933	-.009	.007
		Low Hyperopes	-.004(*)	.002	.025	-.008	.000
	Low Hyperopes	Low Myopes	.003	.003	.536	-.004	.011
		Emmetropes	.004(*)	.002	.025	.000	.008
Secondary Astigmatism RMS	Low Myopes	Emmetropes	.000	.004	.997	-.010	.009
		Low Hyperopes	-.007	.004	.117	-.016	.001
	Emmetropes	Low Myopes	.000	.004	.997	-.009	.010
		Low Hyperopes	-.007(*)	.002	.001	-.012	-.002
	Low Hyperopes	Low Myopes	.007	.004	.117	-.001	.016
		Emmetropes	.007(*)	.002	.001	.002	.012
Higher Orders RMS	Low Myopes	Emmetropes	.004	.010	.922	-.020	.028
		Low Hyperopes	-.012	.009	.440	-.035	.011
	Emmetropes	Low Myopes	-.004	.010	.922	-.028	.020
		Low Hyperopes	-.016(*)	.005	.011	-.028	-.003
	Low Hyperopes	Low Myopes	.012	.009	.440	-.011	.035
		Emmetropes	.016(*)	.005	.011	.003	.028
Total Aberrations RMS	Low Myopes	Emmetropes	.792(*)	.087	.000	.577	1.007
		Low Hyperopes	.417(*)	.088	.000	.201	.633
	Emmetropes	Low Myopes	-.792(*)	.087	.000	-1.007	-.577
		Low Hyperopes	-.375(*)	.019	.000	-.418	-.331
	Low Hyperopes	Low Myopes	-.417(*)	.088	.000	-.633	-.201
		Emmetropes	.375(*)	.019	.000	.331	.418

** The mean difference is significant at the .05 level*

RMS of Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for East Asian group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Defocus RMS	Low Myopes	Emmetropes	1.425(*)	.108	.000	1.164	1.687
		Low Hyperopes	1.242(*)	.112	.000	.973	1.512
	Emmetropes	Low Myopes	-1.425(*)	.108	.000	-1.687	-1.164
		Low Hyperopes	-.183(*)	.044	.000	-.288	-.079
	Low Hyperopes	Low Myopes	-1.242(*)	.112	.000	-1.512	-.973
		Emmetropes	.183(*)	.044	.000	.079	.288
Astigmatism RMS	Low Myopes	Emmetropes	.031	.026	.446	-.030	.093
		Low Hyperopes	.020	.028	.746	-.046	.087
	Emmetropes	Low Myopes	-.031	.026	.446	-.093	.030
		Low Hyperopes	-.011	.021	.865	-.062	.040
	Low Hyperopes	Low Myopes	-.020	.028	.746	-.087	.046
		Emmetropes	.011	.021	.865	-.040	.062
Coma RMS	Low Myopes	Emmetropes	.036(*)	.013	.022	.004	.068
		Low Hyperopes	.023	.014	.243	-.011	.058
	Emmetropes	Low Myopes	-.036(*)	.013	.022	-.068	-.004
		Low Hyperopes	-.013	.011	.482	-.039	.013
	Low Hyperopes	Low Myopes	-.023	.014	.243	-.058	.011
		Emmetropes	.013	.011	.482	-.013	.039
Trefoil RMS	Low Myopes	Emmetropes	.011	.010	.517	-.012	.034
		Low Hyperopes	.013	.009	.337	-.009	.036
	Emmetropes	Low Myopes	-.011	.010	.517	-.034	.012
		Low Hyperopes	.003	.009	.950	-.018	.024
	Low Hyperopes	Low Myopes	-.013	.009	.337	-.036	.009
		Emmetropes	-.003	.009	.950	-.024	.018
Spherical Aberration RMS	Low Myopes	Emmetropes	-.007	.008	.607	-.026	.011
		Low Hyperopes	-.034(*)	.012	.017	-.062	-.005
	Emmetropes	Low Myopes	.007	.008	.607	-.011	.026
		Low Hyperopes	-.026	.012	.083	-.055	.003
	Low Hyperopes	Low Myopes	.034(*)	.012	.017	.005	.062
		Emmetropes	.026	.012	.083	-.003	.055
Quatrefoil RMS	Low Myopes	Emmetropes	-.001	.005	.989	-.012	.011
		Low Hyperopes	-.003	.005	.789	-.015	.009
	Emmetropes	Low Myopes	.001	.005	.989	-.011	.012
		Low Hyperopes	-.003	.004	.761	-.011	.006
	Low Hyperopes	Low Myopes	.003	.005	.789	-.009	.015
		Emmetropes	.003	.004	.761	-.006	.011
Secondary Astigmatism RMS	Low Myopes	Emmetropes	-.004	.003	.426	-.012	.004
		Low Hyperopes	-.014	.006	.091	-.029	.002
	Emmetropes	Low Myopes	.004	.003	.426	-.004	.012
		Low Hyperopes	-.010	.006	.293	-.025	.006
	Low Hyperopes	Low Myopes	.014	.006	.091	-.002	.029
		Emmetropes	.010	.006	.293	-.006	.025
Higher Orders RMS	Low Myopes	Emmetropes	.024	.013	.147	-.006	.054
		Low Hyperopes	.001	.017	.998	-.040	.042
	Emmetropes	Low Myopes	-.024	.013	.147	-.054	.006
		Low Hyperopes	-.023	.016	.309	-.060	.014
	Low Hyperopes	Low Myopes	-.001	.017	.998	-.042	.040
		Emmetropes	.023	.016	.309	-.014	.060
Total Aberrations RMS	Low Myopes	Emmetropes	1.311(*)	.104	.000	1.060	1.562
		Low Hyperopes	1.155(*)	.107	.000	.897	1.413
	Emmetropes	Low Myopes	-1.311(*)	.104	.000	-1.562	-1.060
		Low Hyperopes	-.156(*)	.039	.000	-.250	-.062
	Low Hyperopes	Low Myopes	-1.155(*)	.107	.000	-1.413	-.897
		Emmetropes	.156(*)	.039	.000	.062	.250

** The mean difference is significant at the .05 level*

RMS of Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for Indian/Pakistani/Sri Lankan group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Defocus RMS	Low Myopes	Emmetropes	1.557(*)	.160	.000	1.156	1.959
		Low Hyperopes	1.214(*)	.162	.000	.808	1.620
	Emmetropes	Low Myopes	-1.557(*)	.160	.000	-1.959	-1.156
		Low Hyperopes	-.344(*)	.054	.000	-.474	-.213
	Low Hyperopes	Low Myopes	-1.214(*)	.162	.000	-1.620	-.808
		Emmetropes	.344(*)	.054	.000	.213	.474
Astigmatism RMS	Low Myopes	Emmetropes	-.066	.032	.117	-.144	.013
		Low Hyperopes	.000	.026	1.000	-.063	.063
	Emmetropes	Low Myopes	.066	.032	.117	-.013	.144
		Low Hyperopes	.065	.034	.148	-.017	.148
	Low Hyperopes	Low Myopes	.000	.026	1.000	-.063	.063
		Emmetropes	-.065	.034	.148	-.148	.017
Coma RMS	Low Myopes	Emmetropes	-.002	.012	.983	-.032	.027
		Low Hyperopes	.003	.014	.970	-.030	.037
	Emmetropes	Low Myopes	.002	.012	.983	-.027	.032
		Low Hyperopes	.005	.013	.915	-.027	.038
	Low Hyperopes	Low Myopes	-.003	.014	.970	-.037	.030
		Emmetropes	-.005	.013	.915	-.038	.027
Trefoil RMS	Low Myopes	Emmetropes	.004	.011	.922	-.022	.030
		Low Hyperopes	-.001	.011	.999	-.028	.026
	Emmetropes	Low Myopes	-.004	.011	.922	-.030	.022
		Low Hyperopes	-.005	.011	.910	-.032	.023
	Low Hyperopes	Low Myopes	.001	.011	.999	-.026	.028
		Emmetropes	.005	.011	.910	-.023	.032
Spherical Aberration RMS	Low Myopes	Emmetropes	.012	.009	.403	-.011	.035
		Low Hyperopes	-.010	.011	.623	-.035	.016
	Emmetropes	Low Myopes	-.012	.009	.403	-.035	.011
		Low Hyperopes	-.022	.009	.058	-.045	.001
	Low Hyperopes	Low Myopes	.010	.011	.623	-.016	.035
		Emmetropes	.022	.009	.058	-.001	.045
Quatrefoil RMS	Low Myopes	Emmetropes	-.003	.005	.818	-.016	.010
		Low Hyperopes	.000	.005	.996	-.013	.012
	Emmetropes	Low Myopes	.003	.005	.818	-.010	.016
		Low Hyperopes	.003	.005	.838	-.009	.015
	Low Hyperopes	Low Myopes	.000	.005	.996	-.012	.013
		Emmetropes	-.003	.005	.838	-.015	.009
Secondary Astigmatism RMS	Low Myopes	Emmetropes	-.007	.006	.462	-.020	.007
		Low Hyperopes	-.011	.005	.050	-.022	.000
	Emmetropes	Low Myopes	.007	.006	.462	-.007	.020
		Low Hyperopes	-.004	.006	.737	-.018	.009
	Low Hyperopes	Low Myopes	.011	.005	.050	.000	.022
		Emmetropes	.004	.006	.737	-.009	.018
Higher Orders RMS	Low Myopes	Emmetropes	-.003	.010	.959	-.028	.022
		Low Hyperopes	-.010	.012	.682	-.040	.019
	Emmetropes	Low Myopes	.003	.010	.959	-.022	.028
		Low Hyperopes	-.007	.011	.793	-.035	.020
	Low Hyperopes	Low Myopes	.010	.012	.682	-.019	.040
		Emmetropes	.007	.011	.793	-.020	.035
Total Aberrations RMS	Low Myopes	Emmetropes	1.373(*)	.156	.000	.980	1.766
		Low Hyperopes	1.147(*)	.156	.000	.754	1.540
	Emmetropes	Low Myopes	-1.373(*)	.156	.000	-1.766	-.980
		Low Hyperopes	-.226(*)	.045	.000	-.334	-.117
	Low Hyperopes	Low Myopes	-1.147(*)	.156	.000	-1.540	-.754
		Emmetropes	.226(*)	.045	.000	.117	.334

** The mean difference is significant at the .05 level*

RMS of Zernike terms analysis of variance Brown-Forsythe: Games-Howell post-hoc multiple comparisons tests for Middle Eastern group

Dependent Variable	(I) Refractive Error Groups	(J) Refractive Error Groups	Mean Difference (I-J)	SE	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Defocus RMS	Low Myopes	Emmetropes	.877	.283	.073	-.116	1.870
		Low Hyperopes	.370	.286	.465	-.616	1.355
	Emmetropes	Low Myopes	-.877	.283	.073	-1.870	.116
		Low Hyperopes	-.508(*)	.066	.000	-.665	-.350
	Low Hyperopes	Low Myopes	-.370	.286	.465	-1.355	.616
		Emmetropes	.508(*)	.066	.000	.350	.665
Astigmatism RMS	Low Myopes	Emmetropes	.099	.061	.327	-.106	.303
		Low Hyperopes	.114	.061	.247	-.091	.319
	Emmetropes	Low Myopes	-.099	.061	.327	-.303	.106
		Low Hyperopes	.015	.022	.778	-.039	.069
	Low Hyperopes	Low Myopes	-.114	.061	.247	-.319	.091
		Emmetropes	-.015	.022	.778	-.069	.039
Coma RMS	Low Myopes	Emmetropes	.017	.027	.817	-.066	.100
		Low Hyperopes	.015	.025	.829	-.069	.099
	Emmetropes	Low Myopes	-.017	.027	.817	-.100	.066
		Low Hyperopes	-.002	.015	.993	-.037	.034
	Low Hyperopes	Low Myopes	-.015	.025	.829	-.099	.069
		Emmetropes	.002	.015	.993	-.034	.037
Trefoil RMS	Low Myopes	Emmetropes	-.007	.018	.923	-.059	.046
		Low Hyperopes	-.007	.016	.913	-.060	.046
	Emmetropes	Low Myopes	.007	.018	.923	-.046	.059
		Low Hyperopes	.000	.011	1.000	-.025	.026
	Low Hyperopes	Low Myopes	.007	.016	.913	-.046	.060
		Emmetropes	.000	.011	1.000	-.026	.025
Spherical Aberration RMS	Low Myopes	Emmetropes	-.025	.010	.067	-.051	.002
		Low Hyperopes	-.036(*)	.008	.004	-.059	-.013
	Emmetropes	Low Myopes	.025	.010	.067	-.002	.051
		Low Hyperopes	-.011	.009	.446	-.034	.011
	Low Hyperopes	Low Myopes	.036(*)	.008	.004	.013	.059
		Emmetropes	.011	.009	.446	-.011	.034
Quatrefoil RMS	Low Myopes	Emmetropes	-.007	.004	.188	-.016	.003
		Low Hyperopes	-.002	.003	.746	-.009	.005
	Emmetropes	Low Myopes	.007	.004	.188	-.003	.016
		Low Hyperopes	.005	.004	.531	-.006	.015
	Low Hyperopes	Low Myopes	.002	.003	.746	-.005	.009
		Emmetropes	-.005	.004	.531	-.015	.006
Secondary Astigmatism RMS	Low Myopes	Emmetropes	-.019(*)	.006	.011	-.034	-.005
		Low Hyperopes	-.019(*)	.005	.010	-.033	-.006
	Emmetropes	Low Myopes	.019(*)	.006	.011	.005	.034
		Low Hyperopes	.000	.004	1.000	-.011	.011
	Low Hyperopes	Low Myopes	.019(*)	.005	.010	.006	.033
		Emmetropes	.000	.004	1.000	-.011	.011
Higher Orders RMS	Low Myopes	Emmetropes	-.012	.018	.795	-.061	.038
		Low Hyperopes	-.014	.016	.675	-.062	.034
	Emmetropes	Low Myopes	.012	.018	.795	-.038	.061
		Low Hyperopes	-.002	.013	.989	-.034	.030
	Low Hyperopes	Low Myopes	.014	.016	.675	-.034	.062
		Emmetropes	.002	.013	.989	-.030	.034
Total Aberrations RMS	Low Myopes	Emmetropes	.778	.276	.097	-.196	1.752
		Low Hyperopes	.365	.279	.459	-.600	1.331
	Emmetropes	Low Myopes	-.778	.276	.097	-1.752	.196
		Low Hyperopes	-.413(*)	.059	.000	-.553	-.273
	Low Hyperopes	Low Myopes	-.365	.279	.459	-1.331	.600
		Emmetropes	.413(*)	.059	.000	.273	.553

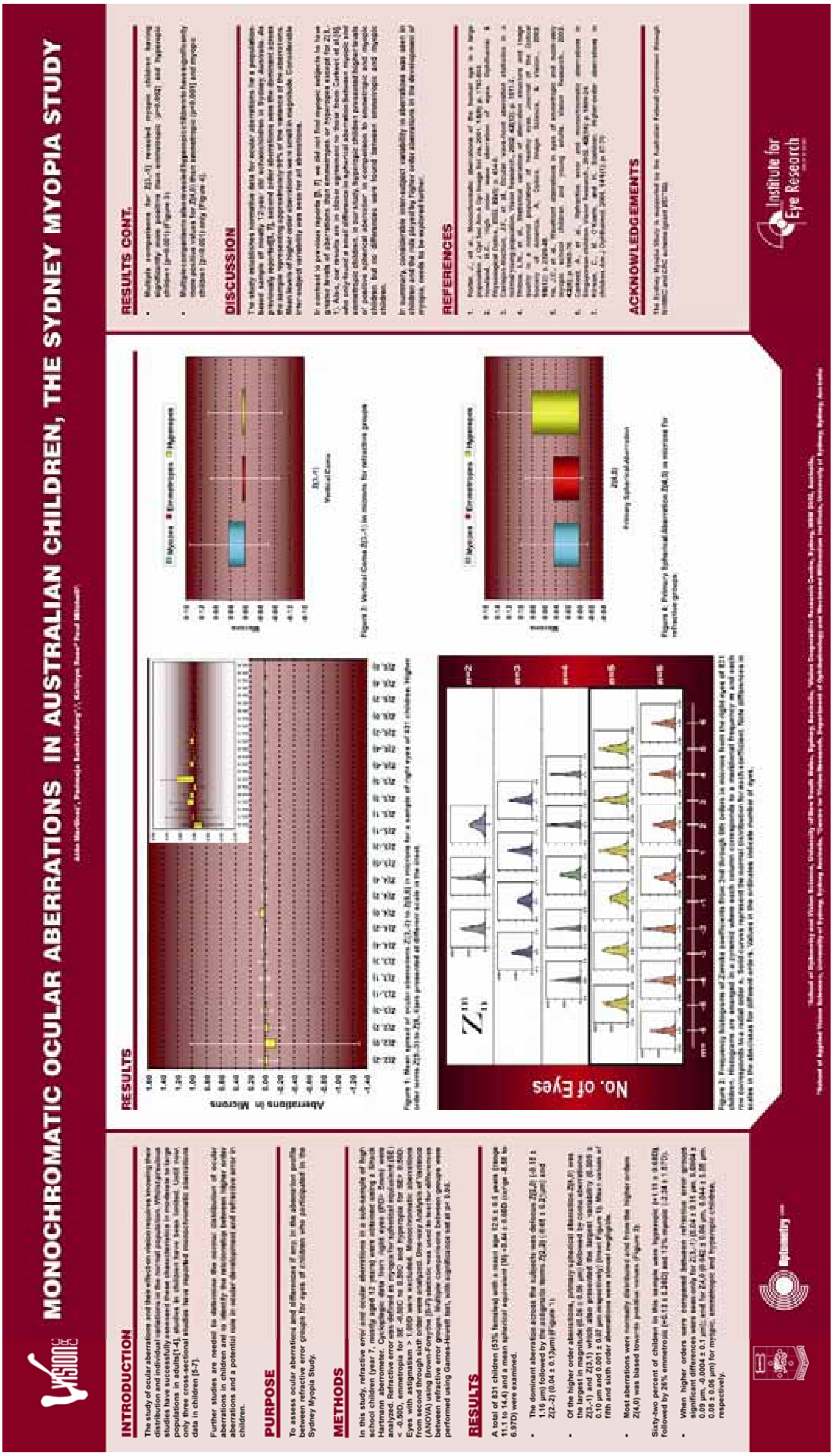
** The mean difference is significant at the .05 level*

APPENDIX G

POSTER
"MONOCHROMATIC OCULAR ABERRATIONS IN AUSTRALIAN CHILDREN, THE SYDNEY MYOPIA STUDY"

Presented at the 2006 ARVO Annual Meeting,
Fort Lauderdale, Florida, USA

Abstract published in Investigative Ophthalmology and Vision Science Journal
Volume 47, E-Abstract 47, May 2006


MONOCHROMATIC OCULAR ABERRATIONS IN AUSTRALIAN CHILDREN, THE SYDNEY MYOPIA STUDY
INTRODUCTION
PURPOSE
METHODS
RESULTS
RESULTS CONT.
DISCUSSION
REFERENCES
ACKNOWLEDGEMENTS
No. of Eyes
Institute for Eye Research

APPENDIX H:

POSTER
"HIGHER ORDER ABERRATIONS IN MYOPIC CHILDREN FROM DIFFERENT ETHNICAL BACKGROUNDS"

Presented at the 11th International Myopia Conference
16-18 August 2006, Singapore

Abstract published in Ophthalmic and Physiological Optics Journal
Volume 26, Supplement 1, August 2006

HIGHER ORDER ABERRATIONS IN MYOPIC CHILDREN FROM DIFFERENT ETHNICAL BACKGROUNDS (P057)

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INTRODUCTION

Myopia is a significant problem that affects nearly 80% of children aged 15 years and above in some countries in Asia.[1-4] It has been suggested that high levels of aberrations, especially higher order aberrations, could play a role in the development of myopia. Nevertheless, most studies have found no difference[5,6] or small differences[7,8] in the amount of higher order aberrations between myopic and emmetropic eyes. Recently, one study found inter-racial differences in the amount of ocular aberrations in children[9] suggesting that ethnicity could play a role in the levels of ocular aberrations and therefore probably a role in the development of refractive errors such as myopia.

AIM

To study the inter-racial differences, if any, in low and high order aberrations in a group of myopic children from three different ethnical backgrounds.

METHODS

- Cycloplegic refraction and ocular aberrations were obtained from both eyes using a COAS G200 aberrometer (Wavefront Sciences Inc, USA) on a sample of high school children (Year 7, mostly aged 12 years old) participating in the Sydney Myopia Study.
- Myopia was defined as spherical equivalent (M)[10] ≤ -0.50D. Eyes with refractive astigmatism > 1.00D in one or both eyes or with pupil diameter < 5mm were excluded from analysis. Ethnicity information was obtained from a 193-item questionnaire administered to the parents.
- Zernike coefficients up to the 6th order were fitted to the aberration data for a pupil diameter of 5mm following the standards of the Optical Society of America.[12]
- Multivariate-adjusted analyses were performed to analyse the effect of ethnicity on Zernike coefficients and RMS with significance levels calculated using Pillai's trace. Adjusted-multiple comparisons Bonferroni test was used to test for differences between ethnical groups. Linear regression was used to examine the effect of Zernike coefficients in M. Level of significance was set at $p<0.05$.

RESULTS

A total of 121 children were included in the analysis. Distribution by ethnical background: Caucasians (Group A) 29%, East Asians (Group B) 62% and Indian/Pakistani/Sri Lankan (Group C) 18%. Mean M of the three groups is presented in Table 1. The mean M of Group B was significantly higher than Group A ($p<0.001$).

Table 1
Mean M ± SD from right eyes of 121 myopic children

Group	Ethnicity	Mean M ± SD (D)	Range (D)
A	Caucasian (n = 35)	[illegible]	[illegible]
B	East Asian (n = 64)	[illegible]	[illegible]
C	Indian/Pakistani/Sri Lankan (n = 22)	[illegible]	[illegible]

Table 2
Association of Z(2,2) and Z(3,-1) with M

Factor	Partial r	p value	Multiple R	R^2	R^2 (adjusted for Z(2, 0))
Z(2, 2)	0.18	<0.001	0.28	0.08	0.05
Z(3,-1)	0.21	0.02			

Results of linear regression of Z(2,2) and Z(3,-1) with M are presented and Table 2.

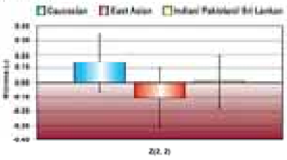

Figure 1
Mean Horizontal / Vertical Astigmatism Z(2, 2) for ethnical groups. Error bars indicate 1 ± Standard Deviation.

Multivariate analysis of Zernike coefficients after adjusting for M revealed differences between ethnic groups for Z(2,2) ($p<0.001$) and Z(3,-1) ($p=0.003$) only. Differences in Z(2,2) were found between Group A (0.14 ± 0.20 μm) and Group B (-0.11 ± 0.21 μm) ($p<0.001$) (Figure 1).

Multivariate analysis of defocus, astigmatism, coma, spherical aberration, higher orders and total RMS after adjusting for M, did not show any association of ethnicity with differences in RMS (Pillai's Trace 0.17, F 1.1762, $p=0.056$).

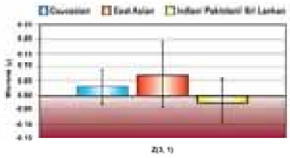

Figure 2
Mean Horizontal / Vertical coma Z(3,-1) for ethnical groups. Error bars indicate 1 ± Standard Deviation

For Z(3,-1), differences were found between Group B (0.07 ± 0.12 μm) and Group C (-0.02 ± 0.07 μm) ($p=0.002$) (Figure 2).

DISCUSSION

Though inter-race differences existed in mean M in this group of myopic children, differences in lower and higher order aberrations were found for Z(2,2) and Z(3,-1) only. Myopic caucasian children had higher levels of against-the-rule astigmatism (ATR) than East Asian children who had higher levels of with-the-rule astigmatism (WTR). Also, myopic East Asian children had higher levels of vertical/horizontal coma than Indian/ Pakistani/Sri Lankan children. It is possible that inter-racial differences in the optical elements (cornea, pupil, and lens) could have accounted for these differences.

Astigmatism has been found to have an association with myopia development in children[13] and coma aberrations play a dominant role in reducing retinal image.[14] In this study, while significant, the combined contribution of Z(2,2) and Z(3,3) in the total variation of M was 8%, and when adjusted for Z(2,0) the contribution further reduces to 5% only.

CONCLUSIONS

Small inter-racial differences of astigmatism Z(2,2) and coma (3,-1) exist in myopic children; however, the effect that these terms have in the variation of the spherical equivalent was small, suggesting that factors other than monochromatic aberrations contribute to the inter-racial differences found in myopic refractive error in children.

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The University of Sydney

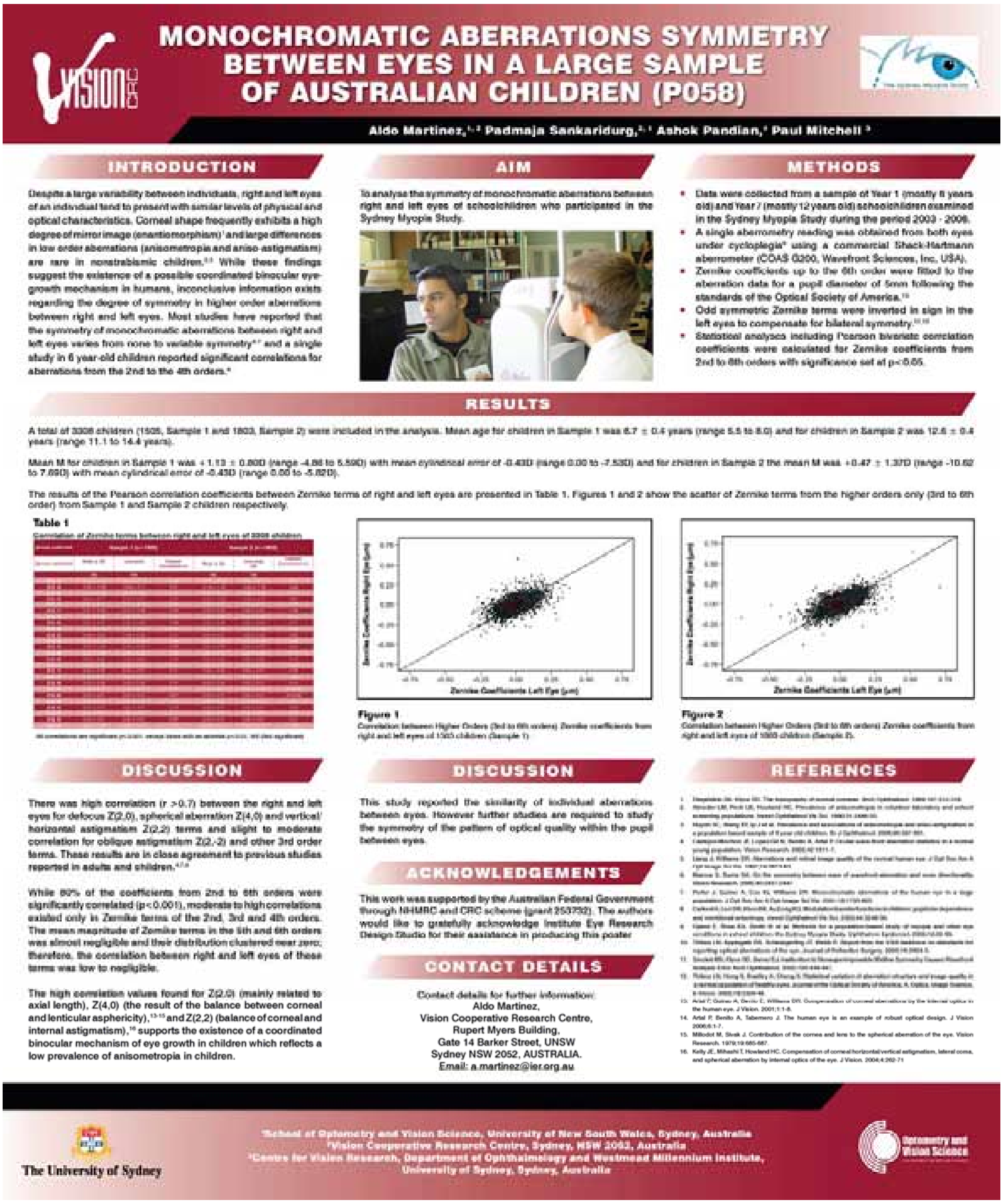
Optometry and Vision Science

APPENDIX I:

POSTER
"MONOCHROMATIC ABERRATIONS SYMMETRY BETWEEN EYES IN A LARGE SAMPLE OF AUSTRALIAN CHILDREN"

Presented at the 11th International Myopia Conference
16-18 August 2006, Singapore

Abstract published in Ophthalmic and Physiological Optics Journal
Volume 26, Supplement 1, August 2006


MONOCHROMATIC ABERRATIONS SYMMETRY BETWEEN EYES IN A LARGE SAMPLE OF AUSTRALIAN CHILDREN (P058)
Aldo Martinez,[1,2] Padmaja Sankaridurg,[2,1] Ashok Pandian,[3] Paul Mitchell [3]
INTRODUCTION
Despite a large variability between individuals, right and left eyes of an individual tend to present with similar levels of physical and optical characteristics. Corneal shape frequently exhibits a high degree of mirror image (enantiomorphism)[1] and large differences in low order aberrations (anisometropia and aniso-astigmatism) are rare in nonstrabismic children.[2,3] While these findings suggest the existence of a possible coordinated binocular eye-growth mechanism in humans, inconclusive information exists regarding the degree of symmetry in higher order aberrations between right and left eyes. Most studies have reported that the symmetry of monochromatic aberrations between right and left eyes varies from none to variable symmetry[4-7] and a single study in 6 year-old children reported significant correlations for aberrations from the 2nd to the 4th orders.[8]
AIM
To analyse the symmetry of monochromatic aberrations between right and left eyes of schoolchildren who participated in the Sydney Myopia Study.
METHODS
Data were collected from a sample of Year 1 (mostly 6 years old) and Year 7 (mostly 12 years old) schoolchildren examined in the Sydney Myopia Study during the period 2003 - 2005.
A single aberrometry reading was obtained from both eyes under cycloplegia[9] using a commercial Shack-Hartmann aberrometer (COAS G200, Wavefront Sciences, Inc, USA).
Zernike coefficients up to the 6th order were fitted to the aberration data for a pupil diameter of 5mm following the standards of the Optical Society of America.[10]
Odd symmetric Zernike terms were inverted in sign in the left eyes to compensate for bilateral symmetry.[11,12]
Statistical analyses including Pearson bivariate correlation coefficients were calculated for Zernike coefficients from 2nd to 6th orders with significance set at p<0.05.
RESULTS
A total of 3308 children (1505, Sample 1 and 1803, Sample 2) were included in the analysis. Mean age for children in Sample 1 was 6.7 ± 0.4 years (range 5.5 to 8.0) and for children in Sample 2 was 12.6 ± 0.4 years (range 11.1 to 14.4 years).
Mean M for children in Sample 1 was +1.13 ± 0.80D (range -4.86 to 5.59D) with mean cylindrical error of -0.43D (range 0.00 to -7.53D) and for children in Sample 2 the mean M was +0.47 ± 1.37D (range -10.62 to 7.69D) with mean cylindrical error of -0.43D (range 0.00 to -5.82D).
The results of the Pearson correlation coefficients between Zernike terms of right and left eyes are presented in Table 1. Figures 1 and 2 show the scatter of Zernike terms from the higher orders only (3rd to 6th order) from Sample 1 and Sample 2 children respectively.
Table 1
Correlation of Zernike terms between right and left eyes of 3308 children
Zernike Coefficients Right Eye (μm)
Zernike Coefficients Left Eye (μm)
Figure 1
Correlation between Higher Orders (3rd to 6th orders) Zernike coefficients from right and left eyes of 1505 children (Sample 1).
Figure 2
Correlation between Higher Orders (3rd to 6th orders) Zernike coefficients from right and left eyes of 1803 children (Sample 2).
DISCUSSION
There was high correlation (r >0.7) between the right and left eyes for defocus Z(2,0), spherical aberration Z(4,0) and vertical/horizontal astigmatism Z(2,2) terms and slight to moderate correlation for oblique astigmatism Z(2,-2) and other 3rd order terms. These results are in close agreement to previous studies reported in adults and children.[4,7,8]
While 80% of the coefficients from 2nd to 6th orders were significantly correlated (p<0.001), moderate to high correlations existed only in Zernike terms of the 2nd, 3rd and 4th orders. The mean magnitude of Zernike terms in the 5th and 6th orders was almost negligible and their distribution clustered near zero; therefore, the correlation between right and left eyes of these terms was low to negligible.
The high correlation values found for Z(2,0) (mainly related to axial length), Z(4,0) (the result of the balance between corneal and lenticular asphericity),[13-15] and Z(2,2) (balance of corneal and internal astigmatism),[16] supports the existence of a coordinated binocular mechanism of eye growth in children which reflects a low prevalence of anisometropia in children.
DISCUSSION
This study reported the similarity of individual aberrations between eyes. However further studies are required to study the symmetry of the pattern of optical quality within the pupil between eyes.
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Optometry and Vision Science

APPENDIX J:

PAPER
"COMPARISON OF MONOCHROMATIC ABERRATIONS IN MYOPIC AND EMMETROPIC CHILDREN"

Presented at the 11th International Myopia Conference
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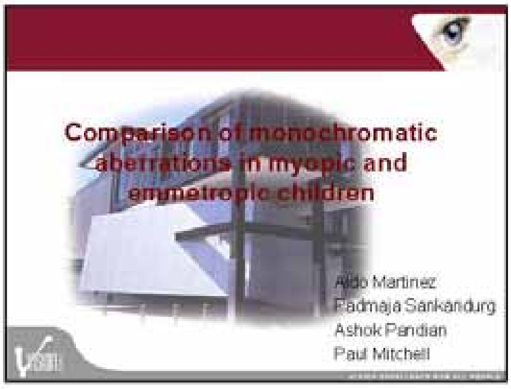
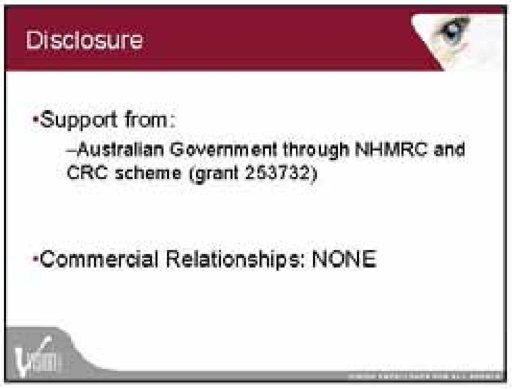
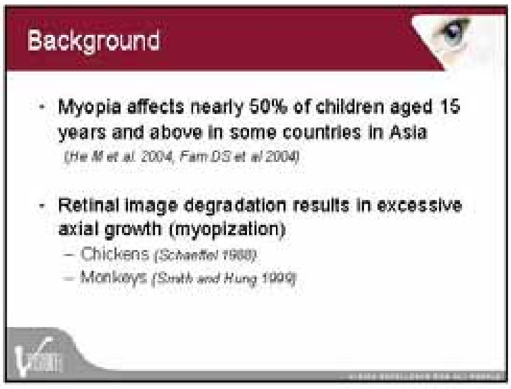
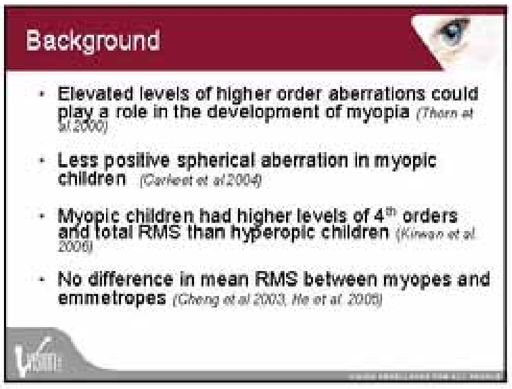
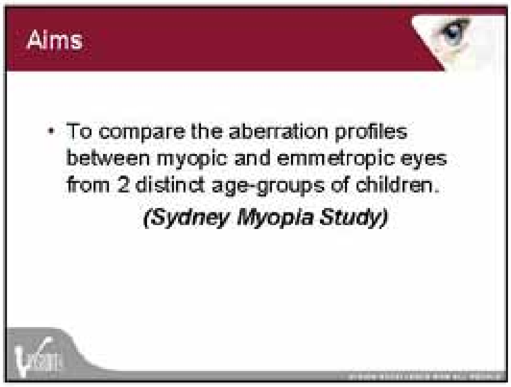
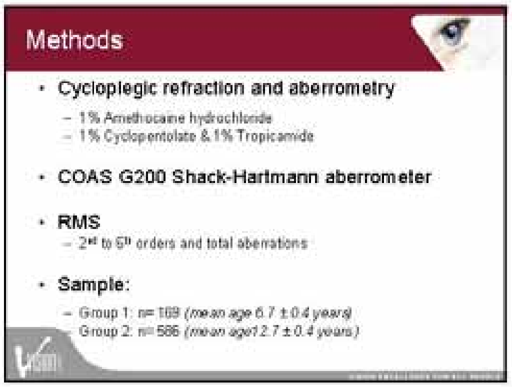

Comparison of monochromatic aberrations in myopic and emmetropic children
Aldo Martinez
Padmaja Sankaridurg
Ashok Pandian
Paul Mitchell


Disclosure
•Support from:
–Australian Government through NHMRC and CRC scheme (grant 253732)
•Commercial Relationships: NONE


Background
• Myopia affects nearly 50% of children aged 15 years and above in some countries in Asia (He M et al. 2004, Fam DS et al 2004)
• Retinal image degradation results in excessive axial growth (myopization)
– Chickens (Schaeffel 1988)
– Monkeys (Smith and Hung 1999)


Background
• Elevated levels of higher order aberrations could play a role in the development of myopia (Thorn et al 2000)
• Less positive spherical aberration in myopic children (Carkeet et al 2004)
• Myopic children had higher levels of 4th orders and total RMS than hyperopic children (Kirwan et al. 2006)
• No difference in mean RMS between myopes and emmetropes (Cheng et al 2003, He et al. 2005)


Aims
• To compare the aberration profiles between myopic and emmetropic eyes from 2 distinct age-groups of children.
(Sydney Myopia Study)


Methods
• Cycloplegic refraction and aberrometry
– 1% Amethocaine hydrochloride
– 1% Cyclopentolate & 1% Tropicamide
• COAS G200 Shack-Hartmann aberrometer
• RMS
– 2nd to 6th orders and total aberrations
• Sample:
– Group 1: n= 169 (mean age 6.7 ± 0.4 years)
– Group 2: n= 586 (mean age12.7 ± 0.4 years)

Methods

- Refractive groups:
  - Emmetropia (SE >-0.50 to +0.50D)
  - Myopia (SE -0.50D to -3.00D)
  - Astigmatism <1.00D
  - Analysis Pupil Diameter (5.00mm)

Statistical Analysis

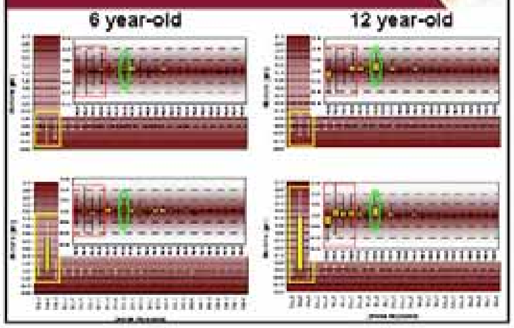
- Independent samples *t*-test
- Multivariate-adjusted analyses *(Pillai's trace)*
- Level of significance set at p<0.05

Results

	6 year-old		12 year-old	
	n	Mean SE ± SD (D)	n	Mean SE ± SD (D)
Emmetropes	140	0.18 ± 0.25	449	0.14 ± 0.26
Myopes	29	-0.94 ± 0.39 *	137	-1.42 ± 0.78 *

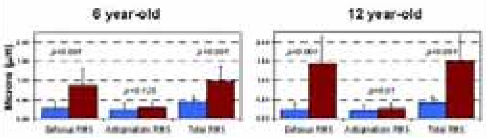
* *p<0.001*

Results



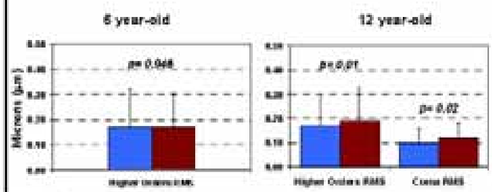
Results

Emmetropes Myopes

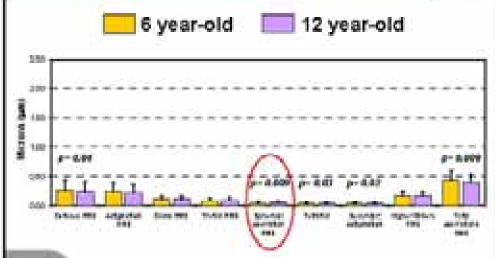


Results

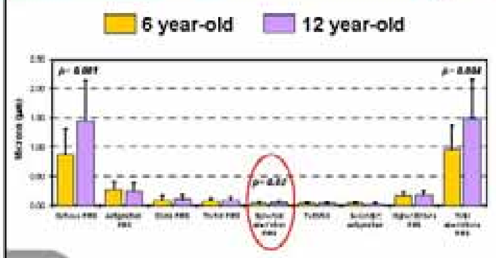
Emmetropes Myopes



Results (*Emmetropes*)



Results (*Myopes*)



Discussion

- Second-order aberrations were the dominant aberrations in all groups.
- We found differences in Defocus and Total RMS between myopic and emmetropic eyes.
- Small differences were found for HO RMS (Coma RMS) between emmetropic and myopic eyes in 12-year-old children only.
- Higher levels of SA RMS in emmetropic and myopic eyes in 12-year-old children.

Conclusions

- High variability in aberrations in emmetropic and myopic eyes in 6 and 12 year-old children.
- Small difference in Coma RMS between myopic and emmetropic eyes (12-year-old).
- Higher levels of SA RMS in emmetropic and myopic eyes in older children.

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APPENDIX K:

PAPER
"COMPARISON OF ABERROMETER AND AUTOREFRACTOR MEASURES OF REFRACTIVE ERROR IN CHILDREN"

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OPTOMETRY AND VISION SCIENCE

ORIGINAL ARTICLE

Comparison of Aberrometer and Autorefractor Measures of Refractive Error in Children

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ABSTRACT
Purpose. The purpose of this study was to evaluate and compare the Complete Ophthalmic Analysis System (COAS) G200 Aberrometer (Wavefront Sciences Inc., Albuquerque, NM) and Canon RK-F1 Autorefractor (Canon Inc., Tokyo, Japan) for measuring refractive errors in young children.
Methods. The Sydney Myopia Study is a population-based study of refractive error and eye health in young Australian children. Cycloplegic refractions were performed on 1504 school year 1 students (mostly 6 years old) and 890 school year 7 (mostly 12 years old) students using both the COAS G200 Aberrometer and Canon RK-F1 autorefractor. Refractive data were analyzed using power vectors. Mean differences and 95% limits of agreement were determined for refractive components between the two instruments.
Results. The mean age ± standard deviation was 6.7 ± 0.4 years (range, 5.5–9.1 years) and 12.6 ± 0.5 years (range, 11.1–14.4 years) for the year 1 and year 7 students, respectively. Mean paired differences for the M component (spherical equivalent) between the COAS G200 and Canon RK-F1 were <0.25 D in both age groups and were statistically significant in the year 1 group only ($p < 0.001$). Small significant differences were found in the astigmatic components (J0 and J45) in both groups. A smaller coefficient of agreement for the M component was found in the older group (0.54 D), whereas the coefficients of agreement of the astigmatic components (J0 and J45) were similar for both groups.
Conclusions. The COAS G200 aberrometer was an easy-to-use instrument for the measurement of refractive error in children. In addition to being able to measure higher and lower order aberrations, the COAS G200 provides refractive error measurements comparable to those of an autorefractor.
(Optom Vis Sci 2006;83:E811–E817)

Key Words: refractive error, automated refraction, Shack-Hartmann aberrometer, power vector analysis, Sydney Myopia Study, Sydney Childhood Eye Study

The ability to reliably measure refractive error in children is important in vision screening, clinical evaluation, and research. In epidemiologic studies such as those investigating the development of refractive error, repeatable and accurate methods are needed to detect longitudinal changes.

Although subjective refraction is considered the gold standard for measuring refraction, its use in children presents some distinct disadvantages. These relate to the child's ability to comprehend the test, the need for cooperation, and duration of testing. In addition, the repeatability of subjective refraction in adults is lower than automated refraction,[1,2] and in children, it may be even lower. These limitations can significantly affect refraction findings in children in both clinical and research settings. Therefore, there is a need for alternative methods of measuring refraction in children that can adequately overcome these issues.

One such alternative method is automated refraction. Automated refractors have been used extensively in epidemiologic studies of refractive error around the world. These instruments range from portable handheld devices[3–5] to more comprehensive instruments that can measure other ocular parameters such as corneal curvature.[6–8] Although some instruments have been shown to be highly accurate,[9–11] others are not reliable or accurate.[12]

Although differences between automated refractors in measuring refractive error in normal subjects are minimal,[13] potential problems can arise when results are compared between studies that use different instruments because these instruments are likely to differ in accuracy and repeatability. Quantifying the differences between instruments will facilitate critical appraisal of findings between such studies.

Although automated refractors are widely used, a new class of instruments known as *wavefront sensors* or *aberrometers* has recently been developed. These instruments are based on a variety of different optical principles, all of which differ from automated refractors. Aberrometers provide detailed assessment of higher order aberrations in addition to spherical and cylindrical errors. Shack-Hartmann type aberrometers are currently the most popular.

The Complete Ophthalmic Analysis System (COAS) by Wavefront Sciences, Inc. (Albuquerque, NM) is one of the first commercially available Shack-Hartmann aberrometers. The repeatability and accuracy of this instrument for measuring refractive error and monochromatic aberrations in model eyes[14] and human eyes[15,16] have been evaluated and the instrument is considered to be comparable to existing automated refractors.

To our knowledge, no study has reported the use of the COAS aberrometer for the measurement of refractive error in young children. The purpose of this study was to examine the reliability of cycloplegic refractive error measurement by the COAS G200 and its comparability to a known automatic refractor (Canon RK-F1; Canon Inc., Tokyo, Japan) using a large population of young children.

METHODS

This study presents cycloplegic refraction data collected during the Sydney Myopia Study from a large sample of year 1 (mostly 6 years old) and year 7 (mostly 12 years old) schoolchildren. Children in the year 1 group ($n = 1504$) were measured during 2003 to 2004 and children in the year 7 group ($n = 890$) were measured during 2004 to 2005.

The Sydney Myopia Study is a population-based study of refraction and eye health of Australian schoolchildren. Detailed study methods have been described elsewhere.[17] Briefly, 34 primary schools and 21 high schools within the Sydney Metropolitan Area were randomly selected using a cluster sampling design. Children in first and seventh grades of school were invited to participate. All examinations took place at the schools during school hours.

Approval for the study was obtained from the University of Sydney Human Research Ethics Committee and the New South Wales State Department of Education and Training, Australia. Informed written consent from at least one parent and verbal assent from each child were obtained.

Cycloplegia was induced following the same protocol in all children. First, one drop of 1% amethocaine hydrochloride (MINIMS; Chauvin Pharmaceuticals Ltd., London, England) was instilled in both eyes to improve comfort and also to enhance the absorption of the subsequent drops.[18] Cycloplegia/mydriasis of each eye were then attained with two cycles of cyclopentolate 1% (one drop) and tropicamide 1% (one drop) instilled 5 minutes apart. Tropicamide 1%[19] and cyclopentolate 1% are both effective cycloplegic agents in school-aged children after 30 minutes of instillation[20] and when combined, they provide adequate effect for cycloplegic refractions 30 minutes after instillation even in the dark irises of black children.[21]

Although we maximized the cycloplegic effect using tropicamide 1% and cyclopentolate 1%, a small proportion of children were slow to dilate and these also received up to two drops of 2.5% phenylephrine. Autorefraction was performed 25 to 30 minutes after the last drop was instilled. Aberrometry was done 5 to 10 minutes after autorefraction.

The mean of five readings taken with the autorefractor in automatic mode (K-R mode) was obtained from each eye for analysis. According to the manufacturer, the RK-F1 autorefractor has a dioptric measuring range of -30 to + 22 D for sphere power, 0 to ± 10 D for cylinder power, and 1° to 180° for axis with increments of 1°. In addition, the instrument requires a minimum pupil diameter of 2.5 mm to provide reliable refractometry (personal communication with Canon Inc.). The instrument controls for accommodation using an automatic fogging system and also provides measurements of corneal power (range, 33.75–61.25 D), interpupillary distance, and corneal and pupil diameters.[22]

The Canon RK-F1 shares the same measurement principle with a previous device (Canon RK-5) and both instruments seem to have the same accuracy in measuring normal subjects (personal communication with Canon Inc.). The use of the Canon RK-5 in previous large-scale studies of myopia is well supported.[6,7]

The specifications of the COAS have been published elsewhere.[14,16,23,24] We found that our instrument was highly repeatable in measuring low-order modes (see Appendix available online at www.optvissci.com), so we obtained and recorded only one reading for analysis from both eyes with the COAS G200 in autorefraction mode (Auto-acquire mode) following the instructions provided by the manufacturer.

Although it could be appropriate to match the pupil diameter for analysis of the aberrometer and the autorefractor to measure the agreement between both instruments, we considered that this approach would not reflect a typical clinical scenario for the aberrometer in measuring such small pupil diameters. Therefore, we chose to set the pupil diameter for analysis in the COAS G200 to 5 mm. This approach also allowed us to sample a larger area of low- and high-order aberrations of the eye and maybe to obtain a better calculation of refractive error.

The COAS G200 calculates the refractive error from Zernike polynomials of the second order: Z_2^{-2} and Z_2^2 for astigmatism and Z_2^0 for spherical equivalent using a least squares fitting of the wavefront. This method has been found to be an inaccurate indicator in determining the spherical equivalent of the refractive error as determined by subjective refraction, whereas other methods such as paraxial curvature matching accurately predict subjective refraction.[25] The COAS G200 offers an option similar to the paraxial curvature matching method called the "Seidel Sphere" option.[16] In this option, the aberrometer incorporates the Z_4^0 term (primary spherical aberration) in the calculation of spherical equivalent. For this study, the Seidel Sphere option was chosen for the calculation of refractive error.

In a small number of cases, the pupil diameter obtained was <5mm and these subjects were excluded from the analysis. All measurements were calculated at the corneal plane in the aberrometer and autorefractor.

The dioptric refractive data obtained with both instruments—S (sphere), C (negative cylinder), α (axis in degrees)—were converted into power vectors following the method suggested by Thibos et al.[26,27]: a spherical lens of power M (= sphere + [cylinder/2]); Jackson cross cylinder at axis 0° with power J_0 (= −[cylinder/2] cos[2*axis]); Jackson cross cylinder at axis 45° with power J_{45} (= −[cylinder/2] sin[2*axis]); magnitude of the power vector $|P| = \sqrt{M^2+J_0^2+J_{45}^2}$.

The agreement between both instruments was evaluated using the method suggested by Bland and Altman.[28] The differences between instruments were tested with a two-tailed *t* test for paired observations. Differences were considered to be statistically significant when $p < 0.05$. For purposes of this study, the Canon RK-F1 served as the gold standard, and we defined and calculated the coefficient of agreement (CoA) between the COAS G200 and the Canon RK-F1 as 1.96 times the standard deviation of the differences between the two instruments.[29] Data analysis was performed using SPSS (version 12.0.1) statistical software.

RESULTS

The mean ages (± standard deviation) of the children in year 1 and in year 7 were 6.7 ± 0.43 years (range, 5.50–9.13 years) and 12.6 ± 0.45 years (range, 11.06–14.44 years), respectively. Fifty-two percent of the year 1 group and 57% of the year 7 group were boys. The majority of children in both groups were white (55% in year 1, 49% in year 7) with the remaining children from diverse ethnic backgrounds (East Asian, Indian/Pakistani/Sri Lankan, Middle Eastern, and others).

Mean right eye spherical error in the year 1 group measured with the Canon RK-F1 was +1.37 ± 0.72 D (range, −3.90 to +6.75 D) with mean cylindrical error of −0.29 D (range, 0.00 to −4.27 D). For the year 7 group, the mean spherical error was 0.55 ± 1.44 D (range, −8.62 to + 6.87 D) with a mean cylindrical error of −0.38 D (range, 0.00 to −5.25 D). The mean vector components obtained with the Canon RK-F1 and the COAS G200 from both eyes of year 1 and year 7 groups are presented in Tables 1 and 2, respectively. Because there was a high correlation between right and left eye spherical equivalent in both year 1 and year 7 groups for both the autorefractor ($r = 0.924$, $r = 0.932$, $p < 0.001$) and the aberrometer ($r = 0.893$, $r = 0.921$, $p < 0.001$), further analyses were limited to right eyes only.

In the year 1 group, a two-tailed *t* test indicated a significant difference ($p < 0.001$) between the Canon RK-F1 and the COAS G200 for the 3 vectors (M, J_0 and J_{45}). The mean difference between the readings obtained in the year 1 group with the Canon RK-F1 and the COAS G200 (M, J_0, and J_{45}, respectively) as a function of their mean are plotted in (Fig. 1A–C). Positive values from the mean indicate that COAS G200 measured more minus than the Canon RK-F1 and negative values from the mean indicate that the COAS G200 measured more plus than the Canon RK-F1. The mean paired differences and 95% limits of agreement between the two instruments in the year 1 group are summarized in Table 3. On average, the COAS G200 measured 0.10 D more myopia than the Canon RK-F1 in the year 1 group.

For the year 7 group, statistically significant differences were found for J_0 (two-tailed *t* test, $p < 0.001$) and for J_{45} (two-tailed *t* test, $p < 0.001$) only. The plot in Figure 1D–F shows the mean difference between readings obtained with the Canon RK-F1 and the COAS G200 (M, J_0, and J_{45}, respectively) as a function of their

TABLE 1.
Mean cycloplegic refractive components of year 1 children (n = 1504) obtained with the Canon RK-F1 autorefractor and the COAS G200 aberrometer

	Canon RK-F1				COAS G200			
	Right Eye		Left Eye		Right Eye		Left Eye	
Refractive Component	Mean (D)	SD	Mean (D)	SD	Mean (D)	SD	Mean (D)	SD
M	1.22	0.70	1.28	0.73	1.12	0.80	1.15	0.82
J_0	0.02	0.22	0.04	0.20	0.09	0.24	0.11	0.23
J_{45}	−0.02	0.10	−0.03	0.09	0.01	0.13	−0.03	0.11

SD, standard deviation.

TABLE 2.
Mean cycloplegic refractive components of year 7 children (n = 890) obtained with the Canon RK-F1 autorefractor and the COAS G200 aberrometer

	Canon RK-F1				COAS G200			
	Right Eye		Left Eye		Right Eye		Left Eye	
Refractive Component	Mean (D)	SD	Mean (D)	SD	Mean (D)	SD	Mean (D)	SD
M	0.36	1.45	0.43	1.48	0.34	1.50	0.37	1.55
J_0	−0.04	0.27	−0.02	0.25	0.06	0.27	0.09	0.25
J_{45}	−0.03	0.12	−0.03	0.11	0.04	0.14	−0.05	0.13

SD, standard deviation.

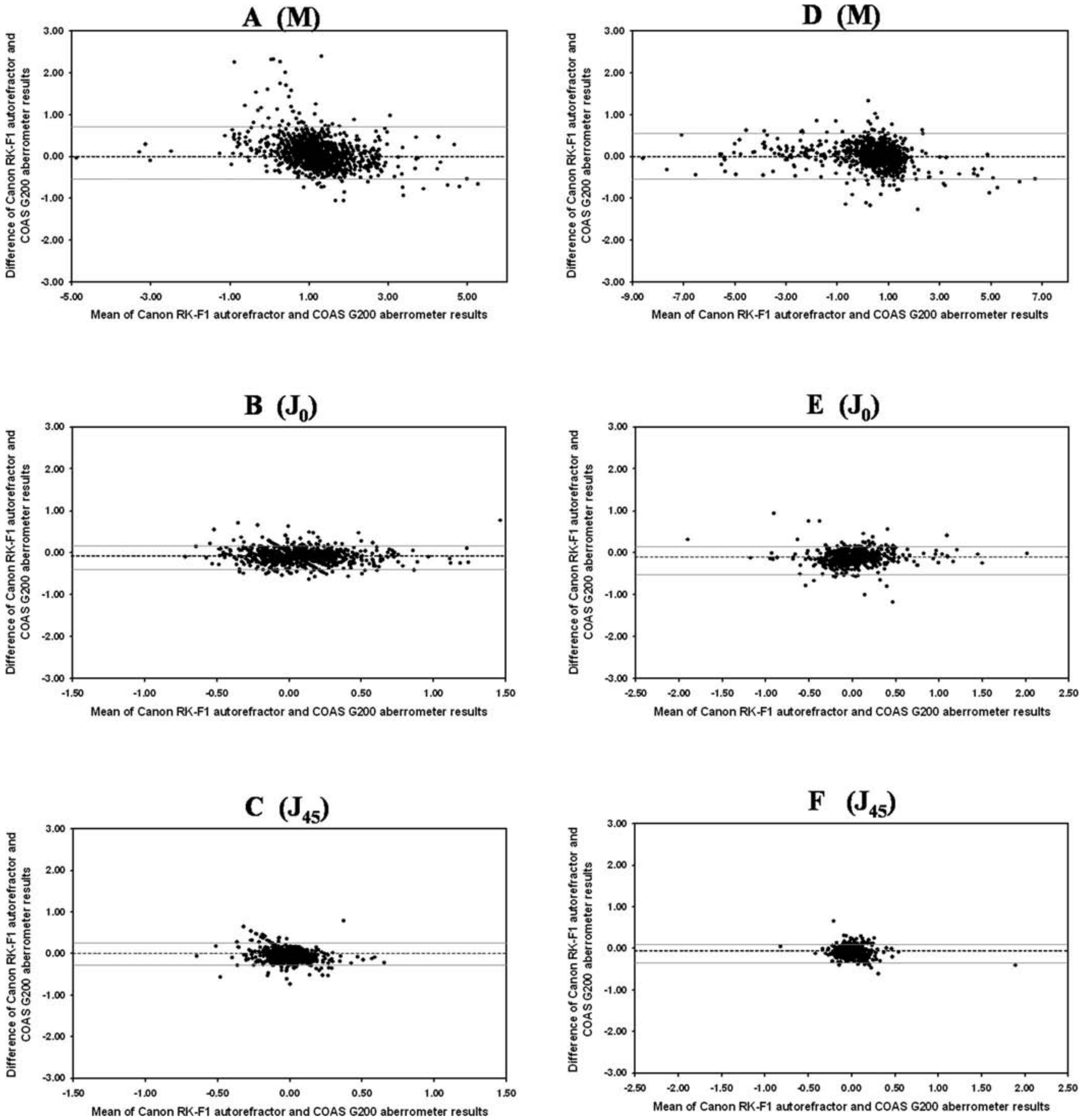

FIGURE 1.

Mean difference between Canon RK-F1 autorefractor and COAS G200 aberrometer results plotted as a function of their mean. The upper and lower solid lines indicate 95% limits of agreement, and the dashed line indicates the mean. Positive values from the mean indicate the aberrometer measured more minus than the autorefractor. Data are shown from the (A–C) right eyes of 1504 children in year 1 and (D–F) 890 children in year 7. (A and D) M vector; (B and E) J_0 vector; (C and F) J_{45} vector.

mean in the year 7 group. Positive values from the mean indicate that COAS G200 measured more minus than the Canon RK-F1 and negative values from the mean indicate that the COAS G200 measured more plus than the Canon RK-F1. Table 4 summarizes the mean paired differences and the 95% limits of agreement between the two instruments for the year 7 group.

The coefficients of agreement found for the M, J_0, and J_{45} components between the Canon RK-F1 and the COAS G200 were 0.64, 0.28, and 0.23 D, respectively, in the year 1 group. For the year 7 group, these coefficients of agreement were 0.54, 0.31, and 0.21 D, respectively.

DISCUSSION

Our study followed similar procedures and setup as Carkeet et al.'s[30] study that assessed the association of myopia and abnormal

TABLE 3.
Mean paired differences and limits of agreement between the Canon RK-F1 autorefractor and the COAS G200 aberrometer for each refractive component from right eyes of children in year 1[a]

	Paired Differences			
Refractive Component	Mean (D)	Standard Deviation	95% Limits of Agreement	Two-Tailed *t* Test p Values
M	0.10	0.33	−0.54 to +0.74	<0.001
J_0	−0.07	0.14	−0.48 to +0.48	<0.001
J_{45}	−0.03	0.12	−0.52 to +0.51	<0.001

[a]A positive value in M indicates that the COAS G200 measured more myopia than the Canon RK-F1 autorefractor.

TABLE 4.
Mean paired differences and limits of agreement between the Canon RK-F1 autorefractor and the COAS G200 aberrometer for each refractive component from right eyes of children in year 7[a]

	Paired Differences			
Refractive Component	Mean (D)	Standard Deviation	95% Limits of Agreement	Two-Tailed *t* Test p Values
M	0.02	0.28	−0.52 to +0.56	0.065
J_0	−0.10	0.16	−0.41 to +0.21	<0.001
J_{45}	−0.07	0.11	−0.28 to +0.14	<0.001

[a]A positive value in M indicates that the COAS G200 measured more myopia than the Canon RK-F1 autorefractor.

levels of monochromatic aberrations in children. In Carkeet et al.'s study, the investigators used an autorefractor (Canon RK-5) and a Shack-Hartmann aberrometer (Zywave; Bausch & Lomb Australia Pty, Ltd., Sydney, Australia) after induced cycloplegia for the determination of refractive error and monochromatic aberrations. However, Carkeet et al.'s study did not compare the refractions obtained with the two instruments and only used the autorefractor readings to classify refractive errors into different refractive groups for analysis. This could be because the Zywave aberrometer was found to have a significant myopic bias compared with both subjective refraction and cycloplegic refraction while measuring myopic eyes.[31]

Salmon et al.[16] evaluated the accuracy of the COAS and an autorefractor (Nidek ARK-2000, Nidek Co. Ltd., Gamagori, Japan) when measuring myopic refractive errors in adults and found that the mean difference of the power vector (in our case, ¦P¦) between the COAS (PD 4 mm, non-Seidel sphere) and subjective refraction was 0.31 ± 0.04D. In our study, the mean difference of ¦P¦ between the Canon RK-F1 and the COAS G200 was 0.05 ± 0.28D (two-tailed *t* test, $p < 0.001$) for the year 1 group and −0.03 ± 0.25D (two-tailed *t* test, $p = 0.001$) for the year 7 group.

We found a better agreement between the two instruments for the M vector in the year 7 group than in the year 1 group. In the year 1 group, we found a number of cases ($n = 25$) in which the COAS G200 measured more than 1.00 D more myopic than the Canon RK-F1. Close inspection of the aberrometry data from these cases, including astigmatism, higher order aberrations, RMS (square root of the sum of squared Zernike coefficients, excluding first-order aberrations), and pupil diameter, did not reveal any evident explanation for this clinically significant difference. This large difference in these subjects could be attributed to the difference in pupil size, method of estimating refractive error, alignment, and other fundamental differences between the two instruments. It could also be that partial cycloplegia allowed some accommodation that affected measurements with the COAS G200 only. We ruled out misalignment of the COAS G200 during measurement as a possible cause because as reported by Cheng et al.,[14] small axial and lateral displacements with the COAS had little effect on measurement of myopic or hyperopic eyes. We also examined the effect that these extreme cases may have had on the differences in vector components between the two instruments in the year 1 group. When we removed these cases from analysis, the mean paired difference for M was 0.08 ± 0.27 D and remained significant (two-tailed *t* test, $p < 0.001$). No change was found for the astigmatic components.

In this study, we compared the differences in the measurement of the refractive state in a population-based sample of children between a clinical aberrometer and an autorefractor. Although the COAS in previous studies have presented some degree of error when compared with the subjective refraction (gold standard), the differences between the instrument and a Canon RK-F1 autorefractor proved to be minimal for measuring spherocylindrical errors. Because of the nature of the study, we did not have the opportunity to compare the accuracy of the COAS G200 with cycloplegic subjective refraction. The results obtained in this study from children under cycloplegia with the COAS G200 were comparable to those from a reliable autorefractor. The COAS can be used as a reliable tool in the detection of refractive errors in population-based studies of refraction in young children.

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APPENDIX

Cycloplegic refractive data obtained from both eyes of 81 subjects from a different subsample of year 7 children from the Sydney Myopia Study following the same procedure as described in the "Methods" section of this article were analyzed. Subjects with a wide range of refractive errors were selected for this study: mean right eye spherical equivalent (± SD) −0.11 ± 1.98 D (range, −6.22 to 5.05 D) and mean astigmatic error of −0.40 D (range, −0.05 to -2.39 D).

The pupil diameter used for analysis was set to 5 mm and the Seidel sphere option was also selected. Two consecutive measurements were obtained from the right eye and then from the left eye with the patient remaining on the chinrest (mean time difference 10 ± 03 seconds). A few minutes later, a third measurement that required realignment of the instrument and repositioning of the patient on the instrument was also obtained (mean time difference 25 ± 15 minutes).

The coefficient of repeatability (CR) of the COAS G200 in measuring low-order modes (sphere and cylinder) in children was obtained following two methods. First, we computed the CR using the method suggested by Salmon et al.[15,16] We found that this method as published was missing a square root operation (see bullet 5), which we included in our calculations. When the square root is not included in the calculation, the variance is obtained and not the standard deviation, which is needed for the calculation of the CR. Personal communications with Dr Salmon confirmed that the authors included this operation in their calculations; however, as a result of a typographical error, it was omitted in the text of both publications. The method for calculating the CR was as follows: 1. Refractive data were converted to power vectors; 2. The mean of the three original power vectors was computed; 3. Three difference vectors were obtained (subtracting the mean from each of the three original power vectors); 4. The magnitude of each difference vector and the mean of the three magnitudes were computed to obtain the mean deviation for each eye; 5. The RMS deviation (standard deviation of the differences)[29] was obtained by squaring and adding up the mean deviations for 81 eyes, dividing by 81, and then taking the square root; and 6. The RMS deviation was multiplied by 1.96 to obtain the coefficient of repeatability for CR.

The second method consisted of the calculation of the 95% confidence intervals (sum of the mean differences ± 1.96 * standard error) of the magnitude of the power vector (P) from all subjects to obtain the CR (1.96 * standard deviation). This well-known method was used for comparison with the results obtained with the method from Salmon et al.

The CR obtained was 0.23 D (method 1) and 0.24 D (95% confidence interval, -0.026 to 0.028) (method 2). This CR was very similar to that found by Salmon et al.[15] in which a marginally better mean repeatability was found with the default sphere option of 0.17 D compared with the Seidel sphere option of 0.22 D. The repeatability of the COAS G200 was slightly lower than the specified by the manufacturer for sphere, cylinder, and axis (±0.05 D) but similar to what can be expected from cycloplegic autorefraction.[1] From these results, we were confident that obtaining only one measurement from each eye with the COAS G200 would provide a very close estimate of the refractive error of the subject.

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