Ocular biometric change in orthokeratology. An investigation into the effects of orthokeratology on ocular biometry and refractive error in an adult population.

Ocular Biometric Change in Orthokeratology

An investigation into the effects of orthokeratology on ocular biometry and refractive error in an adult population

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ABSTRACT

Aim; This study looks at the effect of orthokeratology on a number of biometric parameters and refractive error in an adult population.

Method; Forty three myopic subjects were recruited to a twelve month study into the effects of orthokeratology on ocular biometry and refractive error. Two different back surface lens designs were applied right eye) pentacurve and left eye) aspheric. The aspheric design was chosen to more closely mimic the cornea's natural shape. Anterior and posterior apical radii and p-values; corneal thickness and anterior chamber depth were measured using the Orbscan IIz; together with ocular biometry by IOL Master and a standard clinical refraction. All measurements were repeated at one night, one week, one, three, six and twelve months. Refractive changes were analysed against biometric changes.

Results; Twenty seven participants completed one month of lens wear. Twelve subjects completed twelve months of lens wear. Subjects with myopia ≤ -4.00DS were successfully treated with orthokeratology. Both anterior and posterior apical radii and p values were altered by orthokeratology. Corneal thickness changes were in agreement with previously published studies. Axial length and anterior chamber depth were unaffected by the treatment.

Conclusion; Orthokeratology should be available as an alternative to laser refractive surgery. It is best restricted to myopes of up to -4.00DS with low levels of with the rule corneal astigmatism. The use of an aspheric back design contact lens did not produce a significant benefit over that of a pentacurve.

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CHAPTER 1 INTRODUCTION

1.1 Historical perspective

Leonardo da Vinci and Rene Descartes described contact lenses as far back as the 16th century. In the late 19th century, Eugen Fick, a Swiss physician and Edouard Kalt, a Paris optician described the use of contact lenses to correct errors of sight. The majority of people would probably consider the contact lens to be a 20th century phenomenon with manufacturers carrying out research and development to produce the "ideal" contact lens. These developments have seen the move from blown glass scleral lenses in the late 19th century to modern gas permeable materials with high oxygen permeability. Similar developments have occurred for soft lenses although somewhat later in the polymers used. In most of these cases the contact lenses have been intended to correct the refractive error rather than to induce changes to it.

The use of contact lenses for the control of myopia progression particularly in children has been the subject of a number of long term research projects. The Contact Lens and Myopia Progression (CLAMP) study for example was a randomised clinical trial to examine the effects of RGP lenses on myopia progression in children (Walline, 2001). In her paper published in 1973 Stone (1973) refers to the use of rigid contact lenses in the control of myopia in the young myope. She makes it very clear that this study is using conventionally fitted lenses and not orthokeratology (OK). The findings of this research team were that these conventionally fitted PMMA lenses could retard the development of myopia. However this retardation was not brought about due to effects on the cornea but was more likely to be due to an alteration in the rate of change of the axial length (Stone, 1975).

The last 40 years have seen the development of the technique of fitting rigid contact lenses to manipulate the corneal shape. This manipulation enables the reduction of the manifest error of myopia present. Jessen (1962) explained his use of this technique which he called Orthofocus. In his 1962 paper he suggested that one factor which may

contribute to the development of myopia could be excessive eyelid pressure. He felt that this eyelid pressure was due to uncorrected myopes squinting. He proposed therefore, that control of this pressure could assist in myopia control. He suggested that patients who wore rigid contact lenses simulated a loose lid status and therefore were less likely to progress.

In his Orthofocus technique he fitted individuals with Polymethyl methacrylate (PMMA) lenses which were flatter than the measured corneal curvature (K). He developed this principle as a result of observations of spectacle blur induced by the change in K readings seen in individuals fitted with traditional contact lenses. It was felt that spectacle blur occurred as a consequence of wearing flat fitting lenses. Since PMMA is impervious to oxygen then tear exchange below the lenses is required to allow oxygen to flow underneath the contact lenses. In order to facilitate this, conventional PMMA lenses were fitted up to 0.1mm flatter than flattest K. Corneal oedema, due to the hypoxia which occurred behind the PMMA lenses, was also thought to contribute to the blur experienced by the contact lens wearer.

Jessen made use of the post-lens tear film to create the refractive correction required. The lenses themselves were plano in air. He developed his Orthofocus formula by fitting the lens flatter than the K reading by the desired amount of correction; i.e. back optic zone radius (BOZR) = flattest corneal meridian (in dioptres) - the amount of myopia reduction (in dioptres) required.

Unfortunately the patients in Jessen's study found the lenses very uncomfortable due to the flat fit. Problems also occurred with these flat lenses since they were unstable on the eye. Jessen improved the centration of the lenses by increasing the diameter he used to between 9.5 and 10.5mm total diameter. At the time conventional PMMA lenses had a diameter in the order of 9mm maximum to minimise the risk of corneal hypoxia. The maximum myopia correction attempted using the Orthofocus technique was -3.00DS. The subject involved had worn the lenses on a daily basis for two months and still required several hours of wear each day in order to maintain the correction.

Jessen did not limit his technique simply to the correction of myopia. He also proposed the use of lenses steeper than measured K for the treatment of hypermetropia or with toric back surfaces for astigmatism. In fact he found the treatment of both hypermetropia and astigmatism easier than myopia. The small steep lenses required to correct hypermetropia centred well and were more comfortable than those for myopia. Jessen (1964) talked about using a reverse de Carle bifocal design in order to achieve centration in the flat lenses they were fitting. The de Carle bifocal had a steep back surface central zone to provide the distance correction with a flatter peripheral curve to create the near addition. Jessen's design typically had a flat central zone of 5.5mm diameter with a steeper peripheral zone of 8mm diameter. The lens also had 1 ½ prism dioptres of ballast and was truncated to 8.8mm diameter. The steep zone helped to eliminate the tendency for flat lenses to ride high. The final curve had a radius of 11mm allowing tear exchange to occur under the lens. Jessen considered his lenses as "transparent pressure bandages" for the eye to prevent eye growth.

Neilson, Grant and May (1964) proposed that emmetropisation through the use of contact lenses could be possible. An evaluation of their findings led them to propose that orthokeratology was feasible. Following an analysis of a number of studies they proposed that the initial lens should be selected to be 0.12 - 0.37D flatter than flattest K. Anything flatter than this led paradoxically to corneal steepening, possibly as a consequence of poor centration leading to high riding lenses. Having secured a myopia reduction then the lenses were removed and further K readings taken which were used to select the next lens usually 0.25D flatter. Once emmetropia was achieved then the patient was given plano lenses as retainer lenses. Retention of the new corneal shape varied according to the length of time the lenses had been worn.

Jessen (1964) described Barraquer's procedure of lathing frozen donor corneas, keratophakia. In 1949 Barraquer (Swinger and Barraquer, 1981) had proposed that frozen sections of donor cornea could be modified on a contact lens lathe to produce the required refractive correction. This frozen cornea was then applied to the recipient's

cornea as a lamellar graft in order to correct myopia. A later procedure, keratomileusis, involved a lamellar keratectomy being performed on the patient's own cornea. This corneal section was then frozen, the stroma lathed and then replaced on the eye to achieve the appropriate correction. Jessen said that given the interest in surgical modification of the cornea in order to address refractive error; this could only foster more interest in the use of contact lenses for similar purposes. He likened the deliberate use of a contact lens to modify the cornea to that of an orthodontist using a brace to modify dentition. It seems that even in the early 1960's refractive surgery and contact lens wear were in competition.

Ziff (1968) measured corneal curvature using Photo-electric keratometry (PEK). From these measurements lenses were fitted with increasingly flatter base curves over a period of several months (up to a year) in order to achieve maturity. Ziff interpreted maturity as the point at which growth ceased or the end of adolescence between 18 and 22 years of age. Having achieved maturity then retainer lenses were required. Ziff appears to be the first person to mention sleeping in the lenses in order to maintain a lens free normal acuity in the day. He found that 7 – 10 hours of overnight wear was needed to retain clear vision all day. Interestingly this article was preceded by a disclaimer from the American Optometric Association that the printing of the article did not imply their support of Ziff's claims for orthokeratology.

Rengstorff (1969) attempted to evaluate the correlation between the change in corneal curvature achieved and the myopic shift seen after the use of standard daily wear rigid contact lenses. He evaluated 100 eyes following contact lens removal and found that changes in corneal curvature and myopia did not follow a consistent pattern in all cases. In fact, in extreme cases there was a 4.00D difference in the direction of change between the corneal curvature and the myopia. Rengstorff's conclusion was that the change in refractive error seen in contact lens wear was not simply due to the corneal flattening but that there must be another element in the equation.

One of the problems with a significant number of the early articles and papers published on orthokeratology is that they are based on clinical observation rather than on structured research projects, so that in many cases the evidence could be considered to be anecdotal. In fact Grant and May (1970) point out in their paper that their work is clinical in nature and based on practical application rather than theoretical evaluation. Subjects in their study were initially fitted with conventional rigid lenses. These subjects were then evaluated after three days and again after ten days of wear. Any change in their corneal curvature and refractive error induced by conventional lenses could be assessed at each of these visits. Having established that change in either corneal curvature, refractive error or both had occurred then the process of orthokeratology could commence. One interesting observation made by Grant and May at this point was that a number of individuals showed change in their refractive error without a change in corneal curvature. These individuals were more likely to be those in whom they suspected over accommodation. As a result of this they felt that the application of orthokeratology lenses produced an effect on the whole visual system and not just the cornea. Their report does not indicate that any of their subjects were re-examined using cycloplegia to address their presumption of over accommodation.

Having established that their subject would benefit from the orthokeratology lenses, Grant and May selected their first lens to have a base curve no more than 0.37D flatter than flattest K. Once the cornea had been moulded to this degree of flattening further flatter lenses were prescribed until such time as the desired effect had been achieved. The decision to provide flatter lenses was made on the basis of a plus over refraction of the lenses or a measured change in corneal curvature. The BOZR for the next lenses were selected on the basis of the measured corneal curvature. The lens power was calculated by adding the amount of plus power accepted over the old lens to the power difference between the old and new corneal curvature measures. The lens diameter was increased by 0.2mm for every dioptre of flattening. Successful treatment was said to have occurred when 20/20 vision was achieved and the lenses were plano in power.

This process could take up to five years. Having reached 20/20 vision the subject then required retainer lenses in order for the corneal moulding to be maintained. These retainer lenses were worn on a full time basis for six months and then their wearing time was reduced systematically down to zero. The implication from this paper was that adult patients could then discontinue lens wear and their myopia would have been eliminated. For children the retainer lenses were worn until the eye had reached maturity.

Grant and May still felt there were two unanswered questions at this time. How much change can be induced? How long would the effects last? In the case of the first question they had achieved up to three dioptres of reduction in myopia and as for the second they had had subjects who had maintained clear vision for two years without lenses. Grant and May had also carried out their procedure on hypermetropes. In this case the lenses were fitted steeper than original K readings with the lens changes being made when a negative over refraction was seen. In all other respects the process was the same. They had been able to correct hypermetropia of up to two dioptres. For astigmatism their approach had been to initially create a spherical cornea; a process which could involve an increase in refractive error, and then to further mould the spherical cornea to produce a plano result.

Nolan (1971) proposed that the best group for orthokeratology procedures were young teenagers aged under 14 and < 2.00D myopia. Given the age of the subjects and the relative infancy of the technique, this could be considered a controversial statement at this stage. The lens was fitted according to the amount of correction required i.e. the tear lens provided the optical correction; the lenses were plano in air. Diameters ranged from 7.7 - 9.8mm. Nolan used an increase in wearing time rather than a change in lens form to bring about the desired correction. Patients built up to 10 hours a day for one month and then were reassessed. Anyone who was dissatisfied at this stage was advised to build up to 12 hours. Patients were then advised to reduce their wearing time gradually until they found the minimum time for the shape change to be

maintained. Nolan did not aim for the overcorrection proposed by more recent orthokeratologists to allow for the daily regression. He suggested that patients were so grateful to have been improved from 20/300 – 20/60 that the application of a buffer zone was not necessary.

Grant and May (1972) were particularly interested in the relationship between the change in refractive error and the corneal curvature. They observed that this did not follow a one to one relationship. They gathered clinical data on pre and post orthokeratology results for refraction, corneal curvature and visual acuity from a number of orthokeratologists. Their findings were that in 50% of cases the rate of change in refractive error was twice that of the change in corneal curvature. Since their data were gathered from a number of sources, following a number of different techniques, it is hard to accept the validity of their conclusions. Their evaluation of the effect of corneal curvature change on visual acuity raised an interesting question. Accepted norms for the effect of refractive error on visual acuity appeared to be disrupted by the process of orthokeratology e.g. a 4.00 dioptre myope (vision 20/400) achieved vision of 20/40 after a 1.00 dioptre reduction in refractive error. At this time Grant and May had no means of determining what the unknown factor could be which would account for this variation from the accepted norm. Investigations into the effect of orthokeratology on the ocular aberrations may well help to answer this question.

At this time clinicians who were opposed to the concept of deliberately altering the corneal shape began to raise concerns. In response to this concern The American Optometric Association set up a special project team to look at the issue of orthokeratology in 1974 (Kerns, 1976a). The team raised concerns about the lack of research into the safety and efficacy of the procedure. Clinicians actively involved in orthokeratology at this time such as Jessen and Grant and May had published the results of clinical trials. However these trials often had inadequate controls, such as masking or randomization, which limited their validity. Masking of longitudinal studies can be very difficult. Binder, May and Grant (1980) in their masked and randomized

trial deliberately gave subjects wearing conventional contact lenses new lenses to mask the lens type from observers. They felt that the observer's expectation would be that those undergoing orthokeratology would need a series of flatter lenses to achieve myopia reduction. The conventional group however would not receive a change of lenses once an optimum fit had been achieved. Subjects who received no new lenses would therefore be revealed as members of the conventional group.

Having concluded that further research was required the American Optometric Association team did propose a definition for orthokeratology stating

"Orthokeratology is the reduction, modification, or elimination of refractive anomalies by the programmed application of contact lenses or other related procedures."

Patterson (1975), like Grant and May, was also concerned with evaluating the refractive changes which could be induced in an eye whilst wearing orthokeratology lenses. His concern was that the refractive change seen in some subjects did not correlate with the change seen in corneal curvature.

He hypothesised that there were three possible variables.

1. Is there a greater change in the anterior corneal surface than the posterior surface and therefore a corneal thickness change?
2. If the cornea changes as a whole is there a change in axial length?
3. Do the ocular components change their structure or is the position or tonus of the crystalline lens altered in some way?

Using retrospective data from 28 patients (54 eyes) fitted with a custom designed one piece bifocal type orthokeratology lens with a 6mm central zone he found that 50 eyes were flatter after lens wear, two were unchanged and two were steeper. Of the 50 eyes, 35 had flattening which was less than the overall refractive change, four had equal flattening and refractive change and 10 had more flattening than refractive change. A

comparison was then made between these findings and the ratio proposed by Grant and May (1972) that the change in corneal curvature is usually ½ the change in refraction (1:2). Patterson's findings gave a ratio of 1:2.1. This finding could not be considered to be significantly different from that of Grant and May.

Using the sag formula

$$s = r - \sqrt{(r^2 - y^2)}$$

he calculated the change in sag (Δs)

$$\Delta s = s_2 - s_1$$

where

s_1 = sag pre lens wear

s_2 = sag post lens wear

Since he had no means of measuring the axial length of the eyes involved in this study he used Gullstrand's constants, stating that a 1mm change in axial length was equivalent to 2.42 dioptres. He then used the Gullstrand constant to convert the change in corneal sagittal depth from millimetres to dioptres. Results from the 54 eyes showed a mean change in sagittal depth of 0.032mm or 0.0785 dioptres. This represented only 11.9% of the difference between the total change in refractive power and the change due to flattening of the corneal curvature. This left 88.1% of the change unaccounted for. He speculated that this 88.1% could be accounted for by any or all of the three hypotheses he lists at the beginning of the paper.

Since his calculations are based on a hypothetical eye and not on actual measurement, his conclusions remain speculative. In fact Patterson himself stated that proper measurement of the axial length, with ultrasound, on a per eye basis should improve our understanding of the changes which may occur. He also suggested that investigation of corneal thickness changes should be made.

This paper was preceded by a disclaimer from the American Optometric Association. They state that publication of the paper should not be taken as an endorsement of the

procedure of orthokeratology. In fact they suggest that it is a controversial procedure requiring more research and study.

Kerns (1976a) in response to the concerns mentioned above looked at designing an experimental protocol to validate the procedure of orthokeratology. He particularly wanted to look at a comparison between non-lens wearers, conventional lens wearers and orthokeratology lens wearers. All candidates had to fall within the same range for age, refraction and corneal curvature. He then looked at changes in corneal curvature (both horizontal and vertical), changes in refractive error, unaided acuity and topography. Kerns (1976b), published the results of his study having followed the groups of participants for up to 700 days. He concluded that when non lens wearers were compared with orthokeratology lens wearers then statistically significant changes were seen in horizontal corneal curvature and refraction from as early as 100 days with horizontal topography changes reaching significance by 300 days. A similar effect was seen when the orthokeratology subjects were compared with conventional lens wearers. In this case he found that both conventional alignment fitting lenses and orthokeratology lenses led to flattening of the horizontal keratometry reading although the conventional lenses had a much smaller effect. Surprisingly in both conventional and orthokeratology lenses whilst change occurred in the vertical corneal keratometry readings it never reached statistical significance. Kerns found an increase in astigmatism in 56% of the subjects in his study. 79% of these subjects showed an increase up to and including 1.00 dioptre. He hypothesised that the increase occurred when lenses were fitted more than 0.50D flatter than K. He found that a steepening of the vertical corneal meridian (0.12D) occurred with these flatter lenses. This steepening, accompanied by the relative flattening of the horizontal meridian, led to the increase in corneal toricity. His suggestion was that this occurred due to the reduction of upper lid pressure when a spherical base curve lens was fitted on a cornea which manifested with the rule astigmatism.

Interestingly a large proportion of the individuals (44%), who were fitted with orthokeratology lenses by Kerns, had against the rule astigmatism. With the rule astigmatism is more commonly found in younger individuals, with an increase in against the rule as the eye ages. The proportion of against the rule astigmats had decreased to 17% at the end of the study. This would be consistent with the orthokeratology lenses creating more flattening in the horizontal meridian. Since corneas which display against the rule astigmatism are steeper in the horizontal meridian, any flattening of this meridian may well convert corneas to with the rule astigmatism from against the rule.

Kerns published his final results, conclusion and discussions from the study conducted in 1976 (Kerns,1978). He found that whilst the direction of change induced by the orthokeratology lenses could be predicted, the magnitude of change and therefore the degree of refractive correction could not. He commented that the vertical meridian was particularly unorderly in its responses and most difficult to control. He pointed out that although corneal moulding occurred, in that the cornea flattened, it did not adopt the base curve of the contact lens used. This situation along with the fact that flattening did not occur in every individual fitted with the orthokeratology lenses led him to hypothesise that corneal rigidity could be one factor in this mismatch of responses. Ocular rigidity has been a known factor in Schiotz tonometry for example. Friedenwald nomograms have been used to allow the accurate measurement of intraocular pressure irrespective of the patient's ocular rigidity. More recent work has begun to look at the biomechanical properties of the cornea and its effect on orthokeratology responses. (See Section 1.8 Biomechanics)

Kerns found that as the cornea lost its asphericity then little or no further flattening occurred. He hypothesised that at the point at which the cornea becomes spherical the bearing pressure from the lens is equal in all meridians and this lack of focalized pressure reduced the incentive for corneal change. He commented that as the central

cornea flattens the normal relationship of steep centre and flatter periphery will be disrupted. Once this relationship change occurred there would be no area for displacement of the central corneal curvature. This, he suggested, could be a further reason why flattening slowed significantly. He concluded that only when the mechanisms involved in the corneal change are fully understood would there be a more widespread uptake of orthokeratology.

Erickson and Thorn (1977) began to look at the question of whether the refractive error change induced by orthokeratology was in fact twice that of the change in keratometry. Patterson (1975) had already supported this finding by stating a ratio of 2.1:1 although as previously mentioned this difference may not be statistically significant. In their evaluation of a number of studies Erickson and Thorn concluded that this relationship was not valid. Having plotted the change in keratometry against the change in refractive error they found the relationship to be

$$y = 0.68x + 0.72$$

y = change in refractive error

x = change in keratometry (measured as dioptric power assuming a refractive index of 1.3375)

This led them to the conclusion that there is a 0.72D change in refractive error without any measurable change in the keratometry reading.

They felt that the sources of error could have included;

i. Initial flattening occurs within the central zone which is not detected by keratometry and yet subjective refraction will show a decrease in myopia. Keratometers generally evaluate an annulus with an internal diameter of 2.5 – 3mm and therefore any change within this zone will be missed.

ii) Corneal thickness changes induced by lens wear may occur which would influence the apical radius and therefore the refractive error but would again not be detected by the keratometer.

iii) An expectation on the part of the practitioner to see the rate of change in the refractive error occur at twice that of the keratometer changes and therefore unintentional bias occurs in the recording of the data.

In the UK it is customary to use the radius of curvature to describe the corneal surface for contact lens manufacture, whereas practitioners in the USA use the concept of corneal surface power. The use of the power scale on the keratometer rather than the radius scale may introduce a margin of error. The keratometer establishes the anterior radius of curvature of the cornea by a direct comparison of the object and image size. If this value of r were to be substituted into the power equation

$$F = \frac{n-1}{r}$$

using n = 1.376 would only establish the power of the anterior corneal surface and take no account of the contribution of the posterior corneal surface to the total corneal power. Since it is the total corneal power which contributes to the refractive power of the eye then some method of incorporating the posterior corneal power provision is required. One method is for the keratometer manufacturer to use n = 1.3375 and not 1.376 in the creation of the power scale values. In this case an assumption is made that the posterior corneal surface contributes 10% of the total corneal power. An examination of the values for the Gullstrand schematic eye shows the ratio of the anterior and posterior surfaces to be 12% if the cornea is considered to act as a thin lens. If the corneal thickness is considered this ratio reduces to 11.8% (Douthwaite, 2006). Some instrument manufacturers have chosen to use different refractive indices in their instrument scales: Zeiss n =1.332 and American Optical n = 1.336. This variation in refractive index can lead to a power differential of up to 0.75 dioptres for the same measured radius of curvature. All of these potential variations contribute to a lack of correlation between topography and keratometry when dioptre values and not radii

are used. This can lead to difficulties when comparisons are made between study groups as corneal power values will vary according to the refractive index chosen.

As with most of the early studies Erickson and Thorn (1977) concluded that further longitudinal studies were required. They suggested that these studies should select a more accurate method than keratometry for evaluating change in the central cornea. Thomas Tredici (1979) an ophthalmologist in the American Air Force expressed his concerns about orthokeratology. He commented that orthokeratology was disproportionately costly in time and money for the results achieved. He felt that there were risks of corneal warpage and serious corneal abrasion from the orthokeratology lenses. The need for retainer lenses during the day meant that conventional rigid lenses should continue to be the method of choice for myopic individuals. He again pointed out the need for controlled studies into orthokeratology to increase the understanding of the mechanisms involved and therefore the predictability of the process.

Binder et al (1980) looked at 20 patients fitted with orthokeratology lenses following the Grant and May method and compared their responses to those of ten patients fitted with standard contact lenses. They found in the group of 20 orthokeratology patients that five failed to respond. These five were those members of the group with the more significant refractive errors and whose corneas showed only a slight flattening in the horizontal meridian i.e. their corneas were more spherical. Subjects classed as moderate or good responders had an initial refractive error in the region of 2.00D less than the poor group. Evaluation of their corneal shape showed no significant difference between these groups and the poor responders. Binder also suggested that the presence of against the rule astigmatism, albeit slight in nature, may contribute to success in orthokeratology. This is in contrast to many other researchers who state that orthokeratology causes an increase in against the rule astigmatism and therefore recommend limiting participants to those with astigmatism less than 1.50D. Binder reached the same conclusion as Kerns (1978) that due to the unpredictability of the

process of orthokeratology at this time, pre-analysis of the corneal shape did not provide further information from which to assess the likelihood of success.

Binder et al (1980) noted an anomaly in his paper where a number of individuals, with low myopic corrections, did not respond to orthokeratology. He offered an explanation that axial myopes may differ in their response from refractive myopes. The study did not have data to support this hypothesis, but it may offer another explanation for idiosyncratic results. Surprisingly Binder also found seven eyes which demonstrated an increase in myopia (up to -1.37) despite being fitted with orthokeratology lenses. This group fell within the low myope group i.e. mean refractive error -1.87 dioptres. Subjects in Binder's study had an average age of 24 and it could be speculated that the myopic shift over the period of follow up was simply the normal progression which can occur in this age group. Polse et al (1983c) suggested that normal myopic progression could explain the increase in myopia seen in three individuals in their study of 80 patients (age range 21 – 27 years).

1.1.1 The Berkeley Orthokeratology Study

The Berkeley OK study (Brand,1983) evaluated orthokeratology using daily worn lenses in 40 subjects whose responses were compared with 40 subjects wearing conventional hard lenses. In both cases the lenses were made of PMMA although a number of subjects were transferred to a PMMA/silicone combination later on in the study in order to resolve corneal oedema. Subjects in both groups were followed for 12 months in a masked randomised trial. The study findings were that individuals who received lenses for Orthokeratology purposes required larger, thicker lenses. The interaction between the base curve of the lens and the cornea was evaluated by measuring the bearing relationship i.e. the base curve radius of the lens (BOZR) minus the minimum of the horizontal and vertical corneal curvatures.

Having completed the study outlined above the subjects under went further evaluation to look at the rate of regression of the induced corneal changes. The conclusions were

that after four months some subjects had not returned to their original refractive status, although at 95 days 70% had returned to their baseline refraction. A similar finding occurred for corneal curvature, where 80% returned to baseline at 95 days. A rapid change was seen in the first 30 days of lens discontinuation followed by a slower phase. Polse et al (1983a) further evaluated the subjects from the Berkeley study and charted the rate and degree of regression, the so called persistence of change. They noted that despite the fact that the treatment group (orthokeratology) showed approximately twice the degree of refractive change (1.00D), when compared to the control group (conventional PMMA), after 364 days of wear; the final outcome (persistence of change) after lens wear had been discontinued (on average for 68 days) for both groups is not significantly different. The surprising finding here could be that conventional wear of hard lenses had led to a 0.50D change in refraction. This is likely to be a consequence of the normal procedure of fitting PMMA lenses 0.1mm flatter then flattest K to encourage tear exchange below the lens. A fitting 0.1mm flatter than flattest K is equal to 0.50D.

Polse et al (1983b) also expressed concerns that the change in corneal curvature is consistently 0.50D less than the change seen in refractive power. They postulate, as did Erickson and Thorn (1977) that the reason for this is that keratometers measure an area well outside the treatment zone of the lens where the majority of the refractive change will take place. Polse et al (1983c) concluded that the use of orthokeratology lenses could on average only achieve a 1.00 dioptre reduction in myopia.

Since the process of orthokeratology involves the deliberate manipulation of the cornea then safety is of paramount importance. As part of the Berkeley Orthokeratology study Polse et al (1983b) looked at

- Corneal oedema by evaluating pachymetry changes
- Corneal curvature using keratometry
- Refractive astigmatism particularly to look at irregular astigmatism
- Spectacle blur
- Slit lamp examination to evaluate staining and corneal oedema
- Endothelial cell density using specular microscopy

All assessments were made at the subjects' morning visits except for the slit lamp examination which was repeated in the afternoon. In conclusion they found no substantial change in corneal integrity or vision even in individuals with a significant change in refractive error, in the region of 3.75 dioptres. One of the consequences of fitting contact lenses which are flatter than the corneal apex is the difference in effect on the two principal meridians. This will give rise to a change in the measured regular astigmatism. This assumes that only the two principal meridians will be affected. Since flat fitting contact lenses have a tendency to decentre superiorly and therefore off the apex of the cornea the influence on corneal shape will be asymmetric. It is likely that the affected meridians will not be at 90^0 to each other as would be expected in regular astigmatism. This irregular astigmatism cannot be corrected by conventional refractive methods and may explain the reduction in best corrected acuity seen at the collection appointments.

A small number of subjects in both the treatment and control group showed a grade 3 oedema response (6 – 9 %). These individuals were asked to attend for a complications visit. Subjects from both the treatment and control group required complication visits with the treatment group requiring approximately 25% more visits. 16% of the treatment group had no complication visit. The main reason for the treatment visit was classified as altered corneal physiology. The group did not define the corneal signs which they felt indicated a change in corneal physiology. Measures of corneal oedema and staining showed that, whilst there were differences between the two groups, no values reached clinical significance. Comfort and visual acuity issues

were the next two most common complaints. Analysis of the data on endothelial cell count showed an unexplained increase in the number of cells which was put down to measurement error. In view of the additional complication visits required by their orthokeratology subjects, Polse et al suggested that more follow up visits will be required by orthokeratology patients in order to monitor optimal corneal physiology. They made no recommendation for the number or frequency of these visits.

Inevitably in any longitudinal study a number of subjects will withdraw. Analysis of their dropout candidates was that no one left the study due to significant adverse reactions to orthokeratology lens wear. A number of subjects were withdrawn by the observers due to poor compliance with the study protocol. Since the potential for severe adverse reactions is greater in this more invasive procedure. Any indication of lack of compliance on the part of the subject should be viewed as a significant reason to withdraw the lenses. The complications associated with orthokeratology will be discussed later.

1.1.2 The Tabb method

Paradoxically the Tabb method (Coon, 1984) used PMMA lenses fitted steeper than flattest K (K + 0.25D). The steeper lens helped to improve centration. He also felt that this would avoid the induction of with the rule astigmatism. Apical clearance was maintained in this method and the cornea was manipulated by means of altering the tear reservoir. He felt that the fluid forces at work under the lens could achieve the desired refractive error change. The tear reservoir (TR) i.e. the percentage of the posterior lens surface occupied by the intermediate and peripheral curve area was calculated using the formula:

TR = 1 – Area OZD / Area OAD x 100%

OZD = optic zone diameter (BOZD)

OAD = overall contact lens diameter = K_f + 1mm (TD)

K_f = flattest corneal curvature (in mm)

Manipulation of the tear reservoir was brought about by keeping the base curve and total diameter constant but reducing the optic zone diameter. In this way the tear reservoir could be increased gradually from 32.5% to 45% for subjects undergoing orthokeratology. The control group's lens reservoir was maintained at the 30% level for the duration of the study. Lens designs which allowed a reservoir of beyond 45% were found to be unstable. This instability was addressed by altering the lens total diameter. Coon found that a small number of the control subjects experienced an improvement in unaided vision with four out of 30 achieving 20/20 at some time in the 80 weeks of the study. This compared with 23 of the 48 subjects fitted with orthokeratology lenses.

When examined as a whole the change in refraction i.e. reduction in myopia across both groups was 0.49D @ 180 and 0.43D @ 90 for the control group and in the orthokeratology group 0.56D @ 180 and 0.60D @ 90. Although myopia reduction occurred in both groups the orthokeratology group were found to show a more consistent reduction in myopia particularly in the later stages of the study.

Previous studies (Kerns, 1978), (Binder, 1980) have noted an increase in with-the-rule astigmatism. Coon found no significant increase in with-the-rule astigmatism in either the orthokeratology or the control group using the Tabb method. He assumed that this was because of the careful control of the relationship between the cornea and the lens which reduced the risk of decentration. Most orthokeratology researchers at this time reported that lens decentration led to an increase in corneal toricity and therefore astigmatism.

1.2 Reverse Geometry Lenses (circa 1989)

Fontana (1972) described a lens which he called a one piece bifocal. This lens was possibly the first example of a reverse geometry lens. Reverse geometry lenses have an intermediate peripheral curve which has a steeper radius than the BOZR. This is contrary to normal RGP design in which the peripheral radii flatten towards the lens edge. The central 6mm zone of the lens had a BOZR 1.00D flatter than the paracentral

curve which is fitted on alignment. The final peripheral curve was produced to give acceptable edge clearance. These lenses were still worn on a daily basis. Fontana continued to use the principle of fitting progressively flatter lenses until the desired refractive change was achieved. The initial driver for the work on this one piece bifocal had been a desire to reduce the amount of *with the rule* astigmatism induced by the fitting of flat lenses.

It was assumed that the benefit of this steeper secondary curve was to ease the migration of the central corneal epithelium. As the small central zone was flattened, it was claimed that there was thickening of the mid peripheral cornea. The increased clearance created by the reverse curve acted to facilitate this thickening. The secondary action of the reverse curve was to improve the centration of the lens. Phillips (1995) comments, that this second steeper curve created a negative pressure on the corneal surface which further facilitated the epithelial migration. Epithelial migration will be discussed in Section 1.4 looking at the effect of orthokeratology on corneal thickness.

Wlodyga, an optometrist and Stoyan, from the contact lens manufacturer Contex Laboratories, produced a set of reverse geometry orthokeratology lenses known as the “OK series”. They used the term “Accelerated Orthokeratology” to describe their method of lens fitting. Wlodyga and Bryla (Wlodyga, 1989) in their work with the “Ortho–K 60” series of orthokeratology lenses used a reverse geometry principle. Initial evaluation of the patient involved a comparison of the central keratometry readings with the temporal keratometry reading. The temporal keratometry readings were obtained by asking the patient to fixate nasally on the keratometer. If the temporal readings were flatter than the central then this was taken as an indicator of a successful outcome. This flattening of the temporal cornea, with respect to the central area, confirms the presence of corneal asphericity. Each patient required three or four pairs of lenses with each pair being one dioptre (0.2mm) flatter than the current flattest K. Their wearing schedule involved wearing the first lens for up to two days, the second flatter lens from

two days to a week, the third flatter lens from one to three weeks and the fourth flatter lens from three to six weeks. After six weeks retainer lenses were dispensed which the subject continued to wear until they achieved a consistent 20/20 acuity throughout the day. At this point the subject would begin to reduce the amount of time they wore their retainer lenses. Wlodyga and Stoyan suggested that the best practise was to wear the lens for four hours in the morning, then remove the lens for four hours and then put the lens back in. In this way the process of corneal moulding occurred in approximately 42 days and not 365 days as previously found by Jessen (1962), Grant and May (1970), Kerns (1978) and Binder (1980).

By 1989 overnight wear of orthokeratology lenses had begun. *(*See section 1.3*)* Wlogdya and Bryla (1989) advised against overnight wear of their particular lens design because of the risk of debris entrapment beneath the lens. They felt that overnight lens wear would interfere with the normal sloughing of the epithelium. Subjects who did follow the sleep mode wore lenses for 36 hours and then had 12 hours off i.e. lenses were only worn on alternate nights. They claimed that the Ortho-K 60 lens had the potential to reduce even greater amounts of myopia than previous lens designs. In this particular study their best case achieved a reduction in myopia of 4.00D. They put forward a formula to estimate the amount of myopia reduction possible for any individual.

In this they stated:

$$\text{Estimate of myopia reduction} = (CK - TK) \times 2$$

Where CK = central keratometry reading TK = temporal keratometry reading

The use of the difference between the central and temporal keratometry readings, as a predictor of myopia reduction, confirms the suggestion that corneal asphericity is a determining factor in the success of orthokeratology. As mentioned earlier temporal K readings are achieved by asking the patient to fixate nasally rather than centrally at the keratometer. Since it is difficult to control the patient's fixation and therefore the

accuracy of the temporal K readings it is difficult to see how these measurements could offer any significant information to a practitioner of orthokeratology. They also state that there will be an accompanying 1.00D reduction in axial length which will add to the overall myopic reduction. The study offered no evidence to support their claim of axial length reduction. Coon (1984) found no change in axial length amongst subjects undergoing orthokeratology in his two year study.

Winkler and Kame (1995) recommend that the upper limit of myopia correction with reverse geometry lenses is 3.00 dioptres if a resulting unaided vision of 20/20 is required. Having evaluated their subjects they ordered a series of reverse geometry lenses. The first lens being ordered 1.50 dioptres flatter than the initial k reading. Each subsequent lens was 0.50 dioptres flatter than the previous. The decision on when to change to the next lens was made on the basis of a positive over refraction or a change to an alignment fluorescein fit from a flat fit. Patients were evaluated every one to two days but no set pattern for lens change was established. Having achieved the desired refractive change a retainer lens was prescribed. These retainer lenses were either of a reverse geometry design or a conventional RGP design fitted to the new K reading. In many cases the subject's final reverse geometry lens was used as the retainer lens. The number of hours in the day the patient needed to wear these lenses in order to achieve 20/20 vision all day varied from individual to individual. Since the early reverse geometry lenses had small optic zone diameters 6.0 - 6.5mm some individuals found that this led to ghosting of the image despite a successful reduction in myopia. In these individuals, it was suggested that fitting a retainer lens with a conventional back surface design would allow a larger BOZD to be used and that this could minimise the residual "ghosting".

1.3 Overnight Wear of Lenses

Regular overnight wear of lenses began in the 1990's although as mentioned earlier Wlogdya and Bryla (1989) had commented on sleep mode lenses. Paragon Vision Sciences (Mesa AZ) were the first company to receive FDA approval for the use of their orthokeratology lens for overnight wear in 2002. Overnight wear could really only proceed once high DK materials such as Boston XO (permeability 100Dk) became available.

Walline, Rah and Jones (2004) reported on the Children's Overnight Orthokeratology Investigation (COOKI) pilot study in which 29, eight to 11 year olds had been fitted with orthokeratology lenses, 23 of whom were followed for a period of six months. This initial study was intended to evaluate the degree of refractive error that could be dealt with and the safety of carrying out this procedure in children. Participants were limited to refractive errors between -0.75 and -5.00DS. Astigmatic corrections were limited to -2.00 DC if *with the rule* astigmatism (within 20 degrees of the horizontal) for all other axes a limit of -1.00DC was applied. The mean refractive error at the baseline visit was -2.44 +/- 1.38D and by the six month visit it was -0.16 +/- 0.66D. Contrary to previous studies no significant increase in astigmatism was found.

Of the original group of 29, two subjects achieved unacceptable lens fitting. A further assessment of these two children showed that they had flat corneas (41.50 and 39.50D) which it was not possible to manipulate further in order to achieve the required level of myopia reduction. The remaining children achieved acceptable levels of unaided acuity within one week of commencement of lens wear. On average they required two weeks of wear to achieve sustainable levels of acuity i.e. all day without requiring refractive correction. No child suffered any significant adverse effects during the study. 60% of the children were found to have mild punctate staining of the cornea at their aftercare visits.

1.4 Corneal Changes associated with Orthokeratology

Erickson and Thorn (1977) had hypothesised that changes in corneal thickness may be a factor in the mismatch between the change in refraction and keratometry. In this section research into the effects of orthokeratology on corneal thickness, corneal sag and the cornea's anterior and posterior radii will be discussed.

Binder et al (1980) and Polse et al (1983b) found no significant change in corneal thickness between treatment and control groups. Coon (1984) in his study found that there was a statistically significant difference in central corneal thickness between the control and treatment groups at the end of the two year study. Both groups showed peripheral corneal thickening over the study period. The control group showed an equivalent thickening in the central cornea whilst the treatment group showed central corneal thinning.

Swarbrick, Wong and O'Leary (1998) followed six subjects during 28 days of "accelerated" orthokeratology lens wear. The individuals involved wore the Contex design of lens as advocated by Wlogdya and Bryla; they were not involved in overnight wear of the lenses. Full corneal thickness and corneal epithelial thickness were measured, using a modified optical pachometer, at eight positions along the horizontal meridian (8.25 mm diameter) at each visit. These measurements were compared with the baseline data acquired on two separate occasions prior to the commencement of the study. They found that there was statistically significant mid peripheral thickening of the cornea by day 14. The central corneal thinning did not reach statistical significance during the study but the corneal epithelium did show statistically significant thinning by day 28. The epithelial thinning followed a linear progression such that the corneal epithelium reduced in thickness by almost 10% over the 28 days of the study.

Swarbrick et al express concerns about the safety issues associated with the corneal thinning. They offer a number of possible explanations for the corneal thinning suggesting that compression or loss of cell layers could account for the change. At the time of this study only one adverse incident associated with orthokeratology had been

reported. All of the individuals involved with the study showed a reduction in myopia (mean change 1.71 +/- 0.59D). In contrast to the changes in corneal thickness the most significant change in refractive error occurred in day one. Both the central corneal topography (5-6mm diameter) and the corneal curvature also showed statistically significant changes at this time.

In a later study, Alharbi and Swarbrick (2003) evaluated the effects of overnight wear of orthokeratology lenses. They again reached the conclusion that the cornea undergoes central thinning and midperipheral thickening in response to the wearing of an orthokeratology lens. In this study they also found that 70% of the changes in corneal thickness occurred in the first ten days of wear indicating a rapid corneal response to this modality of lens wear. Choo, Caroline and Harlin (2008) questioned how the cornea changed under orthokeratology lenses. They suggest that the lamellar structure of the stroma would make it resistant to rapid remodelling. They also dismiss the suggestion that epithelial cell redistribution is the basis of the refractive change seen in orthokeratology. They point out that since the epithelial cells are intimately linked together e.g. desmosomes, orthokeratology would need to induce a breakdown in these junctions to allow cell movement. They postulate that the epithelial thinning noted by Swarbrick et al (1998) may occur as a result of intracellular fluid transfer from the central to the mid peripheral epithelial cells. The group also put forward two hypotheses for the midperipheral changes. They suggest that the pressure of the lens on the cornea may induce cellular mitosis. Alternatively the combination of the lens and closed eyelid may reduce the overnight sloughing of epithelial cells. Finally they speculate that the short term effects of the interaction between the lens and corneal epithelium may induce long term stromal changes. Choo et al (2008) suggest that further work is needed to ascertain which if any of these mechanisms account for the corneal changes seen in orthokeratology.

Swarbrick et al (1998) and Alharbi and Swarbrick (2003) also compared the measured changes in corneal sag with the predicted change required to account for the refractive

error change seen using the Munnerlyn formula[1]. In both studies their conclusions were that the change in corneal sag amongst the subjects (based on thickness change) corresponded with the ablation depth calculated from the Munnerlyn formula and therefore accounted for the change in refractive error. Swarbrick et al (1998) concluded that the posterior surface of the cornea is therefore not involved in orthokeratology. They based this conclusion on the fact that laser ablation involves only the anterior surface. Alharbi and Swarbrick (2003) further concluded that the close relationship between their measured thickness changes and the Munnerlyn formula results indicated that the refractive changes seen in orthokeratology occur only as a result of corneal thinning. They suggest therefore that the "bending" or "moulding "of the corneal tissue which had been postulated by earlier researchers did not occur.

In comparison, Fan et al (1999) looked at corneal thickness changes in 54 subjects undergoing overnight orthokeratology and found no statistically significant difference even after six months of wear. They also evaluated the endothelial cell count and found this to be unchanged despite six months of overnight wear. They did agree with the Swarbrick (1998) study in that they felt that the first two weeks were the most critical in terms of refractive error change.

Garner and Owens (2004) questioned the use of the Munnerlyn formula for both the calculation of ablation depth and the change in refractive error seen in orthokeratology for a given change in corneal thickness. Their concerns centred on the use of a formula which is based on spherical surfaces when the cornea is an elliptical surface and the assumption, in the case of the Swarbrick (1998) study, that the posterior surface is not involved in the refractive change seen in orthokeratology. They found that if the Munnerlyn formula was used, assuming that the corneal sag changed but the asphericity (p-value) remained constant, the formula overestimated the refractive change. The degree of overestimation increased as the p-value increased. In a second

[1] The Munnerlyn formula $t = -S^2 * D/8(n-1)$ is used to determine ablation depth (µm) in refractive surgery, where t is ablation depth; S is ablation diameter and D the desired refractive change. Assuming that n = 1.377 simplifies the integer to 3.

situation, which follows more closely the accepted effect of orthokeratology, they assumed that both corneal curvature and p-value changed. In this case the formula underestimated the refractive change by -0.34 dioptres. MacKenzie (2008) and Shah, Edgar, Rabbetts, Harle et al (2009) found that the reproducibility of subjective refractive results could differ by up to +/- 0.75 dioptres. In this case, without a very accurate measurement of refractive error change in orthokeratology, it cannot be assumed that the posterior corneal surface is not involved.

Owens, Garner, Craig and Gamble (2004) examined the change in the posterior corneal radius of curvature associated with orthokeratology in 19 myopic subjects (-1.00 to -4.00D).They used the Purkinje image method described by Royston, Dunne and Barnes (1990) to calculate the posterior corneal radius of curvature. The method employed by Royston et al is described in chapter five. Owens and Garner found that the posterior surface underwent statistically significant flattening between one night and one week of overnight lens wear. This change occurred both centrally and mid – peripherally (2.5mm from pupil centre). After one week the posterior surface flattening began to return towards the baseline value. They point out that although the contribution of any change in the posterior corneal surface to the overall refractive change is very small, it requires consideration.

Soni and Nguyen (2002) examined the change in both anterior and posterior corneal curvature and corneal thickness in nineteen eyes fitted with orthokeratology lenses. They found that after 60 minutes of wear the anterior corneal curvature had undergone changes which were statistically significant. These changes included flattening of the central corneal curvature (up to 1.5mm from the centre) and steepening of the peripheral cornea (beyond 2.5mm from the centre). In the area between 1.5 and 2.5mm from the cornea no change was seen between pre and post lens wear. They found that there was no statistically significant change in the posterior corneal curvature. The corneal thickness showed no change other than a tendency for the nasal cornea to thicken slightly between 1.5 – 3mm from the centre.

Tsukiyama, Shiro, Masahiko, Yoshikazu et al (2008) examined the changes in anterior and posterior corneal curvatures in nine individuals undergoing orthokeratology. They found that whilst the anterior corneal curvature underwent statistically significant changes at no point in the 53 weeks of the study was any significant change seen in the posterior corneal curvature. Both Soni and Nguyen (2002) and Tsukiyama et al (2008) found that the change in refractive error seen correlated with the change in anterior corneal curvature. In contrast to both of these findings Owens et al (2004) found significant flattening of the posterior corneal radii of their nineteen subjects after the first week of lens wear.

In a recent report Reinstein, Gobbe, Archer, Couch, et al (2009) evaluated corneal thickness changes in one subject. Using high frequency ultrasound they were able to measure changes in both the corneal epithelium and the stroma of this individual. They found that thinning occurred in the central epithelium with an annular thickening in the mid periphery. The stroma was seen to thicken centrally with some mid peripheral thinning. Whilst this report appears to support the findings of Swarbrick et al (1998) the use of only one subject means that its evidence can only be seen as anecdotal.

1.5 Predicting success with Orthokeratology

Carkeet, Mountford and Carney (1995) attempted to define a way of predicting success with orthokeratology lenses. This group carried out a retrospective analysis of a group of nine OK subjects to look at characteristics which could potentially influence the success of orthokeratology. Their analyses included:

- Initial refractive error
- Central corneal thickness
- Corneal thickness profile i.e. thickness measured at various known intervals across the cornea. Analysis of this data by plotting the chord diameter against

thickness measures and then fitting a parabolic function to the data ($y = a + bx^2$) where b now describes the rate of change of thickness for the cornea.

- Axial length, vitreous chamber depth, anterior chamber depth, lens thickness
- Corneal epithelial fragility threshold – using the Millodot method i.e. the point at which an aesthesiometer will just produce staining on the cornea. This was checked both centrally and peripherally.
- Ocular rigidity - using Schiotz tonometer and Friedenwald nomograms best fit at weights of 5.5gm, 7.5gm and 10gm.

The orthokeratology groups were identified as:

Poor responders	< -0.75D change in 6 hours wear
Moderate responders	-0.75 – -1.50D in 6 hours wear
Good responders	> -1.50D in 6 hours wear

Poor responders were found to have the highest initial value of myopia (mean SE -6.13 +/- 0.53D). They concluded that none of the other measured characteristics were useful in predicting the outcome of orthokeratology.

Joe, Marsden and Edrington (1996) in a further attempt to look at the possibility of predicting success carried out a study to see if it was possible to establish a direct relationship between corneal asphericity and the improvement in visual acuity found in orthokeratology. Since the majority of patients would consider the achievement of an unaided vision of 6/6 as a successful outcome, a method which allowed the prediction of this outcome, ahead of lens fitting, would be very useful. It would also avoid the issues of commencing treatment in individuals with little chance of success.

In order to assess the relationship they recruited 15 subjects of whom 11 completed the trial. Subjects on this trial were not involved in the overnight wear of lenses but built up to a minimum of eight hours wear per day. As with other studies the subject was supplied with a new pair of flatter lenses (base curve 0.50 dioptres flatter) when the

current pair had become tight and showed no movement on examination. Once a subject showed no change in refraction on three consecutive visits then the lens which was currently being worn was supplied as the retainer lens. For subjects who displayed a +1.00D subjective refraction then the lens being worn at this time became the retainer lens for the remainder of the study. Once the subject completed the study they were supplied with a retainer lens which gave an over refraction at or near to Plano.

Analysis of the results showed that initial corneal asphericity could not be used as a predictor of success in orthokeratology. In fact the only parameter which showed any correlation was between the initial vision and final visual acuity and IOP, although not at a level which could be considered statistically significant. Ironically in this paper they point out that at this time orthokeratology is more an art than a science.

1.6 A Mathematical Model of the Cornea

In the schematic eye, the cornea is often constructed as a simple sphere or sphere/cylinder. In the latter case each of the two principal meridians, positioned at 90^0 to each other, would have a broadly spherical profile. Mandell and St Helen (1971) showed that the prolate ellipse was actually a more acceptable profile for the cornea. They found that for a given apical radius only one spherical or one parabolic measurement were available however between these two measures an infinite number of ellipses could occur. They suggest that the hyperbola would not be a good descriptor of the corneal shape as the eccentricity is too high. Mandell and St Helen also considered a number of sigmoid curves of a given apical radius. In this case they found that all the curves flattened more rapidly than the parabola which made them unsuitable as models of the corneal shape. They conceded that the ellipse was not a perfect analogy for the corneal shape and suggested that more complex curves which are a more accurate fit may be found. However for calculations involving the central cornea they concluded that the ellipse was an adequate representation of the cornea.

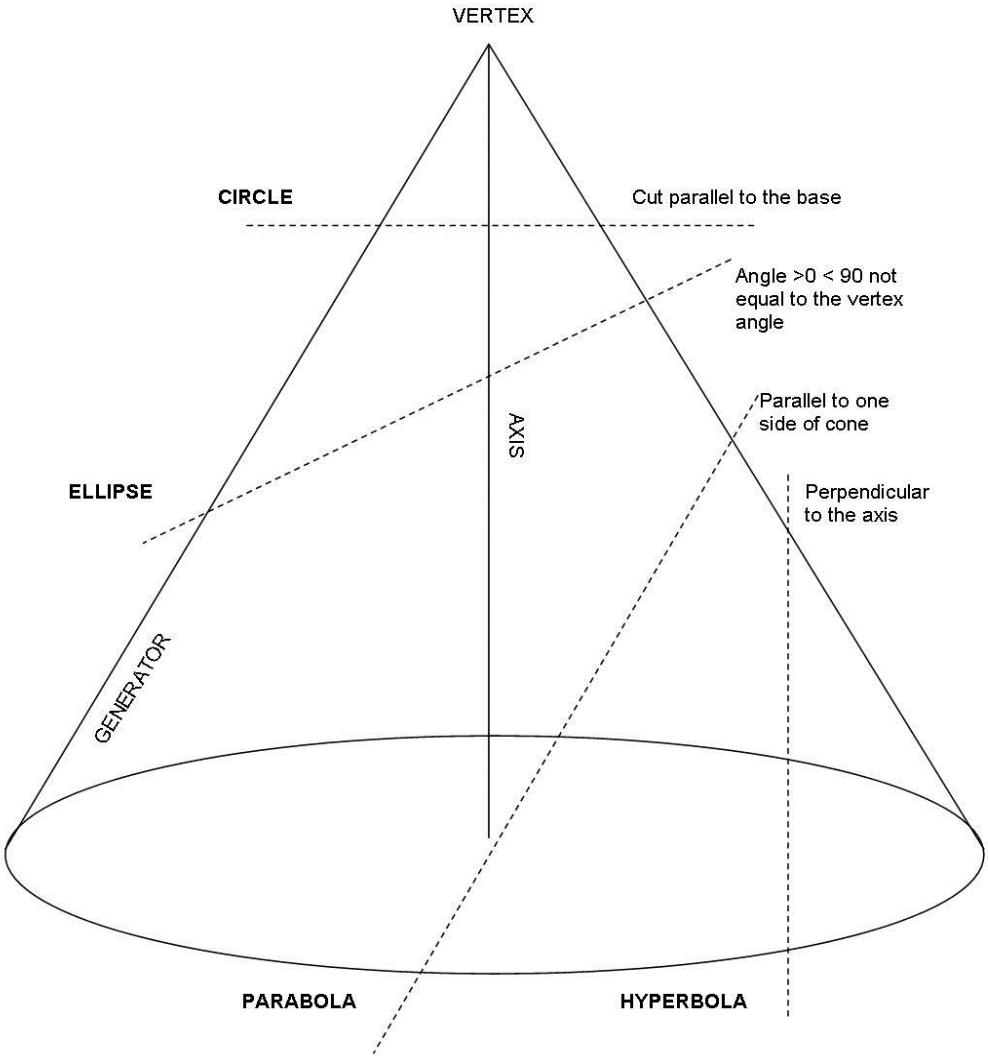


Fig 1.1 Conic section generation

The axis (Fig 1.1) is the central line about which the cone is symmetrical. The generator (Fig 1.1) is the line which when rotated will sweep out a cone. The vertex is the angle between the axis and the generator.

The ellipse is a conic section i.e. it is generated by making an oblique cut through a circular cone, as shown above Fig 1.1. All ellipses have a major and a minor axis as shown in Fig 1.2.

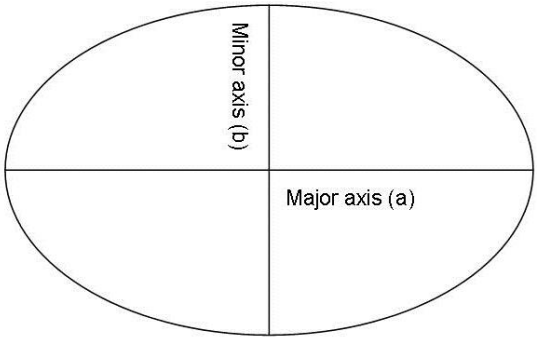


Fig 1.2 Major and minor axes of the ellipse generated by the rotation of the conic section shown in Fig 1.1

If the ellipse is rotated about its axis of symmetry it will produce an ellipsoid which is a more true description of the corneal surface. A rotation about the minor axis would produce a prolate ellipsoid whilst rotation about the major axis would produce an oblate.

In order to evaluate the interaction between a contact lens and the cornea it is necessary to be able to describe the corneal surface profile. The radius of curvature, as measured by the keratometer, gives only a measurement of the apex of the cornea along its two principal meridians. Since the cornea is a prolate ellipsoid, information about the apex gives no indication of the rate of flattening.

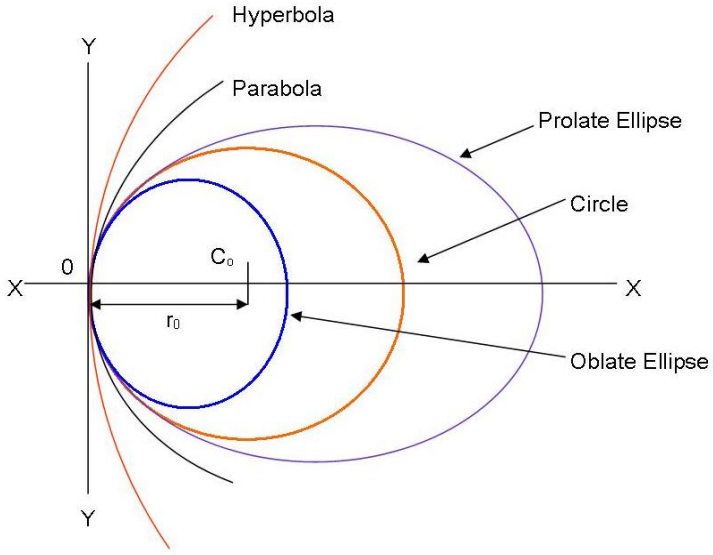


Fig 1.3 Conic sections with same apical radius (r_0) (Courtesy of WAD)

The conic sections shown above (Fig 1.3) all have the same apical radius (r_0) but the rate of flattening or steepening is different in all cases.

Baker (1943) suggested an equation which could be used to describe all conic sections

$$y^2 = 2r_0x - px^2$$

r_0 is the apical radius

x is the sagitta for the semi chord y

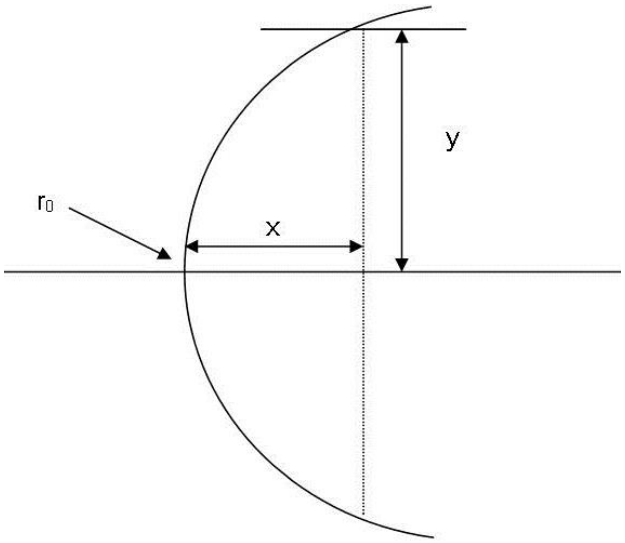


Fig 1.4 The relationship between r_0 and sag for a given chord diameter of y.

Using the Baker equation we find that

$$p = (2r_0 x - y^2) / x^2$$

The value of p can then be used to describe the rate of flattening or steepening of the conic section i.e. p indicates the degree of asphericity of a surface. *p* has also been called the *shape factor*. The term *shape factor* is usually applied to thick lens theory to indicate the magnification produced by a lens. For this reason it is more appropriate to use the term p-value as a measure of asphericity.

The p-values for the conic sections shown in Fig 1.3 are:

Hyperbola	$p < 0$
Parabola	$p = 0$
Prolate Ellipse	$0 < p < 1$
Circle	$p = 1$
Oblate Ellipse	$p > 1$

A number of other terms have been used to describe the asphericity of the cornea these are eccentricity (e), shape factor (e^2) and asphericity (Q).

1.6.1 Eccentricity (e)

A conicoid can also be described in terms of its eccentricity (e). Fig 1.5 shows a point B which is a perpendicular distance AB from a fixed directrix and distance BF from a fixed focus. If the relationship between the distance AB and BF has a constant ratio such that;

$$BF = eAB$$

Then all points of B that satisfy this equation will lie on a curve.

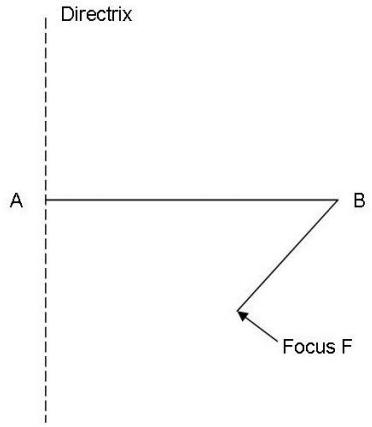


Fig 1.5 Generation of eccentricity (e) from a fixed directrix and focus point F

In this case the values of e will be

Ellipse	0 < e < 1
Circle	e = 1
Hyperbola	e > 1

Whilst eccentricity (e) is an appropriate descriptor of a conic section; Bennett (1969) (quoted in Douthwaite 2006) felt that this term was unsatisfactory. He felt that it was difficult to perceive the effect of a change in eccentricity on the change in the shape of the ellipsoid.

1.6.2 Shape factor (e^2)

Townsley (1970) spoke about the shape factor which he termed e^2.

In Fig 1.2 the major and minor axes of the ellipse are shown. If the major axis is defined as length (*a*) and the minor axis as length (*b)* then the shape factor (e^2) can be defined as;

$$e^2 = 1 - b^2/a^2$$

For a prolate ellipse i.e. an ellipse generated by rotation around the minor axis b < a; e^2 will be a positive value (Lindsay, Smith and Atchison 1998)

Bennett (1969) (quoted in Douthwaite 2006) gave the expression

$$y^2 = 2r_0x - (1 - e^2)\, x^2$$

from this we find the relationship between p-value and e to be

$$p = 1 - e^2 \text{ or } \quad e = \sqrt{(1-p)}$$

If we consider an oblate ellipse i.e. one which is rotated about the major axis b > a; then e^2 will be negative. Townsley called this a mathematically improper term as negative values of e^2 are meaningless. It is not possible therefore to use the term e^2 to describe an oblate (steepening) ellipse.

1.6.3 Asphericity (Q)

Kiely, Smith and Carney (1982) showed the equation for a symmetrical conicoid as

$$x^2 + y^2 + (1+Q)\,Z^2 - 2ZR = 0$$

where:

R is the radius of the corneal apex

Z is the axis of revolution of the conicoid which corresponds to the optical axis of the cornea.

The value of Q then describes the asphericity of the conicoid.

Hyperbola	Q < -1
Parabola	Q = -1
Prolate Ellipse	-1 < Q < 0
Circle	Q = 0
Oblate Ellipse	Q > 0

The asphericity Q can also be related to the eccentricity (e^2) using the equation

$$Q = -e^2$$

The relationship between p and Q is

$$Q = p - 1$$

Mountford (1997) did suggest a predictive value for the degree of myopic change based on corneal asphericity (eccentricity).

where:

$$y = 0.21x$$

y is the eccentricity change and x is the refractive change

In this case Mountford suggests that an average corneal eccentricity of 0.5 would predict a change of ≈ -2.50 dioptres. The greater the eccentricity, the greater the degree of refractive change possible e.g. y = 0.6 refractive change ≈ -3.00 dioptres. These predictive values were based on measurements taken using the EyeSys videokeratoscope. Mountford found that the EyeSys was capable of measuring eccentricity for spherical corneas. He raised concerns about whether the machine was capable of analysing oblate corneas. Since eccentricity cannot be used to describe oblate surfaces the use of p value is more appropriate in this case. Both Kerns and Binder had previously suggested that orthokeratology will have achieved its maximum refractive error change when the cornea becomes spherical.

Mountford's study agreed with the earlier findings of Erickson (1977) that up to 0.75 dioptres of refractive change had been induced before a measurable change in keratometry occurred. He cautions commencing orthokeratology on individuals whose required refractive change is not reflected in their corneal asphericity as indicated earlier. Guillon, Lydon, Wilson (1986) deduced that the average p-value is 0.85 +/- 0.18. Using the equation

$$\text{p value} = 1 - e^2$$

The average corneal eccentricity is therefore 0.39. This suggests that the majority of individuals who are suitable for orthokeratology would have refractive errors between -0.75D and -2.00D. Guillon et al corrected the data produced by Kiely et al (1982) to give a p value from the Q value (p = 1 + Q). This produced a mean p value of 0.74 +/- 0.18. Douthwaite, Hough, Edwards and Notay (1999) found an average apical radius of 7.93mm and p value of 0.76 in the horizontal meridian in their EyeSys study. These two studies gave a value for eccentricity of 0.51 and 0.49 respectively which is in agreement with Mountford. Douthwaite (2003) reanalysed the data from the earlier study (Douthwaite et al 1999) to look at the effect of corneal tilt i.e. the angle between the corneal apex and the videokeratoscope axis. Corneal tilt has the potential to affect

the measurement of corneal asphericity. Douthwaite (2003) found that corneal tilt was unrelated to either apical radius or asphericity.

Fan et al (1999) dispute the relationship between asphericity and refractive error. In their study of 54 adolescent myopes they found that there was no relationship between the two factors. Liubinas and de Jong (1998) in a series of case reports evaluated the change in corneal asphericity at a number of points in a year long study. They found that initial changes in asphericity did correlate with the change in refractive error i.e. a 0.21 change in asphericity, as reported by Mountford (1997), corresponded to a 1.00 dioptre change in refractive error. Once individuals had achieved near emmetropia and began to wear lenses on every second or third night then the asphericity returned towards its prefitting value and yet the refractive error reduction remained. This study reported on only two individuals and as such has limited statistical value. Liubinas and de Jong (1998) suggest that because of the change in asphericity then there must be another underlying factor at work in the longstanding change in refractive error seen in orthokeratology.

1. 7 Axial edge lift in contact lens design

Axial edge lift (AEL) is defined as the distance, measured parallel to the lens axis (ab), between a point on the back surface of a lens at a specified diameter (cd) and the continuation of the back central zone (dashed line e-f and g-h) (Fig 1.6). Early contact lens design research showed that conventional rigid lens fitting was improved by using lenses with a constant axial edge lift. The selection of the appropriate peripheral curves avoided the problem of excessive edge clearance on steep corneas or inadequate clearance on flat corneas. The axial edge lift of a lens may be calculated by calculating the individual sag measurements which contribute to the overall sag of the lens (os).

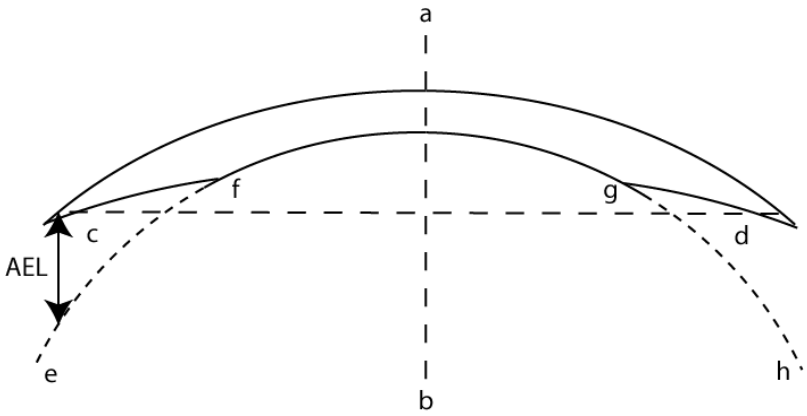


Fig 1.6 Axial edge lift shown for a bicurve lens

The sag equation shown below;

$$s = r - \sqrt{(r^2 - y^2)}$$

where r = surface radius

y = semi meridian

allows these individual measurements to be calculated by substituting into the equation the respective radii and diameters from the lens parameters. The overall sag (os) for the bicurve lens shown in Fig 1.6 is (s1 + s2 – s3). Sag s1 is calculated for the back optic zone radius (BOZR) and the back optic zone diameter (BOZD), sag s2 is calculated for the back peripheral radius (BPR) and the lens total diameter (TD) and sag s3 is calculated for the BPR and the BOZD. The overall sag (os) is then deducted from the sag (s0) where s0 is calculated for the BOZR and the TD. The values for BOZR, BOZD, BPR and TD are obtained from the lens specification.

For the lens in Fig 1.6

$$AEL = s0 - (s1 + s2 – s3)$$

The peripheral curve radii may be selected so that the axial edge lift is a constant. The value for axial edge lift is usually between 0.09 to 0.15mm. Calculation of the AEL for an orthokeratology lens may be calculated in the same manner. For lenses with more peripheral curves their contribution to the overall sag must be incorporated. Douthwaite (2006) provides a useful tool to assist in this. He states that after s1 all even sags are added and all odd sags are subtracted to calculate the final overall sag.

1.8 Retention and Regression

Polse et al (1983a) looked at the rate at which patients regressed to their original refractive error. 80 subjects commenced the study with 40 in a treatment group and 40 in the control group. 56 subjects completed the study. They found that three subjects retained a spherical equivalent change of -0.75 dioptres at the end of the regression phase of on average 26.4 days with the remaining 53 subjects showing retention in the region of ≤ 0.60 dioptres. This included the control group subjects who had had RGP lenses fitted to normal conventions.

Mountford (1998) looked at retention and regression in subjects who had undergone accelerated orthokeratology as distinct from Polse (1983a) who looked at regression following an earlier method of orthokeratology fitting i.e. the use of increasingly flatter lenses for daytime wear. Mountford found the majority of the reduction in the manifest refraction occurred in the first 30 days of lens wear. The first seven days of lens wear induced the greatest degree of change. The persistence of the change through the day increased with the duration of lens wear up to 90 days of lens wear. They found no statistically significant relationship between the degree of refractive change and the rate of regression.

Both Mountford and Polse felt that the regression rate in the corneal moulding was due to the cornea's inherent elastic properties. Any variation in the measured rate of regression is therefore simply a factor of individual differences in the visco-elasticity of the cornea. Sjontoft quoted in (Mountford 1998) used the term relaxation to describe the inherent corneal memory which returns the cornea to its natural shape after a period of moulding. This change mimics that seen in the cornea following a period of orthokeratology lens wear; therefore regression and relaxation are synonymous. Sjontoft also wrote about creep to indicate the continued change in corneal shape which follows the cessation of any period of moulding. This is seen as a continuation of the flattening in the cornea following lens removal. This may manifest as a further decrease in myopia after lens removal. Mountford found increased corneal flattening or

creep in 20% of his subjects at seven days of wear. This had reduced to only 8% by the 30 day visit, and at the 90 day evaluation only 2% continued to show creep over time.

Sridharan and Swarbrick (2003) looked at the short term response of the cornea to the wearing of orthokeratology lenses. They found that, even after only 10 minutes of daily lens wear, change had occurred in uncorrected visual acuity, apical corneal power, keratometry readings both horizontal and vertical, corneal toricity and asphericity. The magnitude and duration of the response improved with the length of time the lenses were worn with the maximum response being seen after eight hours of overnight wear. All of the other measurements involved daily lens wear. Corneal thickness measurements are not available for this study. They suggest that in light of their earlier study (Swarbrick et al 1998) the corneal epithelium and stroma are capable of rapid response to the forces induced by the reverse geometry lenses. The biomechanical responses seen in orthokeratology are discussed later.

Sridharan and Swarbrick (2003) further suggest that the assumption that the cornea is simply moulded by the lens back surface is incorrect. They found that the refractive error correction obtained after only 10 minutes of lens wear persisted for more than an hour. They conclude that this retention of effect indicates that a mechanism other than moulding is present. This is in line with comments made by Choo et al (2008) about the underlying mechanisms of the short term response to orthokeratology.

Lu, Fonn, Simpson and Sorbara (2008) in their study of the malleability of the ocular surface in response to orthokeratology, support the findings of Sridharan and Swarbrick (2003). The study involved twenty myopes who had one eye fitted with an orthokeratology lens whilst the other eye was used as a control. Corneal thickness and corneal epithelial thickness were then measured after 15, 30 and 60 minutes of wear. Lu et al (2008) found that the central corneal epithelium underwent significant thinning after only 15 minutes of lens wear. The mid-peripheral corneal epithelium increased in thickness over the corresponding time frame. No statistically significant change was

seen in the control eyes. A comparison of the corneal thickness at 60 minutes between the treated eyes and the control eyes showed no statistically significant difference in the thickness.

Swarbrick and Lum (2006) examined the influence of Dk/t on the orthokeratology responses and found that the higher the Dk/t the greater the clinical response. Low Dk/t lenses were also associated, as would be expected, with greater central corneal oedema after one night of wear. Whilst this initial oedema response reduced during the two week period of the trial the low Dk lens still showed a greater oedema response. It may be that the increased corneal oedema acts against the corneal thinning which Swarbrick et al (1998 & 2003) suggest is the main factor in the refractive changes seen in orthokeratology.

1.9 Corneal Biomechanics and Mechanisms of Orthokeratology

Mountford (2004) suggests that the forces involved in the corneal response to orthokeratology occur either as a result of lid action or fluid forces produced by the tear film/ lid interaction. Several researchers have looked at the effect of lid action on the cornea. Lydon and Tait (1988) looked at the corneal response to lid action, without the presence of a contact lens, and found that the force was insufficient to disrupt the normal corneal surface. Mountford states that the addition of a rigid contact lens to the eye increases the lid tension and therefore the force applied to the cornea. By applying the equation proposed by Lydon and Tait, Mountford suggests that the lid/lens combination creates a force which is sufficient to displace the globe by 0.25mm. Since this lid pressure requires a blink response and the majority of orthokeratologists now use overnight wear of lenses, when the blink response is absent, it could be assumed that lid pressure has little influence on the corneal response to orthokeratology. The lens insulates the cornea from the lids response.

Tahhan, Sarfraz, Raad, Raad, et al (2003) looked specifically at the interrelationship between the lens and the eyelid in 26 subjects fitted with orthokeratology lenses. The

subjects first wore the lens in an open eye situation and the lens centration and refractive effect were evaluated using topography and refraction data. After a week of no lens wear the subjects wore the lens for an hour with their eye closed and the measurements were repeated. They found that both lens centration and refractive change were unaffected by the eyelid position. They concluded that

i. Lens centration in the open eye could be assumed to match the lens centration in the closed eye.
ii. There was no relationship between lid tension and myopia reduction.

In contrast to Mountford they suggest that lid forces play little part in the process of corneal change in orthokeratology.

If the lid has little influence on the action of the orthokeratology lenses then the tear film/ lens interaction becomes more significant. A number of researchers (Allaire & Flack (1980); Hayashi & Fatt (1980); Conway (1982)) have examined the pressure profile of the precorneal tear film beneath a contact lens. They conclude that the pressure profile is created by the interaction between the minimum and maximum tear thicknesses. The pressure induced by the lid/tear film interaction will be reduced in the closed eye environment since the pressure forces rely on the blink action.

Alharbi, La Hood and Swarbrick (2005) found that the overnight wear of orthokeratology lenses inhibited the stromal oedema response. They found that the predicted levels of corneal oedema, based on Dk/t, only occurred in the mid periphery and the periphery in the orthokeratology group. The control group who wore conventional RGP lenses overnight showed expected levels of oedema both centrally and peripherally. The expected levels of oedema were calculated using the Holden-Mertz formula[2]; this revealed an expected overnight swelling of 6.7% for the conventional lenses and 7.5% for the orthokeratology lenses. The findings were in the conventional contact lens wearers central corneal oedema was 6.2% whilst in the orthokeratology lenses central corneal oedema was 1.2%. They hypothesised that the

[2] The Holden Mertz formula was originally derived from measurements of the corneal oedema responses to the overnight wear of hydrogel lenses. The approximation works for all lens materials.

positive pressure exerted by the lens on the cornea acted as a clamp preventing the predicted stromal swelling. They also suggest that this positive pressure may be further enhanced by the effect of the intraocular pressure. Whilst the lens/IOP combination may clamp the anterior surface it would have no effect on the posterior surface.

Recent concerns about the interaction between corneal thickness and intraocular pressure measurements have led to the development of instruments to measure the corneal resistance. If the cornea resists deformation by contact tonometry, might it also resist moulding by orthokeratology lenses? Gonzalez-Meijome, Villar-Collar, Queiros, Jorge Jorge et al (2008) conducted a pilot study on the corneal biomechanical properties which may influence orthokeratology responses. Using the Ocular Response Analyser (Reichert) they measured the corneal hysteresis (CH) i.e. the ability of the cornea to absorb energy, and the corneal resistance factor (CRF), a measure of the cornea's elastic properties. They found that corneas with a lower CH, i.e. less able to absorb energy, and a lower CRF, i.e. less elastic, showed a more rapid response to orthokeratology. Corneas with these properties also had a more rapid return to normal. Corneal thickness was significantly correlated with CH for the onset phase of orthokeratology but not the recovery phase. No correlation was found with CRF in either phase. In their pilot study Chen, Lam and Cho (2009) found that the CRF was significantly reduced by the overnight wear of orthokeratology lenses whilst the CH was unaffected. Chen et al only evaluated change in the CRF after one night of lens wear. If the reduction in CRF by the overnight wear of OK lenses is another factor to be considered in our understanding of the mechanisms of orthokeratology; a longer study is required. Mountford (1998) indicated that the corneal changes are stable by one month of overnight wear; an investigation of the change in CRF and CH over this timescale would be useful.

Mountford (2004) produced a series of theoretical models for the forces acting under reverse geometry lenses. Using an engineering model developed to examine the stresses experienced by structures in order to improve their design, he suggested that

the compressive forces below the lens would continue to act until a state of equilibrium was reached. This equilibrium would occur when the cornea becomes spherical beneath the lens. He also used this model to explain both “smiley face” (Flat lens) and “central island” (Steep lens) topographies in poorly fitting reverse geometry lenses. Whilst this model appears to explain the corneal change it remains hypothetical. Mountford also looked at the effect of hydrostatic forces on the cornea to see if they can explain the changes seen in orthokeratology. In this model it is assumed that the lens remains static on the eye. The lens and tear film interaction acts to create a form of vacuum. The vacuum action will then mould the cornea to the curvature of the back surface of the lens.

1.10 Comparative lens design studies in Orthokeratology

Tahhan, Du Toit, Papas, Chung et al (2003) compared four reverse geometry design lenses for overnight wear. Each of the lenses was a commercially available design at that time. The sixty subjects had one eye fitted with the same lens (R & R; Danker laboratories, Sarasota, Fl.). This lens may be either a quatracurve or pentacurve lens whose fitting curves are based on i) the degree of myopia reduction required plus an additional -0.75DS to allow for regression and the eccentricity of the cornea. The choice of eye was randomly assigned and masked from the subject. The group was then divided into three subgroups (20 each). Each subgroup had their second eye fitted with either a Contex D Series 4 Zone lens (Contex, Sherman Oaks, CA.), or a Dreimlens (Dreimlens, Melbourne, Florida) or a Mountford BE lens (BE; Ultravision Capricornia, QLD, Australia). Subjects were again masked from the lens design.

The Contex D Series 4 Zone lens is a quatracurve lens with an aspheric periphery whose back surface design is based on the subject’s central keratometry reading and their corneal eccentricity.The Dreimlens is also a quatracurve lens whose back surface design is calculated using the central keratometry reading and the temporal

keratometry reading. This latter measure will give an indication of the corneal asphericity. The Mountford BE lens is a pentacurve lens which uses a customised computer program and a custom fitting set to produce the final lens design. The computer program requires the input of the central apical radius and eccentricity value (Mountford, Rushton, Dave 2004b). Due to commercial interests exact details of the lens designs are difficult to obtain. All the lenses were made in Boston XO material (Polymer Technology Corp Wilmington MA) with a nominal Dk/t of 100 x 10^{-11} cm^2/s). All the lenses were fitted according to the individual manufacturer's instructions. The unaided vision, best corrected visual acuity (BCVA), lens centration, corneal topography and a full slit lamp biomicroscopy examination were carried out at each visit (one night, one week and one month). The corneal topography measurements were used to evaluate the horizontal treatment zone for each of the lens types.

The group found no statistically significant difference in any of the lens types in their effect on unaided vision, subjective sphere or cylinder, corneal apical radius, horizontal centration of the treatment zone and BCVA at high and low contrast at high illumination (146 ± 8 cd/m^2) and low contrast BCVA at low illumination levels (3 ± 1 cd/m^2) at all visits. In the case of high contrast charts in low illumination at one month they found that the Contex lens produced a BCVA of one line poorer than the BE lens. The group also found that the BE lens produced a larger treatment zone at one month of wear when compared to that of the Contex or R&R lens. An evaluation of the subjects' visual quality (day and night vision, haloes and ghosting) and BCVA by the group found no correlation between these factors and the treatment zone size. The group concluded that the four lens types were effective in the reduction of manifest myopic refractive errors. They postulated that the design protocol for the BE lens may be the factor leading to the larger treatment zone for this lens.

In a later study Maldonado-Codina, Efron, Morgan and Hough (2005) compared the BE lens with an experimental design lens. The experimental lens was fitted empirically

whilst the BE lens was fitted using the trial set provided by the manufacturer. The experimental lens was essentially a pentacurve design. The central curve was based on the keratometry reading and the peripheral curves were calculated on the basis of a model eye with an eccentricity (e) of 0.45, since $p = 1 - e^2$ this would translate to a p value of 0.7975. The BOZR was calculated to correct the required degree of myopia plus -0.75D. This latter element which they called the Jessen factor was incorporated to allow for any regression during the day. Once fitted with the lenses subjects were followed for seven nights with assessments being made after one night and seven nights of lens wear. Measurements were made on two occasions during the day the first within one hour of waking and then five hours later. Subjects attended for the first appointment with the lenses in situ. Measurements made at these visits were keratometry, corneal topography, visual acuity, both unaided and best corrected and at high and low contrast. Each subject underwent a detailed slit lamp assessment at every visit to evaluate any physiological change. Subjects were also asked to score lens comfort at the morning visit and the quality of their unaided vision at both visits using a scale of 0 – 100. Nine subjects completed the seven days of the study. The group found that both lenses were effective in reducing myopia to within +/- 1.00D of the desired correction by seven nights. The BE lens did produce an over correction of up to +1.00D in three individuals. Despite these findings subjects gave equal scores to the quality of their unaided vision.

Both of these studies found that multicurve back surface reverse geometry lens designs were effective in the reduction of myopia (Tahhan et al 2003; Maldonado - Codina et al 2005). The refractive correction was achieved by seven days of lens wear with the major change in refractive error being achieved after one night. Maldonado – Codina et al recommend that access to a videokeratoscope or corneal topographer is essential for the ongoing care and monitoring of orthokeratology subjects. One limitation of both of these studies was the use of the EyeSys topographer to evaluate corneal shape change. The EyeSys uses eccentricity as an indicator of corneal shape

and as mentioned earlier eccentricity cannot be used to assess oblate surfaces. Tahhan et al (2003) showed a change in eccentricity for all lens types which indicated a trend towards the cornea becoming spherical with orthokeratology lens wear. Maldonado- Codina et al (2005) gave oblate corneas a value of 0.00.

In the current study it is proposed to fit the right eye of the participants with a similar multicurve design. The left eye will be fitted with a full back surface aspheric design not simply the periphery as in the Contex D Series 4 Zone lens.

1.11 Control of Myopia with Orthokeratology

Harris (1972) proposed that orthokeratology could be used to "explain developmental myopia". He defined this as myopia which is acquired as a result of a continued near point environment. He based his proposal on an analysis of the various orthokeratology studies which had taken place up to June 1972. Many of these studies were simply case reports rather than clinical trials and their principal aim had been the reduction of manifest myopia. A number of subjects involved in these early trials had coincidentally shown a reduction in their rate of myopia progression.

Harris felt that since orthokeratology affected the corneal curvature and corneal thickness, changes in these two parameters and their effect on myopia progression could be evaluated. He also suggested that orthokeratology may inhibit axial length changes by reducing the over accommodation. It was this near stress which he felt could be the trigger for axial extension.

In more recent times, studies have begun involving populations where myopia progression is of concern due to its endemic nature. In particular these studies have begun to look more at how the provision of orthokeratology lenses to children may delay myopia progression. Cheung, Cho and Fan (2004) report on the fitting of an 11 year old child with an orthokeratology lens in one eye only, due to anisometropia. During two years of follow up the eye fitted with the contact lens showed only a 0.13mm increase in axial length. The eye without a contact lens showed a 0.34mm

increase in axial length with the corresponding increase in myopia (0.75 dioptres). The group suggest that this supports the hypothesis that orthokeratology can be used in myopia control. Cho, Cheung and Edwards (2005) reported on their initial study of 35 children aged between seven and twelve who had been fitted with orthokeratology lenses. They concluded that whilst orthokeratology did appear to be capable of preventing the progression of myopia the magnitude of any control was unpredictable.

The Corneal Reshaping and Yearly Observation of Nearsightedness (CRAYON) study (Walline,Jones and Sinott 2009) reported on 40 subjects aged eight to eleven years old fitted with orthokeratology lenses. Twenty eight of these children were followed for two years and their myopia progression compared with a group of age matched children wearing soft lenses. The pilot study findings were that orthokeratology lenses were associated with a reduction in the increase in axial length in the children involved in the study. A-scan ultrasound measurements were made at the initial, one year and two year visits. In both groups of children the axial length increased, the soft lens wearers however showed a 0.1mm faster rate of extension. A similar response was seen in the vitreous chamber depth. The group also looked at the change in the anterior chamber depth and found that the soft lens group showed 0.06mm greater change than the orthokeratology group. Walline et al point out that whilst this study confirms the findings of a number of other studies a randomised clinical trial is required in order to give a definitive answer. If corneal reshaping is an effective means of slowing myopia progression further studies into the rate of change in axial length after the cessation of lens wear are also required.

1.12 Complications associated with Orthokeratology

1.12.1 Corneal staining in Orthokeratology

Cho, Cheung, Edwards and Fung (2003a) commented on the incidence of adverse corneal staining amongst a group of 61 orthokeratology patients in Hong Kong. Sixteen of the patients had corneal staining of sufficient magnitude to advise them to cease lens wear. Four of the patients reported eye infections, two having been advised by ophthalmologists to cease lens wear. None of this specific group of patients had experienced any long term loss of visual acuity or corneal integrity as a result of the infection. They concluded that the risk of corneal staining, sufficient to advise a patient to cease lens wear, increased with the duration of lens wear. By far the commonest complaint amongst the group of patients was lens binding. Only 2% of the group reported this as very often, with 26% reporting no occurrence.

Chui and Cho (2003) reported on a case of recurrent lens binding in a 12 year old girl. After one overnight wear the lenses were difficult to mobilise even with additional lubrication and forced blinking. Once the lens was removed a Grade 2+ (Efron scale) corneal stain was observed and the girl was advised to cease lens wear. Chui and Cho reached the conclusion that this particular individual had “soft” corneal tissue. They based this assumption on the girl’s rapid response to orthokeratology lens wear. In order to address the persistent lens binding, despite the use of several different lens designs. A decision was reached to offer only a partial correction of myopia and thereby reduce the pressure on the cornea. If this degree of epithelial damage is reflected in other young subjects then this may also be a contributory factor in the higher incidence of microbial keratitis seen in orthokeratology (See Section 1.10.2). It is possible that fenestration of the lenses, in the reverse curve, could also have helped to reduce lens binding. In this case a full correction could have then been offered.

In 2012 Cho, Chan, Cheung and Mountford (2012) investigated the effects of fenestration on the performance of orthokeratology lenses. Twenty two individuals were

fitted with a pair of orthokeratology lenses. One of the lenses had three 0.20mm fenestrations evenly distributed (120^0 intervals) around the lens between the reverse and alignment curves. The fenestrated lens was randomly assigned to one eye of each participant. Fifteen individuals were classed as achieving a full correction with the lenses. These participants were asked to grade the degree of lens binding each morning on waking (Fig 1.7). Following the instillation of one drop of artificial tears and three or four normal blinks, subjects assessed the lens binding using a mirror and the following grading scale.

Grade	Definition
0	No binding observed. Lens moves freely
1	Lens bound and loosens up spontaneously after five forced blinks
2	Lens bound and loosens up after one episode of pressure on the upper lid, then repeated on the lower lid and five forced blinks.
3	As grade 2, but two pressure pushes on the lids and five forced blinks
4	As grade 2, but three pressure pushes on the lids and five forced blinks

Fig 1.7 Lens binding grading scales (from Cho, Chan, Cheung and Mountford (2012))

In the eyes wearing fenestrated lenses, the group found a statistically significant reduction in lens binding at the twelve month visit. At previous visits (one month, three months and six months) the fenestrated lenses showed less binding but the results did not reach statistical significance. They also found the fenestrations had no statistically significant effect on the refractive outcome or visual performance of the lenses. Fenestration of the lenses had no effect on the level of corneal staining seen in these individuals. Corneal staining was commensurate with that reported by Cho et al (2003a).

1.12.2 Microbial Keratitis in Orthokeratology

As mentioned in the earlier section microbial keratitis is the most serious side effect reported up to this present time. Hutchinson and Apel (2002) presented a case report on two individuals undergoing orthokeratology who developed microbial keratitis. The first, a 60 year old woman, was found to have a Pseudomonas infection which resolved with medication. The resulting corneal damage was a 2.5mm scar in the central cornea which reduced the vision to 6/12. The second case, a 29 year old male, was found to have an Acanthamoeba infection which also resulted in a corneal opacity. In this individual the acuity was reduced to 6/36. Hutchinson et al expressed concern about these serious side effects associated with a temporary procedure. His use of the term "ill fitting" to describe the characteristics of the orthokeratology lenses being used could also be considered controversial. Poole, Frangouli and Ionides (2003) report a case of a 22 year old male who developed a microbial keratitis following orthokeratology lens wear. The initial infection was sufficient to reduce his acuity to perception of light. Treatment with half hourly antibiotics for a period of 24 hours followed by two days of hourly doses improved the acuity to 6/18. The scar finally resolved after two months and the subject was left with acuity of 6/9.

Sun, Chen, Zhang, Wang et al (2003) reported on four cases of Acanthamoeba keratitis associated with orthokeratology. The four teenagers had a history of between 6 and 24 months of lens wear prior to the development of the infection. Only one of the cases resolved without residual visual impairment. In a further report (Sun, Deng, Zhao, Zhang et al 2006) 28 cases of microbial keratitis associated with orthokeratology were reported. This group had also been wearing lenses for at least six months before the onset of symptoms. Acanthamoeba and Pseudomonas were the infective organisms in 24 of the 28 cases. Lang and Rah (2004) reported the first case series of adverse corneal events related to orthokeratology in the USA. The five cases included two cases of microbial keratitis, one of infiltrates, one case of toxic keratitis and one case of corneal abrasion. The more serious complications had occurred in individuals who

were non-compliant with wearing schedules. One child (12 years old) with microbial keratitis had removed the lenses only once or twice a week for cleaning. The child (12 years old) with toxic keratitis admitted to over wearing his lenses (32 hours continuous wear) and also to not washing his hands prior to lens insertion. Lang and Rah concluded that he had introduced his topical acne medication into his eye along with his lenses. The two children were taken out of orthokeratology lenses. All of the cases resolved without any loss of best corrected visual acuity. This case series clearly illustrate that despite being given full instructions patient compliance must be monitored at all aftercare visits.

Tseng, Fong, Chen, Hou et al (2005) carried out a retrospective analysis of nine patients (10 eyes) who presented with microbial keratitis following orthokeratology lens wear. These patients were all under 18 years old (eight to 17 years) and were undergoing accelerated (overnight wear) orthokeratology. The subjects had been using the lenses for between one and 24 months. After an analysis of all predisposing factors for keratitis in this age group had been performed, the only common factor was found to be orthokeratology. Cultures taken from the 10 corneas revealed a variety of infectious agents, both gram positive and gram negative[3]. In only four of the patients were the infectious agents positively identified. 90% of the corneal infiltrative events occurred in the central cornea. Since this is the area of the cornea which undergoes maximum moulding with orthokeratology lenses this adds further to the concern about the safety of this procedure. As Cho (2003a) pointed out this is the area where corneal stain is seen in most orthokeratology patients and where Alharbi and Swarbrick (2003) found significant epithelial thinning.

All the patients evaluated by Tseng et al (2005) were treated with appropriate antimicrobials and all corneas showed resolution of the corneal infiltrates and re-epithelialisation occurred. The recovery of visual function was more limited with all eyes

[3] Gram positive and Gram negative refer to a method of staining bacteria. Gram positive bacteria retain the initial stain and appear violet on microscopic examination. Gram negative bacteria lose the initial stain and take up the counter stain and appear red on microscopic examination. Variations in the structure of the cell walls of the different bacteria give rise to these differences.

being left with some degree of corneal scarring. Four eyes had acuity of < 20/30 with one individual being left with hand movements at 20cms. This last individual had a complicated recovery which involved the development of secondary glaucoma which would have further compromised the corneal recovery.

Hsiao, Ma, Huang, Yeh et al (2005) looked at a group of 20 young people (mean age 14 years) who had presented with infectious keratitis following orthokeratology lens wear. Eight eyes showed central corneal infiltrates and 13 paracentral infiltrates, one individual had bilateral disease. The microorganism involved was identified in 13 of the cases. The majority of these cases were due to Pseudomonas (nine) with only one case of Acanthamoeba. In contrast to the Tseng group 16 of the affected individuals made a full recovery with acuity returning to 20/20. One individual however was left with acuity of 20/200 due to central corneal scarring. Watt and Swarbrick (2005) evaluated the first 50 worldwide reported cases of orthokeratology related microbial keratitis. They concluded that the risk factors in these cases were that patients were of Asian origin and aged between 9 and 15 years of age. Patients experiencing an episode of keratitis were more likely to be non-compliant with lens and case cleaning procedures particularly with respect to the use of tap water with lenses. These individuals were also more likely to have continued to wear their lenses despite the onset of discomfort. The higher incidence amongst the Asian population is more likely to reflect the greater uptake of the procedure by individuals in those countries with a higher incidence of myopia.

In a report from Taiwan, Hsiao, Yeung, Ma, Chen et al (2007) reviewed hospital cases of microbial keratitis occurring in children. In 33 of the 78 cases contact lens wear was found to be a predisposing factor. Eight of these cases were undergoing overnight orthokeratology and six of these cases involved children less than 12 years of age. Concerns have to be raised when such young children are put at risk of serious corneal damage for what could still be considered an experimental procedure. Hsiao felt that the increased incidence of contact lens related keratitis in this age group, when

compared to other groups, was associated with the degree of myopia found amongst the Taiwanese people and the subsequent degree of contact lens wear. This result was consistent with the incidence of microbial keratitis seen in the adult population of Taiwan. Studies amongst children from similar age groups suggested that trauma, either from accident or surgery rather than contact lens wear was the most common predisposing factor in microbial corneal infection (Cruz, Sabir, Capo, Alfonso, 1993; Kunimoto, Sharma, Reddy, Gopinathan et al 1998). Hsaio et al (2005) advise caution when considering fitting orthokeratology lenses to children for what they too call a temporary procedure.

Watt, Swarbrick, Boneham (2007) reported on the Australian experience of microbial keratitis in orthokeratology. The background to the study was an attempt to identify the demographics for orthokeratology within Australia. As part of the questionnaire practitioners were asked to report adverse responses to orthokeratology. Of the 33 practitioners who responded nine cases of microbial keratitis were reported. Two of these nine cases are those reported by Hutchinson (2002). Both Pseudomonas and Acanthamoeba were identified as infective organisms in this series of patients which corresponds with both the Tseng et al (2005), Hsaio et al (2005) and Hutchinson (2002) studies. These first three studies found orthokeratology as a predisposing factor in microbial keratitis whilst the Watt et al (2007) study began from the premise of looking for adverse effects from orthokeratology. Both the Tseng et al (2005) and Hsaio et al (2005) studies found a high incidence of microbial keratitis amongst patients under 16 which was not reflected in the Watt et al (2007) study.

As a result of the prevalence of myopia in East Asia (Morgan, Ohno-Matsui, Saw, 2012) orthokeratology is being used as a possible means of myopia control. As a consequence of this, orthokeratology patients in these countries show a younger age profile than countries such as the United States and Australia. It seems unlikely that the under 16's are more susceptible to microbial keratitis but simply that the higher number of fittings amongst this age group has increased the apparent incidence. Lam, Houang,

Fan, Lyon et al (2002) compared the incidence of microbial keratitis in Hong Kong with that of Europe and North America and found that rates were comparable with those of Scotland and the United States. Watt et al (2007) also examined the worldwide trends in microbial keratitis associated with orthokeratology. They evaluated all the published cases (123) between 2001 and 2007; this report included the 50 cases reported in 2005. They concluded that the majority of cases were of East Asian origin as in 2005 and that a significant number of these cases occurred at a time when there was very little regulation of the procedure of orthokeratology. As with the other reported studies the organisms involved were predominantly Pseudomonas or Acanthamoeba.

The Watt et al study (2007) found, that of the nine cases of microbial keratitis they identified, seven of them were non-compliant with aftercare or lens case care procedures. No evidence was offered regarding lens care procedures in the other studies. These findings confirm the need to ensure patients are fully informed about the need for appropriate lens and case care and regular aftercare. No attempt was made in the case series presented by Sun (2003) to assess whether inappropriate lens care had contributed to the disease process. The use of tap water to wash lenses or cases is probably the highest risk factor in the development of Acanthamoeba keratitis. Robertson, McCulley and Cavanagh (2007) report on the case of a 19 year old man who suffered permanent loss of vision in one eye as a result of Acanthamoeba keratitis secondary to orthokeratology. This young man, unknown to his optometric practitioners, had stored his lenses in tap water for several years prior to the infection developing.

Boost and Cho (2005) looked at the effect of orthokeratology on the normal microbial flora of the tears in individuals undergoing orthokeratology. The microbial flora of each individual was assessed on two occasions before they commenced lens wear. Further samples were taken at six aftercare visits once orthokeratology had commenced. No change was found in the conjunctival contents over this period of time. The same group of patients also had their lenses, lens cases and suction holders processed for microbial contamination. Individuals involved in this study removed their lenses using

suction holders. Cho, Cheung, Edwards and Fung (2003a), in their survey of twelve experienced orthokeratology practitioners, reported that in Hong Kong patients were advised to remove their lenses with suction holders. They reported that the background for this practise was seminars and workshops provided by orthokeratology lens companies. Of the twelve practitioners surveyed five taught their patients to remove the lenses by digital manipulation after the adaptation period had been completed. Their analysis of the patients lens removal habits showed that as few as 20% removed their lenses without using suction holders. Organisms isolated from the lenses and accessories were not the same as those found in the conjunctival swabs. Individuals who were assessed as having poor compliance with lens hygiene procedures had the highest levels of contamination. Despite these findings none of the individuals involved in the study experienced an infective episode.

Cho, Boost and Cheng (2009) further examined the microbial contamination of the solutions, cases and accessories used by orthokeratology patients in their clinic. They again found that the highest levels of contamination were found in the accessories, tweezers and suction holders, used by the patients (46%). 33% of the containers of artificial tears used by the patients were also contaminated. The highest levels of bacteria were of the type Staphylococcus Aureus and Serratia Marcescens. Patient education regarding the risks of contamination improved the rates of contamination in the accessories but did not have any impact on contact lens case contamination. Tseng et al (2005) point out in their study that individuals in the age group eight to 17 may not be as capable of following a strict hygiene regime as an adult. If this is the case then they advise caution in the use of orthokeratology. This is of particular concern where orthokeratology is being used with young children as a means of myopia control.

Hsaio et al (2005) point out that the use of orthokeratology with children and adolescents must be approached with caution due to the inherent risk. It is clear that parents involved in making the decision about the possibility of orthokeratology for their

children need clear and detailed consent advice before a child commences treatment. Other researchers (Wilhelmus 2005; Yepes,Lee, Hill,Ashenhurst et al 2005) also concluded that the use of orthokeratology in children required careful evaluation due to the increased risk of microbial keratitis.

Dart, Radford, Minassian, Verma et al (2008), Stapleton, Keay, Edwards, Naduvilath et al (2008) and Stapleton, Edwards, Keay, Naduvilath et al (2012) looked at the incidence of microbial keratitis in traditional contact lens wearers. All three studies showed that overnight use of all forms of contact lenses increased the risk of microbial keratitis by a factor of up to five. The incidence of infection amongst RGP lens wearers in these studies (Dart 2008; Stapleton et al 2008 & 2012) was 1:10 000. None of the studies reported a case of microbial keratitis associated with the overnight wear of RGP lenses. Individuals who reported overnight wear of lenses were not further classified into traditional or orthokeratology lens wearers.

Young, Leung, Cheng, Law et al (2004) reported five of the six cases of orthokeratology related corneal ulcer they found were culture positive for Pseudomonas. Keay, Edwards, Naduvilath, Forde et al (2006) in their study on factors affecting the morbidity associated with soft contact lens related microbial keratitis found that the most significant factor was the underlying causative organism. They found that individuals infected with Pseudomonas had larger corneal ulcers with a higher incidence of vision loss. Wang and Lim (2003) in a case report noted that their patient's Pseudomonas related corneal ulcer was stellar in shape rather than circular. They hypothesised that the unusual shape had occurred as a result of the lens creating stellate splits in the epithelium which allowed an opportunistic infection to occur. Araki, Takatsuka, Asari, Mutoh, Nishi et al (2005) reported on a case of microbial keratitis associated with Pseudomonas. They found that Pseudomonas was more resistant to antibiotic therapy under slightly hypoxic situations. Overnight hypoxia is an inherent difficulty with any contact lens wear in a closed eye situation. The bacteria were also capable of coating the lenses with glycocalyx slime. This slime may well further reduce

the efficacy of any antibiotic therapy given. These two factors could therefore contribute to both the incidence and the severity of the infection seen in orthokeratology related microbial keratitis.

Choo, Holden, Papas, Willcox (2009) looked at the binding of Pseudomonas Aeruginosa to both orthokeratology and conventional RGP lenses. They found that orthokeratology lenses retained more bacteria than the conventional lenses. This study was carried out on cats and the lenses were soaked in a solution of Pseudomonas Aeruginosa prior to being inserted into the cat's eyes. They conclude as a result of this increased binding of bacteria to the lens surface that orthokeratology patients may be exposed to a higher risk of corneal infection.

When Fleiszig and Evans (2010) looked at the pathogenesis of microbial keratitis, they found that fluorescein staining was a poor predictor of the risk of infection in their animal models. They did find that hypoxia could increase the cornea's susceptibility to infection. They also found that extended wear of lenses reduced the corneal epithelial cells ability to up-regulate antimicrobial peptides. Fleizig and Evans (2010) suggested that contact lenses which sit too close to the corneal surface and therefore reduce tear exchange; would increase the risk of corneal infection. This lack of tear exchange would reduce the rate of removal of bacteria from the corneal surface increasing the risk of a bacterial infection. They postulate that in the case of orthokeratology overnight wear, coincident hypoxia, reduced tear exchange and increased bacterial load may explain the increased incidence of microbial keratitis in orthokeratology.

One further concern associated with contact lens wear has always been the potential for reduction in corneal sensitivity. This reduction in sensitivity was originally thought to be related to oedema secondary to hypoxia. As high Dk lens materials have become available this risk has been significantly reduced. In young patients involved in orthokeratology the combination of prolonged wear time to allow for myopia control, potentially softer corneal epithelium, potentially reduced corneal sensitivity and poor compliance with hygiene instructions gives cause for concern as to the long term

benefits of this procedure. Chee, Lim and Tan (2007) reached this conclusion after reporting on the incidence of infectious keratitis in five children (aged nine to 14 years) undergoing orthokeratology. All five subjects tested positive for Pseudomonas aeruginosa. All subjects were left with some degree of scarring in the central or paracentral cornea. Hiraoka, Kaji, Okamoto and Oshika (2009a) investigated the effect of orthokeratology on corneal sensation using the Cochet-Bonnet aesthesiometer. The adult subjects used in this study (23.5 +/- 3.2 years) had myopia ranging from -1.00 to – 4.00 dioptres. Subjects were evaluated before the commencement of the treatment and after three months of overnight wear of reverse geometry lenses produced in Boston XO material (Polymer Technology Corp, Wilmington, MA). Five corneal locations were evaluated, the corneal apex, superior, inferior, temporal and nasal locations two millimetres from the limbal margin. At the end of the three month period all zones showed a statistically significant reduction in sensitivity from the baseline measure. The five zones showed no statistically significant difference between each other either at baseline or after three months of treatment. Hiraoka et al also looked at the interaction between the change in central corneal sensation and the degree of myopic correction and found that there was no correlation between these two factors.

Lipson (2008) conducted a retrospective analysis of 296 cases of orthokeratology fitted in one practice. He wanted to evaluate the comparative risks for individuals of 12 years and under against those aged 12 years, one month and older. In this large group only three adverse events, defined as microbial keratitis, corneal ulcer, corneal abrasion sufficient to require medical intervention, loss of best corrected visual acuity or corneal scar were reported. The three cases all occurred in individuals less than 12 years of age but all resolved satisfactorily. The individuals involved were able to continue wearing the orthokeratology lenses.

1.12.3 Iron ring deposition in Orthokeratology

Cho, Chui et al (2002a) reported the first incident of the appearance of a brown ring in the cornea of a subject undergoing orthokeratology. The first signs of this ring in the inferior cornea commenced after only two weeks of wear with an almost complete and well defined ring being present by week four. The ring appeared to form at the edge of the bull's eye fluorescein pattern. The patient was asymptomatic and all other aspects of corneal health were normal.

They point out that the rings are similar in appearance to Fleischer rings seen in keratoconus. The aetiology of the Fleischer ring in keratoconus is thought to be the deposition of iron in the corneal epithelium. These iron deposits occur at points of sudden change in corneal contour such as would be seen in both keratoconus and orthokeratology. A number of hypotheses have been proposed for the cause of the deposit. It is now generally accepted that for an iron ring to form there must be a sudden change in corneal curvature which allows pooling of the tears. This description applies to the principle of orthokeratology fitting with the reverse and alignment curves producing the sudden change in corneal curvature and the tear pooling.

Rah, Barr and Bailey (2002) reported on six cases of pigment deposits in the cornea of orthokeratology patients and concluded that the incidence was associated with individuals with darker irides and more significant refractive change. Other researchers (Liang, Chou, Wu, Lee 2003; Hiraoka, Furuya, Matsumoto, Okamoto, Kakita et al 2004) have also reported on the incidence of iron rings in orthokeratology. All of the researchers conclude that these rings are benign in nature and should not prevent patients from continuing to wear their contact lenses. Hiraoka, et al (2004) conducted specular biomicroscopy on their subject. This indicated no significant change in the number, shape or density of the endothelial cells between the pre-lens fitting and annual aftercare appointments. They point out that the presence of an iron ring has only been reported in subjects wearing lenses during sleep. They suggest that stagnation of the tears in the reverse curve overnight leads to the iron deposition.

Individuals wearing orthokeratology lenses in the open eye state will have continuous replenishment of the tear film due the action of the blink. Cho, Chui and Cheung (2003b) examined two subjects to assess reversibility of the iron ring after cessation of lens wear and found that all evidence of the ring had disappeared within two months.

In a further study Cho, Chui and Cheung (2005) looked at the incidence of iron ring and factors which could be associated with its appearance. After 12 months of lens wear 90% of the 35 subjects had evidence of the iron ring. The group conclude that the factors influencing the presence of the ring are baseline refractive sphere or spherical equivalent, the target amount of myopia reduction and the change in apical radius. They found, however, that there was no statistically significant relationship between the magnitude of the changes induced and the first appearance of the ring. The intensity of the ring also appeared to increase over time. A further complication of the pigmented ring was reported by Cheung, Cho and Cheung (2005). In one patient (10 year old female) a white lesion developed within the ring after two years of lens wear which had increased in density at the end of the third year. They suggest that the white lesion may be indicative of increasing stress on the cornea. The child was allowed to continue lens wear but the group advise caution in the assessment of corneal health in orthokeratology patients.

Gonzalez-Meijome, Gonzalez-Perez, Garcia-Porta, Diaz-Rey et al (2012) reported on the incidence of iron ring in two Caucasian subjects. The two subjects had undergone unremarkable orthokeratology treatment for a period of six months. As with the previous reports (Cho et al 2002, Rah et al 2002, Liang, et al. 2003, Hiraoka et al. 2004, Cho et al 2005) the iron ring was found at the base of the reverse curve. Gonzalez-Meijome et al point out that the previously reported incidents of iron ring had been in subjects of Asian ethnicity. They suggest that as the individuals in their report were Caucasian this reduces the possibility of an ethnic element to the development of iron ring. Rah et al (2002) had suggested that the incidence of iron ring was associated

with those with darker irides. Gonzalez-Meijome et al (2012) do not indicate the iris colour of the two subjects in their study.

All of the reported studies indicate that corneas which manifest the iron ring are otherwise healthy. The recent paper by Gonzalez-Meijome (2012) suggests that all orthokeratology lens wearers and not just those with dark irides should be advised of the possibility of this deposit occurring. They should be reassured of its benign nature if it should occur. Further research into the relationship between iris colour and the incidence of iron ring, and into the degree of refractive change prior to the appearance of the iron ring would allow practitioners to offer more appropriate advice.

1.12.4 Other corneal events in Orthokeratology

A further benign corneal change reported by some researchers (Cheung, Cho, Bron, Chui et al 2006; Lum & Swarbrick 2007) is the presence of fibrillary lines. These lines appear in the central cornea, within 3mm of the corneal apex, and are most noticeable in the lower cornea. Cheung et al (2006) report their presence after their subject had been wearing the orthokeratology lenses for 12 months, however Lum and Swarbrick (2007) noted their presence after only five weeks. The lines appear to lie in the subepithelial / anterior stromal layers of the cornea and their presence has also been noted in normal and keratoconic corneas. Their true origin is unknown although Cheung et al (2006) suggest that they are nerves of the sub-basal plexus whose arrangement has been altered by the change in epithelial migratory patterns induced by orthokeratology. They further suggest that the change may be pressure induced. In earlier reports the identification of these fibrillary lines as originating in the corneal nerves was questioned (Kurteeva, Affeldt, Albini, Agarwal 2002; Hsu, Affeldt & Meallet 2004). Both studies suggested that they represent a variant of corneal verticillata and were in fact epithelial cells which had undergone neurotrophic damage.

Ng (2006) reports a case of central corneal epitheliopathy in an asymptomatic 12 year old girl. The girl had been wearing orthokeratology lenses successfully for a period of

three and a half years. At a routine aftercare she was found to have a “dellen” like area in the central cornea. This flattened depression showed minimal staining and no microbial activity. The girl was advised to cease lens wear in this eye and the lesion resolved in four months. The lesion returned within six weeks of the girl returning to lens wear. The lens parameters were altered to reduce the pressure on the central cornea. This was achieved by reducing the amount of correction required from -3.75D to -2.50D and flattening the alignment curves by 0.50D. It was hoped, that as well as reducing the pressure the flattened peripheral curves would encourage tear flow and therefore reduce any drying element associated with the lesions formation. The girl returned to lens wear with this new lens and the lesion showed almost total resolution.

Corneal dellen normally form peripherally adjacent to an area of poor wetting. This may be as a result of a raised pingueculae or at the edge of an RGP lens which shows poor mobility. The loss of the mucin layer in these areas leads to degeneration of the corneal epithelium and compaction of the anterior stroma and subsequent corneal thinning. Ng suggests that the atypical presentation in this case may be due to changes in the corneal epithelium induced by orthokeratology. Swarbrick (1998) suggests that the central corneal epithelium is thinned and the mid-peripheral cornea thickens in orthokeratology. Ng (2006) surmises that the “dellen like” lesion is formed at the interface of these two corneal areas.

Ng (2008) also reports a case of an asymptomatic foreign body under an orthokeratology lens in an eight year old child. Under normoxia the central cornea would show the greatest sensitivity. Ng found that in this child the central corneal sensitivity in both eyes was reduced. As mentioned earlier it has been accepted for many years that the wearing of contact lenses, particularly rigid lenses, does lead to a reduction in corneal sensitivity. Orthokeratology in this case is therefore no greater a culprit than any rigid lens wear. However it does highlight the need to warn patients about the possibility of foreign material getting under the lens and to make them aware of checking the eye’s appearance on a regular basis.

In a report, published by the American Academy of Ophthalmology (Van Meter, Musch, Jacobs, Kaufman et al, 2008), concerns were raised that no well designed cohort studies or randomised controlled studies had been conducted into the safety of orthokeratology. The report recommends that, until these studies have been conducted, a wide margin of safety should be applied to the procedure. The authors did not make any suggestions about what this margin of safety should be.

1.13 Non Orthokeratology uses of Reverse Geometry lenses

1.13.1 Trauma

Martin and de Juan (2007) reported the use of reverse geometry lenses in a case of corneal irregularity secondary to trauma. This lens gave a significant improvement in acuity for the patient. The chair time involved to produce this was significantly reduced when compared to the fitting of a standard aspheric RGP. There was however no intention to induce any corneal refractive change. They suggest that the reduced chair time could prove beneficial in cases such as this.

1.13.2 Post Operative complications of refractive surgery

Hau and Ehrlich (2003) fitted 19 eyes with reverse geometry RGP lenses following unsuccessful refractive surgery. They found that the flatter the post operative K the more likely the patient was to require a reverse geometry lens. 12 of these individuals had an improvement in visual acuity with the lens when compared with that of post operative spectacles. They cite the custom design nature of these lenses as a drawback, suggesting that most practitioners would prefer a compromised fit from a conventional RGP. They comment that, as the tendency to treat ever greater degrees of myopia continues, the central ablation zone will become flatter leading to a greater tendency to have to use reverse geometry lenses.

Steele (2007) in his review document on post LASIK contact lens fitting also supports the use of reverse geometry RGP lenses when the ablated central zone is significantly flatter than the periphery.

1.13.3 Post operative management of corneal graft surgery

Szczotha and Lindsay (2003) in their commentary on contact lens fitting after keratoplasty suggest the use of a reverse geometry lens for graft buttons which are proud of the cornea. The secondary reverse curve allows the contact lens to lie over the raised area. Lagnado, Rubinstein et al (2004) reported on the management of 11 patients who showed flat corneal topography post keratoplasty. All 11 patients required a reverse geometry lens to achieve a satisfactory contact lens fit. The reverse geometry lenses met with a varying degree of subjective success and only six of the patients continued with the contact lenses. The remainder of the group chose to wear spectacles or were content to continue without refractive enhancement.

1.14 Summary

A critical part of continuing research is the submission of findings and conclusions to peer review. Many of the early journals appear to have applied only editorial review rather than peer review to the papers they published. Whilst this does not negate the findings of the individual researchers the conclusions could be considered as personal opinions only. These early papers had little theoretical evaluation of their findings and at times made speculative claims for the procedure. An example of this is the suggestion by Wlogdya and Bryla (1989) that there is a 1.00D reduction in axial length when orthokeratology lenses are applied; this despite the fact that no measurements of axial length were made during the study. The early publications on the process of orthokeratology are based on clinical observations rather than structured research projects in fact Grant and May (1970) actually pointed this out in their paper. Concerns around this are reflected in the response of the American Optometric Association to

add disclaimers ahead of papers published in their journal (Ziff 1968, Patterson 1975). As late as 1975 the American Optometric association were calling orthokeratology a controversial procedure requiring more research and study (Patterson 1975). Their response was to establish a research group to provide a more structured approach to the investigation of orthokeratology (Kerns 1976a, b & 1978).

Kerns (1976a, b & 1978) as indicated earlier had matched his three study groups for age, refraction and corneal curvature. In this way he minimised the variation in subject response created by these three factors. The introduction of the control group against which change could be measured improved the ability of the experiment to identify a change in response created only by the orthokeratology lenses. In contrast Binder et al (1980) in their comparative study did not match their subjects for refractive error with the conventional group having an average refractive error of twice that of the orthokeratology group. Whist both groups showed a change in manifest refractive error by the application of orthokeratology lenses the Kerns studies have more validity due to the matched samples.

Following on from the research of Kerns a more structured approach has been applied to our understanding of orthokeratology. The Berkeley Orthokeratology study (Brand 1983, Polse et al 1983 a, b, c) introduced the concept of masking into the study of orthokeratology. Masking of the lens type from the investigator and also the subjects reduces the potential for bias in the interpretation of clinical measures or subjective responses. A further improvement to reduce unintentional bias from experimental results is to randomly assign subjects to specific research groups.

Many of the early researchers pointed out the need for structured longitudinal studies into orthokeratology (Erickson and Thorn 1977). Whilst the early studies were by nature longitudinal in that they involved the provision of a series of increasingly flatter lenses. Each individual involved in the study proceeded at a different rate which limits the translation of the findings to a wider group (Winkler and Kame (1995). Coon (1984)

followed his research and control groups for a period of 80 weeks. Whilst this was not a masked and randomised study it benefitted from the inclusion of a control group. Some of the researchers applied retrospective analyses to their studies or compiled responses from a number of studies (Neilson, Grant & May (1964), Erickson & Thorn (1977)). In both of these cases the aspect of control is absent from the data collection.

Erickson and Thorn (1977) pointed out that changes in corneal power would be better evaluated with an instrument other than the keratometer. The results of the early studies would have benefitted from the use of corneal topographers to assess corneal shape change. As computerised corneal topography became available in the 1980's this has improved our understanding of the mechanism involved in orthokeratology. The same also applies to the investigation of anterior chamber depth and axial length change with the availability of the IOL Master since 2000.

Swarbrick et al (1998) and Alharbi and Swarbrick (2003) reported on corneal thickness change both centrally and mid peripherally. Their first paper was based on only six subjects who wore the lenses in an open eye situation. The latter paper did involve overnight wear of orthokeratology lenses. This study was conducted over three months of lens wear and involved 18 subjects. The optical pachometer used is very repeatable (centre +/- 2µm and mid periphery +/- 4.3µm) but this level of repeatability can only be achieved by an experienced pachometrist. Swarbrick et al had expressed concerns about the thickness changes induced by orthokeratology. If orthokeratology is to be offered on a commercial basis it would be useful to have information from an instrument which is readily available and non invasive.

A number of studies have used the Munnerlyn formula developed to calculate the ablation depth in refractive surgery to assess change in orthokeratology (Swarbrick et al 1998 and Alharbi and Swarbrick 2003). This formula is based on spherical surfaces and as such concerns must be raised about its use on prolate or oblate ellipses. Garner and Owens (2004) found that the formula either under estimated the change in

refractive error if the p value was kept constant or over estimated the change if the p value were changed.

In order to address the concerns expressed in this section during the current study a longitudinal design will be applied. Corneal topography will be evaluated using the Orbscan topographer rather than keratometry. The Orbscan will also be used to assess the corneal thickness changes to reduce the need for an experienced pachometrist. The IOL Master will be used for the investigation of any induced change in anterior chamber depth or axial length. Changes in corneal power will be calculated from first principles to avoid the use of the Munnerlyn formula. As indicated earlier an ideal study would have randomised participants and masked the lens design from the researcher. This has not been possible with this study firstly because all the participants will wear the two lens designs. Randomisation could only be applied by assigning some participants to wear the aspheric lens in the left eye and some the right with the pentacurve being worn in the opposite eye. Secondly the two lens designs have been produced in different tints to allow participants to differentiate the two lenses. The study rationale is outlined in Section 1.15.

1.15 Study Rationale and Aims

This study aims to address the following aspects of the investigation of the effects of orthokeratology on ocular biometry.

- Maldonado-Codina et al (2005) used an experimental lens with an aspheric periphery design based on the eccentricity of a model eye. The aspheric design lens in this study will be individualised to the asphericity of each of the subjects. This will be compared with a pentacurve design lens whose peripheral curves will be calculated using the asphericity of each individual subject. These lenses will be designed using software from Douthwaite (2006). The lens designs will be compared to establish whether the aspheric design produces more acceptable results.
- The early researchers suggested a need for longitudinal studies (Erickson and Thorn 1977). Most of the current studies into overnight orthokeratology have followed the adult subjects for no more than 30 days (Alharbi & Swarbrick 2003). The studies suggest that the majority of change has occurred in the first month. Walline et al (2004) had followed a group of children for six months and found that the majority of them had achieved acceptable levels of unaided vision after two weeks of lens wear. This study will follow subjects for twelve months in order to assess whether the changes are complete after one month and what change if any occurs after this time. This evaluation will be applied to
    - Anterior apical radius and p value
    - Posterior apical radius and p value
    - Refractive error
- Kerns (1978) suggested that any effect on the refractive error would stop once the cornea became spherical. Studies which have employed the EyeSys have been unable to assess this as the EyeSys cannot be used to assess oblate surfaces. The Orbscan IIz is capable of measuring oblate surfaces this will

allow us to assess the effect on the p value of the cornea. A comparison between the p value and the refractive error will be made to assess if the effect stopped when the cornea became spherical.

- Swarbrick et al (1998) published data regarding the change in corneal thickness seen in orthokeratology in open eye lens wear. Alharbi and Swarbrick (2003) produced similar results for overnight orthokeratology. They found midperipheral thickening and central thinning. Thickness was measured in both cases using a modified pachometer and measurements were made up to three months of lens wear. This study will look at corneal thickness change over twelve months to see if the corneal thickness changes agree with those of Swarbrick et al (1998) and Alharbi & Swarbrick (2003).
- The early researchers (Grant & May (1972); Patterson (1975) and Erickson & Thorn (1977)) suggested that there was a 2:1 relationship between the change in refractive error and the corneal power. It has been suggested that the reason for this is that the keratometers used are not able to assess the central corneal zone where maximum change will occur. The Orbscan IIz topographer will allow us to assess the central cornea. The relationship between the refractive error and corneal power will be confirmed.
- Swarbrick et al (1998) found that the change in the corneal sag was in close agreement with the predicted change found using the Munnerlyn formula. Concerns arise from the use of this formula which applies to spherical surfaces and not the prolate ellipse of the cornea (Garner and Owens 2004). A comparison will be made between the calculated corneal sag and the refractive error change.
- Swarbrick et al (1998) also suggested that as there was close agreement between the change in corneal sag and the refractive error change the posterior cornea is not affected by the process of orthokeratology. As the Orbscan IIz allows us to evaluate the posterior cornea the change in posterior

apical radius and p value will be evaluated to assess whether it is involved in the refractive error change.

- What about the vertical cornea? Kerns (1978) suggested that the vertical cornea was unorderly in its response to orthokeratology. At that time the lenses were being worn during the day. Soni et al (2003) had evaluated the change in the vertical cornea using the keratometer. The Orbscan IIz will allow the full extent of the vertical cornea to be evaluated.
- Studies have suggested that there is an increase in against the rule astigmatism. A breakdown of the change in refractive error will be made to evaluate the change in astigmatism over twelve months.
- The upper limit of the refraction will be extended to - 6.00DS most current studies have suggested an upper limit of – 4.00DS. The study will look at the acceptability of extending the upper limit of correction.
- What if any effect did we find in the anterior chamber depth and axial length? Cheung et al (2004), Cho et al (2005) and Walline et al (2009) reported the use of orthokeratology in the control of myopia. All of these studies reported a reduction in the increase in axial length amongst the children in their studies. This study will evaluate whether change occurs in an adult population.

CHAPTER 2 PRELIMINARY STUDIES

In the following chapter the details of the instruments which will be used in the investigation of the rationale detailed in chapter one are outlined. In any clinical investigation a number of factors can influence the measurements being taken for example subject variation both inter and intra, interobserver variation, measurement error of the instrument being used. Subject variation is outside the control of the observer but can be minimised by the use of specific protocols. The protocols for this longitudinal study are outlined in chapter three. The use of a single observer for data collection reduces interobserver errors and the specific protocols referred to earlier minimise the risk of intraobserver variation. Knowledge of the repeatability of the instruments used in any study will allow appropriate interpretation of any measurements which have been taken. A discussion on measurement error indices, repeatability and the use of Bland Altman plots for the assessment of measurement differences can be found in section 2.1

A repeatability study of the Orbscan II for both the anterior and posterior cornea was conducted. In particular the preliminary study on the anterior surface was

1. To examine the repeatability of apical radius (r_0) and p values derived from the topographical maps produced by the Orbscan II corneal topographer on normal human corneas.
2. To calculate the number of repeated measurements required to produce an accurate evaluation of the corneal shape.

A study on the repeatability of the Orbscan II to measure posterior surfaces was also conducted. This latter study was carried out after a literature review revealed that there are no previous studies reported on the ability of the Orbscan II to measure posterior surfaces. A literature review of the Orbscan's repeatability on pachymetry measures is given. The EyeSys Corneal Analysis system 2000 (EyeSys) will be used to establish the lens parameters for both the pentacurve and the aspheric design lenses. A

literature review on the repeatability of the EyeSys topographer is presented. A similar review of the IOL Master is also presented as this instrument will be used to measure the anterior chamber depth and axial length of both eyes on each of the participants at each of the visits.

Experimental procedures and data are presented to show the use of the collar and pillar method for the checking of the aspheric back surface design lenses. Initial experimental data are presented to show the calculation of the pillar diameters. These initial investigations are made using lenses of known parameter. Since the pillar diameter is a critical value in the calculation of the lens sagitta it is necessary to know the true diameter rather than accept a nominal value. Having established the true dimension of the pillars; the lens sagitta for an unknown lens can then be calculated. The collar and pillar technique will be applied to the pentacurve design lens to allow comparison of the ordered lens sag with that which was supplied. The back optic zone radius of the pentacurve design will also be checked using the conventional measurement method i.e. by use of the radiuscope.

2.1 Measurement error and repeatability

2.1.1 Measurement error

Measurements made on the same subject on a number of occasions will show a variety of values. This variation arises either as a result of natural variation within the subject or because of variation in the measurement tool. The investigator may also introduce measurement error but the effect can be minimised by the following the same set of protocols for each measure. The measures made will tend to vary around the true value of the parameter being investigated. The true value of the parameter may not be known but is accepted as the average measure found from a series of measurements on the same subject. The degree of variation or measurement error within these measurements could be evaluated using the standard deviation, if at least two measurements have been taken. This is known as the within subject standard deviation (S_w). Where multiple readings have been taken the within subjects standard deviation may be found using a one way analysis of variance (ANOVA) with subject as the factor. This mechanism for recording measurement error is only useful if the standard deviation is the same for all subjects. If the size of the error depends on the measurement i.e. the magnitude of the error increases as the measurement increases then the use of standard deviation would be inappropriate (Bland and Altman 1996a).

Correlation coefficients have also been used to express measurement error. The Pearson correlation coefficient is the one most commonly quoted. Difficulties arise with the use of correlation coefficients because if the subjects are closely related then this will give a small correlation coefficient however when subjects are selected from a random sample the correlation coefficient will be inflated. A strong correlation may not necessarily indicate a strong agreement between measurements (McAlinden, Khadka & Pesudovs 2011).

In some situations the correlation coefficient may be reported to indicate the test-retest reliability. As well as being affected by the sample the correlation coefficient may also

be affected by the order in which the measures are taken. This effect can be avoided by using the intra-class correlation. The intra-class correlation estimates the average correlation among all possible orders of pairs of measures. The method may also be extended to more than two measures. The higher the intra-class correlation the better the discrimination between individuals but this does not help with decisions about the precision of the measurement (Bland & Altman 1996b)

Measurement error may also be described using the within subject coefficient of variation. The coefficient of variation is equal to the standard deviation of the measurements divided by the mean. Use of the coefficient of variation to describe measurement error is only useful when the standard deviation is proportional to the mean. A scatter plot of the absolute value of the difference against the mean will identify if the relationship exists (Bland 2000)

2.1.2 Repeatability

Bland and Altman (1999) recommend that measurement error may also be reported in terms of repeatability. This may also be described as the precision of the measurement. Repeatability is calculated using $1.96.\sqrt{2}$ (S_w) which is equal to $2.77(S_w)$. The British Standards Institute recommends that the 95% repeatability coefficient be defined using two standard deviations (quoted in Bland & Altman 1986). This allows the calculation of the 95% repeatability coefficient. We would expect 95% of the repeated measures by the same method to lie within these values. This criterion will only apply if the measurement errors are normally distributed. Using this method it is assumed that the mean difference between measures is zero.

Bland and Altman (1986) initially applied this method to the comparison of two methods of clinical measurement in order to look at the agreement between the two methods. They argued that two instruments being used to measure the same factor may be highly correlated and yet may not be in agreement. In these circumstances they may

not necessarily be interchangeable. They suggested a method whereby the magnitude of the lack of agreement between two methods could be calculated. The difference between the two measures should be plotted against the mean. This will demonstrate if there is any relationship between the measurement error and the unknown true value. As indicated in the earlier section (2.1.1) the mean of a series of measures may be taken to indicate the best estimate of the true value where this is an unknown quantity. The mean of the difference (d) between the measures indicates if there is any bias and the standard deviation of the differences (s) will help to assess the agreement or otherwise between the measures. In this case the 95% limits of agreement (LoA) are calculated using +/- 2s. For two instruments measuring the same factor we would expect the bias (d) to be close to zero if the instruments were in agreement. Examples of the use of Bland Altman plots to assess agreement between two methods of measurement are shown in Figs 2.20 a, b and c. Bland and Altman advise that if the magnitude of d +/- 2s would not be clinically significant then the two methods may be used interchangeably. A comparison of the repeatability coefficient for each instrument to the limits of agreement calculated for the comparison of the two methods can help to explain any lack of agreement between the two methods. If the limits of agreement and the repeatability coefficients are similar in magnitude this indicates that the lack of agreement results from a lack of repeatability. If the two measures are widely separated i.e. the limits of agreement are greater than the repeatability coefficient then some other factor must be involved in the lack of agreement (Bland & Altman 1999).

One difficulty with the use of the limits of agreement is that they will change if the measurements were to be repeated on a second group of individuals. Bland and Altman (1986) suggest the use of the standard error and confidence intervals to assess the precision of the bias and the limits of agreement. The standard error for the bias (d) may be calculated using $\sqrt{(s^2/n)}$ where n is the sample size. The standard error for the limits of agreement approximate to $\sqrt{(3s^2/n)}$. The 95% confidence limits are calculated by finding the value in t tables which corresponds to n-1 degrees of freedom in the 0.05

column. The confidence intervals each of the limits of agreement becomes LoA +/- t standard errors. The wider the confidence intervals the less in agreement the two methods are. In the following study we have not applied confidence limits to the Bland Altman plots as the subject group is the same throughout.

2.2 The Orbscan II

2.2.1 Introduction

The use of slit scanning technology allied to the quantitative evaluation of Placido disc reflection, along with the availability of computerised analysis, have allowed more detailed investigation of both the anterior and posterior corneal surfaces. One instrument which combines these two technologies is the Orbscan II (Bausch & Lomb, Rochester, NY 14604 USA). Orbscan II is a videokeratoscope which relies on a projection based system to evaluate the corneal surface. In this method, data from an image of a Placido disc projected onto the anterior surface of the cornea and a series of scanning slits are analysed. The system uses triangulation to identify the height of each point on the cornea.

The Orbscan II projects 20 slit images on to the cornea from the right as it travels across the cornea and then projects 20 slits from the left as it returns. By employing the Scheimpflug projection system the anterior and posterior corneal surfaces are in focus at the same time along with the iris and anterior lens surfaces. This enhanced depth of focus allows the Orbscan to produce data regarding anterior chamber depth as well as details of corneal topography and thickness. Once the 40 slit images have been captured, 8000 points on the images are analysed. This takes the form of triangulation of the slit beams against a reference plane at a known distance from the objective lens of the camera (Fig 2.1).

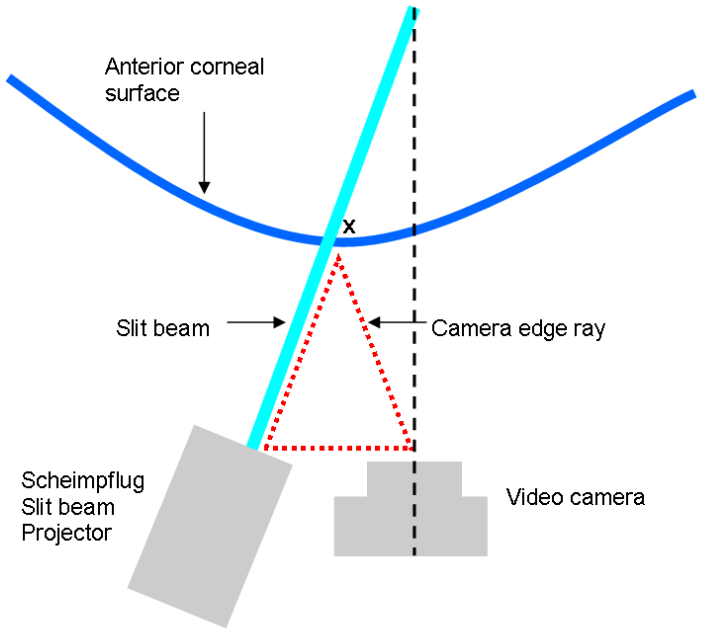


Fig 2.1 Orbscan slit scanning system; the dotted triangle indicates the triangulation system used to determine the height of X. (Courtesy of WAD)

Cartesian co-ordinates are recorded for both the leading and trailing edges of each of the slits; the sagittal height of the slit beam can then be determined. As each of the slits produces a discrete measurement with a separation of approximately 250μm the program extrapolates the intermediate points by use of low order polynomials, so called smoothing splines. (Cairns, Collins & McGhee 2003; Douthwaite, 2006)

Orbscan I consisted of only the slit scanning system. The addition of the Placido disc system in Orbscan II allowed the “shape factor” of the cornea to be evaluated. This offered further information regarding the flattening or steepening of the corneal surface. The combination of the slit scanning and Placido disc systems therefore delivered the advantages of both whilst minimising their disadvantages.

2.2.2 Image production (topography maps)

The image is then analysed against a “best fit sphere”. The benefit of using the best fit sphere technique is that the cornea is being compared against a curved surface. The radius of the best fit sphere is determined by the software and based on an analysis of the corneal curvatures in the population as a whole, with 7.8mm (43.5D) being the average and therefore assigned the colour green. In the topography displays, green areas indicate those which align with the best fit sphere (BFS). Warm colours, red/ orange/yellow indicate areas which are steeper than the BFS and cold colours blue/purple indicate areas which are flatter than BFS. Each best fit sphere is individual to that subject. Since the normal cornea is a prolate ellipse which flattens to the periphery, the periphery will generally appear as blue with the centre varying from green to red. It was observed in the present study that the central corneas appeared in the yellow/orange band prior to the commencement of treatment. In subsequent image captures, following orthokeratology lens wear, the central corneas generally appeared green to blue.

The American Academy of Ophthalmology (1999), in their report on corneal topography, point out that there are two scales used by topographers. The absolute scale in which the colours, step sizes and range are kept constant. This display is the most appropriate for the assessment of change since all maps will use the same scale. A relative scale, in which the range is determined by the flattest and steepest value of the cornea, will vary for each image processed. This image specific form of scaling is inappropriate for the assessment of change. The relative scale may also overemphasise small changes in topography. The Orbscan II uses the absolute form of scaling. The default scales are 5μm for corneal surface elevation maps, 1.0D intervals for the keratometric map and 20μm intervals for the pachymetry maps (Wei, Lim, Chan and Tan 2006)

Tanabe, Oshika, Tomidokoro, Amano, et al (2002) point out that there is no standardised scale for colour coding of the corneal topography maps produced by slit

scanning topographers. They found that in order to assess normality, the anterior and posterior elevation maps should be considered differently. They recommended that the anterior surface should use a 10μm scale for the colour scales whilst the posterior surface should be viewed using a 20μm scale. These scale increments gave the highest sensitivity and specificity for the assessment of normality in a cornea under assessment. As a further confirmation of normality they concluded that corneal topography maps which showed more than three colours, within the central three millimetre zone, should be considered to be abnormal.

Gatinel, Malet, Hoang-Xuan and Azar (2011) looked at the impact of differing corneal asphericity on the best fit sphere results. They found that as the cornea became more aspheric i.e. p value increases, the best fit sphere radius increased. The increase in best fit sphere radius also occurred as the apical radius became steeper. In contrast to this as the apical radius increased the distance between the best fit sphere and the corneal apex decreased. As scale colours are assigned according to the variance between the corneal shape and the BFS, these findings raise concerns about using only the colour maps to assess change in corneal topography.

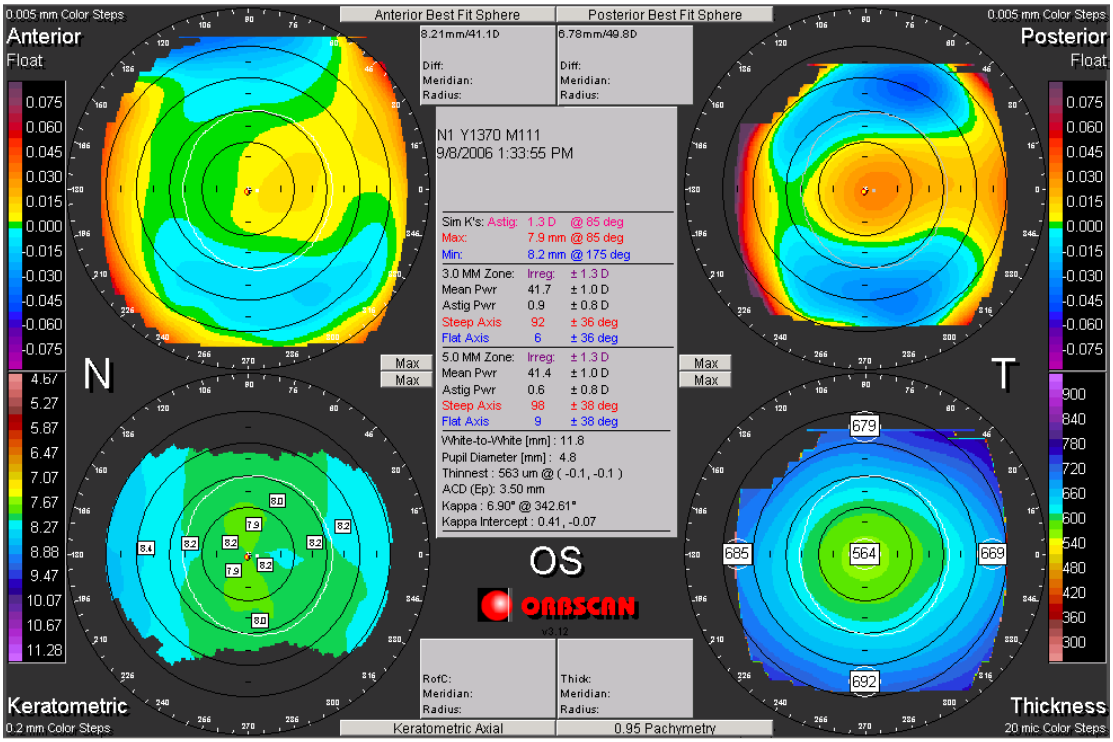


Fig 2.2 Example of a Pre-Fit Orbscan topography of the left eye of subject PV

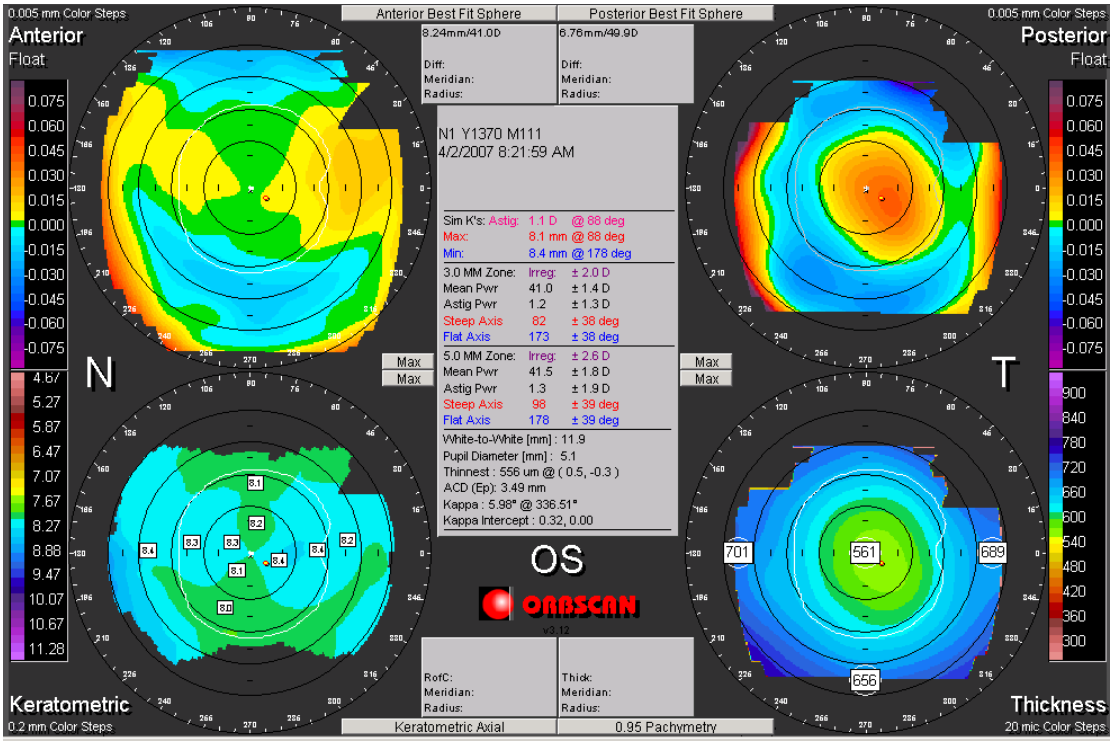


Fig 2.3 Example of a three month post fit Orbscan topography of the left eye of subject PV

Topographical data, both anterior and posterior and corneal thickness measurements are particularly relevant in refractive surgery, orthokeratology and the monitoring of corneal changes in disease processes such as keratoconus. Sonmez, Doan, Hamilton (2007) found that the use of the slit scanning technology of the Orbscan II could assist in the identification of keratoconic individuals particularly when the condition is sub-clinical. Since keratoconus is a contraindication for refractive surgery, accurate identification of patients with the sub-clinical form of the disease would reduce the risk of patients developing keratoconus or other keratectasia in the post-surgical period. Further to this Rao, Raviv, Majmudar & Epstein (2002) investigated individuals who had positive results with either the Rabinowitz[4] or Klyce/Maeda[5] screening methods for keratoconus. They found that comparison of the results for the anterior and posterior elevations and thinnest pachymetry could more accurately predict which of those individuals had the greatest risk of corneal ectasia following corneal refractive surgery.

Liu, Huang & Pflugfelder (1999) in their study developed a set of normal parameters against which corneal topography and thickness results could be evaluated. Although only a small study (94 eyes) they used the 5 patterns previously identified by Naufal, Granet, Hess, Friedlander (1997) as a basis to produce terms of reference for the Orbscan results. They concluded that the topography maps could be used to assess "normality", allowing diseased corneas to be identified more accurately. This was particularly true for conditions affecting the posterior corneal surface since Placido disc topographers produce data for the anterior surface only. Destrempes, Brunette, Meunier, Beyrouthy et al (2002) also proposed the development of a topography-based screening process to identify corneas which have previously undergone LASIK procedures. This was in response to concerns about the use of these corneas in any future corneal transplant surgery.

[4] Rabinowitz screening method uses two indices the central K and the I-S index Rabinowitz (1995)
[5] Klyce/Maeda screening method uses the KCI index Naoyuki (1994)

Leyland (2004) looked to validate the measurement of posterior corneal curvature using the Orbscan II with respect to the calculation of intraocular lens (IOL) power. Calculation of the IOL power can be a problem in eyes which have previously undergone some form of refractive surgery. Traditionally the IOL power was calculated by measuring the anterior corneal curvature and making an assumption about the relationship between the anterior and posterior corneal surfaces. The structure could then be considered as a single refracting surface and not treated as a "thick lens". Once the anterior surface has been altered in refractive surgery then this relationship no longer applies. Using 15 normal corneas a comparison was made between corneal power calculations following the traditional method and those found by measuring the posterior corneal surface and then using the "thick lens" formula. Leyland found that there was close correlation between the two methods if the anterior surface keratometry was measured by a Javal-Schiotz keratometer and not the simulated K's generated by the Orbscan II. The reverse applied when used on corneas which had previously undergone laser refractive surgery when Orbscan simulated K's (SimK) were more accurate than keratometry.

Cairns and McGhee (2005) in their review paper noted that as yet there is no peer reviewed data available for the reproducibility of posterior surface measurements. They advise caution in the evaluation of images where data is missing due to eyelids, eyelashes, reflections etc. Orbscan II defaults are set to create a best fit sphere over the whole anterior surface, where peripheral, flatter data is missing the resulting Best Fit Sphere (BFS) will be steeper than expected. Maldonado et al (2006) looked at both the repeatability and reproducibility of the posterior corneal curvature after LASIK. For the purposes of repeatability 10 images were taken from each of 22 LASIK patients, all the readings were taken at the same session by the same individual. They found the repeatability coefficient ($1.96 \times s_{w,}$ where s_w is the standard deviation of the mean of the 10 readings) for the posterior best fit sphere to be 0.09 with 95% confidence intervals (0.08 -0.10). The intra-class correlation co-efficient for this series was found to be 0.98

(0.96 -0.99 95% confidence limits). Whilst these results appeared to show excellent repeatability, the accuracy of the measurements cannot be confirmed because there is currently no validated standard to compare them with.

Quisling, Goins, Sutphin, Sjoberg et al (2006) compared the posterior corneal surface topography of keratoconic individuals using the Orbscan II and the Pentacam. Their findings showed a statistically significant difference in the posterior elevations above the best fit sphere despite no difference in the radii of curvature of the sphere. The Orbscan II recorded the best fit sphere above that of the Pentacam. They postulated that the difference in the elevations may be a result of the two methods used to measure the cornea i.e. slit scanning versus Scheimpflug technology. This small study was unable to say which of the two methods was the correct one and recommended further investigations using standardised test objects.

2.2.3 Pachymetry

There have been several studies which have looked at the accuracy and repeatability of pachymetry measurements using the Orbscan II. Van de Pol and Salmon (2001) found that corneal shape and curvature had no significant effect on the repeatability of pachymetry measures. They did find that central corneal measures were more repeatable than those for the periphery. These findings are confirmed by Jonuscheit and Doughty (2007) who found a mean correlation of variance of 0.77% for the 1mm central zone which fell to 0.86% if the central point only was considered. This fell further to 1.0% if the peripheral cornea was considered beyond 2.5mm radius both temporally and nasally. Poor repeatability was felt to be due to lack of available data at the extremes of the corneal diameter i.e. 4 – 4.5mm from the corneal centre. Cho et al (2002b) in their study reported that not only was central corneal pachymetry more repeatable than the periphery, further examination of the peripheral results showed that the superior periphery was the least repeatable. They also found that in order to have a precision of 2% for the central cornea no more than 2 readings were required whilst 1

reading gave rise to a precision of 3%. Since they looked only at the repeatability of measurements it is not possible to give the degree of accuracy as no corroborative measurements were taken.

In contradiction to this, Fam, Lim and Reinstein (2005) found that the vertical peripheral measures were more repeatable than the horizontal measures with the greatest repeatability occurring over an area of 3.0mm horizontal and 4.0mm vertical diameters. They suggest that one reason for the improvement in repeatability in the vertical periphery is due to the vertical slits used by the Orbscan II. Yaylali, Kaufman & Thompson (1997) also found that the Orbscan II showed repeatability comparable to that of ultrasound pachymetry, often considered the “gold standard”, but that differences between the two measures were statistically significant such that the two results were not interchangeable.

Several studies have found that Orbscan pachymetry measures are consistently greater than those found by ultrasound and have suggested that this is due to the acoustic factor value found in the Orbscan software. Prisant, Calderon, Chastang, Gatinel et al (2003) compared results using the default acoustic factor of 0.92 finding an underestimation of the ultrasound results. An adjustment of the factor to 0.946 compensated for this.

Lackner, Funovics, Skorpik, Scmidinger et al (2005) produced similar results and noted that whilst the Orbscan, Pentacam and ultrasound showed excellent repeatability it was not possible to say which of them was closest to the “true value” since all three systems showed “systematic and random errors” from each other. Liu et al (1999) suggest that the reason for the difference between the ultrasound and the Orbscan results was as a result of the Orbscan including the mucous layer in the thickness measure. This would account for a 40µm difference between the readings. As the ultrasound pachymeter makes contact with the corneal surface the mucous layer is bypassed. Gonzalez-Mejome, Cervino, Yebra-Pimentel & Parafita (2003) found that the application of the acoustic factor across the whole cornea was inappropriate; this is

particularly true for thicker corneas (> 576µm). They suggest that further investigation is required to establish new algorithms and that until then, correction factors for each corneal location and each corneal thickness would need to be applied.

2.3 Previous Orbscan Repeatability Studies

2.3.1 Anterior

Few studies have looked at the repeatability of the Orbscan in relation to the assessment of anterior corneal topography. In those studies which have been reported, the majority have evaluated the Orbscan's accuracy and repeatability using test surfaces. Beyrouthy, Brunette, Horner, Munger et al (2001) used black PMMA spheres to evaluate accuracy and repeatability between Orbscan instruments. Intra-class correlation coefficients for radii were found to be 0.96 and for asphericity 0.91. Cairns, McGhee, Collins and Owens et al (2002) also measured opaque black PMMA spheres supplied by the manufacturers of the Orbscan and a second series of black spheres made from a research material. This second material was also PMMA with an infused black dye, giving rise to a semi-transparent material. The results showed that the Orbscan could more accurately measure the opaque material rather than the translucent one. Cairns suggests that the Orbscan is at its most accurate when measuring surfaces which scatter light evenly across the surface. This is obviously not true for the cornea and must therefore be a source of potential error in any investigation of the repeatability of corneal topography measurements by the Orbscan. Gonzalez Perez, Cervino, Giraldez, Parafita et al (2004) used calibrated steel balls in their study of the accuracy and precision of the EyeSys and Orbscan systems. They found that the EyeSys system was more accurate than the Orbscan on these steel balls. In light of the Cairns study this may be as a result of the light scatter across the surface and the different measurement processes for the two instruments. Douthwaite and Mallen (2007) found that the Orbscan under read when compared with the EyeSys system on both test surfaces and corneas. Whilst the apical radius and p-value measurements were found to be statistically significantly different from each other, they conclude that clinically they may not be. The repeatability of both instruments as defined by Bland and Altman (1999) was found to be comparable.

Rabsilber, Becker & Auffarth (2005) assessed the reliability of the Orbscan measurements with respect to various refractive conditions. Their study agreed with the previous findings that reliability decreased as the more peripheral aspects of the cornea were evaluated. This was particularly apparent when the results from individuals with hypermetropia were compared with the emmetropic control group. They note that the hypermetropic group were not age matched with the control group and suggest that one possible explanation for their findings could be related to the age of the subjects and therefore not a lack of reliability in the Orbscan. Cho, Lam, Mountford & Ng (2002) compared the performance of four corneal topographers including the Orbscan. They excluded the results from the Orbscan from their final analysis because of the poor repeatability and reproducibility. Two readings were taken by the same examiner at the same session in order to assess repeatability with a further reading on another day being used to assess reproducibility. This study was looking particularly at the use of topographers for the fitting of orthokeratology lenses which require a measurement precision of 0.01mm BOZR or 2μm elevation data. Cho calculated the minimum number of readings required to deliver the measurement precision required using the standard error formula.

$$\mathbf{SE} = \mathbf{SR}/\sqrt{\mathbf{n}}$$

where

S_E is the standard error

S_R is the repeatability standard deviation

n is the number of readings taken

The findings from the study were that 552 readings were required for the Orbscan to deliver this degree of precision.

Buehren, Davis, Lingelbach, Collins et al (2001) reported on the influence of the tear film stability in the post blink period on corneal topography. Using subjects with tear break up times (TBUT) of between 9 and 36 seconds they found that the superior and inferior corneal topography (2-4mm from the corneal centre) can change significantly over the course of the time taken to acquire the images. Nemeth et al (2001) although using the TMS corneal topographer, found that even a short pause in blinking could affect the corneal topography. Since most patients are asked to stare wide immediately prior to image capture then variance in the tear film could influence the repeatability and reproducibility of Orbscan measures. This effect is further supported by Liu et al's (1999) suggestion that the Orbscan evaluates the pre-corneal mucous layer.

2.3.2 Posterior repeatability

Swarbrick (1998) and Alharbi and Swarbrick (2003) have stated that the refractive effects of orthokeratology are achieved as a result of changes in the epithelium. In both papers they apply the Munnerlyn formula to the refractive change seen in orthokeratology. The formula assumes that the posterior cornea is not involved in the refractive change seen in corneal refractive surgery. Alharbi and Swarbrick concluded that as the change in corneal sag seen in their orthokeratology study matched the calculated sag using the Munnerlyn formula there should be no effect on the posterior surface of the cornea. Owens and Garner (2004) have challenged the findings of Alharbi and Swarbrick in their study. They found that the posterior corneal surface flattened significantly at one week of orthokeratology lens wear. In order to establish any change in the posterior cornea amongst the participants in the current study we evaluated the repeatability of measures of the posterior apical radius and p value using the Orbscan II corneal topographer. The number of measures required to produce an accurate evaluation of the shape of the posterior cornea were also investigated. A number of investigators have questioned the accuracy of the Orbscan II both for assessment of the anterior surface ((Beyrouthy et al, 2001, Cairns et al, 2002,

Gonzalez Perez et al, 2004, Cairns et al, 2005, Douthwaite and Mallen, 2007, Cho et al., 2002) and posterior surfaces of the cornea. ((Leyland, 2004, Cairns and McGhee, 2005, Quisling et al., 2006, Maldonado et al., 2006)) Leyland concluded that Orbscan II is an appropriate instrument to use in the assessment of the posterior corneal surface for the calculation of IOL lens power. Both Cairns and McGhee (2005) and Quisling et al (2006) advise caution in the use of Orbscan II for the assessment of the posterior surface. Cairns and McGhee (2005) particularly point out that there are currently no studies on the reproducibility of the posterior corneal surface using the Orbscan. Maldonado, Nieto, Diez-Cuenca, Pinero (2006) stated that the Orbscan measures of the posterior cornea were repeatable but could not comment on the accuracy of the values as there was no accepted norm at that time.

The second study, using posterior corneal data from the twenty participants recruited for the anterior study, was completed to look at the validity and precision of the posterior measurements.

2.4 Orbscan Repeatability

It was hoped that this repeatability study would address the concerns about the Orbscan raised by Cho et al (2002).

2.4.1 Anterior repeatability on corneas

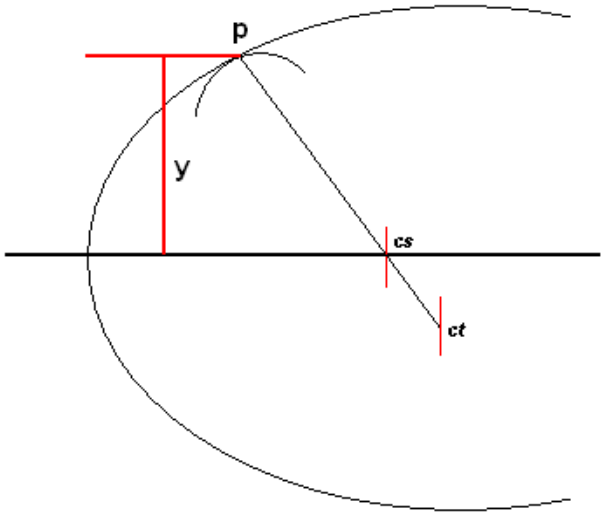
2.4.1.1 Method

Twenty healthy participants were recruited from within the Bradford School of Optometry and Vision Science. The subjects comprised 14 females and 6 males aged 21 – 43 years, median 27.5. Participants were treated in accordance with the tenets of the Declaration of Helsinki and informed consent was obtained. These participants were not involved in the subsequent study into the effects of orthokeratology on the cornea. Ten independent measures of the cornea were made on the twenty participants by the same investigator. The measures for each individual were taken at the same sitting. To avoid any inter eye bias only measurements from the right eyes of the participants were used.

In accordance with the manufacturer's instructions, the left eye was occluded and participants were asked to view the fixation target in the centre of the Orbscan placido disc image. As image captures take approximately five seconds, during which time the subject should not blink, participants were asked to take three good blinks prior to image capture. The image of the Orbscan's placido disc rings in the participant's cornea could be seen on the computer screen display. Image captures were only made once all of the rings were clearly imaged in the cornea. This minimised any loss of image quality due to tear film effects (Buehren et al., 2001). As the upper lid can restrict the acquisition of data in the vertical meridian of the images, individuals were asked to stare wide following the three good blinks. Participants were repositioned on the chin rest between each image capture.

Once all the images had been acquired, image analysis commenced. Global measures of the cornea (mean of all meridians) are available via the View/ Elevation/ Anterior selected/ Aconic route in the Orbscan software menu. To allow global analysis the corneal zone selected was from 2.6 to 7.0mm diameter. The Orbscan software gives the apical radius and the p value for the global mean. The Orbscan actually lists the p value as the shape factor, which is contrary to recommendations from the British Standards Institute (2005).

After consultation with Orbtek Research (Feldkirchen, Germany) access was given to additional software, which is not available in the standard Orbscan package. This allows the raw data for each image to be obtained. Image data for each capture was obtained via the Tools/ Statistics/ Recorder/ Anterior Axial route in the software menu. The raw data obtained consists of the saggital radii (r_s) and perpendicular distance (y) for a number of points on a selected corneal meridian Fig 2.4



Sagittal radius (rs) = p*cs*

Tangential radius (rt) = p*ct*

At point p a distance y from the major axis

Fig 2.4 Diagram to illustrate the relationship between the sagittal and tangential radii.

For the Orbscan the tangential radius is referred to as the meridional curvature and the sagittal radius as the axial curvature. For a prolate ellipse, such as the cornea, the tangential radius will always be longer than the sagittal.

In this case sixteen points along the flattest meridian, as indicated by the keratometry results, were selected for analysis. The zone chosen for the single measure analysis was from 2.5 – 7.0mm. The 7.0mm diameter allows the capture of sufficient data but avoids potential interference from the more peripheral cornea where the profile ceases to follow a conic section. It was possible to examine the 7.0mm vertical diameter in all participants. The vertical meridian is most susceptible to the loss of data due to the upper lid position. This potential loss of data was managed by requesting that participants stare wide during image capture. The inner diameter (2.5mm) was chosen to avoid lack of precision from the smallest placido disc ring images. These small ring images will show only minimal changes if there is a variation in either radius or p value. These small changes will not have the precision seen in the larger rings.

Having obtained the sagittal radii (r_s) and perpendicular distance (y) from the computer display the apical radius (r_0) and p value can now be calculated. The relationship between r_s, y, r_0 and p is shown in an equation derived by Bennett (Bennett, 1988)

$$r_s^2 = r_0^2 + (1-p)\, y^2 \qquad \text{Eq. 2.1}$$

where:

r_0 and p are therefore constants of the surface section.

If r_s^2 is plotted against y^2 this will generate a straight line. R02 is the intercept on the y axis, when y = 0 and the slope of the line is 1-p. It is possible therefore to describe the surface section in mathematical terms. A typical result of an r_s^2 against y^2 is shown is shown in Fig 2.12a Concerns have been raised in the past about asymmetry between the two semi meridians of the cornea. Douthwaite (2003) showed that this asymmetry occurred as a result of the tilt of the cornea with respect to the optical axis of the instrument being used to measure the corneal topography. The effect of the tilt can be eliminated by averaging the two semi meridians (Fig 2.12b).

2.4.2 Posterior repeatability on corneas

2.4.2.1 Method

The images from the twenty participants recruited for the anterior repeatability study were reanalysed to evaluate the repeatability of the posterior apical radius and p value. The analysis was completed following the methods described previously (Douthwaite and Parkinson, 2009). In this study global measures of the posterior cornea (mean of all meridians) were retrieved via the View/ Elevation/ Posterior selected/ Aconic route in the menu. To allow global analysis the corneal zone selected was from 2.6 to 7.0mm.

Using the software referred to in the previous section on the anterior apical radius and p value, the raw data for each image was obtained. This allowed the analysis of a single meridian. The zone chosen for the single measure analysis was from 2.5 – 7.0mm. This aligned with the zone chosen for the posterior global measure and is in accordance with the previous study of the anterior measures by Douthwaite and Parkinson (2009). In the case of the posterior surface study the 180^0 meridian was selected to allow maximum data points to be recorded. Cairns and McGhee (2005) cautioned about using images with missing data for analysis. The image data was retrieved via the Tools/ Statistics/ Recorder/ Posterior Axial route in the software menu. The sagittal radii and perpendicular distances for sixteen points across the horizontal meridian were obtained. The apical radius and p value for each of the ten posterior surface images of the twenty participants were calculated using the method described for the anterior surface (Douthwaite and Parkinson 2009). Once all the data were retrieved they were analysed following the same procedures indicated in the anterior study (Section 2.5.1).

2.4.3 Posterior repeatability using test surfaces.

A number of researchers have looked at the anterior surface repeatability using test surfaces (Beyrouthy et al 2001; Cairns et al 2002; Gonzalez-Perez 2004; Douthwaite & Mallen 2007). There are no reports of posterior surface analysis using surfaces.

2.4.3.1 Method

Two series of rigid contact lenses were ordered. The parameters for the first series are detailed in a later section in which the procedure for verification of the orthokeratology lenses is described. As the posterior corneal radius is steeper than that of the anterior a second series of steeper monocurve lenses was ordered (Table 2.7). In order to mimic a corneal surface more closely three of the lenses in this second series were ordered with a central thickness of 0.5mm, all the other lenses were 0.22mm central thickness. Three independent measures of the back optic zone radii were made using a radiuscope. The results are also shown in Table 2.7.

In order to obtain measurements from the Orbscan the lenses were mounted in a custom built wet cell filled with normal saline. Two wet cells were produced to allow the two different diameter lenses to be appropriately positioned. The lenses were sealed into the wet cell using Blutack©. This temporary adhesive allowed the lenses to be exchanged but provided an adequate seal to prevent leakage of the saline. This wet cell was then positioned in line with the measurement axis of the Orbscan.

The Orbscan was set to measure test surfaces and ten independent measures of each of the sixteen lenses were made. Bland Altman plots were produced to examine the difference between the radiuscope measurements and the Orbscan.

2.5 Orbscan Repeatability Results

2.5.1 Anterior

2.5.1.1 Global measure

A repeated measures ANOVA for the global measures of the twenty participants showed they were not statistically different; anterior radius ($F_{(9,171)} = 0.905$, $P = .523$) and shape factor ($F_{(9,171)} = 0.923$, $P = .507$). As the same method of measurement is being applied to the ten measures this statistical result is as expected. It is possible to examine repeatability by investigating the difference between measures. The true measure of the anterior apical radius (r_0) and shape factor are unknown but we could use the mean of a number of measures as being indicative of the true value. In this study the mean of the ten measures was taken as the best estimate of the true value for the anterior apical radius and p value. By examining the difference between the individual measure and the mean of ten we can assess the error in each of the individual measures.

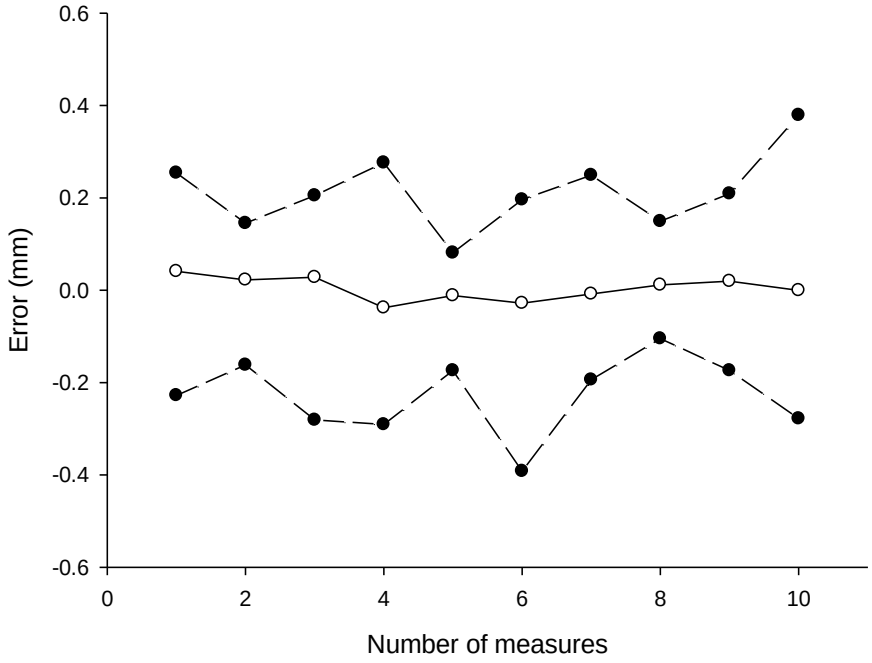
A series of running averages were also calculated in which measure one was the same as before, measure two the mean of two measures, etc., until the final measure was the mean of ten measures. The difference between the mean of ten and each of the other mean measures should indicate the error of each of the running average measures. These error measures were calculated by subtracting the mean of ten measures from each of the other means. Since the mean of the ten running averages and the mean of the ten measures will be the same then the error in this case will be zero. The same analyses were applied to the global p value measures.

Figs 2.5 and 2.6 show the results for the apical radius and p value for the global measure for both the repeated measurements and the running average. As only twenty individuals were evaluated the non-parametric statistical measures of median and

range were used to indicate the maximum error for an individual rather than the mean and standard deviation which indicate the extent of the error for the group.

One concern with the use of the global analysis of the Orbscan is the inclusion of all meridians in the analysis. A number of studies have shown that the anterior corneal shape varies between the two meridians; horizontal and vertical (Eghbali, Young, Maloney 1995; Douthwaite et al 1999; Douthwaite 2003). Analysis of the raw data for the flattest meridian should overcome the concerns raised by the global measure data. The flattest meridian was that identified by the keratometry result provided by the Orbscan.

a)



b)

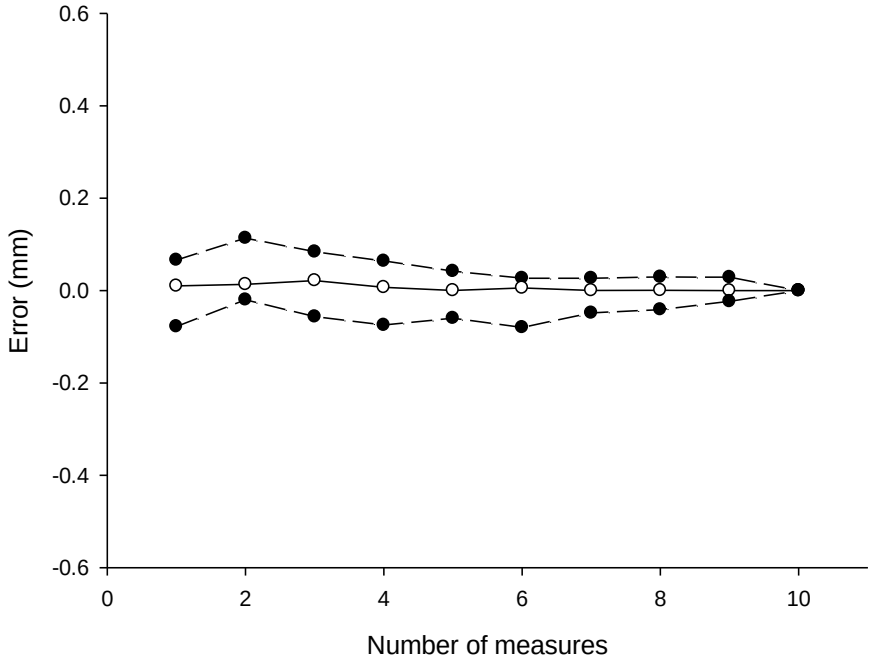
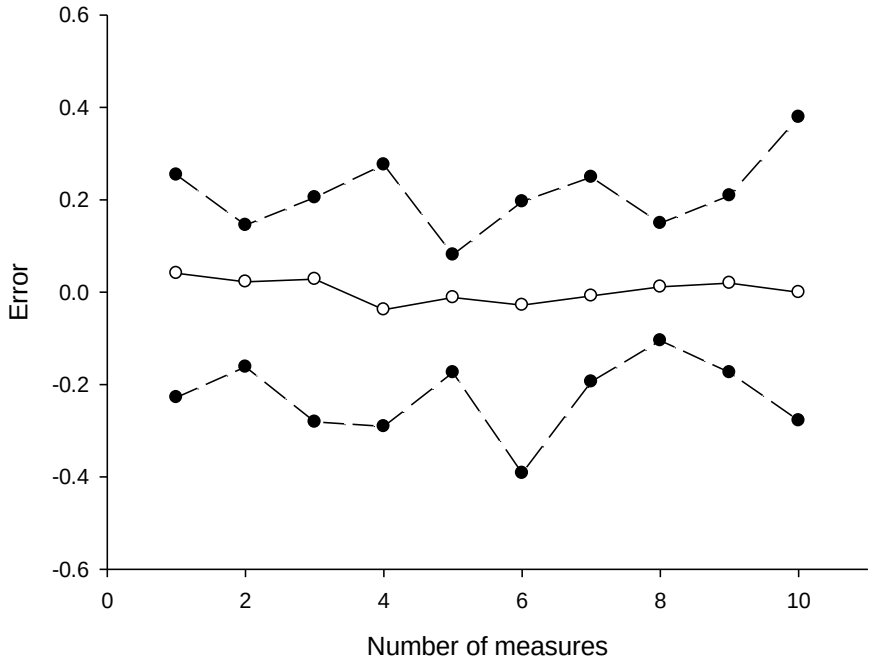


Fig 2.5 The apical radius measurements of the surface. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

a)



b)

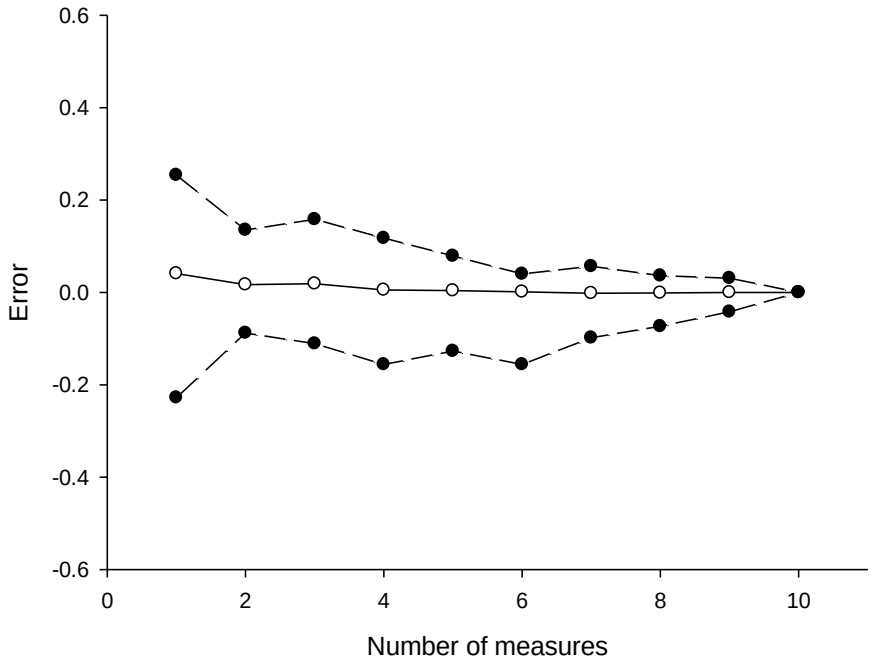
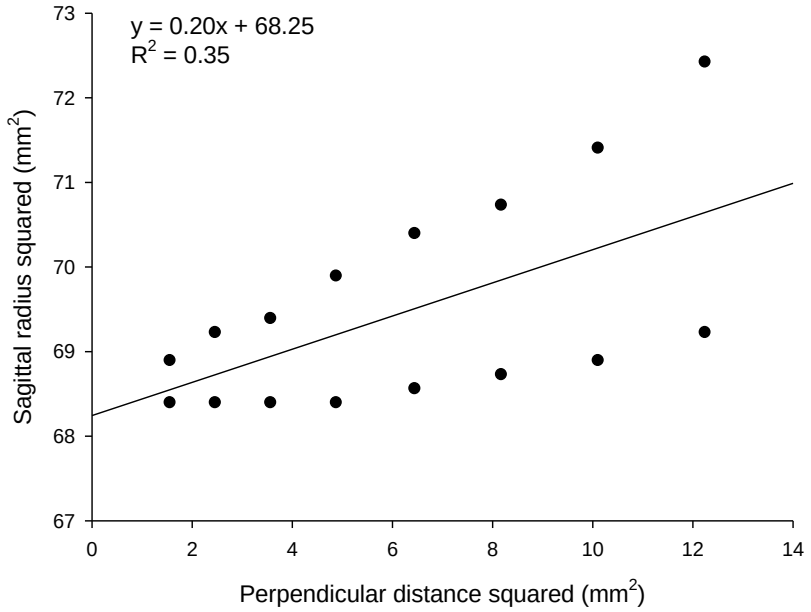


Fig 2.6 The shape factor measurements of the surface. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

2.5.1.2 Single meridian

As shown in Fig 2.7 a scatterplot of the averaged values of the sagittal radii (r_s^2) of the two semi-meridians and the perpendicular distance (y^2) from the corneal apex were obtained for each individual measure. The averaged points lie on a straight line whose equation allowed the apical radius and p value to be calculated using equation 2.1. The results for the example shown in Fig 2.7 are apical radius (r_0) 8.26mm and p-value 0.80. The coefficient of determination of 0.98 indicates that this corneal section approximates closely to that of a conic section. The coefficient of determination R^2 was also found for each of the scatterplots. The R^2 value indicates how well the selected corneal meridian follows a conic section. The lowest R^2 value for any anterior measure was 0.88. The same analyses outlined in the global analysis section were applied to the single meridian data. The results for the apical radius (r_0) and p value repeated measurements and running averages are shown in Figs 2.8 and 2.9.

a)



b)

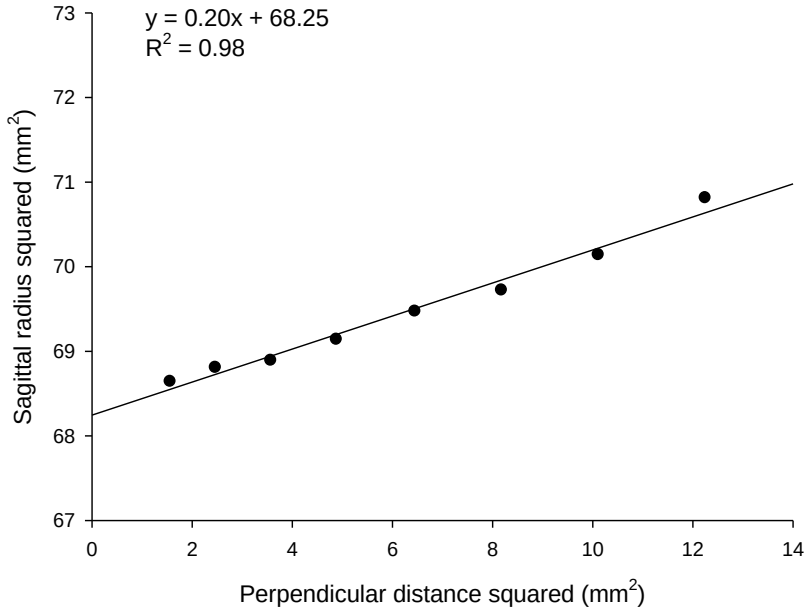
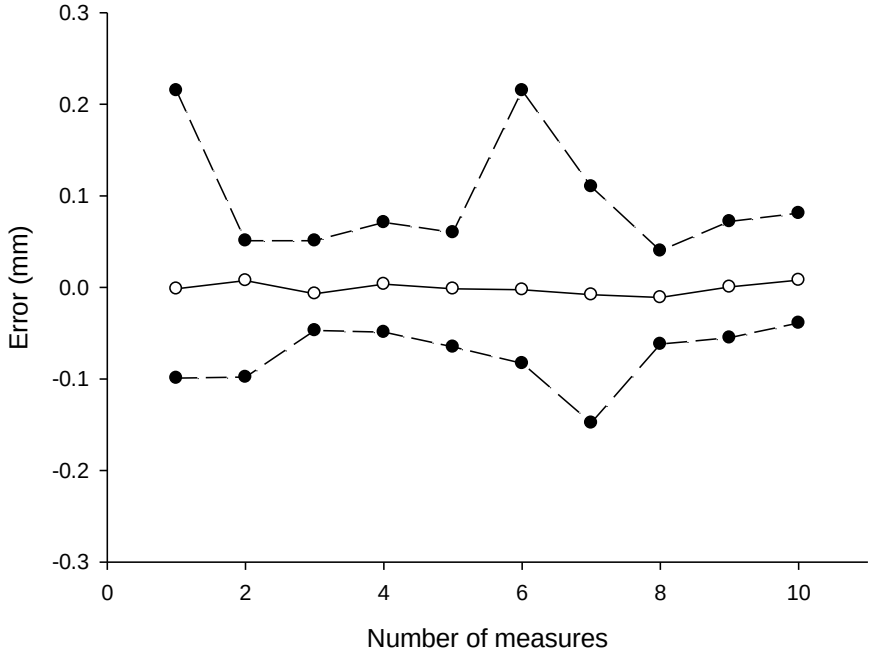


Fig 2.7 Scatterplot of sagittal radius squared versus perpendicular distance squared on the near horizontal principal meridian of the right cornea of subject HB. a) illustrates semi-meridian asphericity, b) illustrates the result when semi-meridian averaging is applied.

a)



b)

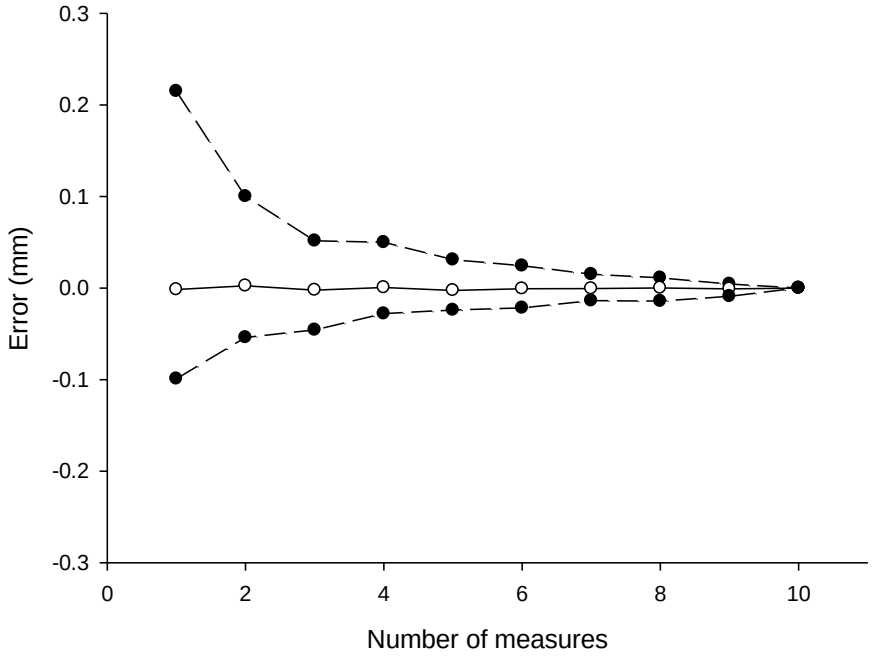
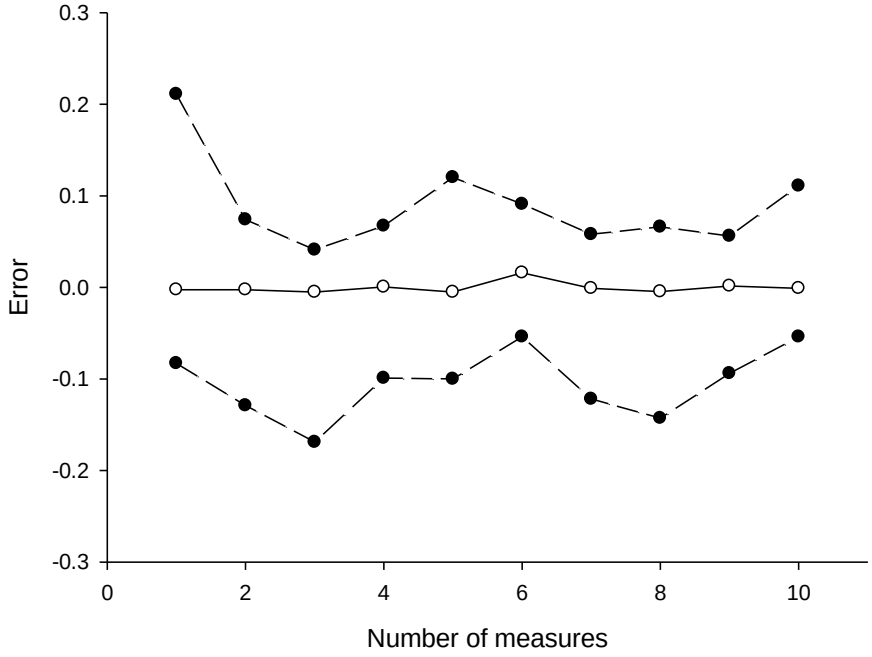


Fig 2.8 The apical radius measurements of a single meridian. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

a)



b)

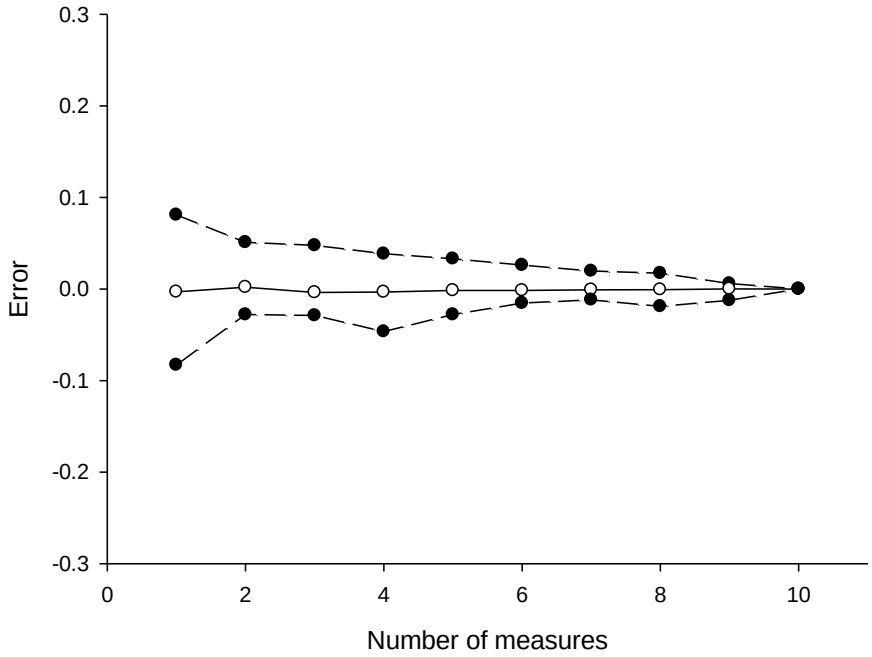


Fig 2.9 The p-value measurements of a single meridian. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

Another method to examine repeatability is to compare a single measure against the measurement provided by the mean of a number of measures. These results are shown in Table 2.3 where the difference between measure 1 and measure 6 was compared with the difference between the mean of measures 1 - 3 and 6 - 8 and these two results were compared with the difference in the mean of measures 1- 5 and 6 - 10. For a sample which has a normal distribution the British Standards Institute (2005) recommend that the repeatability be defined as twice the standard deviation of the differences. An investigation of the errors in the r_0 and p values, for both the global and single meridian analysis, using the Kolmogorov-Smirnov d test showed that they were not statistically significantly different form a normal distribution.

Table 2.1 Comparison of the repeatability of the global analysis based on the difference between measures

	Mean	Standard deviation
Apical radius (mm)		
M1-M6	-0.035	0.119
(M1+M2+M3)/3 – (M6+M7+M8)/3	-0.019	0.045
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	-0.002	0.041
Shape factor		
M1-M6	-0.056	0.178
(M1+M2+M3)/3 – (M6+M7+M8)/3	-0.022	0.075
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	0.004	0.077

Table 2.2 Comparison of the repeatability of the single meridian based on the difference between measures

	Mean	Standard deviation
Apical radius (mm)		
M1-M6	0.010	0.095
(M1+M2+M3)/3 – (M6+M7+M8)/3	-0.003	0.034
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	0.001	0.031
Shape factor		
M1-M6	0.005	0.058
(M1+M2+M3)/3 – (M6+M7+M8)/3	0.000	0.025
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	0.001	0.030

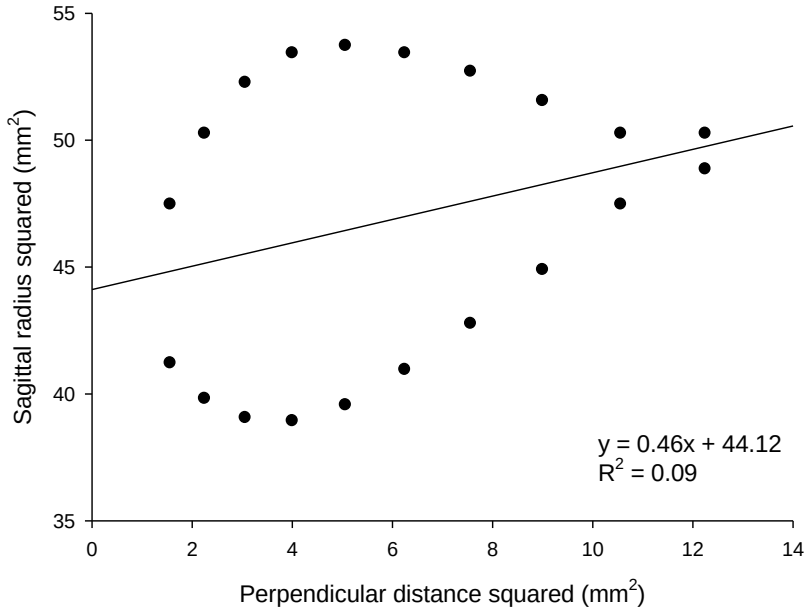
Table 2.3 Repeatability

Orbscan Global measures		Single meridian	
Apical radius (mm)		Apical radius (mm)	
Single measurement	0.239	Single measurement	0.190
Mean of three measurements	0.090	Mean of three measurements	0.069
Mean of five measurements	0.083	Mean of five measurements	0.061
Shape factor (asphericity)		p value (asphericity)	
Single measurement	0.356	Single measurement	0.116
Mean of three measurements	0.151	Mean of three measurements	0.051
Mean of five measurements	0.155	Mean of five measurements	0.060

2.5.2 Posterior repeatability on corneas results

The straight line equation for the scatterplot Fig 2.10 is y = 0.48x + 43.86. This gives the apical radius as 6.62 mm and the p-value is 0.52. The coefficient of determination (R^2) of 0.99 indicates that this corneal section approximates closely to that of a conic section. Critical value tables for Pearson correlation coefficient were consulted to find the appropriate R^2 value. This showed the critical value of r for a two tailed t test with nine degrees of freedom is 0.602. This gives a value for R^2 of 0.36. This is in contrast to the anterior surface measures where R^2 was not less than 0.88 for any measure. Any measurement with an R^2 value below 0.36 was removed from the analysis. Fifteen measurements were removed from the 200 measurements taken. The greatest number of measurements eliminated for any one individual was four.

a)



b)

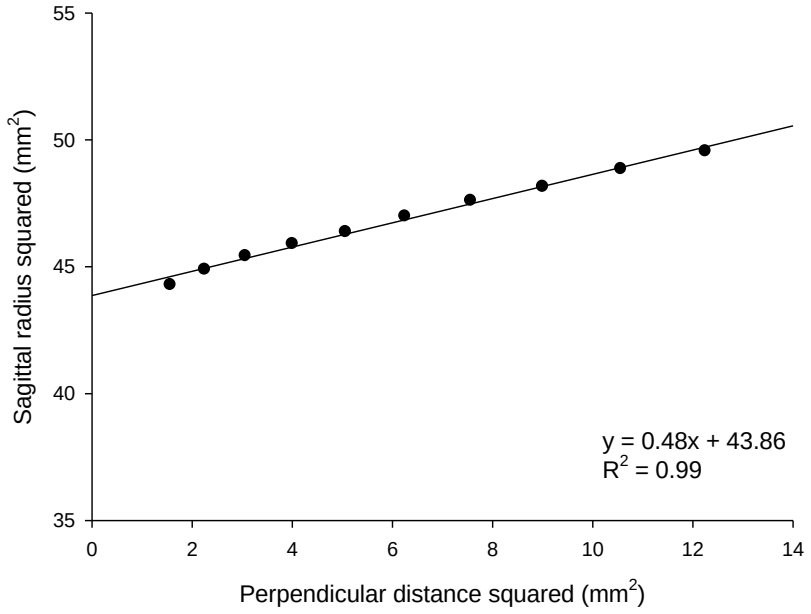


Fig 2.10 Scatterplot of sagittal radius squared versus perpendicular distance squared on the near horizontal principal meridian of the right cornea of subject MC. (a) illustrates semi-meridian asphericity, (b) illustrates the result when semi-meridian averaging is applied.

2.5.2.1 Global measure

A repeated measure ANOVA of the posterior results for the Orbscan global analysis showed no statistical difference between the ten measures for the twenty participants posterior radius ($F_{(9,171)}$ =0.528) and shape factor ($F_{(9,171)}$ = 0.615). This is consistent with the findings for the anterior surface. The mean of the ten measurements was again taken to give the best estimate of the value for the posterior radius and shape factor. The difference between the mean of ten measures and each individual measure is shown in Fig 2.11 for the posterior apical radius and shape factor. Fig 2.12 shows the running average measurement errors for the Orbscan global results for the same measurements.

The individual images were re-evaluated using the additional analysis software so that data from only the horizontal meridian (180^0) could be included.

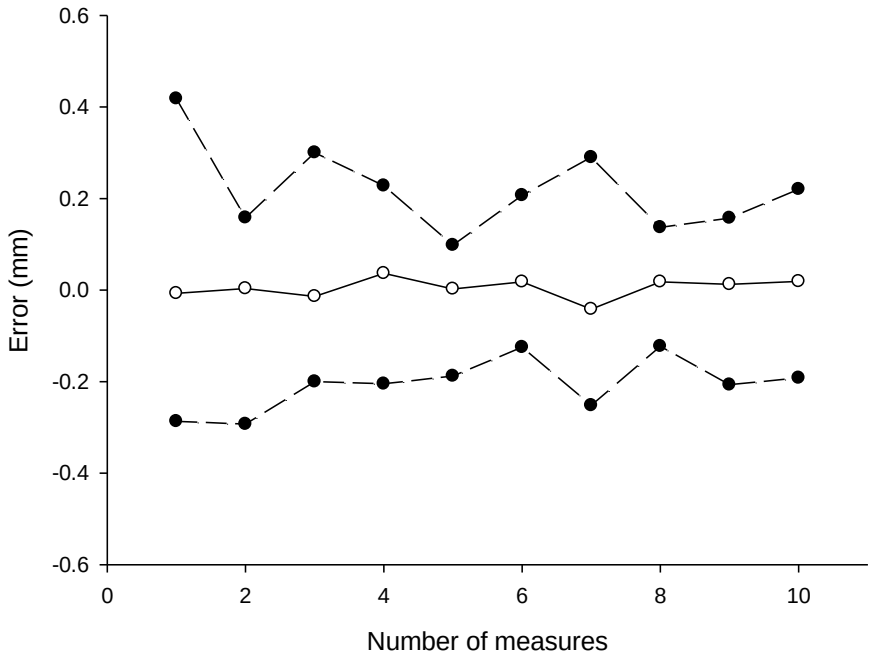
Table 2.4 Comparison of the repeatability of the global analysis of the posterior cornea based on the difference between measures

	Mean	Standard deviation
Apical radius (mm)		
M1-M6	-0.009	0.137
(M1+M2+M3)/3 – (M6+M7+M8)/3	0.001	0.080
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	0.004	0.067
Shape factor		
M1-M6	0.008	0.188
(M1+M2+M3)/3 – (M6+M7+M8)/3	-0.013	0.119
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	0.005	0.101

Table 2.5 Comparison of the repeatability of the single meridian of the posterior cornea based on the difference between measures

	Mean	Standard deviation
Apical radius (mm)		
M1-M6	-0.008	0.298
(M1+M2+M3)/3 – (M6+M7+M8)/3	0.046	0.116
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	-0.007	0.088
Shape factor		
M1-M6	-0.069	0.410
(M1+M2+M3)/3 – (M6+M7+M8)/3	0.048	0.185
(M1+M2+M3+M4+M5)/5 – (M6+M7+M8+M9+M10)/5	0.001	0.144

a)



b)

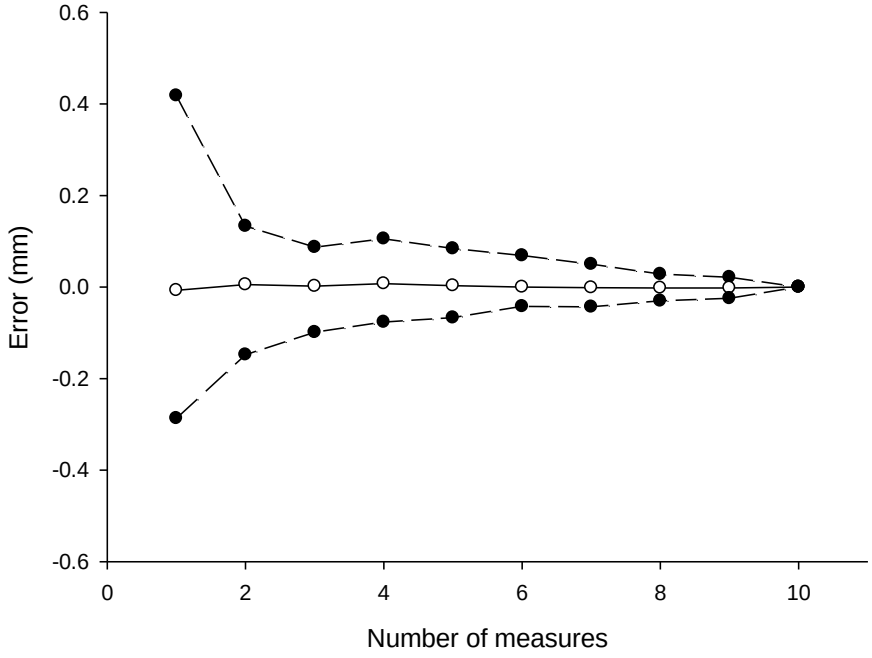
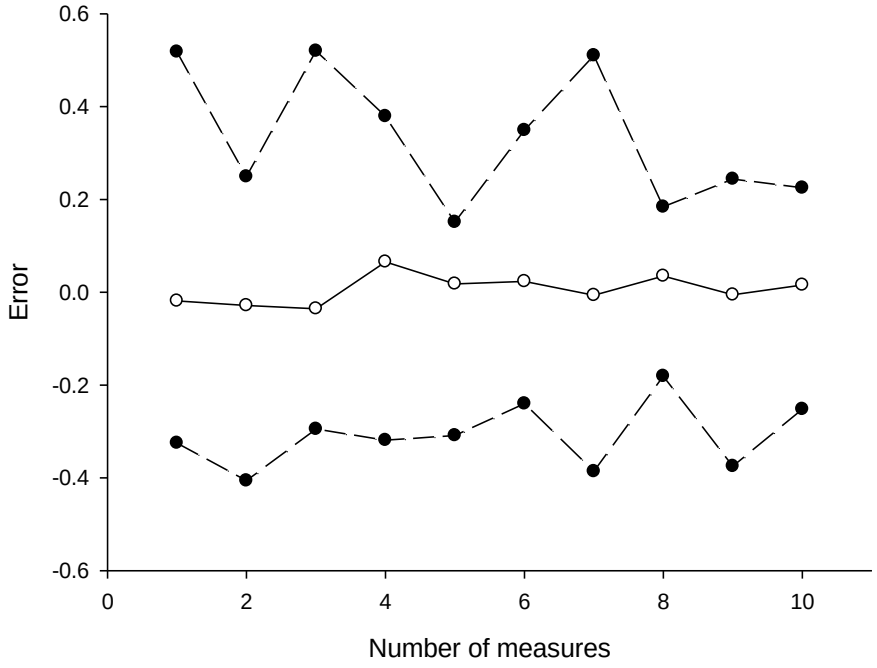


Fig 2.11 The apical radius measurements of the surface. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

a)



b)

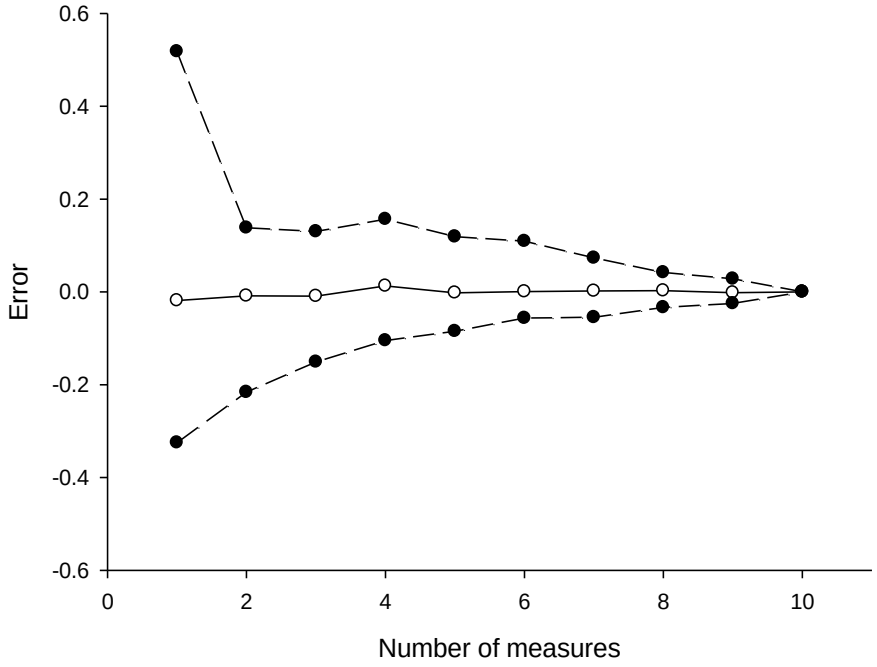


Fig 2.12 The shape factor measurements of the surface. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

2.5.2.2 Single meridian

The sagittal radii (r_s) and perpendicular distance (y) were analysed using scatterplots as detailed in the results for the anterior study. The horizontal meridian results were then analysed as previously described for the global analysis. The results are shown in Fig 2.13.

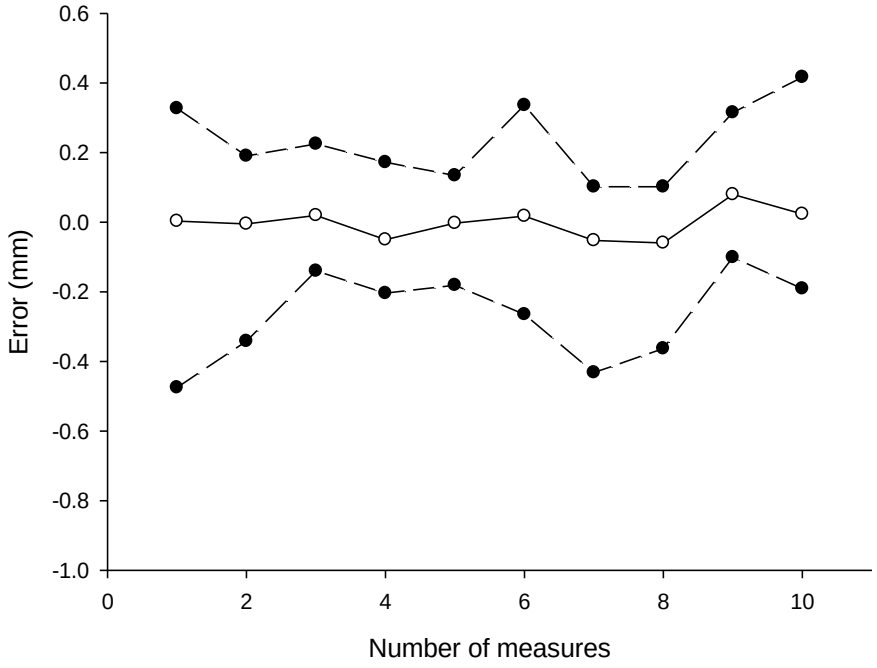
The error values for the posterior apical radius and p value for both the global and single meridian measurements were analysed to confirm that they were part of a normal distribution. This would follow the British Standards Institute recommendation that repeatability may be defined as twice the standard deviation of the mean. The Kolmogorov- Smirnov d test shows that the error results for the global and single meridian posterior radii and p values are not statistically different from a normal distribution. The repeatability of the posterior measures are shown in Table 2.6.

The same repeatability analysis applied to the anterior surface was applied to the posterior measures (Table 2.6)

Table 2.6 Repeatability of the posterior corneal measurements

Orbscan Global measures		**Single meridian**	
Apical radius (mm)		Apical radius (mm)	
Single measurement	0.274	Single measurement	0.596
Mean of three measurements	0.160	Mean of three measurements	0.232
Mean of five measurements	0.134	Mean of five measurements	0.176
Shape factor (asphericity)		p value (asphericity)	
Single measurement	0.376	Single measurement	0.820
Mean of three measurements	0.238	Mean of three measurements	0.370
Mean of five measurements	0.202	Mean of five measurements	0.288

a)



b)

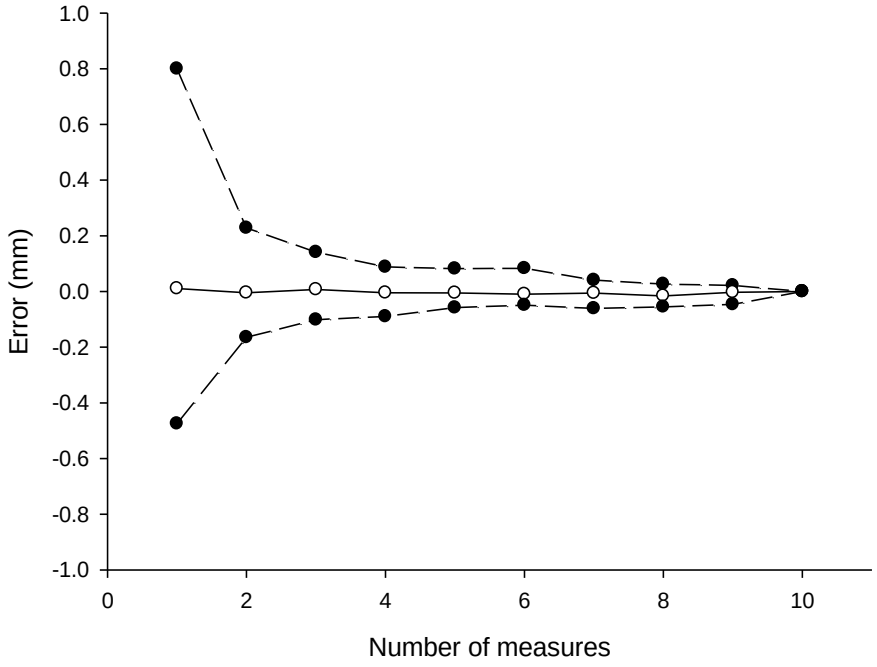
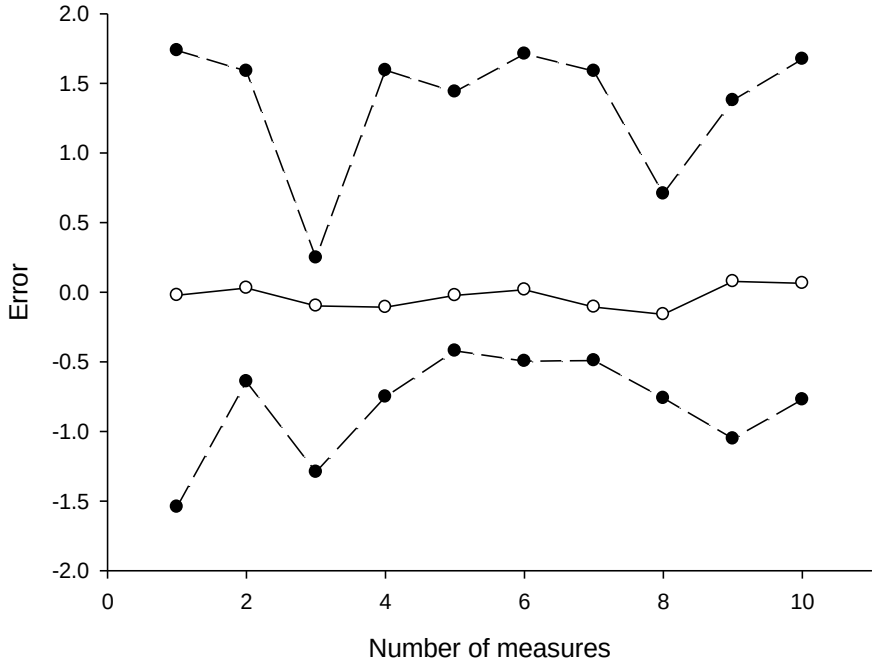


Fig 2.13 The apical radius measurements of a single meridian. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

a)



b)

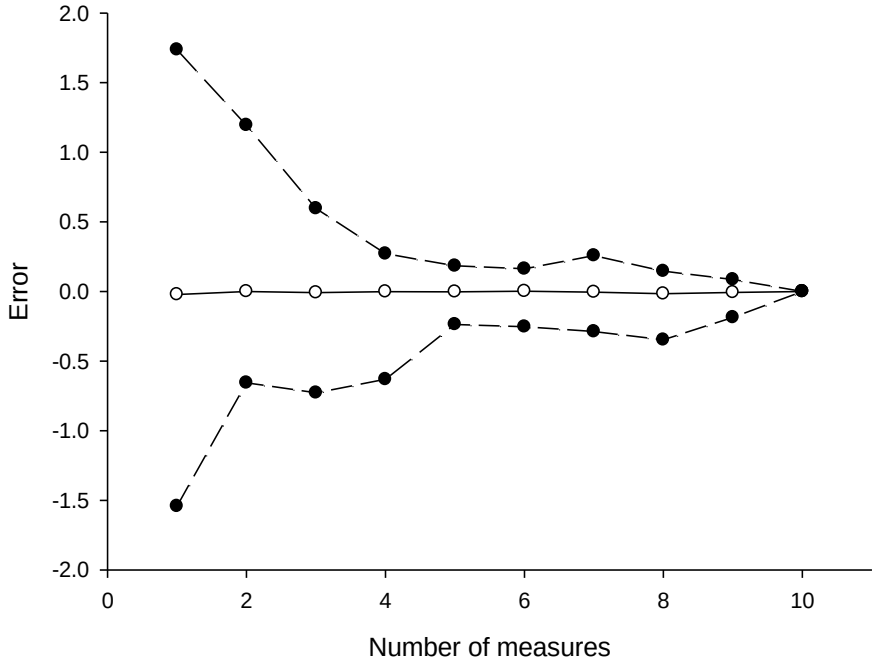


Fig 2.14 The p-value measurements of a single meridian. (a) indicates the median and the range of the results from 20 subjects for each of the ten measurements. (b) indicates the running averages where it can be seen that the spread of the results decreases as more measurements contribute to the running average.

2.5.2.3 Results Posterior Repeatability on Surfaces

Table 2.7 Results of the measures of the sixteen surfaces.

Radiuscope measure (mm)	Orbscan measure (mm)	Centre thickness (mm)	Difference Radiuscope – Orbscan (mm)	Mean of Radiuscope and Orbscan (mm)
7.01	7.09	0.22	-0.08	7.05
7.52	7.50	0.22	0.02	7.51
8.03	8.07	0.22	-0.04	8.05
8.55	8.53	0.22	0.02	8.54
9.04	9.02	0.22	0.03	9.03
5.52	5.57	0.22	-0.05	5.54
6.00	6.10	0.22	-0.10	6.05
6.53	6.55	0.22	-0.02	6.54
7.01	7.05	0.22	-0.04	7.03
7.53	7.59	0.22	-0.06	7.56
8.02	8.10	0.22	-0.08	8.06
8.53	8.63	0.22	-0.10	8.58
9.01	9.13	0.22	-0.12	9.07
6.03	6.15	0.50	-0.12	6.09
6.53	6.68	0.50	-0.14	6.61
7.04	7.19	0.50	-0.15	7.12

a)

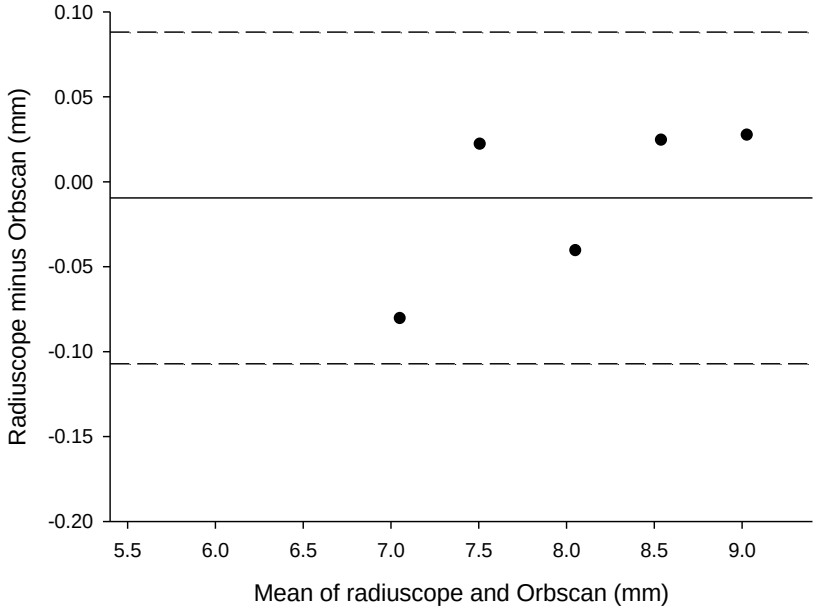


Fig 2.15 a) Bland Altman plot for the 10.6mm diameter surfaces with 0.22mm centre thickness

b)

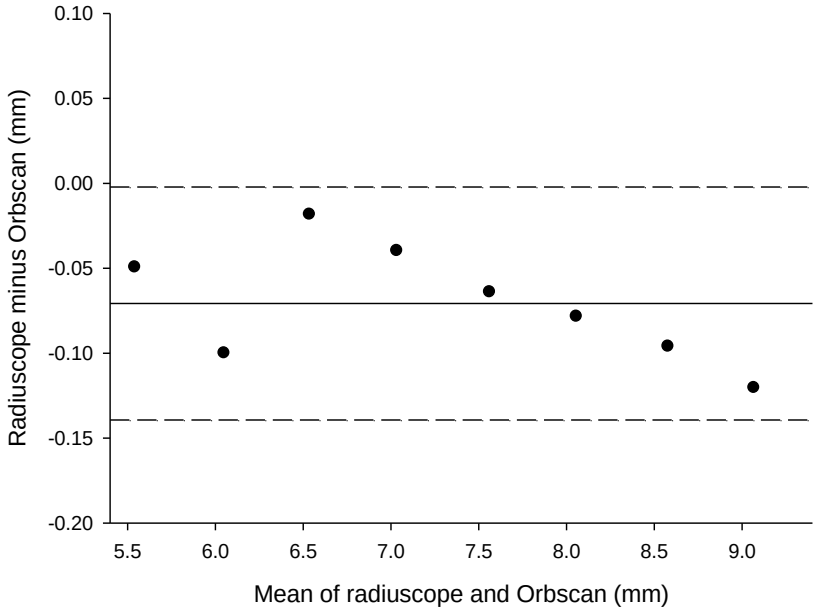


Fig 2.15 b) Bland Altman plot for the 11.2mm diameter surfaces with 0.22mm centre thickness

c)

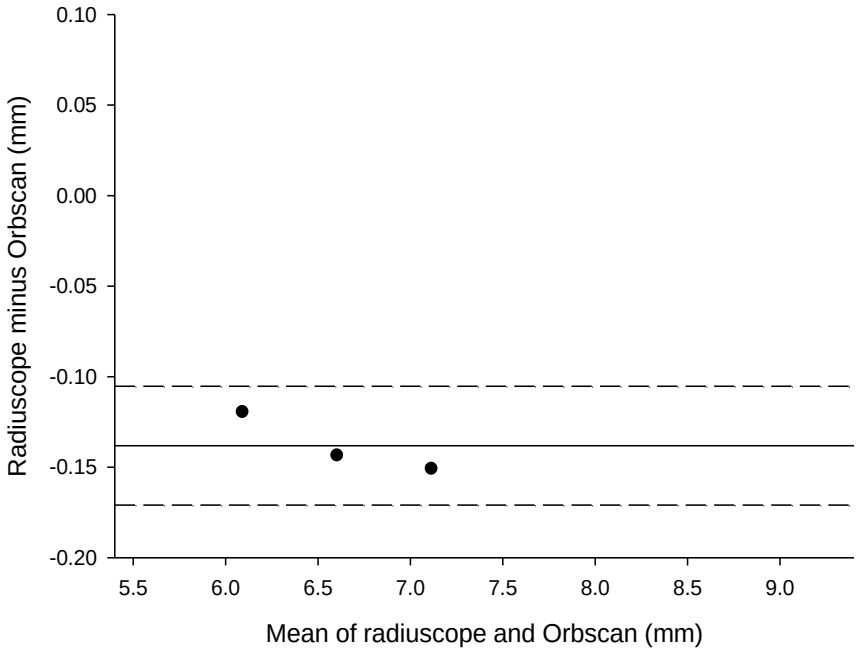


Figure 2.15 c) Bland Altman plot for the 11.2mm diameter surface with 0.5mm centre thickness.

The Bland Altman results for the posterior surface measures show that the mean bias for the 10.6mm surface as shown in Fig 2.15 a) is -0.098mm (solid line) with the limits of agreement being from -0.107 to +0.088mm (dashed lines). For the 11.2mm (0.22mm) surface the mean bias is -0.06 mm (solid line) with the limits of agreement of – 0.141 to -0.018mm (dashed line) (Fig 2.15 b). The results for the 11.2mm diameter lens with a 0.5mm centre thickness are shown in Fig 2.15 c. The mean result for this is -0.136mm with the limits of agreement of -0.167 to -0.106mm; these points are indicated on the graph following the same protocol as Figs 2.15 a and b.

2.6 Orbscan Discussion

2.6.1 Anterior Cornea

In chapter one the terms which may be used to describe the corneal shape were illustrated. The apical radius is a universal term but the terminology used to describe asphericity is more varied. The Orbscan uses the term shape factor to indicate the asphericity of the global measure this is in fact the p value of the total surface.

Figure 2.10 show the range of errors of the individual measures when compared to the mean of ten measures for both the global and single meridian analyses of the apical radius and p value. The repeated measurement plots for both the global and single meridian analyses show no trend to an increase or decrease in the error values with increasing numbers of measurements. The maximum error for the global analysis of the apical radius is 0.2mm. A similar result was found for the single meridian apical radius results. The p value error for the global measure was approximately 0.4. The single meridian p value maximum error was found to be approximately 0.2. This reduction in the latter maximum error supports the use of the single meridian analysis for the investigation of corneal asphericity when using the Orbscan.

Figure 2.11 shows the running average measurement results for the Orbscan global measures of apical radius and p value showing that the mean of increasing numbers of measurements reduces the error. The improvement in the error measurement seen by increasing the number of measures in the mean falls such that after three to four measures are included little further benefit is gained. When the single meridian data is analysed a similar result is found. Only the horizontal data is presented as this provides maximum data points which are not unduly influenced by the action of the upper lid on the corneal or tear film surfaces.

In Table 2.5 we see the reduction in the repeatability results as more measurements are added to the mean. For the global measure apical radius; when a single

measurement difference is compared with the difference between the mean of three measurements the difference is reduced to 38% of the single value. When the difference of the mean of five measurements is compared with the single measurement the result is further reduced to 35% of the single. For the p value results the reductions are 42% and 45% respectively. A similar analysis of the single meridian results shows that when the difference of the mean of three measures is compared to that of the single measurement a reduction to 36% of the single value occurs. This result falls further to 32% of the single measurement when the difference of the mean of five measurements is compared. For both the global apical radius and p value and the single meridian apical radius and p value a reduction in the difference was seen when the mean of three measurements were compared with the single measurement. The difference obtained when further measurements were added i.e. a five measurement mean, made no substantial improvement.

The findings for the repeatability of the global measure s show that there is a substantial improvement in the repeatability if more measures are included in the result. Cho et al (2002) used only two measures at the initial visit with a single measurement at the second. There was no attempt to average the results to improve the repeatability. The group also analysed a 9.0mm corneal chord which would include more peripheral data where the cornea can fail to follow a conic section. In the current study a 7.0mm corneal zone was chosen to specifically avoid this problem.

As Table 2.5 shows the results for the single meridian analysis were consistently better than those for the global measure. This led to the conclusion that, for the purposes of the analysis of change in the anterior corneal surface in this study, the single meridian data should be analysed. Since the mean of three measures showed a substantial improvement in the repeatability measures; three measures should be taken of the corneal topography for each visit.

2.6.2 Posterior Cornea

Figure 2.18 show the repeated measurement results for the global analysis of the posterior apical radius and p value provided by the Orbscan software. This shows that there was no trend in the measurement error as more measures were added. The maximum error for the posterior apical radius for both the global and single meridian measurements was 0.4mm. The maximum error for the global analysis p value was 0.4 whilst that for the single meridian was 0.8. This large difference may reflect the findings of Dubbelmann and Sicam (2006) who found that the posterior corneal asphericity varied significantly between meridians. As with the anterior surface the algorithms employed by the Orbscan software to produce its global measures are unknown. It may be that averaging across the meridians gives rise to the discrepancy. The mean posterior apical radii of the twenty subjects for both the global and single meridian results are 6.21 +/- 0.07mm and 6.29 +/- 0.07mm respectively. The standard error is quoted here as these results are comparisons of mean results. For the p values the results are global measure p = 0.69 +/- 0.03 and for the single meridian p = 0.41 +/- 0.07. Lam and Douthwaite (1997) in their study found the p value of the posterior cornea to be 0.34 +/- 0.38. The single meridian p value obtained in this study appears to be more in agreement with this than the global measure.

This repeatability study was not designed to find a true measure of the posterior asphericity but more to look at the validity and precision of the measurements taken. Table 2.8 shows the repeatability results for both the global and single meridian measurements for the apical radius and p value of the posterior surface. For the global measure of the apical radius the difference measurement reduces to 58% of the single measurement if the three measurement mean difference is used. The difference reduces to 49% of the single measurement if the five measurement mean difference is compared. For the global p value the reductions are 63% and 54% respectively. For the posterior surface, in contrast to the anterior surface, the apical radius and p value single measurement differences are greater than those obtained from the Orbscan

global analysis. An examination of the reduction in the difference in the measures obtained by including more measurements into the results shows that the apical radius difference is improved to 39% of the single measurement difference when the mean of three measures is used. If the five measurement mean is considered the reduction is 30%. The p value results for the single meridian are a reduction to 45% and 35% respectively.

In contrast to the anterior surface the single meridian posterior results appear less repeatable than the global measure. The reduction in the difference when further measurements are added to the result (mean of three) shows a greater improvement (39%) than the corresponding improvement in the global measure. The raw data analysis of the single meridian allowed the calculation of the coefficient of determination (R^2) and this in turn confirmed how well the posterior cornea was represented by a conic section. Each of the images had a coefficient of determination available and those which did not meet the critical value were rejected. This facility was not available for the global measure.

In conclusion it was found that the posterior surface analysis should be completed in the same manner as the anterior i.e. the mean of three measures would be analysed to produce a posterior apical radius and p value at each visit.

2.6.3 Posterior Surfaces

In contrast to the study by Cairns et al (2002), who found difficulty in measuring translucent surfaces, no difficulties were experienced in measuring the transparent contact lenses. The Bland Altman plots of the posterior surface measures shown in Figure 2.15 indicate that there is no trend in the measures for any of the surfaces. In all cases the Orbscan over reads the surface result when compared to the radiuscope measure. The results for the two thinner lenses are in agreement with Cairns et al (2005) with repeatability limits between 0.08 and -0.10. The magnitude of the

measurement error increases with the two larger diameter lenses and is particularly apparent for the 0.5mm surface. This thickness was selected as being close to that of the human cornea and as such raises concerns about the Orbscan's ability to measure the posterior cornea. The Orbscan produces the anterior co-ordinates using the Cartesian system described in section 2.1 and the slit scanning procedure records the corneal thickness. From these two measures the Orbscan employs an algorithm to produce the topographical map of the posterior surface. One unknown factor in the Orbscan's construction of the posterior surface is the algorithm employed by its software. In view of these results the posterior surface analysis results for the participants in the study will be treated with caution.

2.7 Study limitation

One aspect of the investigation of the corneal response to orthokeratology is the ability to assess whether the cornea becomes oblate in shape. The repeatability study has been completed using only prolate shapes and as such this limits the translation of the repeatability to oblate surfaces.

2.8 The EyeSys Corneal Analysis System 2000

2.8.1 Introduction

For the purposes of lens design the EyeSys Corneal Analysis system 2000 (EyeSys) was employed. This corneal topographer has a set of eight placido rings an image of which is projected onto the cornea. Analysis of the image created allows the corneal shape to be evaluated. Once a focussed image of the ring pattern on the cornea has been obtained, the instrument software locates the dark/light interfaces of the eight rings. Since both the inner and outer edges of each of the rings is identified this gives 16 interfaces. Each of these interfaces is then analysed at one degree intervals through the 360^0 of each ring. This gives approximately 5760 data points (Dave, Rushton, Fowler 1998a). From these data points, it is possible to obtain the sagittal radii at a specific meridian on the cornea and for a specific distance from the corneal apex.

A number of researchers have looked at the validity and repeatability of the EyeSys. Early studies assessed the EyeSys's ability to measure spherical surfaces (Verity, Wilson, Conger 1991; Gonzalez Perez, Cervino, Giraldez, Parafita et al 2004). As the cornea is a prolate ellipse the ability to evaluate aspheric surfaces would give a more representative assessment of its function. A number of studies have looked at the measurement of calibrated aspheres as well as normal corneas. Douthwaite (1995) in his assessment of the EyeSys against calibrated ellipsoid surfaces found that the EyeSys values for both vertex radius and p value were higher than those of the Form Talysurf analysis on the surfaces used. Form Talysurf analysis is used in the engineering industry to compare an unknown surface against an agreed reference surface or standard. A stylus is applied to the surface under analysis along the requested meridian. Using laser interferometry the progression of the stylus across the surface can be transmitted to the computer for comparison. The accuracy of the analysis is said to be within parallel plates separated by 1µm over a 20mm scan (Douthwaite and Mallen 2007). Douthwaite found that the EyeSys produced repeatable

results which were accurate enough for comparative studies but had concerns about the accuracy of the absolute values produced.

Vamosi, Sohajda, Modis, Vamosi and Berta (1998) evaluated the EyeSys against three keratometers, the Haag Streit, the Shin-Nippon and the Carl Zeiss 110. The authors do not provide the model numbers for the Haag Streit and Shin-Nippon keratometers which makes comparison of these results with other studies difficult. Measurements were conducted on three calibrated steel balls and 22 normal corneas. The group found that the EyeSys had a repeatability of +/- 0.25D on both horizontal and vertical meridians. The EyeSys gave comparable results for both principal meridians. All of the keratometers used in this study showed considerable variance between the two principal meridians. Vamosi et al (1998) concluded that for clinical evaluation, where 0.25D is the smallest division prescribed, the EyeSys was comparable with the three keratometers. The keratometers showed an accuracy of +/- 0.1D. Vamosi et al (1998) suggested that for the purposes of rigid contact lens prescribing keratometry, particularly using the Carl Zeiss keratometer, would be the method of choice. In contrast they pointed out that, in the case of marked or irregular astigmatism, the EyeSys was the instrument of choice.

Pardhan and Douthwaite (1998) also compared the EyeSys vertex radius and p value measures, for both corneas and ellipsoid surfaces, against similar measurements made using the Topcon KR-3500 keratometer. A comparison of the repeatability of the vertex radius results for corneas found by the two instruments showed that the keratometer gave confidence limits of +/- 0.028mm for vertex radius whilst the Eye Sys gave +/- 0.090mm. Similar results were found for the p value (Topcon +/- 0.073, EyeSys +/- 0.332) Pardhan and Douthwaite suggested that one reason for lack of agreement between the two instruments may be the large area of cornea sampled by the EyeSys (5.5mm semi meridian). They found that comparison of the EyeSys, using an equivalent diameter to that assessed by the keratometer (3.5mm semi meridians),

improved the agreement between the two measures (EyeSys vertex radius +/- 0.086 and p value +/- 0.115).

Dave, Ruston and Fowler (1998a,1998b) carried out evaluations of the EyeSys in a clinical assessment and on convex aspheric surfaces. In their first study they compared the repeatability of the SimK readings of the EyeSys with those of a Bausch and Lomb keratometer. The repeatability of mean corneal power and peripheral radii measurements from the EyeSys were assessed by comparison of two independent measures made by the same observer on the same day. In order to compare the SimK readings of the EyeSys with those of the Bausch and Lomb keratometer a point 1.5mm from the corneal vertex was selected. Dave et al (1998a) found that the two instruments produced measurements of mean corneal power (sphere plus half of the cylindrical component of the corneal power) which were significantly different at a clinical level. For the purposes of the current study we only wished to look at the repeatability of the EyeSys. The group found that the mean difference between repeated measures was 0.112D with limits of agreement between -0.029 and +0.253D for mean corneal power.

The EyeSys software produces a table of data showing the sagittal radius at specified intervals from the corneal apex. Dave et al (1998a) found no significant bias in sagittal radii measurements out to 4mm from the corneal apex along any of the four principal meridians. The inferior and temporal meridians produced the most repeatable measures (bias 0.029mm and 0.024mm respectively). They felt that the reason for the increased bias for the superior and nasal meridians (0.079mm and 0.059mm respectively) was the reduced data set available along these two aspects. The upper lid may prevent the acquisition of accurate placido ring data for the superior cornea. Nasal shadow may equally obscure the outer rings on the nasal cornea. When Dave et al (1998a) further analysed their data looking at four corneal zones, semi meridians of 0-1mm, 1-2mm, 2-3mm and 3-4mm, they found that the central 4mm area i.e. zones 1

and 2 produced similar bias levels in all four meridians (range 0.020 to 0.043mm) suggesting that repeatability is most valid in this central zone.

In their second study on the repeatability of the EyeSys, Dave et al (1998b) compared the accuracy of the measurement of calibrated aspheric surfaces against Form Talysurf analysis results. Parameters for these surfaces were selected to mimic the range of apical radii and p values seen in the human cornea. They found that for the central sagittal radii repeatability was bias 0.042 (limits of agreement +0.121mm to -0.037mm). It is difficult to compare this with their earlier study as results for this were reported in dioptre and not millimetre values. One important finding was that as the p value increased i.e. the surfaces became more spherical, the bias reduced, indicating that the EyeSys is at its most repeatable for spherical surfaces. Dave et al (1998b) repeated their investigation of the peripheral radii on the calibrated aspheres, as they had done with the cornea in the earlier study. They found a clear trend that the repeatability of peripheral radii measurements deteriorated as the surfaces became more aspheric. Investigation of the four principal meridians of the calibrated aspheres indicated no difference between the measures, in contrast to their first study. Douthwaite (1995) in his evaluation of the EyeSys on calibrated ellipsoidal surfaces found that the accuracy of the EyeSys to measure p value deteriorated as the surface became more aspheric.

Jeandervin and Barr (1998) compared the repeatability of the EyeSys against three other videokeratographers and a manual keratometer on twelve corneas. They found that the EyeSys was the most repeatable in a clinical setting. Repeated measures analysis of variance for the five instruments revealed no statistically significant difference in repeatability between them. Hough and Edwards (1999) investigated both repeatability and reproducibility of the EyeSys by comparing the results from the same eight participants measured eight times on four different EyeSys instruments. Repeatability is a measure of results made using the same instrument on independent occasions. Reproducibility refers to test results made by the same method using an

identical instrument in a different laboratory. Hough and Edwards found that the reproducibility for a single measure of apical radius was +/- 0.208mm (95% confidence limits). The reproducibility could be improved by taking the mean of three measures (+/-0.10mm 95% confidence limits). A similar improvement was demonstrated for the p value, with a single measure giving 95% confidence limits of +/- 0.11 whilst the mean of three measures gave +/- 0.07.

2.9 EyeSys Method

2.9.1 Image capture

Image acquisition commenced by selecting the basic method of examination from the EyeSys software display. In order to capture multiple images, as suggested by Hough and Edwards (1999), it is necessary to select either right or left and not both eyes. The subject was positioned with their chin on the chin rest and forehead firmly against the head rest. Subjects were asked to keep both eyes open during the image capture phase. They were instructed to turn their head slightly to one side to eliminate the shadow created by the nose i.e. for the right eye the head should be turned to the left. The subject was then asked to fixate the central target, a green flashing light. The EyeSys provided a continuous video stream of the eye under examination. The instrument was then focussed using the joystick. The focus was achieved when the central line was aligned with the breaks in the central block.

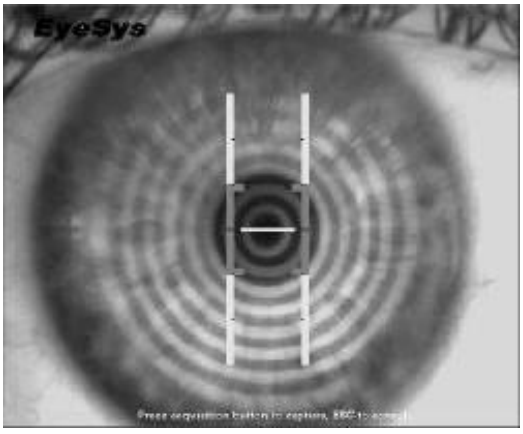


Fig 2.16 Photo from EyeSys System 2000 Software Operators Manual 1998

Subjects were asked to make one or two full blinks to ensure the tear film was full and smooth over the corneal surface. The image was then captured using the capture button on the joystick. The EyeSys software required verification that the image has been placed at the corneal apex. (Fig 2.17) Any images which did not coincide with the corneal apex were repeated.

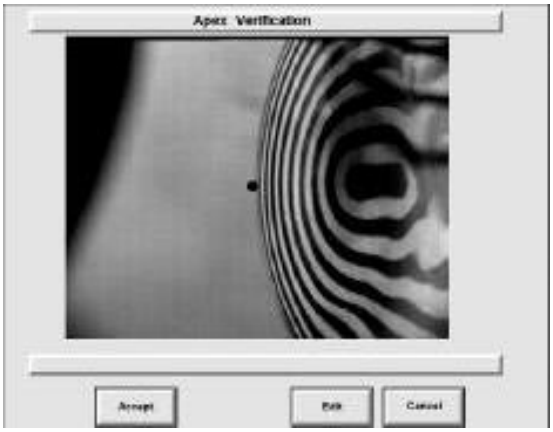


Fig 2.17 Photo from EyeSys System 2000 Software Operators Manual 1998

When the processed image was seen on the screen the image was checked for the completeness of the rings from five to twelve. Details of these rings were required to complete the analysis. Images with insufficient data were repeated.

Fig 2.18 Photo from EyeSys System 2000 Software Operators Manual 1998

This was in line with the study by Douthwaite et al (1999). They found that inclusion of rings one to four were unreliable when used to evaluate the apical radius and p values. They also noted that, due to the nasal shadow, it was difficult to obtain the equivalent number of rings for the temporal and nasal meridians beyond ring twelve. No pupil data were saved in this study. Each individual capture session was then saved until three acceptable data sets for each eye had been achieved.

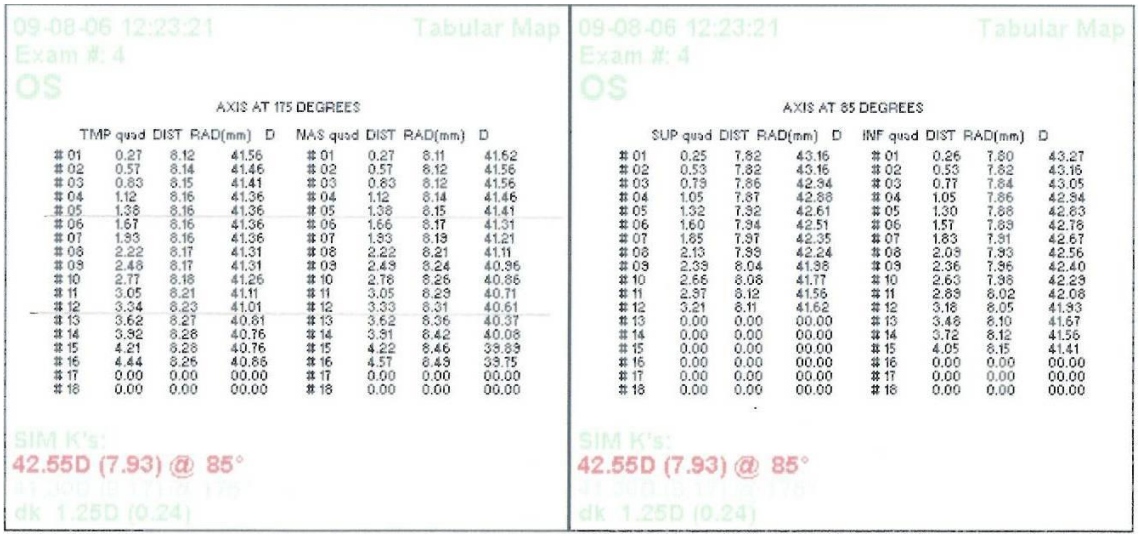


Fig 2.19 Example of EyeSys topography results for the left eye of subject PV used in lens design

2.9.2 Analysis

When a capture session had been completed for each eye, the images were analysed using the EyeSys software. From the main screen, the option to display patient data was selected. The six complete capture sessions were displayed. Once an individual session was highlighted, the software offered a number of analysis possibilities. The 2-Map display was selected with the option to display in tabular form. A table containing dioptres, radius of curvature (mm) and distance from the centre (mm) was displayed for the four semi meridians. The initial table displayed the raw data along the principal meridians (0^0 and 180^0). The axes of the flattest and steepest meridians are also displayed. Using the options button it was possible to have the table reconfigured to

display the raw data along the flattest and steepest semi meridians. Tables for each of the six capture sessions were then printed for each of the participants (Fig 2.19).

It was now possible to analyse these data in the same manner as that applied to the Orbscan i.e. r_s^2 against y^2 to produce an apical radius and a p value for the cornea in question. This analysis was applied to each of the three measures for each cornea. The mean apical radius (r_0) and p value for each eye was then calculated.

2.10 Results Comparison of Orbscan and EyeSys apical radius and p value

In this study the initial lens design was calculated using the apical radius and p value derived from the EyeSys image analysis. The monitoring of any subsequent corneal changes was to be evaluated using the images from the Orbscan II. This decision was made because of the additional elements available from the Orbscan topographer i.e. corneal thickness, posterior corneal topography and anterior chamber depth. It was therefore necessary to look at the correlation between the Orbscan and EyeSys values for the subjects prior to any lens fitting.

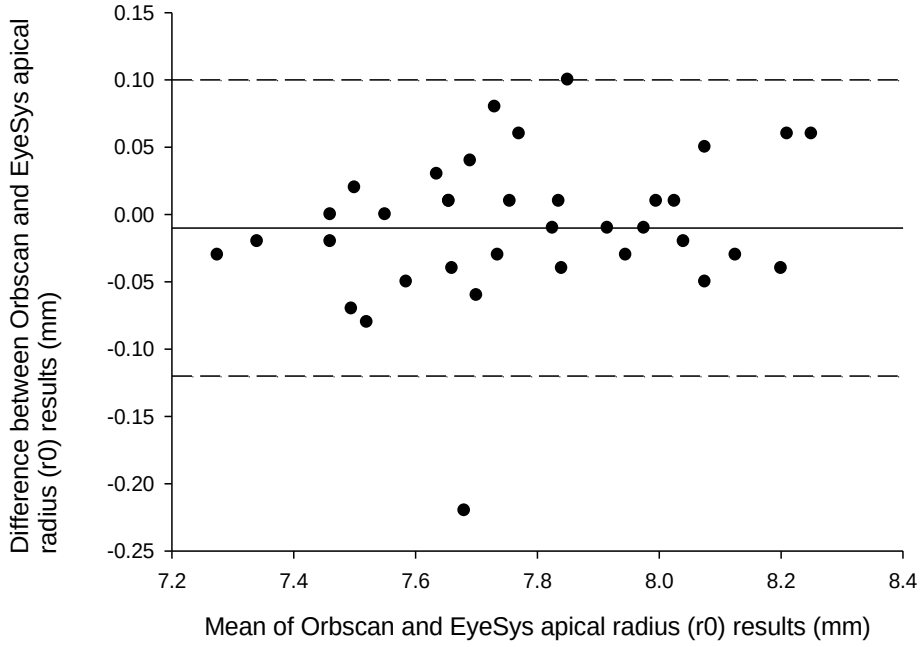
Bland Altman analyses were plotted for both apical radius and p value for each eye (Fig 2.19 a,b,c,d). The mean bias and limits of agreement for the four measurements are shown in Table 2.8.

Table 2.8 Mean bias and limits of agreement for apical radius and p value Orbscan and EyeSys

	Apical radius (r0)(mm)	p value
Right	-0.01 LoA +0.10 to -0.12	-0.02 LoA +0.12 to -0.17
Left	0.02 LoA +0.17 to -0.13	0.01 LoA +0.12 to -0.10

The results for the Orbscan and EyeSys were also plotted against each other (Figs 2.20 a,b,c,d). The correlation results are apical radius; right eye $r^2 = 0.95$, left eye $r^2 = 0.92$ and p value; right eye $r^2 = 0.49$, left eye $r^2 = 0.65$. Paired t test results for the two measures are right r_0 $t_{(42)} = -0.90$, p= 0.38; p value $t_{(42)} = -2.06$ p = 0.05 and left r_0 $t_{(42)} = 1.83$, p = 0.08; p value $t_{(42)} = 0.67$ p = 0.51. In Figs 2.19 the two dotted lines indicate +/- 2SD and the solid line the mean bias of the measures shown in Table 2.8.

.a) right



b) left

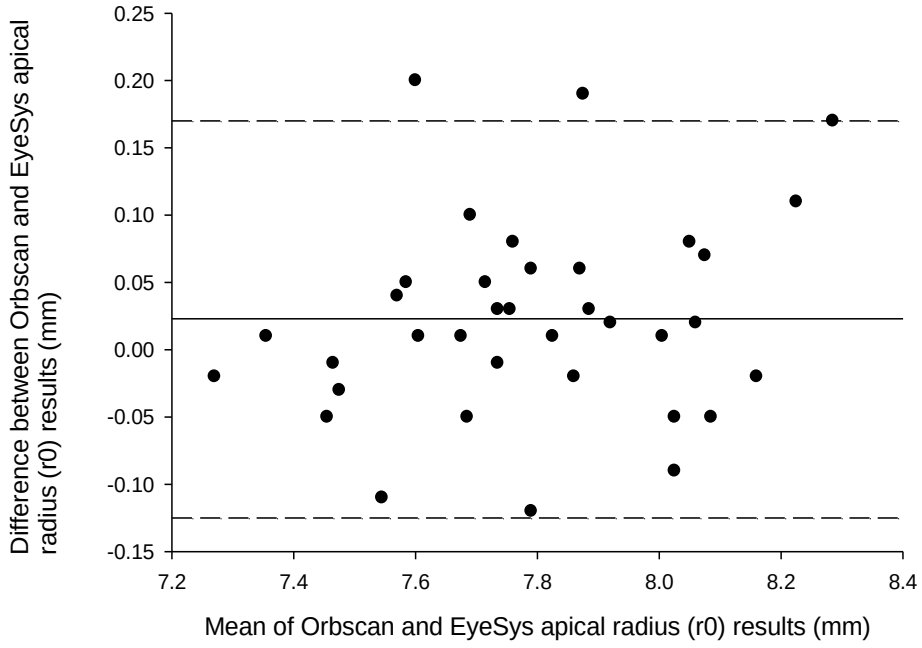
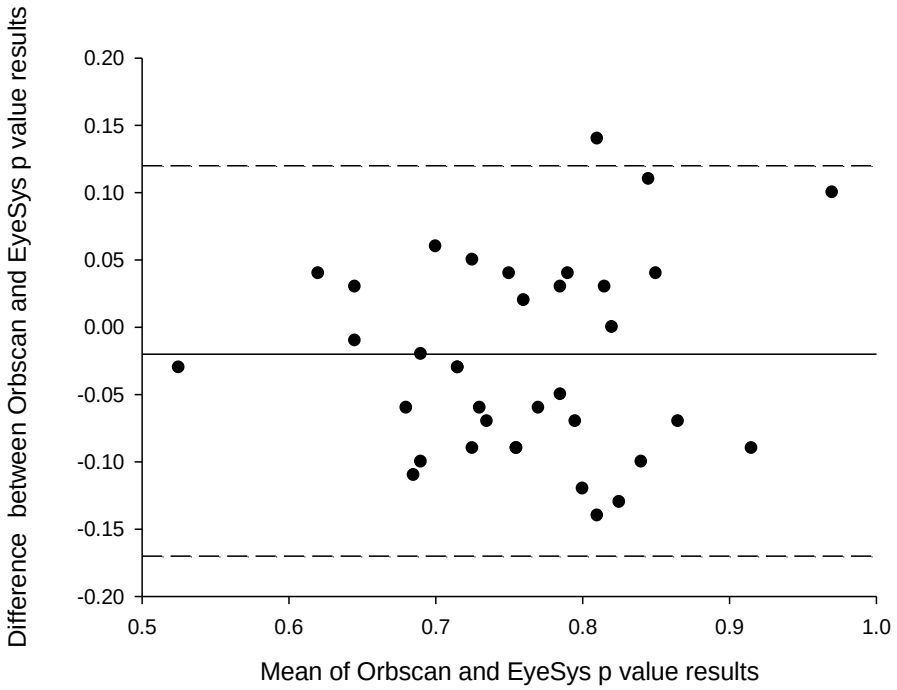


Fig 2.19 Bland Altman Plots of apical radius (mm) for a) right and b) left eyes.

c) right



d) left

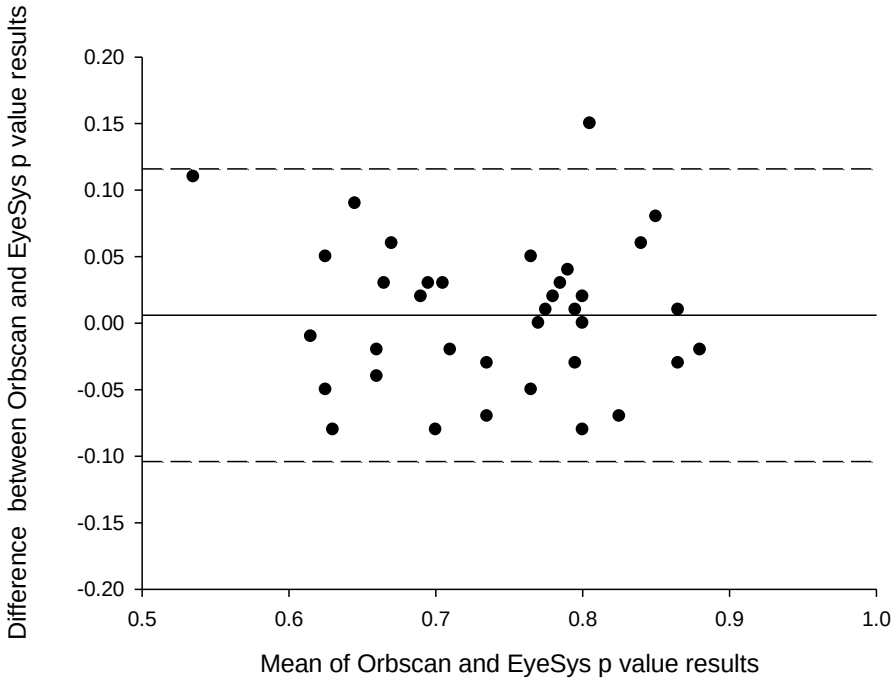
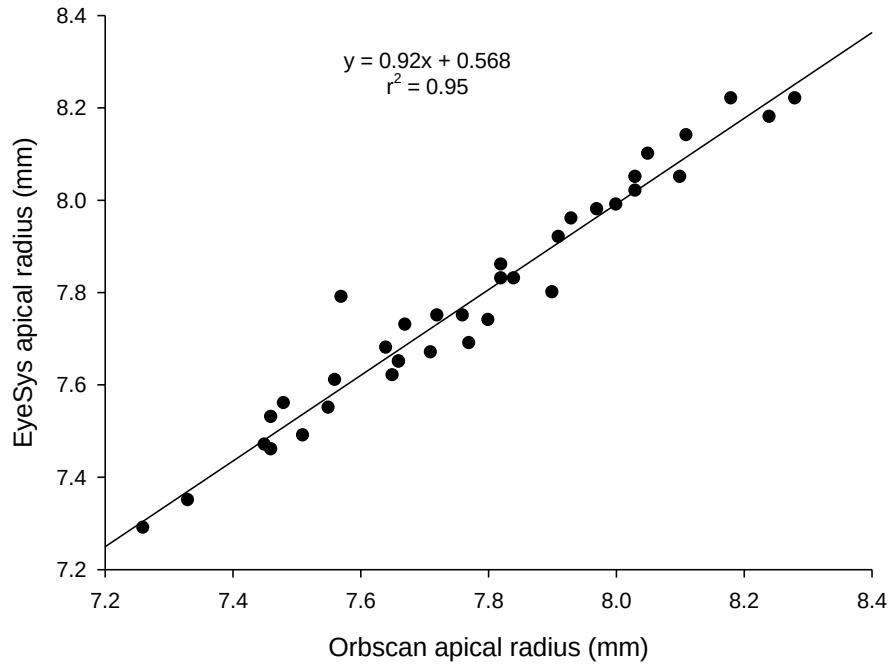


Fig 2.19 Bland Altman Plots of p value for c) right and d) left eyes.

a) right



b) left

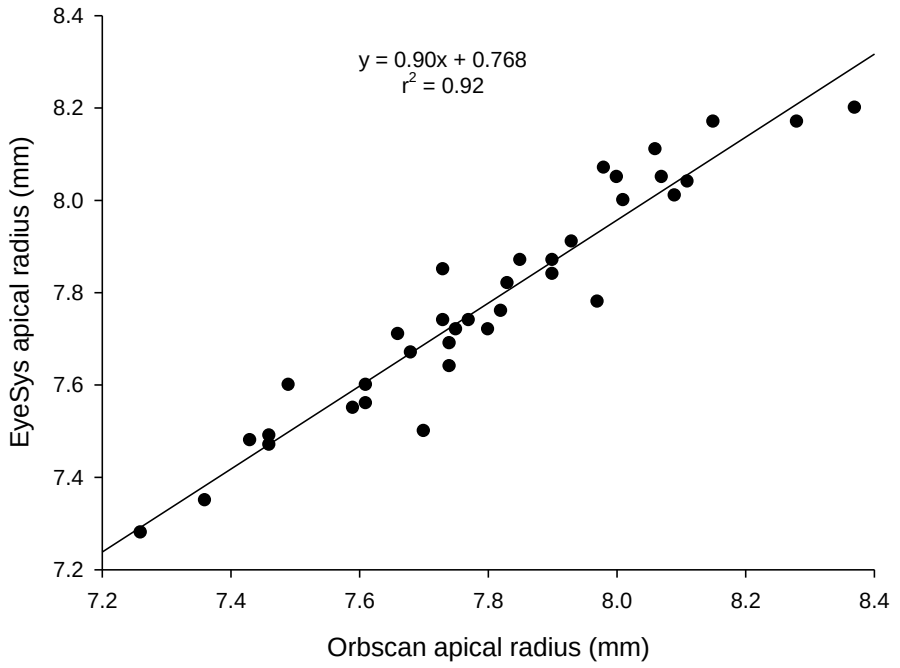
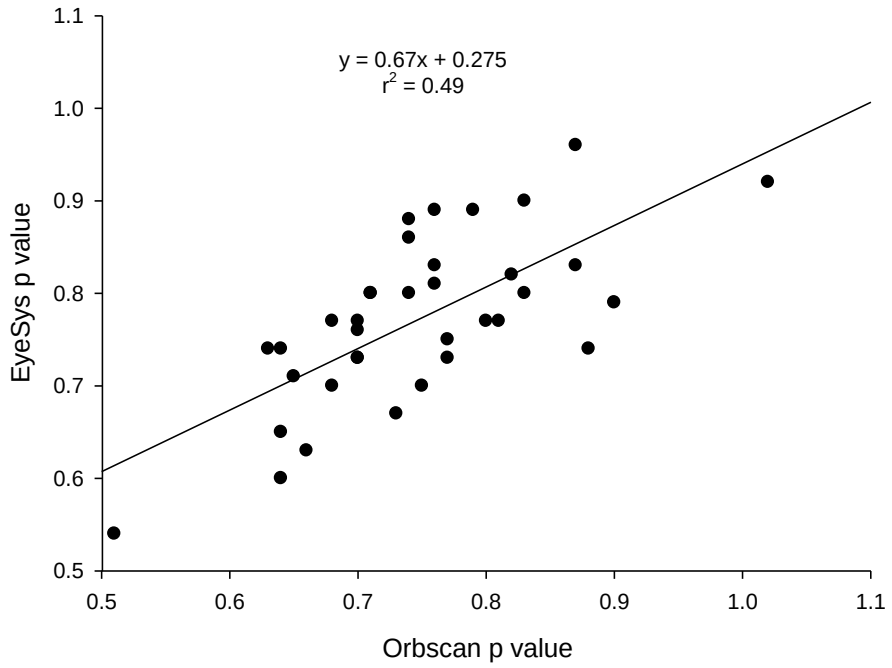


Fig 2.20 Orbscan versus EyeSys apical radius for both a) right and b) left eyes

c) right



d) Left

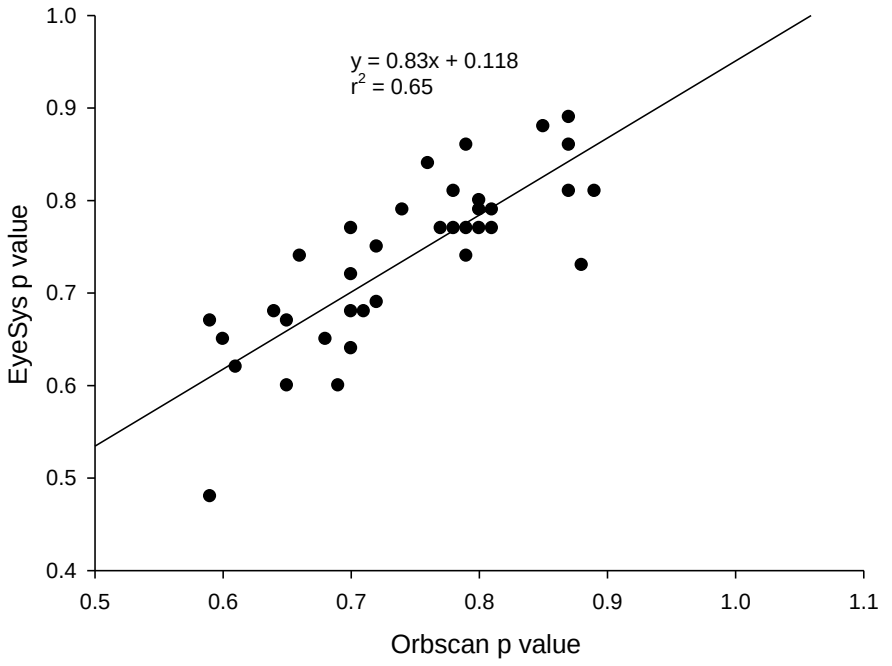


Fig 2.20 Orbscan versus EyeSys p value for both c) right and d) left eyes

2.11 Discussion

Gonzalez Perez et al 2004 compared the accuracy and precision of the Eyesys and Orbscan on test surfaces. They found that the two instruments showed close agreement with a mean bias of < +/- 0.05mm. The group found that the EyeSys was slightly more precise than the Orbscan but felt that both provided appropriate clinical measurements. Douthwaite and Mallen (2007) compared the EyeSys with the Orbscan II on both aspheric buttons and normal corneas. They found that, when the two instruments were compared, the Orbscan under read the corneal apical radius between 0.020 and 0.070mm. The corneal p value was similarly under read by the Orbscan by 0.01 to 0.086. The Bland Altman results from the current study are in keeping with the two published studies (Gonzalez-Perez et al 2004, Douthwaite & Mallen 2007).

If two instruments produce the same value for each of the parameters measured then the results should show a high degree of correlation (r^2). The values for r^2 should be close to 1. For the two instruments the correlation measures for r_0 are right 0.96 and left 0.92. For the p value the correlation measures are lower right 0.49 and left 0.66. If we look at critical values for r we find that r (34) = 0.325, $p<0.05$. All measures are therefore significantly correlated. It would seem appropriate therefore to use the EyeSys for the lens design but to continue to use the Orbscan for on-going analysis and patient monitoring.

2.12 The IOL Master

2.12.1 Introduction

The IOL Master (Carl Zeiss Meditec, Inc., Dublin, CA), a partial coherence interferometer, can be used to measure corneal curvature, anterior chamber depth and axial length. In order to measure anterior chamber depth a 0.7mm slit beam is directed through the anterior segment at an angle of 38^0 to the visual axis. The camera of the IOL Master is aligned so that the slit beam is imaged as an optical section. The instrument software then measures the distance between the cornea's anterior pole and the lens anterior capsule.

Partial coherence interferometry is applied to the measurement of axial length based on the principle of the Michelson interferometer. A laser diode generates infra-red light (λ 780μm) of short coherence length (C_L = 160μm). The light is reflected in to the eye by two mirrors after being split into two equal coaxial beams by a beam splitter. The separation of the two coaxial beams is equal to twice the displacement of the mirror. As the beams enter the eye reflections occur at the corneal and retinal interfaces. As the beams leave the eye the difference in the frequency between the two is detected by a photo-detector after passing through a second beam splitter. During the measurement procedure the mirror is moved at a constant speed which creates a Doppler effect. The displacement of the mirror can then be precisely determined and related to the reflected signals detected at the photo detector. This allows accurate measurements of the axial length between anterior corneal pole and retinal pigment epithelium.

For the purposes of this study, individuals had anterior chamber depth and axial length measurements made at baseline and at each subsequent visit. Lam, Chan and Pang (2001) compared the measurements of anterior chamber depth and axial length using the IOL Master with that of ultrasound biometry. IOL Master measurements were made by two observers; each observer's results were masked from the other. A third

observer made the ultrasound measurements. In order to compensate for the two different reflecting surfaces used in the two instruments, retinal pigment epithelium for the laser of the IOL and inner limiting membrane for the ultrasound waves, a correction factor has been added to the IOL Master software. A comparison of the axial length measures, from the two observers making the IOL Master measurements, found no statistically significant difference between them, indicating the instrument is repeatable. A further comparison between these axial length measures and those of the ultrasound biometer also showed no statistical significance, confirming the validity of the instrument.

Santodomingo-Rubido, Mallen, Gilmartin and Wolffsohn (2002) also evaluated the IOL Master for validity and repeatability. They too compared measurements of axial length using ultrasound A-scan, the accepted method at that time, with that of the IOL Master. Their conclusions were that the two methods were valid with no statistically significant difference between them. Their findings on the repeatability of the IOL Master were that measurements were highly repeatable with no significant bias. Kielhorn, Rajan, Tesha, Subryan et al (2003) also evaluated the IOL Master and ultrasound in measuring axial length when used by trained and untrained observers. They found that both groups of observers achieved a coefficient of repeatability of 0.07mm for axial length.

Lam et al (2001) did raise concerns about the anterior chamber depth measurements. Here their findings were that the IOL Master readings were significantly deeper than those of the ultrasound biometer. They suggested that the mechanism applied by the IOL Master to measure anterior chamber depth, a slit beam applied on the temporal side, may not measure the axial anterior chamber depth. Santodomingo-Rubido et al (2002) in their study also compared IOL Master anterior chamber depth measurements with those of an ultrasound biometer. In their study they found that the IOL Master results were significantly shorter than those of the ultrasound biometer. They concluded that the small difference, though statistically significant, was smaller than the

resolution of the ultrasound biometer and not clinically significant. The IOL Master measures the anterior chamber depth from the anterior corneal surface to the anterior lens surface. The true anterior chamber depth is therefore the IOL Master measure minus the corneal thickness.

Sheng, Bottjer and Bullimore (2004) compared the IOL Master results for anterior chamber depth, axial length and corneal curvature with that of A scan ultrasound. Measurements were made by both an experienced and an inexperienced observer. They found that whilst ultrasound measurements made by an experienced observer were more repeatable than those made by an inexperienced observer, this did not apply to the use of the IOL Master. Sheng et al also agreed with both Lam et al (2001) and Santodomingo-Rubido et al (2002) in finding longer anterior chamber depth measures with the IOL Master than ultrasound.

More recently Buckhurst, Wolffsohn, Shah, Naroo et al (2009) compared the IOL Master with a new optical low coherence reflectometry device, Lenstar (Haag-Streit). The Lenstar is capable of measuring corneal and lens thickness as well as anterior chamber depth and axial length. They found that for axial length measures the Lenstar produced measures which were slightly greater than those of the IOL Master. Whilst the differences were statistically significant they were not found to be of clinical significance. Doors, Cruysberg, Verbakel, Berendschot et al (2009) found similar results in their study comparing the IOL Master, Lens Star and the Visante anterior segment optical coherence tomographer.

2.13 IOL Master Method

2.13.1 Axial length measurements

All participants had axial length measurements taken, at each visit, using the IOL Master. Measurements were taken in accordance with the procedures outlined in the user guide provided by the manufacturer (Carl Zeiss Jena GmbH). Participants were asked to place their chin on the chin rest and to bring their forehead into place against the brow bar. The chinrest was positioned so that the patient's eyes were approximately aligned with the canthus markers on the headrest. At this point the instrument was in overview mode. The subject was directed to look at the yellow fixation light and the IOL Master was then brought into line with the subject's central cornea. Centration of the instrument was facilitated by the presence of a ring of lights bisected by cross hairs which were centred on the subject's pupil. Once the instrument was aligned then the axial length mode was selected. At this point the fixation light became red and subjects were reminded to continuing fixating on the light.

Subjects were then asked to make one complete blink. Both Santodomingo- Rubido et al (2002) and Buckhurst et al (2009) in their studies asked their candidates to have one good blink before measures were made. This was to ensure an optically smooth surface on the cornea to facilitate the focussing of the IOL Master prior to measurements being taken. The crosshairs and circle were brought into focus and the fixation light was placed within the circle prior to a measurement being made. Only measures which had a signal to noise ratio (SNR) of greater than 2.0 were used. The SNR indicates the quality of the measurements being made. The manufacturers recommend that measures with SNR values of between 1.6 and 2.0 are unreliable. Any measurements with inappropriate SNR values were repeated. The IOL Master software also indicated where any measures differed by more than 0.2mm from the others. In this case, further measurements were taken until all subjects had five

acceptable measures of axial length. These readings were then repeated for the other eye.

As mentioned earlier the IOL Master requires an optically smooth surface in order to make accurate measurements. Difficulties were experienced in taking measurements on some individuals on the study at visits subsequent to the initial one. The corneal surface was not optically smooth immediately following orthokeratology lens removal. In this instance, as per the IOL Master manual, the fixation light was focussed at the upper or lower extremes of the circle.

The IOL Master provides a running average of the axial length measures as well as the five individual measures along with their SNR. Both sets of readings were recorded for each eye of each subject and for each visit.

2.13.2 Anterior chamber depth measurements

Prior to anterior chamber depth measures the IOL Master requires keratometry measures to be taken. As per the manufacturer's instructions the participants were asked to make one or two complete blinks to create an optically smooth tear film. The IOL Master produces five keratometry readings within 0.5 secs provided the 6 peripheral measuring points are focussed within the circles. Once satisfactory keratometry readings had been obtained then the anterior chamber depth measures could be completed.

The participants were instructed to continue looking at the fixation light. The fixation point was brought into focus and placed within the square displayed on the screen. The instrument was positioned so that no corneal reflections were seen. The presence of any specular reflection from the anterior corneal surface prevents accurate readings. Further adjustments were made until the anterior lens surface was seen within the square target. At this point the trigger was pressed. The IOL Master produces five

readings of the anterior chamber depth along with the calculated mean. The need for an optically smooth tear film for the keratometry readings and anterior chamber depth measures was again a problem for some participants at later visits. Where problems occurred the measurements were repeated. The measures were then completed for the second eye. Anterior chamber depth measurements from the IOL Master are taken between the anterior corneal apex and the anterior lens surface. The true anterior chamber depth requires the central corneal thickness measurement to be deducted. The IOL Master, unlike the Lenstar, has no facility for corneal thickness measurements to be made. Corneal thickness measurements, obtained at the same visit, from the Orbscan were used to make the correction.

2.14 Collar and Pillar

2.14.1 Introduction

In order to verify the lens sagittas ordered for the subjects participating in this study the collar and pillar technique was applied. This process was first proposed by Douthwaite and Hurst (1998a,1998b) for the purposes of measuring axial edge lift.

The device consists of a pillar whose upper diameter is equivalent to that of the chord diameter to be investigated. The pillars lower diameter should correspond to the inner diameter of the collar which in turn should be equivalent to the overall diameter of the contact lens under investigation taking into account the tolerance limits of lens total diameter. (Fig 2.21)

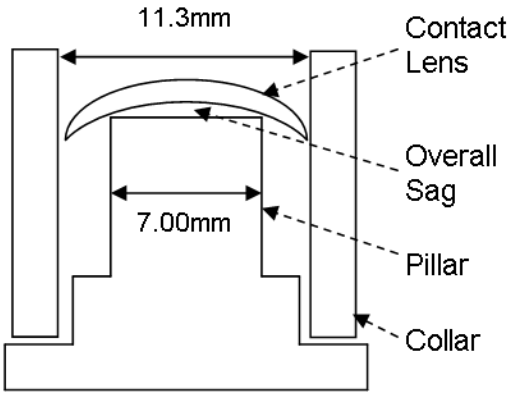


Fig 2.21 The collar and pillar arrangement for measuring the overall sagitta for a diameter of 7.00mm when the lens total diameter is 11.20mm.

(Courtesy of WAD)

The collar acts as a centring device. Its height should be sufficient to retain the lens centrally over the pillar.

Dietze, Cox, Douthwaite (2003) also employed the collar and pillar method when evaluating methods of verification of aspheric back surfaces of rigid contact lenses. They expressed concerns about accuracy and precision with a recommendation that

large pillar diameters be used to improve precision in the measurement of conicoidal asphericity.

Since the measurement of lens sagittas is an integral part of the calculation of the axial edge lift, this technique can be applied to the lenses in this study for the purposes of verification of lens sagittas. Sag measurements can then be compared with the theoretical calculated sag generated by the computer program Douthwaite (2006) used for the design of the Orthokeratology contact lenses.

2.15 Calculation of pillar diameters

2.15.1 Method

For the Orthokeratology lenses it was necessary to measure the lens sag at a number of chord diameters. To facilitate this, a series of pillars were created. (Table 2.9) Each of the pillar and collar combinations were unique i.e. a 9.00mm pillar used with a 10.9mm collar could not be interchanged with the 9.00mm pillar for use with an 11.3mm collar.

Table 2.9: Pillar and Collar diameters ordered for sag measurement verification

Collar Diameter (mm)	Pillar Diameters (mm)						
10.9	5.0	5.3	7.0	9.0	9.55	10.6	
11.3			7.0	9.0	9.55	10.6	10.9

In order to use the pillar and collar method for the measurement of sag in the orthokeratology contact lenses it was necessary to accurately determine the pillar diameters. Each of the pillars had been machined to a nominal diameter but due to manufacturing tolerances this was not necessarily the actual diameter on which the contact lens rests.

Monocurve contact lenses without edge finish were ordered (Table 2.10)

Table 2.10: Diameter and Radii of monocurve lenses ordered for verification purposes

Lens Diameter (mm)	Radii (mm)				
10.6	7.0	7.5	8.0	8.5	9.0
11.2	7.0	7.5	8.0	8.5	9.0

The monocurve lenses represent the simplest surface for manufacture and assessment. The lack of edge treatment eliminates any error created by an edge profile. The lenses were manufactured from ML92, a fluoro-silicone acrylate material. This polymer produces lenses with high mechanical stability. As the lenses were to be used for the verification of the pillar diameters it was essential that the lens dimensions remained consistent throughout the measurement process.

2.15.2 BOZR measurement

The lens radius recorded was derived from 3 independent measures of the BOZR *(r_0)* using the radiuscope. McMonnies (1998) reported on the causes of potential measurement errors with the radiuscope. These may be due to poor quality images either surface or aerial. Errors of this nature may be avoided by ensuring

i) The lens surface is clean and polished

ii) The lens support has sufficient fluid within it to create a continuous fluid layer below the lens.

Failure to locate the lens surface normal to the measurement axis will also lead to measurement error. To minimise these errors the lenses were cleaned and polished before measurement and sufficient fluid placed in the lens support to ensure a continuous layer of fluid below the lens. Normal measurement was ensured by centring the centre of curvature image in the eyepiece of the field of view.

2.15.3 Sag Measurement

The appropriate pillar and collar combination was positioned on the radiuscope in place of the normal concave lens support and the table was then centred below the radiuscope. The upper surface of the pillar was then brought into focus. At this point the radiuscope scale was zeroed.

The contact lens was then placed onto the pillar inside the collar, concave side down (Fig 2.21). Positioning of the contact lens can be difficult particularly with the small diameter pillars. The space between the pillar and collar means that the lens can overbalance and come to rest at an angle. To avoid this it was necessary to use a wire speculum to ensure that the contact lens was level on the pillar. The collar height was sufficient to allow the lens to remain centred over the pillar.

The radiuscope was then refocused onto the front apex of the contact lens. This is the second image which is seen, the first image being that of the horizontal surface of the pillar. The distance the platform moves is equal to the overall lens sag (*os*) plus the lens centre thickness (t_c). The centre thickness was measured with a contact lens centre thickness dial gauge.

Three independent measures of (t_c + *os*) were made for each of the five lenses on each of the 11 pillars. Three independent measures of the centre thickness (t_c) were also made on each lens, (*os* = (t_c + *os*) - (t_c)).The mean of these measurements was recorded.

The overall sag (*os*):

$$os = r_0 - \sqrt{(r_0^2 - y^2)} \qquad (1)$$

where r_0 = BOZR, y = the semi chord diameter and os = calculated overall sag.

Rearrangement of equation (1) gives

$$y = \sqrt{r_0^2 - (r_0 - os)^2} \qquad (2)$$

Equation (2) allows calculation of the pillar diameter on which the lenses rest.

Having calculated the pillar diameter for all 5 lenses the mean of these 5 results was then taken to be the actual pillar diameter. (See Table 2.11 for an example)

Further verification of the precision of the measurements was made by comparing the measured sag *(os)* for each of the five lenses against the calculated sag using the calculated pillar diameter and equation (3)

$$os = r_0 - \sqrt{(r_0^2 - y^2)} \qquad (3)$$

The pillar diameter was taken to be the mean of the measures as indicated above, *y* the semi chord is therefore equal to half of the value in equation (3).

2.15.4 Measurement of lens sag for an unknown lens

Having now established the pillar dimensions using lenses of known BOZR and diameter, the pillars can be used to check lens sagittas for the orthokeratology lenses used in the study. For lenses with a polynomial back surface design three independent measures of sagitta were made on each of three pillars (nominally 7mm, 10.6mm and 10.9mm diameter). Sagitta measurements for lenses with a C5 back surface design were made using only the 7mm and 10.9mm pillars. Three independent measures of lens centre thickness (t_c) were also made using the contact lens centre thickness dial gauge.

The upper surface of each of the pillars was brought into focus with the radiuscope and then the lens was placed on the pillar within the collar (see Fig 2.21). The radiuscope was then refocused onto the front surface of the contact lens and the distance travelled (t_c +*os*) noted. The measured overall sag was then calculated (*os* = (t_c +*os*)-t_c) for each set of 3 readings.

The computer program used in the lens design (Douthwaite 2006) was then used to calculate the expected sagitta results for the lens parameters which had been ordered. The mean of the three readings for measured sagitta was then compared with the calculated sagitta result.

2.15.5 Example of calculation of sag for comparison with the three pillar diameters used for verification purposes.

Using the sag equation

$$s = \frac{r - \sqrt{r^2 - py^2}}{p}$$

where:

r = apical radius

p = p value

y = semi diameter of the pillar

Apical radius = 7.91mm

p value = 0.68

Refractive error = -1.50DS

The calculated sag for the 7mm pillar which has a measured diameter of 6.88mm is 0.785mm.

The sag is adjusted for the amount of correction required and the tear lens thickness at the corneal apex = 0.06 – 0.005

The calculated sag for the lens = 0.73mm

The calculated sag for the 10.6mm pillar which has a measured diameter of 10.41mm is 1.85mm. As this is the diameter at which the alignment curve is required the sag of the lens and cornea will be equal.

The calculated sag for the 10.9mm pillar which has a measured diameter of 10.51mm is 1.90mm. The measured sag includes an allowance for the axial edge lift of the lens.

2.15.6 Verification of Orthokeratology lenses

Once the ordered lenses were received from the supplier they were checked for accuracy following the procedure laid out previously. In addition, as the C5 design lenses have a spherical central optic zone, the back optic zone radius (BOZR) was also measured. The same radiuscope used for sag measurements was used in its traditional setting for these measurements. The pillars, described previously, were replaced with the standard lens mount.

2.16 Results:

Table 2.11: Example of Sag and Diameter Measures for 9.0mm pillar and 10.9mm collar. All measurements are in mm.

Nominal Contact Lens Radius (r_0)	Mean of the 3 independent measures			Calculated Pillar Diameter	Calculated Sag	Measured Sag (os - t_c)
	(r_0)	(t_c + os)	t_c			
7.00	7.01	1.75	0.22	8.74	1.52	1.53
7.50	7.52	1.60	0.21	8.71	1.39	1.39
8.00	8.01	1.50	0.20	8.74	1.29	1.30
8.50	8.55	1.41	0.22	8.69	1.19	1.19
9.00	9.04	1.32	0.20	8.71	1.12	1.12
Mean and SD				8.72 +/- 0.02	1.30 +/- 0.16	1.30 +/- 0.16

Table 2.11 shows the results for the 9.0mm pillar in conjunction with a 10.9mm collar. The calculated pillar diameter of 8.72mm was used in the sag equation to find the calculated sag. Similar tables were constructed for the other ten pillar and collar combinations used in the study. The combined results for these measurements are shown in Table 2.12.

Table 2.12: Mean Values for Pillar Diameters and Sag Measures. All measurements are in mm.

Pillar and Collar Diameter ordered	Pillar Diameter measured	Measured Sag *(Mean and SD)*	Calculated Sag *(Assuming the pillar diameters found in column 2)*
Collar 10.9			
5.0	5.67	0.52 +/- 0.04	0.52
5.3	5.14	0.43 +/- 0.05	0.43
7.0	6.91	0.79 +/- 0.08	0.79
9.0	8.72	1.30 +/- 0.16	1.30
9.55	9.50	1.58 +/- 0.19	1.58
10.6	10.45	1.96 +/- 0.26	1.96
Collar 11.3			
7.0	6.88	0.78 +/- 0.08	0.78
9.0	8.66	1.29 +/- 0.17	1.29
9.55	9.42	1.55 +/- 0.19	1.55
10.6	10.41	1.95 +/- 0.25	1.95
10.9	10.58	2.03 +/- 0.26	2.03

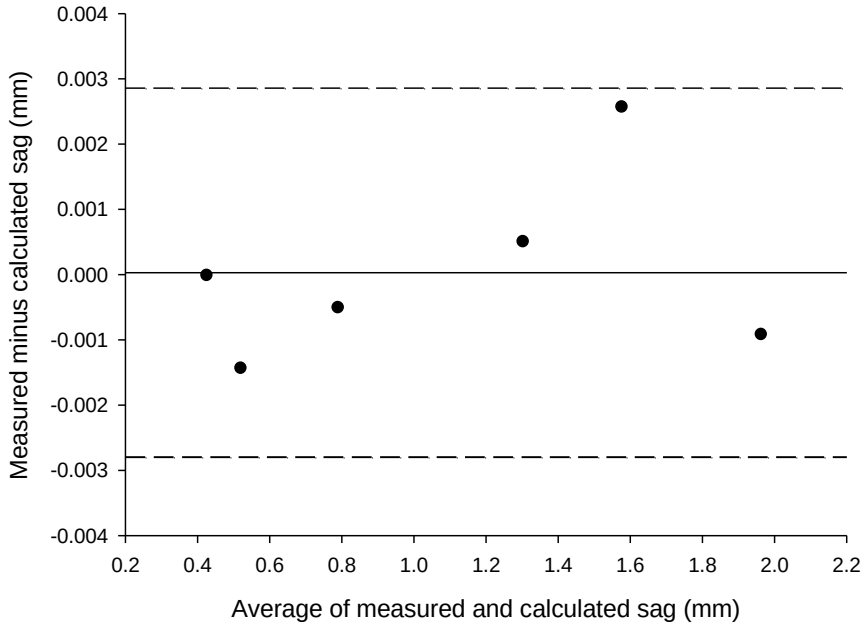
Table 2.12 shows the lens sagitta results for the eleven pillars**.**

Table 2.13: Mean and Difference Results for the 10.9mm and 11.3mm Collars. All measurements are in mm

Pillars used with Collar diameter 10.9mm	Difference between Measured and Calculated Sag	Mean of Measured and Calculated Sag	Pillars used with Collar diameter 11.3mm	Difference between Measured and Calculated Sag	Mean of Measured and Calculated Sag
5	-0.0014	0.5209	7	-0.0007	0.7837
5.3	0.0000	0.4267	9	0.0022	1.2875
7	-0.0005	0.7903	9.55	-0.0004	1.5482
9	0.0005	1.3031	10.6	-0.0011	1.9519
9.55	0.0026	1.5771	10.9	-0.0016	2.0268
10.6	-0.0009	1.9638			
Mean	0.0000		Mean	-0.0003	
SD	0.0014		SD	0.0015	

Table 2.13 shows the difference between the two sag measures (calculated and measured) and the mean of the two measures for both sets of collar and pillar combinations. It is possible to assess the agreement between two methods of clinical measurement by plotting the mean of the two measurements against the difference between the two measurements. The results for the two pillar and collar combinations are shown in Figs 2.22.

a)



b)

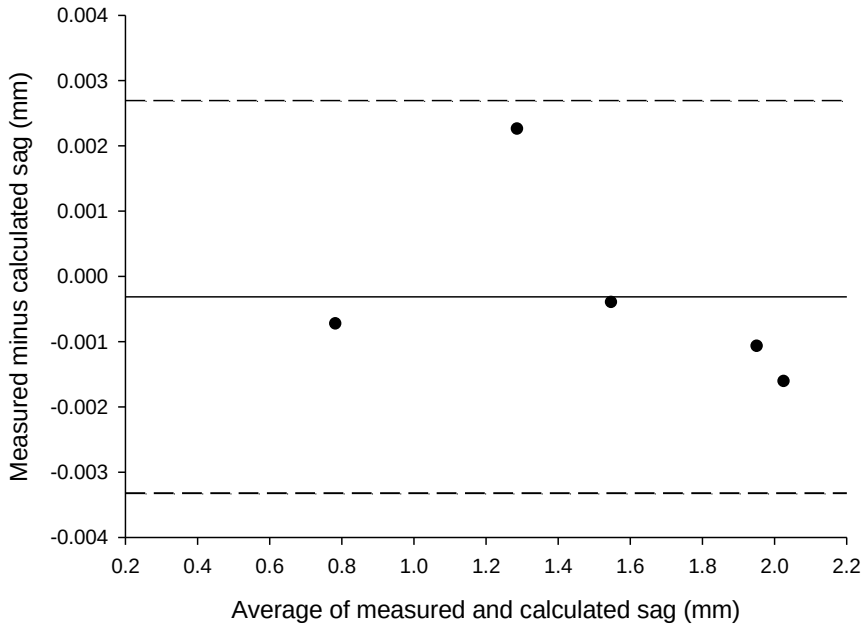


Fig 2.22 Bland Altman plots of the Collar and Pillar combinations

a) 10.9 mm pillar collar combination b) 11.3mm pillar collar combination

Fig 2.22a shows the mean difference or bias (solid line) in the sag measures is 0.000mm and the limits of agreement (+/- 2SD) (dashed line) whilst Fig 2.22b shows the mean difference to be -0.0003mm. Twice the standard deviation of the difference between two measurements is said to be a good indication of the comparability of two clinical measures (Bland, 1986). This was less than 0.003mm for both collars.

2.16.1 C5 Design Results

Three independent measures of the BOZR and sag measures (7.0mm and 10.9mm collar and pillar combinations) were taken and the mean of these three readings was calculated. Bland Altman plots were then created comparing the measured BOZR against the ordered BOZR Fig 2.23.

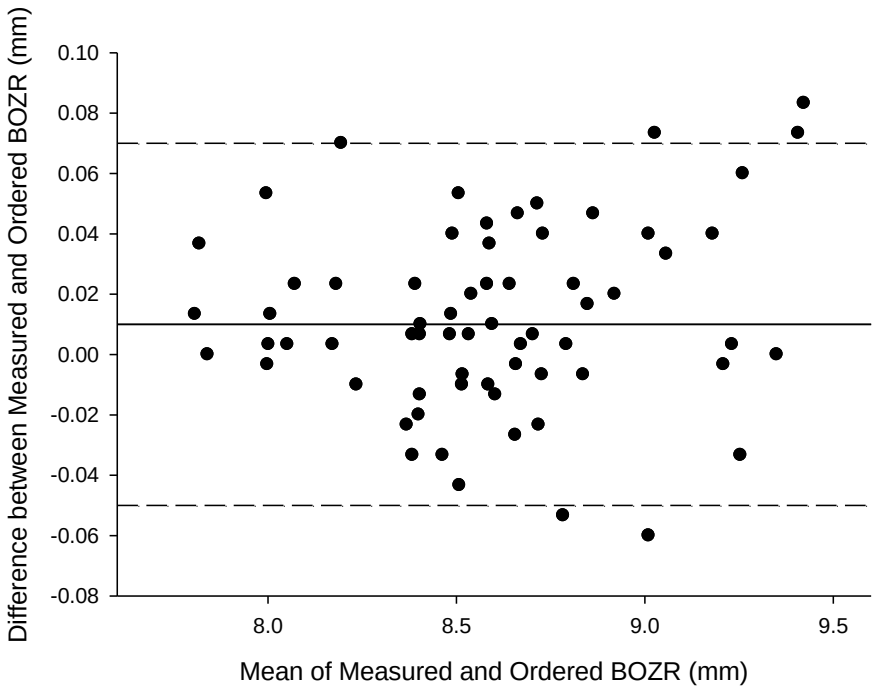
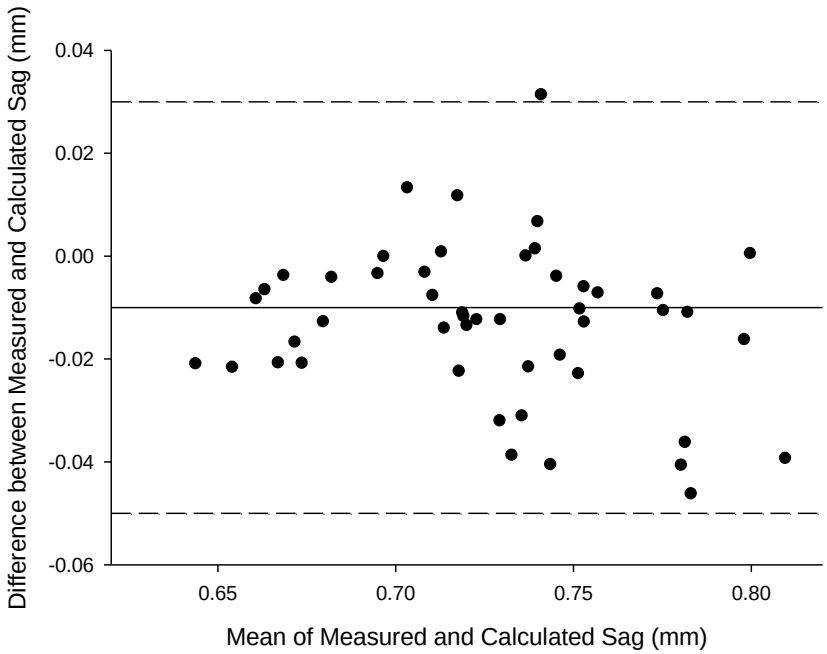


Fig 2.23 Back Optic Zone Radius (BOZR) comparison for the C5 design lens

Figure 2.24 shows the Mean (bias) for the two measures was found to be 0.01mm. The limits of agreement (2SD ((Bland, 1986)) are -0.05 to 0.07mm. The use of two standard deviations indicates the 95% confidence limits if three standard deviations were to be applied i.e. 99% confidence limits then all the BOZR measures would fall within these limits (-0.08 to 0.10). The British Standard for Contact Lens Tolerances (BS EN ISO 18369-2 (2006)) states the tolerance for the measurement of the BOZR to be +/- 0.05mm.

a)



b)

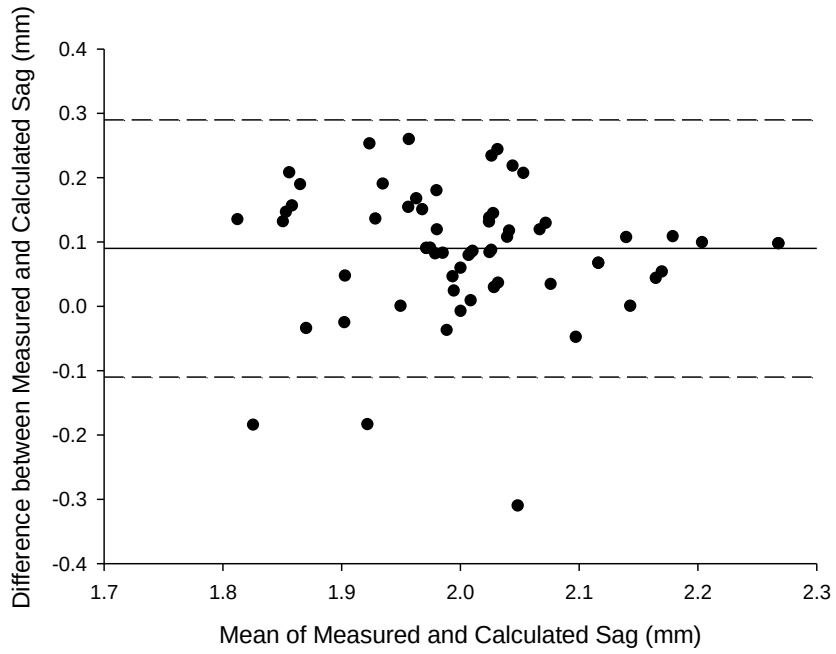
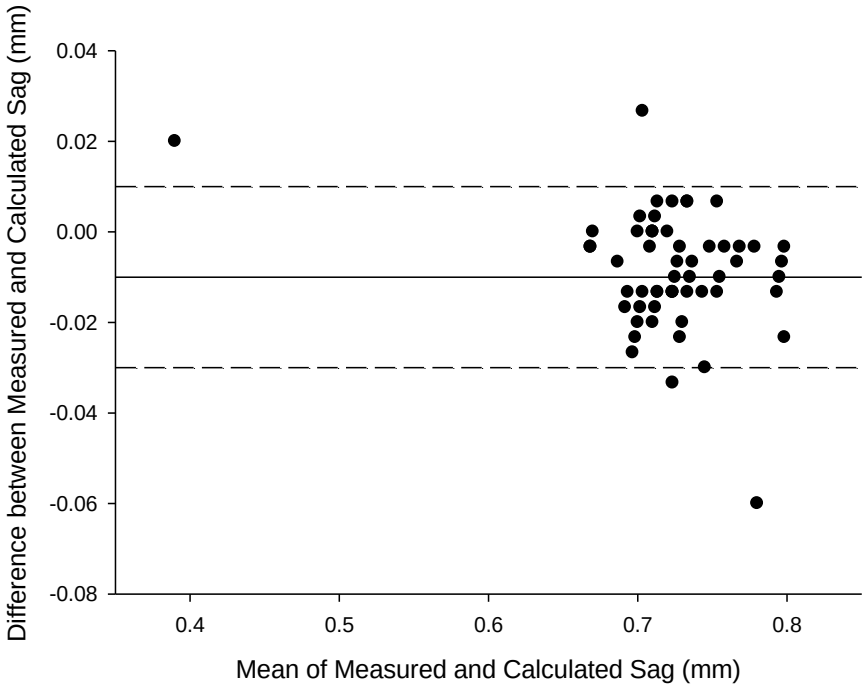


Fig 2.24 Lens Sags measured with 7.0mm and 10.9mm pillars a) The mean (bias) for the 7.0mm pillar was -0.01mm with the limits of agreement -0.05 to 0.03.b) The mean (bias) for the 10.9mm pillar was 0.09mm with the limits of agreement being -0.11 to 0.29

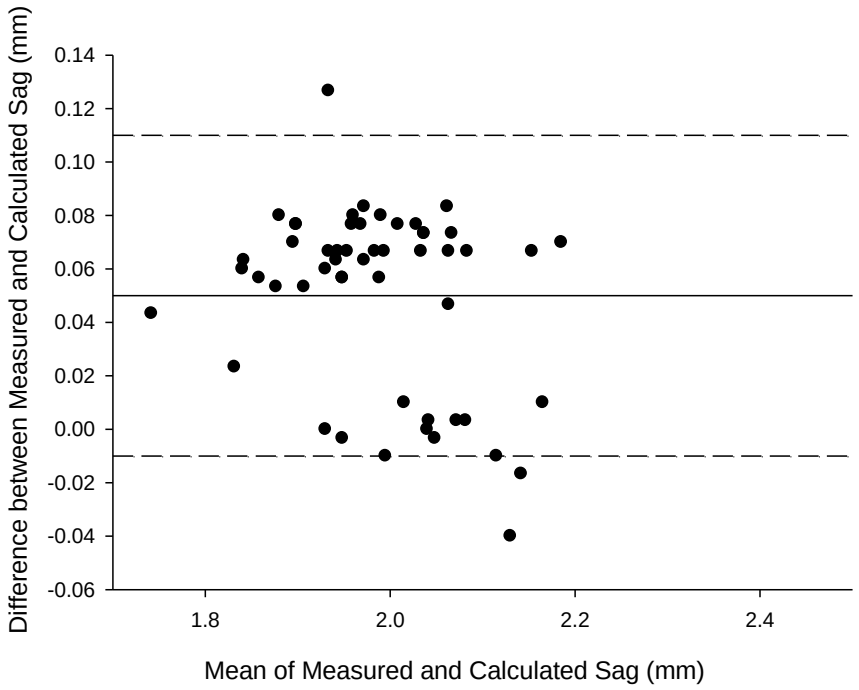
2.16.2 Aspheric Design Results

Three independent measures of the sag measures (7.0mm, 10.9mm and 11.3 collar and pillar combinations) were taken and the mean of these three readings was calculated. Bland Altman plots were then created comparing the measured BOZR against the ordered BOZR Fig 2.25.

a)



b)



c)

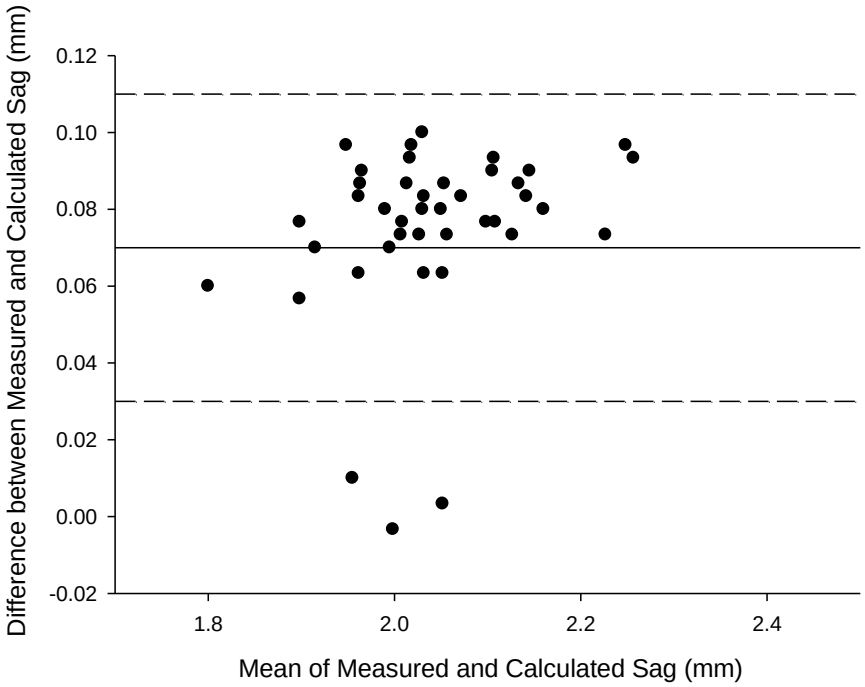


Fig 2.25 Aspheric lens sags measured with 7.0, 10.6 and 10.9mm pillars a) The Mean (bias) was -0.01 with the limits of agreement -0.03 to 0.01 b) The Mean (bias) was 0.05 with the limits of agreement -0.01 to 0.11 c) The Mean (bias) was 0.07 with the limits of agreement 0.03 to 0.11.

2.17 Discussion

Accurate measurement of the lens sag is dependent upon a clear focus of the pillar surface being achieved. This can be quite difficult if the upper surface of the pillar has coarse tooling marks. This coarse surface then leads to a range of apparent focus points. In the case of the small diameter pillars this can be particularly troublesome as the sag measurements are very small. The other difficulty with these small pillars was that the lenses tended to overbalance. In order to facilitate the placing of the lens onto the pillar the initial collar height was reduced. Since the purpose of the collar is to act as a centring device for the lens only a small height differential is required. This difficulty applied to both the C5 and aspheric design lenses.

An analysis of the outliers using the Bland Altman plots (Figs 2.22) showed no systematic error i.e. no single subject's lens measures were outside the 95% limits of agreement for more than one sag measure. The mean bias for the two central measurements was found to be -0.01mm this indicated that the sag measured by the collar and pillar technique tended to under read by 0.01mm. The results indicate that this method would be appropriate for the verification of the ordered orthokeratology lenses.

CHAPTER 3 PROTOCOLS AND INITIAL OUTCOMES

3.1 Introduction

The aim of this study was to look at the effect of orthokeratology on a number of biometric measures. In this chapter the recruitment process for the subjects who participated in the study is outlined. The inclusion and exclusion criteria which were applied are detailed and the research evidence to support these. Having recruited the subjects the data collection protocols are shown for each of the visits. The data will enable the main outcome measures of the assessment of the change in;

- anterior apical radius and p value
- posterior apical radius and p value
- corneal sag and corneal power
- refractive error and the associated change in vision and best corrected visual acuity (BCVA).
- the correlation between the change in corneal sag and corneal power and the refractive error change
- changes in corneal thickness both centrally and in the mid periphery over time
- Anterior chamber depth and axial length change, if any, will be evaluated.

The results of these investigations are outlined in chapters four to eight.

Section 3.4 gives an explanation of the use of power vectors (Thibos, Wheeler and Horner 1997) for the recording of refractive error measurements. An illustration of the two lens designs used in the study is shown in section 3.6. Finally the statistical analysis procedures used in the study and the power calculations applied are detailed in sections 3.9 and 3.10.

3.2 Subject recruitment for Orthokeratology study

In order to recruit subjects for the full study a web advert was placed on the University home page (Figure 3.1). No subjects from the previous precision study were used in this later study.

Are you short sighted?

Would you consider an alternative to Laser surgery?

Would you be interested in participating in a study where your corneal shape is changed to eliminate your short sight by wearing contact lenses during sleep?

If the answer to these questions is yes then please contact a.parkinson@bradford.ac.uk for further information.

Fig 3.1 Recruitment advert for the university website

The university home page is visible to members of the university and to members of the public searching the university website. Ninety four responses were received and subjects were sent an initial information letter. Subjects responding at this stage were self-selecting and motivated by the prospect of myopia elimination. No financial incentive was offered at any stage during the recruitment or study phases. The orthokeratology lenses and contact lens care products were provided free of charge for the duration of the study. A new pair of lenses was provided for subjects who completed the twelve month study, and wished to continue with orthokeratology treatment. These lenses were supplied after the last data collection appointment. Subjects who continued with orthokeratology have been provided with annual aftercare appointments either at the Bradford School of Optometry Eye clinic or have been transferred to another optometrist with an interest in orthokeratology. Due to reports from previous investigators (Rah et al 2002; Tahhan et al 2003; Maldonado-Codina et al 2005) of the large scale drop out of recruits to orthokeratology studies no limit was placed on the number of initial enquiries that would be invited for further evaluation.

3.3 Initial assessment

Fifty six people responded positively on receipt of the initial information letter. These subjects were invited to attend for an initial evaluation appointment. A full list of the inclusion and exclusion criteria is shown in Table 3.2. In order to eliminate subjects who had had previous adverse reactions to contact lens wear a full history and symptoms assessment was carried out. Subject's general health status and any medications being taken on a regular basis were recorded. All the subjects reported they were in good general health at the time of their initial assessment and no subject was taking long term medication. Subject's unaided vision was measured using directly viewed high contrast logMAR charts (Numbers 4 and 5) at six metres. The two charts were randomly selected with a different chart being used for each eye to minimise any learning effect. Subjects who were unable to read the top three lines at six metres were brought forward to three metres. If the subject was still unable to read the top three lines they were moved forward to 1.5 metres from the chart. Scores achieved at these shorter viewing distances were corrected for the appropriate distance in accordance with the scale indicated on the logMAR charts (Table 3.1). LogMAR charts are considered to be the most appropriate method of assessment for both vision and visual acuity in clinical studies (Ferris and Bailey (1996). The results were recorded as Visual Acuity Rating scores (VAR) rather than logMAR scores.

VAR scores are equivalent to 100 – 50(logMAR)

e.g. VAR for 0.00 logMAR is 100 – 50(log (MAR1.0))

VAR = 100.

VAR scores were chosen to avoid the use of negative scores for acuities better than log MAR 0.00

e.g. LogMAR -0.30 (MAR = 0.5 degrees) is equivalent to VAR 115.

Table 3.1 Correction factors for reduced viewing distances (VAR)

Measurement at 6 metres	No correction
Measurement at 3 metres	-15
Measurement at 1.5 metres	-30

A full subjective refraction using trial frame and lenses was then carried out. The back vertex distance of the trial frame was recorded for any subjects whose refractive error exceeded 5.00 dioptres in any meridian. The visual acuity achieved was recorded following the method outlined above. Subjects who were over 35 years old at the time of recruitment had their amplitude of accommodation measured using the RAF rule. A full slit lamp assessment of the subject's anterior eyes was carried out to ensure the eyes were capable of undergoing orthokeratology treatment. All subjects had undergone a full eye examination within the last two years. No subjects reported any posterior segment pathology.

Eleven people were rejected at this initial stage. Four subjects had refractive errors outside the study protocol.

Refractive error limits were set at;

- Myopia no greater than -6.50 dioptres,
- With the rule astigmatism no greater than -1.50DC,
- Against the rule astigmatism no greater than -0.75DC.

The lower limit for against the rule astigmatism was set in light of the reported increase seen in this form of astigmatism in previous studies (Kerns 1976a, Kerns 1978, Binder et al 1980). One volunteer was rejected having been found to have corneal pathology, i.e. keratoconus.

Six of the volunteers were optometry students. As optometry undergraduates are involved in mastering the skills of retinoscopy, direct ophthalmoscopy and other

methods of ocular assessment in mesopic illumination concerns were raised about the effects of orthokeratology on visual function under these conditions. Berntsen, Barr and Mitchell (2005) in their study reported that there was a loss of low contrast best corrected visual acuity of logMAR 0.11 +/- 0.09. Following one month of orthokeratology treatment this loss increased to 0.19 +/- 0.12 if the pupil was dilated to five millimetres. Joslin, Wu, McMahon, Shahidi (2003) , Berntsen et al (2005), Hiraoka, Matsumoto, Okamoto, Yamaguchi et al (2005) have all reported on the effect of orthokeratology on the higher order aberrations. The effect on higher order aberrations becomes more apparent with the larger pupils induced in mesopic illumination. This, coupled with the loss of low contrast acuity with a dilated pupil, meant that it was considered appropriate to exclude optometry undergraduates from the study.

Students from other disciplines within the university, who were less dependent on mesopic vision, were allowed to join the study. A number of volunteers were presbyopic. No age exclusion was applied however two presbyopic subjects decided not to continue with the study at this point. These two individuals benefitted from using their uncorrected myopia as a form of reading correction. They felt that the exchange of distance spectacles for reading spectacles did not justify their participation in the study.

Table 3.2 Inclusion and Exclusion criteria for the study

Inclusion Criteria	Exclusion Criteria
At least 18 years of age, no upper age limit was applied.	No history of anterior eye disease which would preclude contact lens wear
Able to make an informed judgement about the procedure	No previous refractive surgery
Willing to follow the study protocol	No general health conditions which would contraindicate contact lens wear
Sphere ≤ -6.50DS With the rule astigmatism ≤ -1.50DCyl Against the rule astigmatism ≤ -0.75DCyl	Agreement between corneal and spectacle astigmatism to minimise effects of uncorrected lenticular astigmatism
Visual acuity of VAR 100 or better in each eye	No topical medication
Achieve a successful fit and visual acuity through the lenses	No systemic medication which would be associated with adverse response in the anterior eye.
Able to insert and remove the lenses safely	No pregnant or lactating mothers
Achieve a myopia reduction after a brief period of open eye lens wear (1 – 2 hours)	No history of posterior segment disease
	Optometry undergraduates

3.4 Power vectors (Thibos, Wheeler and Horner 1997)

In order to allow the change in manifest refractive error to be recorded in a manner which would allow statistical evaluation the sphero-cylindrical errors were converted to power vectors. Thibos et al (1997) proposed a series of power vectors which allowed the description of refractive errors using Fourier analysis. Researchers have shown that orthokeratology can lead to a change in the form of astigmatism present e.g. an increase in against the rule. A method of recording the manifest refractive error which simply involved the calculation of the mean sphere would potentially disguise this change. Power vector analysis deconstructs the refractive error into a spherical component and a pair of Jackson Cross Cylinder lenses (JCC). The benefit of the JCC lens is that it has a mean sphere equivalent of zero. A JCC lens may also be

represented either by a single phase shifted cosine wave or the sum of a pure cosine and sine wave. These wave forms lend themselves to the principle of Fourier analysis.

In the paper Thibos et al describe a number of forms of power vector analysis. The rectangular form of Fourier decomposition which is described here is more useful for statistical analysis. In this form the power profile of any lens may be represented by the equation;

$$P(\theta) = M + J_0 \cos 2\theta + J_{45} \sin 2\theta$$

Where P (θ) = the variation of lens power with meridian

In order to convert from conventional sphere cylinder notation (S, - C x α) to the Fourier rectangular form Thibos et al offer the following equations;

M = S + C/2

J0 = -C/2 cos2α

J45 = -C/2 sin2α

This rectangular form of Fourier decomposition means that the elements within a lens or a refractive error can be considered separately when any change is being analysed.

Fig 3.2 shows the three elements of the Fourier decomposition.

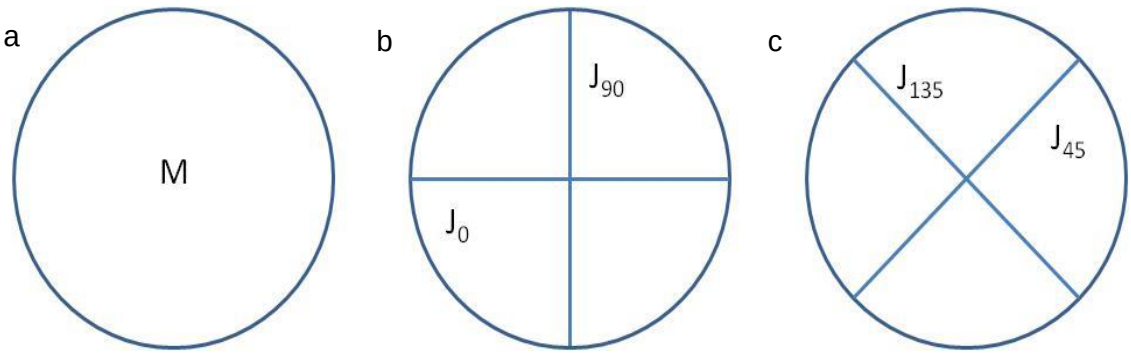


Fig 3.2 Elements of the Fourier decomposition (rectangular form)

The crossed cylinders shown as elements b and c could be represented by a sphere cylinder combinations of

b) $J_0 / (J_{90} – J_0) \times 90$

c) $J_{45} / (J_{135} – J_{45}) \times 135$

The example below shows the decomposition of the initial and one year refractive errors for the right eye (pentacurve design) of one of the subjects into the Fourier decomposition.

Table 3.3 Fourier decomposition (rectangular form) for the right eye of subject DR initial and one year refractive errors. (All values are in dioptres)

	Sphere (S)	Cyl (C)	Axis (α)	M	J_0	J_{45}
Initial	-2.75	-0.75	165	-3.13	-0.32	0.19
One year	-0.50	-0.50	175	0.25	-0.25	0.04

A Microsoft Excel © spreadsheet was created to calculate the power vectors for each eye of each subject at each visit for the twelve months of the study.

3.5 Lens design appointment

Forty three subjects were then invited for a lens design appointment. Subjects who were wearing contact lenses were only admitted to the study after a period without lens wear. For subjects wearing soft lenses a period of at least one week without lenses was required prior to lens design measurements being made. Mountford Ruston and Dave (2004) pointed out that conventional rigid lens wear may induce some corneal flattening. They noted that long term rigid lens wearers may not manifest their full refractive error unless they spend a period of time without their lenses. Subramaniam, Bennett, Lakshminarayanan and Morgan (2007), found in their study, that rigid gas permeable lens wearers showed a residual degree of myopia (-0.29 +/- 0.55D) after 30 days of orthokeratology lens wear when compared to a group of soft lens or spectacle

wearers. Subramaniam et al (2007) asked their subjects to leave out their lenses for three weeks prior to lens design measurements. They did not use topography measurements to confirm the corneal status. Only one subject for the current study was an established rigid gas permeable lens wearer. Mountford, Ruston and Dave (2004) recommended that rigid gas permeable lens wearers should not be fitted with orthokeratology lenses, until they have two consecutive topography maps which show no significant difference. This procedure was followed for the one subject noted above.

At the lens design visit the following measurements were made; (Table 3.2)

Table 3.4 Lens design appointment measurements

Eyesys Corneal Analysis System	Three independent measurements were made on each eye following the procedure outlined in Chapter 2
Orbscan II Corneal topographer	Three independent measurements were made on each eye following the procedure outlined in Chapter 2
IOL Master axial length	Five independent measurements were made on each eye following the procedure outlined in Chapter 2
IOL Master anterior chamber depth	One measurement was made following the procedure outlined in Chapter 2
Contact lens refraction	Subjective refractive errors were adjusted for BVD and the mean spherical error (sphere power plus half of the cylindrical element) calculated.
Horizontal visible iris diameter (HVID)	A graticule eyepiece was placed in one of the the slit lamp eyepieces to allow accurate measurement of the horizontal visible iris diameter.

3.6 Lens design protocols

Following the lens design appointment the results from the EyeSys were analysed. Sagittal radii and perpendicular distance data were retrieved for each of the subjects as indicated in Chapter 2 Section EyeSys procedures. These data were then analysed following the procedure outlined in Chapter 2 Section 2.2.1. These analyses produced three measures of apical radius and p value along both principal meridians for each eye of each subject. The mean value of the apical radius and p value were then calculated. The mean results for the horizontal meridian were used to design the orthokeratology lenses using the computer program available on the CD rom issued with Contact Lens Optics and Lens Design Douthwaite (2006).

In this study two lens designs were used. Subjects had their right eye fitted with a traditional pentacurve (C5) design lens. The left eye was fitted with a custom designed aspheric back surface orthokeratology lens. Both lenses were produced in Boston XO material ((Polymer Technology Corp Wilmington MA) with a nominal Dk/t of 100×10^{-11} cm^2/s) by No7 Laboratories (Hastings West Sussex). To assist subjects in identification of the lenses, the pentacurve lens was made from lilac tinted and the aspheric lens from blue tinted Boston XO material. The light neutral tints present in Boston XO material are usually used to facilitate the visualisation of an RGP lens where a transparent lens would prove a problem. No subject reported any difficulty in colour perception despite wearing the two differently tinted lenses.

3.6.1 C5 design

Having selected the orthokeratology programme the C5 design option was chosen. The programme was used to calculate the required back optic zone radius (BOZR). The calculation is made on the basis that the required BOZR is equal to the apical radius flattened by the subject's refractive error plus -1.00D. The additional dioptre is included to allow for regression in the refractive correction during the day. Mountford recommended at least a -0.50 dioptre overcorrection when lens parameters were selected (Mountford 1998). The change in radius per dioptre is approximately 0.2mm per dioptre.

The calculation of the BOZR is made using

$$r = (n - 1)/F$$

The refractive index used in this calculation is n = 1.3375, as previously mentioned this refractive index accounts for the contribution made by the posterior corneal surface to the total corneal power.

For example

Flattest meridian Apical radius = 7.55mm

Corneal power = 337.5/7.55 = 44.70D

Correction required = - 1.50 + (-1.00) = -2.50D

New corneal power = 42.20D

OK BOZR = 337.5/ 39.27 = 8.00mm

The reverse curve radius was calculated to give a tear lens thickness (TLT) of 0.005mm. The first alignment curve gives a clearance of 0.01mm reducing to alignment by the second peripheral curve. 0.08mm edge clearance is created by the selection of the peripheral curve. The tear lens profile of the pentacurve design is shown in Fig 3.2. The diameter measures for the five curves are shown in Table 3.3 and the tear lens profile for this lens is shown in Fig 3.2

Table 3.5 Lens diameters for C5 lens design

C1	C2	C3	C4	C5
7.00mm	8.00mm	9.00mm	10.00mm	11.20mm
BOZR	Reverse curve	Alignment curve	Alignment curve	Peripheral curve

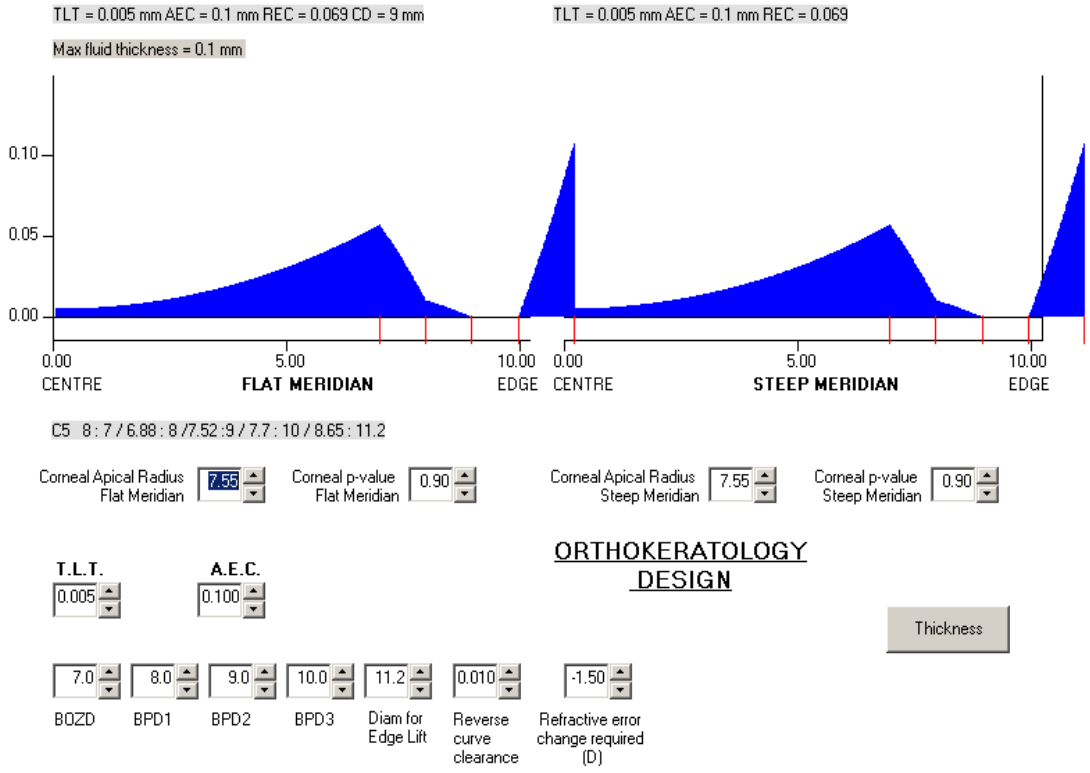


Fig 3.3 Tear lens profile for C5 design lens

3.6.2 Aspheric design

The aspheric lens design programme was selected for the left lens. Using the apical radius and p values calculated from the initial data the lens details were generated by the programme software. Since the aspheric lens had an elliptical back surface it could not be ordered using a series of radii. The programme generated a series of sag measures for the back optic zone diameter (BOZD), the corneal contact diameter and the total diameter (TD).

For example; for a cornea of apical radius = 7.56mm and p value 0.81

- Standard aspheric RGP lens (Fig 3.4a)

  Using the sag equation:

$$s = \frac{r - \sqrt{r^2 - py^2}}{p}$$

The corneal sag at 7mm diameter is 0.849mm. If the apical clearance required is 0.02mm then the contact lens sag (s_1) at 7mm must be 0.869mm.

The corneal sag at 9.6mm diameter is 1.674mm. The change in the contact lens and corneal sags must be equal. The change in the corneal sag over this diameter is 0.825mm. The contact lens sag (s_2) at 9.6mm diameter should then be 1.694mm.

The corneal sag at 11.2mm diameter is 2.377mm. The axial edge clearance at this diameter should be 0.1mm. The lens sag must therefore be 0.1mm less than that of the cornea. The change in the corneal sag is 0.703mm and therefore the change in lens sag will be 0.603mm. This gives the lens sag (s_3) of 2.297mm at 11.2mm total diameter.

- Orthokeratology lens (Fig 3.4b)

For the orthokeratology lens we needed to reduce the central sag to produce the appropriate refractive correction.

Change in sag per dioptre = 0.024mm for a 7mm diameter zone

Correction required = -1.50 + (-1.00) = -2.50D

Change in sag required = 0.06mm

TLT = 0.005mm

New sag = 0.805mm at 7mm diameter

$$r = \frac{(y^2+s^2)}{2s}$$

BOZR = 8.01 mm

The sag at 9.6mm i.e. the corneal contact diameter must be 1.679mm to allow a TLT of 0.005mm.

The sag at 11.2mm must be 2.262mm allowing an edge clearance of 0.12mm. The tear lens profile for the lens design calculated above is shown in Figure 3.5.

a)

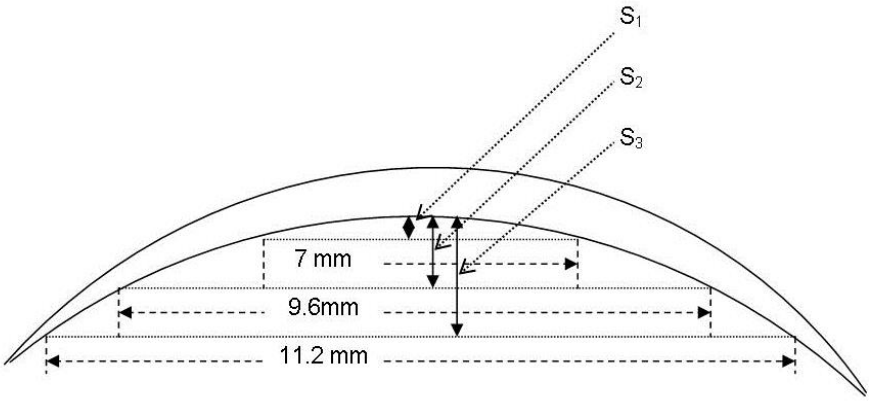


Fig 3.4a sag measures for an aspheric design lens

b)

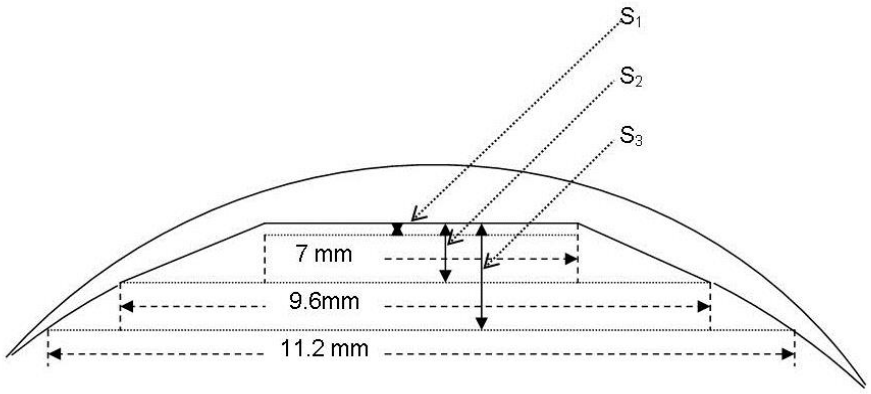


Fig 3.4b sag measures for a reverse geometry lens

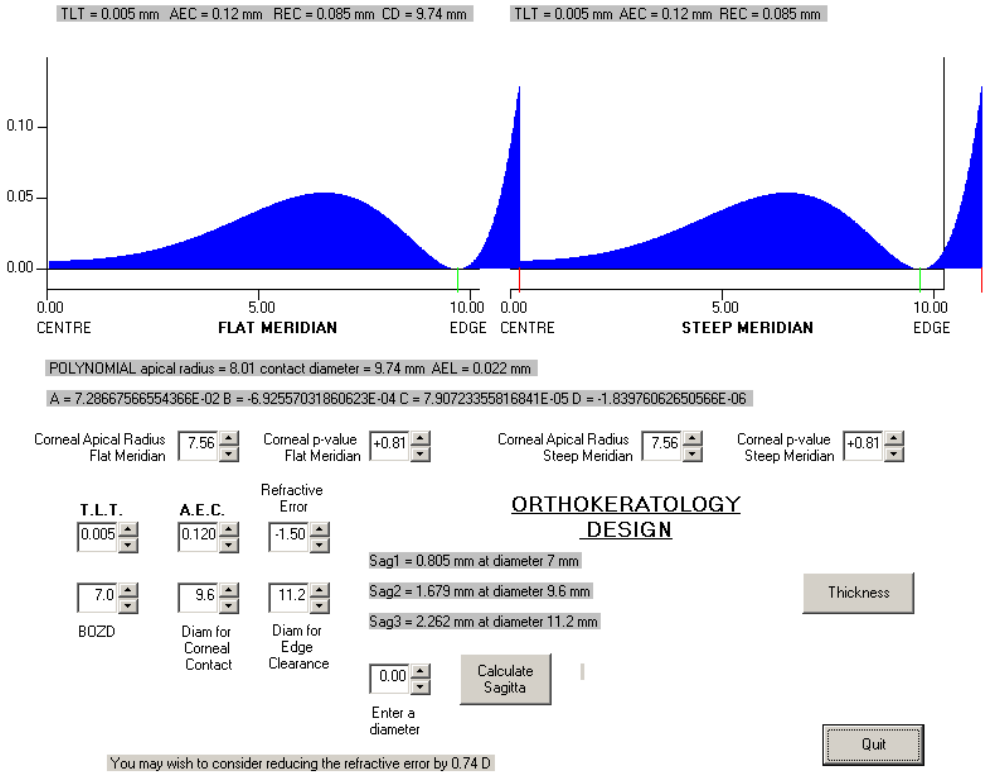


Fig 3.5 Tear lens profile for aspheric design lens

The computer programme provided all the lens details once the apical radius, p value and refractive correction were entered.

For both lens designs the back vertex power (BVP) was ordered as +1.00D to compensate for the overcorrection in the tear lens profile. This allowed the subjects to have good acuity through the lenses in open eye situations. It was felt that acceptable acuity through the lenses in open eye situations would facilitate the adaptation period. Good acuity through the lenses would also be indicative of an appropriate lens fit. Subjects could wear the lenses later in the day if they experienced regression of the orthokeratology effect before the end of the day.

The centre thickness, for both designs, was originally selected to be 0.18mm. This was in agreement with the centre thicknesses listed for orthokeratology lenses in the ACLM handbook both 2007 and 2011 (range 0.14 to 0.17mm). After problems with breakages in the earlier lenses the centre thickness was increased to 0.20mm. This lens thickness is consistent with that used in conventional rigid gas permeable lenses (0.12 – 0.23mm ACLM handbook 2007). Lens thickness in conventional RGP lenses is determined by the refractive correction required.

An initial total diameter (TD) of 11.2mm was selected for both lens designs. The decision on the total diameter was based on the subject's corneal diameter (HVID). Individuals with HVID < 12mm were fitted with lenses of 10.9mm (TD). The total diameter of standard fitting rigid gas permeable is normally selected to be 2mm smaller than the HVID (Gasson and Morris 2003). This large total diameter was chosen for the orthokeratology lenses to improve centration. As the eye rotates upward and outward during sleep small diameter lenses tended to displace. This displacement would lead to decentration of the flattened zone. Hiraoka, Mihashi, Okamoto, Okamoto et al (Hiraoka et al., 2009b) looked at the effects of a decentred orthokeratology lens. They found that contrast sensitivity and low contrast visual acuity were significantly correlated with the degree of decentration. Changes in the third and fourth order aberrations were also correlated with the degree of decentration. Hiroaka et al found no significant correlation between the degree of decentration and the corrected distance acuity. Whilst participants may achieve acceptable levels of uncorrected visual acuity following orthokeratology lens wear; changes in contrast sensitivity and higher order aberrations would be interpreted by participants as a reduction in visual quality.

The large diameter also improves the initial comfort of the lenses. In conventional RGP lenses, with total diameters smaller than the HVID, contact between the upper lid margin and the lens edge can be a source of patient discomfort (Phillips 1997). Reference to the ACLM handbook (2007) showed that total diameters between 10.0

and 12.7mm were available commercially at this time. The ACLM handbook for (2011) listed lenses of up to 17.0mm total diameter.

3.7 Collection protocol

When the lenses were received from the manufacturer they were verified following the procedures outlined in Chapter 2. Subjects were then invited to attend for a collection appointment. At this appointment all subjects were instructed in the insertion and removal procedure and care procedures for their orthokeratology lenses. In order to ensure that the reverse curve of the lenses was completely filled with solution, subjects were instructed to fill the lens with normal saline (Sensitive Eyes® Plus Bausch and Lomb). They were then instructed to insert the lenses whilst holding their face parallel to the table. This is in contrast to the insertion procedure for traditional rigid gas permeable lenses where the subject would generally hold their head upright. As subjects were inserting their lenses immediately before going to sleep there was little time for the tears to displace any air trapped in the reverse curve. Any air trapped under the lens would lead to excessive drying and staining of the cornea under the reverse curve. The large diameter lenses also reduce the rate of active tear exchange.

A further concern was that as subjects would have little or no tear exchange under the lenses whilst they were asleep, saline would be preferable to rigid lens wetting solution. Under normal rigid gas permeable wearing conditions the tear exchange instigated by blinking would dissipate any wetting solution and its accompanying chemical constituents. In their in vitro study Begley, Waggoner, Hafner, Tokarski (1991) investigated the effect of three different wetting solutions including Boston Conditioning solution on rabbit corneal epithelium. They found that Boston Conditioning solution did affect the microscopic structures of the cornea when used in quantities which were commensurate with that of normal contact lens wear. Begley et al commented that extrapolation of the damage in the rabbit to that of the human cornea should be used with caution. The rabbit has a reduced blink rate compared to that of the human which

they point out would lead to an increased concentration of the solution. This reduced blink rate would also apply to our subjects as the lenses were being worn during sleep.

Furrer, Mayer and Gurny (2002) in their review article looked at the ocular tolerance of preservatives in both ocular drugs and contact lens solutions. They point out that prolonged exposure to chlorhexidine has been associated with corneal desquamation. Boston Conditioning solution is preserved with 0.006% chlorhexidine gluconate. In soft contact lens wear these responses are seen because of desorption from soft lens materials. Paugh, Marsden, Edrington, Deland et al (2007) advised the use of a carboxymethylcellulose based lubricant to reduce the corneal staining induced by the use of multipurpose solutions in soft lens wearers. Since our lenses were filled with saline prior to insertion it was concluded that this should reduce solution related corneal stain. Carnt, Jalbert, Stretton, Naduvilath et al (2007) also looked at solution toxicity. In their study of soft lens wearers they found that hydrogen peroxide-based solutions led to the lowest incidence of solution toxicity. For the purposes of this study it was felt that the small risk of a subject inadvertently inserting their lenses without neutralising the hydrogen peroxide did not outweigh the benefits of an unpreserved solution.

Due to the large diameter of the lenses, subjects were instructed to remove their lenses by manipulating the upper lid to dislodge the lens from the cornea whilst holding the lower lid firmly against the globe. Cho, Cheung, Mountford and White (2008) reported that some individuals wearing orthokeratology lenses had lens suckers available to remove their lenses. As indicated in chapter one these were found to be a source of potential microbial contamination (Boost and Cho 2005). Cho et al (2008) advised that digital manipulation was good practice for lens removal. Only those subjects therefore who could remove the lenses using digital manipulation were allowed to continue with the study. Subjects were advised that the lenses should be mobilised on the eye before any attempts to remove the lenses were made. Ocular lubricants could be used first thing in the morning to assist in lens mobilisation prior to removal (Cho et al 2008).

These procedures were refined in pre study evaluations with one volunteer. Five people were unable or unwilling to handle the lenses at this time and asked to be removed from the study.

Once subjects were confident with the insertion and removal procedures the lens fit was evaluated using fluorescein. Mountford, Cho and Chui (2005) point out that fluorescein pattern analysis alone is a poor predictor of the accuracy of orthokeratology lenses. The patterns should be viewed alongside corneal topography measurements. At this time if the fluorescein pattern showed the classic bull's eye appearance then the collection visit was allowed to continue. The subjects' visual acuity and over refraction were checked at this stage. It was essential that subjects could achieve acceptable levels of vision whilst wearing the lenses. Whilst the lenses were not intended for daily wear it was important to provide some form of visual correction during the early phases of the procedure when the full effect of orthokeratology had not been achieved.

Subjects were instructed to wear the lenses for at least one hour in an open eye situation and then to return for a further assessment. At this time the lenses were removed. Unaided vision, subjective refraction to assess the residual refractive error and visual acuity measurements were carried out. Only subjects who demonstrated a reduction in their manifest myopic error were allowed to continue. As the two eyes had undergone different forms of treatment, right eye – C5 lens and left eye – aspheric lens the results are reported separately (Table 3.4). Sridharan and Swarbrick (2003) found that even ten minutes of open eye orthokeratology lens wear induced a significant change in the unaided logMAR visual acuity.

Table 3.6 Mean change in vision, sphere power and best corrected visual acuity at the collection appointment

	Pentacurve	Aspheric
Change in vision (VAR)	25.48	24.91
Change in sphere (dioptres)	1.53	1.34
Change in best corrected visual acuity (VAR)	-3.8	-7.36

The mean change in unaided vision of 25.20 letters was commensurate with the change in mean sphere of 1.44 dioptres for the two eyes. The loss in best corrected visual acuity (BCVA) which was seen after the period of open eye wear of the lenses was not anticipated. Paired t tests of the loss in BCVA for each eye individually showed that the loss was statistically significant (Pentacurve $p = 0.003$ and Aspheric $p = < 0.0001$). A paired t test of the difference between the pentacurve and aspheric results, for change in BCVA, showed that this difference was also statistically significant ($p = 0.003$). Paired t tests for the change in vision and change in mean sphere, between the two eyes, showed that they were not statistically significantly different; $p = 0.848$ and $p = 0.261$ respectively. BCVA for these individuals was measured with high contrast logMAR charts.

Thirty five of the thirty six subjects showed a reduction in their myopia. The thirty sixth subject showed no change in refractive error after two hours. This subject was the oldest subject recruited for the trial (age 57 years). Jayakumar and Swarbrick (2005) evaluated the orthokeratology response in three age groups, children (mean age 9.5 +/- 1.7years), young adults (mean age 24.6 +/- 3.7years) and older adults (mean age 43.9 +/- 6.1 years). Subjects in the three groups were evaluated after one hour of open eye wear of orthokeratology lenses. They found that, whilst all age groups responded, the older subjects showed significantly less change. In light of these findings this subject was allowed to proceed to the first overnight wear stage. This subject would be removed from the study at this stage if an inappropriate response was seen.

Subjects were issued with the lenses and normal saline (Sensitive Eyes® Plus Bausch and Lomb) for lens insertion. Boston Cleaner solution (Bausch and Lomb) was issued for subjects to use to clean their lenses when they removed them in the morning. Once the lenses had been removed, cleaned and rinsed with saline, they were stored in Boston Conditioning solution (Bausch and Lomb) during the day. As all the subjects, except for one, were naive rigid lens wearers they were advised to wear their lenses during the day and not to sleep in them for one week. Any subjects experiencing difficulty during this phase were advised to return immediately. All subjects were successful and proceeded to the first overnight wear session.

3.8 Protocol for first overnight visit

This visit was scheduled only when subjects could attend the following morning between 8.00 and 9.00a.m. Subjects were instructed to attend wearing their lenses. Two subjects, who collected their lenses, were unsuccessful in completing one night of wear and were removed from the study. At this visit the following measurements were made (Table 3.7). This procedure was followed for all the other data collection visits at one week (OW), one month (OW), three months (OQ), six months (6M) and twelve months (OY). Any subjects with concerns about their eyes were given emergency contact details (Appendix C).

Table 3.7 First overnight (ON) measurements

Over refraction of lenses and visual acuity	
Lens fit and centration	
Slit lamp assessment including corneal stain assessment	
Vision, over refraction and visual acuity	
Orbscan II Corneal topographer	Three independent measurements (procedure as Chapter 2)
IOL Master axial length	Five independent measurements (procedure as Chapter 2)
IOL Master anterior chamber depth	One measurement (procedure as Chapter 2)

3.9 Study profiles

The age and gender profiles for the subjects accepted onto the study are shown in Table 3.6. These profiles reflect the subjects who completed one night, one month and one year of lens wear. These discrete points were selected as phases in the study which correspond with previously published investigations into the effects of orthokeratology to allow comparison. The gender bias towards female subjects in the study is in keeping with a number of recent studies into contact lens wear (Efron, Morgan & Woods (2010), Morgan, Efron & Woods (2011), Swanson (2012). Efron et al (2010) in their ten year survey of contact lens prescribing in Australia reported that 65% of those fitted with lenses were women. Morgan et al (2011), in an international survey which looked particularly at presbyopic contact lens correction, reported a ratio of male to female of 34:66 for presbyopes ($\geq$ 45 years) and 29:71 for pre-presbyopes (15-44 years). Swanson (2012) in a large population study in the United States reported that women were 40% more likely to wear contact lenses than men.

Efron et al (2010) reported the peak age for contact lens fitting was 21 to 25 years. 80% of the lens wearers surveyed by Morgan et al (2011) were pre-presbyopic with only 16% falling into the presbyopic category. Swanson (2012) reported that the number of contact lens wearers reduced with increasing age, the median age of wearers in the US being 31.4 years. Whilst the age profile for the current study did show a decrease in median age between the one night and one year groups, this decrease was not a statistically significant difference ($F_{(2,22)}$ =.910 p>0.05) . Investigation of the correlation between age and initial refractive error showed that there was a weak negative correlation (RE R^2=0.0882; LE R^2 = 0.0982) i.e. older subjects tended to manifest higher levels of myopia. This correlation (R^2) did not reach statistical significance for either eye. No significant difference was recorded in the degree of myopia between the right and left eyes.

A number of factors may have influenced the initial age and refractive error profiles. Since subjects for this study were self selecting, it could be speculated that those individuals who had already worn spectacles or contact lenses for a number of years may volunteer for a new refractive procedure. This could influence the initial age profile. Secondly, individuals with higher refractive errors may be more willing to seek alternative methods of refractive correction. Unfortunately those subjects with higher refractive errors were the ones who were more likely to experience unsatisfactory results in terms of vision quality and stability. Any withdrawals in this higher refractive error group accompanied by its weak association with age would also lead to a reduction in the mean age of the cohort. Two of the older subjects also withdrew from the study due to incipient presbyopia. The full reasons for withdrawal from the study are given in Fig 3.6.

Power vector analysis (Thibos, Wheeler, and Horner 1997) was applied to the subjective refractive errors found at the initial assessment visit. Volunteers were excluded from the study if they had spectacle astigmatism greater than 1.50D of with

the rule or 0.75D if against the rule. The power vector analysis shows that the astigmatism within the three discrete groups was not statistically significantly different (right eye J_0 $F_{(2,22)}$ =.670, J_{45} $F_{(2,22)}$ = 2.049; left eye J_0 $F_{(2,22)}$ =.643, J_{45} $F_{(2,22)}$ =.502 p>0.05 for all results). The group completing twelve months of lens wear had a lower initial value for M which was statistically significant (right eye $t_{(34)}$ = -2.532 p = 0.016; left eye $t_{(34)}$ = -2.278 p = 0.029). Kolmogorov-Smirnov tests of the refraction data indicated that the two groups were normally distributed.

Table 3.8 Age and Gender Profiles

Time	Gender		Age (years)		Range
	M	F	Mean	SD	
One Night	11	25	30.31	+/- 10.31	18 - 57
One Month	9	19	28.80	+/- 9.60	18 - 57
One Year	5	7	27.70	+/- 10.50	18 - 57

Age and gender profiles for subjects at discrete points within the study; the age reflects the subject's age at the commencement of the study.

Table 3.9 Refractive Error Profiles

Time	Number of subjects	Eye	Mean refractive error (dioptres)		
			M (+/-SD)	J0 (+/-SD)	J45 (+/-SD)
One night	36	R	-3.25 +/- 1.40	0.03 +/- 0.23	-0.03 +/- 0.16
		L	-3.14 +/- 1.33	-0.02 +/- 0.25	-0.04 +/- 0.16
One Month	28	R	-3.23 +/- 1.60	0.00 +/- 0.14	0.00 +/- 0.16
		L	-3.13 +/- 1.53	-0.04 +/- 0.19	-0.05 +/- 0.16
One Year	12	R	-2.43 +/- 1.13	0.00 +/- 0.16	0.03 +/- 0.16
		L	-2.46 +/- 1.11	0.05 +/- 0.19	-0.08 +/- 0.16

Mean refractive error profiles at the same discrete points as those of the Age and Gender profiles in Table 3.6. These values represent the mean initial refractive errors of the subjects in the study.

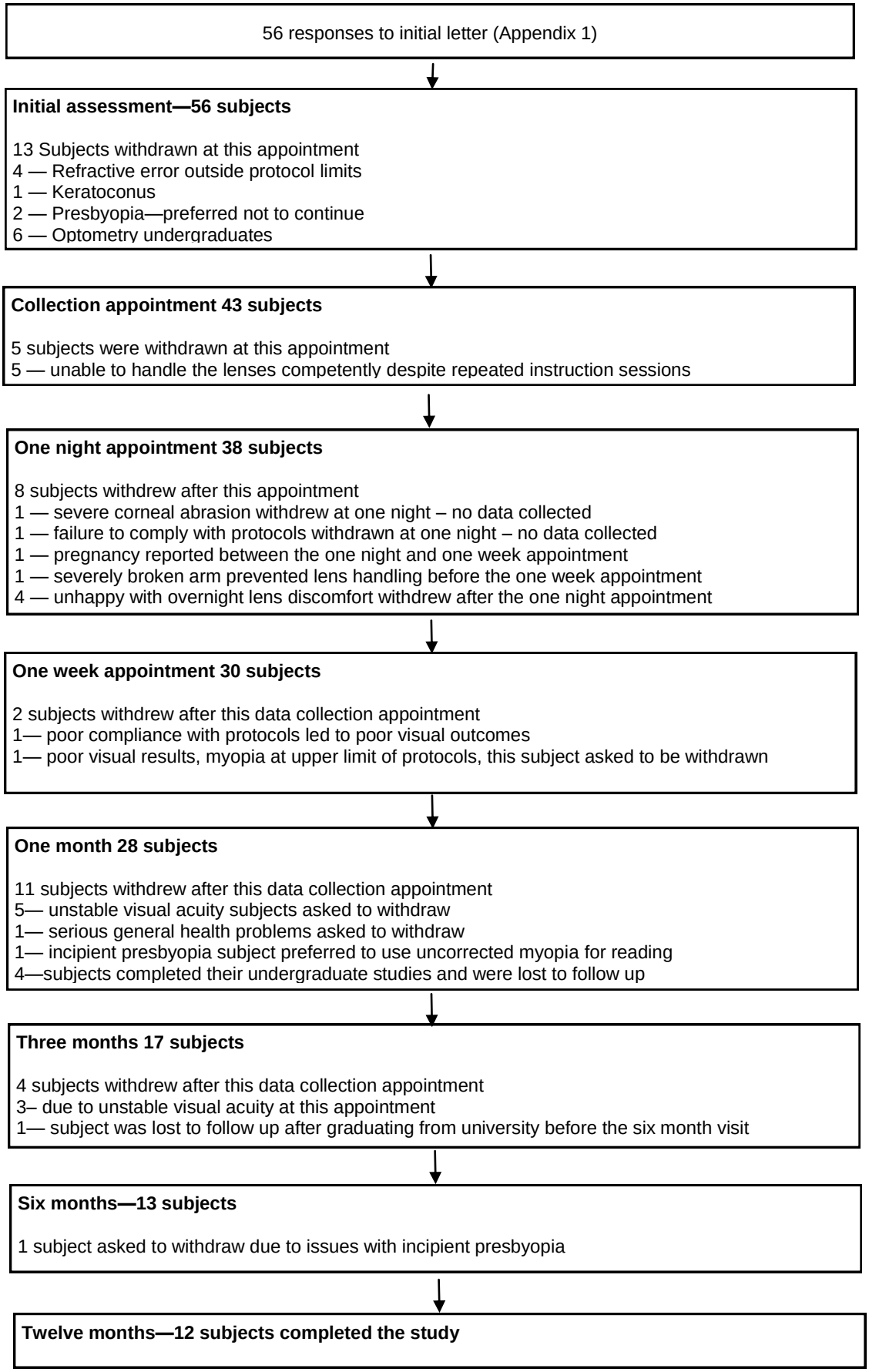


Fig 3.6 Flowchart of withdrawals from the study including reasons

3.10 Statistical analyses

Statistical analysis will be carried out using IBM SPSS (version 19). Two way repeated measures ANOVA with lens design and time of visit as the within subject factors was applied. This will allow evaluation of the difference, if any, between the actions of the pentacurve and aspheric lenses. Repeated measures ANOVA was chosen as the same subjects were involved with each of the two factors. The threshold for statistical significance was set at the p = 0.05 level. Where two means are compared a paired t test was applied. The same level of statistical significance was applied to this test i.e. p = 0.05. Where Mauchly's test of sphericity was significant then the Greenhouse-Geisser correction was applied to the data.

3.11 Power analysis (A Priori)

An a priori power analysis using G*Power 3.1.6 was applied to the various parameters being measured in the study. As the study involved the comparison of the potential difference in effect between the two lens designs an ANOVA repeat measures within factors design was selected. For each of the parameters an alpha level of 0.05 and power of 95% was selected. Using the previously published data for the Orbscan repeatability for the anterior apical radius; if we wish to detect a 0.1mm change in the anterior apical radius a sample size of nine would deliver a 95% power result. Detection of a 0.1 change in apical radius would equate to a 0.50D change in anterior corneal power. Since the radius of the anterior corneal surface is the major factor in the eyes refractive power detection of this small change should allow us to evaluate the response appropriately. Using previously published p value data it was found that a sample size of 12 would also be required to detect a 0.1 change in the anterior p value. Calculation of the sample size for the posterior surface measurements proved more difficult. Concerns have been raised about the Orbscan's ability to evaluate the posterior corneal surface. For this reason we chose to use a change value of 0.2mm in the posterior radius. G* Power calculates a sample size of eight is required. No data is available for the p value results for the posterior surface measured by the Orbscan.

Using the same change parameter for the posterior p value a sample size of 25 is required. Jonuscheit and Doughty (2009) published their data for the repeatability of the central corneal thickness measurements using the Orbscan and found a repeatability of +/- 0.009mm. If we wish to detect a change in central corneal thickness of 0.01mm then this will need a sample size of eight.

One of the principal measures for the study is the effect of orthokeratology on the refractive error of the subjects. Detection of a change of 0.50D in the manifest refractive error would equate with the change being measured in the anterior apical radius. G*Power 3.1.6 indicates that the sample size of four would be appropriate to detect this change. Detection of a change in axial length of 0.1mm would require a sample size of five whilst a detection of a 0.1mm change in anterior chamber depth would require a sample of 14.

Table 3.10 Effect size and Critical F values for study parameters

Parameter	Effect Size	Critical F value
Anterior apical radius	0.58	2.53
Anterior p value	0.41	2.40
Posterior apical radius	0.50	2.53
Posterior p value	0.26	2.29
Central corneal thickness	0.50	2.53
Refractive error	1.41	3.33
Axial length	0.71	2.71
Anterior chamber depth	0.38	2.37

Table 3.10 shows the effect size and critical F value for the parameters indicated in column one. The effect size is calculated using the magnitude of change to be detected in each of the parameters and previously known repeatability measures where available.

Due to the large attrition rates found in previous studies and as indicated earlier in the chapter subject numbers were over recruited to allow for dropouts. Post hoc analyses of the power of the findings are presented in chapter nine.

CHAPTER 4 ANTERIOR CORNEAL RESPONSE

4.1 Introduction

In chapter one Swarbrick and Alharbi (2005) reported that the dominant effect of orthokeratology occurred in the anterior cornea. In this chapter the anterior corneal responses found in this study are reported. These changes include the effects on the anterior apical radius and p value for both the horizontal and vertical meridians. As the lenses have been designed to manipulate the corneal surface the correlation between the back optic zone radius (BOZR) of the penatcurve lens and the right corneal apical radius will be presented. The aspheric lens is designed using sag measurements and not radii. The correlation between the left corneal sag and the aspheric lens sag will also be shown. As the anterior cornea is the principal element in the refractive power of the eye both the change in refractive error and the change in the total corneal power will be shown. Since the change in refractive error should be accompanied by an equivalent improvement in uncorrected visual acuity these results are also shown. Previous authors have reported some small residual refractive errors at the end of the treatment period. The best corrected visual acuity results are also reported. The diameter of the treatment zone is an important factor in the success of orthokeratology. If this treatment zone were to be significantly decentred then this would tend to counteract the benefits of a large treatment zone. The results for the two lenses treatment zones in both the horizontal and vertical directions are shown along with the equivalent decentrations, horizontal and vertical, from the geometric centre of the cornea are reported. In chapter one the current findings regarding the physiological effects of orthokeratology were outlined. In this chapter the physiological responses noted during this study are reported.

4.1.1 Anterior apical radius

A number of studies of corneal topography have attempted to classify the topographical maps in order to assess the normality of the cornea. Dingeldein and Klyce (1989) looked at the topographic images from 22 normal subjects (44 corneas). They found that there was considerable similarity between the right and left eye corneal power maps (18 out of 22 subjects). The images from the two eyes were often mirror images of each other. The aim of the study had been to develop a set of normative images for corneal topography which was associated with excellent visual acuity. They concluded that at that time this was of little value. Bogan, Waring, Ibrahim, Drews et al (1990) used the images from 399 normal corneas to create a classification system for their topographical maps. Three independent masked ophthalmologists classified the images into round, oval, symmetric bowtie, asymmetric bowtie and irregular. In this study only 7.1% of corneas showed an irregular topographical pattern. They found no statistically significant difference in the patterns of the left and right eyes.

Rabinowitz, Yang, Brickman, Akkina et al (1996) also sought to produce a database of normal topographic images using the TMS-1 topographer. Their study involved 195 normal subjects (390 corneas). In order to improve the classification of the topographical images Rabinowitz et al (1996) subdivided Bogan et al's (1990) original five patterns to give ten classifications. The study found that the majority of the subjects (66%) had symmetric patterns (round, oval, symmetric bowtie) as previously classified by Bogan et al (1990). 5.9% of the corneas classified by Rabinowitz et al (1996) showed an irregular pattern. 43% of the images of the left and right eyes were mirror images of each other. In their retrospective analyses of myopes presenting for LASIK pre-assessment using the Orbscan II, Myrowitz, Kouzis and O'Brien (2005) and Wei, Lim, Chan and Tan (2006) found that the results from the right and left eyes were highly correlated. Both studies found for example that the correlation coefficient (r) for the average SimK readings of the right and left eyes were 0.90 and 0.91 respectively. The two groups suggest that where individuals are found to have asymmetrical

Orbscan results further clinical investigations should be carried out to rule out pathology. Bogan et al (1990) and Rabinowitz et al (1996) reported that corneal topography patterns were unrelated to age, gender or ethnicity. Whilst the use of topographical patterns may prove useful in the identification of normal or diseased corneas it provides only qualitative rather than quantitative information.

4.1.2 Asphericity

Carney, Mainstone and Henderson (1997) in their cross sectional study looked at the relationship between corneal topography and myopia. They found a tendency for the cornea to flatten more slowly for higher degrees of myopia (spherical equivalent > -4.00DS). Using the term Q for asphericity they found a mean value of Q = -0.330 +/- 0.229 within their four groups i.e. emmetropes, low, medium and high myopes. As previously noted Q = p – 1 giving a value for p of 0.670. 95% of the corneas in their study showed flattening towards the periphery i.e. a prolate ellipse. They concluded that there was a statistically significant relationship between corneal asphericity and spherical equivalent refractive error. Whilst they also found a positive correlation between the corneal curvature and spherical equivalent refractive error, it did not reach statistical significance.

The asphericity value (Q = -0.330 or p = 0.670) found in this study agreed with earlier findings by both Kiely (1982) and Eghbali et al (1995). This is in contrast to the studies of Guillon et al (1986) who found p values of 0.85 +/- 0.18 and Sheridan and Douthwaite (1989) who found p values of 0.88 for emmetropes and 0.89 for myopes and hypermertropes. Douthwaite, Hough, Edwards and Notay (1999) in their study of the EyeSys found the mean horizontal p value to be 0.76. In this latter study no details of the participant's refractive errors were given. Davis, Raasch, Mitchell, Mutti et al (2005) conducted a retrospective analysis of the corneal topographies of 643 children recruited to the Orinda Longitudinal Study of Myopia. They found a mean asphericity value of Q = -0.346 (p = 0.654) with 99.7% of the corneas being prolate in shape. An

evaluation of the same corneas over a five year period showed that the corneas had become less prolate over time.

Read, Collins, Carney and Franklin (2006) investigated the topography of the central and peripheral cornea in a group of young adults. Using the Medmont E300 corneal topographer (Medmont Pty Ltd Victoria, Australia) topographical images were obtained from the central cornea using the topographer in its normal configuration. Six peripheral images were then obtained using an external fixation target positioned at 0^0, 60^0, 120^0, 180^0, 240^0 and 300^0. The seven images were then combined to produce a topographical image which provides 46 rings of data rather than the normal 32 rings. Concerns were raised regarding the effect of extraocular muscle tension on peripheral corneal topography when the subject was fixating off axis. Investigations by Read et al (2006) found that at the fixation points used (approximately 11^0 off axis) any induced change was not significant. The study found that as a wider corneal diameter was evaluated in the topographical image a statistically significant change was seen in r_0 and Q. The mean value for r_0 and Q for a 6mm diameter were 7.77 +/- 0.2mm and -0.19 +/- 0.1 and for a 10mm diameter were 7.72 +/- 0.2 and -0.36 +/- 0.2 respectively. Since $Q = p - 1$ this would give the mean value of p as 0.81 +/- 0.1 for a 6mm diameter and 0.64 +/- 0.2 for a 10mm diameter. These values for p confirm that the normal cornea shows an increasing rate of flattening towards the periphery.

Read et al (2006) also evaluated the agreement between the corneal topography and a conic section. They found that as an increasing diameter of the cornea was evaluated the agreement between the cornea and a conic section broke down. This lack of correspondence meant that at a 10mm diameter cornea a ninth order polynomial function was required to produce an adequate fit. The deviation of the cornea from a conic section as more peripheral areas are included means that the use of r0 and p or Q as descriptors becomes increasingly invalid.

4.1.3 Effect of orthokeratology on refractive error

Jessen (1962), as indicated in chapter one, found that a person's refractive error could be reduced by fitting contact lenses with a back optic zone radius which was flatter than the measured cornea. His Orthofocus technique was the precursor of modern orthokeratology. Wlogdya and Bryla (1989) produced the first set of reverse geometry lenses which enabled the refractive error change to be induced in a period of forty two days instead of the 365 days of earlier studies (Jessen 1962; Grant 1970; Kerns 1978 & Binder et al 1980). Swarbrick, Wong and O'Leary (1998) followed six individuals wearing reverse geometry lenses in open eye conditions (minimum of two hours lens wear) for 28 days. They found that after 28 days the myopia had been significantly reduced (mean change 1.71 +/- 0.59D).

Lui, Edwards and Cho (2000) also looked at the efficacy of reverse geometry lenses for the reduction of myopia in open eye wear. They restricted their study to myopes of up to -3.50D with corneal astigmatism of < -2.00D. Subjects were followed for 100 days and were expected to wear the lenses for eight hours a day once adaptation had been achieved. The results of the orthokeratology lens wearers were compared with a matched group wearing conventional alignment fit lenses. The mean reduction of myopia in the orthokeratology group was -1.50D +/- 0.45 whilst the alignment fit group showed a mean change of 0.01D +/- 0.05. Statistically significant changes in myopia occurred up to day 40 in the orthokeratology group. Lui and Edwards found that there was an increase in astigmatism of -0.09D +/- 0.32 by day 70 which was statistically significant but may not be considered to be clinically significant.

Nichols, Marsich, Nguyen, Barr et al (2000) in their study of myopes also limited their refractive sphere to -3.50D with astigmatism up to -1.00DC. They followed their subjects for up to 60 days of overnight lens wear. No control group was recruited for this study. Eight subjects completed the 60 day trial. Nichols et al found that the majority of the myopic reduction occurred between nights one and seven with the mean

change throughout the study of +1.83 +/- 1.23D. They found no statistically significant change after day seven. Nichols et al established the change in refractive error by both standard clinical methods and by auto-refraction. They found that when the refraction was measured by the auto-refractor a statistically significant difference in the degree of myopia reduction was found +0.64 +/- 0.52D. Nichols et al suggest that this difference could be explained either by the large entrance pupil of the auto-refractor or the weighting of the evaluation of the refractive error to the peripheral cornea. They suggest that the incorporation of data from the peripheral cornea, where less refractive change occurs in orthokeratology, may have accounted for this difference. In the present study all refractive results have been determined by the use of standard clinical methods and not by auto refractor.

Rah, Jackson, Jones, Marsden, Bailey and Barr (2002) reported their preliminary results from the Lenses and Overnight Orthokeratology (LOOK) study. They found that the mean change in the sphere of the right eye at the one month visit was 2.11 +/- 0.97D with the left being very similar (2.20 +/- 0.99D). This change in refraction meant that the mean spherical error at the one month visit was R 0.01 +/- 0.78 and L 0.08 +/- 0.68. The group did examine participants after one night and one week of lens wear but results for these visits were not reported. Rah et al reported that 11% and 20% of their participants were >1.00D away from their target refraction in the right and left eyes respectively at one month. The majority of these (right 9% and left 17%) were under-corrected. The results had improved by the three month visit to 10% of the subjects being under-corrected by > 1.00D in either eye. In the current study 96% of the subjects were within 1.00D of the target refraction for the right eye i.e. 4% were under-corrected. Results for the left eyes, which had been fitted with the aspheric design lens, were 93% within 1.00D of the target refraction with 7% overcorrected by >1.00D. The group found no significant change in the astigmatic element of the refraction at the one month visit. All participants were re-evaluated at the one month and three month visits

after at least six hours of no lens wear. At both visits a regression of between 0.25 and 0.50D was noted at the afternoon visit.

Soni, Nguyen and Bonanno (2003) in a small study (eight participants completed) found that the full effect of orthokeratology had been achieved after one week of overnight wear. The induced change (2.12 D) was maintained throughout the day. Tahhan et al (2003) in their study looked at the effect on refractive error of four different commercially available reverse geometry lenses. They found that there was no statistically significant difference between the four lens types in their effect on the change in subjective sphere. Whilst the level of change in subjective sphere was not reported they did confirm that the one week and one month visit data differed significantly from that at one day but not significantly from each other. All three visits were significantly different from the baseline findings. Walline et al (2004), in their study of the effects of overnight orthokeratology lens wear in children (COOKI), found after six months of lens wear the mean change in refractive sphere was -2.48 +/- 1.57D. This change had occurred by two weeks into the study.

Sorbara, Fonn, Simpson and Kort (2005), in their study of 30 participants with an initial mean sphere of -3.00 +/- 1.03, found that after one night the mean sphere had reduced to – 1.70 +/- 0.53. After 28 nights of lens wear the mean sphere had reduced further to -0.41 +/-0.77 as with Rah et al (2002). Sorbara et al reported the percentage of participants who had not achieved their attempted correction at the 28 day visit i.e. within +/- 1.00D of the target refraction. They reported that 13% were under-corrected at this time with no one over-corrected. Johnson, Carney, Mountford, Collins, Cluff et al (2007) reported on their eight day study into the effect of orthokeratology on visual performance. Their participants were restricted to < 3.00D of myopia and < 1.50D of with the rule astigmatism. Individuals with any against the rule corneal astigmatism were excluded. This latter restriction is in agreement with the suggestion of Kerns (1978) and Binder (1980) that orthokeratology causes an increase in against the rule

astigmatism. Johnson et al (2007) also excluded individuals with any lenticular astigmatism. Since lenticular astigmatism cannot be corrected by orthokeratology any residual error in the lens would obviously impact on the performance measures employed in the study i.e. residual refractive error and high and low contrast visual acuities. In this study Johnson et al fitted only one eye with a lens allowing the participants other eye to be used as a control. They found that by day eight the spherical component of the refractive error had changed from -2.10 +/-0.89DS to +0.25 +/- 0.25DS. Johnson et al also recorded the regression of the orthokeratology effect over the day and found that this reduced after eight days of lens wear. This is in agreement with previous studies (Nichols et al 2000; Soni 2003)

Cheung, Cho, Chui and Woo (2007) looked at the initial and residual refractive errors in 31 individuals who had worn orthokeratology lenses for at least one month. They compared the best and worst eye responses. Decisions about the best and worst eyes were based on the visual acuity achieved on a 90% contrast chart and not on the refractive response achieved. They found that the better eye had achieved 92% +/- 11% reduction in M (Thibos 1997) whilst the worst eye showed only an 84% +/- 14% reduction. This difference between the best and worst eyes increased with the use of low contrast acuity charts. Cheung et al recommend that orthokeratology patients are evaluated using both high and low contrast acuity charts.

4.1.4 Effect of orthokeratology on astigmatism

Mountford and Pesudovs (2002) analysed the effect of overnight orthokeratology on astigmatism. Using two different vector analysis methods, the Bailey-Carney designed for use to analyse contact lens induced corneal shape changes and the Alpins designed for use in the assessment of surgically altered corneas, they calculated the change in astigmatism. They also looked at the corneal topography results obtained using the EyeSys 2000 videokeratoscope. In their retrospective analysis of 23

successful orthokeratology lens wearers they found that orthokeratology could produce a mean reduction in astigmatism of 50% in 93% of cases. By using the Alpins vector analysis they calculated that for the orthokeratology lenses to have completely eliminated the pre-treatment astigmatism they would need to be 80% more efficient. The EyeSys 2000 topography images indicated that the majority of the reduction in astigmatism occurred over the central cornea up to 2mm either side of the centre. Mountford and Pesudovs suggested that, when a patient is evaluated for orthokeratology lens fitting, the potential residual astigmatic correction should be estimated. Any uncorrected astigmatism will obviously impact adversely on the patient's visual acuity and therefore the success of the procedure.

Tahhan et al (2003) in the study mentioned earlier found no statistically significant change in astigmatism after one month of orthokeratology. Subjects in their study were restricted to ≤-1.50DC in any meridian. Hiraoka, Furuya, Matsumoto, Okamoto, Sakata, Hiratsuka, Kakita, and Oshika (2004) examined the change in regular and irregular astigmatism using Fourier analysis in 39 patients undergoing three months of successful orthokeratology. Hiroaka et al defined success as those subjects achieving an uncorrected visual acuity (UCVA) of 20/20 or better by logMAR. The mean regular astigmatism prior to treatment was 0.53 +/- 0.23D; all subjects had less than 1.00D of refractive astigmatism. The group found that regular astigmatism increased significantly following orthokeratology to 0.63 +/- 0.40D. The asymmetry which the group defined as lower order irregular astigmatism also increased significantly (0.35 +/- 0.22D to 0.64 +/- 0.40D). This irregular astigmatism could not be corrected by sphero-cylindrical lenses. Hiroaka et al found that the increase in irregular astigmatism was correlated with the amount of myopic correction required. They also found that their results for irregular astigmatism were similar to the effects seen in PRK and LASIK. They recommend that the impact of the increase in irregular astigmatism on visual function requires further investigation. Walline et al (2004) found the initial astigmatism in the COOKI study was J_0 +0.50D and J_{45} -0.47D. The group found no statistically significant increase in

astigmatism during the six month study. Sorbara et al (2005), in their 28 day study, found no significant change in the cylindrical element of the refraction during the study.

Cheung, Cho and Chan (2009) used the Thibos (1997) vector analysis to look at the change in astigmatism associated with successful orthokeratology. Retrospective records from the right eye of seventy four young people (7 to 16 years) were evaluated in this study. All the subjects had undergone at least six months of orthokeratology. These subjects were further divided into non-astigmats ≤ -0.50DC; low with the rule (WTR –ve cyl axis at 180 +/- 30^0) -0.75 to -1.50DC; moderate WTR -1.75 to -2.25 and three subjects who had either against the rule (ATR -ve cyl axis at 90 +/- 30^0) or oblique astigmatism. Cheung et al defined oblique astigmatism as any axis whose orientation was not within the previous two definitions. Only seven subjects were included in the latter two categories, moderate WTR and ATR or oblique astigmatism. The low numbers of ATR subjects is in agreement with Kerns (1978) and Binder (1980) who recommended against fitting orthokeratology lenses to individuals with against the rule astigmatism. The low numbers of moderate ATR subjects occurred as a result of the difficulty of fitting a spherical back surface lens on to a toric cornea. Cheung et al found that both J_0 and J_{45} for the refractive astigmatism were significantly different from the baseline measures at six months. They note that a significant decrease in J_0 was accompanied by a small increase in J_{45}. Similar effects were not seen in the corneal toricity post-orthokeratology. The study showed that the effect of orthokeratology on the astigmatic elements of the cornea is seen only in those subjects classed as astigmats.

4.2 Anterior Corneal Response Methods

4.2.1 Anterior apical radius and p value change

The anterior apical radius was calculated for each subject at each visit. The method employed was that previously described in chapter two (Douthwaite and Parkinson 2009). Once the anterior apical radii and p values had been calculated it was possible to look at the change in the two parameters at each visit. Initial mean apical radii and p values for the right and left eyes are shown in Table 4.1.

4.2.2 Corneal Sag change

The corneal sag was calculated for all visits made by the participants.

Using the sag formula

$$s = \frac{r - \sqrt{(r^2 - py^2)}}{p}$$

where:

r = apical radius (r0)

p = p value calculated from the Orbscan data for each visit

y = the semi-meridian evaluated

The corneal diameter chosen was seven millimetres as this corresponds with the central optic zone of both the C5 and the aspheric design lenses. This gives a value of 3.5mm for y.

4.2.3 Agreement between contact lens BOZR and anterior apical radius of the right eye.

An evaluation of the agreement between the BOZR and the anterior apical radius at one month was conducted. The right eye of the participants had been fitted with the pentacurve (C5) design lens. The BOZR of the lenses had been selected to induce the required degree of myopic correction plus an extra dioptre (lens design chapter 3). This extra dioptre was to compensate for any regression of the orthokeratology effect over the day. The data are shown in Fig 4.12. The one month point was selected as this was the point at which the refractive changes reached the limit of significant change.

4.2.4 Agreement between contact lens sag and corneal sag of the left eye.

The left eye of the participants had been fitted with an aspheric back surface design lens. The agreement between the lens sag and corneal sag at a 7mm diameter was evaluated. The lens sag at this diameter had been previously selected to elicit the required refractive change in the aspheric lens (lens design chapter 3). The one month interval was again chosen as the point at which significant change in refractive error had ceased.

4.2.5 Refractive error

At each visit the subject's manifest refractive error was evaluated using standard clinical methods and recorded in conventional sphere/cyl/axis notation. These values were then transformed to power vectors (Thibos 1997) to facilitate comparison of the data as outlined in chapter three.

4.2.6 Corneal Power change

Corneal power was calculated for each visit using the following step along method;

L_1 =	0.00D
Anterior corneal power (F_{ac}) = L_2	$((n_{cornea} - n_{air}) / r_{anterior\ cornea})D$
l_2 =	$1000 / (L_2)$ mm
L_3 =	$(1000 /(l_2 + (\text{Central corneal thickness}/ n_{cornea}))$ D
Posterior corneal power (F_{pc})	$((n_{aqueous} - n_{cornea}) / r_{posterior\ cornea})$ D
Total corneal power L_4 =	$(L_3 + (F_{pc}))$ D

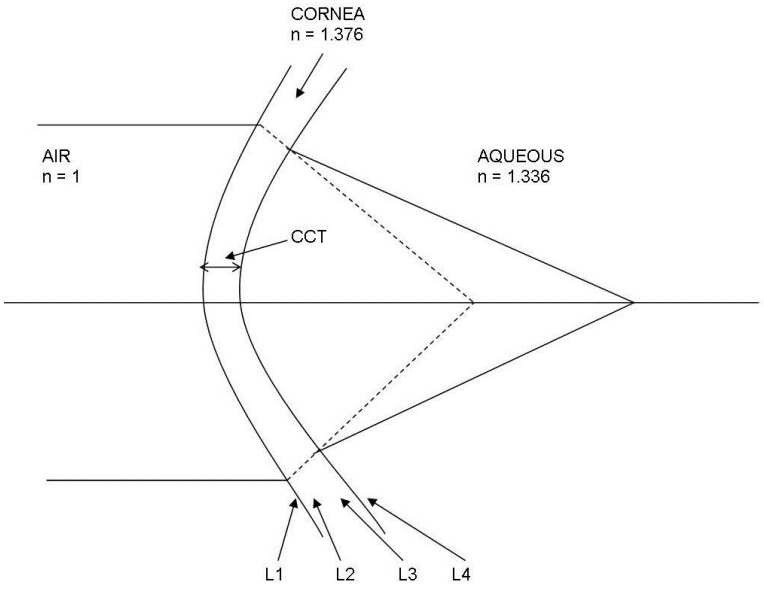


Fig 4.1 Total corneal power calculation by the step along method.

4.2.7 Anterior vertical cornea

The Orbscan images of the vertical cornea were analysed in the same manner as that described in Chapter 2. The results are shown in Table 4.12.

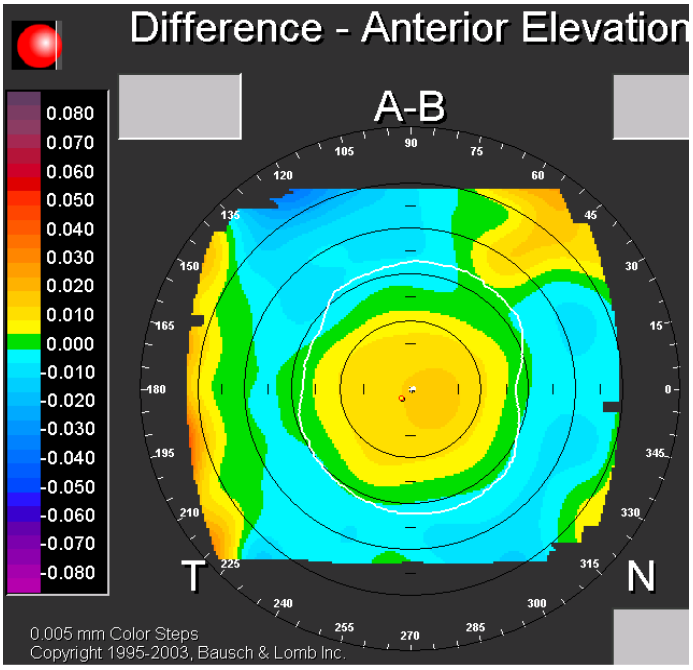
4.2.8 VAR Rating

Following the procedures outlined in chapter three the vision (V) and best corrected visual acuity (BCVA) were recorded at each visit for the pentacurve and aspheric lenses. The results were recorded as visual acuity ratings. The mean results for each lens for each visit are shown in table 4.13.

4.2.9 Treatment zone diameter and decentration

The treatment zone is defined as the diameter of the area of the cornea which shows no difference in the apical radius measurement between visits. This diameter was found using the difference maps produced by the Orbscan. Maps from the one night, one week and one month visit were subtracted from the initial topography map. The difference map produced shows the point of no difference between the two visits in green. Examples of difference maps are shown in Figs 4.2 (right eye a-c & left eye d-f). Once the difference map was produced the treatment zone diameter (TD) was found by moving the cursor over the map to note the extremes of the area where change had occurred. The decentration of the treatment zone was found by recording the temporal semi meridian as minus and the nasal semi meridian as positive with respect to the centre of the cornea. This allowed the total horizontal diameter (a+b) and the decentration (x) of the geometric centre of the zone to be calculated. The decentration (x) is calculated by subtracting the temporal semi meridian from half of the horizontal treatment zone. The vertical treatment zone (c+d) was evaluated in the same manner as the horizontal. In this case the superior semi meridian was recorded as positive and the inferior as negative. This allowed the vertical decentration of the treatment zone (y) to be calculated by subtracting the inferior semi meridian from half of the vertical diameter (Fig 4.3).

a)


Difference - Anterior Elevation
A-B
0.080
0.070
0.060
0.050
0.040
0.030
0.020
0.010
0.000
-0.010
-0.020
-0.030
-0.040
-0.050
-0.060
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-0.080
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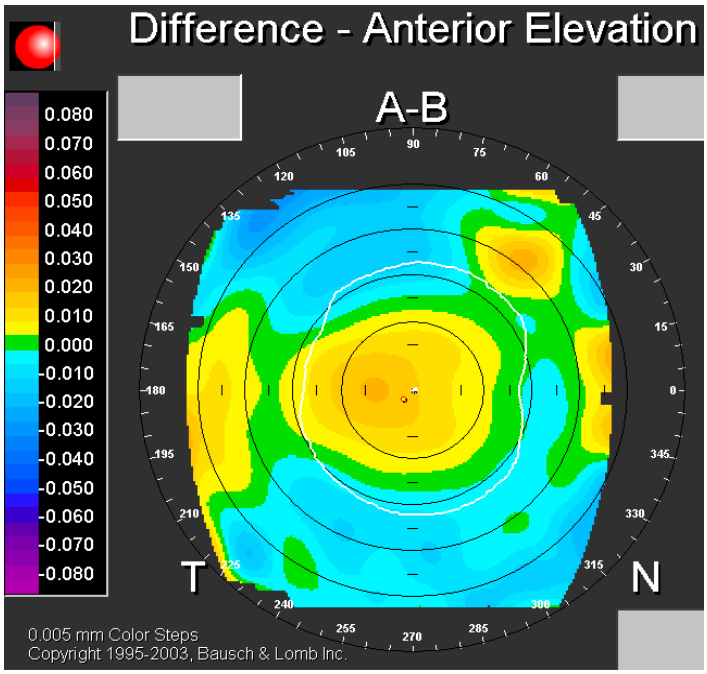
0.005 mm Color Steps
Copyright 1995-2003, Bausch & Lomb Inc.

b)


Difference - Anterior Elevation
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0.080
0.070
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-0.030
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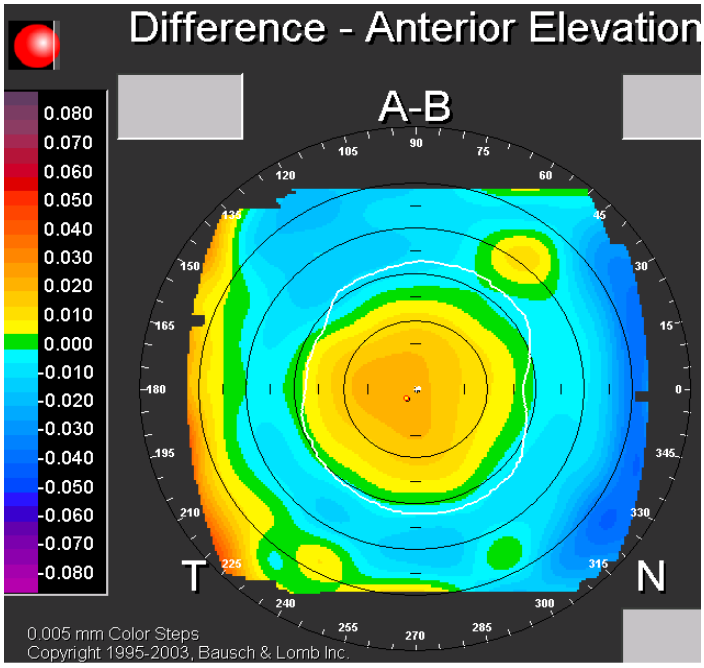
Difference - Anterior Elevation
A-B
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Copyright 1995-2003, Bausch & Lomb Inc.

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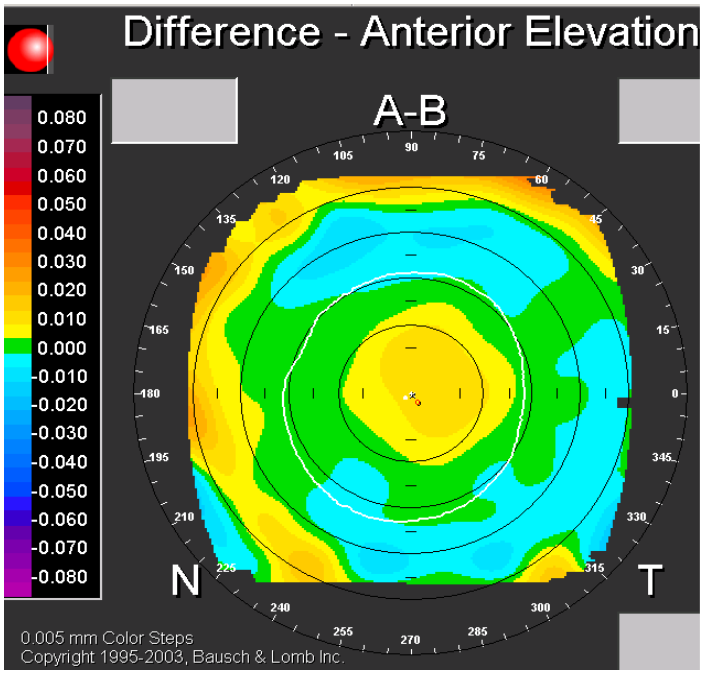
Difference - Anterior Elevation
A-B
0.080
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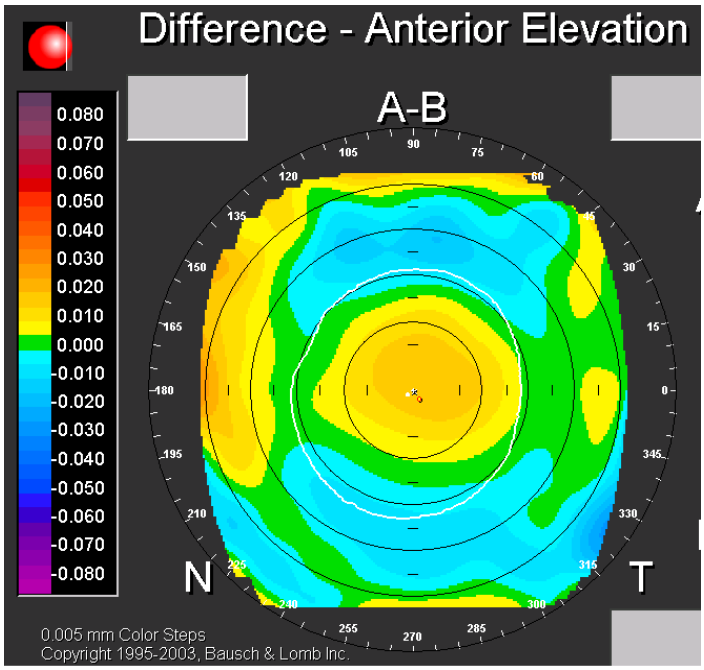
Copyright 1995-2003, Bausch & Lomb Inc.

e)



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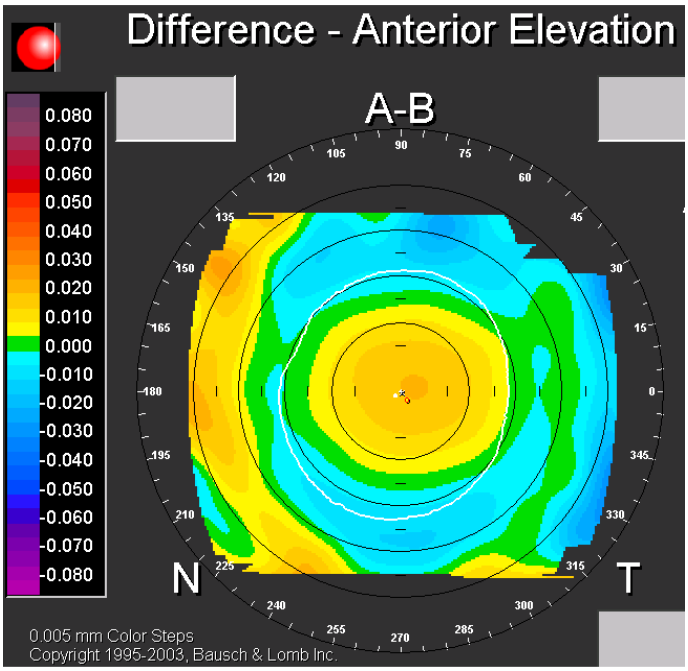


Fig 4.2 Examples of Difference Maps for subject DM. Image A is the initial topography and Image B is that generated at the one night, one week or one month visit respectively. Images (a-c) represent the pentacurve lens and images (d-f) represent the aspheric lens.

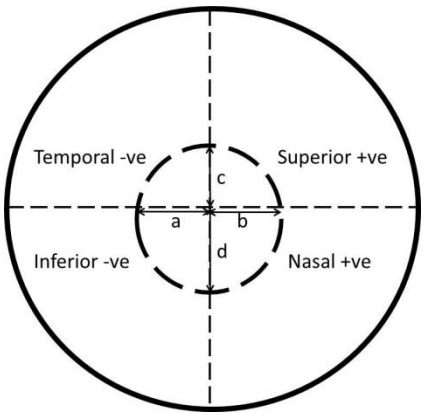


Fig 4.3 Treatment zone diameter (dashed line) shown with respect to the corneal diameter (solid line).

4.2.10 Physiological response of the cornea

All subjects had a full slit lamp assessment completed at every visit in order to assess the physiological response in the cornea to the two lenses. This assessment included a white light assessment with the major slit lamp and an assessment of the corneal staining using Fluorescein sodium and a cobalt blue filter. The staining patterns were enhanced using a Wratten (12) filter over the observation system and graded according to the Efron grading scale for corneal staining (Efron 2004). As recommended the five scale divisions were further subdivided into 0.1 units to increase the level of discrimination between subjects and also between visits made by individual subjects. For assessment visits subjects were asked to attend wearing their lenses so that a fitting analysis could be made. The lenses were then mobilised from the cornea and removed by the subjects. Corneal staining was assessed at this point using the method outline above. The corneal stain results are presented in Fig 4.23. Any subject who experienced any adverse reactions between visits was given an emergency contact number. Subjects were spoken to and offered immediate advice over the telephone and were then assessed as soon as possible after this time and appropriate treatment given. As well as corneal stain any other corneal changes were noted during the slit lamp assessment.

4.3 Results

4.3.2 Anterior apical radius and p value

Table 4.1 The initial mean values for the apical radius for the right and left eyes of the 36 subjects recruited to the study. The corneal diameter evaluated was 7mm in diameter.

	Apical radius (r0) mm	p value	Q
Right	7.77 +/- 0.26	0.76 +/- 0.12	-0.24 +/- 0.12
Left	7.80 +/- 0.26	0.74 +/- 0.09	-0.26 +/- 0.09

The right eye was fitted with the pentacurve lens and the left eye with the aspheric back surface design. Results from this point forward will be identified as pentacurve and aspheric rather than right and left.

Table 4.2 Group mean anterior apical radius (mm) for each visit

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	7.77 +/- 0.26	7.80 +/- 0.26
One night	36	8.08 +/- 0.29	8.09 +/- 0.38
One week	30	8.16 +/- 0.33	8.28 +/- 0.42
One month	28	8.27 +/- 0.38	8.28 +/- 0.41
One quarter	17	8.32 +/- 0.28	8.33 +/- 0.45
Six months	13	8.12 +/- 0.37	8.18 +/- 0.25
Twelve months	12	8.11 +/- 0.11	8.19 +/- 0.28

Table 4.3 Group mean anterior p values for each visit

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	0.76 +/- 0.12	0.74 +/- 0.09
One night	36	1.29 +/- 0.38	1.17 +/- 0.43
One week	30	1.28 +/- 0.54	1.51 +/- 0.83
One month	28	1.51 +/- 0.52	1.55 +/- 0.60
One quarter	17	1.41 +/- 0.77	1.67 +/- 0.41
Six months	13	1.24 +/- 0.48	1.34 +/- 0.29
One year	12	1.23 +/-0.32	1.30 +/- 0.51

Table 4.4 Change in anterior apical radius (r0) (mm) and p value at each visit after the initial

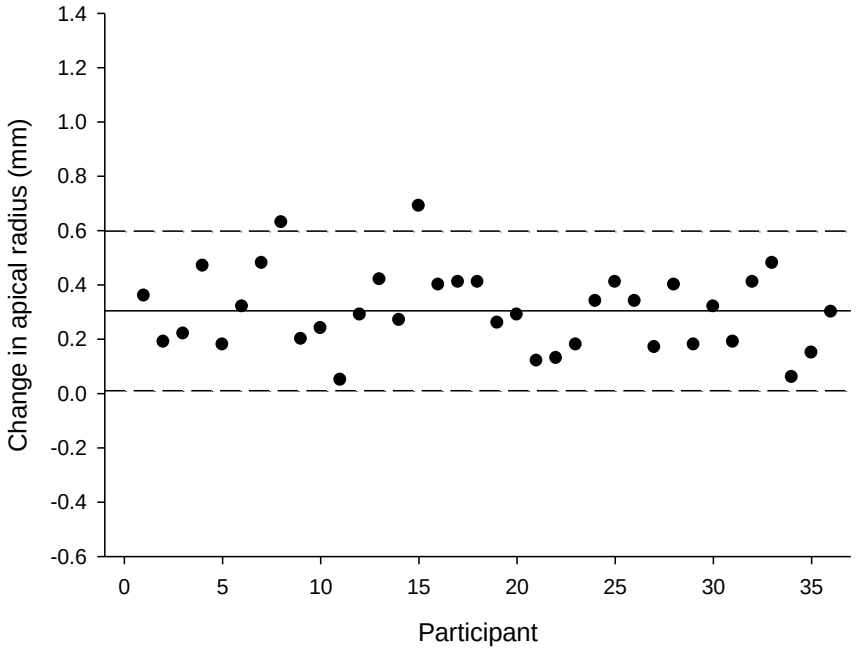
	Number of subjects	Anterior apical radius		p value	
Visit		Pentacurve	Aspheric	Pentacurve	Aspheric
One night	36	0.30	0.29	0.53	0.43
One week	30	0.38	0.48	0.52	0.76
One month	28	0.48	0.46	0.75	0.79
One quarter	17	0.48	0.47	0.72	0.94
Six months	13	0.35	0.38	0.45	0.57
One year	12	0.33	0.40	0.41	0.54

Table 4.5 Change in anterior apical radius (r0) (mm) and p value at each visit after the initial for subjects completing twelve months of lens wear

	Number of subjects	Anterior apical radius		p value	
Visit		Pentacurve	Aspheric	Pentacurve	Aspheric
One night	36	0.25	0.23	0.40	0.38
One week	30	0.30	0.48	0.40	0.71
One month	28	0.36	0.43	0.53	0.65
One quarter	17	0.39	0.53	0.46	0.77
Six months	13	0.35	0.38	0.45	0.57
One year	12	0.33	0.40	0.41	0.54

The data in Table 4.5 indicates that both corneas undergo significant flattening at the one night visit (paired t tests; pentacurve r0 $t_{(35)} = -12.43$ $p<0.05$; p value $t_{(35)} = -8.55$ $p<0.05$ and aspheric r0 $t_{(35)} = -7.40$ $p<0.05$; p value $t_{(35)} = -5.73$ $p<0.05$). Figs 4.4, 4.5, 4.6 and 4.7 show the change in apical radius and p value at each of the visits for each lens. The use of two standard deviations indicates 95% confidence limits. This analysis reveals that there is no systematic bias in the measurements.

a)


Change in apical radius (mm)
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1.2
1.0
0.8
0.6
0.4
0.2
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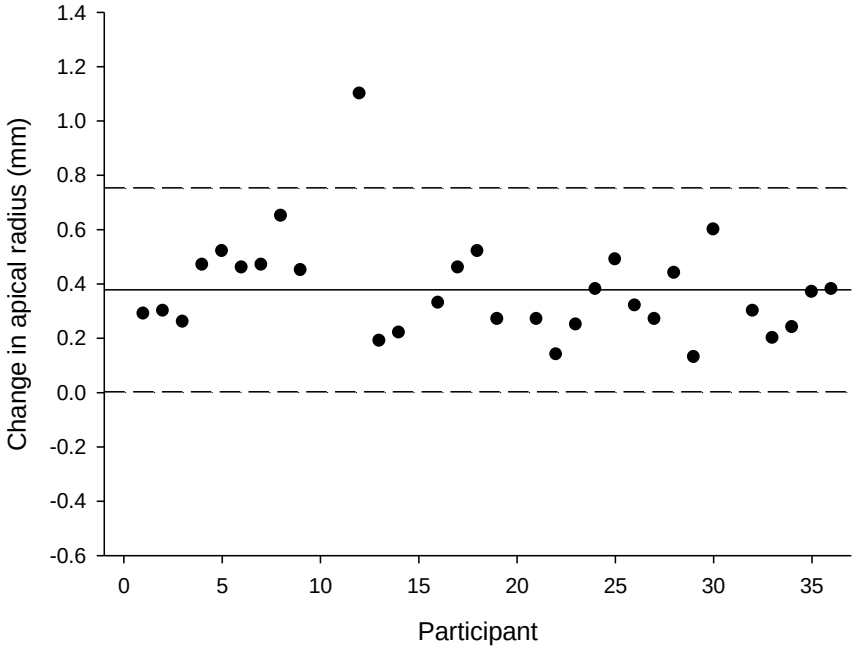
-0.4
-0.6
0
5
10
15
20
25
30
35
Participant

b)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0.6
0.4
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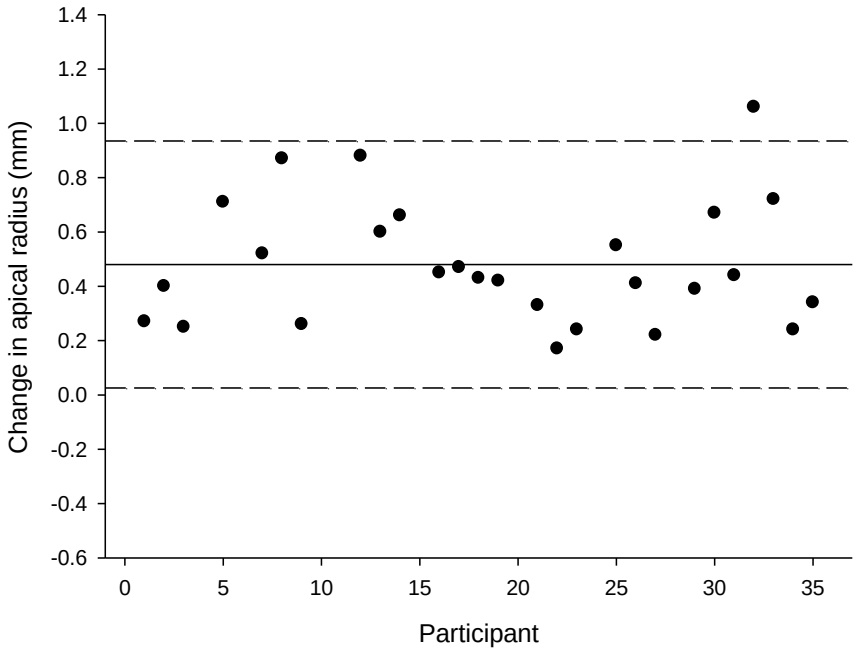
0
5
10
15
20
25
30
35
Participant

c)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0.4
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-0.6
0
5
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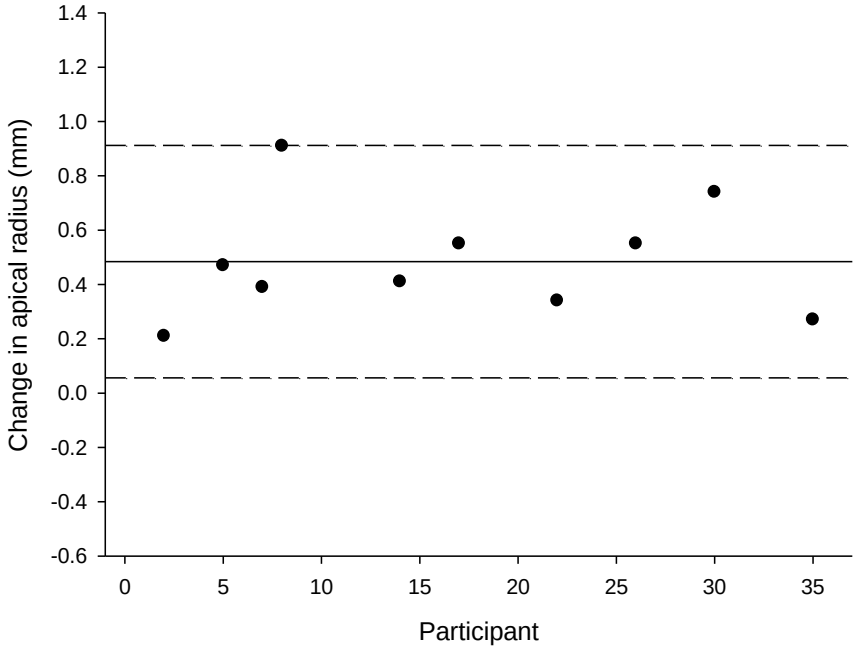
30
35
Participant

d)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0.4
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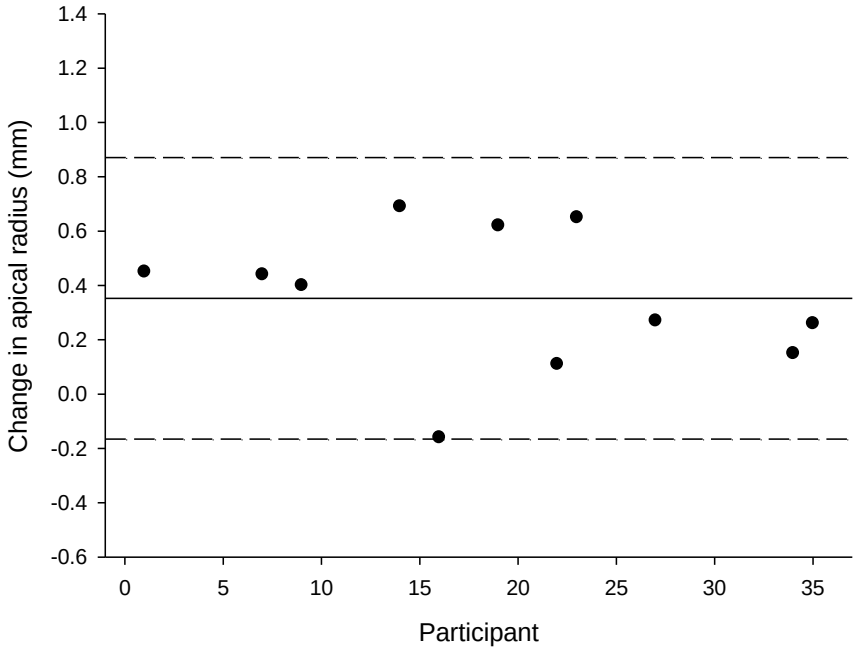
30
35
Participant

e)



f)

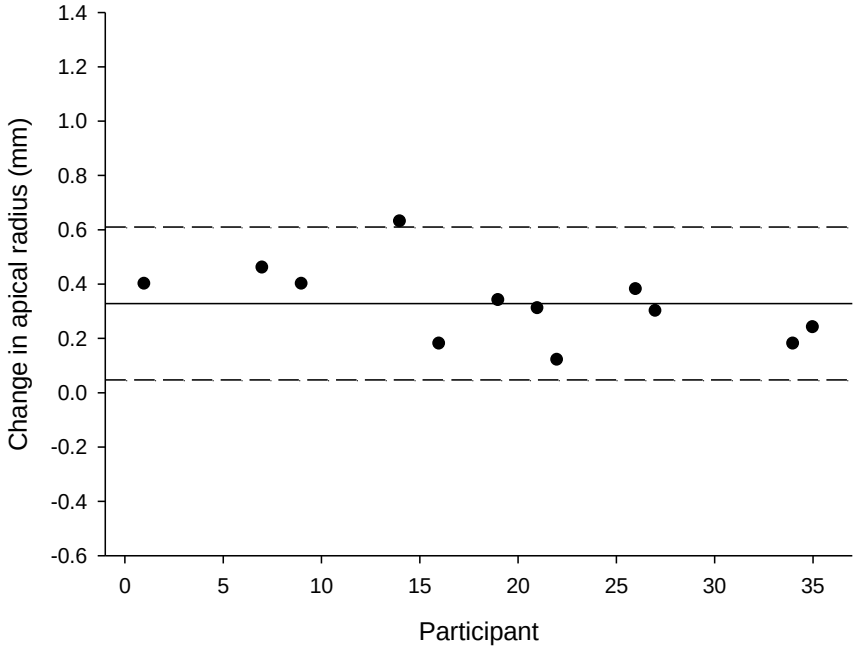
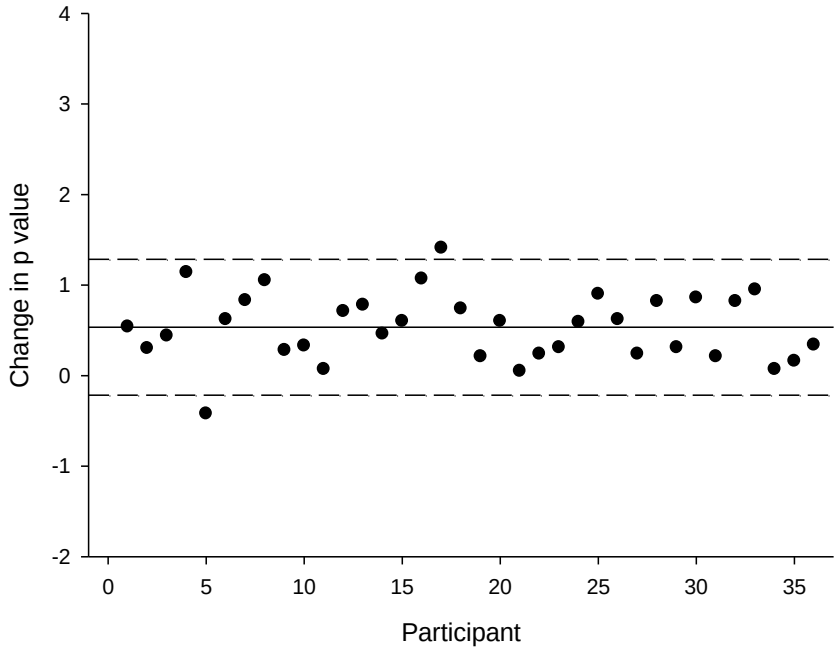


Fig 4.4 Difference plots of the change in the apical radius for the pentacurve lens a) initial to ON, b) initial to OW, c) initial to OM, d) initial to OQ, e) initial to 6M and f) initial to OY. The initial measurement was deducted from the measure obtained at each visit. The broken lines indicate two standard deviations.

a)


Change in p value
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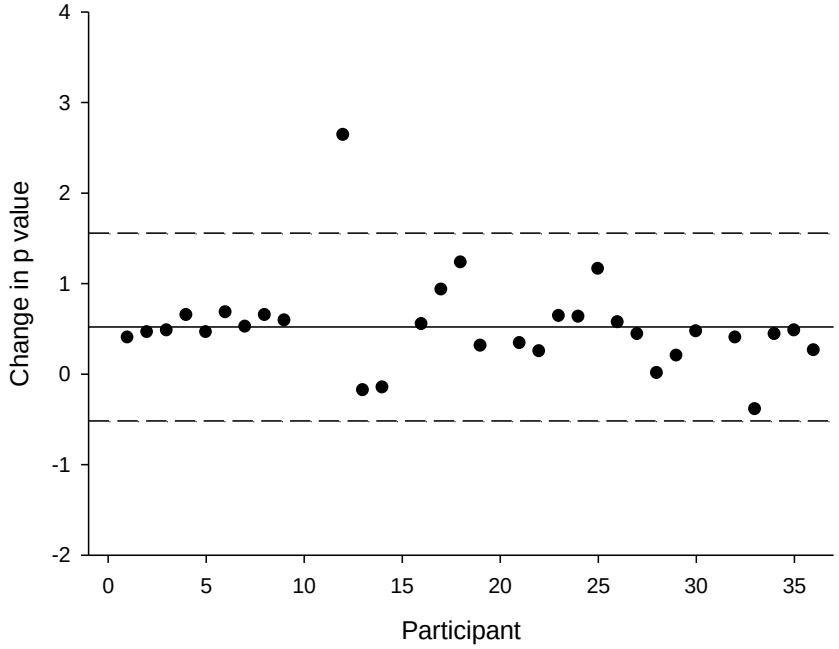
3
2
1
0
-1
-2
0
5
10
15
20
25
30
35
Participant

b)


Change in p value
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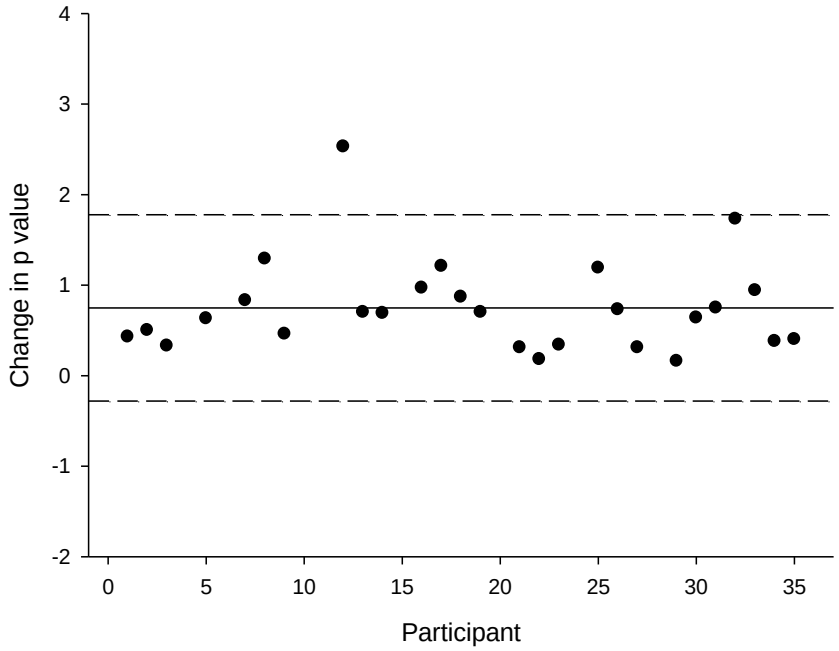
2
1
0
-1
-2
0
5
10
15
20
25
30
35
Participant

c)


Change in p value
Participant
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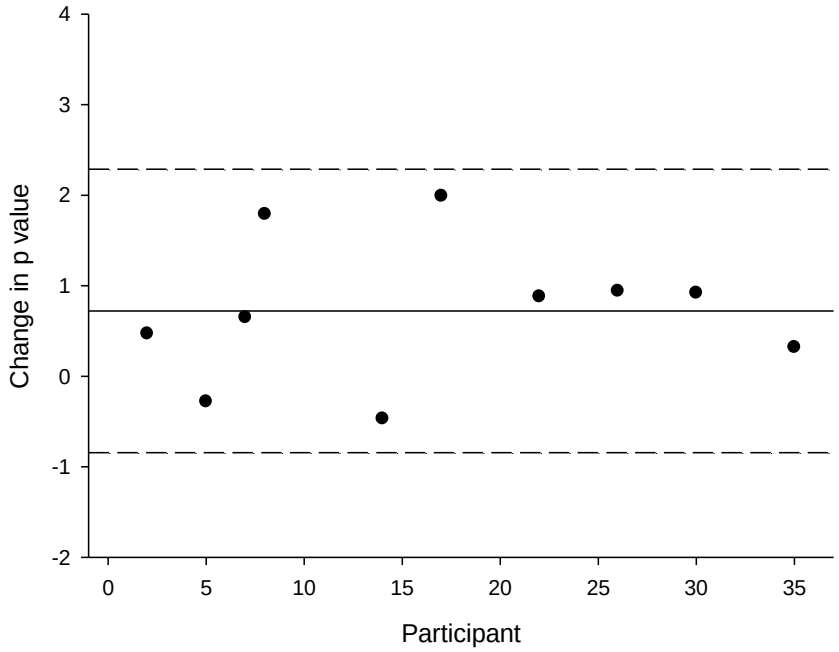
-1
-2
0
5
10
15
20
25
30
35

d)


Change in p value
Participant
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0
5
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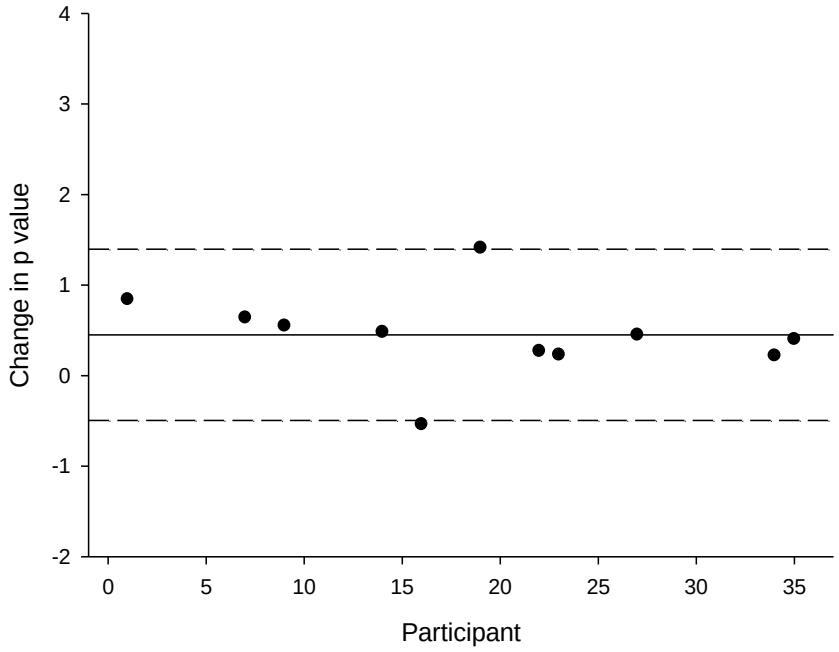
25
30
35

e)



f)

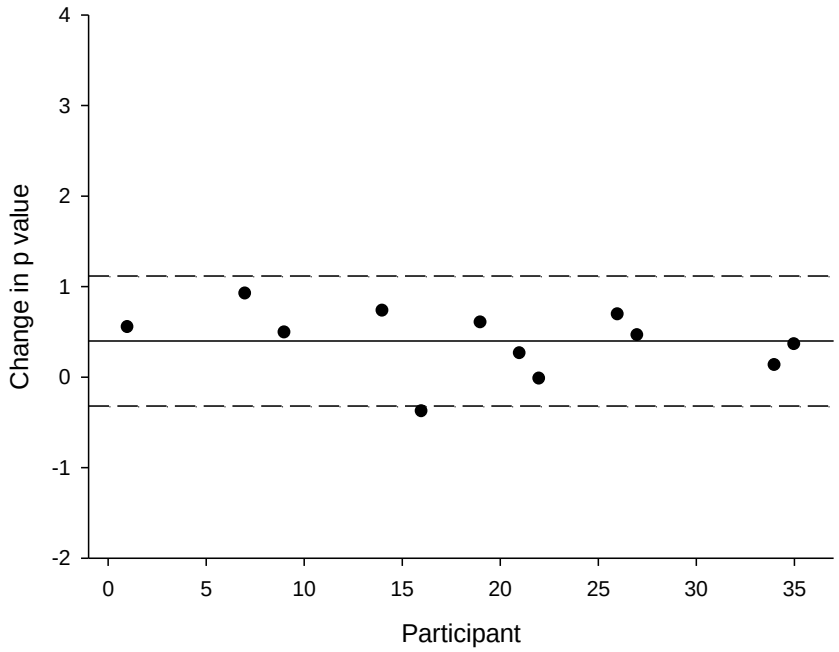
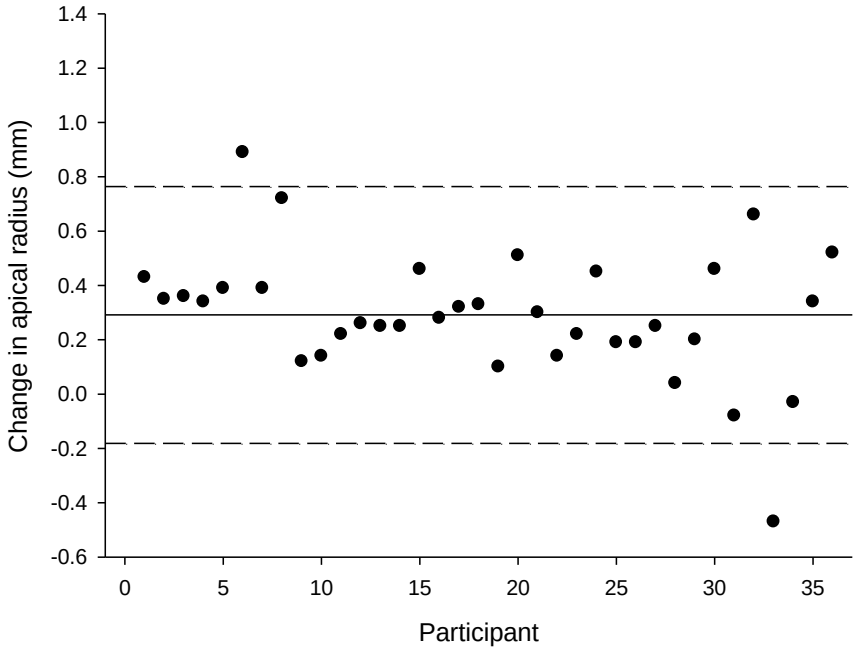
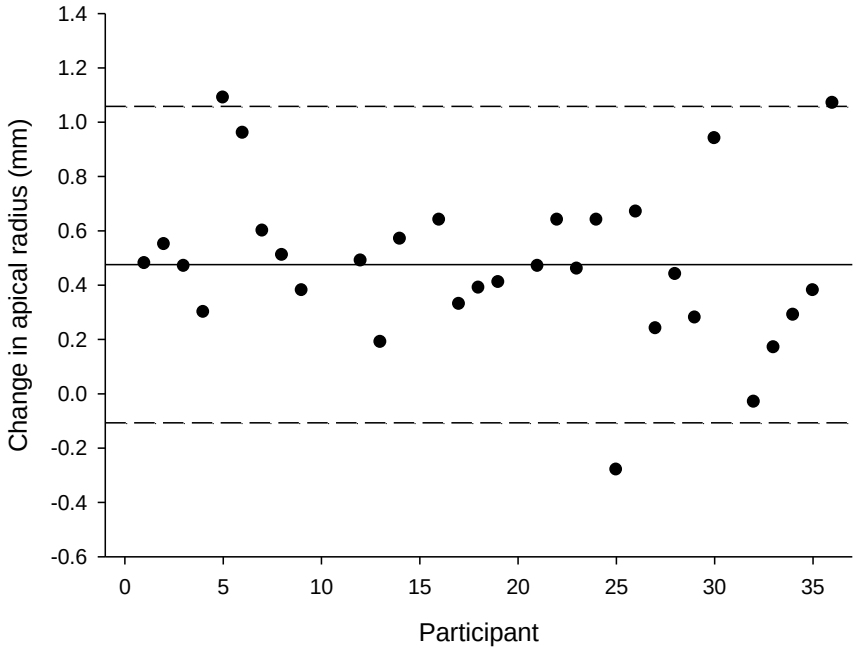


Fig 4.5 Difference plots of the change in the p value for the pentacurve lens a) initial to ON, b) initial to OW, c) initial to OM, d) initial to OQ, e) initial to 6M and f) initial to OY. The initial measurement was deducted from the measure obtained at each visit. The broken lines indicate two standard deviations.

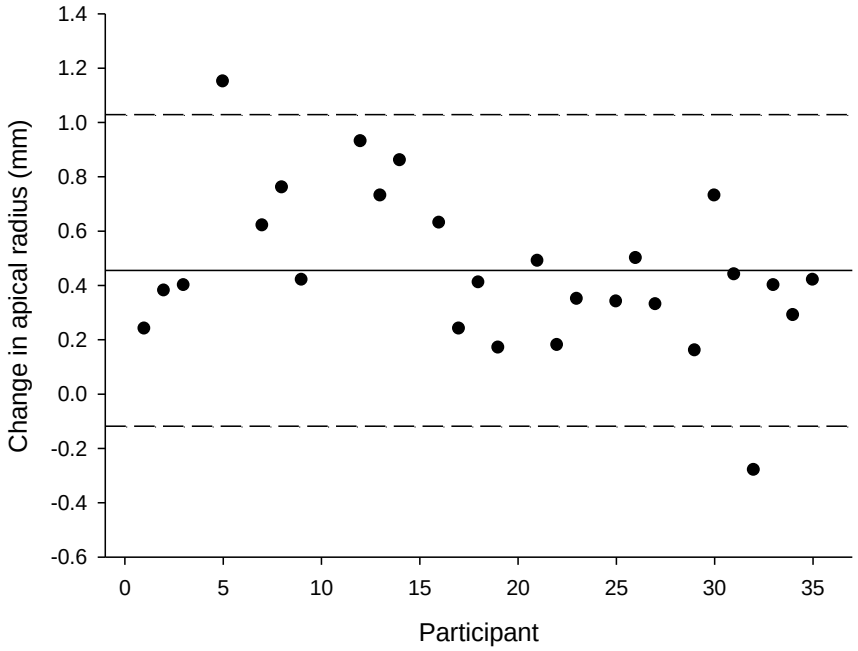
a)


Change in apical radius (mm)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
0
5
10
15
20
25
30
35
Participant

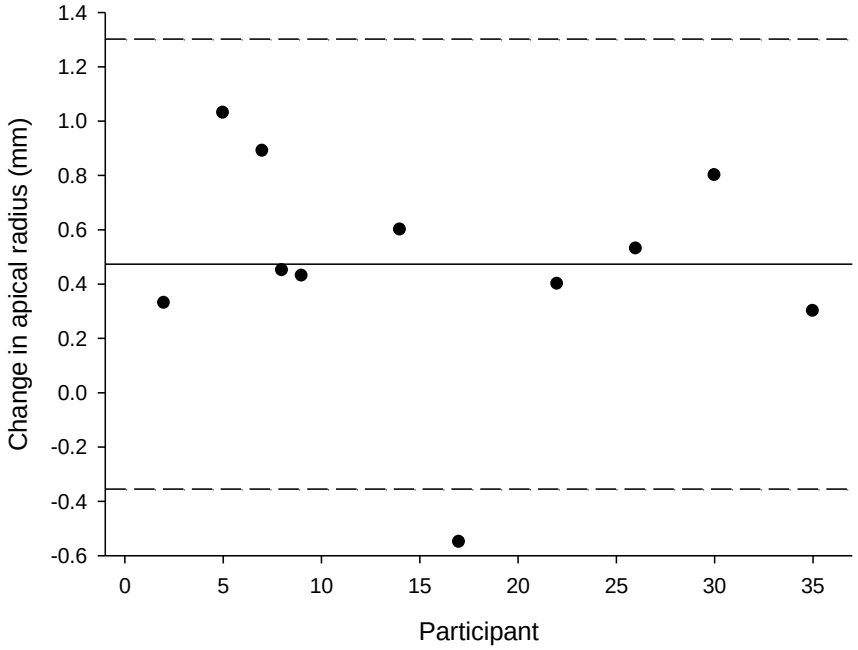
b)


Change in apical radius (mm)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
0
5
10
15
20
25
30
35
Participant

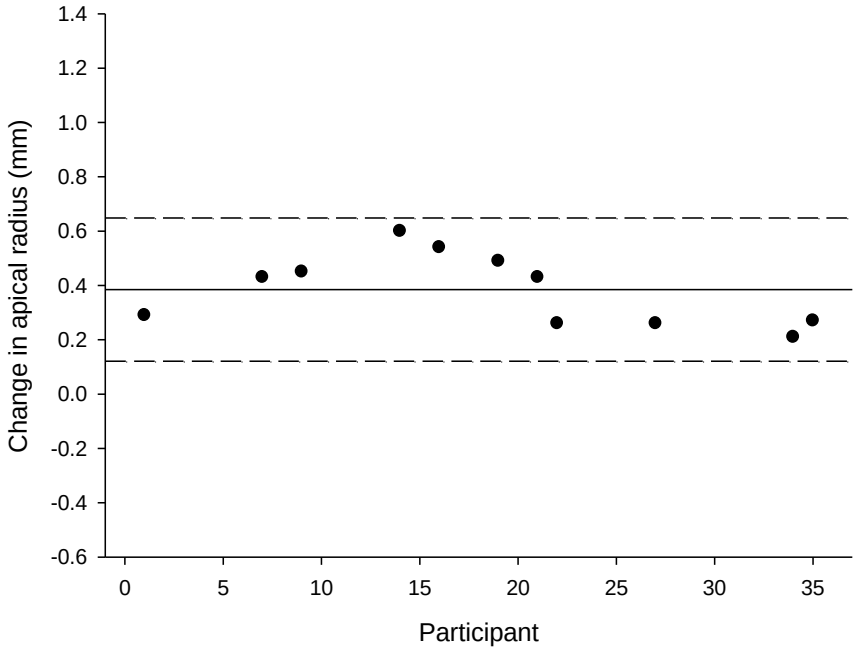
c)


Change in apical radius (mm)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
0
5
10
15
20
25
30
35
Participant

d)


Change in apical radius (mm)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
0
5
10
15
20
25
30
35
Participant

e)



f)

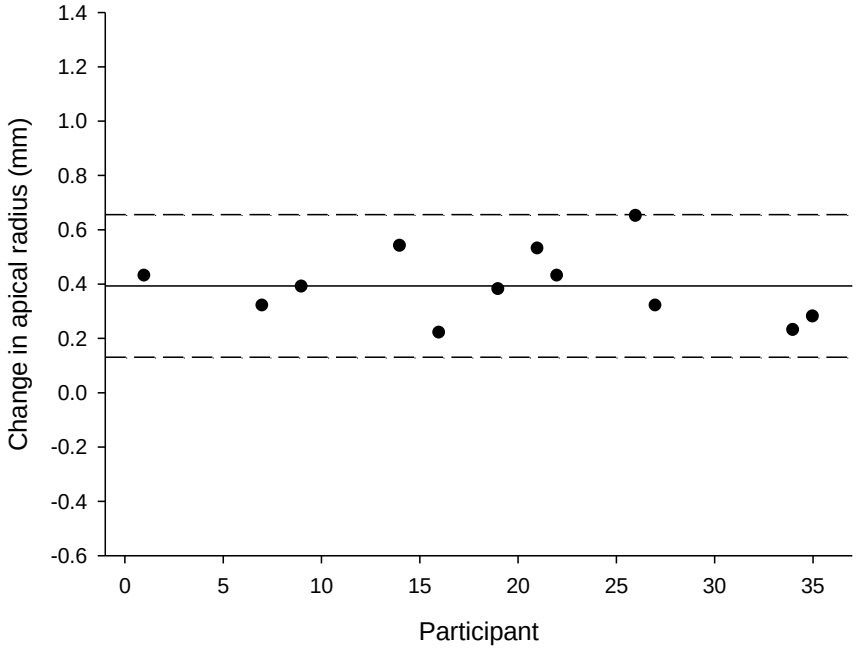
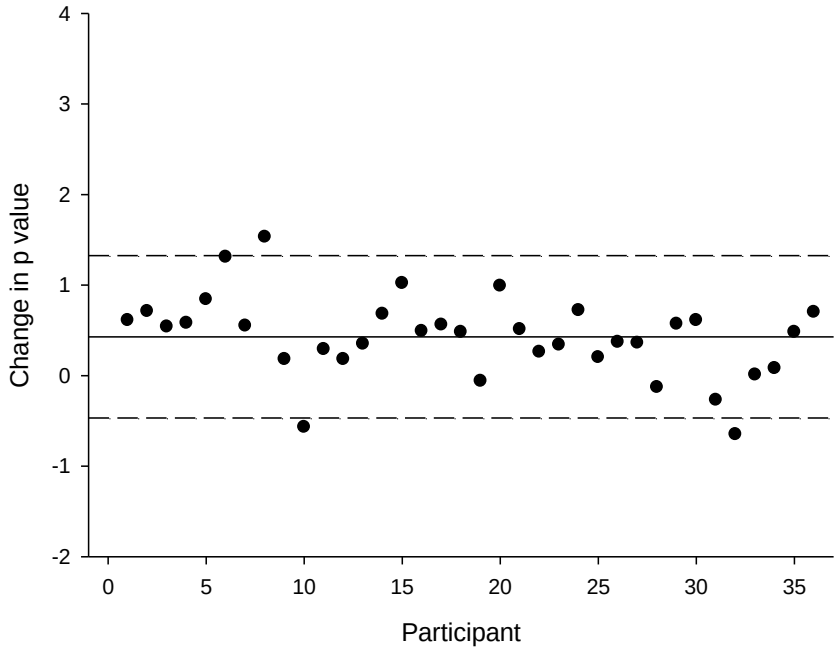


Fig 4.6 Difference plots of the change in the apical radius for the aspheric design a) initial to ON, b) initial to OW, c) initial to OM, d) initial to OQ, e) initial to 6M and f) initial to OY. The initial measurement was deducted from the measure obtained at each visit. The broken lines indicate two standard deviations.

a)


Change in p value
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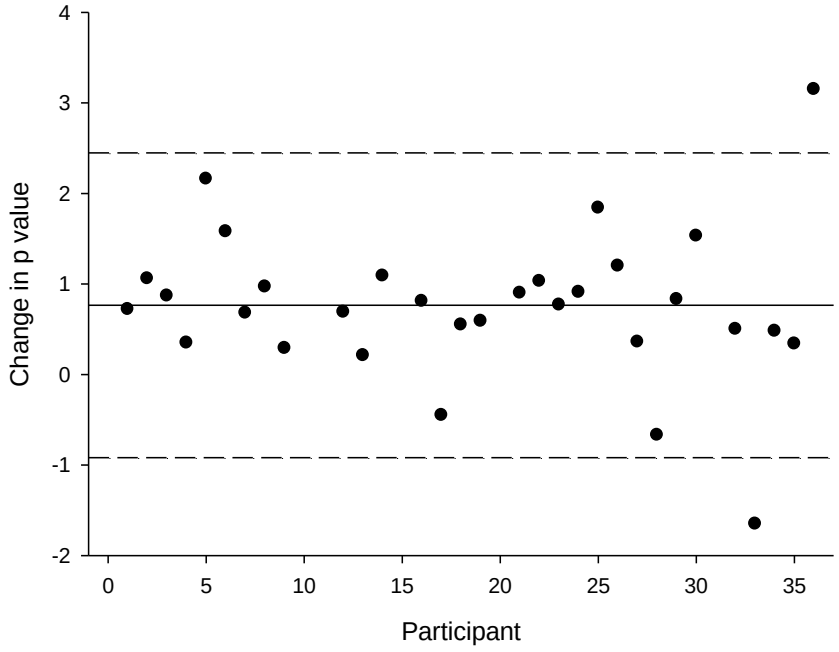
2
1
0
-1
-2
0
5
10
15
20
25
30
35
Participant

b)


Change in p value
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2
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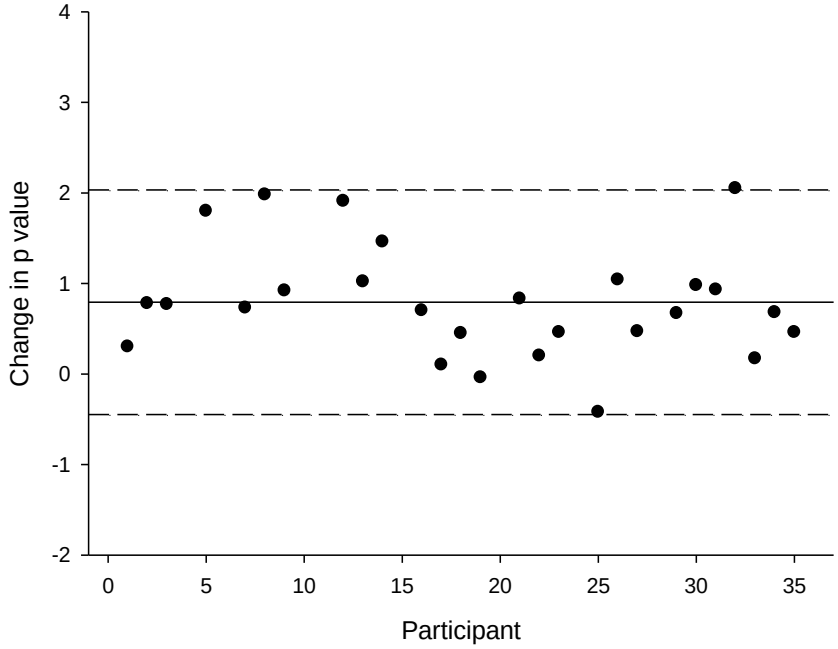
0
-1
-2
0
5
10
15
20
25
30
35
Participant

c)


Change in p value
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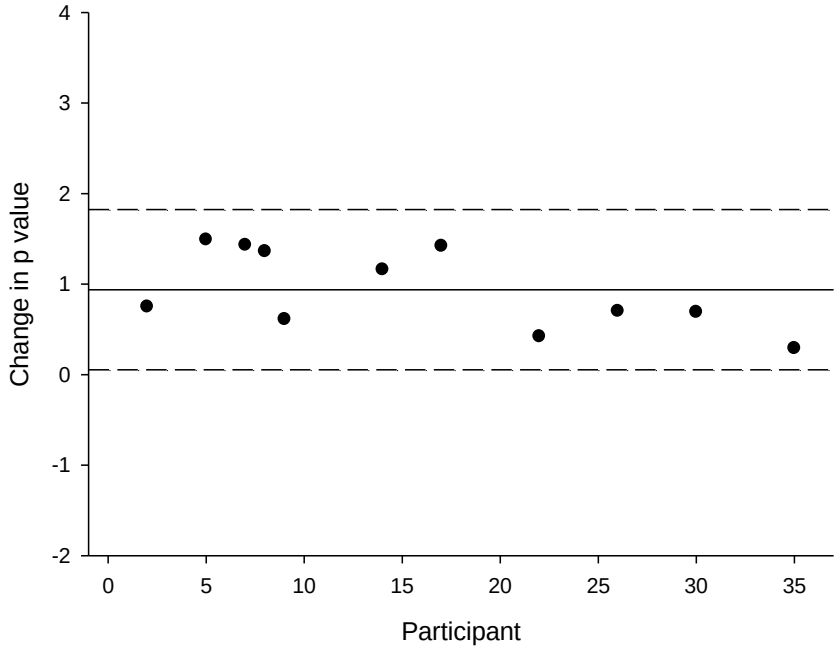
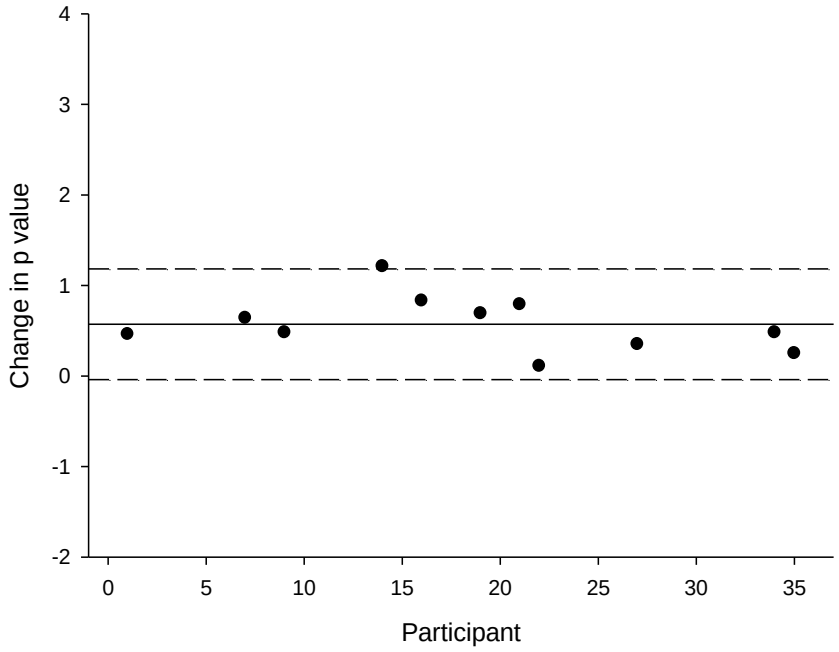
2
1
0
-1
-2
0
5
10
15
20
25
30
35
Participant

d)


Change in p value
4
3
2
1
0
-1
-2
0
5
10
15
20
25
30
35
Participant

e)



f)

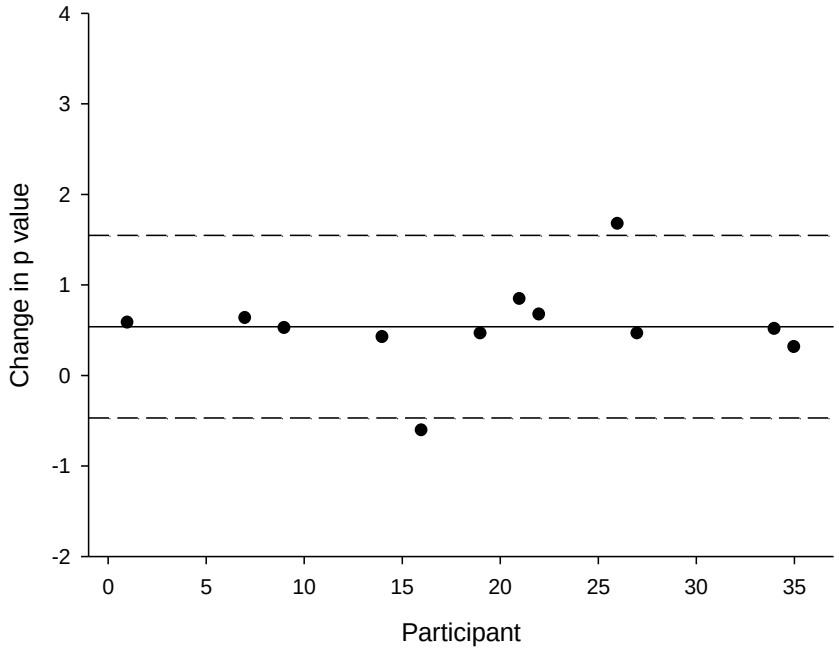
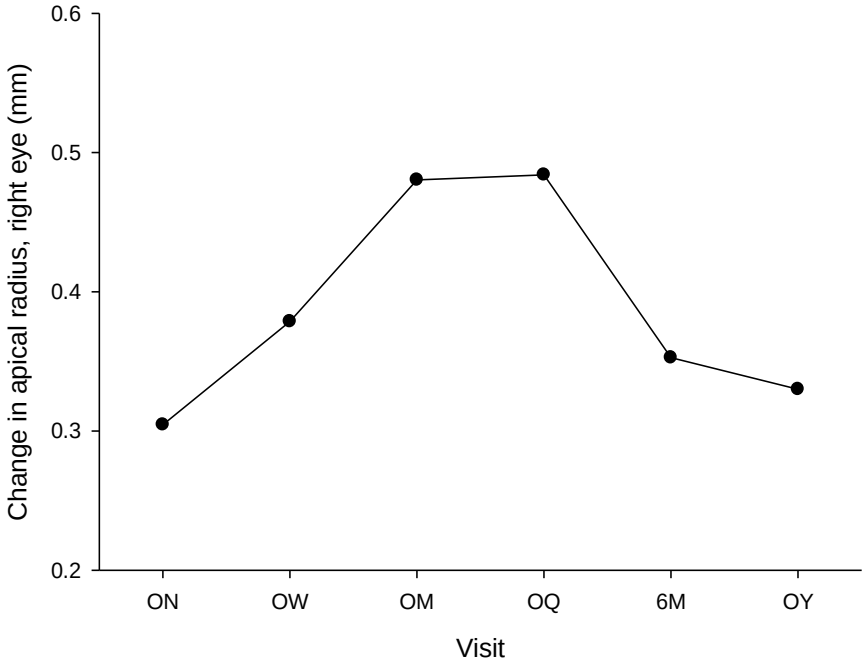


Fig 4.7 Difference plots of the change in the p value for the aspheric design a) initial to ON, b) initial to OW, c) initial to OM, d) initial to OQ, e) initial to 6M and f) initial to OY. The initial measurement was deducted from the measure obtained at each visit. The broken lines indicate two standard deviations.

A repeated measures ANOVA of the pentacurve anterior apical radii measured at each visit showed that there was a significant difference in the apical radius over time ($F_{(5,50)} = 12.71$ $p = 0.00$) for the twelve subjects. A repeated measure ANOVA of the right (pentacurve) p value for the same subjects showed that there was a significant difference in the p value over time although this was only just significant. ($F_{(1.91, 19.12)} = 3.768$ $p = 0.043$). A correction for sphericity was applied to the pentacurve p value findings. The same repeated measures analyses were applied to the aspheric design. They showed that for both the apical radius ($F_{(5,50)} = 23.51$ $p = 0.00$) and for the p value ($F_{(5,50)} = 8.686$ $p = 0.00$) a significant difference had occurred over the twelve months. Bonferroni post hoc tests were applied to the results for the pentacurve anterior apical radius and showed that the initial apical radius values were significantly different from all visits ($p< 0.05$). The apical radii results at one night were not significantly different from any of the subsequent visit data. This condition applied to visits at one week, one month, six months and one year. Bonferroni post hoc tests for the pentacurve anterior p value revealed that the initial measurement was significantly different at one night, one week, one month ($p<0.05$) but not from the six month and twelve month data. The p value measures at one night, one week, one month were also significantly different from each other ($p<0.05$) the six month and twelve month visit data were not significantly different from each other. When a similar analysis was applied to the aspheric design apical radius results the initial value was found to be different from all the subsequent visits ($p<0.05$). The one night result was also significantly different from the one week visit data ($p <0.05$) with no significant difference after this. For the aspheric design p value the initial visit data was significantly different from all other visits. The one night, one week, one month, six month and twelve month results were not significantly different from each other. The three month visit data was excluded from these results as there were insufficient participants available for data collection at this visit. A two way repeated measures ANOVA with lens and visit as the factors

showed no significant difference between the effect of the two lenses on the apical radius ($F_{(5,45)} = 2.121$ $p = 0.078$) or p value ($F_{(5,45)} = 1.083$ $p = 0.381$)

a)



b)

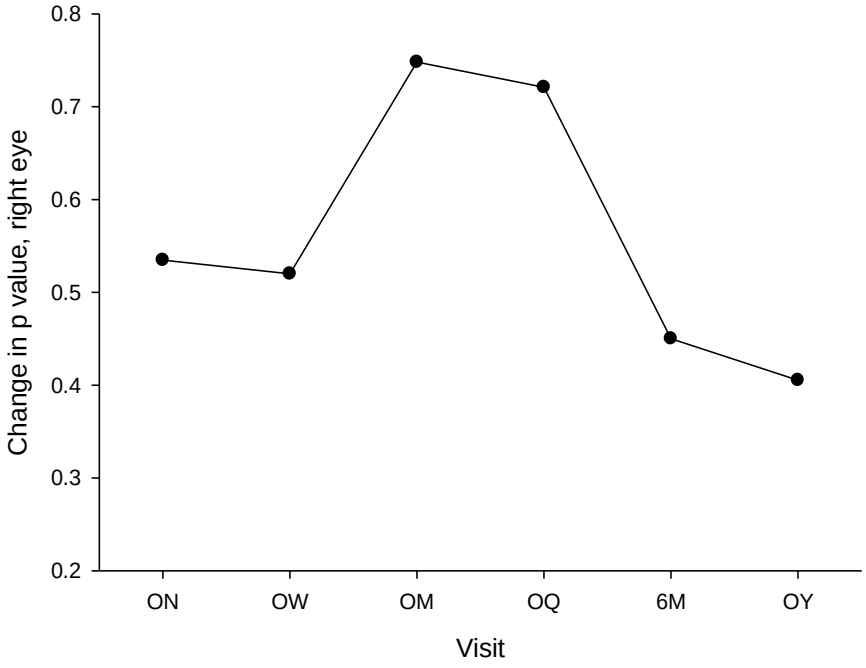
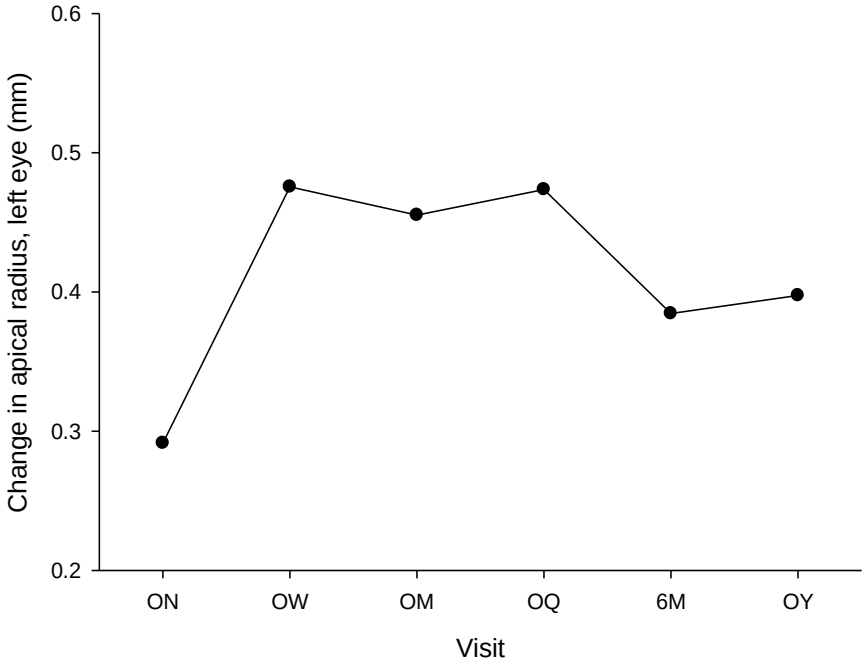


Fig 4.8 Pentacurve group mean change in a) apical radius and b) p value for the twelve months

a)



b)

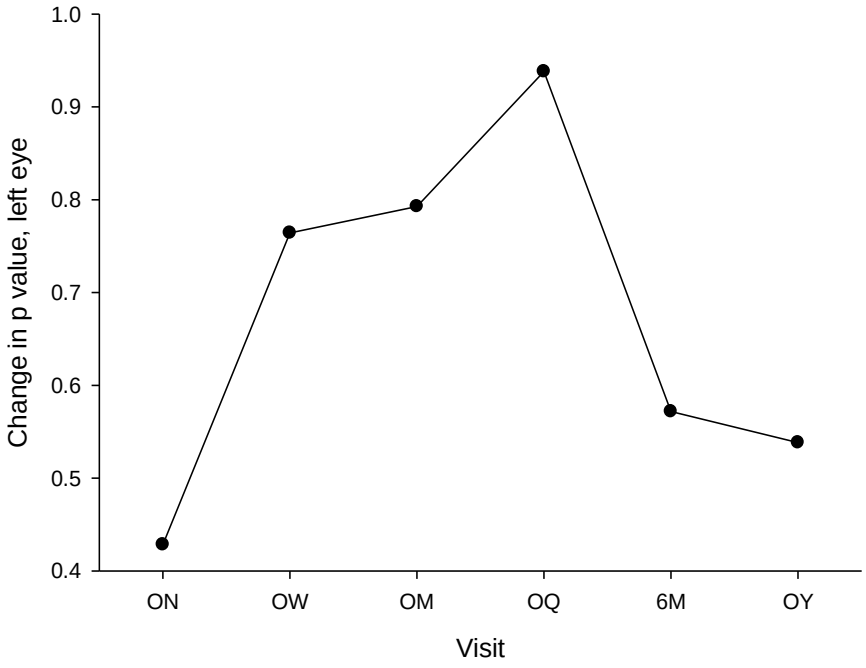
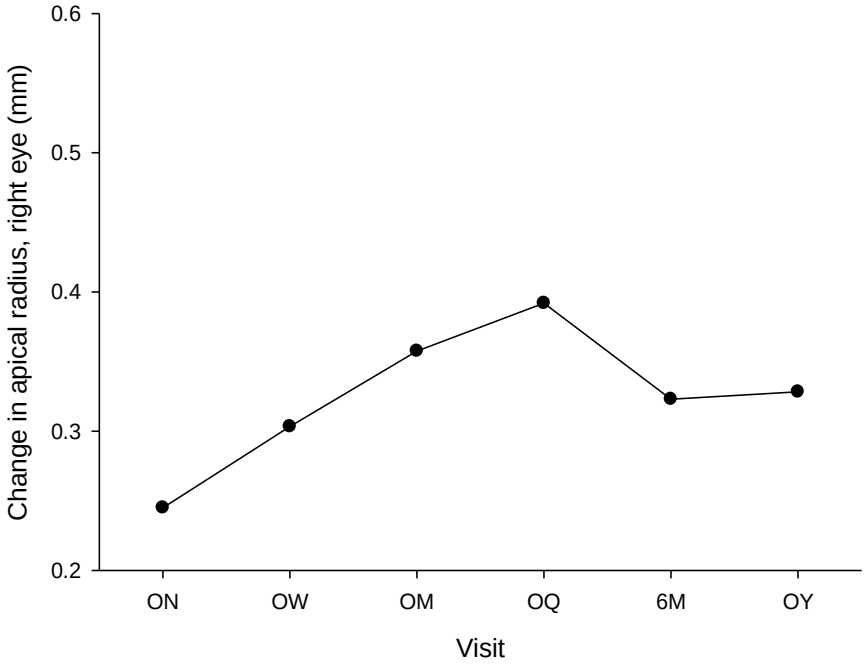


Fig 4.9 Aspheric design group mean change in a) apical radius and b) p value for the twelve months

a)



b)

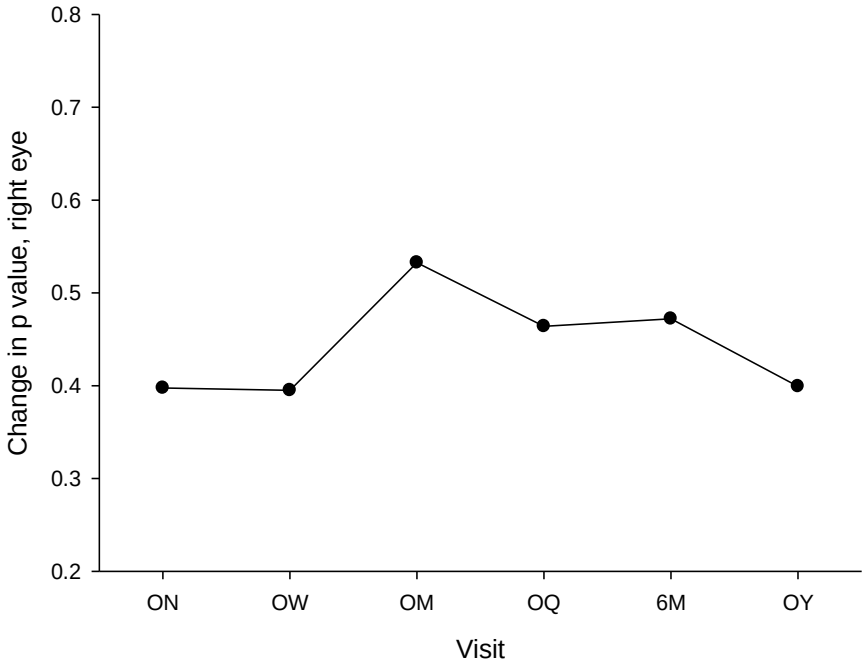
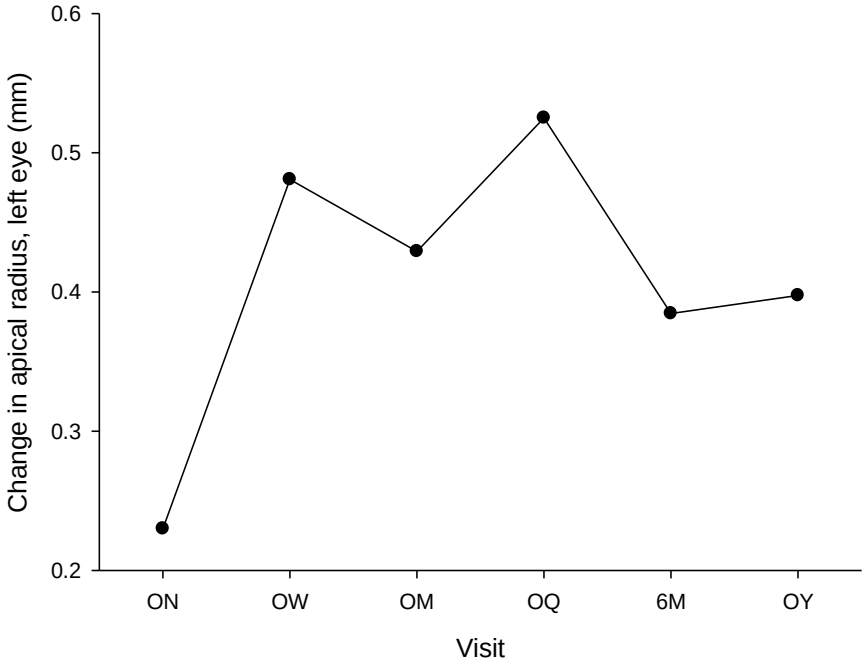


Fig 4.10 Pentacurve results for the12 subjects who wore the lenses for one year a) apical radius change b) p value change.

a)



b)

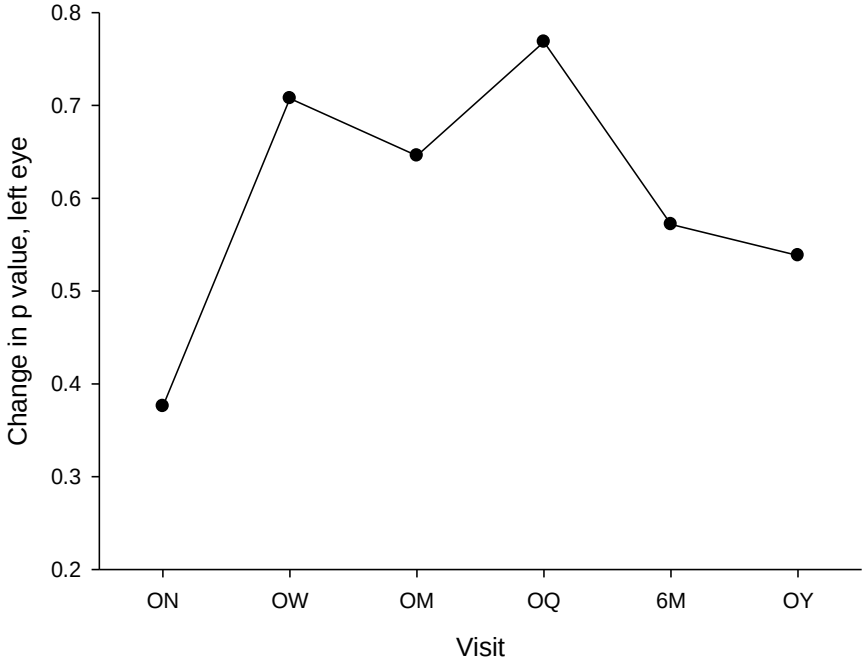


Fig 4.11 Aspheric design results for the12 subjects who wore the lenses for one year a) apical radius change b) p value change.

4.3.2 Results for Corneal Sag

Table 4.6 Mean corneal sag (mm) results for each visit

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	0.82 +/- 0.03	0.82 +/- 0.03
One night	36	0.81 +/- 0.03	0.80 +/- 0.04
One week	30	0.80 +/- 0.04	0.80 +/- 0.06
One month	28	0.80 +/- 0.04	0.80 +/- 0.05
One quarter	17	0.79 +/- 0.04	0.80 +/- 0.06
Six months	13	0.80 +/- 0.04	0.80 +/- 0.03
One year	12	0.81 +/- 0.03	0.80 +/- 0.03

The corneal sag changes at one night in both eyes are statistically significant. A paired t test shows R $t_{(35)} = 5.10$ $p < 0.05$ and L $t_{(35)} = 3.83$ $p < 0.05$. A repeated measures ANOVA for the pentacurve corneal sag for the twelve subjects who completed twelve months of lens wear shows ($F_{(5,50)} = 12.10$ $p = 0.00$) and for the aspheric design ($F_{(5,50)} = 10.22$ $p = 0.00$). These results show that a significant change occurred in both corneal sags. Bonferroni post hoc tests showed that the initial pentacurve corneal sag is statistically significantly different from the other five measures ($p < 0.05$). For the aspheric design the Bonferroni post hoc tests show that the one night sag measure is not statistically significantly different from the initial measure ($p = 0.146$). The change in sag at one week is significantly different from the initial. The one night, one week, one month, six and twelve month visits are not significantly different from each other. A two way repeated measures ANOVA with lens design and time as the two factors showed that there was no significant difference in the change in corneal sag between the two lens designs ($F_{(5,45)} = 0.640$ $p = 0.670$).

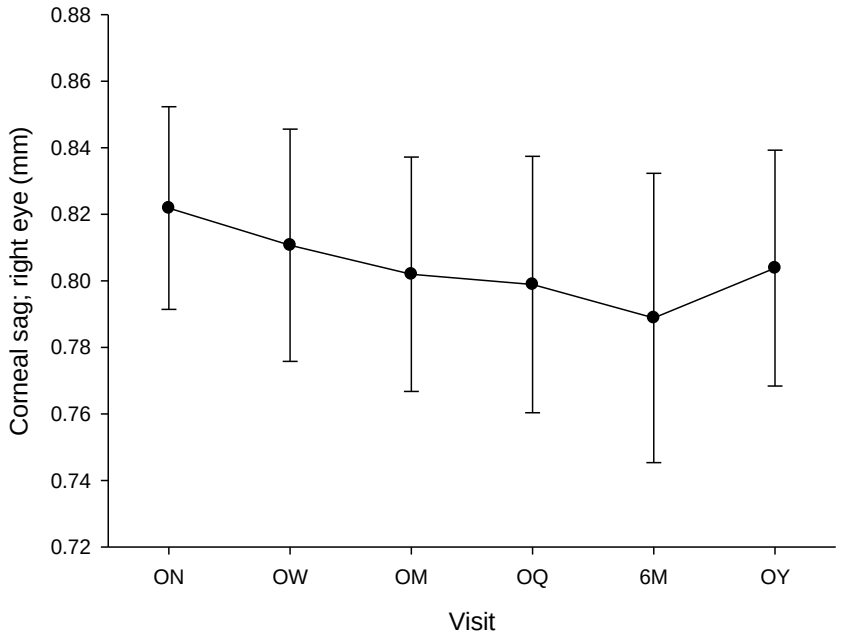


Fig 4.12 Pentacurve corneal sag measure at each visit

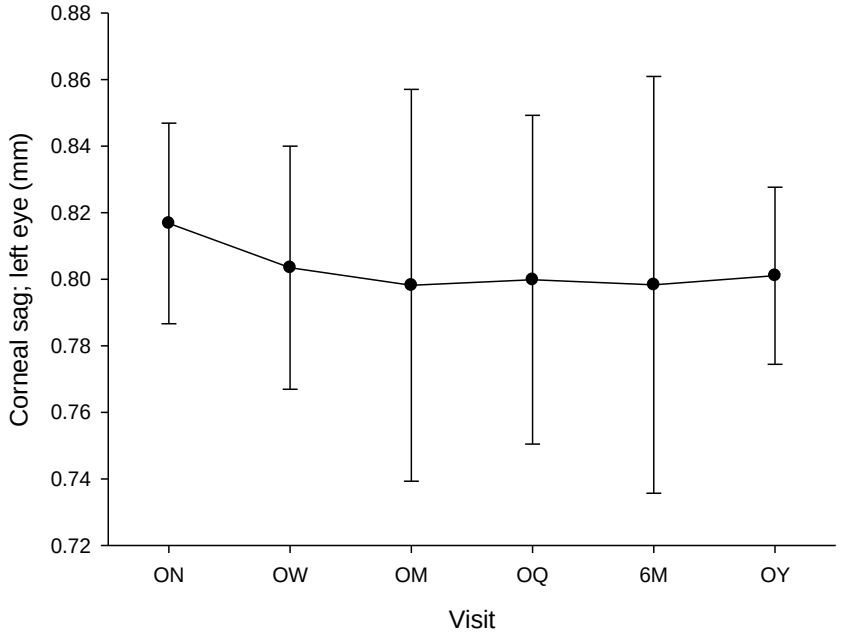


Fig 4.13 Aspheric corneal sag measure at each visit

4.3.3 Results for Pentacurve BOZR and right apical radius and the Aspheric design lens sag and corneal sag

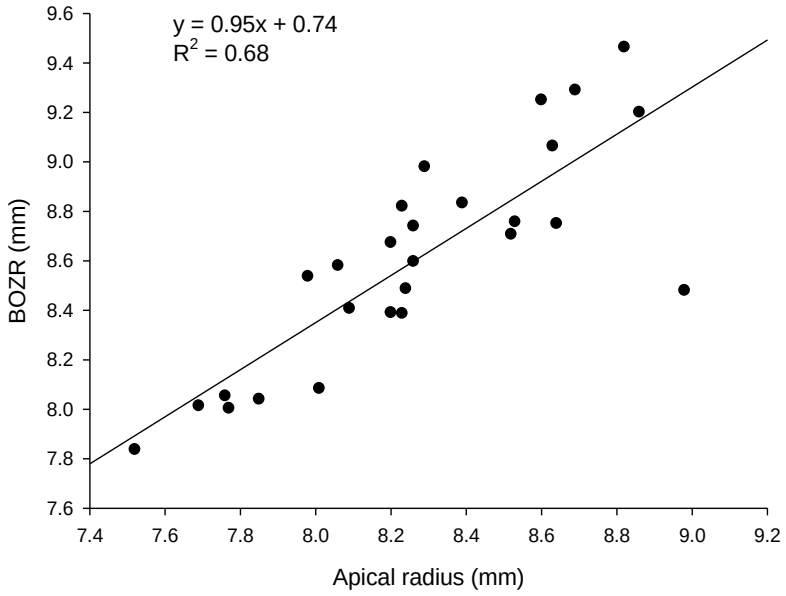


Fig 4.14 Pentacurve mean BOZR compared with right eye anterior apical radius (r_0) at one month.

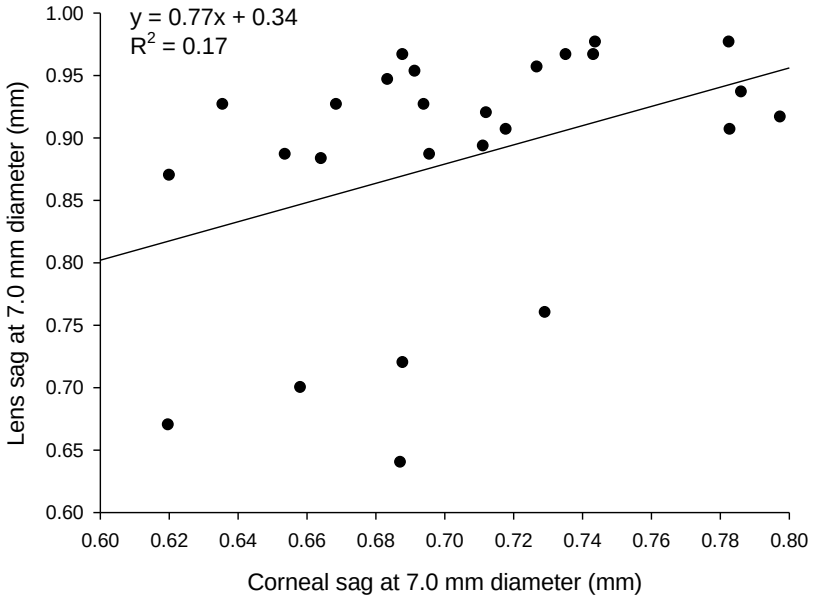


Fig 4.15 Aspheric lens sag compared with the corneal sag at one month both measured over a 7mm radius.

4.3.4 Results for the corneal sag

Table 4.7 Effect of change in apical radius (r0), p value (p) and corneal diameter (y) on corneal sag.

r0 (mm)	p	y (mm)	Sag (mm)
7.8	0.5	3.5	0.81
7.8	1.0	3.5	0.83
7.8	1..5	3.5	0.86
7.8	2.0	3.5	0.89
7.8	2.5	3.5	0.92
7.8	3.0	3.5	0.96
7.0	0.8	3.5	0.92
7.5	0.8	3.5	0.86
8.0	0.8	3.5	0.80
8.5	0.8	3.5	0.75
9.0	0.8	3.5	0.70
9.5	0.8	3.5	0.66
7.8	0.8	2.0	0.26
7.8	0.8	2.5	0.41
7.8	0.8	3.0	0.60
7.8	0.8	3.5	0.82
7.8	0.8	4.0	1.09
7.8	0.8	4.5	1.40

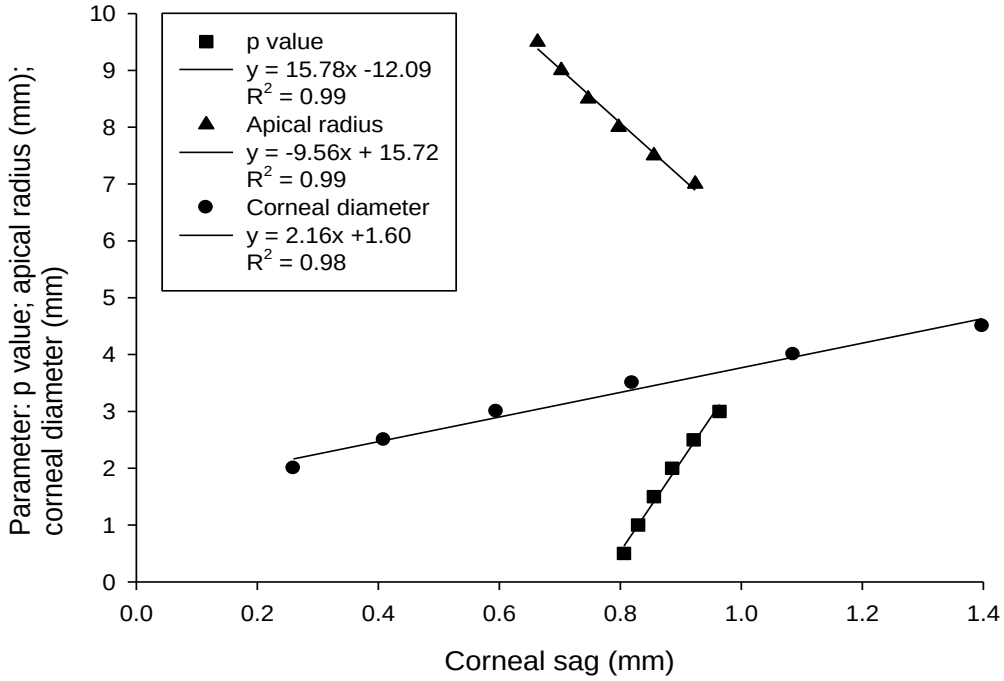


Fig 4.16 Graphical display of the effect of change in apical radius (r0), p value (p) and corneal diameter (y) on corneal sag.

It can be seen from Table 4.7 and Fig 4.16 that a change in the corneal diameter assessed has the largest impact on corneal sag. The results for the pentacurve BOZR and the right apical radius at one month are shown in Fig 4.14. A paired t test of the BOZR and r_0 at one month shows the two results are significantly different ($t_{(26)} = 7.209$ $p = 0.00$). The results for the aspheric lens sag and left corneal sag at one month are shown in Figs 4.15. A paired t test of the lens sag and the corneal sag at one month shows that they are also significantly different from each other ($t_{(26)} = 10.239$ $p = 0.00$)

Figs 4.17a and 4.17b show the results of the change in corneal sag at one month against the equivalent change in apical radius for both the pentacurve and aspheric lens designs. The correlation between the change in sag and apical radius for the pentacurve lens did not reach statistical significance if the full group were included ($t_{(24)} = 2.43$ $p > 0.05$). Examination of the data shows that one participant is a significant outlier with an excessive change in the apical radius (0.88). Removal of this participant's result from the data produces a correlation which is statistically significant ($t_{(23)} = 4.48$ $p < 0.001$). The participant whose results were removed had an initial spherical refraction (M = -5.00D) which was at the upper limit of that normally fitted with orthokeratology lenses (Mountford 1997; Walline 2004). The effect of orthokeratology on the refractive error is discussed in Section 4.1.3. For the aspheric design the t test also reaches statistical significance ($t_{(23)} = 5.54$ $p < 0.001$) if the outlier is removed. It is possible that this increased correlation for the aspheric lens is a consequence of the method of lens design. As indicated in chapter three, the aspheric lens parameters were based on creating the appropriate sags at 7.0, 9.6 and 11.2mm of the lens diameter. One subject was visually identified as an outlier in the sag data. The result for this individual did not reach a statistically significant value when outlier protocols were applied. This individual showed an abnormal p value result (2.79) at the one month visit. This individual had a myopic correction which was at the upper limit of acceptance into the study (M = -5.63D).

a) pentacurve

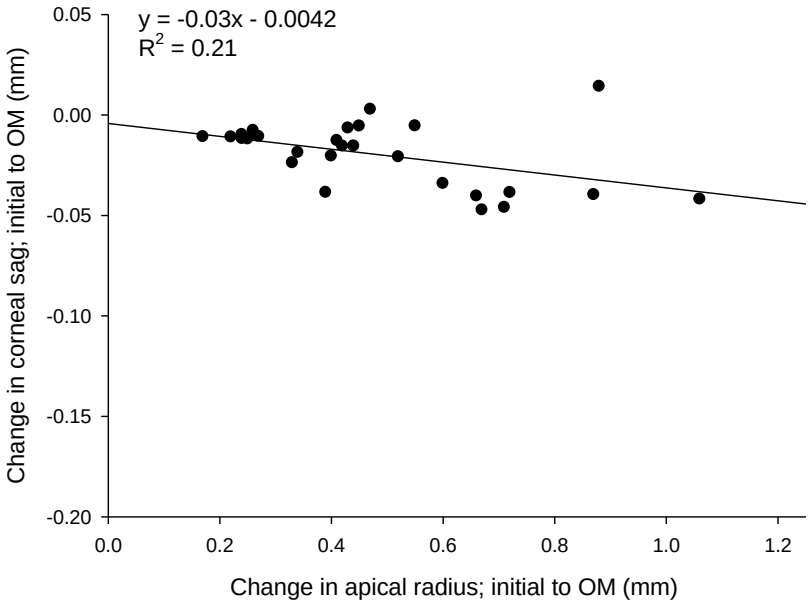


Fig 4.17a Change in apical radius at one month compared to change in corneal sag at one month (Pentacurve).

b) Aspheric

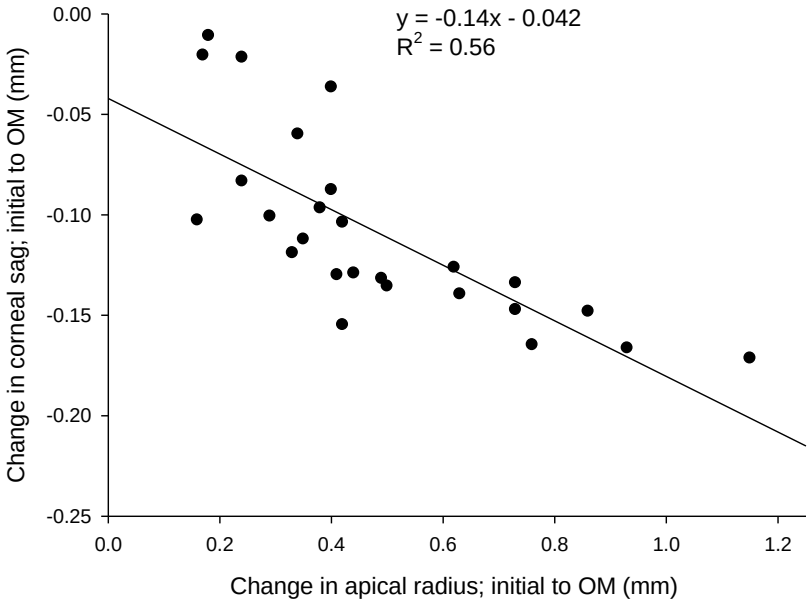


Fig 4.17b Change in apical radius at one month compared to change in corneal sag at one month (Aspheric).

4.3.5 Results for refractive error

Table 4.8 Mean refractive error (dioptres) results for each visit a) pentacurve and b) aspheric design.

a) Pentacurve

Visit	Number of subjects	M	J_0	J_{45}
Initial	36	-3.25 +/- 1.40	0.03 +/- 0.23	-0.03 +/- 0.16
One night	36	-0.73 +/- 0.71	-0.00 +/- 0.17	0.00 +/- 0.18
One week	30	-0.13 +/- 0.15	-0.01 +/- 0.15	-0.02 +/- 0.15
One month	28	0.09 +/- 0.30	-0.00 +/- 0.07	0.01 +/- 0.10
One quarter	17	-0.09 +/- 0.49	-0.00 +/- 0.09	0.05 +/- 0.15
Six month	13	0.23 +/- 0.56	0.00 +/- 0.00	0.03 +/- 0.08
One year	12	-0.04 +/- 0.38	-0.05 +/- 0.17	0.04 +/- 0.07

b) Aspheric

Visit	Number of subjects	M	J_0	J_{45}
Initial	36	-3.14 +/- 1.33	0.02 +/- 0.25	-0.04 +/- 0.16
One night	36	-0.71 +/- 0.89	-0.02 +/- 0.24	-0.00 +/- 0.15
One week	30	0.15 +/- 0.55	0.01 +/- 0.19	0.00 +/- 0.14
One month	28	0.24 +/- 0.76	-0.02 +/- 0.11	0.00 +/- 0.12
One quarter	17	0.22 +/- 0.83	0.03 +/- 0.11	-0.06 +/- 0.11
Six month	13	0.23 +/- 0.77	-0.06 +/- 0.12	-0.04 +/- 0.13
One year	12	0.15 +/- 0.55	-0.02 +/- 0.14	-0.03 +/- 0.19

The results for change in refractive error are shown in Tables 4.8 a) and b). A repeated measures ANOVA shows that the for the pentacurve design M ($F_{(2.3, 25.4)}$ =29.76 p = 0.00), $J_{0\ (6,66)}$ p = 0.83, $J_{45\ (6,66)}$ p = 1.89. The results show that there was a statistically significant change in M but no statistically significant change in either J_0 or J_{45}. The tests of within-subject contrasts show that the change in M is significant at one night (p = 0.001) and also at one week (p= 0.002) but not at the one, three, six and twelve months visits. The within-subject tests for J_0 and J_{45} show that there is no significant

change at any visit. For the aspheric design the repeated measure ANOVA shows M ($F_{(6, 66)} = 28.77$ $p = 0.00$), $J_{0\ (3.10, 34.14)}$ $p = 0.69$, $J_{45\ (6, 66)}$ $p = 0.72$. The results for the aspheric design are, as expected, similar to those of the pentacurve with a statistically significant change in M but not for J_0 and J_{45}. The tests of within-subject contrasts for the aspheric design also show that for M the change is significant at one night ($p = 0.00$) and at one week ($p = 0.017$) but not at any of the other four visits. The results for the within-subjects contrasts for J_0 and J_{45} are the same as for the pentacurve i.e. no significant change at any of the six visits. The two way ANOVA with lens and visit as factors showed no statistically significant difference between the two lenses for M ($F_{(5,45)} = 1.035$ $p = 0.407$), J_0 ($F_{(1,2.989)} = 1.012$ $p = 0.4$) and J_{45} ($F_{(5,45)} = 1.479$ $p = 0.212$). The Greenhouse Geisser correction was applied to the results for the J_0 results. The three month visit data was excluded from the two way ANOVA due to low numbers of participants at this visit.

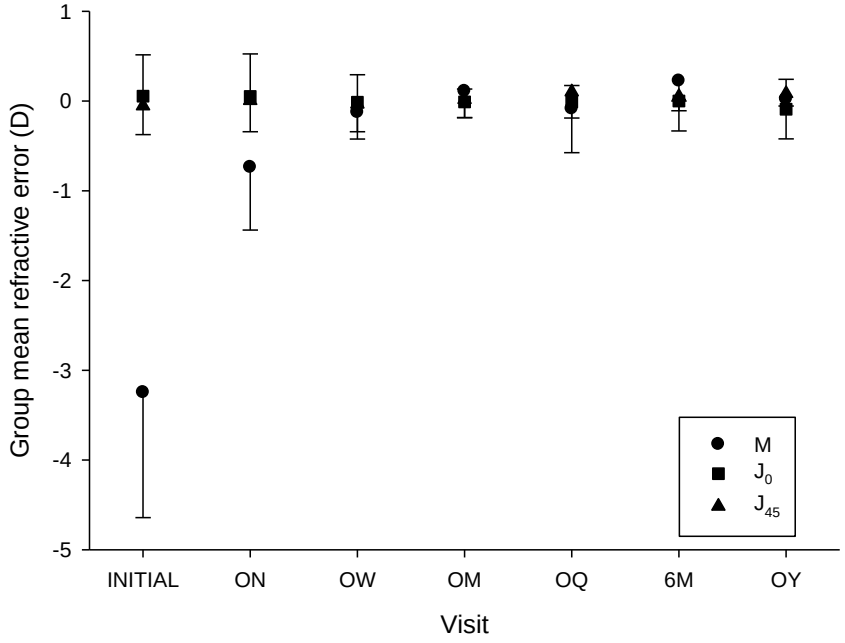


Fig 4.18 Mean refractive error change for the pentacurve design for twelve months

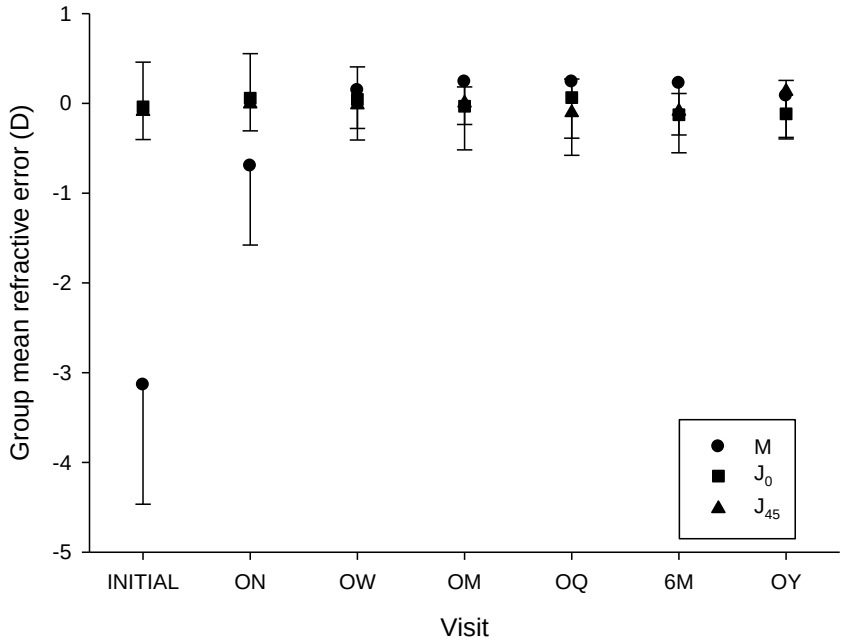


Fig 4.18 Mean refractive error change for the aspheric design for twelve months

Table 4.9 Mean astigmatic error (dioptres) present at each visit.

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	-0.41 +/- 0.38	-0.49 +/- 0.32
One night	36	-0.55 +/- 0.33	-0.60 +/- 0.33
One week	30	-0.50 +/- 0.19	-0.49 +/- 0.17
One month	28	-0.44 +/- 0.18	-0.50 +/- 0.18
One quarter	17	-0.63 +/- 0.31	-0.60 +/- 0.13
Six month	13	-0.33 +/- 0.29	-0.50 +/- 0.14
One year	12	-0.50 +/- 0.16	-0.50 +/- 0.18

For clarity the mean astigmatic error present in each eye for the group at each of the visits is presented in Table 4.9.

4.3.6 Results for corneal power

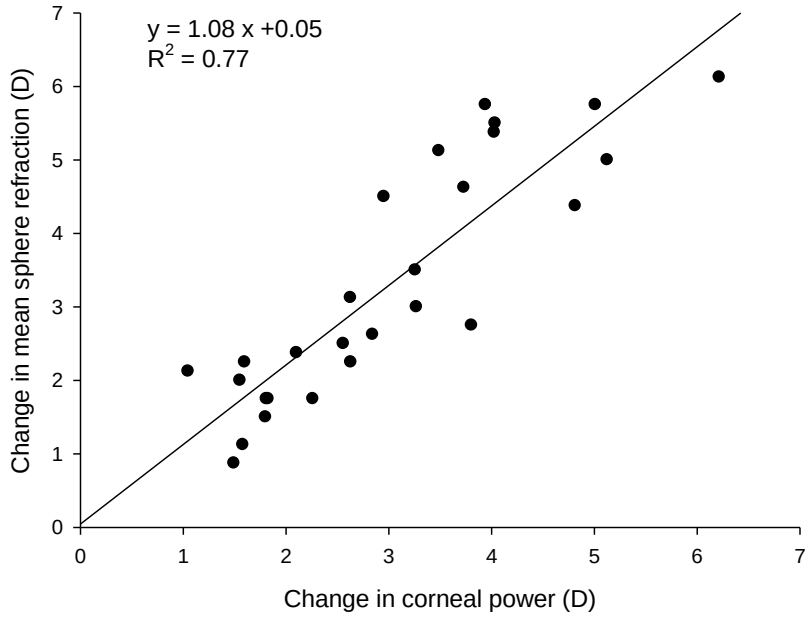
Table 4.10 Mean corneal power results for each visit measured in dioptres.

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	43.14 +/- 1.55	42.97 +/- 1.50
One night	36	40.91 +/- 2.18	41.00 +/- 2.19
One week	30	40.65 +/- 1.75	39.95 +/- 2.39
One month	28	40.15 +/- 2.03	40.21 +/- 2.03
One quarter	17	39.70 +/- 1.43	39.57 +/- 2.54
Six months	13	40.92 +/- 2.10	40.51 +/- 1.48
One year	12	40.95 +/- 1.52	40.47 +/- 1.44

Table 4.11 Change in mean corneal power at each visit measured in dioptres

Visit	Number of subjects	Pentacurve	Aspheric
One night	36	-2.22	-1.97
One week	30	-0.26	-1.05
One month	28	-0.51	0.26
One quarter	17	-0.45	-0.64
Six months	13	1.22	0.93
One year	12	-0.02	-0.04

a) pentacurve



b) aspheric

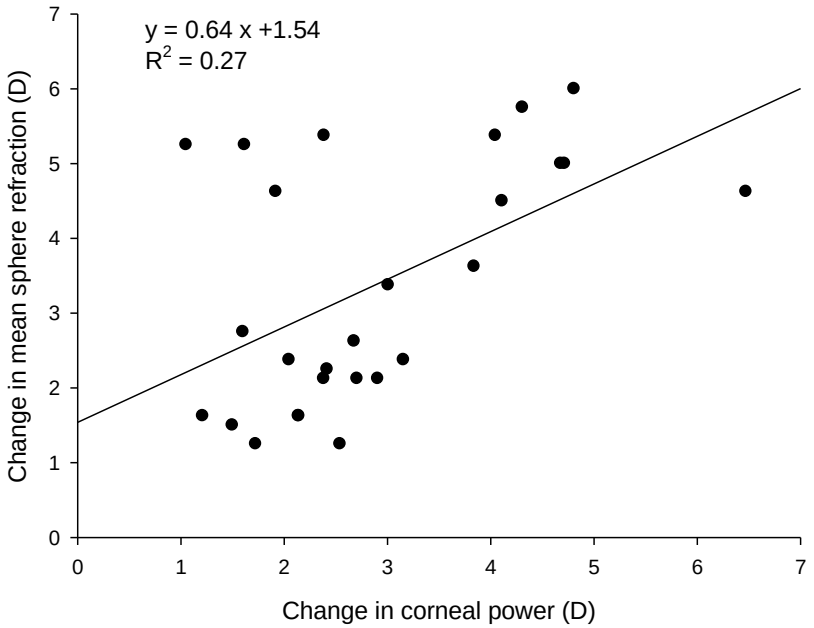


Fig 4.19 show the correlation between the change in mean sphere refraction (ΔM) and the change in corneal power (ΔACP) for the pentacurve and aspheric designs at one month of lens wear.

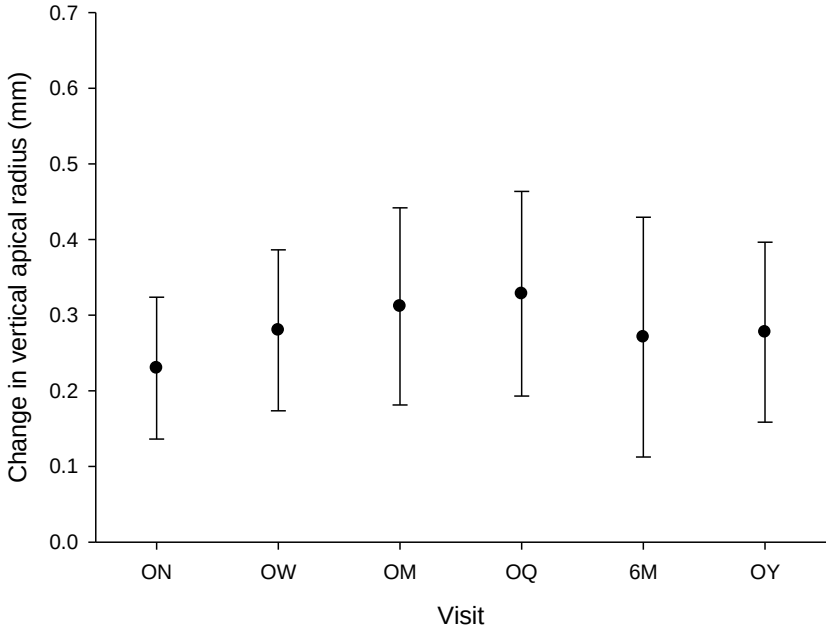
4.3.7 Results for vertical cornea

Table 4.12 Vertical apical radius (r0) (mm) and p value for the pentacurve and aspheric lens designs for participants completing twelve months of the study.

	Number of subjects	Pentacurve		Aspheric	
Visit		Apical radius	p value	Apical radius	p value
Initial	36	7.69 +/- 0.25	0.91 +/- 0.11	7.71 +/- 0.22	0.91 +/- 0.11
One night	36	7.92 +/- 0.29	1.29 +/- 0.23	7.92 +/- 0.24	1.20 +/- 0.24
One week	30	7.97 +/- 0.24	1.21 +/- 0.32	8.13 +/- 0.23	1.59 +/- 0.44
One month	28	8.01 +/- 0.31	1.22 +/- 0.18	8.08 +/- 0.32	1.40 +/- 0.38
One quarter	17	8.03 +/- 0.32	1.09 +/- 0.32	8.18 +/- 0.33	1.48 +/- 0.27
Six months	13	7.99 +/- 0.31	1.18 +/- 0.35	8.08 +/- 0.23	1.39 +/- 0.18
One year	12	7.97 +/- 0.28	1.06 +/- 0.22	8.03 +/- 0.27	1.23 +/- 0.36

Repeated measures ANOVA for the vertical radius shows no statistically significant change over time in either eye; pentacurve ($F_{(1,11)} = 1.023$ $p = 0.334$) and aspheric ($F_{(1,11)} = 1.05$ $p = 0.398$). A repeated measures ANOVA for the p value of the vertical cornea of both eyes show a statistically significant change over time; pentacurve ($F_{(2.5,27.8)} = 3.548$ $p = 0.033$) and aspheric ($F_{(3.2,34.7)} = 7.435$ $p = 0.00$). In both cases the Greenhouse-Geisser correction was applied. A two way repeated measures ANOVA for the vertical apical radius showed that there was a statistically significant difference between the effect of the two lenses on vertical apical radius ($F_{(5,50)} = 2.893$, $p = 0.023$). The results for the vertical p value also showed a statistically significant difference between the two lenses ($F(2.3, 23) = 3.445$, $p = 0.043$). The Greenhouse-Geisser correction was applied in the latter case. It can be seen from Table 4.12 that the aspheric lens produces a flatter and more oblate corneal response.

a) pentacurve



b) aspheric

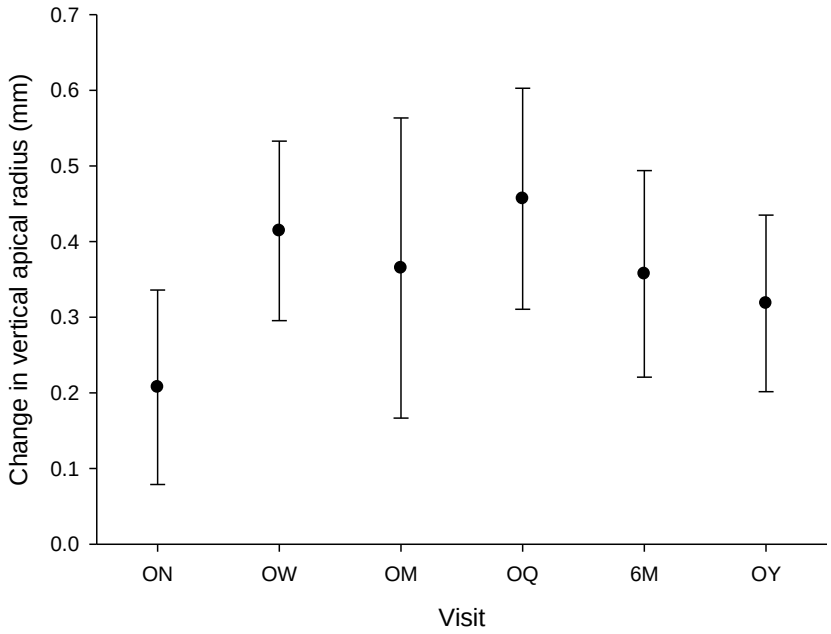
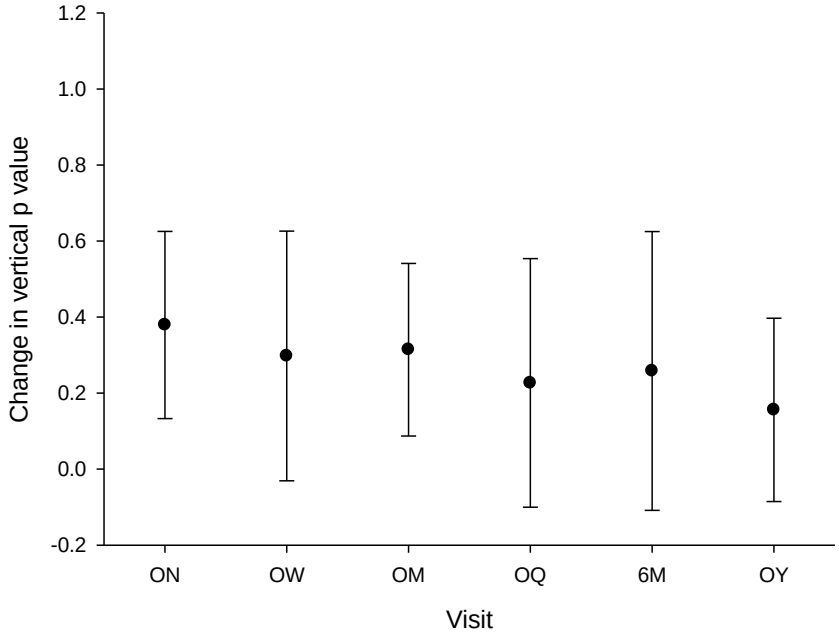


Fig 4.20 Change in the vertical apical radius for the twelve subjects completing twelve months of lens wear; a) pentacurve, b) aspheric.

a) pentacurve



b) aspheric

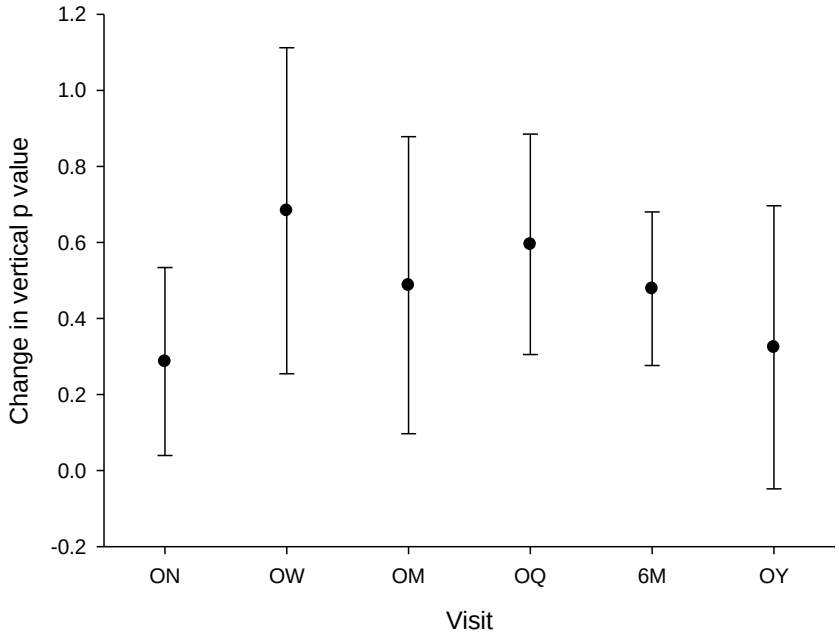


Fig 4.21 Change in the vertical p value for the twelve subjects completing twelve months of lens wear; a) pentacurve, b) aspheric.

4.3.8 Results for VAR

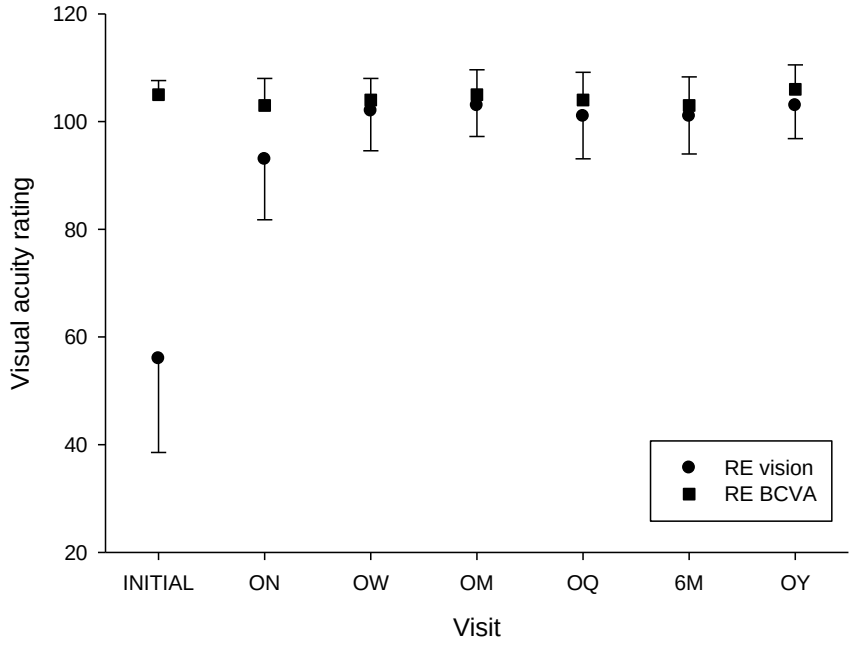
Table 4.13 Mean change in vision and best corrected visual acuity (BCVA) for the pentacurve and aspheric lens designs over twelve months. Results are recorded as Visual Acuity Ratings (VAR)

	Number of subjects	Pentacurve		Aspheric	
Visit		Vision	BCVA	Vision	BCVA
Initial	36	56 +/- 17	105 +/- 3	56 +/- 16	105 +/- 3
One night	36	93 +/- 11	103 +/- 5	90 +/- 13	99 +/- 6
One week	30	102 +/- 7	104 +/- 4	97 +/- 8	101 +/- 6
One month	28	103 +/- 6	105 +/- 5	99 +/- 8	101 +/- 6
One quarter	17	101 +/- 8	104 +/- 5	98 +/- 6	99 +/- 6
Six month	13	101 +/- 7	103 +/- 5	98 +/- 8	100 +/- 6
One year	12	103 +/- 6	106 +/- 5	100 +/- 7	103 +/- 5

Table 4.13 shows the best corrected visual acuity, this is the acuity achieved after any residual refractive error had been corrected. A paired sample t test of the initial vision and BCVA results of the two eyes showed that they were not statistically different from each other (Vision $t_{(35)} = -.157$ $p = 0.877$; BCVA $t_{(35)} = -1.22$ $p = 0.230$). Paired sample t tests were repeated on the vision and BCVA data of the two eyes at twelve months (Vision $t_{(11)} = 2.88$ $p < 0.015$; BCVA $t_{(11)} = 2.22$ $p = 0.05$). The t tests revealed that despite undergoing the same length of treatment the two eyes had responded differently. The lens designs applied to the two eyes were described in chapter 3. The statistical results are only just significant p=0.05 for the BCVA. A two way repeated measures ANOVA for the BCVA with lens and time as factors showed that the effect of the lens and visit were statistically significant ($F_{(1,10)} = 23.104$, $p = 0.001$) and ($F_{(5,50)} = 3.372$, $p = 0.011$) respectively. The interaction between the lens and the visit was not statistically significant ($F_{(5,50)} = 1.409$, $p = 0.237$). A similar two way repeated measures ANOVA applied to the results for unaided vision showed that the lens type and visit had a statistically significant effect (Lens - ($F_{(1,10)} = 16.958$ $p = 0.002$, Visit - $F_{(1.75, 17.47)} =$

61.69, p = 0.000). the lens visit interaction was again shown not to be statistically significant ($F_{(2.68,\ 26.82)} = 0.8$, p = 0.492). For the latter two results the Greenhouse-Geisser correction was applied. Table 4.13 shows that the pentacurve lens produces a higher level of both vision and best corrected visual acuity when compared to the aspheric design over the twelve month period.

a) pentacurve



b) aspheric

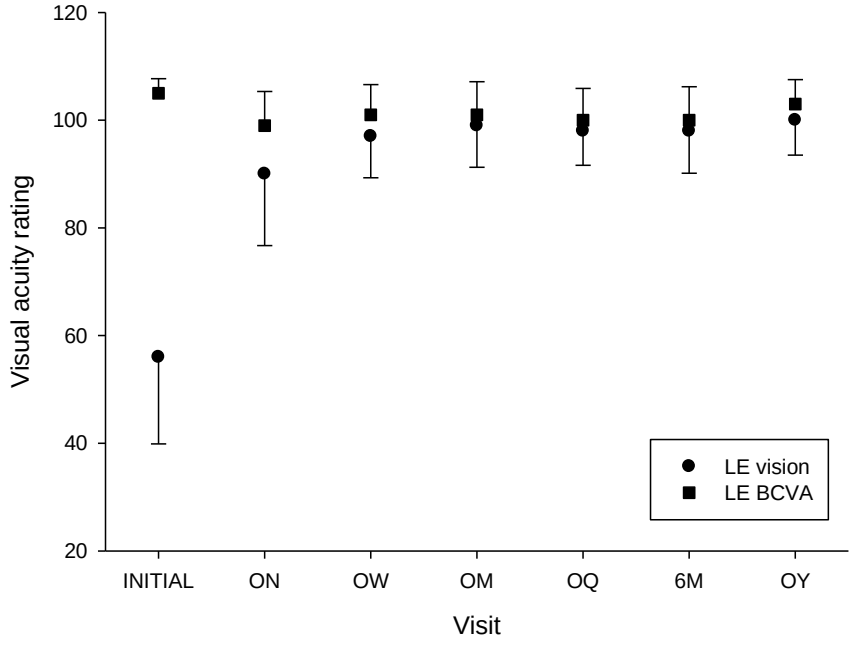


Fig 4.22 Vision and best corrected visual acuity results for the pentacurve and aspheric designs for twelve months.

4.3.9 Results for the treatment zone

Table 4.14 Treatment zone diameter (TD) and horizontal decentration (x) and vertical decentration (y) for the pentacurve (a) and aspheric lens (b) designs for all subjects to one month of lens wear. (All measurements are in mm)

a)

Visit	Number of subjects	Pentacurve			
		Horizontal TD	Vertical TD	x	y
One Night	36	2.5 +/- 1.1	2.8 +/- 1.3	-0.3 +/- 0.4	-0.1 +/- 0.6
One Week	30	3.3 +/- 0.8	3.3 +/- 0.9	-0.3 +/- 0.5	0.0 +/- 0.5
One Month	28	3.3 +/- 0.7	3.2 +/- 0.9	-0.2 +/- 0.4	-0.2 +/- 0.5

b)

Visit	Number of subjects	Aspheric			
		Horizontal TD	Vertical TD	x	y
One Night	36	3.0 +/- 0.9	3.0 +/- 0.9	-0.3 +/- 0.5	-0.1 +/- 0.6
One Week	30	3.4 +/- 0.5	3.6 +/- 0.5	-0.2 +/- 0.5	-0.1 +/- 0.5
One Month	28	3.3 +/- 0.6	3.7 +/- 0.8	-0.1 +/- 0.5	-0.2 +/- 0.5

A two way repeated measures ANOVA with lens and visit as the two factors show that there was no statistically significant change in the horizontal treatment zone diameter between visits or between the two lens designs ($F_{(1.20, 40.70)} = 2.711$, $p = 0.101$). For the vertical treatment zone diameter there was a statistically significant difference between the two lenses ($F_{(1, 34)} = 6.462$, $p = 0.016$). There was no significant change in the vertical treatment zone diameter over time ($F_{(2,68)} = 0.337$, $p = 0.715$). Table 4.14 shows that the aspheric lens design produced a larger vertical treatment zone than the pentacurve lens.

An assessment of the results for the displacement of the treatment zone shows that both lenses are minimally displaced in the infero-temporal direction. A two way repeated measures ANOVA for the horizontal displacement shows that there is no significant difference in the effect of the two lenses ($F_{(1,25)} = 0.340$, $p = 0.565$) and that there was no significant interaction between the lens and visit data ($F_{(2,50)} = 1.599$, $p = 0.212$). The two way ANOVA did reveal that there was a significant effect between the visits ($F_{(2,50)} = 5.835$, $p = 0.005$). An examination of the pairwise comparisons shows that no significant difference occurred between the one night and one week visit. There was a significant difference between the one week and the one month visit although this was only just significant ($p = 0.048$). The most significant change occurred between the one night and the one month visit ($p = 0.014$). An evaluation of the vertical displacement using two way repeated measures ANOVA shows that there is no statistical difference in the effect of the two lenses ($F_{(1,25)} = 0.512$, $p = 0.481$) or in the interaction of the lens and visit results ($F_{(2,50)} = 1.433$, $p = 0.248$). A statistically significant difference was shown for the visit data ($F_{(2,50)} = 3.582$, $p = 0.035$). However an examination of the pairwise comparisons showed that none of these reached statistical significance. The within subjects contrasts showed that the difference between the one week and the one month visit almost reached significance ($p = 0.052$).

4.3.10 Results for physiological responses

The results of the corneal stain assessment at each visit for all the individuals in the study are presented in Fig 4.23

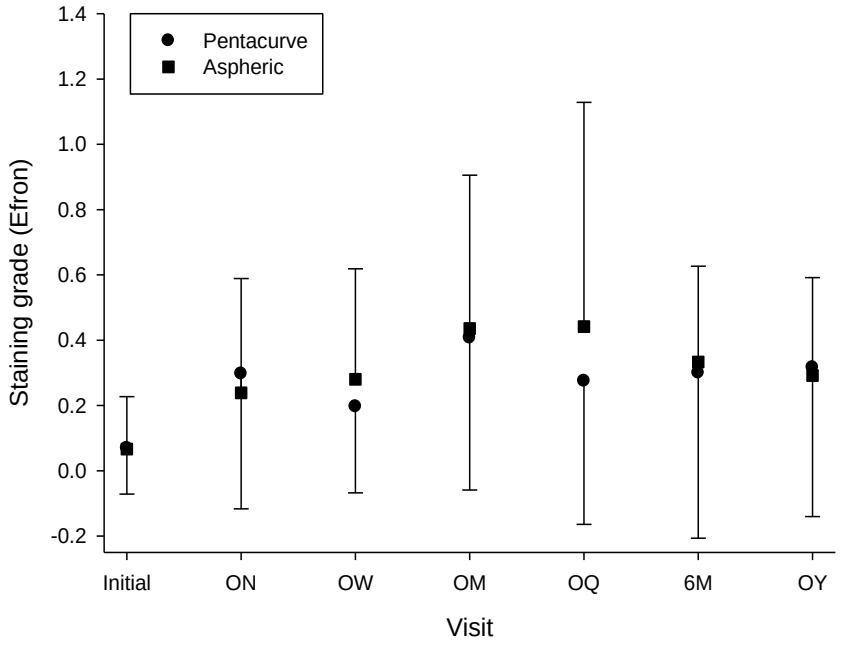


Fig 4.23 Corneal stain results for the pentacurve and aspheric lens designs for twelve months

A two way repeated measures ANOVA for the staining associated with the pentacurve and aspheric design lenses showed there was no statistically significant difference between the effect of the two lenses over the period of the study ($F_{(1,10)}$ = 0.001, p = 0.973). The two way ANOVA did reveal that there was a statistically significant difference in the grade of corneal staining between visits ($F_{(2.6,26.02)}$ = 3.467, p = 0.036). An examination of the within subjects contrasts did not reveal a significant difference at any of the comparison points. No statistically significant effect was found for the lens / occasion interaction ($F_{(2.45, 24.51)}$ = 0.299, p = 0.786).

Seven subjects contacted the researcher due to discomfort on waking. These individuals underwent a full slit lamp assessment as soon as possible after the phone call. Two individuals had central corneal stain above Grade 2. The first occurred prior to any data collection and the second after five weeks of lens wear. The other five individuals had corneal stain between Efron Grade 1 and 2. These events occurred in three individuals between the one night and the one week visit, in one individual between one week and one month and in one individual between one month and three months.

Four individuals had foreign body type traces at their routine appointments. One individual contacted the researcher for an emergency appointment after two weeks of lens wear and was found to have a foreign body in the right eye. One individual was found to have corneal iron rings in both eyes at the six month assessment visit. A full case study for this individual is presented in Appendix D. One individual contracted conjunctivitis after one month of lens wear. This proved to be recurrent and difficult to treat. New lenses, with unchanged parameters, were provided for this individual in case of bacterial contamination. This subject struggled to return to lens wear and withdrew from the study. No individual presented with microbial keratitis at any point during the study.

4.4 Discussion

4.4.1 Apical radius and p value change

The values for r0 are in agreement with those shown by Kiely et al (1982), Guillon et al (1986), Eghbali et al (1995), Douthwaite et al (1999), and Read et al (2006). The values for p are in broad agreement with those of Douthwaite et al (1999). The results differ from Guillon et al (1986) and Sheridan et al (1989) in that the corneas in this study appear to flatten more quickly. Similarly the corneas in the present study differ from the results of Carney et al (1997) and Davis et al (2005) in that they flatten more slowly. These differences may be accounted for by the different methods used to determine p in the studies. Guillon et al (1986) calculated p values for a nine millimetre cornea. Sheridan calculated the p value by comparing keratometry readings taken on axis and at points up to 25 degrees off axis. Carney et al (1997) used a curve fitting program on the raw data produced by the TMS-1 topographer using a diameter of six millimetres. Davis et al (2005) used the same analysis method as Douthwaite et al (1999); however the TMS-1 topographer produces results in apical power and not apical radius values. Davis et al converted the apical power (ACP) values to radii using the equation

$$r0 = (n - 1) \div ACP \quad \text{(n = 1.3375)}$$

As previously indicated this value for n takes account of the contribution of the posterior corneal surface to the total corneal power. The Davis et al study (2005) used an eight millimetre diameter. Since the p value and the semi-meridian (x) under examination are linked by Baker's equation

$$y^2 = 2r0x - px^2$$

a variation in the corneal semi meridian studied may account for the variation in p values noted. Although Bogan et al (1990), Rabinowitz et al (1996), Myrowitz et al (2005) and Wei et al (2006) report significant correlations between the right and left

eyes of individuals. The two eyes will be considered separately in this study as two different orthokeratology lens designs were used.

The data in Tables 4.4 and 4.5 indicates that both corneas undergo significant flattening at the one night visit. This flattening is as expected as both designs of orthokeratology lenses have been fitted to induce this change. The anterior p value (pentacurve and aspheric) at one night indicates a change from the initial prolate ellipse i.e. $0 < p < 1$ to an oblate ellipse where p is greater than 1. The change in apical radius and p value are in keeping with that of Sridharan and Swarbrick (2003). They found that as little as ten minutes of open eye lens wear induced a statistically significant change in the anterior apical radius. This significant change after ten minutes was not reflected in the p value. In this case eight hours of overnight wear was required for the change to reach significance (Sridharan and Swarbrick 2003). In a more recent study Villa-Collar, Gonzalez-Meijome, Queiros, Jorge (2009) also looked at the corneal response in open eye wear of orthokeratology lenses. Villa-Collar et al found that the corneal response occurred more quickly in those subjects requiring a greater level of correction. This difference in the rate of response was only seen after 60 minutes of lens wear.

In the current study the anterior apical radius continued to change up to one month of lens wear for the pentacurve design. The aspheric design showed the most significant change up to one week of wear and then produced little further change. It was expected that after one month no further change in anterior apical radius would be seen in keeping with other studies (Mountford 1998, Nichols 2000, Rah 2002). The change in apical radius for the twelve months of the study is shown in Fig 4.6. This shows that for the pentacurve lens after one month of wear no further change in apical radius had occurred. For the aspheric design (Fig 4.7) no change is seen after one week. This may indicate that the back surface aspheric design of the left lens initiates a more rapid effect on apical radius. It is not possible to reach that conclusion from the current data. A further experiment, possibly following similar principles to Sridharan and

Swarbrick (2003) or Villa-Collar et al (2009) would help to confirm this hypothesis i.e. short term open eye situation. Participants in the current study did wear the aspheric lens in an open eye situation during the collection appointment. The results of this appointment are detailed in chapter three. All but one participant had a positive response i.e. they achieved a reduction in their manifest refractive error. An explanation for the one exception is given in chapter three. A paired t test of the change in M at the collection appointment showed no statistically significant difference between the two lenses ($t_{(35)} = 1.14$, $p=0.26$). The length of time participants wore the lenses at the collection appointment varied between one and two hours. Another experiment with careful control of the wearing time would help to clarify this hypothesis.

The anterior apical radius data for both eyes appears to show that the corneas steepened following six months of lens wear. Due to subjects leaving the study for a variety of reasons only twelve subjects were available for data collection at the six month visit. It was felt appropriate to examine data for the full twelve months from only these twelve subjects. Their results are shown in Figs 4.8 and 4.9. The change in the anterior apical radius to one month is as expected for the larger group. The ANOVA results for the apical radius of both eyes show that the differences are not significant after the first night for the pentacurve and the first week for the aspheric. The small numbers in the later group (12) make statistical analysis less robust.

It can be seen that the p value for the anterior surface of the right and left eyes follows a similar pattern to that of the apical radius. As these two parameters are calculated from the same set of data this is to be expected. Table 4.3 shows that the p values from one night are all greater than one. Since a p value of one would indicate a spherical surface the suggestion by Kerns (1978) that any change in refraction would stop once the cornea became spherical did not occur in this study. The p value data for the twelve subjects completing twelve months was again plotted. This also indicated that the cornea became oblate after one night of lens wear.

4.4.2 BOZR and Apical radius and lens sag and corneal sag

Kerns (1978) had noted that the degree of corneal flattening was poorly correlated with the BOZR. Kerns found that once the BOZR was 0.50 dioptres flatter than the corneal apical radius, as measured by keratometry, the variability in the response increased substantially. Brand et al (1983) in the Berkeley Orthokeratology Study looked at the bearing relationship i.e. the BOZR – the minimum of the horizontal and vertical corneal curvatures. The group found no systematic agreement between the two parameters. Coon (1984) found similar results in the study evaluating the Tabb method of orthokeratology lens fitting. Mountford (2004b) found the relationship between the BOZR and corneal power differed according to the lens back surface design. Mountford concluded that if the lens had a direct moulding effect on the corneal epithelium then there should be a 1:1 relationship between the BOZR (D) and the change in the apical corneal power (r_0 (D) – BOZR (D)). The highest correlation he found was $r^2 = 0.80$ ($P< 0.0001$, df 59). This result was for a theoretical lens design with a constant tear layer profile. The result for our design (Fig 4.12) of $R^2 =0.68$ shows that the two parameters are significantly related. The pentacurve lens in the study was designed to create a constant tear layer profile on the eye.

The benefits of fitting rigid contact lenses using the sag method where both apical radius and asphericity are considered have been described by Young (1998). He found that the inclusion of the asphericity value improved the percentage of corneal alignment. Fig 4.13 indicates that for the orthokeratology lens design (aspheric) in this study there was no agreement between the achieved corneal sag and lens sag values. If, as Young (1998), the asphericity value were to be included in the lens design then this lack of correlation is not unsurprising. Orthokeratology lenses are only aligned at the mid peripheral curves and not centrally where they need to produce corneal flattening.

4.4.3 The relationship between corneal power and refractive error in orthokeratology.

Erickson and Thorn (1977) suggested that the refractive error changed at twice the rate of the change in corneal power. Corneal power changes in this study were assessed using keratometry which, as shown in chapter one, has limitations. In a more recent study Chan, Cho and Mountford (Chan et al., 2010) looked at the correlation between the change in apical corneal power (ΔACP) and the change in refractive error (ΔM) in 128 subjects. They also looked at the maximum change in corneal power across the treatment zone. The treatment zone was defined as that area of the cornea which showed no change in power between the initial and two week visit. This zone was found by moving the cursor across the difference map created by the topographer from the results of the measurements taken at the two visits and noting the diameter. They found that the relationship between the change in corneal power and refractive error was $\Delta M = 0.91\Delta ACP + 0.57$. In an earlier study Mountford (1997) had found the relationship between the corneal power and refractive error change to be $\Delta M = 0.92\Delta ACP + 0.15$. The Pearson correlation coefficient for the two studies were $r = 0.78$ and $r = 0.95$ respectively. Chan et al suggest that the small differences between the two studies may result from the different topographers used. Mountford used the EyeSys videokeratoscope in the 1997 study whilst Chan et al used the Medmont topographer in their study.

Applying the same analysis to the data from the pentacurve design (Fig 4.18a) in the current study shows that the relationship is $\Delta M = 1.08\Delta ACP + 0.05$ with a Pearson correlation coefficient of $R^2 = 0.77$. The small difference between the findings for this study and the earlier two may well be due to the use of yet another topographer (Orbscan). The Mountford and Chan et al studies used conventional C4 or C5 design lenses. In the current study the left eye has been fitted with an aspheric back surface design lens. Fig 4.18b shows the change in refractive error and corneal power for this eye. In this case the relationship is defined as $\Delta M = 0.64\Delta ACP + 1.54$ and the Pearson

correlation coefficient is $R^2 = 0.27$. This lower correlation coefficient appears to indicate that the aspheric lens design has a less well defined effect on the corneal power.

The results for refractive error correction in the study group were better than those reported by Rah et al (2002). After one month only 3% of the eyes wearing the pentacurve design were more than 1.00D away from full correction. This was one individual who remained under corrected at this visit. The results for the aspheric design were slightly worse with 18.5% of the subjects being more than one dioptre from the desired correction. In this case three participants were overcorrected by more than one dioptre with only two participants being undercorrected.

4.4.4 Vertical cornea

Scatterplots of the change in the vertical apical radius and p value for the pentacurve and aspheric designs lenses are shown in Fig 4.19 a) and b) and Fig 4.20 a) and b). The vertical apical radii results for both eyes indicate that there is a small degree of flattening in the vertical meridian. The p value indicates that the vertical cornea changes from a prolate ellipse to an oblate ellipse after the first night of lens wear. These data show that the right eye, fitted with the C5 design, appears to show a more regular response to the orthokeratology treatment. The left eye (aspheric) data, both for apical radius and p value, are more unstable in appearance. A search of the literature revealed that no studies looking specifically at the effect of overnight orthokeratology on the vertical cornea had taken place. Kerns (1976a) had looked at the effect of flat fitting lenses on both the horizontal and vertical corneal curvature assessed by keratometry. He found that both conventional and orthokeratology lens wearers showed a flattening of the vertical cornea but this did not reach statistical significance in either case.

Soni et al (2003) had looked at the change in the keratometry of the vertical cornea over the day after one night, one week, one month and three months of lens wear.

They found that the cornea flattened significantly overnight and remained so throughout the day. This change seemed most marked after one night with the effect reducing over the ensuing three months. The difficulty with keratometry assessment of the cornea has been discussed in chapter one. It is possible that the change in the central zone where the orthokeratology lenses exert their maximum action was missed in this method of examination. Hiroaka et al (2005) in their investigation of the change in higher order aberrations as a result of orthokeratology treatment noted that there was a change in direction of the vertical and horizontal coma. They speculated that this occurred as a result of the superior cornea becoming flatter than the inferior. This may be reflected in the present study with the increase in the p value from a prolate to an oblate ellipse. The difference between the central and peripheral apical radius measurements can be used to estimate the rate of flattening of the cornea. In the current study however, the analysis applied to the raw data from the Orbscan involved the combination of the two semi meridians, superior and inferior, onto one axis to eliminate the effect of tilt. This combination should serve to reduce the effect of the difference. It could be argued that the lack of any statistical change in the astigmatic elements of the refractive error over the course of the study indicate that some change must occur in the vertical cornea. If change were to occur only in the horizontal meridian there would be a corresponding increase in the corneal cylinder.

4.4.5 Visual acuity and orthokeratology (VAR) results

Raasch, Bailey and Bullimore (1998) looked at the repeatability of visual acuity measurements. They reported that the test - retest standard deviation is two to three letters (VAR) or 0.04 – 0.06 log units. It could be argued that the apparent difference between the vision and BCVA measures for each eye are simply a factor of test-retest repeatability. Cousens, Rosser, Murdoch and Laidlaw (2004) also looked at test-retest variability in visual acuity measurements. They found that any change in visual acuity must approach 1.84 times the size of the change criterion (1.96 x SD) to show both

95% specificity and sensitivity. They suggest that there are ways to improve the detection of true change in visual acuity measures. These are the use of logMAR charts, scoring by letter and not line, using strict measurement protocols and avoiding uncorrected refractive errors. These recommendations were applicable to the current study where the visual acuity measurements were made using logMAR charts and VAR rating to score individual letters. All data was gathered by one practitioner to an established protocol. Visual acuity data was measured after participants had had any residual error corrected.

The pattern of change in the vision and BCVA mimic that of the change seen in the refractive error. The maximum change in both vision and BCVA occurs by one month with no significant change after this time. Rah et al (2002) repeated visual acuity measures at morning and evening appointments and found that visual acuity was maintained after six hours without lens wear once lenses had been worn for three months. In the current study participants attended only in the morning. A number of subjects reported that they were able to wear their lenses on alternate nights and still maintain vision which they felt to be subjectively acceptable. These individuals were those with lower degrees of myopia on entry ($M \approx -1.50$).

One aspect of this investigation had been to see if an aspheric back design orthokeratology lens, as fitted in the left eye, would provide a more natural corneal surface and therefore improve the acceptance of orthokeratology. A general view of the aspheric design data shows that the lens is inconsistent in its effects on the anterior surface. This lack of predictability of outcome means that this current aspheric lens design is inappropriate despite producing acceptable refractive error correction. The pentacurve fitted in the right eye was more stable in its action.

4.4.6 Treatment zone diameter

Averaging of the results disguises some aspects of the treatment zone diameter and displacement. A visual inspection of the difference maps showed that at one night the zones were less well defined. By one week the zones were well centred and regular in shape. Tahhan et al (2003) used the EyeSys topographer axial difference maps to locate the treatment zone. They comment that the treatment zones in their subjects were stable after the one night assessment. The treatment zones found by Tahhan et al were wider than those found in the current study (≈ 5.5mm). The EyeSys produces corneal topography maps using the placido disc system and as outlined in chapter two this can limit the validity of central corneal measures. The BE lens produced a larger diameter treatment zone than any of the other three lenses they used. They suggested that this difference may occur as a result of the BE method of lens design. The BE lens relies on hydraulic forces in the tears to create the change in corneal shape required to correct the myopia. Tahhan et al found no association between the treatment zone and subjective reports of visual quality or visual acuity.

In their study into the short term effects of orthokeratology Sridharan & Swarbrick (2003) evaluated the treatment zone using the Medmont Corneal topographer. They found that the treatment zone diameter was well established after ten minutes of open eye lens wear (3.86 +/- 0.88mm) and increased up to eight hours of lens wear (5.59 +/- 0.83mm). This latter situation involved closed eye lens wear. Their criterion for the assessment of the treatment zone diameter was the horizontal distance from inner edge to inner edge of the zero dioptre change zone. In their investigation of the posterior corneal changes seen in orthokeratology Owens, Garner, Craig and Gamble (2004) found an increase in the treatment zone diameter between one night (3.32 +/- 1.08mm) and four weeks (4.66 +/- 0.56). In this study which also used the EyeEys Topographer only the vertical extent of the treatment zone was reported. They report difficulty with the assessment of the one night diameter due to a lack of clarity at the edge of the zone. They suggest this is the cause of the large SD at this point.

Lu, Simpson, Sorbara and Fonn (2007) investigated the relationship between the treatment zone diameter and visual, optical and subjective performance in orthokeratology. They found similar results to this study in the treatment zone diameter. They found this was 3.41 +/- 0.09mm after one night increasing to 3.61 +/- 0.07mm after 28 nights of lens wear. Lu et al also evaluated the treatment zone after four and 10 nights and concluded that the treatment zone changed up to 10 nights of lens wear. They also found that the diameter of the treatment zone was associated with the unaided vision, subjective visual quality, residual refractive error and ocular aberrations. Lu et al (2007) point out that the difference between their treatment zone and that of Tahhan et al (2003) could be explained by the use of different corneal topographers. Chan, Cho and Mountford (2010) in their retrospective study evaluated the treatment zone diameter but did not report the diameter found. They made use of the zone to evaluate the apical corneal power change as reported in section 4.4.3.

4.4.7 Physiological response

The results of the corneal stain analysis in this study were commensurate with that reported by other researchers (Cho et al 2003a; Maldonado-Codina et al 2005). Two individuals were withdrawn from the study as a result of corneal staining of greater than Efron Grade 2. The first individual had removed her lenses after the first night of lens wear prior to attending for measurements which was contrary to the advised protocol. This individual was referred to the local hospital due to severe pain and photopohobia which was not responding to ocular lubricants. The subject confirmed that she had failed to mobilise the lens from the cornea prior to attempting to remove the lens. Despite the significant corneal deficit she suffered no long term effects. The second individual was seen as an emergency between the one month and three month visit. He had a corneal stain of Efron grade 2 on presentation. He was treated with ocular lubricants and reviewed regularly throughout the day. The level of corneal stain had improved to Efron Grade 1.5 by the evening appointment. He was advised to continue

to use the ocular lubricants throughout the evening and prior to going to sleep and to cease lens wear until reviewed. The next morning the corneal stain had resolved and no discomfort or visual loss was reported. These two individuals were the only ones who withdrew from the study as a direct result of corneal insult. Maldonado-Codina et al (2005) reported a number of individuals with dimple veil type staining in the reverse curve zone. This stain type it is suggested is due to tiny air bubbles trapped in this area. In this study only one individual was found to have an air bubble in the reverse curve zone and she was not found to have any form of dimple stain. The reduction in the number of individuals with this dimple stain may be due to the insertion procedure used in this study. As mentioned in chapter three, subjects were advised to fill the lens with saline prior to insertion. They then inserted the lens whilst their head was in a horizontal position rather than the normal upright position for lens insertion.

One interesting finding was that a number of individuals were found to have fluorescein pooling in the mid periphery. This was not as a result of staining but appeared to correspond with the reverse curve zone of the lens. This fluorescein pooling would appear to correspond to the effects seen in corneal warpage which has been reported by researchers looking at corneal ectasia such as keratoconus. No grading scale exists to evaluate corneal warpage.

Of the five individuals who were found to have corneal foreign bodies only one reported symptoms. None of the individuals required medical treatment for the foreign bodies. These asymptomatic foreign bodies correspond with the findings of Ng (2008) who reported on an incidence of an asymptomatic foreign body in a child undergoing orthokeratology. As indicated in chapter one this raises concerns about the possible reduction in corneal sensation associated with orthokeratology lens wear. Investigations into whether the effect of orthokeratology has a greater effect on corneal sensation than that seen in long term RGP lens wear would help to address concerns regarding the use of orthokeratology as a means of myopia control in children.

4.5 Conclusion

Alharbi and Swarbrick (2003) suggested that the principal source of change induced by orthokeratology was in the anterior aspects of the cornea. In this chapter the study has shown that both lenses created change in the anterior and posterior radii and their respective p values. Refractive error, vision and visual acuity changes are as expected. An analysis of the action of the two lenses shows that both lenses produced similar effects upon the anterior corneal surface apart from the vertical apical radius and the vertical treatment zone diameter. These results are discussed further in chapter nine.

CHAPTER 5 TOPOGRAPHY – POSTERIOR

5.1 Introduction

Difficulties arise in the evaluation of the posterior corneal surface as it can only be imaged through the anterior cornea. Royston, Dunne & Barnes (1990) calculated the posterior corneal parameters using the Purkinje image method. In this method a series of annular LEDs were projected onto the corneal surface and the resultant images recorded by still photography. The ring of LEDs are seen as Purkinje image I from the anterior corneal surface and Purkinje image II from the posterior corneal surface

Using equation (5.1) the actual posterior corneal radius can be calculated.

$$r_2 = (n / (F_1 + (1/ (r_2' + d')))) - d \qquad (5.1)$$

r_2 = posterior corneal radius

n = corneal refractive index

F_1 = anterior corneal power

r_2' = apparent posterior corneal radius, this is due to refraction at the anterior corneal surface.

d' = apparent corneal thickness

d = actual corneal thickness

This method assumes that the posterior cornea is a spherical surface. The initial study involved the evaluation of 15 eyes. Dunne, Royston and Barnes (1991) repeated the technique to look at the toricity of the posterior corneal surface. Lam and Douthwaite (1997) also evaluated the posterior corneal surface using the Purkinje technique. The results of these three studies are shown in Table 5.1.

Table 5.1 Results from studies using Purkinje method for posterior corneal radius

Study	Sample size	Posterior apical radius
Royston et al (1990)	15 eyes	6.40mm
Dunne et al (1991)	60 eyes	6.78mm (SE 0.03)
Lam & Douthwaite (1997a)	30 eyes	6.64mm (SE 0.05)

Lam and Douthwaite (1997b) in a further study, deduced the posterior corneal radius and asphericity using the anterior corneal topography and the corneal thickness in different regions. They found the horizontal posterior radius to be 6.51mm +/- 0.40 by this method. Dubbelman, Sicam and Van der Heijde (2006) using Scheimpflug imaging of the cornea recorded the shape of the anterior and posterior cornea. In their study of 114 eyes they found the average posterior radius to be 6.53mm +/- 0.25.

As previously indicated Leyland (2004) validated the Orbscan II for the assessment of the posterior corneal surface. He found that the Orbscan II was an appropriate instrument to assess the posterior corneal curvature for intra-ocular lens power calculation prior to cataract surgery. Quisling et al (2006) compared the Orbscan II with the Pentacam in the assessment of posterior corneal curvature in keratoconic eyes. They found the Orbscan overestimated the posterior radius by 0.03mm with 95% confidence limits of -0.46 – 0.40. Cheng, Rao and Lam (2007) evaluated the accuracy of the Orbscan II in a group of 304 eyes undergoing myopic LASIK. They found that whilst there was a statistically significant error in assessing the posterior corneal curvature post LASIK (0.14 +/- 0.13 mm); this result was felt to not be of clinical significance. Cheng, Ho, Lau and Lam (2009) produced a mathematical model to compensate for the error in the posterior curvature measures found by the Orbscan. This was in response to an analysis by Nawa, Masuda, Ueda, Hara et al (2005). Nawa et al (2005) felt that reported ectasia secondary to LASIK, occurred as a result of a change in the magnification of the posterior corneal surface when it was imaged through the flattened anterior surface. They calculated that the posterior image of a cornea which had undergone laser ablation to achieve a 10.00D reduction in refractive power would be smaller by 0.778%. Cheng et al (2009) found that when the correction was applied the apparent change in the pre and postoperative dimensions of the posterior surface was no longer statistically significant. They suggest that their model should be used with caution since it assumes that the ablation zone is accurately centred with the pre and postoperative corneal apex.

5.1 1 The effect of orthokeratology on the posterior cornea

Owens et al (2004) investigated the effects of overnight orthokeratology on the posterior corneal surface. In their study they evaluated posterior corneal change in 19 subjects over a period of one month. Measurements were taken at one night, one, two and four weeks of overnight wear. Anterior topography measurements were made using the EyeSys corneal topographer and corneal thickness by ultrasound pachymetry and the posterior surface by the Purkinje method described previously. Their results for the posterior corneal surface were 6.38mm +/- 0.26

Owens et al found the central and paracentral anterior surface changes followed the expected pattern, with the flattening of the anterior surface (5mm diameter) reaching statistical significance at all visits after one night. The posterior corneal surface was also found to show flattening but this reached statistical significance only at the one week visit. This posterior flattening reduced with prolonged lens wear. A comparison of the changes in the two surfaces with those of the myopia reduction achieved revealed that the anterior surface changes were the major source of refractive modification. The changes in the posterior cornea were small in comparison to those of the anterior surface. This is consistent with the contribution of the posterior surface in the untreated cornea where the posterior corneal power contributes approximately 12% of the total power. Owens et al postulate that the initial changes in the cornea occur as a result of corneal bending and that the later changes occur as a result of more extensive tissue redistribution. Swarbrick et al (1998) in their study suggested that the posterior corneal surface was unaffected by the wearing of orthokeratology lenses.

Stillitano, Chalita, Schor, Maidana et al (2007) followed fourteen subjects (26 eyes) for eight nights of orthokeratology lens wear. Using the Orbscan IIz they looked at the change in the highest and lowest elevation points for the Posterior Float map. In contrast to Owens et al (2004) they found no statistically significant change in the posterior corneal surface by this method. Tsukiyama, Miyamoto, Higaki, Fukuda and Shimomura (2008) followed nine subjects (18 eyes) for 53 weeks of orthokeratology

lens wear. Using the Pentacam they evaluated the change in the anterior and posterior corneal radii. They found that whilst there was a statistically significant change in the anterior corneal radius no such change was seen in the posterior radius.

Chen, Lam and Cho (2010) evaluated the change and recovery in the posterior corneal surface after six months of orthokeratology lens wear. Twenty eight individuals were successfully fitted with orthokeratology lenses. The anterior and posterior corneal topographies were captured after one night, one week, one, two, three and six months of lens wear. Chen et al found that after one night of lens wear the posterior corneal radius showed statistically significant steepening. This change was not seen at any of the other visits. This study also looked at the diurnal change in the anterior and posterior cornea once subjects were established wearers i.e. after six months of overnight wear. They found that the posterior corneal radius did flatten significantly during the day i.e. between two - eight hours of lens removal when compared to the results on immediate lens removal. Individuals involved in this study ceased lens wear after the six month visit. Recovery of the posterior corneal surface was monitored after one week, two weeks, one month and two months of lens wear cessation. Chen et al found that there was no statistically significant change over this two month period.

Queirós, Villa-Collar, Gutiérrez, Jorge et al (2011) compared the changes in the anterior and posterior corneal elevation following standard and customised LASIK and orthokeratology. In order to examine any differences which could occur as a result of the three treatment modalities the refractive error range chosen was that normally used in orthokeratology (-2.25 to -5.00D with astigmatism < 1.00D). Elevation measurements were made at the centre and at 1mm intervals out to 4mm on both the nasal and temporal sides. The results from the right eyes of sixty one patients, who were successfully treated by one of the three methods, were reported. Queirós et al (2011) found, that for all three modalities, there was no statistically significant change in the posterior elevation at any of the measured points. These readings were taken at the three month post treatment assessment visit.

Lam and Douthwaite (1997) looked at the posterior corneal asphericity along the horizontal meridian and found a p value of 0.34 +/- 0.38; participants in this study were students in Hong Kong. Dubbelman, Sicam, and Van der Heijde (2006) found that the posterior corneal asphericity varied between the two meridians. They also found that the asphericity of the posterior surface increased with age. They found that for subjects aged between 18 and 65 the cornea shows a gradual increase in asphericity. The posterior corneal asphericity in young people was found to be close to p = 1.0. In older subjects the asphericity tends towards p = 0.5. The majority of participants involved in the current study would fall in the younger category of this study and would be expected to have a p value closer to 1.0.

5.2 Posterior Surface

5.2.1 Method

The apical radii and p values for the posterior corneal surface were calculated following the same procedure as those for the anterior surface indicated in chapter two. Results are shown for the apical radius and p value of the posterior cornea for the twelve months of the study in Table 5.2.

5.2.2 Results

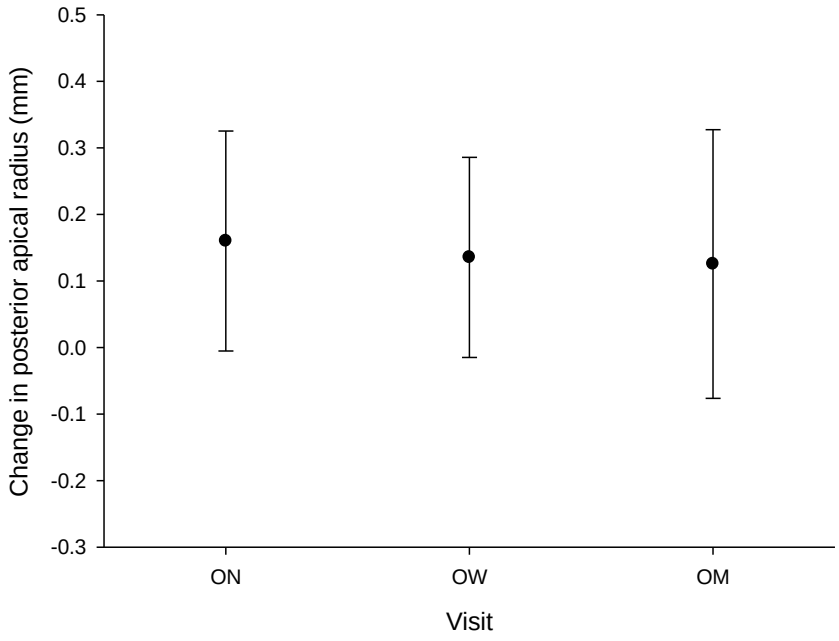
Table 5.2 Posterior apical radius (r0) (mm) and p value for the pentacurve and aspheric lens designs for the twelve months of the study

	Number of subjects	Pentacurve		Aspheric	
Visit		Apical radius	p value	Apical radius	p value
Initial	36	6.40 +/- 0.26	0.74 +/- 0.30	6.40 +/- 0.28	0.68 +/- 0.33
One night	36	6.24 +/- 0.26	0.45 +/- 0.44	6.19 +/- 0.27	0.35 +/- 0.41
One week	30	6.27 +/- 0.29	0.51 +/- 0.39	6.24 +/- 0.31	0.45 +/- 0.41
One month	28	6.29 +/- 0.30	0.60 +/- 0.41	6.30 +/- 0.30	0.65 +/- 0.55
One quarter	17	6.26 +/- 0.37	0.42 +/- 0.40	6.14 +/- 0.28	0.20 +/- 0.36
Six months	13	6.32 +/- 0.37	0.71 +/- 0.39	6.32 +/- 0.31	0.61 +/- 0.45
One year	12	6.33 +/- 0.29	0.66 +/- 0.25	6.26 +/- 0.52	0.52 +/- 0.30

A repeated measures ANOVA for the pentacurve posterior apical radius shows there is no statistically significant change over the course of the study ($F_{(1.04, 10.36)} = 0.885$ $p = 0.372$). Bonferroni post hoc tests show that the pentacurve design effect on the posterior apical radius was significantly different at one week from the initial visit but not at any other time. For the aspheric design, the results show that the effect on the posterior apical radius for the repeated measures ANOVA was ($F_{(2.94, 34.97)} = 0.842$ $p=0.388$) again showing no statistically significant change over time. For the aspheric design the Bonferroni post hoc tests showed that the results were significantly different

at one night from the initial but not at any other visit. A two way repeated measures ANOVA confirmed that there was no statistically significant difference between the effects of the two lenses ($F_{(1,10)} = 3.092$, $p = 0.109$), the Greenhouse Geisser correction was applied to this result. For both posterior p values the repeated measures ANOVA were pentacurve ($F_{(2.52, 25.16)} = 1.019$ $p = 0.390$) and aspheric ($F_{(1.74, 17.37)} = 2.04$ $p = 0.164$). The Bonferroni post hoc tests in both cases showed no significant change at any visit. The Greenhouse Geisser correction was applied in all cases. A two way repeated measures ANOVA did show a statistically significant difference in effect between the two lenses ($F_{(1,10)} = 7.537$, $p = 0.021$). Table 5.2 shows that the aspheric lens design produces a more prolate profile to the posterior corneal surface.

a) pentacurve



b) aspheric

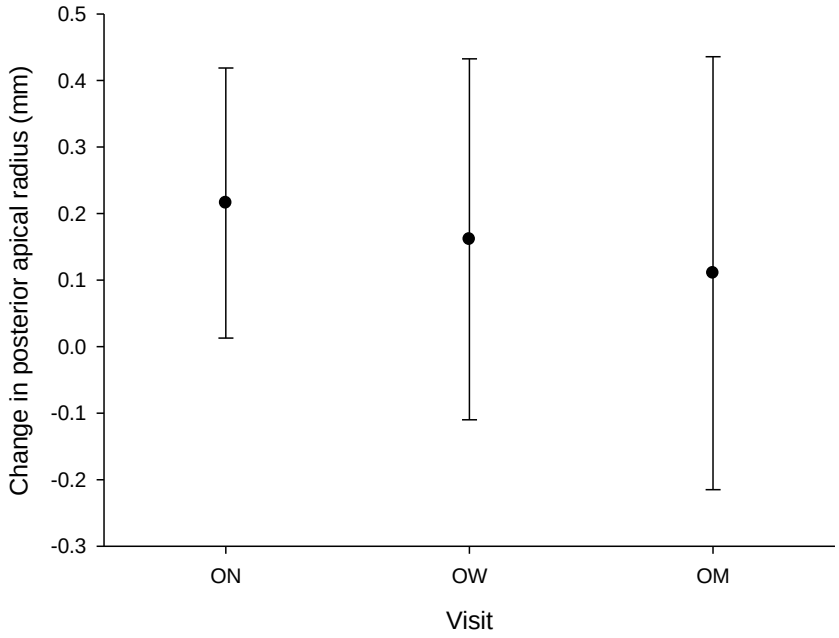
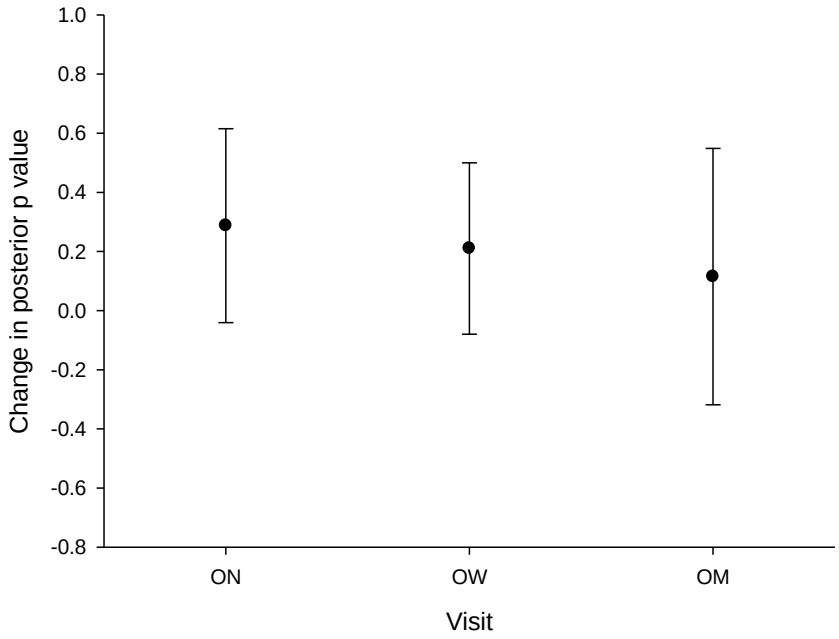


Fig 5.1 a) and b) show the posterior apical radius (mm) for the pentacurve and aspheric designs.

a) pentacurve



b) aspheric

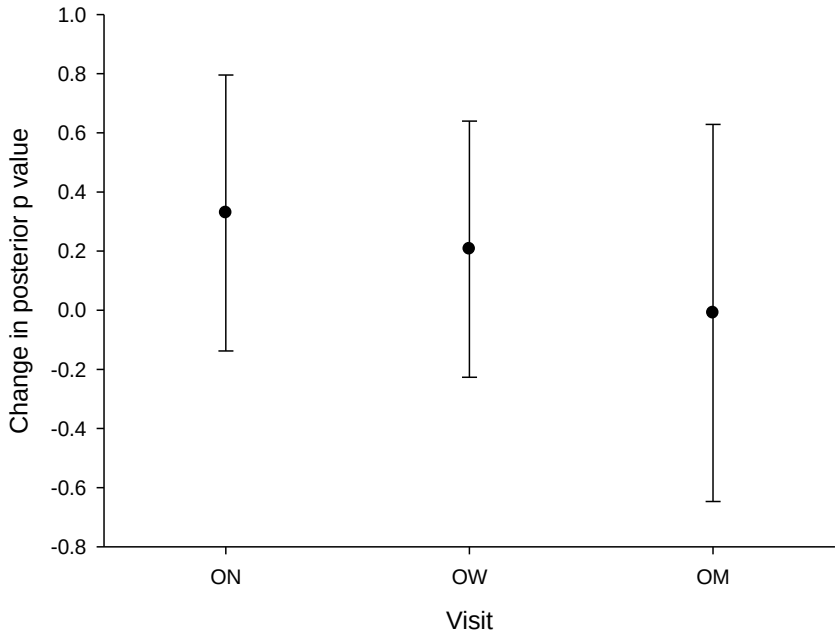


Fig 5.2 a) and b) show the posterior p value for the pentacurve and aspheric designs.

5.3 Discussion

Results for the present study for the pentacurve design revealed that the change in the posterior surface did not reach statistical significance until one week of lens wear. This agrees with the findings of Owens et al (2004). For the aspheric design the results agree with the findings of Chen et al (2010) that the cornea undergoes statistically significant steepening after one night of lens wear. The change in the pentacurve design posterior apical radius returns to its original values over the course of twelve months (Fig 5.1 a). The results for the aspheric design are more variable (Fig 5.1 b). A significant steepening is seen initially followed by a return towards the original measure at the one month visit. The results at three months are not statistically significantly different from those at one month.

An examination of a number of the participant's individual posterior p values revealed that they were < 0. Measures of this kind would indicate that the posterior corneal surface had become hyperbolic in curvature. This extreme curvature of the posterior corneal surface, which would not normally be seen, would lead to an increase in the aberrations associated with the posterior surface. The effect of orthokeratology on the ocular aberrations is discussed in chapter eight. The findings in chapter two regarding the repeatability of the posterior surface analysis from the Orbscan mean that the results require a degree of caution to be applied when conclusions are drawn. A further study using an instrument which is able to directly analyse the posterior surface would allow for a more definitive answer to the question about the effect of orthokeratology on the posterior corneal surface. A more definitive answer here would assist in the decision of whether the two lens designs did produce a different effect on the posterior surface. At this time the apparent difference may be artefactual.

CHAPTER 6 CORNEAL THICKNESS RESPONSE

6.1 Introduction

In this chapter the effect of orthokeratology on the corneal thickness will be investigated.

6.1.1 Effect of orthokeratology on corneal thickness

In chapter one it was noted that Swarbrick et al (1998) were the first group to look specifically at corneal thickness to try and explain the effects of orthokeratology on the cornea. Binder et al (1980) and Polse et al (1983b) had previously reported no statistically significant change in corneal thickness. Coon et al (1984) had reported a statistically significant change in central corneal thickness (0.02mm) in the orthokeratology groups. They also noted a peripheral thickening in both the control and orthokeratology group. The lens material being used in the Coon et al (1984) study was PMMA. Since this material is impermeable to oxygen then some corneal oedema and therefore an associated increase in corneal thickness could have been anticipated (Holden and Mertz 1984).

Swarbrick et al (1998) followed six myopes wearing reverse geometry lenses for 28 days. This study involved open eye and not overnight lens wear. Assessment of the total corneal thickness showed statistically significant thickening of the mid peripheral cornea (2.5mm from the corneal apex) by day 14. The group noted central corneal thinning which did not reach statistical significance throughout the study. Swarbrick et al (1998) also evaluated changes in corneal epithelial thickness. They found that the central corneal epithelium (1mm either side of the corneal apex) thinned by up to 10% at the end of the study. Swarbrick et al (1998) concluded that the majority of the central thinning was epithelial in origin whilst the mid peripheral thickening was stromal in origin.

Nicholls et al (2000) in their study measured corneal thickness using the Orbscan I. This instrument uses only the slit scanning facility and not the placido disc facility of the

Orbscan II. Corneal thickness measurements were taken at 1, 7, 14, 30 and 60 days of overnight lens wear. Nicholls et al (2000) found that the reduction in central corneal thickness reached statistical significance by day 7 of the trial. Measurements of the peripheral cornea (3mm from the apex) in the superior, inferior, temporal and nasal areas showed no statistically significant change in thickness at any point in the study.

Alharbi and Swarbrick (2003) looked at the effects of three months of overnight orthokeratology wear on corneal thickness in eighteen young myopes. Total corneal and stromal thickness was measured using a Holden-Payor optical pachometer. Epithelial thickness was calculated by subtracting the stromal thickness from the total. Measurements were made across the horizontal meridian at 0.25, 3.50 and 5.00mm nasal and 3.25 and 4.75mm temporal of the centre. As a control measure ten other young myopes were fitted with conventional RGP lenses to be worn overnight. The lenses for both groups were made of Boston XO material. Thickness measurements were taken on days 1, 4,10,30,60 and 90 for the orthokeratology group and at days 1,4,10 and 30 for the control group. Measurements for both groups were made in the morning immediately after lens removal and again after eight to ten hours of no lens wear. Only the evening data was reported. Alharbi et al reported that the morning results mirrored or slightly exceeded the evening results.

Alharbi and Swarbrick (2003) also found the orthokeratology group showed statistically significant changes in the central corneal epithelial thickness as early as day one of the study. The total central corneal thickness showed a similar response. The central epithelial and total corneal thinning was stable by day ten with no statistically significant change after this time. Central stromal thickness showed no statistically significant change throughout the study. Evaluation of the nasal and temporal mid peripheral corneal thickness showed an increase which reached significant levels by day four and stabilised by day ten. In contrast to the central thinning, which was epithelial in origin, the mid peripheral thickness changes were situated in the stroma. No statistically significant change was found in any of the parameters for the control group either

centrally or peripherally. Neither group showed any statistically significant change for epithelial, stromal, or total thickness measures in the peripheral cornea.

Soni, Nguyen and Bonanno (2003) used the Orbscan to measure corneal thickness in their study. As previously noted Marsich and Bullimore (2000) had found the Orbscan to be the most repeatable instrument when compared to optical or ultrasound pachymetry. Soni et al found no significant change in central corneal thickness using the Orbscan over the three months of their study. They also looked at epithelial thickness using confocal microscopy and found that the epithelium was significantly thinned after three months of lens wear.

6.1.2 Central Corneal Thickness measures by Orbscan

The effect of Orthokeratology on corneal thickness has been investigated by a number of authors (Swarbrick et al 1998, Nichols et al 2000, Alharbi & Swarbrick 2003, Haque et al 2005). We chose to assess the effects of the orthokeratology lenses, used in this study, with the Orbscan IIz instrument. Yaylali, Kaufman and Thompson (1997) evaluated the Orbscan I against ultrasound pachymetry; whilst Marsich and Bullimore (2000) reported on the repeatability of pachymetry using Orbscan I when compared to that of both optical and ultrasonic pachymetry. Both groups found that the Orbscan I gave repeatable measures of corneal thickness. In fact, Marisch and Bullimore (2000) pointed out that in their results, the Orbscan I gave the most repeatable measures. In both studies the Orbscan I results varied significantly from that of both optical and ultrasonic pachymetry and as such, Orbscan values are not interchangeable with other forms of pachymetry. Liu, Huang and Pflugfelder (1999) carried out an evaluation of corneal thickness in normal eyes using the Orbscan I. They concluded that it was a useful tool for evaluating corneal thickness. Modifications were made to the Orbscan I acquisition process (Orbscan IIz) with the addition of placido disc imaging to the slit scanning mechanism. The combination of these two methods sought to improve the instruments analysis, particularly of corneal topography.

Jonuscheit and Doughty (2009) reported on their study into the repeatability of the corneal thickness measures using the Orbscan IIz. They looked at the repeatability of corneal thickness measures on both right and left eyes. They used the central point corneal thickness (CPCT) value in their assessment. The CPCT was defined as, the thickness at the intersection of the horizontal and vertical meridians of the pachymetry data map produced by the Orbscan software. Both spectacle and contact lens wearers were included in the study; lens wearers removed their lenses just prior to the measurements being taken. They compared the difference in the mean between the first and third measures, finding the difference in both right and left eyes to be ≤ 0.002mm. The SD of the third and first measures was 0.009 giving limits of agreement (LoA) for the third and first measures of +/- 0.018mm. In order to assess the repeatability of their measures they used the Coefficient of Variation (COV) to indicate the relative dispersion of the results. They found their COV results to be close to 1% with no significant difference between the right and left eyes. The COV may also be used to indicate the measurement error of an instrument.

In contrast to Jonuscheit and Doughty (2009) Martin, De Juan, Rodriguez, Fonseca et al (2009) looked at corneal thickness change induced by extended wear soft contact lenses using both ultrasound pachymetry and Orbscan II. Corneal thickness was measured in four peripheral locations (superior, inferior, temporal and nasal) within 2.5mm of the nearest limbus. The central cornea was also measured. Measurements were made one week before lens wear commenced and after one week of lens wear. They found that the Orbscan was more repeatable than ultrasound at all five locations both with and without contact lens wear. Lam and Chan (2003) investigated the corneal thickness at three reference points selected by the Orbscan IIz software. These were the fixation point, the corneal apex and the thinnest point of the cornea. Although there were differences in measures between the three points these were not of statistical significance. Whilst this lack of statistical significance may be the case, they concluded that studies should use the same point for all participants in the group.

6.2 Repeatability of the initial corneal thickness measures

6.2.1 Method and Data analysis

The corneal thicknesses of 72 eyes (36 individuals) were evaluated using the Orbscan IIz. This was the baseline data for the initial recruits to the orthokeratology study. Each individual had three independent measures of the corneal thickness of both the right and left eyes taken. As with the study of Jonuscheit and Doughty (2009), both spectacle and contact lens wearers were included in the study. Contact lens wearers were asked to leave their lenses out for one week prior to the measurements being taken. The values used for the corneal thickness were those of the central cornea as designated by the Orbscan IIz. Since Lam and Chan (2003) found no statistically significant difference in the three corneal measures it was considered appropriate to use this measure to evaluate repeatability in our subjects.

The repeatability of the central corneal thickness data from the study were compared using the techniques described by Jonuscheit and Doughty (2009). Firstly the mean and standard deviation of the group mean for the three measures was calculated. The limits of agreement were calculated (+/- 1.96 x SD of the difference) between the first and third measurements and the coefficient of variation i.e. the (standard deviation/average) x 100%. The results for the three measures for the right and left eyes are summarised in Table 6.2

6.3 Change in corneal thickness at each visit for the twelve months of the study

6.3.1 Method and Data analysis

All participants had their corneal thickness measured using the Orbscan at their initial assessment visit. After completing the successful fitting of orthokeratology lenses the corneal thickness was measured at each subsequent visit using the Orbscan. Each individual had three measures of the corneal thickness taken following the procedure outlined in chapter three. Using the Orbscan software it is possible to select a numeric overlay for the pachymetry map display. This numeric overlay allows the thickness measures to be retrieved at 0.5mm intervals across a given meridian. The horizontal meridian (180^0) was selected in order to maximise the available data. The three results were combined to produce a mean of the three measurements for each visit.

The change in the corneal thickness from the initial value was calculated for each 0.5mm point across the horizontal meridian. The standard error for each of the measures was calculated. The standard error rather than the standard deviation is used in this case because each of the values is a mean rather than a single measure. The graphical displays show the limits of two standard errors. This is consistent with the use of two standard deviations to encompass 95% of the agreement of measures. Values which fall outside the two standard errors indicate true change.

6.4 Results

6.4.1 Repeatability of the initial corneal thickness measures

Table 6.1 Mean (+/- SD) of central corneal thickness (mm) for both right and left eyes

	Number of subjects	Measure 1	Measure 2	Measure 3	Mean of three measures	Difference in measure 3 - 1
Right	36	0.574 +/- 0.036	0.575 +/- 0.036	0.575 +/- 0.035	0.575 +/- 0.036	0.001 +/- 0.005
Left	36	0.576 +/- 0.039	0.577 +/- 0.039	0.576 +/- 0.038	0.577 +/- 0.038	0.000 +/- 0.005

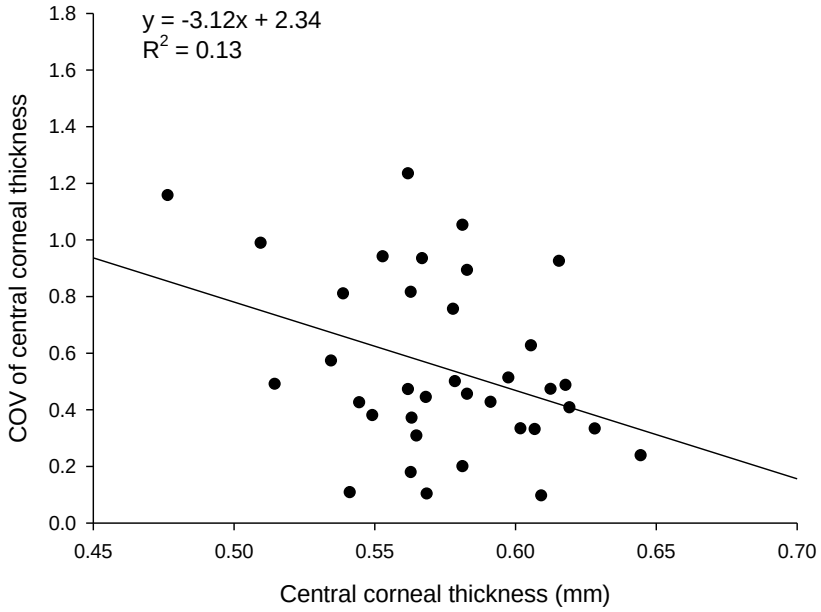
These results give LoA for the both right and left eyes of +/- 0.010. The right corneal thickness falls between 0.565 and 0.585mm and the left between 0.567 and 0.587mm. The COV results for the two eyes are shown below. Table 6.2 and Fig 6.1a and b

Table 6.2 COV mean and range for right and left eyes

COV	Number of subjects	Mean	Minimum	Maximum
Right	36	0.548 +/- 0.309	0.095	1.233
Left	36	0.539 +/- 0.358	0.000	1.728

The coefficient of variation shows that the two eyes show a similar degree of variation of approximately 0.5%.

a) right



b) left

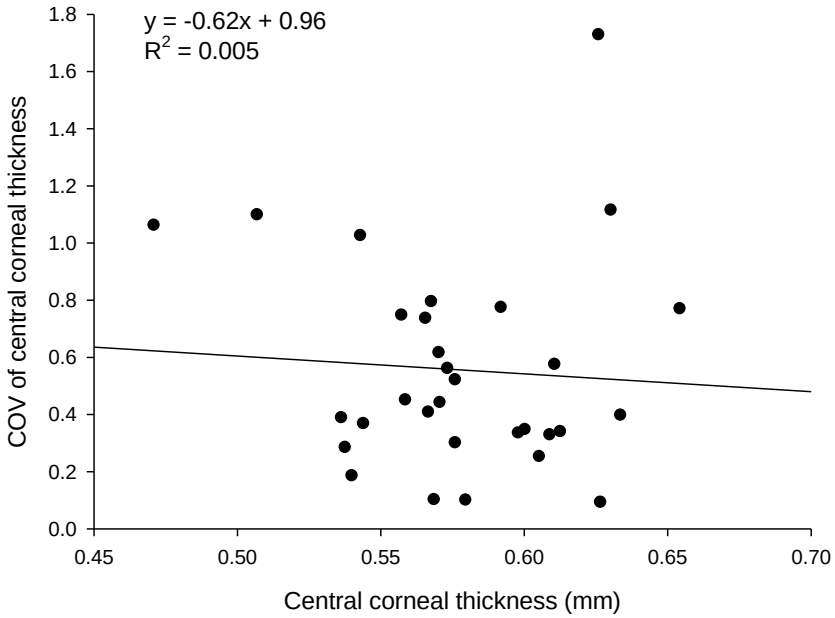


Fig 6.1 a) COV results for the Right eyes and b) COV results for the Left eyes.

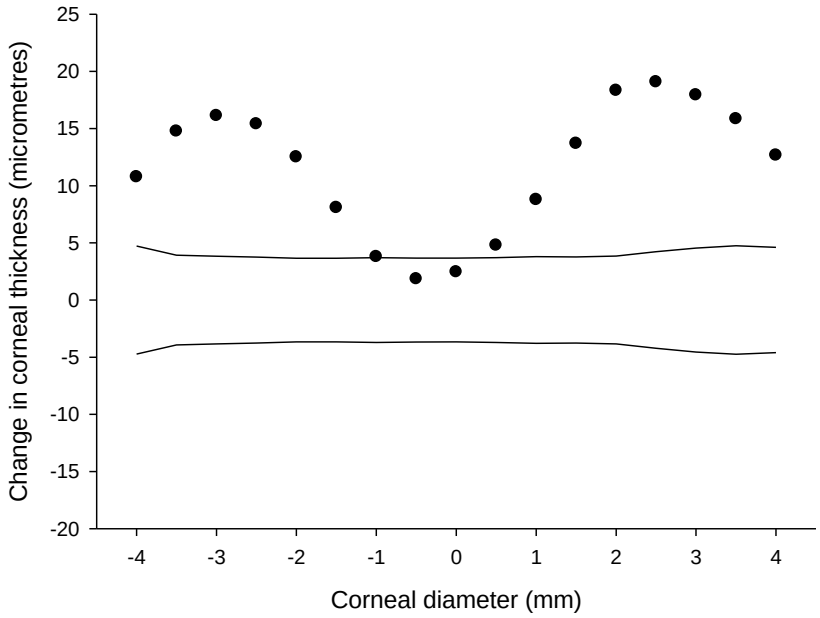
The linear regression lines show that there is a slight negative correlation between central corneal thickness and COV, more for the right eye than the left.

6.4.2 Change in corneal thickness at each visit for the twelve months of the study

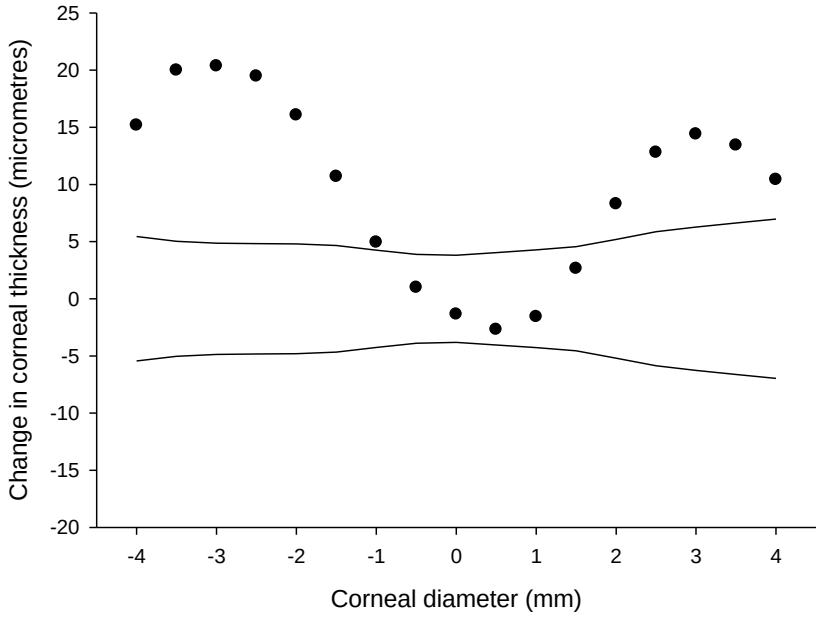
The scatterplots of the pentacurve and aspheric design effects on corneal thickness at one night are shown in Fig 6.2. This shows that the change in the central corneal thickness did not exceed any measurement error for either lens design. The scatterplot for the aspheric design shows that the thinnest point of the cornea is displaced temporally. The change in the mid peripheral thickness in the pentacurve design shows that both the nasal and temporal mid peripheral measures are thickened. For the aspheric design only the nasal thickness showed a significant increase. The group results show a similar appearance in the corneal thickness profile at the one week visit. The aspheric lens design still shows an asymmetric thickening with only the nasal mid periphery showing a significant change.

At the one month visit the pentacurve design still shows a small degree of mid peripheral thickening with no significant change in the central cornea. The aspheric design still has a significant nasal mid peripheral thickening and for the first time the central thickness is just outside the standard error measure. This is the first time the central thickness has shown significant thinning. For the last three visits only twelve subjects remained in the study and the standard error measures become very large in comparison to the thickness change measures. The general corneal profile continues to follow the expected pattern of central thinning and mid peripheral thickening.

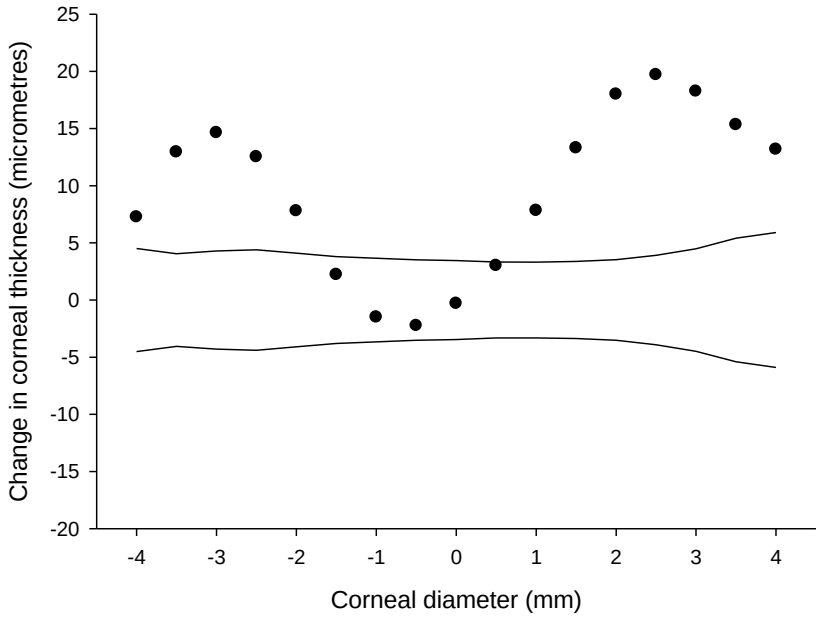
One Night (36 subjects)
a) pentacurve



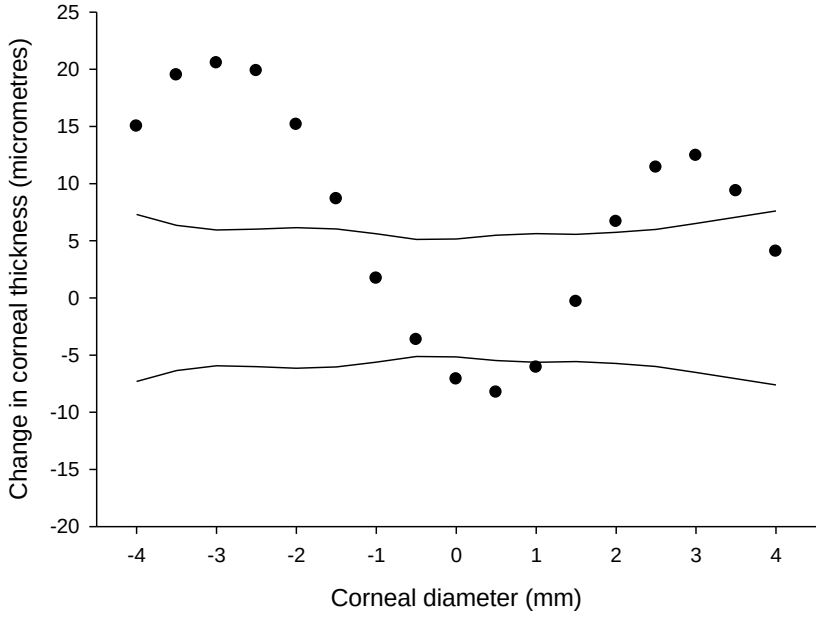
b) aspheric



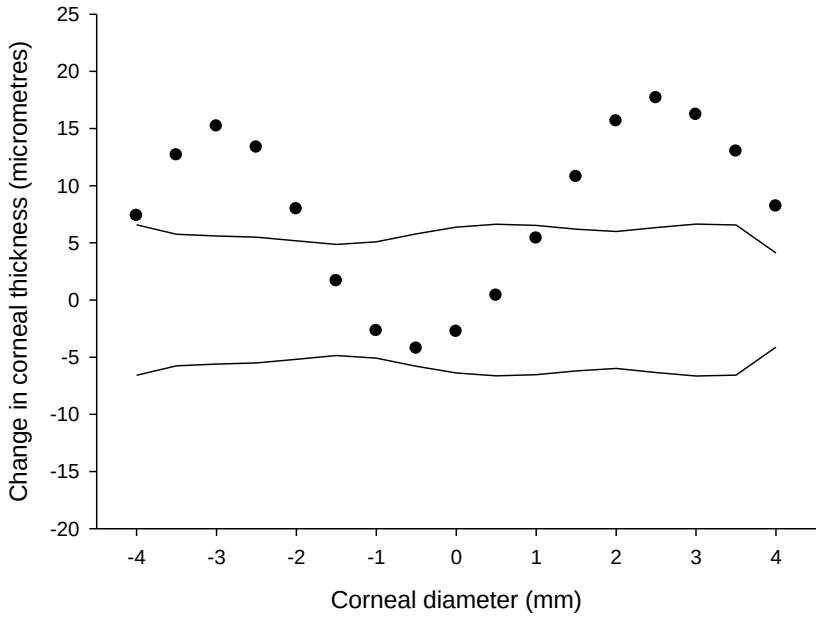
One week (30 subjects)
a) pentacurve



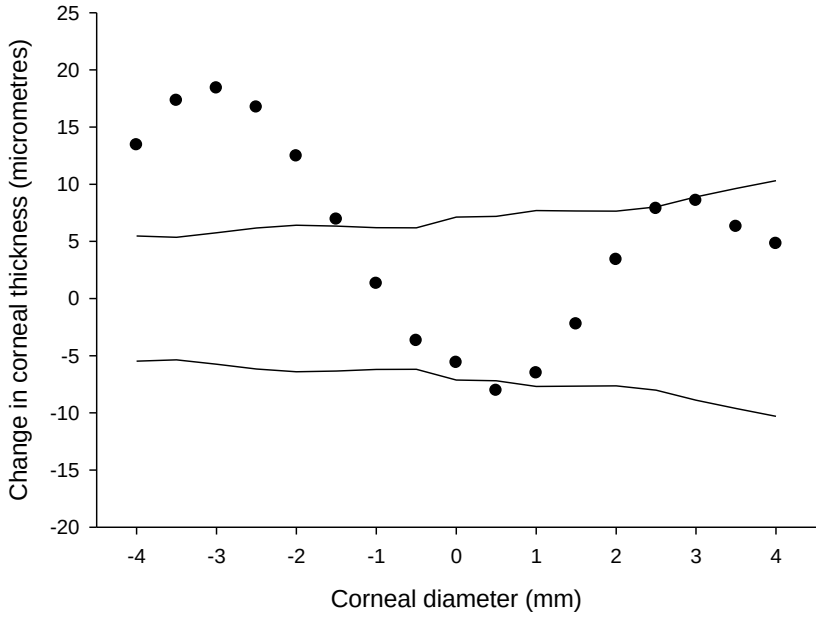
b) aspheric



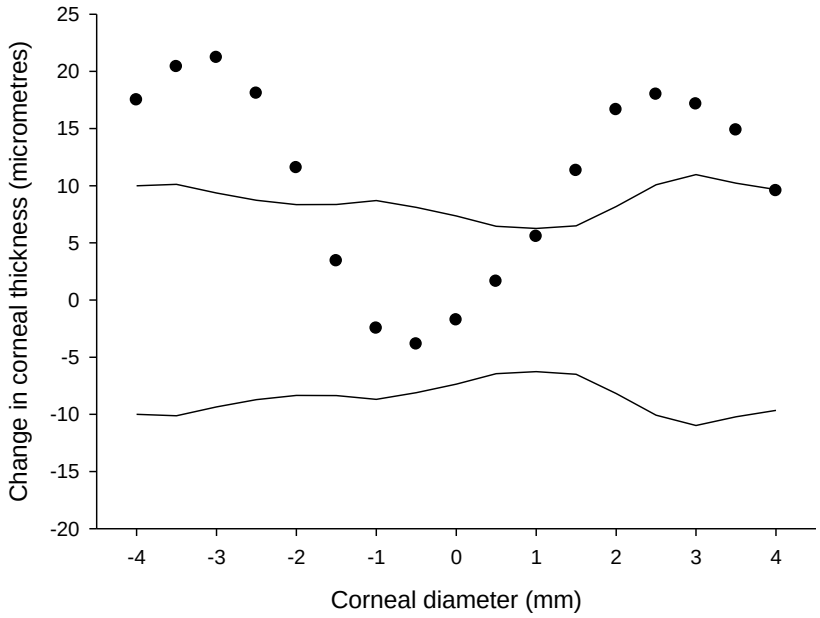
One Month (28 subjects)
a) pentacurve



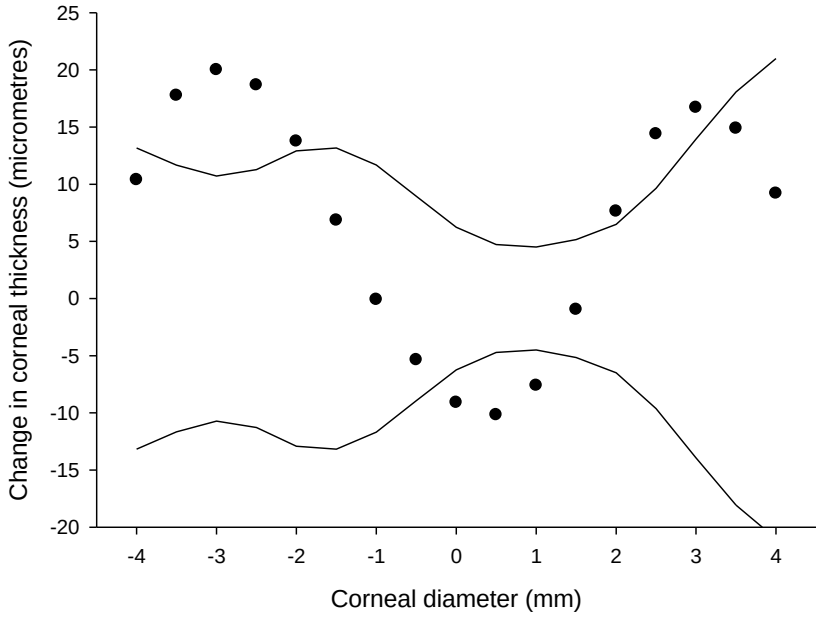
b) aspheric



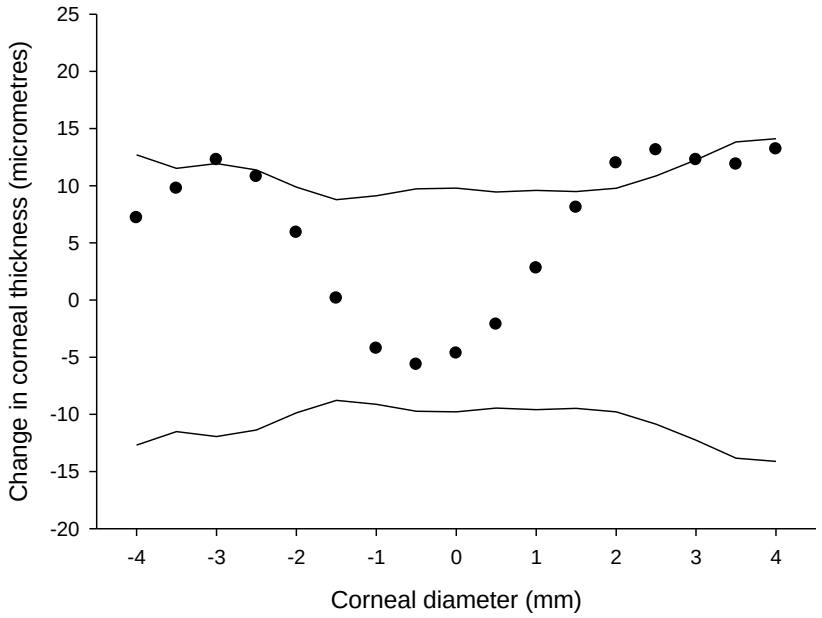
Three Months (17 subjects)
a) pentacurve



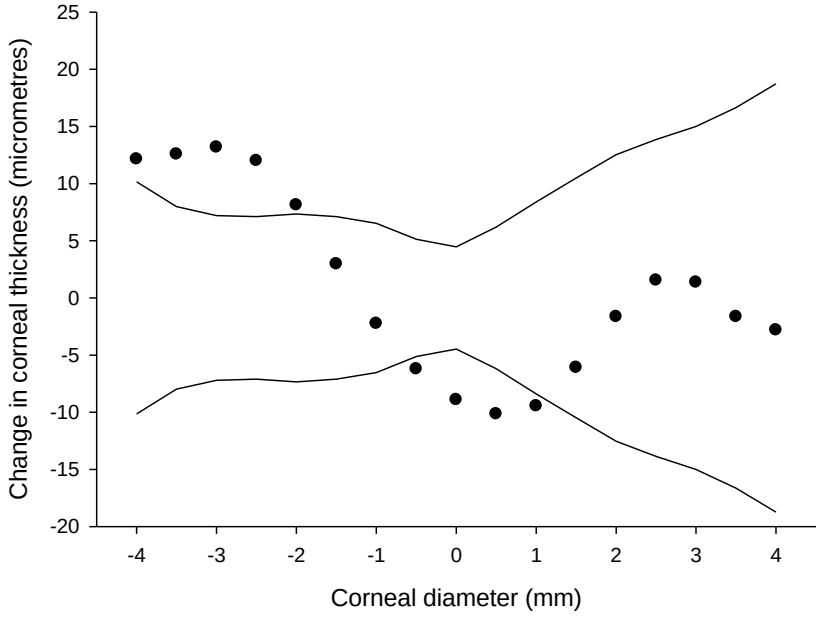
b) aspheric



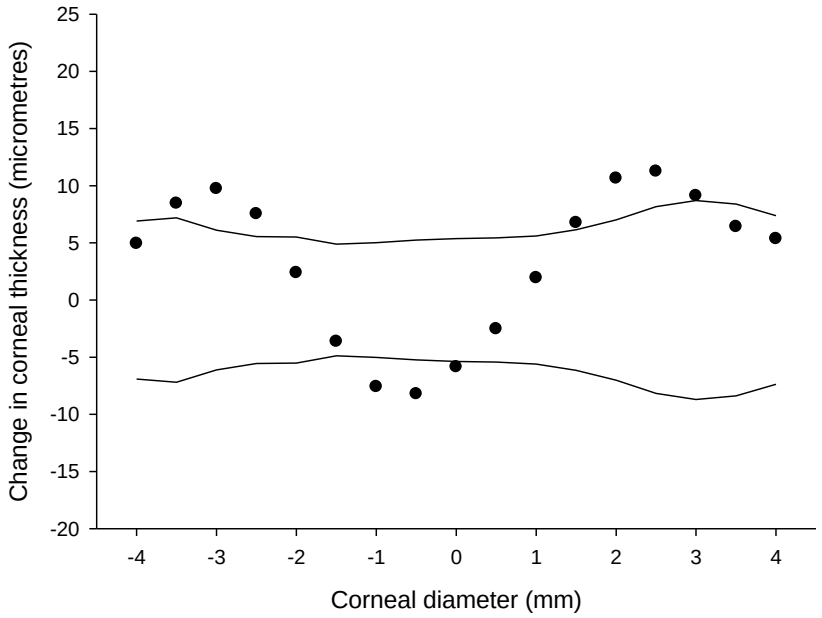
Six Months (13 subjects)
a) pentacurve



b) aspheric



Twelve months (12 subjects)
a) pentacurve



b) aspheric

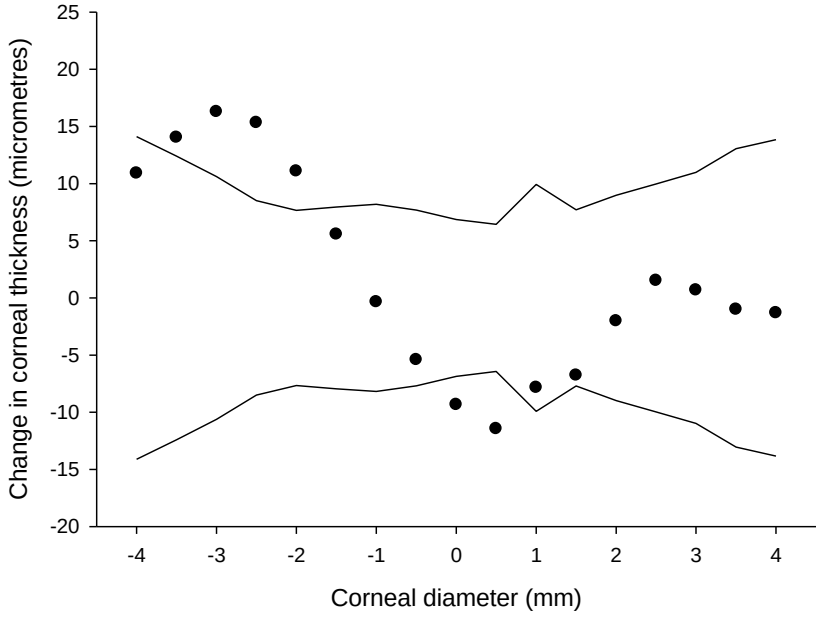


Fig 6.2 Group mean change in corneal thickness against diameter for the 12 months of the study.

6.4 Discussion

The coefficient of variation results for the Orbscan (Table 6.2) show that the central corneal thickness measurements reach acceptable repeatability. The small negative correlation between the coefficient of variation and central corneal thickness is in agreement with the findings of Jonuscheit and Doughty (2009). This slight correlation suggests that the thicker corneas are more repeatable in their measurements. The small measurement error shown between the three measurements (Table 6.1) indicates that the Orbscan is a repeatable instrument for the assessment of corneal thickness and that the use of the mean of three measurements is valid. This repeatability agrees with the findings of Yaylali et al (1997), Van de Pol and Salmon (2001), Cho et al (2002b), Fam et al (2005) and Jonuscheit and Doughty (2007).

The present study results of corneal thickness change agree with the findings of Swarbrick et al (1998) in which they found an increase in the total corneal thickness in the mid periphery. This change was noted after day fourteen. We found that even at one night of lens wear the total thickness change for the pentacurve design followed this profile and continued to do so for the twelve months of the study. The mid periphery of the aspheric design was less predictable in its effect on the corneal thickness with a significant effect on the nasal mid periphery and not the temporal. This effect could possibly have occurred with a lens which showed a significant degree of decentration. Fluorescein evaluation of the fit of the lenses carried out at each visit did not indicate that this was the case. Individuals achieved the expected degree of refractive correction from the aspheric lens and acceptable levels of visual acuity. As indicated in chapter four there was a small but statistically significant difference in the achieved vision when the two VAR results were compared at the twelve month visit. In a later study Alharbi and Swarbrick (2003) showed that the changes in corneal thickness occurred within two different layers of the cornea. In the central cornea the thinning occurred in the corneal epithelium whilst the mid peripheral thickening was

associated with the corneal stroma. In this investigation Alharbi and Swarbrick used a modified pachometer which allowed the differentiation of the corneal layers. This facility is not available in the Orbscan.

In 2004 Haque, Fonn, Simpson and Jones evaluated the change in the epithelial and total corneal thickness using optical coherence tomography. They evaluated a 10mm chord diameter across the horizontal cornea at nine points, central, 0.8, 1.6, 2.7 and 3.6mm to either side of the centre. Individuals had their corneal thickness assessed immediately on waking and throughout the day, at 1, 3, 7, and 14 hours after lens removal and at days 4, 10 and 28 of orthokeratology lens wear. Corneal thickness was also measured three days after lens wear had ceased. Haque et al found that the cornea showed maximal swelling in the first hour of the morning after the first night of lens wear. This swelling affected both the central and paracentral areas and reduced over the day. One concern in this study is their location of the paracentral position; they used the mean thickness from the 0.8 and 1.6mm zones to either side of fixation. In the current study we have used a point at 3mm to either side of fixation. This point coincides with the beginning of the transition from the central flattened curve to the reverse curve in the pentacurve and similarly in the aspheric design. This was more in agreement with the Alharbi and Swarbrick (2003) study who used a point at 3.5mm to either side of the central cornea. Haque et al report central and paracentral corneal swelling immediately on lens removal which had returned to baseline by three hours after lens removal. In their evaluation of the epithelial responses Haque et al found that the central epithelium showed thinning immediately on lens removal which was maintained through the day (14 hours open eye). In contrast the mid peripheral increase resolved over the day. This pattern continued throughout the course of the study. Haque et al also noted that the degree of total corneal swelling both centrally and paracentrally decreased over the duration of lens wear. They suggest that this may indicate an adaptive process to the cornea's response. They also found the corneal

thickness recovered to baseline after 72 hours of no lens wear confirming the reversibility of the effect of orthokeratology on the corneal thickness.

In a case study Reinstein, Gobbe, Archer, Couch et al (2009) used high frequency digital ultrasound to scan a 10mm diameter of the cornea. The individual was assessed after 30 days of orthokeratology lens wear. They found a 2mm central zone of thinning in the right eye and a 1mm zone of thinning in the left eye. The right eye showed no significant paracentral thickening whilst the left showed up to 7µm of thickening. The group suggest that this occurred as a result of the patient wearing two different lens designs. In the Reinstein et al case both lenses are of a multicurve design rather than an aspheric and a multicurve in the current study.

In a recent study Lian, Shen, Jiang, and Mao et al (2013) used ultra high resolution optical coherence tomography to look at the corneal epithelium and Bowman's layer profiles after orthokeratology. This group looked at both the horizontal and vertical profiles of the cornea. Previous groups have used only the horizontal profile in their analyses. In the current study, use of the vertical profiles provided by the Orbscan can be limited by the availability of the data. As Cairns (2005) reported care should be taken in using images with missing data. Vertical data collection can be difficult even when the subject is asked to stare widely during the image capture. Lian et al (2012) took the OCT measurements two to four hours after the orthokeratology lenses had been removed. This allowed any initial corneal oedema after the overnight wear of lenses to subside. Epithelial measurements were taken after one, seven and 30 days of lens wear.

For the vertical meridian Lian et al found that statistically significant central thinning occurred up to the seventh day of lens wear. At this time the central thinning had reached 14.3% of the baseline measure. A comparison of the superior and inferior meridians showed that there was no mid peripheral thickening. The group actually noted a thinning of the superior corneal epithelium. For the horizontal meridian Lian et

al noted a similar degree of epithelial thinning by day seven (16.4%). The mid periphery in the horizontal meridian also showed statistically significant thickening by day seven. Lian et al speculated about the cause of the superior thinning and suggested that it may be due either to the upper lid causing excessive pressure on this corneal region or to the lens decentring overnight. Lian et al point out that as their measurements were taken after lens removal they were masked from any overnight decentration.

This study also looked at whether changes occurred in the thickness of Bowman's membrane over the thirty days of orthokeratology lens wear and found no effect. This is in contrast to the earlier study of Nieta-Bona, Gonzalez-Mesa, Nieto-Bona, Villa-Collar et all (2011) who found a significant increase in the thickness of Bowman's membrane after one month of orthokeratology lens wear. It may be that the two different techniques, optical coherence tomography and confocal microscopy respectively, applied to the corneal measurements led to these conclusions. Nieta-Bono et al (2011) also used the confocal microscope to look at the effect of orthokeratology on corneal cell morphology after 30 days of lens wear. A group of myopes (SE -2.33+/- 0.95D) fitted with orthokeratology lenses were compared with a group of emmetropes or low myopes who wore no contact lenses. They found the same corneal thickness changes as the earlier studies. They suggest that epithelial thinning occurs as a result of compression of the epithelial cells. The apparent reduction in the number of basal cells they suggest occurs because the compressed cells are more difficult to visualise. Nieto-Bono et al found no statistically significant change in the stroma or endothelium over the thirty days of the study. Zhong, Chen, Xie, Yang et al (2009) also found a decrease in the density of the basal cells but only in a group of patients who had worn orthokeratology lenses for five years. Zhong et al compared this group with a group who had worn their lenses for only one night. The group also found that corneal thickness increased generally after one night of lens wear but after five years of lens wear only the paracentral zone showed thickening although the central epithelium was thinned. The corneal endothelium was unchanged

after five years which Zhong et al felt was an improvement over the effect of conventional contact lenses worn long term. This comment refers to the use of low Dk/t lenses and the group agree that improvements in the Dk value of lens polymers may well address this issue.

These cellular level analyses are outside the scope of this study.

CHAPTER 7 ANTERIOR CHAMBER AND AXIAL LENGTH EFFECTS OF ORTHOKERATOLOGY

7.1 Introduction

The cornea which has been considered in chapters four and five provides the maximum focussing power of the eye. The other contributors to the eyes refractive status are the lens and its position within the eye and the axial length. If the combination of the cornea and lens focal lengths is in agreement with the eyes second principal focus i.e. the retinal surface then the eye will be emmetropic. Where this does not occur then the eye will manifest a degree of ametropia. In the case of myopia the axial length will be longer then the second principal focus. If the corneal power is reduced by flattening the anterior surface then the two focal planes may be brought into alignment.

The eye may however be myopic as a result of the lens being positioned closer to the cornea i.e. a shallow anterior chamber. If orthokeratology were to produce a shallowing of the anterior chamber then this could counteract the reduction of the corneal power achieved by the reverse geometry lenses. If the flattening of the cornea were to also produce a reduction in the axial length then this would enhance the procedure of myopia reduction. In order to investigate this, the anterior chamber depth and axial lengths of the participants were measured throughout the study.

7.1.1 Anterior chamber depth

Rabsilber, Becker, Frisch and Auffarth (2003) looked at anterior chamber depth (ACD) in relation to the refractive status using the IOL Master and the Orbscan. Using the three refractive groups, hypermetropes (SE +4.84 +/- 1.60D), myopes (SE -9.64 +/- 3.79D) and emmetropes (uncorrected visual acuity 20/20, no refractive limits are given) three ACD readings of one eye of each individual were taken using the Orbscan II. The Orbscan II allows measurements to be taken at points other than the corneal apex.

Rabsilber et al (2003) compared the measures between the apex and a 3.0mm diameter zone for all three refractive groups. The IOL Master takes five readings of the ACD at each image capture and provides an average. Whilst all three groups showed a decrease in ACD at the 3.0mm zone, none of the decreases were statistically significant. Rabsilber et al (2003) did find that the ACD of hypermetropes was statistically significantly smaller than the emmetropic group. This difference was not seen in the myopic group. A comparison between the ACD results for the IOL Master and the Orbscan using Bland-Altman plots showed no statistically significant difference between them.

Reddy, Pande, Finn, El-Gogary (2004) compared the ACD measurements between ultrasound, the Orbscan II and the IOL Master. This study on patients awaiting cataract surgery for age related cataracts involved a slightly older age group than the Rabsilber et al (2003) study, 72 years (59 – 94years) and 43.83 years (22 – 82 years) respectively. The ultrasound measures were statistically significantly different from both of the other two measurements (0.40mm lower than the Orbscan and 0.43mm lower than the IOL Master). No statistically significant difference was found between the IOL Master and the Orbscan. Reddy et al cautioned that at the time it was not possible to say if the IOL Master and Orbscan results were interchangeable.

Hashemi, Yazdani, Mehravaran, Fotouhi (2005) completed a similar study to that of Reddy et al (2004). In the Hashemi et al (2005) study the participants were all young myopes (19 – 49years) seeking refractive surgery. In contrast to the Reddy et al (2004) study Hashemi et al (2005) found a statistically significant difference between the ACD measurements of the IOL Master and the Orbscan (mean difference +0.12mm $p< 0.001$). Hashemi et al (2005) made the IOL Master measurements under cycloplegia and the authors state that this may account for the greater ACD seen in these cases. They note that the ACD may increase by between 0.08 and 0.12mm under cycloplegia.

Whilst the differences found were statistically different Hashemi et al (2005) indicated that these differences may not be of clinical significance.

Frisch, Rabsilber, Becker, Reuland et al (2007) in their comparison of ACD measurements between the Orbscan IIz and the IOL Master found no statistically significant difference. They also found that the two instruments produced highly correlated readings (R = 0.95) and as such were clinically interchangeable. Lee, Kim, Kim and Song (2007) compared the Orbscan IIz with ultrasound biomicroscopy. The ultrasound biomicroscope (UBM) required an immersion bath over the cornea. The immersion bath avoids the probe contacting the cornea which has been cited as a possible cause for the reduced ACD measures found with A-scan ultrasound (Reddy et al 2004; Hashemi et al 2005). Lee et al (2007) found that the two instruments produced measurements for the ACD which were statistically significantly different. Measurements from the UBM were found to be greater than those for the Orbscan (0.087 +/- 0.09). The Lee et al (2007) study was evaluating ACD for the purpose of phakic lens implantation. The ease of use of the Orbscan for ACD measurement was considered to outweigh the smaller readings it produced (Lee et al 2007).

Kim, Sun, Chang, Kim (2009) compared the Orbscan and Pentacam in anterior segment measurements including ACD one to five years after refractive surgery. Both LASEK and PRK procedures were considered. The study was conducted in an effort to address the concerns about apparent posterior corneal ectasia in the early post treatment phase of the refractive surgery procedures indicated. Concerns had previously been expressed regarding the accuracy of the Orbscan II for the evaluation of the posterior corneal surface (Cheng, Rao & Lam 2007). Kim et al (2009) postulated that for measurements taken between 12 and 60 months post treatment the posterior cornea could be considered to be stable.

7.1.2 Axial length

Drexler, Findl, Schmetterer, and Hitzenberger (1998) looked at eye elongation during accommodation in emmetropes and myopes using partial coherence interferometry, the same method employed by the IOL Master. Axial length measurements were made with the subjects fixating at their far point and near point. They found that both refractive groups showed elongation with the emmetropes showing a dioptric equivalent of 0.036D and the myopes 0.015D. Drexler et al also found that the anterior chamber depth decreased during maximal accommodative effort (mean 131μm) and the lens thickness increased (mean 175μm) for all refractive groups. The group found no statistically significant difference between the anterior chamber changes in emmetropes and myopes.

Stone, Quinn, Francis, Ying, (2004) investigated the diurnal change in axial length. Using partial coherence interferometry, as Drexler et al (1998), they measured their participant's axial lengths at discrete intervals during a 16 hour period of one day. Their results indicate that the human eye may undergo fluctuations in axial length between 15 and 40μm. Stone et al concluded that as the eyes focal depth is approximately 0.3D these small fluctuations would not be detected subjectively. They also found that axial length fluctuations did not occur on every day. They felt that this phenomenon should be investigated further. Read, Collins and Iskander (2008) used the IOL Master in their study of the diurnal variation in axial length. They too found that axial length did undergo a statistically significant variation during the day. The mean magnitude of the change found in their participants being 0.046 +/- 0.022mm (maximum to minimum difference). The maximum peak of the group mean axial length occurred at 13.00 (mean time of measurement) whilst the minimum group mean axial length occurred at 22.30 (mean time of measurement). Read et al also compared axial length measurement taken on consecutive days to assess day to day fluctuation. Repeated measures ANOVA of the two morning measurements showed no statistically significant difference.

Atchison and Smith (2004) reported on their concerns about the possible errors in axial length measurements when using the IOL Master in the accommodating eye. The IOL Master uses an average group velocity refractive index for the eye of 1.3549 calculated at 780nm and the dimensions of the Gullstrand model eye. It is known that during accommodation the lens of the eye thickens and the anterior chamber depth narrows. The thickening of the lens and the consequent increase in refractive index extend the optical path through the eye and therefore create an overestimation of any change in axial length. Atchison and Smith found that the error in axial length measurement could be estimated using the equation;

$E = OPL_a/n_{ave} - L_u$

where = OPL_a = the optical path length of the accommodated eye

n_{ave} = the average refractive index of the unaccommodated eye

L_u = the geometrical length

They applied this equation for 10.9D of accommodation; the accommodative error used by Gullstrand in the accommodated model eyes, and found errors of 18μm for the shell lens and 26μm for the gradient lens model eye of Gullstrand. This suggests a potential error of between 1.65μm and 2.39μm per dioptre of accommodation.

They point out that by amending the global refractive index used in the instrument to 1.4903 in the unaccommodated eye and 1.4266 in the accommodated eye the correct refraction could be achieved. Since these are not anatomically correct, they derived a more accurate equation for an estimation of the error induced by the use of a single refractive index for the eye, and not a gradient refractive index taking account of the changes in the accommodating lens.

$E = OPL_{LA}/n_L – (L_L + \Delta L_L)$

Where OPL_{LA} = optical path length of the accommodated lens

n_L = average refractive index along the visual axis of the unaccommodated lens

L_L = length of the unaccommodated lens

ΔL_L = actual change in length of the lens in accommodation

Mallen, Kashyap and Hampson (2006) also reported on axial length changes during accommodation. In their study of young emmetropes and myopes they found that there was a transient increase in axial length during the accommodative response. They found that this response was only statistically significant for a 6D accommodative stimulus. In contrast to Drexler et al (1998) they noted that the emmetropic subjects showed a smaller response to this 6D accommodative stimulus than the myopes. The dioptric equivalent of the axial length change was found to be 0.10 dioptres for emmetropes and 0.15 dioptres for myopes. They also noted that both groups showed a reduction in anterior chamber depth during accommodation. The magnitude of these changes was not reported. Mallen et al concluded that the errors in axial length reported by Atchison and Smith (2004) would apply to both of their study groups since the aqueous and lens refractive indices would be similar for the two groups. As a result of this they concluded that the difference in the measured response was true and not an artefact due to measurement error.

In more recent studies Read, Collins, Woodman, and Cheung (2010) and Ghosh, Collins, Read and Davis (2012) have used the Lenstar LS 900 to investigate changes in axial length during accommodation or changes of gaze. Read et al (2010) found that for a 3.00D and 6.00D accommodative stimulus the mean change in corrected axial length change was 5.2 +/- 11.2μm and 7.4+/- 18.9μm respectively. The group used the formulae proposed by Atchison and Smith (2004) to establish the correction factor which should be applied. Read et al (2010) found no statistically significant difference between the two refractive groups. Ghosh et al (2012) looked at the effect of gaze change on axial length. They wanted to look at the effect of the extra-ocular muscles on axial length in all nine cardinal points of gaze. The group found statistically significant increases in axial length for infero-nasal, inferior and supero-nasal gaze and statistically significant decreases in axial length for supero-temporal and superior gaze. No significant changes were seen in the other four directions of gaze.

The group also looked at the effect of time on the axial length change. In this case the subjects were asked to view a distant target for five minutes in all nine cardinal points of gaze; Ghosh et al found that the change in axial length seen on an immediate change of gaze increased significantly if this gaze change persisted for five minutes. They also found that the more myopic individuals experienced a greater change in axial length when they looked in the infero-nasal direction.

7.1.3 Axial length changes in Orthokeratology

Recent studies have suggested that orthokeratology could be used to control myopic progression in children. The flattening of the cornea, induced by the orthokeratology lenses, is known to alter the peripheral refraction (Charman, Mountford, Atchison and Markwell 2006). One result of this may be a reduction in the stimulus for vitreous chamber expansion. A number of studies have compared the increase in axial length seen in spectacle wearing and orthokeratology lens wearing children. Anecdotal evidence of the effect of orthokeratology on axial length change was reported by Cheung, Cho and Fan (2004). In this case an 11 year old child, with unilateral myopia, was fitted with an orthokeratology lens in the affected eye. During two years of follow up the eye fitted with the contact lens showed only a 0.13mm increase in axial length. The eye without a contact lens showed a 0.34mm increase in axial length with the corresponding increase in myopia (0.75 dioptres).

The LORIC study conducted in Hong Kong evaluated the axial length and vitreous chamber depth in 35 children undergoing orthokeratology treatment over a two year period (Cho, Cheung & Edwards 2005). At the end of the two year period the orthokeratology treated children had shown an increase in axial length of 0.29 +/- 0.27mm whilst the spectacle wearing controls had an increase of 0.54 +/- 0.27mm. Vitreous chamber depth findings for the two groups were 0.23 +/- 0.25mm and 0.48 +/- 0.26mm respectively. Walline, Jones and Sinnott (2009), as part of the CRAYON study, report similar findings for both axial length and vitreous chamber depth increases over

a two year period. They report that the children undergoing corneal reshaping treatment (orthokeratology) had, on average, a change in axial length that was 0.16mm per year less than the soft contact lens wearing group. Vitreous chamber depth increase was, on average, 0.1mm greater in the soft lens wearers. Kakita, Hiaoka and Oshika (2011) compared two groups of children, one wearing orthokeratology lenses and a control group wearing spectacles. In comparison to the two earlier studies which compared the orthokeratology lens wearers retrospectively with group data from earlier investigations (Cho, 2005, Walline et al., 2009) Kakita et al (2011) conducted a prospective study. Their findings were that an increase in axial length of 0.39 +/- 0.27mm occurred for the orthokeratology group and 0.61 +/- 0.24mm for the spectacle wearers. No report was made about changes in vitreous chamber depth in this study.

Few studies have looked at the effect of orthokeratology on the anterior chamber depth. Walline et al (2009) reported that children undergoing orthokeratology had no statistically significant increase in anterior chamber depth (mean change -0.01mm $p = 0.63$), the children wearing soft contact lenses had a statistically significant increase in anterior chamber depth over the two year period (mean change 0.05mm $p = 0.0005$). There was no statistically significant change in lens thickness in either group. Tsukiyama, Miyamoto, Higaki, Fukuda et al (2008) report finding no significant change in anterior chamber depth measurements in an adult population undergoing orthokeratology.

7.2 Anterior chamber and axial length measurements

7.2.1 Anterior Chamber method

Both the Orbscan and IOL Master provide measurements for the anterior chamber depth. The IOL Master measures the anterior chamber depth from the corneal apex to the anterior lens capsule surface. The Orbscan allows the selection of anterior chamber depth measurements to be made either from the anterior corneal surface or from the corneal endothelium. For the comparison between the two instruments shown the corneal anterior surface was selected. The IOL Master produces five measures and a mean measurement of the anterior chamber depth. For the Orbscan the anterior chamber depth information was retrieved for each of the three image captures and the mean of the three measurements calculated. The procedures for both image captures are outlined in chapter two.

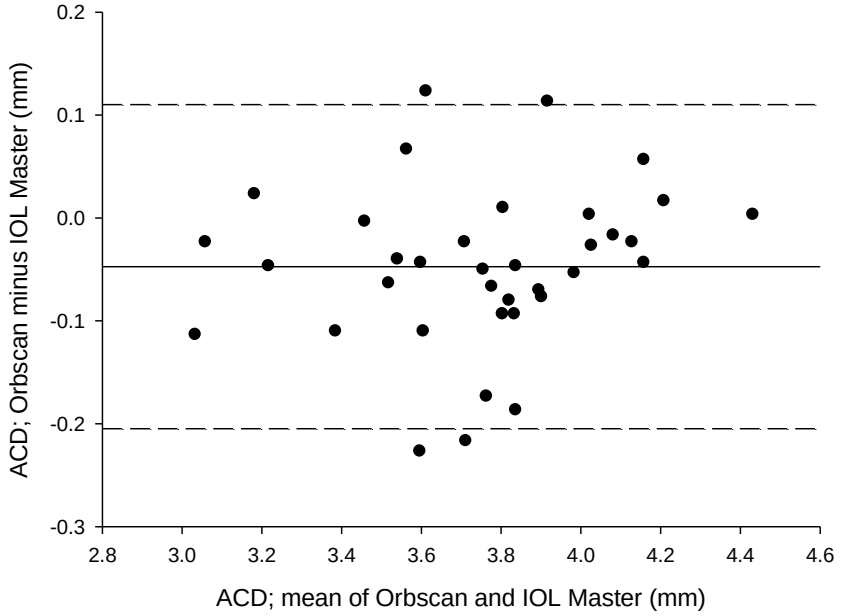
7.2.2 Axial length method

Axial length measurements were made at each visit following the procedure outlined in chapter two. Measurements were made on each eye until five acceptable measurements were achieved. In accordance with the IOL Master handbook axial length measures with a signal to noise ratio of less than 2.0 were deleted and repeated.

7.3 Results

Bland Altman plots were completed for the anterior chamber depth results from the two instruments (Fig 7.1). These plots provide information regarding the correspondence between two instruments or measures; they do not provide information regarding the true measure of the parameter in question. The results indicate there was no systematic bias in the results for either eye. Pearson correlation coefficients for the right and left eyes show R^2 = 0.94 and 0.95 respectively. For the purposes of the orthokeratology study anterior chamber depth measurements using the IOL Master were obtained at each visit following the protocols outlined in chapter two. Two way repeated measures ANOVA for the anterior chamber depth measurements for the twelve participants completing the full study were completed. This showed that there was a statistically significant effect between the two lenses ($F_{(1, 9)}$ = 9.35, p = 0.014). Tables 7.1 and 7.2 show the measurement results for each of the visits; these indicate that the aspheric lens produced a greater shortening of the anterior chamber than the pentacurve lens design. There was also a statistically significant difference between the effects on the anterior chamber at each of the visits where measurements were made ($F_{(5,45)}$ = 9.553, p = 0.000). An examination of the within subjects contrasts showed that there was only one visit at which statistically significant differences occurred (p = 0.008). This was between the one night and the one week visit. An examination of the pairwise comparisons revealed more information showing that the initial measurement was significantly different from the one week, six month and one year data. An examination of the lens / visit interaction showed that this was not statistically significant ($F_{(5,45)}$ = 0.689, p = 0.634).

a) right



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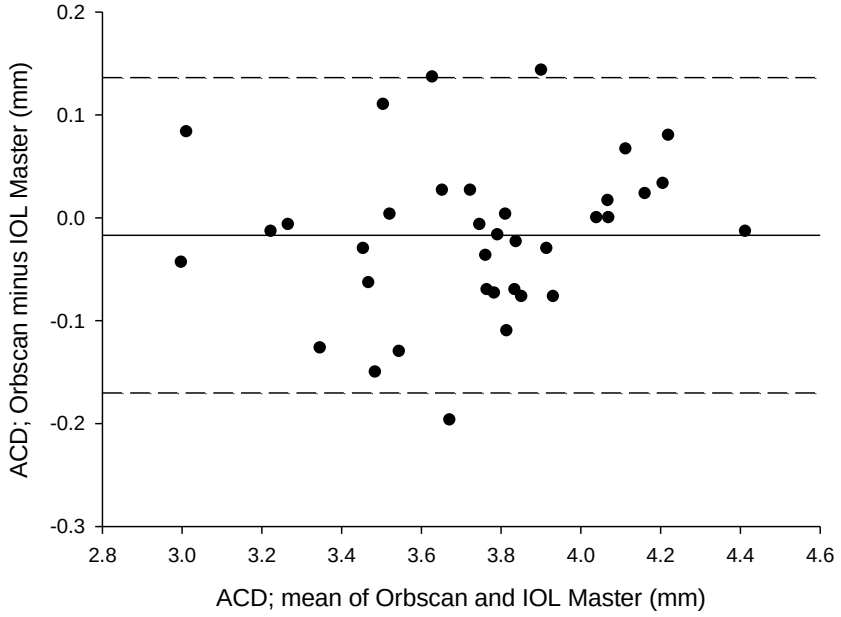
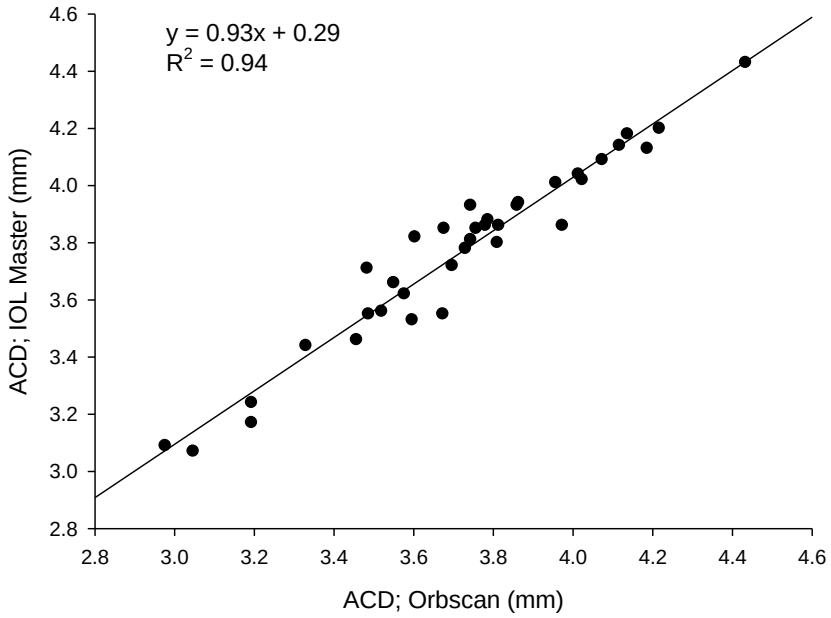


Fig 7.1 Bland Altman plot comparisons of the anterior chamber depth measurements (mm) provided by the IOL Master and Orbscan

a) right



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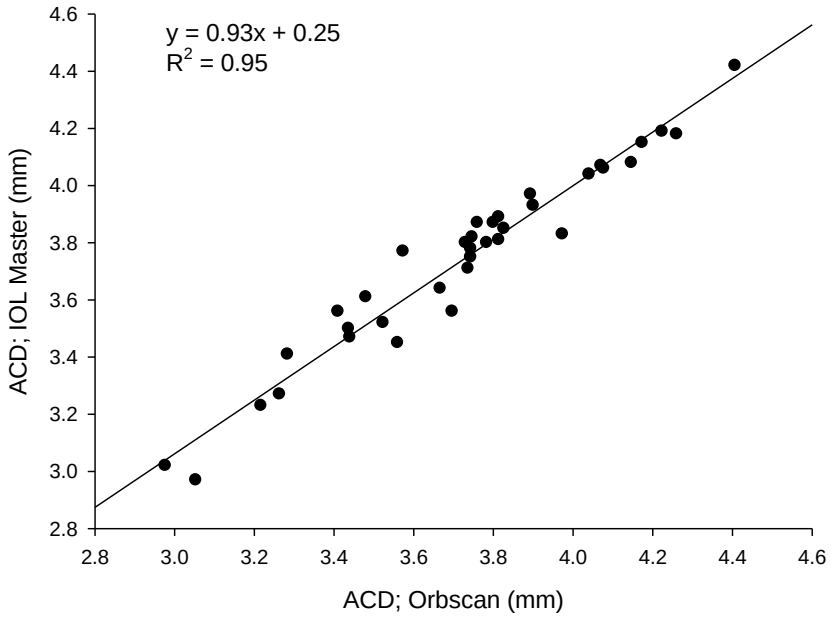


Fig 7.2 Correlation between IOL Master and Orbscan for the anterior chamber depth measurements (mm) of the right and left eye.

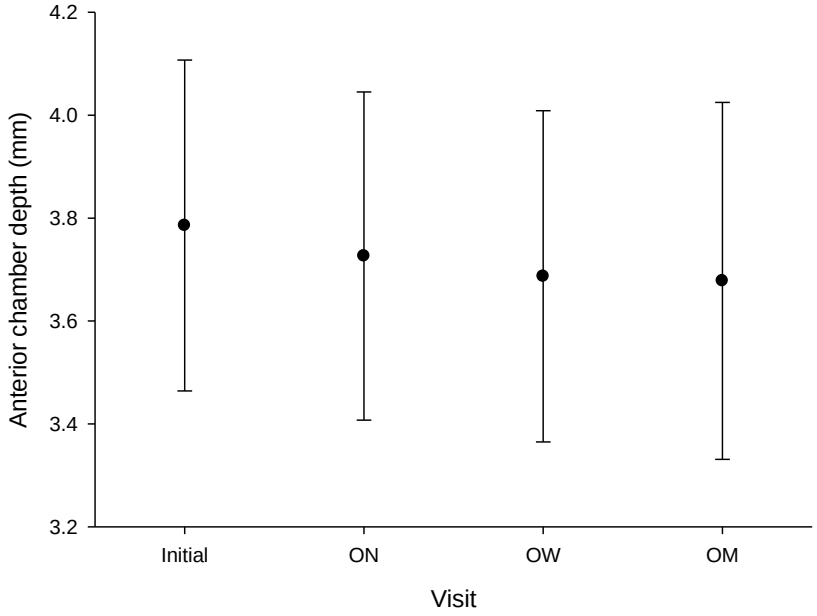
Table 7.1 Mean anterior chamber depth results (mm) from the IOL Master for the pentacurve and aspheric designs for each visit for the twelve months of the study.

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	3.79 +/- 0.33	3.76 +/- 0.34
One night	36	3.73 +/- 0.32	3.70 +/- 0.32
One week	30	3.68 +/- 0.33	3.64 +/- 0.34
One month	28	3.68 +/- 0.33	3.63 +/- 0.32
One quarter	17	3.66 +/- 0.27	3.62 +/- 0.24
Six months	13	3.83 +/- 0.27	3.79 +/- 0.25
One year	12	3.83 +/- 0.26	3.79 +/- 0.25

Table 7.2 Mean anterior chamber depth results (mm) corrected for central corneal thickness (mm) for each visit for the twelve months of the study. The central corneal thickness measures were obtained from the Orbscan.

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	3.19 +/- 0.31	3.16 +/- 0.34
One night	36	3.15 +/- 0.33	3.12 +/-0.33
One week	30	3.10 +/- 0.33	3.05 +/- 0.33
One month	28	3.11 +/- 0.36	3.04 +/-0.35
One quarter	17	3.07 +/- 0.29	3.03 +/- 0.27
Six months	13	3.25 +/- 0.26	3.22 +/- 0.24
One year	12	3.26 +/- 0.25	3.23 +/- 0.24

a) pentacurve



b) aspheric

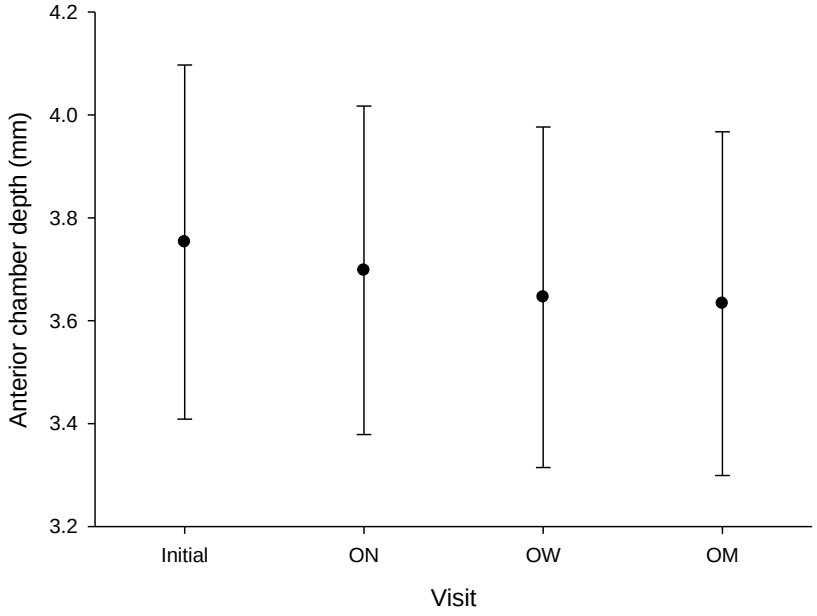


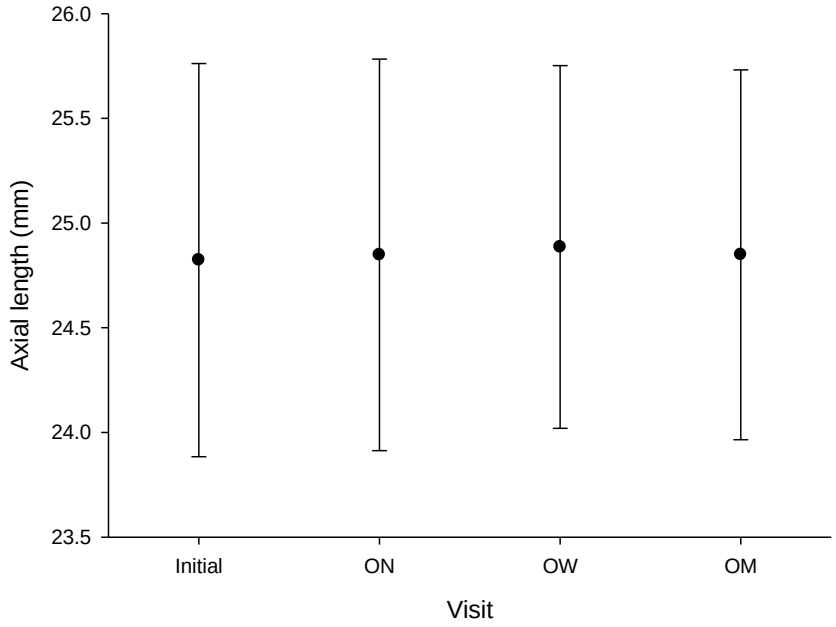
Fig 7.3 Group mean change in anterior chamber depth to one month.

Table 7.3 Axial length measurements (mm) for each visit for the twelve months of the study

Visit	Number of subjects	Pentacurve	Aspheric
Initial	36	24.82 +/- 0.94	24.77 +/- 0.94
One night	36	24.85 +/- 0.93	24.77 +/- 0.94
One week	30	24.89 +/- 0.87	24.80 +/- 0.88
One month	28	24.85 +/- 0.88	24.83 +/- 0.91
One quarter	17	24.87 +/- 0.78	24.78 +/- 0.75
Six months	13	24.79 +/- 0.78	24.70 +/- 0.84
One year	12	24.75 +/- 0.77	24.67 +/- 0.77

A two way repeated measures ANOVA was completed for the pentacurve and aspheric design axial length data. This revealed that there was no statistically significant difference between the lenses ($F_{(1,7)} = 0.474$, $p = 0.513$) or the visit ($F_{(1.317,\ 9.220)} = 0.173$, $p= 0.754$). The ANOVA also confirmed that there was no statistically significant interaction between the lens and the visit ($F_{(2.016,\ 14.109)} = 0.566$, $p = 0.581$). The Greenhouse-Geisser correction was applied in all cases. These results indicate that there was no statistically significant change in axial length for either eye.

a) pentacurve



b) aspheric

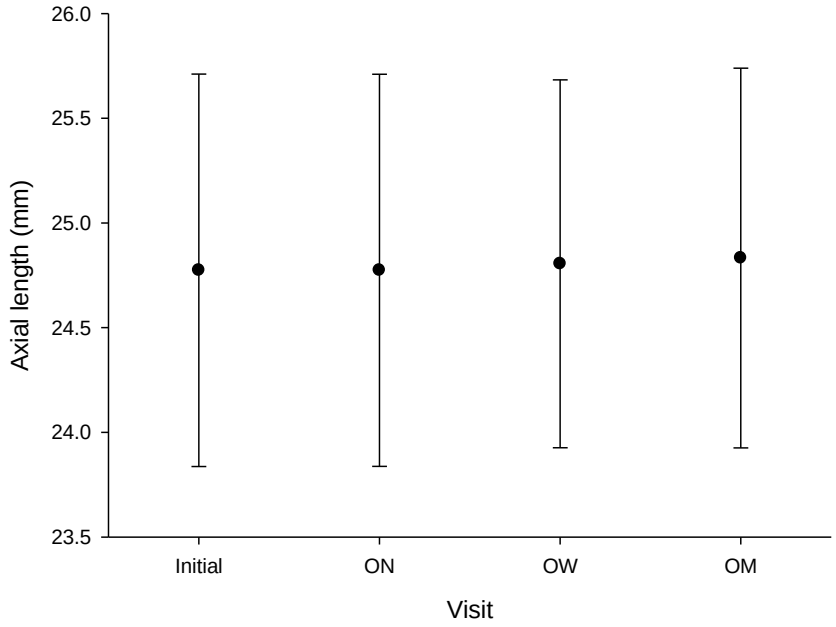


Fig 7.4 Group mean change in axial length to one month.

7.4 Discussion

In view of the findings of Drexler et al (1998), Atchison & Smith (2004) and Mallen et al (2006), the individuals in the current study were encouraged to focus into the distance with the non-fixating eye to reduce the stimulus to accommodation. The findings of Read et al (2008) regarding the diurnal change in axial length were addressed by taking the axial length measurements in the mornings between 8.00 and 9.00am. Read et al had noted that the minimum axial length measurements were achieved at 10.30pm with the maximum measure at 1.00pm. The IOL Master safety mechanism allows only twenty measures of axial length to be taken on an eye in one capture session. In order to collect five measures with a signal to noise ratio greater than 2.0 a number of the participants required up to ten measures to be taken. This was particularly necessary for the post orthokeratology fitting sessions due to the effect of the lenses on the anterior corneal surface. The IOL Master requires an optically smooth surface in order to produce an accurate measure. Post orthokeratology corneas with significant central epithelial staining were more difficult to image.

The statistical analysis showed that the pentacurve design had no effect on the anterior chamber depth throughout the study. This agrees with the findings of Tsukiyama et al (2008) who saw no change in their adult population. The results for the left eye which had been fitted with the aspheric design lens were surprising. The anterior chamber depth measures became significantly smaller after the one week visit. This reduction occurred as a consequence of the corneal apex moving backwards under the action of the orthokeratology lens. If this effect were to occur in isolation then the eye would become more myopic. The refractive error results for the aspheric lens from chapter four do not support this conclusion. If the axial length were also to shorten then no increase in the eyes effective power would occur. The statistical analysis of the axial length data for the two eyes shows that no change in axial length occurred throughout the study. These anomalous results for the aspheric lens may have occurred as a

result of the more unstable corneal profile created by this lens design. The IOL Master can only produce an anterior chamber depth measurement once the corneal curvature is known. In the case of orthokeratology the central corneal profile is considerably flatter than the average (Table 4.2) particularly for the aspheric lens. If the corneal apex is abnormally positioned then the apparent distance between the corneal apex and the lens capsule could be misinterpreted by the IOL Master software.

A number of studies (Cheung et al 2004; Cho et al 2005; Walline et al 2009; Kakita et al 2011) have reported a reduction in the rate of change in axial length seen in children fitted with orthokeratology lenses. Since the IOL Master measures axial length from corneal apex to retinal pigment epithelium, can we be sure that an apparent reduction in axial length indicates only control of the vitreous chamber expansion? If there is a reduction in anterior chamber depth then we would still see a change in overall axial length without necessarily a corresponding decrease in the rate of change of the vitreous chamber. Newer instruments which allow the vitreous chamber depth to be measured as well as the anterior chamber depth and axial length will provide more conclusive evidence for the axial length effects. In the current study no information is available for any change in vitreous chamber depth.

CHAPTER 8 OPTICAL MODELLING

8.1 Ocular aberrations and Orthokeratology

The optical system of the eye, as with other optical systems, has a number of inherent aberrations. The dynamic nature of the eye's optical system, coupled with the non-axial arrangement of the components and minor imperfections in both the cornea and lens mean that these aberrations are more significant than those in a man-made system (Hampson, 2008). Optical systems, such as telescopes are, as a general rule, rotationally symmetrical; this cannot be said of the eyes optical components. This lack of rotational symmetry means that the aberrations will also differ between the eyes two principal meridians. The aberrations of the eye may be divided into chromatic and monochromatic. Chromatic aberrations occur as a result of dispersion i.e. the result of the difference in refraction of the different wavelengths of light. Monochromatic aberrations are indicative of the differences in optical path length which occur as rays pass through different points within the pupil. These differences in optical path length occur as a result of variations in the refractive index of the ocular components and the minor imperfections in the ocular structures mentioned previously (Charman, 2005b),(Hampson, 2008).

The paraxial rays which strike the central cornea reach a point focus which is further from the corneal apex than rays which strike the more peripheral aspects of the cornea. This change in focal point arises due to the increase in corneal power across the surface of the cornea. The natural prolate shape of the cornea serves to minimise the effect of spherical aberration by reducing the increase in refractive power across the corneal shape. This difference in optical path gives rise to positive spherical aberration (Fig 8.2). Since the change in optical path length may be either advanced or retarded, with respect to the perfect wavefront, the magnitude of the aberration may be either

positive or negative. The absolute value of these positive and negative aberrations may be expressed in terms of the root mean square value (RMS).

8.1.1 Root Mean Square (RMS)

The RMS is the statistical deviation of the aberrant wave front from the perfect wave front averaged across the entire wave.

RMS = √ (average of the squared wave front deviations) – (square of the average wave front deviations)

The RMS is expressed in microns. For example a system affected only by defocus would show a RMS of approximately 0.25µm, which equates to 0.25 dioptres at the fovea, in a young healthy eye with a five millimetre pupil (Artal, 2006). In 1947 Maréchal demonstrated that a system in which the RMS was less than or equal to λ/14 could be considered to be aberration free (Maréchal 1947 cited by (Charman, 2005b)). One problem with expressing aberrations in terms of the RMS is that two people may have the same RMS value and yet have completely different aberration components (Charman, 2005b).

8.1.2 Zernike Polynomials

In order to overcome the difficulties of RMS, ocular aberrations may also be identified by means of their Zernike polynomial. The use of Zernike polynomials to describe aberrations replaces the earlier Seidel aberrations, which are now considered to be only of historic interest. Zernike polynomials are used to breakdown complex aberrations into their constituent parts. These polynomials may be identified by their radial (n) and meridional (m) components i.e. Z_n^m. The radial component indicates exponential variation of the polynomial function. The meridional component, which may be either positive or negative, indicates the number of repetitions of the sinusoid around the pupil margin. In this notation system, defocus is identified as Z_2^0, horizontal

coma as Z_3^1, vertical coma as Z_3^{-1}, spherical aberration as Z_4^0. Aberration Zernike polynomials are often shown graphically as a pyramid (Fig 8.1).

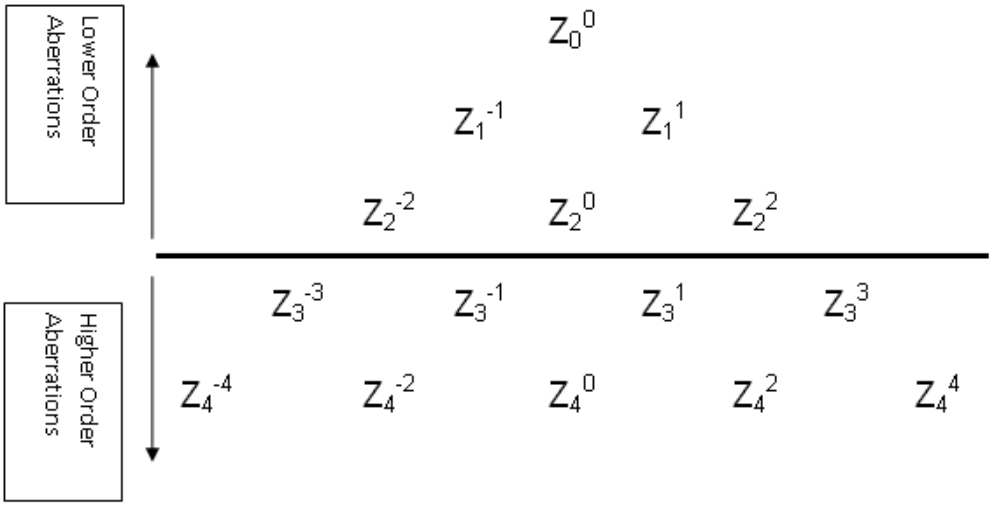


Fig 8.1 Zernike polynomials.

One limitation of the Zernike polynomials is that their values are dependent upon the pupil size of the subject under consideration (Charman, 2005b).

8.1.3 Ocular component contributions to aberrations

The cornea and lens are the principal contributors to the eyes ocular aberrations. The anterior cornea, due to its prolate shape and the major change in refractive index occurring at the air/cornea interface, is the principal source of spherical aberration. The increase in power which occurs across the cornea means that rays which strike the peripheral cornea will reach a focus which is closer to the corneal apex than rays which strike the central cornea (Fig 8.2). This is termed positive spherical aberration. Atchison (2005) found the spherical aberration of the emmetropic eye to be 0.10µm. He also found that spherical aberration increased by 0.007µm per dioptre of refractive error.

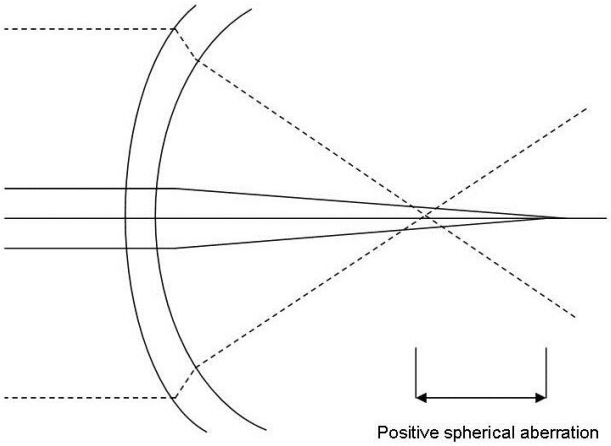


Fig 8.2 Representation of spherical aberration.

Field curvature occurs, in the absence of other aberrations, as a consequence of the change in the image plane as the distance between the object and the axis increases. This curved plane is known as the Petsval surface (Tunnacliffe 1987). This curvature may produce problems for camera lenses as the image plane needs to be flat. For the eye this is less of a problem provided the field curvature corresponds with the far point sphere. This correspondence can only occur for one specific lens power, refractive index and centre of rotation. The unaccommodated Gullstrand simplified schematic eye gives rise to a Petsval surface of radius -17.4mm (Tunnacliffe 1987). The horizontal retinal radius for the emmetrope, as found by Atchison (2006), is -12.91mm. Atchison also found that the retinal radius would flatten by -0.094mm per dioptre. This mismatch between the flatter Petsval surface and the retinal radius means that the image shell will be formed behind the retina. In the young eye this image can be moved into the retinal plane by accommodation (Verkicharia, Mathur, Mallen, Pope et al 2012).

Sicam, Dubbelman and van der Heijde (2006) in their study looked at the spherical aberration of the two corneal surfaces. Using Scheimpflug images and ray tracing they were able to separate the anterior and posterior effects. They evaluated 114 right eyes from individuals aged between 18 and 65 years of age. They found that the anterior corneal surface shows positive spherical aberration which increases slightly with age.

The posterior surface shows negative spherical aberration in the young which reaches zero by approximately 30 years of age. This positive trend continues with age. The lens is particularly dynamic in its effect on aberrations due to its accommodative function. The principal effect of accommodation is to reduce the defocus induced by the proximity of the object of regard. Defocus and astigmatism, second order aberrations, have been corrected by optical methods, spectacles or contact lenses, for many years. Indeed the eye itself will attempt to correct the defocus associated with near objects by means of accommodation. Higher order aberrations such as coma, trefoil and spherical aberration are not corrected by standard clinical methods such as spectacles and contact lenses.

Ocular aberrations are also affected by pupil size. Both spherical aberration and coma increase as the square of the aperture. Pupils with a diameter of three millimetres or less are said to produce a diffraction limited system i.e. aberrations are minimised. As well as increasing with pupil size, coma also increases as the position of the light source becomes more off axis. Second order aberrations, such as oblique astigmatism, dominate at angles of incidence greater than ten degrees (Charman, 2005a).

If the measurements of the aberrations from the anterior cornea and the whole eye are subtracted from each other, it is possible to deduce the aberrations induced by the internal optics i.e. posterior corneal surface and lens. Artal, Guirao, Berrio and Williams (2001) evaluated the individual measures of the aberrations from the anterior cornea and those of the internal optics in six individuals. In all cases they found that the measures from either the anterior cornea or the internal optics were greater than those for the eye as a whole. They felt that this reduction in the measures from the whole eye indicated that the internal optics aberrations compensated for those from the anterior surface. They stated that this compensation would act to improve the final retinal image. He, Gwiazda, Thorn and Held (2003) in their study found that this compensation effect did not apply to all individuals. In their study of 45 young subjects (18 emmetropes and 27 myopes) they found that, whilst the aberrations of the anterior cornea were greater

than those of the whole eye in some individuals, there were individuals whose anterior corneal aberrations were equal to or less than those of the whole eye. He et al also looked at the effects of the higher order aberrations by recalculating the RMS values without astigmatism. This recalculation showed that only 19 eyes had RMS values for the anterior cornea which were greater than those for the whole eye. They identified three typical eyes; one in which the anterior corneal aberrations were greater than the whole eye, one in which the two values were very similar and one in which the whole eye was greater than the anterior cornea.

They then deconstructed the RMS score into individual Zernike functions. For the eye which showed a greater RMS for the anterior cornea than the whole eye. Z8 (x axis coma) was greater in the whole than in the anterior cornea. All other Zernike functions, that were not zero, followed the RMS pattern. Similarly for the eye in which the whole eye aberrations were greater than the anterior cornea the majority of the Zernike functions followed this pattern with the exception of Z8 and Z12 (spherical aberration). In the eye where the anterior cornea and the whole eye aberrations were very similar in magnitude all the Zernike functions followed this pattern. This appears to indicate that the apparent compensation of the anterior corneal aberrations by the internal optics cannot be assumed in all subjects.

In the study by Sicam et al (2006) corneal aberrations undergo minimal changes with increasing age. Guirao, Redondo and Artal (2000) looked specifically at age as a factor in the change in corneal aberrations. They evaluated three age groups, young (20 – 30 years), middle (40 – 50 years) and older (60 – 70 years). Their findings showed that the corneal radius decreases with age and that the cornea becomes more spherical. These changes lead to an increase in spherical aberration in the middle and older groups. Coma and other higher order aberrations were shown to be similarly affected in the aging cornea. Calver and Elliott (1999) looked specifically at the effect of aging on the monochromatic aberrations of the eye. In a comparative study between undergraduates (mean age 24.2 +/- 3 years) and elderly volunteers (mean age 68.0 +/-

5 years) they found the older age group had lower modulation transfer functions (MTF) when the same pupil diameters (4mm and 6mm) were considered. The lower MTF occurred as a result of the effect of the eye's spherical aberrations on the image of the sinusoidal grating being viewed by the subjects. When the natural pupil size was considered (undergraduates pupil diameter 5.10 +/- 0.54mm and elderly volunteers' pupil diameter 4.20 +/- 0.49mm); the two groups were found to have very similar MTF results. The reduction in pupil size seen in the elderly volunteers acted to minimise any effects from the increase in aberrations which may occur as a result of other aging changes in the eye.

The internal surface aberrations are known to increase with age, particularly due to changes in the refractive index, curvature and thickness of the lens. Artal, Berrio, Guirao and Piers (2002) in their study found that the internal ocular aberrations increased at a rate which was ten times that of the corneal change with age. They also evaluated the change in the compensation effect as a result of the change in corneal and internal ocular aberrations. The group found that in patients over 45 years of age the corneal and ocular aberrations became additive and not subtractive as they are in the young eye. Artal et al (2002) evaluated the aberrations in their subjects with a 5.9mm pupil diameter. The ocular aberrations are pupil size dependant (Charman 2005a) and a 5.9mm pupil would be considered a large diameter in the middle and older aged population. As Calver and Elliott (1999) found senile miosis acts to mitigate some of the additive effects of the aberration changes in older subjects.

8.2 Effect of Orthokeratology on higher order ocular aberrations

Whilst a number of studies have examined the effect of laser refractive surgery on higher order ocular aberrations very few have looked at the effect in orthokeratology. Joslin, Wu, McMahon, Shahidi (2003) evaluated whole eye wavefront aberrations in nine myopic subjects; data from the right eyes only were included in the study. Zernike coefficients for orders three to six were calculated for both three and six millimetre pupils at baseline and at one month post fitting. They found that higher order aberrations increased by a factor of 2.66 for the three millimetre pupil and 2.50 for the six millimetre pupil. These values were the mean for the group, there was significant inter subject difference i.e. factors varied between 1.45 and 4.27 for the six millimetre pupil. Spherical aberration (Z_4^0) showed the greatest increase following orthokeratology; inclusion of the spherical aberration (Z_6^0) gave a 3.99 factor increase. Horizontal coma (Z_3^1) was also significantly affected by the procedure: mean baseline 0.051 +/- 0.078 to mean post fit 0.35 +/-0.14µm (p 0.0005). Inter eye variability increased for horizontal coma by a factor of 1.79.

Hiraoka, Matsumoto, Okamoto, Yamaguchi et al (2005) looked at the effect of orthokeratology on higher order aberrations in 39 young myopes. All participants achieved acuities of 20/20 or better and were followed for three months post fitting. Anterior corneal aberrations were calculated for both three and six millimetre pupils from corneal topography measurements. They found that for a three millimetre pupil third order aberrations increased from RMS 0.058 +/- 0.037 to 0.111 +/- 0.081µm (P <0.0001). In the case of the six millimetre pupil the third order aberrations increased from RMS 0.323 +/- 0.165 to 0.633 +/- 0.448µm. Fourth order aberrations also increased from RMS 0.037 +/- 0.028 to 0.079 +/- 0.078µm (P<0.0001) in the three millimetre pupil and for the six millimetre pupil from 0.297 +/- 0.113 to 0.849 +/- 0.339µm (P<0.0001). They also found significant positive correlation between the myopic change induced by the orthokeratology and the increase in higher order

aberrations, for both the three and six millimetre pupils. Changes in the individual coma aberrations showed that vertical coma changed from positive to negative and that horizontal coma increased significantly in the positive direction for both pupil sizes. In order to combine the results from the right and left eyes the sign for the horizontal coma was reversed for the left eyes.

Berntsen, Barr and Mitchell (2005) reported the effect of one month of corneal refractive therapy (orthokeratology) on the higher order aberrations. The highest change was seen in spherical and secondary spherical aberration when measured across a five millimetre pupil. Their findings were similar to those of Joslin et al (2005) with spherical aberration increasing from 0.045µm +/- 0.04 to 0.202µm +/- 0.14. Berntsen et al did not record the increase in horizontal coma seen by Joslin et al (2005). Berntsen et al also evaluated the higher order aberrations across a three millimetre pupil and found that the change in spherical aberration did not reach statistical significance.

Stillitano, Chalita, Schor, Maidana et al (2007b) followed their fourteen myopic individuals for eight days of orthokeratology wear. Using a 6.5 millimetre pupil they found a statistically significant increase in the higher order aberrations after one night which continued to increase to day eight. For the right eyes horizontal coma increased in the positive direction whilst for the left eyes the increase occurred in the negative direction. Vertical coma showed no statistically significant difference between the two eyes. In a later study Stillitano, Schor, Lipener and Hofling-Lima (2007a) measured the stability of the ocular aberrations during the day. The ocular aberrations were measured at 8a.m., 1p.m. and 6p.m. following six months of orthokeratology treatment. The 14 subjects had worn their orthokeratology lenses for eight hours on each night during the previous six months. They found that spherical aberration (Z_4^0) decreased significantly throughout the day. Defocus (Z_2^0) increased significantly between 8a.m. and 1p.m. but did not change significantly after this time. Despite the increase in defocus they found no change in the subject's vision. They hypothesize that the

decrease in spherical aberration compensates for the increase in defocus and this is why there is no loss of vision.

Hiraoka, Okamoto, Ishii, Takahira et al (2007) looked at higher order aberrations in 22 subjects followed for three months of orthokeratology treatment. In these individuals, they particularly wanted to look at the effect of orthokeratology on both mesopic contrast sensitivity and higher order aberrations. Higher order aberrations increased in a similar nature to those reported in their earlier study (Hiraoka, 2005). Mesopic contrast sensitivity, with and without glare, was negatively correlated with the increase in third and fourth order aberrations. Although the aberrations values were greater for the larger pupils no correlation was found between the pupil size and mesopic contrast sensitivity. Hiraoka et al caution that the effect of orthokeratology on mesopic contrast sensitivity should be discussed with patients. They point out that certain professions e.g. pilots or military personnel who have visual requirements, above the average patient, may be adversely affected by this increase in aberrations despite achieving acuities of 20/20 or greater.

Mathur and Atchison (2009) evaluated the effect of orthokeratology on peripheral aberrations in two individuals. The two were successfully fitted with orthokeratology lenses. Ocular aberrations were assessed at baseline and at one and two weeks of lens wear. Peripheral aberrations were measured using a modified Hartmann-Shack aberrometer at each of the three visits. Both subjects showed an increase in spherical aberration in the central visual field after two weeks of lens wear. Horizontal and vertical comas, which were the predominant peripheral aberrations in the untreated eyes, increased following orthokeratology and changed their direction.

In altering the anterior corneal surface, in the process of orthokeratology, it would seem that the compensatory relationship between the anterior cornea aberrations and the aberrations of the internal optics are disrupted, leading to the increase seen in total eye aberrations. Hiraoka, Okamoto, Ishii, Okamoto et al (2009) looked at the recovery of corneal higher order aberrations after orthokeratology lens wear was discontinued.

They found that following twelve months of successful lens wear higher order aberration measures returned to baseline within one month of wear cessation. Oliveira, Ferreira and Franco (2011) raised concerns that many studies either ignored the effect of the posterior corneal surface or incorporated its effect into that of the internal optics of the eye. They state that changes in the anterior cornea's biomechanical response will affect the aberrations induced by the posterior surface. The biomechanical changes seen in orthokeratology were discussed in chapter one. More recently Chen, Lam and Cho (2009) and Hon, Cheung, Cho and Lam (2012) have begun to use the ocular response analyser to look at the biomechanical responses of the cornea in children fitted with orthokeratology lenses. Hon et al (2012) suggest that children fitted with orthokeratology lenses should have the biomechanical changes in their corneas monitored.

8.3 The effect of orthokeratology on higher order ocular aberrations in the study group.

8.3.1 Method

The combined effect of the changes in apical radius, axial length and refractive error were examined for the participants. As the majority of change occurs in the first four weeks of lens wear only data from the three visits after the initial assessment were considered. The refractive error was assessed at each visit and recorded as power vectors following the procedure indicated in chapter three. The anterior apical radius was calculated for each visit using the Orbscan single meridian data. The method of analysis for this data is indicated in chapter two (Douthwaite and Parkinson 2009). The axial length was measured for each participant at each visit using the IOL Master. The procedure for the axial length measurements is also outlined in chapter two. A comparison of the changes in these three parameters will indicate the change in the aberrations which may have occurred. No direct measure of the change in aberrations was available.

8.3.2 Results

Table 8.1a shows the results of the change in the apical radius, axial length and sphere (M) at the one night, one week and one month visits for the pentacurve and aspheric lens designs for all participants. The change was calculated by deducting the initial pre-treatment value for each of the three measures from the results obtained at each visit. Thirty six participants commenced the study and twenty seven participants completed one month of lens wear. For both eyes the apical radii are seen to increase indicating that the cornea is flattening under the influence of the orthokeratology lenses. The change in the anterior radius was discussed in chapter four. A decrease in the degree of change in apical radius was noted in the eye wearing the aspheric design at

the one month visit. To investigate the possible cause for this, the data was recalculated using only the data from the twenty seven participants completing one month of lens wear Table 8.2b. The apical radius data shows the expected change when this adjustment is made. The cornea continues to flatten up to the one month visit (Fig 8.3 a & d). An examination of the results for individual participants shows that two individuals had large changes in apical radius at the one week assessment visit (0.96 and 1.07mm) and left the study at this stage. Removal of their data from the mean result at one week reduces the result leaving the expected change in apical radius over time.

The axial length data for the two eyes indicates small changes occur in this parameter over the month. The pentacurve design shows a small increase in axial length whilst the aspheric lens shows a small decrease. This pattern is seen in the whole group and in the smaller group completing a full month of lens wear (Fig 8.3 b & e). The axial length data was discussed in chapter seven.

The refractive errors obtained at each visit had been analysed using power vectors (Thibos et al 1997) the results for both groups are shown in Fig 8.3 c & f. Both groups show the expected change in the spherical vector (M). The change in the two vectors corresponding to the astigmatic elements J_0 and J_{45} were discussed in chapter four. One way repeated measures ANOVA, with time as a factor, of the astigmatic vector results showed no significant change at any point.

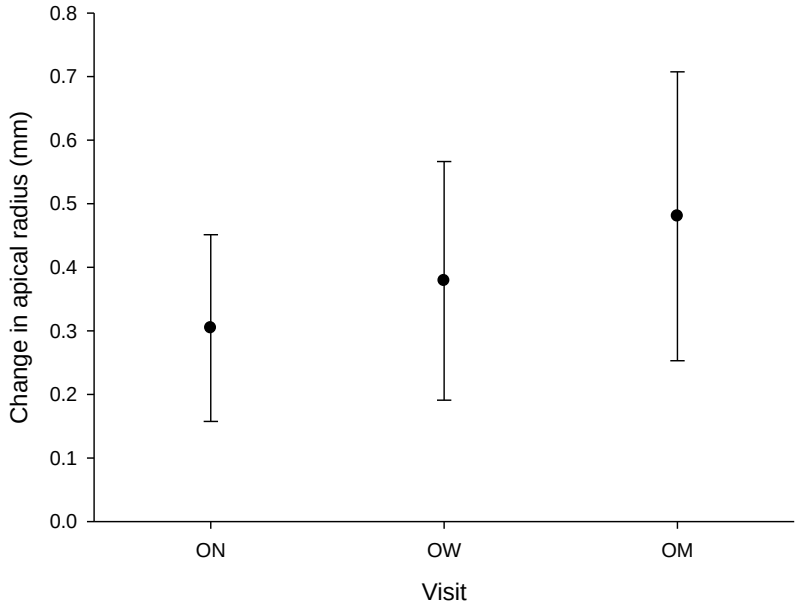
Table 8.1a Mean change in apical radius (r_0), axial length (AXL) and refractive error (M) at one night (ON), one week (OW) and one month (OM) for all participants at each visit.

	Number of subjects	Pentacurve			Aspheric		
Visit		r_0 (mm)	AXL (mm)	M (D)	r_0 (mm)	AXL (mm)	M (D)
ON	36	0.304	0.002	2.531	0.291	0.000	2.476
OW	30	0.379	-0.017	3.165	0.475	-0.019	3.315
OM	28	0.480	-0.024	3.347	0.455	-0.023	3.449

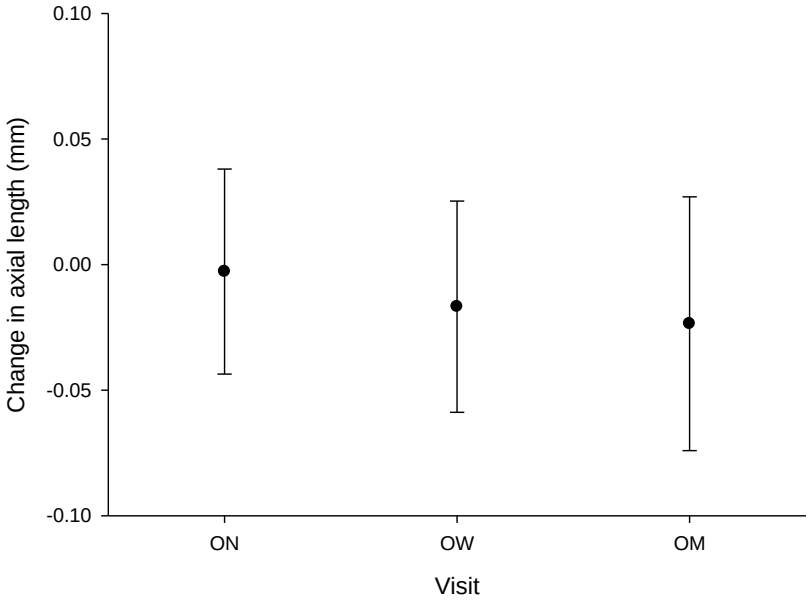
Table 8.1b Mean change in apical radius (r_0), axial length (AXL) and refractive error (M) at one night (ON), one week (OW) and one month (OM) for the twenty seven participants completing one month of wear

	Number of subjects	Pentacurve			Aspheric		
Visit		r_0 (mm)	AXL (mm)	M (D)	r_0 (mm)	AXL (mm)	M (D)
ON	36	0.293	-0.004	2.500	0.256	-0.004	2.500
OW	30	0.370	-0.016	3.134	0.436	-0.017	3.317
OM	28	0.480	-0.024	3.347	0.455	-0.023	3.345

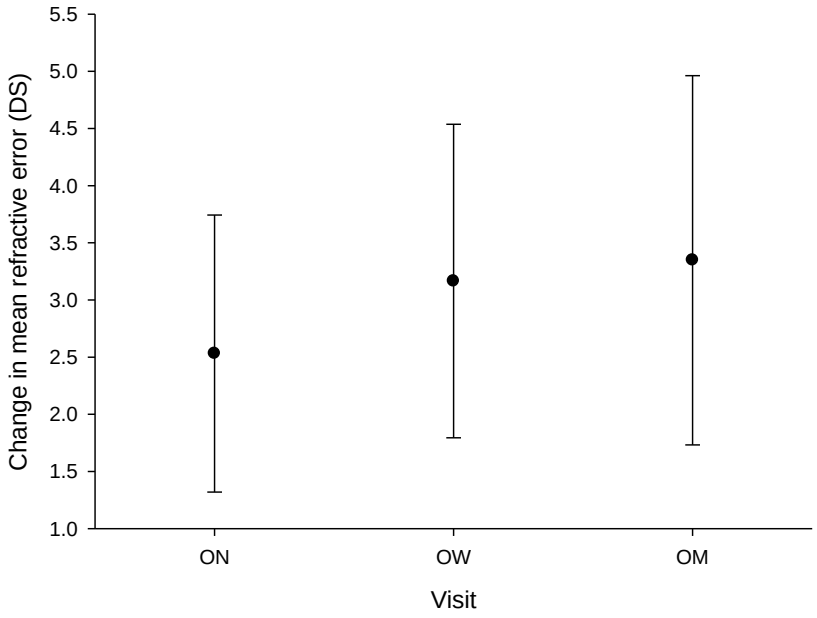
a) pentacurve



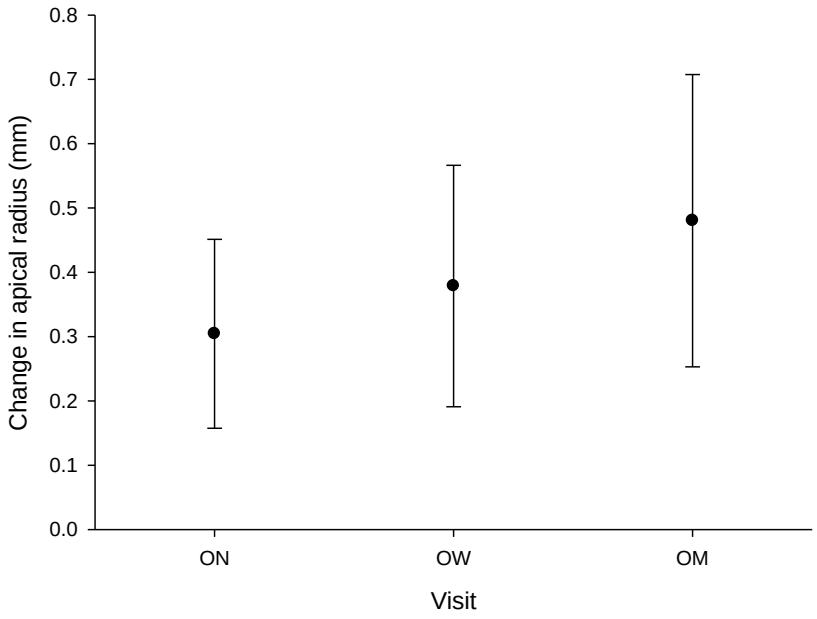
b) pentacurve



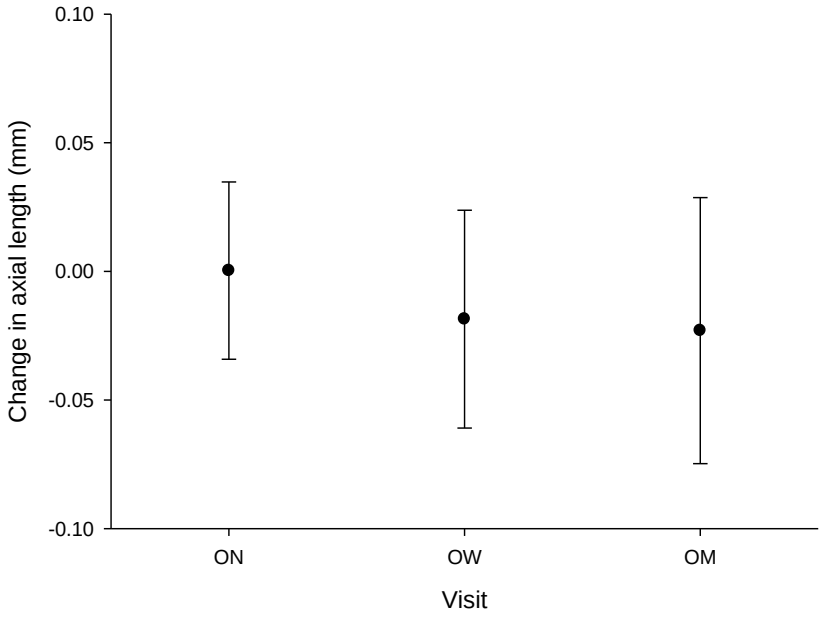
c) pentacurve



d) aspheric



e) aspheric



f) aspheric

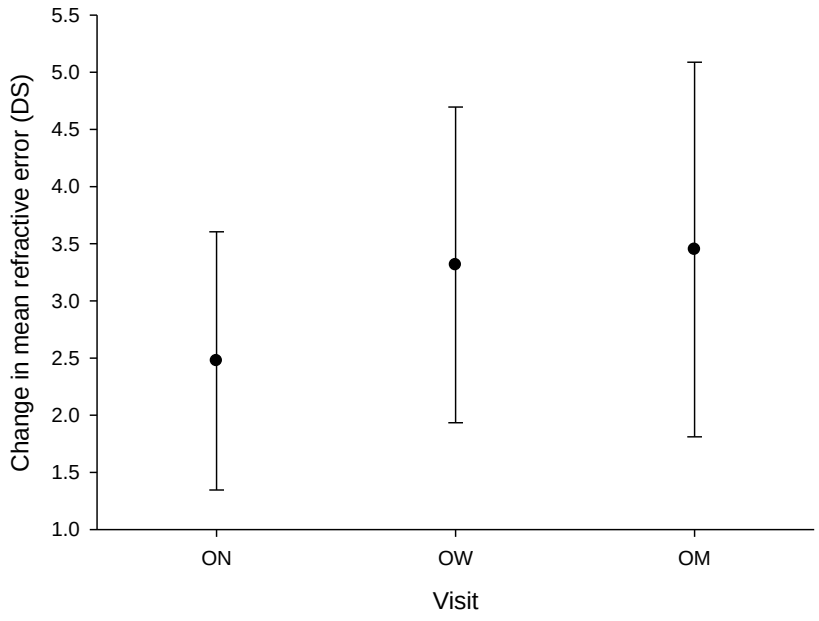


Fig 8.3 Pentacurve (a-c) and Aspheric (d-f) eye change in r_0, axial length and M from one night to one month.

8.4 Discussion

The cornea's natural prolate shape serves to minimise the spherical aberrations present in the eye's optical system. The flattening of the front surface by the addition of the orthokeratology lenses changes the corneal profile to that of an oblate (steepening) ellipse. Flattening of the central zone of the cornea will result in a backward displacement of the paraxial focus of the system, which will correct myopia. However, the marginal rays which may pass through the periphery of the orthokeratology treatment area will undergo a forward shift in the eye relative to the paraxial rays; this will increase the degree of spherical aberration. Stillitano and colleagues (2007) observed a change in spherical aberration from around 0.1 microns pre-treatment to around 0.8 microns at 8 days into an orthokeratology fitting. Increasing spherical aberration will stretch the waist of the point of best focus, which could have the following clinical effects: a reduction in the power of the negative correcting sphere for myopic correction; an increase in the depth of focus; a reduction in best-corrected visual acuity. This may explain part of the mismatch between the degree of corneal power change and the manifest change in refractive error.

Stillitano et al (2007) observed an increase in coma from around 0.25 microns to 0.50 microns following orthokeratology. Changes in coma-like aberrations could be attributed to decentration of the reverse geometry lens, and dynamic shifts that may occur in this during the blink cycle.

8.4.1 Interaction between biometric factors

During this study, small and generally insignificant changes in axial length and anterior chamber depth were observed. Such small changes can be expected following the fitting of reverse geometry contact lenses. A flattening of the central portion of the cornea may result in the backward displacement of the anterior vertex of the cornea, which will reduce both the anterior chamber depth and the overall axial length on the

eye. Such changes will reduce the refractive power of the eye, which could possibly be a factor in the mismatch between corneal power change and overall refractive error change.

The subjects in the current study could fall into any of the three groups proposed by He et al (2003) i.e.

i) group one: anterior corneal aberrations were greater than the whole eye
ii) group two: anterior corneal and whole eye aberrations were very similar
iii) group three: whole eye aberrations were greater than the anterior cornea.

However, all subjects achieved high levels of best corrected visual acuity pre treatment (Table 4.13) and all had well defined refractive end points i.e. they were able to discriminate +/- 0.25DS changes very easily. This is in agreement with their small depth of focus requiring the image and retinal planes to correspond when wearing their refractive correction. The change in the p value of the cornea created by both lens designs would produce the effects indicated earlier of a stretching of the waist of the point of best focus. This was observed by the reduction in the clear end point of the refraction with some individuals being unable to discriminate any difference when shown +/- 0.50DS changes. The p value changes were particularly prominent in the left eye, aspheric design lens. Table 4.5 shows that at one month the group had undergone an increase in p value in the aspheric design (p value change 0.79) of almost twice that of the pentacurve (p value change 0.46). This significant flattening of the cornea under the aspheric lens may also explain why some individuals had changes in refraction which were in excess of the expected values predicted by the lens design. Some individuals showed apparent hypermetropia at their appointments which was in excess of the expected over correction induced to allow for daytime regression (+1.00D). This apparent hypermetropia may also indicate the increased depth of focus and lack of end point definition.

One further explanation for this increased depth of focus could be the blur adaptation i.e. an increase in defocused visual acuity when viewing through blurring lenses, which

takes place in the visual system (Rosenfield, Hong, George 2004, George and Rosenfield 2004). In blur adaptation an individual's visual acuity under initially defocused conditions improves with no apparent change in refractive error. Fig 4.18 shows the change in refractive error against the change in corneal power. For the pentacurve lens this shows that only 77% of the change in the manifest refractive error can be explained by the change in the corneal power. This is contrary to the design parameters for this lens detailed in chapter three. The BOZR of the lens was selected to manipulate the required refractive change in the cornea and yet 23% of this change is unaccounted for. The aspheric design lens fitted to the left was more unpredictable in its action when the change in corneal power was examined. Fig 4.18 shows that only 27% of the change in the refraction was predicted by the change in corneal power. In this case 73% of the refractive change is unaccounted for in the change in corneal power but the mean refractive error measures for the aspheric lens (Table 4.9) at one month shows M = +0.24 +/- 0.70D. The effects of blur adaptation must be particularly effective for the aspheric lens in view of this mismatch.

The increase in aberrations will inevitably mean that the retinal image quality is reduced. The action of blur adaptation means that once the orthokeratology lens is removed in the morning an individual will manifest an improvement in acuity once blur adaptation has occurred. This blur adaptation will persist throughout the day and may account for the subjective perception of good quality vision all day despite an apparent under or overcorrection. Some individuals reported that they could wear their orthokeratology lenses on alternate nights and did not perceive any depreciation in their vision.

Rosenfield et al (2004) in their study of young myopes found an increase in unaided visual acuity from 0.76 to 0.53 logMAR after three hours of blur adaptation. This blur adaptation could account for a two line improvement in logMAR acuity allowing the subjects to maintain 6/6 (VAR 100). The VAR results shown in Table 4.13 show that the aspheric design vision and BCVA at twelve months were statistically significantly

different from the pentacurve. The mean VAR scores of 103 +/- 6 and 100 +/- 7 for the pentacurve and aspheric designs respectively were those measured at the morning visit. At this point the subjects would have had only a short period of blur adaptation. The reported facility to wear lenses on alternate nights may be further indication of blur adaptation taking place.

The change in the vertical cornea induced by orthokeratology is not as fully understood as that of the horizontal. Changes in this meridian must inevitably lead to a change in the coma like aberrations. Mathur and Atchison (2009) reported that the vertical coma changed direction after two weeks of orthokeratology lens wear. The posterior cornea also plays a part in the overall aberrations of the eye. If as is thought the posterior corneal shape acts to reduce the aberrations of the anterior surface then any change here would affect that compensatory action. In the study the posterior cornea shows an early statistical change (pentacurve, one week and aspheric, one night). Due to the concerns regarding the measurement of the posterior cornea it is difficult to draw valid conclusions for the effects.

An increased understanding of the effect of orthokeratology on the higher order aberrations may allow the current treatment range to be extended. Improved back surface designs may allow an appropriate correction to be applied without the inevitable impact on spherical aberration. This may be akin to the work on wavefront guided LASIK.

CHAPTER 9 CONCLUSIONS

9.1 Clinical considerations

In our preliminary studies we produced data for the precision of the Orbscan on anterior apical radius and p value measurements on corneas. This was in response to a lack of information in this area as most previous precision papers had been based on test surfaces (Douthwaite & Parkinson 2006). Cairns and McGhee (2005) reported no studies into the repeatability of the Orbscan measures on the posterior cornea. A further literature search showed no papers available dealing with the Orbscan's precision on posterior surfaces. This study has addressed both of these issues and the results are reported in chapter two.

When this study commenced one of the aims was to look at the possibility of using an aspheric back surface lens to produce the appropriate change in refractive error during overnight wear. Visualisation of the results of the change in the apical radius and p value show that our current aspheric design is unstable in its action. The fluorescein patterns seen at each of the visits showed the bull's eye pattern that was expected and was seen in the right eye. Mountford et al (2005) indicated that fluorescein patterns are not the most appropriate tool to use in the assessment of orthokeratology lens fit. In a clinical setting this is likely to be the most acceptable along with the global topography results. It would be inappropriate to expect practitioners to analyse raw image data for lens fitting purposes. The right lens which had a traditional multicurve back surface design (C5) did achieve the desired result.

Statistical comparison of the results from the two lens designs shows that only five parameters were found to be significantly different. These were the change in the vertical anterior apical radius and p value, the vertical treatment zone diameter, the posterior p value and the anterior chamber depth measurements. The results for the apical radius and p value show that the aspheric lens produces a flatter more oblate cornea in the vertical meridian. Examination of the vertical treatment zone diameter for the aspheric lens reveals a larger diameter than the pentacurve lens at all visits. An

increase in the change in the vertical cornea would suggest that the aspheric lens may induce an increase in the coma type aberrations. This potential change in aberrations was not reflected in the unaided vision and BCVA results recorded for the two lenses. There was also no statistically significant difference in the astigmatic error recorded for the aspheric lens (J_0 and J_{45}) which might have been expected with a greater change in the vertical cornea. Further examination of the statistical analysis for the posterior p value shows that neither the visit or lens/visit interaction reached statistical significance. Concerns exist about the assessment of the posterior surface using the Orbscan because change here cannot be assessed independently of the change in the anterior surface. As indicated in chapter seven the left anterior chamber depth data produced anomalous results such that there appeared to be a decrease in anterior chamber depth which was not reflected in the refractive error measurements found. Tsukiyama et al (2008) had recorded no statistically significant change in anterior chamber depth in their subjects over a 53 week period. Pairwise comparisons of the data showed that only the one night to one week visit showed a statistically significant difference in the depth of the anterior chamber.

The second aim of the study was to examine the time scale for the onset of orthokeratology. Early researchers had suggested that the effects were complete by one month but that the majority of change had occurred after one night. Statistical analysis of the anterior apical radius showed that there was no statistically significant change after one night for the pentacurve lens. The change for the aspheric lens continued to the one week visit with no further change. This could suggest that the aspheric lens has a slower effect on the corneal shape than the pentacurve. In contrast the aspheric lens had a more rapid effect on the p value with no statistical change being seen after the one night visit whilst the pentacurve lens showed change until the one month visit. For the posterior corneal surface the pentacurve lens had no statistical change in effect after the one week visit whilst the aspheric lens had a more rapid response showing no further change after one night. Both lenses showed no

statistically significant change at any visit. These results have to be treated with a degree of caution due to concerns over the assessment of the posterior corneal surface by the Orbscan IIz. For the refractive error changes both lenses showed no statistically significant change in M after one week of lens wear. Neither lens produced any effect on J_0 or J_{45} at any visit.

Our third aim had been to look at the suggestion by Kerns (1978) that the change in refractive error would stop once the cornea became spherical. This study showed that the anterior corneal surface was oblate after one night of lens wear for both designs and for both the horizontal and vertical meridians. The refractive error continued to change until one week of lens wear. These results show that the refractive error effects are not solely dependent on the corneal asphericity achieved.

In chapter six the changes in corneal thickness were reported. The study findings agree with those of Swarbrick et al (1998) and Alharbi and Swarbrick (2003) in that the central cornea did show thinning and there was mid peripheral thickening. The Orbscan IIz is unable to differentiate intracorneal changes so that we could not confirm that the central thinning was based in the corneal epithelium and that the mid peripheral thickening was based in the stroma. Alharbi and Swarbrick (2003) had followed the corneal thickness changes for three months. This study found the corneal thickness response followed the same pattern as Alharbi and Swarbrick (2003) throughout the twelve months of the treatment.

Grant & May (1972); Patterson (1975) and Erickson and Thorn (1977) had suggested a 2:1 relationship between the change in refractive error and corneal power. This study found that for the pentacurve lens the change in refractive error (ΔM) was related to the change in corneal power (ΔACP) by the equation

$$\Delta M = 1.08\Delta CP + 0.05 \quad (R^2 = 0.77)$$

The aspheric lens produced a less predictable response which was expressed by the equation

$$\Delta M = 0.64\Delta CP + 1.54 \; (R^2 = 0.27)$$

It had been suggested that one reason for the apparent 2:1 relationship was the use of keratometry which would not detect the very central zone of change. This study has shown that there is a 1:1 relationship for the multicurve design lens used when the entire cornea is mapped. The aspheric lens equation suggests that this lens design had a greater effect than expected on the refractive error. The poor correlation of the results for the aspheric lens means that this result should be treated with caution.

The use of the Munnerlyn formula to evaluate the change in corneal sag has been used by Swarbrick et al (1998) and questioned by Garner and Owens (2004). Using a formula which is based on the assumption that refractive surgery produces no effect in the posterior corneal surface to prove that there is no change in the posterior surface when orthokeratology is applied is controversial. In chapter seven the results for the change in the posterior cornea were reported. This study found that for the pentacurve design the change in the posterior surface did not reach statistical significance until one week of lens wear. This agrees with the findings of Owens et al (2004). For the aspheric design the results show that the cornea undergoes statistically significant steepening after one night of lens wear which agrees with the findings of Chen et al (2010). The change in the pentacurve design posterior apical radius returns to its original values over the course of twelve months (Fig 5.1 a). The results for the aspheric design are more variable (Fig 5.1 b). The presence of p values which are < 0 indicates a hyperbolic surface shape. Whilst this study has shown a change in the posterior surface; further investigation of these changes are required using a technique which allows an independent assessment of the corneal surface.

One further outcome measure had been to look at the change in the vertical cornea. Previous studies into the effect of orthokeratology on the vertical cornea had been conducted using the keratometer (Kerns 1978; Soni et al 2003). The Orbscan IIz has allowed the evaluation of the central zone of the cornea rather than the annulus of the keratometer. For both lenses there is flattening of the vertical cornea and a move to an oblate shape which corresponds with the change seen in the horizontal meridian.

The refractive error corrections attempted were wider than some studies with participants having refractive errors up to -6.50D of spherical refraction. No subject with a refractive error of this magnitude continued with the study after one month. The degree of flattening required led to significant corneal staining which reduced the clarity of the vision. Inevitably these large refractive corrections would have excessive changes in the p value with the consequent increase in spherical aberration. This leads to the conclusion that orthokeratology should be limited to errors up -4.00D with low levels of with the rule astigmatism. No significant change was seen in either J_0 or J_{45} astigmatic components in the current study, but entry was limited to with the rule astigmatism of no greater than -1.50DC and against the rule of no more than -0.75DC. Control of the amount of astigmatism will regulate the increase in coma-like aberration changes which can occur in orthokeratology.

The changes found in the anterior chamber are more difficult to explain. No change in anterior chamber depth had been anticipated which corresponds with the findings for the pentacurve design. The shortening of the anterior chamber depth at one week did not agree with the refractive error and axial length change findings. We were concerned that the abnormal corneal shape induced by orthokeratology may have caused a problem with the IOL Master software. Further studies into the effect of orthokeratology on the anterior chamber depth possibly using anterior segment OCT may help to clarify these findings. As expected no change was found in the axial length in this adult population.

The significant increase in aberrations which inevitably occur as a result of the flattening of the cornea mean that care should be taken in the selection of orthokeratology patients in a clinical setting. Hiraoka et al (2007) pointed out that care should be taken when offering the procedure to pilots and military personnel who may have visual requirements above that of the normal population. Hiroaka et al found a loss of mesopic contrast sensitivity. In this case concerns must arise for individuals

undergoing orthokeratology living in the United Kingdom and who would be driving in mesopic conditions on a significant number of days in the year.

9.2 Post Hoc Power analyses

Table 9.1 shows the post hoc power analyses for the study. Three discrete points for the power analysis have been selected. These are one night, one month and one year. The points were selected as being clinically significant and are in keeping with analyses applied in chapter three. These visits also represent points at which the number of participants decreased (One night (36), One month (28), and One year (12)).

If we accept that a power of 80% will establish that change has occurred then we see that for the anterior apical radius we were able to detect change at the one night and one year visit but not at one month for the pentacurve lens. For the aspheric lens the power was only sufficient at the one year visit. This loss of power occurs because of the increase in the standard deviation of the measures at the later visits which mask the ability to detect change even though the sample size remained above the a priori calculation. For the anterior p value we see that we had no result for power of over 80% at any visit. This again occurs due to the large standard deviation of the measures at each of the visits compared to the initial standard deviation used to calculate the sample size. This same situation applies to the anterior vertical apical radius, central corneal thickness, anterior chamber depth and axial length measurements. Reductions in the sample size had no effect on the power of the refractive error data which achieved power of ≥ 90% at all visits. The posterior apical radius results show power results of ≥ 95% for the one night and one month visits for both lens designs. The reduction in the sample size at one year again accounts for the reduction in the power to approximately 70%. The posterior p value results show that the results for the pentacurve lens achieved power of > 80% for all visits. The aspheric lens created a larger standard deviation measure for the one month and one year visits which reduced the power of the test at these points. Finally the anterior vertical p value results did

achieve statistical power at the one night and one month visits for the pentacurve lens and at the one night visit for the aspheric design.

Table 9.1 Power Analysis values for the indicated parameters at the one night, one month and one year visits.

		Pentacurve			Aspheric		
Parameter		One night	One month	One year	One night	One month	One year
Subject Numbers		36	28	12	36	28	12
Anterior r0	D	0.1	0.1	0.1	0.1	0.1	0.1
	SD	0.15	0.23	0.13	0.24	0.29	0.13
	ES	0.67	0.43	0.77	0.42	0.34	0.77
Power (%)		99	72	80	79	55	80
Anterior p value	D	0.1	0.1	0.1	0.1	0.1	0.1
	SD	0.38	0.51	0.41	0.45	0.62	0.54
	ES	0.26	0.20	0.24	0.22	0.16	0.19
Power (%)		46	26	20	37	21	15
Posterior r0	D	0.2	0.2	0.2	0.2	0.2	0.2
	SD	0.26	0.30	0.29	0.27	0.30	0.27
	ES	0.77	0.67	0.69	0.74	0.67	0.74
Power (%)		99	96	72	99	96	78
Posterior p value	D	0.2	0.2	0.2	0.2	0.2	0.2
	SD	0.44	0.41	0.25	0.41	0.55	0.30
	ES	0.45	0.49	0.80	0.49	0.36	0.67
Power (%)		85	81	83	89	59	70
Anterior vertical r0	D	0.1	0.1	0.1	0.1	0.1	0.1
	SD	0.29	0.31	0.28	0.24	0.32	0.27
	ES	0.34	0.32	0.36	0.42	0.31	0.37
Power (%)		65	51	31	79	49	35
Anterior vertical p value	D	0.1	0.1	0.1	0.1	0.1	0.1
	SD	0.23	0.18	0.22	0.23	0.38	0.36
	ES	0.43	0.56	0.45	0.43	0.26	0.28
Power (%)		82	89	43	82	39	23
Central corneal thickness	D	0.01	0.01	0.01	0.01	0.01	0.01
	SD	0.04	0.04	0.04	0.04	0.05	0.04
	ES	0.25	0.25	0.25	0.25	0.20	0.25
Power (%)		43	36	20	43	27	20
Refractive error (M)	D	0.50	0.50	0.50	0.50	0.50	0.50
	SD	0.71	0.30	0.38	0.71	0.76	0.55
	ES	0.70	1.67	1.32	0.70	0.66	0.91
Power (%)		99	100	99	99	96	90
Anterior chamber depth	D	0.1	0.1	0.1	0.1	0.1	0.1
	SD	0.33	0.36	0.25	0.33	0.35	0.24
	ES	0.30	0.28	0.4	0.30	0.29	0.42
Power (%)		55	42	36	55	43	39
Axial length	D	0.1	0.1	0.1	0.1	0.1	0.1
	SD	0.93	0.88	0.77	0.94	0.91	0.77
	ES	0.11	0.11	0.13	0.11	0.11	0.13
Power (%)		15	14	11	15	14	11

Table 9.1 shows the power analyses for the parameters indicated in column one. D is the difference we wished to detect; SD is the standard deviation of the measures at each of the visits and ES is the ratio of the two measures which gives the effect size. For the refractive error data only the change in M is reported as there was no statistically significant change in J_0 or J_{45} throughout the study.

In the a priori power analyses an α level of 0.05 was selected to minimise the risk of a Type I error occurring i.e. a 5% risk of rejecting the null hypothesis. In the post hoc power analyses the power level was set to reduce the risk of a Type II error. This is conventionally accepted, as indicated earlier, as $(1 - \beta) \geq 0.8$. Whilst it would be best practice to minimise Type II errors this does not mean that findings with low power are incorrect. Bland (2000) cautions that a population may have a significant difference even if the null hypothesis i.e. no difference between means is true. The principal influences on the power of a test are the effect size, the significance level and the sample size. In this study we had selected the significance level and estimated effect size from population norms to calculate the sample size in our a priori analyses.

In the post hoc results the small effect size found in parameters such as anterior vertical r0 (Table 9.1) due to the large standard deviation in our measurements accounts for the reduced power for these results. If we were to accept that the study required larger changes to be present before change was detected i.e. an increased effect size then these results may also achieve 80% power. The results for the axial length change showed the lowest power results. This occurred as a consequence of the very large standard deviation for this parameter. This is to be expected in a group of myopes with a refractive range between -1.00DS and -6.50DS. Initial axial length measures showed a range of right eye 22.5 – 26.4mm (mean of 24.8 +/- 0.95mm) and left eye 22.7 – 26.4mm (mean 24.7 +/- 0.97mm). Post hoc power analysis for axial length showed that a sample size of 700 subjects was required in order to achieve an

80% power result. This sample size would have been prohibitive in this longitudinal study.

9.3 Limitations of the current study

The number of subjects who left the study for non clinical reasons limited the conclusions that could be drawn. When recruiting for a longitudinal study amongst an undergraduate population there is always the problem of students graduating and no longer being available for data collection. This occurred in a number of the individuals who were initially recruited. This also limited data collection at the three month visit as this coincided with the long summer vacation and students who were away from the university were unable to return for a data collection appointment.

Re examination of the subjects at the end of the day would have allowed us to assess the potential regression of the orthokeratology effect. The morning data has confirmed that there was little further change in response from either lens design after one month. Subjects with refractive errors below – 4.00DS reported that they could continue without lenses throughout the day as reported in chapter four. Individuals with refractive errors of up to -1.50DS have reported that they can achieve acceptable levels of vision throughout a 48 hour period when the lenses were worn on alternate nights. A number of these individuals reported this effect within the first week of lens wear.

In chapter five the effects of orthokeratology on the posterior surface were discussed. At the time that the study commenced no controlled study into the Orbscan's posterior validity had been published (Cairns and McGhee 2005). The availability of an instrument which employs Scheimpflug imaging for the posterior surface, such as the Pentacam, would have given access to an instrument which was capable of measuring the posterior surface directly.

In chapter eight the effects of orthokeratology on the eyes aberrations were discussed. A limitation of the current study is that we had no access to an aberrometer at this time. The adaptive optics laboratory here at Bradford School of Optometry and Vision Science has a binocular aberrometer but this is a research tool requiring bite bar stabilisation for measurements. This aberrometer was in use in other projects during the study. As part of the interest in the effect of aberration changes in orthokeratology pupil size would have allowed a mathematical model to be constructed. The BOZD of both of the lens designs was fixed at 7mm. In conventional lens designs the BOZD would have been amended to allow for the pupil size (Gasson and Morris 2003). VAR results were measured only at high contrast. Access to low contrast VAR results would have allowed further investigation of the effect of orthokeratology on aberrations and their clinical ramifications to be evaluated.

In conclusion this study set out to examine the ocular biometric changes associated with orthokeratology in light of the current research. This study has shown that the anterior corneal surface becomes oblate. The results demonstrate a change in the posterior corneal surface both apical radius and p value. The study found that the vertical corneal apical radius and p value, which have not previously been reported, undergo change during orthokeratology. Anterior chamber depth and axial length are unchanged in an adult population by the procedure. The instrumentation investigations have produced results for precison for the Orbscan IIz for the measurement of the posterior corneal surface and posterior test surfaces.

9.4 Future work

9.4.1 Hyperopic and Toric Orthokeratology

Since this study commenced, hyperopic orthokeratology has also been reported by a number of studies (Lu, Sorbara, Simpson, Fonn 2007; Gifford, Swarbrick 2008). The early researchers found that this was an easier procedure as the steep lenses were less likely to decentre than the flat lenses of myopic orthokeratology. Chan, Cho & de Vecht (2009) have also reported on the use of a toric back surface design lens to correct significant myopic astigmatism (-2.50 DCyl). In view of these recent advances a study of the short term effects of hyperopic and toric orthokeratology is timely.

9.4.2 Aberrations and peripheral refraction

The current study was limited due to a lack of aberrometry measurements at aftercare visits. A short term study of up to one month for example could be conducted easily. It would be useful to correlate the clinical appearance of the lens fit with the changes in higher order aberrations, particularly coma-like aberrations.

9.4.3 Blur adaptation in orthokeratology

It appears to be the case in orthokeratology patients that their vision varies considerably between observers. One factor in this may be the ability of a patient's visual system to respond to blur. It would be interesting to examine any potential correlations between a patient's blur adaptation and their subjective appreciation of their vision post orthokeratology fitting.

9.4.4 OCT of the corneal epithelium

Since the start of the study the availability of commercial instruments, particularly OCT devices for examination of the anterior ocular structures has advanced considerably. A study of the changes in corneal epithelium during the early stages of an orthokeratology fitting, and how these changes stabilise at later stages in the fitting would improve our understanding of the underlying mechanism, of corneal change.

9.4.5 Finite element analysis

Finite element analysis is currently being applied to studies of the human crystalline lens in the investigation of accommodation function and basic changes in presbyopia. This technique could also be applied to the cornea in future studies of orthokeratology. It may help to predict likely success of patients in orthokeratology.

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APPENDIX A Initial contact letter

THE EYE CLINIC, UNIVERSITY OF BRADFORD

BRADFORD BD7 1DP

This document outlines the treatment described as Orthokeratology. Orthokeratology requires that you wear specially designed gas permeable contact lenses overnight that will reshape your cornea during sleep in order to provide acceptable unaided distance vision during waking hours. The Orthokeratology effect is temporary and reversible. The quality of your unaided vision will be dependent on wearing your lenses as prescribed by your practitioner. The quality of your unaided vision will also depend on how much internal astigmatism is present in your eyes, which is not always predictable. If you do not find the results acceptable then your eyes will return to their normal state over a period of time (one to three weeks) during which we will provide soft lenses to correct your vision until your prescription becomes stable.

BENEFITS

These lenses have been designed to provide excellent visual acuity and oxygen transmission to the eye during wear. The lens design should provide a reduction in the refractive error of a treated eye with a resultant improvement in the unaided vision. This change is believed to be completely reversible and temporary in nature.

RISKS

While no harmful health risks to your eyes are anticipated from using these lenses, as with any contact lens, there are potential risks of irritation to the eye, infections or corneal ulcers. Transient distorted vision that is not corrected with spectacle lenses may occur after removal of the lenses. No harmful effects are expected from any of the examination procedures used in the fitting and performance assessment of these lenses. If you develop any unusual symptoms or prolonged discomfort, removing the lenses, in most cases, will provide immediate relief. However, you should also contact the contact lens practitioner immediately.

In the event that it is believed that these lenses present new risks or the possibility of undesirable side effects, you will be advised of this information so that you may determine whether or not you wish to continue as a volunteer patient in this investigation. Patients wearing the contact lenses during sleep induce extra risks over daily wear contact lenses but Orthokeratology is not as risky as wearing extended wear soft contact lenses. Extended wear (wearing lenses for one week without removal)

contact lenses are marketed and are used in normal optometric high street and hospital practice.

PARTICIPATION IN THE STUDY

Participants in the study will be required to attend the University on a number of occasions during the 12 month period of the study. Times for these appointments will be arranged at a mutually convenient time. These visits include:

1. An initial visit when the suitability of the participant for Orthokeratology will be assessed and the various measurements required to design the lenses will be made. This visit will normally last between 60 and 90 minutes. Patients who currently wear soft lenses should not wear them on the day of the initial visit. Individuals who currently wear RGP lenses will need a longer period of time without their lenses before the measurements can be made.

2. The next visit will be a collection appointment when the custom designed lenses will be checked for fitting purposes and instructions regarding the insertion and removal of the lenses will be given. At this visit participants will need to wear the lenses for 1 – 2 hours and then have their refraction reassessed to confirm that the corneal reshaping is taking place. The extent of this corneal reshaping will vary from individual to individual at this visit.

3. The third visit takes place on the morning after the participant has worn the lenses overnight for the first time. The participant will attend the University wearing the lenses so that immediate overnight reactions can be assessed. This visit would normally last 1 hour.

4. Subsequent visits take place at
    a. 1 week of overnight wear
    b. 1 month of overnight wear
    c. 3 months of overnight wear
    d. 6 months of overnight wear
    e. 12 months of overnight wear

    It would be expected that these visits would also last in the region of 1 hour.

Participants will be given contact information for the University staff involved in the study in case of emergency.

APPENDIX B Consent form

THE EYE CLINIC, UNIVERSITY OF BRADFORD
BRADFORD BD7 1DP

This document outlines the treatment described as Orthokeratology. Orthokeratology requires that you wear specially designed gas permeable contact lenses overnight that will reshape your cornea during sleep in order to provide acceptable unaided distance vision during waking hours. The Orthokeratology effect is temporary and reversible and it may be necessary to wear your retainer lenses during some waking hours to maintain satisfactory distance vision, especially if you fail to wear them as advised. The quality of your unaided vision will be dependent on wearing your lenses as prescribed by your practitioner. The quality of your unaided vision will also depend on how much internal astigmatism is present in your eyes, which is not always predictable. If you do not find the results acceptable then your eyes will return to their normal state over a period of time (one to three weeks) during which we will provide soft lenses to correct your vision until your prescription becomes stable.

BENEFITS

These lenses have been designed to provide excellent visual acuity and oxygen transmission to the eye during wear. The lens design should provide a reduction in the refractive error of a treated eye with a resultant improvement in the unaided vision. This change is believed to be completely reversible and temporary in nature.

RISKS

While no harmful health risks to your eyes are anticipated from using these lenses, as with any contact lens, there are potential risks of irritation to the eye, infections or corneal ulcers. Transient distorted vision that is not corrected with spectacle lenses may occur after removal of the lenses. No harmful effects are expected from any of the examination procedures used in the fitting and performance assessment of these lenses. If you develop any unusual symptoms or prolonged discomfort, removing the lenses, in most cases, will provide immediate relief. However, you should also contact the contact lens practitioner immediately.

In the event that it is believed that these lenses present new risks or the possibility of undesirable side effects, you will be advised of this information so that you may determine whether or not you wish to continue as a volunteer patient in this investigation.

Patients wearing the contact lenses during sleep induce extra risks over daily wear contact lenses but Orthokeratology is not as risky as wearing extended wear soft contact lenses. Extended wear (wearing lenses for one week without removal) contact lenses are marketed and are used in normal optometric high street and hospital practice.

The most common complication for extended wear patients is contact lens induced acute red eye. This is an acute reaction that usually requires no treatment. It is painful for a few hours.

All contact lens patients are exposed to extra risks when wearing contact lenses. The condition that creates most concern is microbial keratitis. This is sight threatening but is very rare. It is best avoided by the wearer ensuring clean and hygienic care and handling of their contact lenses

ALTERNATIVES

Currently available alternatives to Orthokeratology lenses are:

1. Spectacles
2. Conventional soft or gas permeable contact lenses
3. Refractive surgery

DECLARATION

I have read all of the above information. I understand what I have read and the process has been explained to me. Although it is impossible for the contact lens practitioner to inform me of every possible complication s/he has answered all of my questions to my satisfaction and has assured me that s/he will advise me of new risks if they develop and will answer any further inquiries I may have about this treatment or wearing this type of lens.

Should any complications occur I agree to contact

Annette Parkinson on:

XXXXXXXXXXX at any time

Prof Douthwaite on:

XXXXXXXXXXX during the working day

OR XXXXXXXXXXX at any other time

Please print

Name ----------

Address ----------

Date ----------

Phone number ----------

Signature ----------

If the patient is under 18 years of age, parent or guardian signature is required

Signature parent / guardian ----------

Relationship to minor ----------

Signature of witness ----------

APPENDIX C Instruction leaflet

Wearing, Cleaning and Handling Instructions for Orthokeratology lenses

Lens Identification

Left lens – BLUE ***Right lens – LILAC***

The lenses should be cleaned each morning when they are removed from your eyes.

1. **ALWAYS WASH YOUR HANDS BEFORE HANDLING YOUR LENSES**
2. Place the lens in the palm of your hand.
3. Shake the bottle of cleaner.
4. Then place one or two drops of Boston cleaner onto the lens surface and rub the lens using your fingertips.
5. Rinse the cleaner from the lens using the saline provided.
6. **NEVER USE TAP WATER ON YOUR CONTACT LENSES**
7. Fill the lens case with the Boston conditioning solution and store your lenses during the day.
8. Always change the solution each day.
9. Your case should be rinsed with boiled hot water every day and allowed to air dry.
10. **Discard** any unused solution **90 days** after opening.

In the initial period you may be advised to wear the lenses during the day whilst you adjust to them. The cleaning instructions given above should then be followed at the end of each period of wear.

At night the lenses should be removed from the case and the conditioning solution rinsed from the lenses with Saline. The lens should then be filled with a drop of saline before insertion.

Before removing the lenses from your eyes in the morning gently massage the lens to mobilise it from the cornea. You may wish to insert a drop of comfort solution to facilitate the mobilisation.

During the first few weeks of the Orthokeratology process your distance vision may vary during the course of the day. The lenses are designed to correct your vision during the day and may be safely worn if at any time you feel your vision is not clear enough. This is particularly important if you are driving, especially in low light levels.

Corneal Infection

A corneal infection or ulcer is the most serious possible side effect of any contact lens wear. In order to reduce the risk of this you should follow all the instructions given above and be aware of the following emergency procedures.

Symptoms

- ***Redness*** – compare your two eyes, if one is particularly red in comparison to the other you should consider this to be suspicious.
- ***Watering*** – particularly if accompanied by significant discomfort (see below)
- ***Light sensitivity (photophobia)*** – if your eyes are more sensitive to light than you normally expect you should consider this to be suspicious.
- ***Discomfort*** – particularly if this appears to increase as the day progresses.

If you experience any of the above symptoms you should immediately remove the contact lenses and contact one of the members of staff from the Optometry Department listed below.

Annette Parkinson	XXXXXXXXXXX
Professor Douthwaite	XXXXXXXXXXX
Alison Alderson	XXXXXXXXXXX
Bradford University Eye Clinic	XXXXXXXXXXX

(9.00am – 5.00pm Mon – Fri)

In the event that you are unable to attend the University you should seek assistance from the nearest Casualty department taking your lenses, solution bottle and case with you.

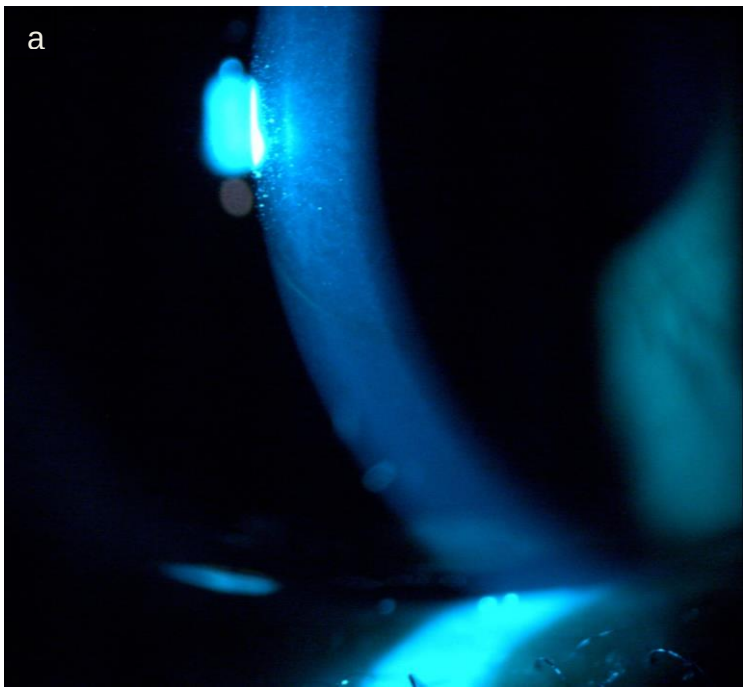
APPENDIX D Iron ring case study

One of the reported complications of orthokeratology had been the appearance of an iron ring in the cornea (Cho et al 2002a & 2005; Rah et al 2002; Liang et al 2003; Hiraoka et al 2004; Cheung et al 2005; Gonzalez-Meijome et al 2012). In the current study an iron ring was seen in only one individual. The results for the main measures of the anterior surface are shown in Table Aiii.1.

Table Aiii.1 Apical radius, p value, central corneal thickness (CCT), refractive error (M), vision and best corrected visual acuity (BCVA) results for subject KR.

	Initial	One night	One day	One month	Six months	Twelve months
Apical radius (mm)	7.55	7.72	7.82	7.77	7.82	7.85
p value	0.83	1.07	1.27	1.14	1.28	1.29
CCT (mm)	0.583	0.590	0.581	0.587	0.582	0.588
M (dioptres)	-1.75	0.25	-0.25	0.50	-0.25	0.50
Vision (VAR)	62	103	103	100	104	105
BCVA (VAR)	105	103	104	100	104	105

The iron ring was noted at the six month aftercare visit (Fig Aiii.1). No data is available for the three month visit as the individual was unable to attend at this time. This individual had dark irides which is in agreement with Rah et al (2002). His initial refractive error of SE -1.75D may be considered as only moderate rather than significant as suggested by Rah et al (2002). This individual had undergone the majority of refractive change after one night of lens wear. The refractive results after the one night visit are within expected repeatability values (Shah et al 2009).



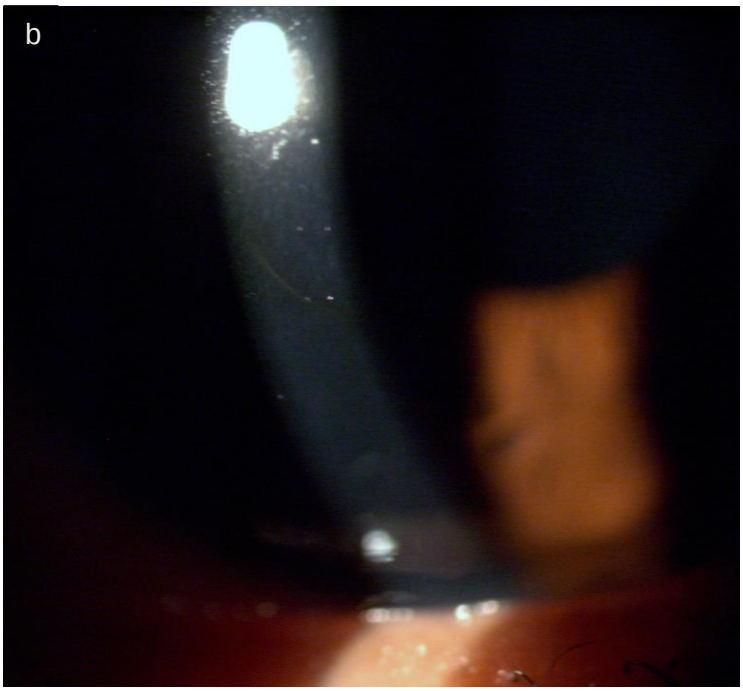


Figure Aiii.1: Iron ring seen in one participant after six months of lens wear. Image a) was taken using the cobalt blue filter; Image b) was taken without filters.

The ring, as seen in Figs Aiii.1a & b, appears in the mid peripheral cornea at the junction of the reverse curve. No other adverse changes were noted and the subject continues to wear orthokeratology lenses.

APPENDIX E: Anonymised example of data collection sheets for each visit

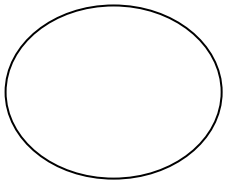
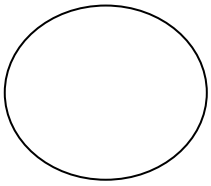
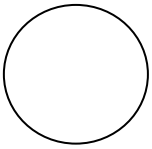
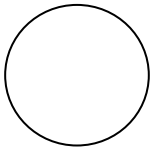
Collection appointment

<table>
<tr><td colspan="2">DATE</td><td colspan="2">10/11/2006</td></tr>
<tr><td colspan="2">NAME</td><td colspan="2">P V</td></tr>
<tr><td colspan="2">APPOINTMENT TYPE</td><td colspan="2">One Hour</td></tr>
<tr><td colspan="4">LENS SPECIFICATION AND TYPE
RIGHT C5 LEFT Aspheric</td></tr>
<tr><td colspan="2">VISUAL ACUITY RIGHT</td><td>LOGMAR 6</td><td>108</td></tr>
<tr><td colspan="2">LEFT</td><td>LOGMAR 6</td><td>100</td></tr>
<tr><td colspan="2">Binocular Acuity</td><td colspan="2">107</td></tr>
<tr><td colspan="2">VISION RIGHT</td><td>LOGMAR 6</td><td>100</td></tr>
<tr><td colspan="2">LEFT</td><td>LOGMAR 6</td><td>106</td></tr>
<tr><td colspan="2">Binocular Acuity</td><td colspan="2">105</td></tr>
<tr><td colspan="2">FLUORESCEIN PATTERN RIGHT
Bull’s eye ring pattern</td><td colspan="2">FLUORESCEIN PATTERN LEFT
Bull’s eye ring pattern</td></tr>
<tr><td colspan="2">STAIN
No stain</td><td colspan="2">STAIN
No stain</td></tr>
<tr><td>REFRACTIVE ERROR RIGHT
-0.50/-0.25*140</td><td>VISUAL ACUITY
108</td><td>REFRACTIVE ERROR LEFT
-0.75/-0.25*180</td><td>VISUAL ACUITY
106</td></tr>
</table>

FURTHER INSTRUCTIONS or COMMENTS

As 1st time RGP wearer then use evening wear sessions to get used to handling and wear for first overnight on Thursday 16th November. Next appointment: 8.30a.m. Friday Nov 17th

First overnight visit

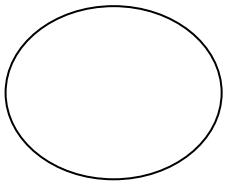
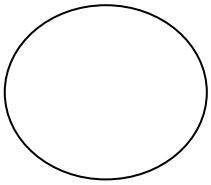
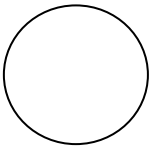
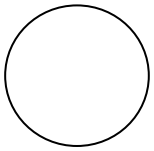
DATE		17/11/2006	
NAME		P V	
APPOINTMENT TYPE		1st overnight	
LENS SPECIFICATION AND TYPE RIGHT C5		LEFT Aspheric	
VISUAL ACUITY RIGHT		LOGMAR 6	
LEFT		LOGMAR 6	
Binocular Acuity			
VISION RIGHT		LOGMAR 6	105
LEFT		LOGMAR 6	108
Binocular Acuity		110	
FLUORESCEIN PATTERN RIGHT Typical ring pattern 		FLUORESCEIN PATTERN LEFT Very Broad ring 	
STAIN Central stain Trace level Efron grade 0.3 		STAIN No Stain 	
REFRACTIVE ERROR RIGHT Plano/-0.25*45	VISUAL ACUITY 105	REFRACTIVE ERROR LEFT plano	VISUAL ACUITY 108

FURTHER INSTRUCTIONS or COMMENTS PTO

Aware of clear portion of vision with inferior ghosting if worn in daylight.

Review 27th November with one week of overnight wear

One week visit

DATE	27/11/2006	
NAME	P V	
APPOINTMENT TYPE	One week	
LENS SPECIFICATION AND TYPE RIGHT C5 LEFT Aspheric		
VISUAL ACUITY RIGHT	LOGMAR 6	
LEFT	LOGMAR 6	
Binocular Acuity		
VISION RIGHT	LOGMAR 6	108
LEFT	LOGMAR 6	108+
Binocular Acuity	109	
FLUORESCEIN PATTERN RIGHT  Lenses removed one hour ago	FLUORESCEIN PATTERN LEFT 	
STAIN  No stain	STAIN No Stain 	

REFRACTIVE ERROR RIGHT	VISUAL ACUITY	REFRACTIVE ERROR LEFT	VISUAL ACUITY
Plano/-0.25*20	108	Plano/-0.50*20	108

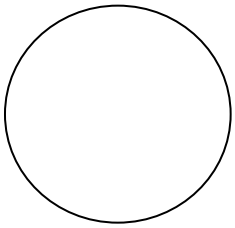
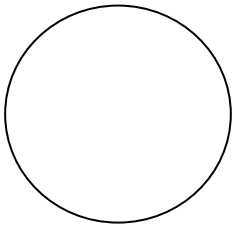
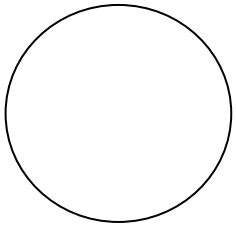
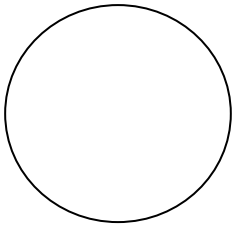
FURTHER INSTRUCTIONS or COMMENTS PTO

No difficulties since last visit

Very happy with lenses

Advised to use rewetting drops in the morning

One month visit

DATE		08/01/2007	
NAME		P V	
APPOINTMENT TYPE		One Month	
LENS SPECIFICATION AND TYPE RIGHT C5 LEFT Aspheric			
VISUAL ACUITY RIGHT		LOGMAR 6	108
LEFT		LOGMAR 6	109
Binocular Acuity		109	
VISION RIGHT		LOGMAR 6	108
LEFT		LOGMAR 6	109
Binocular Acuity			
FLUORESCEIN PATTERN RIGHT Good edge lift Central annular pattern 		FLUORESCEIN PATTERN LEFT Good edge lift Ring pattern less well defined 	
STAIN Superior conjunctival arcuate stain from lens binding 		STAIN Superior conjunctival arcuate stain from lens binding 	
REFRACTIVE ERROR RIGHT Plano/-0.25*70	VISUAL ACUITY 108	REFRACTIVE ERROR LEFT Plano/-0.25*45	VISUAL ACUITY 109

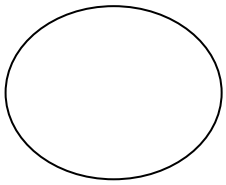
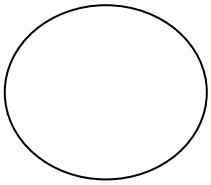
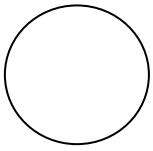
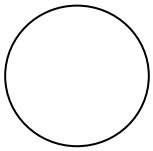
FURTHER INSTRUCTIONS or COMMENTS PTO

No difficulties since last visit

Now able to wear alternate nights without any subjective problems.

Review in 3 months

Three months visit

DATE		02/04/2007	
NAME		P V	
APPOINTMENT TYPE		Three months	
LENS SPECIFICATION AND TYPE RIGHT C5 LEFT Aspheric			
VISUAL ACUITY RIGHT		LOGMAR 6	
LEFT		LOGMAR 6	
Binocular Acuity			
VISION RIGHT		LOGMAR 6	108
LEFT		LOGMAR 6	107
Binocular Acuity		110	
FLUORESCEIN PATTERN RIGHT ½ mm edge lift 		FLUORESCEIN PATTERN LEFT ½ mm edge lift Slightly toric appearance 	
STAIN FB trace 12 o'clock limbus – Efron grade 0.5 Vessels quiet Marked limbal arcades nasal 		STAIN Clear vessels quiet 	
REFRACTIVE ERROR RIGHT plano	VISUAL ACUITY 108	REFRACTIVE ERROR LEFT plano	VISUAL ACUITY 107

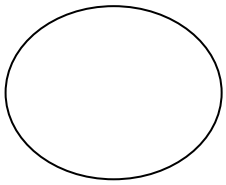
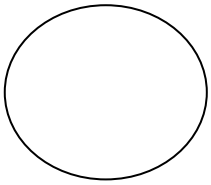
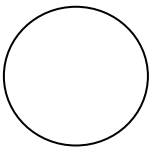
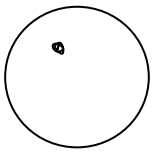
FURTHER INSTRUCTIONS or COMMENTS PTO

No difficulties since last visit

Alternate nights worn

Aware by 5.00pm on second day that vision just beginning to drop.

Six months visit

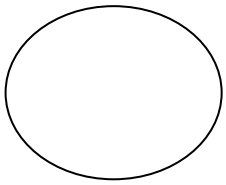
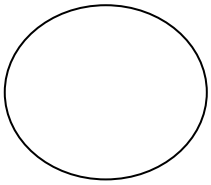
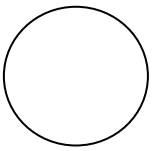
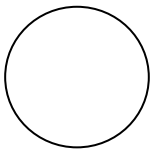
DATE		23/07/2007	
NAME		P V	
APPOINTMENT TYPE		6 months	
LENS SPECIFICATION AND TYPE RIGHT C5 LEFT Aspheric			
VISUAL ACUITY RIGHT		LOGMAR 6	
LEFT		LOGMAR 6	
Binocular Acuity			
VISION RIGHT		LOGMAR 6	107
LEFT		LOGMAR 6	106
Binocular Acuity		109	
FLUORESCEIN PATTERN RIGHT Classic bull's eye 		FLUORESCEIN PATTERN LEFT Classic bull's eye 	
STAIN Minor central punctate stain Efron Grade 0.2 		STAIN Small defect in epithelium Efron Grade 0.4 	
REFRACTIVE ERROR RIGHT -0.25DS	VISUAL ACUITY 107	REFRACTIVE ERROR LEFT -0.25/-0.25*60	VISUAL ACUITY 106

FURTHER INSTRUCTIONS or COMMENTS PTO

No difficulties since last visit

Wearing alternate nights, can leave for two nights but aware of reduction in acuity on second evening

One year visit

DATE		19/11/2007	
NAME		P V	
APPOINTMENT TYPE		12 months	
LENS SPECIFICATION AND TYPE RIGHT C5 LEFT Aspheric			
VISUAL ACUITY RIGHT		LOGMAR 6	108
LEFT		LOGMAR 6	109
Binocular Acuity		110	
VISION RIGHT		LOGMAR 6	108
LEFT		LOGMAR 6	109
Binocular Acuity		109	
FLUORESCEIN PATTERN RIGHT Classic bull's eye 		FLUORESCEIN PATTERN LEFT Classic bull's eye 	
STAIN Minor central punctate stain Efron Grade 0.1 		STAIN Minor central punctuate stain Efron Grade 0.1 	
REFRACTIVE ERROR RIGHT Plano	VISUAL ACUITY 108	REFRACTIVE ERROR LEFT Plano	VISUAL ACUITY 109

FURTHER INSTRUCTIONS or COMMENTS PTO

No difficulties since last visit

Can wear every third night but aware of just beginning to deteriorate in extreme distance