USING CORNEAL CHARACTERISTICS TO PREDICT CORNEAL CHANGE IN OVERNIGHT ORTHOKERATOLOGY

A thesis presented to the graduate faculty of the New England College of Optometry in partial fulfillment of the requirements for the degree of Master of Science

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This manuscript has been read and accepted by the Thesis Committee in satisfaction of the thesis requirement for the degree of Master of Science.

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The New England College of Optometry, 2009

PURPOSE

The primary purpose of this study was to investigate the potential relationships between corneal characteristics (corneal hysteresis (CH) and corneal resistance factor (CRF)) and changes as a result of orthokeratology treatment to see if the corneal properties were predictive of corneal change. Changes in corneal properties throughout the study period were also examined. Another aim of this study was to examine the differences in baseline CH and CRF and outcomes of treatment between adults and children. Patient satisfaction with treatment and perception of eye comfort throughout the study were also investigated.

METHODS

This study included 41 myopic patients new to orthokeratology lens wear. These patients were fit with Contex OK-E system orthokeratology lenses and were followed for three months for a total of six visits each. These visits included baseline, lens dispensing and one day, one week, three week and three month follow up points. Corneal characteristics (CH and CRF) were measured with the Reichert Ocular Response Analyzer at each visit. Other measurements included were uncorrected logMAR visual acuities, manual keratometry, corneal topography using the Humphrey Atlas Topographer, non-cycloplegic subjective refraction and pachymetry using the Sonogage Pachymeter. Patient satisfaction surveys were given at the beginning of the baseline visit and each follow-up visit. Unscheduled visits for adverse events and lens re-fittings were conducted as needed. Refractive measures were converted into power vector format (M, J_{180} and J_{45}). The relationships between corneal properties and measures of corneal change were analyzed using simple linear regression and multiple linear regression analyses.

RESULTS

Thirty patients completed the study and eleven dropped out at various time points before the three month visit. The average age of patients was 24 yrs with a range of 8 yrs to 54 yrs. 46% of the patients were male and 54% were female. A characteristic pattern of corneal change was noted in most patients, with most corneal flattening between the one day and one week follow-up points. There was a statistically significant decrease in central corneal thickness through the study in left eyes only ($p < 0.0008$). Right eyes showed a trend in thinning over time, but the data did not reach statistical significance. There was no difference in mean

baseline CH or CRF for patients successfully completing the study (CH: OD = 10.8, OS = 9.7; CRF: OD = 11.7, OS = 10.8) and those that dropped out (CH: OD = 11.3, OS = 10.1; CRF: OD = 11.2, OS = 10.3; all p-values > 0.01). There was a significant decrease in CRF at the one week and three week time points for right eyes only (p = 0.000003 and p = 0.001 for one and three weeks respectively). Data for left eyes showed a trend for change in CRF but did not reach statistical significance (p-values > 0.01).

With all patient data included as a whole, there were no significant relationships between corneal properties (CH and CRF) and change in corneal apical power, refractive error values or visual acuity (all p-values > 0.01). When patient data was grouped according to baseline refractive error (M), there was a statistically significant relationship between baseline CH and apical power change at the one week time point in group 1 (M = 2.00D or less) (p=0.004, R^2 value=0.631). There was also a statistically significant relationship between baseline CRF and change in visual acuity at the three month time point after adjusting for baseline M values for left eyes only (p=0.007). Otherwise, no significant relationships were found between CH or CRF and corneal apical power, refractive error or visual acuity change when analyzing the data separated into baseline refractive error (M) groups.

There was not a significant difference in CH or CRF between adults and children (all p-values > 0.01). There was a significant difference in mean age for patients successfully completing the study (20.87 yrs) and for patients discontinuing from the study (34.09 yrs) (p=0.005).

Patient satisfaction surveys showed overall lower perceptions of improvement in acuity with treatment at the one day visit (13% excellent and 20% good) compared to the three month visit (48% excellent and 45% good).

CONCLUSIONS

It appears unlikely that corneal characteristics can be used to reliably predict corneal change in orthokeratology, at least in a clinical setting.

Central corneal thickness and CRF values both decreased significantly over the study period, however, the findings were not consistent across both eyes. It is unclear whether or not the change in CRF represents an overall reduction in corneal rigidity brought about by orthokeratology treatment.

It appeared that children were more successful than adults with orthokeratology treatment in this study. This finding was not due to differences in baseline corneal properties between children and adults.

Patients in this study were less satisfied with their vision during the first few weeks of treatment.

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Introduction

Orthokeratology Overview

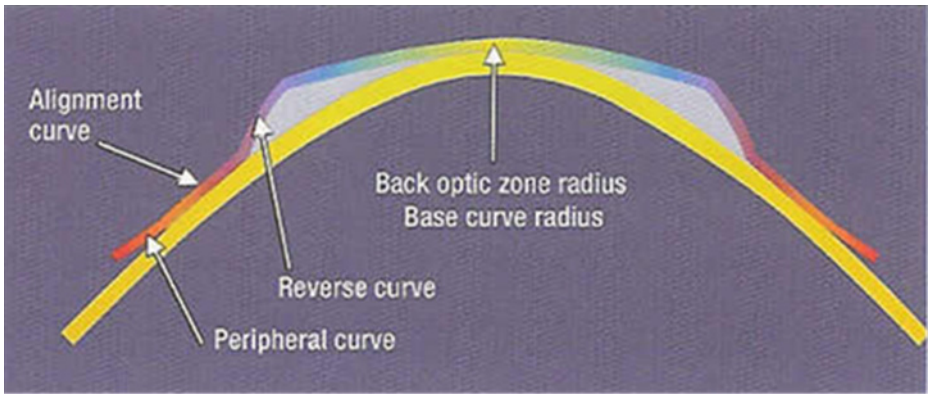
Overnight orthokeratology has been defined as the application of specially designed rigid contact lenses for the purpose of reducing a patient's myopic refractive error (Mountford, 2004). The procedure involves flattening a central area of the cornea, thus reducing its refractive power. This, in turn, reduces the refractive error of the eye. The principle of flattening the cornea with contact lenses was discovered in the early 1950s (Swarbrick, 2006). Doctors noticed that patients' corneas were gradually being flattened with daytime PMMA contact lens wear. This was true especially when the lenses were fit flat with respect to the steepness of the cornea. In the 1960s, George Jessen introduced a technique that he called orthofocus (Swarbrick, 2006). He fit rigid contact lenses slightly flatter than the curvature of the cornea. This produced an overall flattening effect of the cornea and reduced myopic refractive error. This procedure showed modest success but had several problems. The lenses were hard to center on the cornea because of the flat base curve and the reduction in refractive error took weeks to months to occur.

In the 1970s, orthofocus was renamed orthokeratology (Swarbrick, 2006). Several practitioners became interested in the procedure and started making modifications to the lenses. This continued throughout the 80s and 90s with few improvements in treatment time or patient success. The first scientific studies of orthokeratology began in the 1970s as well (Swarbrick, 2006).

In the early 1990s, several changes in rigid contact lenses provided for a renewed interest in orthokeratology. New lens materials were introduced that allowed for a higher level of oxygen to be transmitted through the lens and to the eye (Swarbrick, 2006). These new lens materials were deemed safer for the eye, even for overnight wear. Additionally, a new lens design was introduced during this time period, called the reverse geometry lens (Swarbrick, 2006).

Reverse Geometry Lens Design

In the reverse geometry lens design, the back surface of the lens was modified to create four distinct zones of differing curvatures (Figure 1). The most central zone on the lens is called the back optic zone and is responsible for flattening the central portion of the cornea. Moving from center to periphery, the next area is called the return zone. It is an area of steeper curvature and provides an area of tear film pooling. The next zone is called the alignment zone and it is flatter than the reverse curve. This area is important in centering the lens on the cornea. The most peripheral zone on the lens is called the peripheral curve and is responsible for tear exchange under the lens.



Bausch & Lomb, "A Guide to Overnight Orthokeratology", 2004.

Figure 1: Cross section of an orthokeratology lens on the cornea (yellow line).

The reverse geometry lens, made in the new lens materials, was approved for overnight wear in 2002 (Barr, Rah, Jackson and Jones, 2003). With the new design, the lenses were much easier to center on the cornea and a noticeable reduction in refractive error was seen virtually overnight. Full treatment effects were generally seen within five to ten days of the initiation of treatment. This new method was named accelerated orthokeratology because of the speed at which the treatment effects were achieved. Currently, most patients wear the lenses overnight and the reverse geometry design is used.

Orthokeratology Fitting Philosophy

Orthokeratology lenses were fit using baseline flat keratometry values and spherical refractive error. The lens was fit slightly flatter than the flat keratometry value. By doing this, the lens induces corneal flattening centrally. As a result, the refractive power of the cornea is reduced and the myopic refractive error is reduced or eliminated (Mountford, 2004). Lenses

are obtained from a diagnostic fitting set and the initial lens choice is based on the keratometry and refractive values. The fit is assessed with fluorescein. The fit of the lens is then fine tuned using the fluorescein pattern. Often, several lenses are trialed before an acceptable fit is found. In general, a well fitting orthokeratology lens will center on eye closure and will demonstrate a characteristic fluorescein pattern. This pattern is illustrated in Figure 2. A 3-4mm area of central bearing is surrounded by a 1mm wide ring of pooling. The midperiphery shows alignment and the periphery shows good edge clearance. The diagnostic lens fitting method is the one most often used, however, empirical fitting has also been shown to be an effective method (El Hage, Leach, Miller, Prager, Marsack, Parker, Minavi and Gaume, 2007).

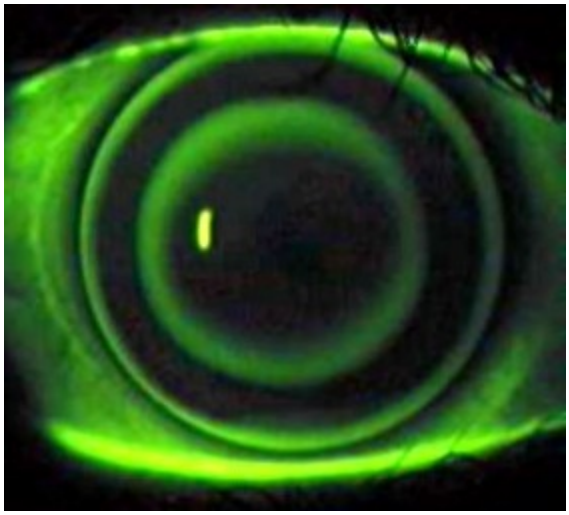


Figure 2: Illustration of fluorescein pattern under a properly fitting orthokeratology lens. Image obtained from http://www.mncontactlensinstitute.com/crt.jpg.

The lenses are worn every night for the first several months of treatment. On average, most patients show full correction around the one week point of lens wear (Swarbrick, 2006). Further corneal changes past the one week point are insignificant in most patients (El Hage et al., 2007). Most patients show a regression in treatment effect throughout the waking hours, generally between 0.25 and 0.75D of a myopic shift (Swarbrick, 2006). For this reason, patients are generally over-corrected by a half Diopter to account for this regression. In addition, a greater magnitude of regression occurs on the first day after lens wear versus the level of regression seen on the eighth day (Johnson, Carney, Mountford, Collins, Cluff and Collins, 2007).

Safety of Orthokeratology Treatment

Orthokeratology is generally considered to be a safe and effective treatment for myopia (Swarbrick, 2006). There is a slightly increased risk of infection associated with overnight lens wear of any type of lens (Swarbrick, 2006). A collection of case reports of microbial keratitis in orthokeratology lens wearers was inconclusive regarding the risk involved in orthokeratology. Clear conclusions about the incidence of microbial keratitis in orthokeratology patients could not be made for several reasons. These included the lack of accurate data regarding the total number of patients wearing the lenses, patient compliance and lens materials (Watt and Swarbrick, 2005). Most patients in this study were from Asian countries and were between the ages of 9 and 15 (Watt and Swarbrick, 2005). In these countries, orthokeratology lenses are often prescribed for children in the hope that they may slow the development of myopia (Watt and Swarbrick, 2005). Only three of fifty cases were

from the United States. It is not clear whether there is a higher risk for adverse events in the Asian population or if the higher incidence of keratitis is due to the presumably higher number of patients wearing the lenses in these areas (Watt and Swarbrick, 2005).

Increased interest in the use of orthokeratology lenses with children has been seen in the literature. This is perhaps due to the large numbers of children and adolescents that wear the lenses worldwide (Watt and Swarbrick, 2005). In a small sample pilot study, correction of myopia using orthokeratology lenses was found to be safe and effective in children and adolescents (Mika, Morgan, Cron, Lotoczky and Pole, 2007). In addition, minimal corneal staining was noted and no cases of microbial keratitis were reported (Mika et al., 2007). In the current study, both children and adults were recruited for participation.

Overall, orthokeratology appears to be an effective option for the correction of myopia and shows minimal side effects. Orthokeratology patients were not shown to have any decrease in best-corrected visual acuity in a short-term study on lens wear (Johnson et al., 2007). In addition, there was no significant change from baseline in contrast sensitivity or high and low contrast visual acuity seen in these patients (Johnson et al., 2007). One of the most common visual side effects from treatment is the experience of glare or halos around lights in dim conditions (Swarbrick, 2006). This side effect can be reduced by increasing the size of the central treatment zone.

Corneal Changes in Orthokeratology

As a result of orthokeratology treatment, the central cornea flattens and the mid-peripheral cornea steepens (Swarbrick, Wong and O'Leary, 1998). It is known that orthokeratology lenses work mainly on the anterior corneal tissue, however it is not clear whether the effect is mainly on the epithelium, anterior stroma, or both (Swarbrick et al., 1998). In addition, there are several theories on which forces are involved in inducing corneal change in orthokeratology. One theory proposed that the downward pressure of the central portion of the orthokeratology lens was flattening the underlying corneal epithelial cells (Swarbrick et. al., 1998). Another theory proposed that the orthokeratology lens created an outward pulling pressure in the tear film. This pressure gradient was thought to pull the epithelial cells peripherally, thus creating a re-distribution of epithelial cells in the cornea (Swarbrick et. al., 1998). As a result of this re-distribution, there is a relative flattening in the central cornea compared to the mid-peripheral cornea. Still another theory proposed that the corneal stroma was being changed by orthokeratology lenses, along with the epithelium (Soni, Nguyen and Bonanno, 2004).

Several histological and morphological studies have investigated the effect of orthokeratology lenses on the corneal cell layers and the forces that may be involved in these changes. A recent study on primate corneas demonstrated cellular changes at the level of the corneal epithelium and stroma after a short period of closed-eye lens wear (Cheah, Norhani, Bariah, Myint, Lye and Azian, 2008). Specifically, the corneal epithelial cells showed focal compression rather than re-distribution or loss of cell layers in the central cornea. The main

changes in cell morphology were seen in the wing and basal cells. In the midperiphery, the corneal epithelium was thickened mainly in the squamous and basal cells. This study also showed central stromal thinning and mid-peripheral stromal thickening. Both mechanical compression and tear film pressure gradients were noted as potential forces acting on the cornea in this study.

Another recent histological study on cat corneas showed thinning of the central corneal epithelium and thickening of the mid-peripheral corneal epithelium (Choo, Caroline, Harlin, Papas and Holden, 2008). This study also showed that in short term wear (4-8 hours), the epithelial cells showed compression. However, with longer wear times (14 days), epithelial cell proliferation was seen in the mid-periphery. This study also showed central stromal thinning after 14 days of lens wear. The exact mechanism contributing to these changes was hypothesized to be cellular metabolic changes, lens-induced pressure forces or corneal edema.

Another study showed that the corneal epithelium was thinned centrally and thickened mid-peripherally in human subjects who wore orthokeratology lenses for one hour (Lu, Simpson, Sorbara, and Fonn, 2008). These changes were found to occur after just fifteen minutes of lens wear in human subjects (Lu et al., 2008). However, these corneal changes were variable depending on the patient, suggesting that there may be individual differences in corneal malleability (Lu et al., 2008). Histological and morphological studies are providing insight into how the cornea is affected by orthokeratology lens wear. Even so, it is still unclear which forces specifically are contributing to these corneal changes.

Predicting Corneal Change with Orthokeratolgy

Research studies have shown that there are only certain patients who are good candidates for orthokeratology treatment. Generally, patients with refractive errors between -1.00 D and -5.00 D are best suited for treatment. Additionally, these patients can have no more than -1.50 D of with the rule astigmatism or -0.75 D of against the rule astigmatism (Caroline, 2001). Since orthokeratology does not fully correct astigmatism, patients outside of these ranges are less likely to be successful with treatment. Currently, there are not many ways to predict how the cornea is going to change in orthokeratology. The initial amount of refractive error can be used to predict how fast the treatment effects will take place (Carkeet, Mountford and Carney, 1995). Specifically, those patients with higher refractive errors take longer, on average, to show full treatment effects. Those patients with lower baseline refractive errors achieve full correction more quickly.

It has also been noted that children's corneas seem to change more quickly than adults with orthokeratology treatment (Subramaniam, Bennett, Lakshminarayanan and Morgan, 2007). Another study on the effects of orthokeratology with respect to age concluded that there was reduced corneal flattening, refractive outcome and central corneal thinning in older patients after one hour of lens wear (Jayakumar and Swarbrick, 2005). The authors hypothesized that this could be due to the reduced wound healing response seen in older corneas. These studies provide general guidelines, but other properties of the cornea may influence how the changes occur during treatment.

Ocular and corneal rigidity have been investigated for possible use as a predictor in orthokeratology (Carkeet et al., 1995). In the past, rigidity was measured using a mathematical equation that included a measurement of eye pressure. The rigidity measurement was thus restricted to the eye as a whole. Recently, a new method of measuring corneal rigidity in isolation was introduced.

Reichert Ocular Response Analyzer

The Reichert Ocular Response Analyzer (ORA) is an automated non contact tonometer with a modified testing procedure and new software that gives intraocular pressure (IOP) readings along with measurements of certain corneal properties. During the testing, a traditional non-contact tonometer flattens the cornea with a puff of air. A light detection system measures when the cornea is in a flattened state, and a pressure measurement is taken. The ORA also flattens the cornea and takes a pressure measurement, but the air puff continues after the first flattening and indents the cornea slightly. The pressure of the air puff is then weakened and the cornea is allowed to "bounce back" to its original shape. During this time, the cornea flattens again, giving another applanation point. At this point in time another pressure measurement is taken. At the conclusion of the exam, a graph illustrating the pressure at the various stages of the test is produced and four measurements are given. An explanation of the graph obtained during analysis is shown in Figure 3.

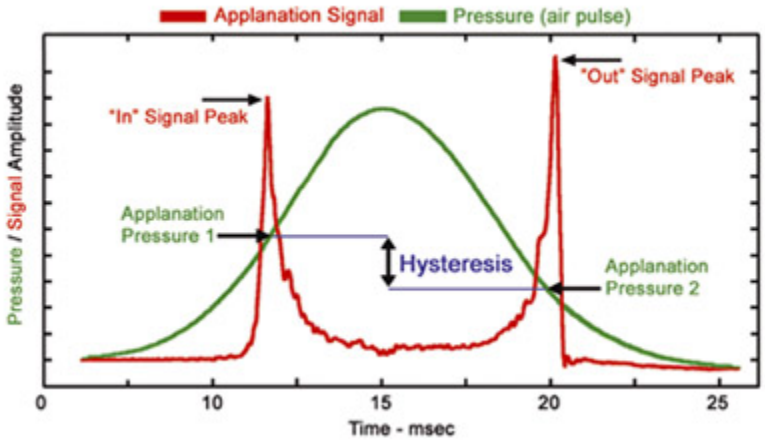


Figure 3: Illustration of the graph obtained from corneal analysis with the Reichert ORA. Green line – pressure output, red line – applanation signal (corneal response). X axis – time in msec, Y axis – pressure and signal amplitude. Applanation pressure readings are taken at the two points where the green and red lines cross. Corneal hysteresis is the difference between the pressure measurements at these two points. Image from: http://www.ocularresponseanalyzer.com/how.html.

The first two measurements, IOP_G and IOP_{CC} are Goldmann-corrected IOP and corneal resistance-corrected IOP respectively (Luce, 2005). The third measurement is called corneal hysteresis (CH) and is a measurement of the visco-elastic properties of the cornea (Luce, 2005). It can be thought of as a measure of the ability of the cornea to both absorb and dissipate energy (Luce, 2005). It is calculated as the difference in the amount of pressure needed to produce the two applanation points. Corneas with lower CH values are considered to be "softer" than those with higher measurements (Luce, 2005). The fourth measurement, corneal resistance factor (CRF) gives a measurement of the overall corneal rigidity or stiffness (Luce, 2005). It is derived from the CH measurement (Luce, 2005). CRF is an indicator of how moldable the cornea is and this could have predictive value in

orthokeratology. CH is also a measurement that could be useful in predicting orthokeratology outcomes.

Several studies have been done with the Reichert ORA in order to determine population norms for CH and CRF values as well as to gain further understanding of the relationship between corneal properties and intraocular pressure measurements. In one study, CH measurements were shown to be repeatable on individual eyes but were different from person to person (Luce, 2005). The CH values for right and left eyes were also highly correlated (Luce, 2005). The average CH value in a population of normal patients was found to be 12 – 13 mmHg with a range between 8 and 18 mmHg and standard deviation of 1.90 mmHg (Luce, 2005). The CH values for adults and children were also found to be similar (Kirwan, O'Keefe and Lanigan, 2006). CH value was not correlated with corneal radius, astigmatism, visual acuity or axial length, suggesting that CH is truly a new parameter for measuring corneal properties (Luce, 2005). It was also shown to be independent of intraocular pressure and to remain constant throughout the day while intraocular pressure showed a diurnal variation (Laiquzzaman, Bhojwani, Cunliffe and Shah, 2006).

CRF is a measurement of the effects of both the viscous and elastic properties of the cornea (Luce, 2005). It was found to be affected by intraocular pressure, but only with significantly high pressures (Luce, 2005). CRF was found to be around the same value as CH in the study of a population of normal patients with a standard deviation of 2.08 mmHg; however, it was considered a distinct and separate measurement from CH. This was because of the person to person variability in the measurement (Luce, 2005).

Relating the Reichert ORA to Orthokeratology

A few recent orthokeratology studies have been done using the Reichert Ocular Response Analyzer to determine corneal properties. A significant correlation between CH and rate of corneal change was found in one study (Gonzalez-Meijome, Villa-Collar, Queiros, Jorge and Parafita, 2008). Specifically, for a three hour period of lens wear, a significant correlation was found between CH and changes in steep keratometry values (Gonzalez-Meijome et al., 2008). CH was also correlated with changes in central corneal thickness in this study. It appeared that corneas with higher CH values showed less change compared to those corneas with lower CH values (Gonzalez-Meijome et al., 2008). There was also a trend for corneas with higher CRF values to show less change over the three hour wearing period, but there was no significant correlation found (Gonzalez-Meijome et al., 2008).

Another study determined that on average, CRF decreased over a period of one month of lens wear (Chen, Lam and Cho, 2008). CH did not change significantly over the six month time period of this study (Chen et al., 2008).

Summary and Purpose

The purpose of this study was to determine if CH and CRF values can be used in a clinical setting for predicting the amount of corneal change in overnight orthokeratology treatment. It was hypothesized that corneas with higher CH and CRF values would be slower to change when compared to corneas with lower CH and CRF measurements. The relationship between patient age and corneal change was also examined. Another aim for this study was to examine the relationship between corneal properties and success with orthokeratology treatment. Finally, patient perceptions of orthokeratology throughout the treatment period were determined through the use of satisfaction surveys.

Methods

Study Design

Patients were examined at six visits throughout the study by the Principal Investigator (Dr. Marjorie Rah) and research assistant (Kristin Glavine). These visits included a baseline visit, lens dispensing visit and four follow-up visits (one day, one week, three weeks and three months after beginning lens wear). Extra visits were included for lens re-fitting or other issues as needed.

Subjects

This study included 41 myopic patients interested in orthokeratology. The patients received free contact lenses, solutions and contact lens cases during the study. Patients were recruited for the study in several ways. The names of some of the study participants were obtained from a waiting list of patients interested in participating in orthokeratology studies maintained by the principal investigator. Other patients in the study were recruited by the principal investigator from the New England Eye Institute Clinic. Any patient attending an exam at the clinic and expressing an interest in trying orthokeratology was informed about the study. Another group of patients was recruited by referral from other patients. Finally, several participants were recruited from a list of patients interested in any upcoming contact lens study. This list was also maintained by the principal investigator.

All patients were treated in accordance with the Declaration of Helsinki and all study procedures were approved by the New England College of Optometry Institutional Review

Board. Patients read and signed informed consent documents before beginning participation in the study. Patients were also able to discontinue their participation in the study at any time.

Inclusion Criteria

Male and female patients of all racial/ethnic and religious backgrounds were recruited into this study without bias. For inclusion in the study, the patients had to meet the entry criteria listed below:

- 8 years or older at the time of the baseline visit
- Non-cycloplegic spherical refractive error of -1.00 to -5.00 D inclusive. Cylindrical refractive error no more than -1.50 DC axis +/- 180 degrees or no more than -0.75 DC at any other axis orientation
- Free of eye disease and binocular vision problems that may have affected contact lens wear
- Free of systemic diseases that may have affected vision or the ability to safely and successfully wear contact lenses

Exclusion Criteria

1. Patients with abnormal or severe dry eye, blepharitis or other ocular conditions that may have interfered with results
2. Patients with signs of keratoconus, or other corneal disorders
3. Patients with pupil size larger than 5 mm in normal lighting
4. Patients who were current rigid gas permeable lens wearers

5. Patients who had intraocular or corneal surgery of any kind
6. Patients who were taking or were planning to take medication that may cause dry eye or affect vision, corneal curvature or healing
7. Patients who were pregnant or nursing or who may have become pregnant during the course of the study

Study Materials

Bausch & Lomb received FDA approval for their Vision Shaping Treatment™ in June 2004. The Vision Shaping Treatment™ includes four different orthokeratology lens designs made with Boston Equalens II (oprifocon A) material. The Vision Shaping Treatment lens used in this study, the Contex OK-E System lens, had a reverse geometry design and was FDA approved for overnight wear. These lenses were fit according to flat K readings, target myopic reduction in Diopters and degree of corneal eccentricity. They are available in the following parameters:

Target Powers	Plano to -5.00 D
Optical Zone	6.0 to 7.0 mm
Flat Central K	41.00 to 46.00 D
Powers	+0.75 to +1.00 D

The lenses for this study were chosen partially for ease of fitting and partially to ensure proper lens wear by the patient. The Contex OK-E system includes a diagnostic fitting set and also allows for lenses to be fit empirically using the patient's refractive error and corneal characteristics. The lenses that are dispensed to patients are tinted red and yellow.

The red lens is worn in the right eye and the yellow lens in the left eye. This ensures that the lenses are not inadvertently switched by the patient.

Study Procedures

Patients must have had a complete eye examination, including dilated fundus examination, performed by a licensed O.D. or M.D. within one year prior to the baseline visit. This requirement was met by obtaining a copy of the patient's medical record. If the patient had not had a complete eye exam, a complete eye exam was performed by a licensed O.D. at the baseline visit of this study. Patients were seen at the same time of day for every visit whenever possible. This was done to reduce variability in the Reichert Ocular Response Analyzer measurement since it is known that there is a diurnal variation in intraocular pressure.

Baseline Visit

Participants were examined for inclusion/exclusion criteria during the baseline visit. At this visit, a brief patient ocular and medical history was taken and a full slit lamp examination was performed.

Orthokeratology lenses were fit at the baseline visit using a diagnostic lens. The initial diagnostic lens was determined from flat K readings, target myopic reduction (manifest sphere refraction) and corneal eccentricity from topography measurements. For some low myopic refractive errors, diagnostic lenses were not available. In these cases, a lens was ordered directly from the manufacturer based on the above criteria.

Anesthetic drops were administered prior to lens insertion. If the fit of the first diagnostic lens was unacceptable, a second diagnostic lens was used with different parameters. This process continued until an acceptable fit was obtained. An acceptable fit was defined as a well-centered lens demonstrated on eye closure, not necessarily while the eye was open. Additionally, the fluorescein pattern demonstrated a 2-4mm area of central bearing surrounded by a bright and narrow ring of fluorescein pooling. All acceptable fits also demonstrated alignment to moderate bearing in the alignment zone and good edge clearance.

All fits were assessed by slit lamp examination of the fluorescein pattern with the lens on the eye. When an acceptable fit was found, lenses were ordered from the manufacturer and the patient returned for a dispensing visit after the lenses arrived.

Dispensing Visit

During the second (dispensing) visit, the fit of the ordered lenses was assessed with a slit lamp using fluorescein stain. If an acceptable fit was found, the patient was instructed to wear the lenses overnight and return the next day for the third visit. The patient was also educated on proper lens care and received lens insertion and removal training. Patient education was supplemented with a take home information sheet (Appendix A). Patients were also provided with disposable soft contact lenses in different powers for use during the first week of treatment. Because vision changes throughout the first few days of treatment, these lenses allowed for clearer vision during this time.

Follow-Up Visits

Four follow up visits were included in this study. The first follow-up visit was the day after the first night of lens wear. The second visit was one week after the first night of wear. For this visit date, there was an accepted range of 6 to 8 days from the initiation of lens wear. The third and fourth visits were at three weeks and three months after the first night of wear, respectively. For each of these visit dates, there was an acceptable range of plus or minus seven days from the actual three week and three month points.

The examination procedures performed at each visit are outlined in Table 1.

Visit	Procedures Performed at Visit
Baseline	• Medical and ocular history (with questionnaire) • Uncorrected logMAR visual acuity (VA_{sc}) • Subjective refraction • Corneal topography and Keratometry • Full slit lamp exam • Non-contact tonometry/CRF measurement • Pachymetry • Diagnostic set fitting of orthokeratology lenses • Snellen visual acuity (VA_{cl}) with orthokeratology lenses • Spherical and cylindrical over-refraction
Dispensing	• Fitting assessment of orthokeratology lenses • Snellen visual acuity (VA_{cl}) with orthokeratology lenses • Spherical and cylindrical over-refraction • Contact lens insertion and removal training • Contact lens care education
All Follow-Up Visits (#1-#4)	• Uncorrected logMAR visual acuity (VA_{sc}) • Full slit lamp exam • Corneal topography and Keratometry • Non-contact tonometry/CRF measurement • Pachymetry • Subjective refraction • Spherical and cylindrical over-refraction

Table 1: Procedures performed at each visit of the study.

Patients were given Boston Simplus™ solution to care for their lenses. Patients were also given contact lens cases and rewetting drops as needed. If patients showed signs or symptoms of solution allergies, they were given Unique pH™ contact lens cleaning and storage system.

Overview of Study Procedures

1. **Visual acuity (VA)**

Patients read standard Bailey-Lovie visual acuity charts to determine uncorrected visual acuities at each visit. Lighting on the chart was kept at a luminance between 96 and 102 cd/m^2. Acuity was measured OD, OS and OU starting at 4 meters. If the patient could not read any letters in the top line at 4 meters, the visual acuity measurement was taken at 2 meters and a correction factor was added to the logMAR calculation. Patients read every letter in each line starting at the top of the chart. The patient was encouraged to read the chart until all letters on a line were missed. LogMAR visual acuities were calculated with the following formula: 0.9-(0.02*Total letters correct) + correction factor. The correction factor for the 4m testing distance was 0.18 and for the 2m testing distance was 0.48.

Snellen visual acuity charts were used to determine best-corrected acuities at the dispensing and follow-up visits at the completion of the subjective refraction. Snellen acuity was measured in a 20 foot room using a standard projector aimed at a reflective surface. The size of the letters on the projected chart were calibrated for the room distance so that a 20/20 letter measured the standard 8.75mm in height.

2. Refraction (non-cycloplegic)

Patients had their spectacle prescriptions determined during subjective refraction at the baseline and all follow-up visits. Refraction was done by the same examiner for all patients and was recorded in spherocylindrical notation. This was later converted to M, J_{45} and J_{180} notation for data analysis.

3. Corneal Topography

Topography maps of the eyes were taken to determine the shape of the cornea at the baseline and all follow up visits. The Humphrey Atlas topographer was used for all patients. A corneal power map was used for data analysis, although tangential and difference maps were used to assess lens fit. Corneal apical power was recorded in diopters for each patient as well as simulated keratometry (SimK) readings.

4. Keratometry

The curvature of the cornea was measured with a B&L standard keratometer. These manual keratometry measurements were compared to the SimK measurements from the topographer to ensure accuracy of data collection.

5. Slit lamp examination

Patients were examined with a slit lamp biomicroscope to assess corneal health and examine the fit of the orthokeratology lenses. Fluorescein (strips wet with sterile saline solution) was used in the patient's eyes during this examination to aid evaluation of corneal staining and lens fit.

6. Ophthalmoscopy/Fundus Biomicroscopy/Binocular Indirect Ophthalmoscopy

The health of the patients' eyes in this study was assessed in one of the aforementioned procedures. In undilated patients, ophthalmoscopy and/or fundus biomicroscopy was performed. In dilated patients (those receiving a complete eye exam at baseline), BIO was performed.

7. Non-contact tonometry

The Reichert Ocular Response Analyzer was used to obtain IOP and corneal property measurements. Three measurements were taken on each eye at the baseline and each follow-up visit. Data points were monitored for accuracy using the corneal waveform graph obtained with each measurement. If the waveform graph suggested an inaccurate measurement, those data points were thrown out and another measurement was taken. The measurement values (IOPg, IOPcc, CH and CRF) were averaged for each visit for each eye.

8. Pachymetry

Patients had central corneal thickness measured by pachymetry using a Sonogage pachymeter. A corneal anesthetic was instilled in each eye before measurement. Five measurements were taken for each eye. These measurements were averaged for each visit. An inaccurate measurement was defined as an outlier more than .015 from the other data points in the set. If this occurred, the data point was deleted and another measurement was taken.

9. **Spherical and cylindrical over refraction using trial lenses**

This procedure assessed the amount of power in the contact lenses and aided in fitting the contact lenses.

Patient Satisfaction Surveys

Patients were given surveys at the baseline and follow up visits to assess satisfaction with orthokeratology treatment at different time points. These surveys were given at the beginning of each exam. The questionnaires also included questions designed to assess visual side effects and comfort. Patients were encouraged to answer honestly and to include additional observations if needed. These surveys are included in Appendix B.

Unscheduled Visits

Unscheduled visits due to lens discomfort, changes in vision or other adverse reactions were given at no charge to the patient at the New England College of Optometry.

Patients were educated fully on the potential risks associated with orthokeratology lens wear. Patients were also educated on proper lens handling and cleaning. In case of an adverse event, patients were instructed to remove the lenses (if wearing them) and to contact the principal investigator or research assistant immediately.

Patients were then examined immediately by the principal investigator, if possible. Patients were also advised to seek care at the New England Eye Institute or at an eyecare professional in the area. Adverse events were reported to the IRB within five days of the occurrence.

Re-fitting Lenses

Several patients' lenses were refit during the study for various reasons. These reasons included patient complaints of visual distortions or halos, poor visual acuity outcome after a reasonable period of lens wear, lens discomfort, lens decentration as evidenced by corneal topography and corneal complications such as increased staining seen on slit lamp examination. The decision to refit lenses was made after the one week time point because that is generally the time at which the full treatment effect is expected. A new pair of lenses was ordered for the patient based on the fit of the previous lens, topography maps, remaining refractive error and any visual symptoms. After assessing the fit of the new lenses, they were dispensed to the patient. If the new fit was acceptable, the patient continued to wear the lenses for the remainder of the study.

If patients needed to discontinue lens wear while in the study due to illness or lens refitting procedures, the follow-up appointment dates were recalculated based on the date when lens wear resumed. This procedure assured that follow-up visit times were standardized and included the same duration of lens wear for all patients.

Data Collection and Management

The primary outcome of this study was change in apical corneal power as measured by corneal topography. Secondary outcomes of this study included change in central corneal thickness, reduction in overall refractive error, subjective changes in visual acuity and changes in CH and CRF. Each outcome was examined for relationships with baseline CH and CRF measurements. Outcomes were also examined for changes over the time course of

the study. Reduction in refractive error was measured in Diopters from subjective refractions. Change in central corneal thickness was calculated (in mm) from pachymetry. Changes in corneal topography were assessed from difference and sagittal maps. Subjective changes in visual acuity were measured from logMAR visual acuity tests and a questionnaire about vision that was given at baseline and each follow up visit (Appendix B). Changes in CH and/or CRF were calculated from Reichert ORA measurements in mmHg.

Statistical Analysis

Data were analyzed using Microsoft Excel. Refractive errors were converted into M, J_{180} and J_{45} notation with the following equations:

$$M = \text{sphere} + (\text{cylinder}/2)$$

$$J_{180} = -(\text{cylinder}/2)\cos(2 \times \text{axis})$$

$$J_{45} = -(\text{cylinder}/2)\sin(2 \times \text{axis})$$

Comparisons between groups were made with two sample t-tests and comparisons between time points were made using paired two sample t-tests. Trends over time were measured with simple linear regression analysis and multiple regression analysis. A more conservative p-value cutoff level of 0.01 for statistical significance was adopted for analyses in this study due to the large number of tests conducted.

Results

Demographics

Thirty patients completed the study and eleven patients dropped out due to various reasons including discomfort with lens wear, visual side effects of treatment and unsatisfactory visual acuity results. The data from ten of these patients was included in the analysis up through the last completed visit in each patient's file. The data from one of the discontinued patients was excluded due to the fact that the patient withdrew from the study before the one day follow-up point. Table 2 summarizes the demographic information for the study patients.

Demographic Characteristics and Baseline Refractive Errors

Age	Mean: 24 Range: 8-54
Gender	Male: 46% Female: 54%
Ethnicity	African American: 9.76% Asian: 19.51% Caucasian: 65.85% Other/Unknown: 4.88%
Mean Spherical Refractive Error at Baseline	Mean OD: -2.96D OS: -2.91D Range OD and OS: -1.00 to -5.00
Number of Patients Completing Each Follow-Up Visit	1 Day: 40 1 Week: 40 3 Week: 36 3 Month: 30

Table 2: Demographic characteristics and mean baseline refractive error of the patients in the study. Total number of patients enrolled in the study at each follow up point.

Pattern of Corneal Change

Over the follow-up period, a characteristic pattern of change was seen in corneal apical power for most patients. This can be described as a gradual central flattening at the first day visit, a large flattening at the one week visit and little to no further change at the next two follow up visits. The most significant changes occurred between the one day and one week follow up points. Change in apical power over time for an average patient is illustrated in Figure 4 (right eye). Similar results were found for both OD and OS in most patients. A typical change in topography patterns from baseline to one week is illustrated in Figure 5.

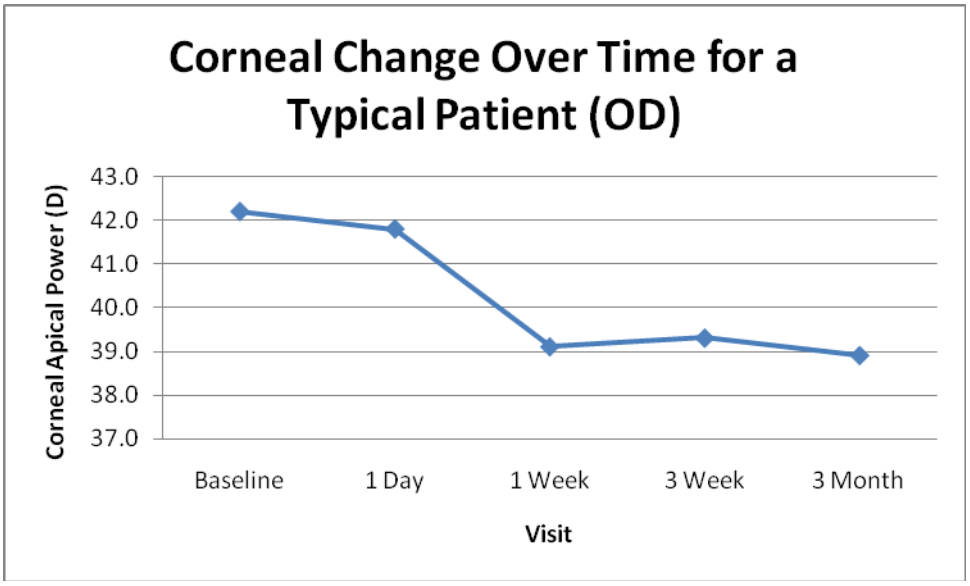


Figure 4: Typical change in corneal apical power from baseline at each follow up visit in the right eye of a single patient. X axis – time of visit, Y axis – corneal apical power in Diopters.

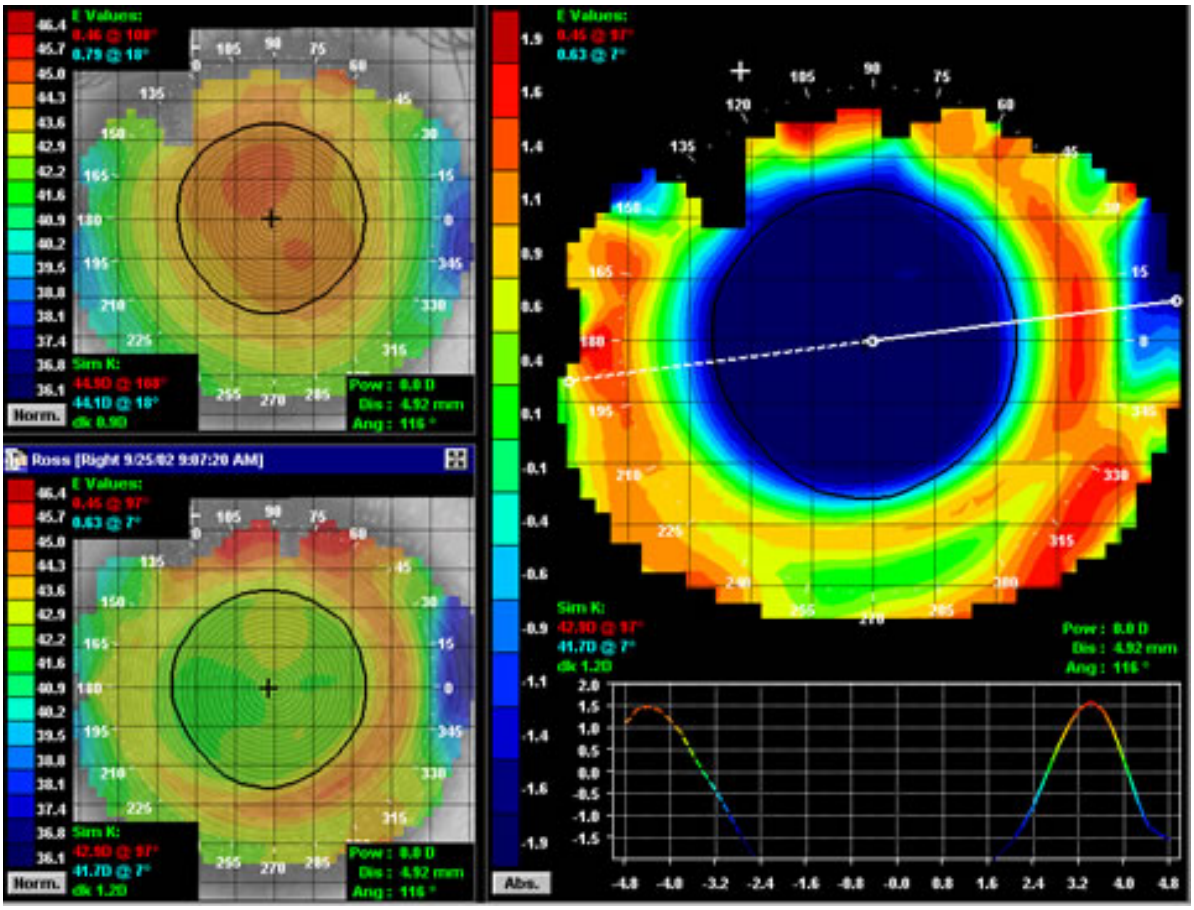


Figure 5: Typical change in corneal topography after one week of orthokeratology lens wear. Top left map – baseline, bottom left map – one week time point. Scale for left maps: red is steepest, blue is flattest. Large right map – difference map between baseline and 1 week maps. Scale for right map: red is relative steepening, blue/green is no change, blue is relative flattening. Image from: http://www.ferris.edu/mco/ptcare/OrthoK/index.htm.

Change in Central Corneal Thickness

There was a statistically significant difference in central corneal thickness as measured by pachymetry when comparing baseline and three weeks as well as baseline and three months for left eyes (p=0.002 and 0.0002 for three weeks and three months respectively). No statistically significant change was seen for the one day or one week time point for left eyes (p=0.714 and 0.092 for one day and one week respectively). No statistically significant changes were seen at any time point for right eyes (p=0.857, 0.053, 0.310 and 0.094 for one day, one week, three weeks and three months respectively). Change in average central corneal thickness over time is demonstrated in Figure 6. Means and standard deviations of central corneal thickness data are included in Table 4.

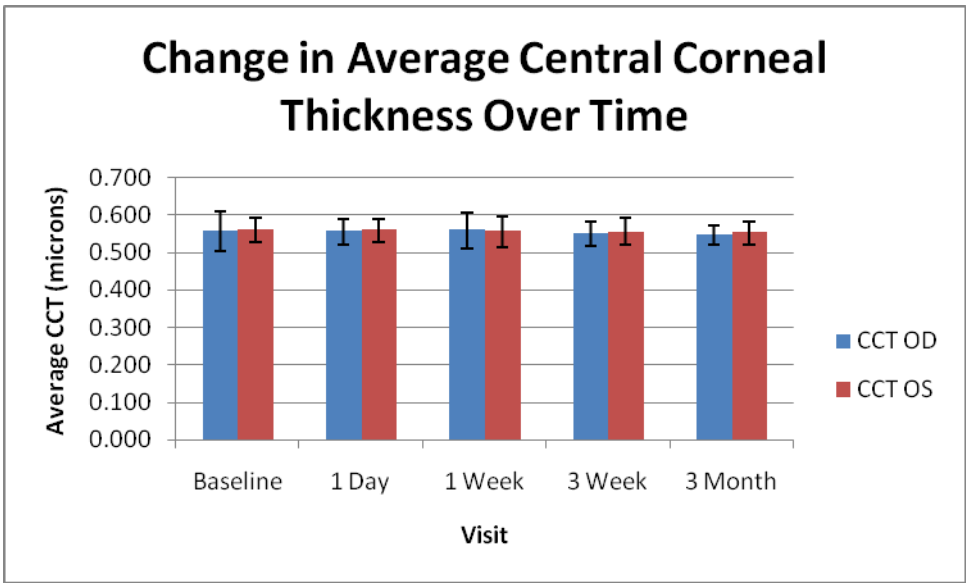


Figure 6: Change in central corneal thickness over time for each eye. X axis: Time of visit, Y axis: central corneal thickness measured in microns.

Central corneal thinning was more pronounced for left eyes in this study. To try and explain this finding, several factors that may be related to change in central corneal thickness were examined for baseline differences between the right and left eyes. There was a statistically significant difference in baseline CH between the right and left eyes in this study ($p = 0.0008$, mean CH = 10.85, 9.88 for right and left eyes respectively). There was also a statistically significant difference in baseline CRF between right and left eyes ($p = 0.0004$, mean CRF = 11.53, 10.70 for right and left eyes respectively). There was no statistically significant difference in baseline refractive error (M) between right and left eyes ($p = 0.196$, mean M = -3.08, -2.99 for right and left eyes respectively).

There was no statistically significant relationship between baseline CH or CRF and change in CCT at the three week or three month time points for either eye in this study (p-values > 0.01 for all comparisons, Table 3).

	CH		CRF	
	OD	OS	OD	OS
Three Weeks	0.004 (0.464)	-0.003 (0.012)	0.003 (0.531)	-0.002 (0.099)
Three Months	0.0001 (0.981)	-0.002 (0.101)	-0.0003 (0.962)	-0.0004 (0.782)

Table 3: Linear regression analysis results for the relationship between baseline CH and CRF with change in central corneal thickness (CCT). Data given as coefficients followed by p-values in parentheses.

Corneal Characteristics and Successful Completion of the Study

There was no statistically significant difference in the mean corneal resistance factor (CRF) for patients successfully completing the study when compared to patients who did not complete the study (OD: mean successful = 11.7 (SD = 3.2), mean unsuccessful = 11.2 (SD =

2.1), p=0.26; OS: mean successful = 10.8 (SD = 2.4), mean unsuccessful = 10.3 (SD = 1.8), p=0.299). There was also no statistically significant difference in mean corneal hysteresis (CH) for patients completing the three month study versus patients who discontinued participation in the study (OD: mean successful = 10.8 (SD = 2.4), mean unsuccessful = 11.3 (SD = 3.9), p=0.42; OS: mean successful = 9.7 (SD = 2.99), mean unsuccessful = 10.1 (SD = 3.2), p=0.74). Figure 7 illustrates the mean baseline (right and left eyes averaged) CRF and CH for patients successfully completing the study and for patients who discontinued from the study. Table 4 includes means and standard deviations of CH and CRF throughout the study.

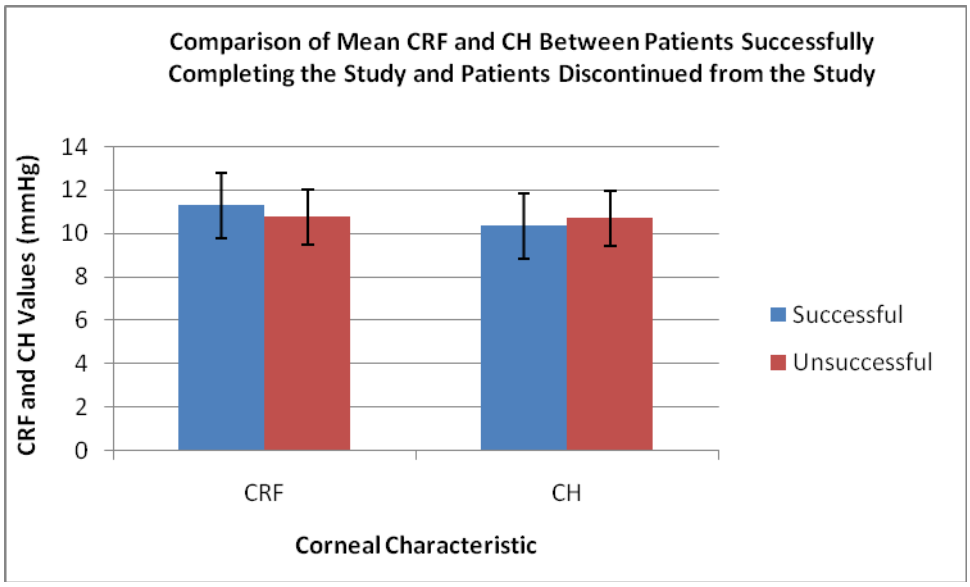


Figure 7: CRF and CH values for patients successfully completing the study (blue) and patients discontinued from the study (red). X axis – corneal characteristic groupings, Y axis – average baseline CRF and CH for right and left eyes measured in mmHg).

		Baseline Mean (SD)	1 Day Mean (SD)	1 Week Mean (SD)	3 Weeks Mean (SD)	3 Months Mean (SD)
CRF (mmHg)	OD	11.53 (1.69)	11.29 (1.90)	10.92 (1.46)	11.10 (2.20)	10.87 (1.89)
	OS	10.70 (1.51)	10.83 (2.30)	10.62 (1.79)	10.62 (1.97)	10.56 (1.59)
CH (mmHg)	OD	10.85 (1.66)	10.94 (1.53)	10.78 (1.45)	11.11 (1.94)	10.71 (1.69)
	OS	9.88 (1.72)	10.47 (2.28)	10.43 (1.71)	10.54 (2.07)	10.32 (1.65)
Central Corneal Thickness (microns)	OD	557 (53)	556 (34)	559 (48)	550 (33)	547 (26)
	OS	559 (34)	558 (31)	555 (42)	555 (36)	552 (31)
M (Diopters)	OD	-3.08 (1.34)	-2.02 (1.25)	-0.66 (1.41)	-0.58 (1.46)	-0.12 (0.57)
	OS	-2.99 (1.31)	-2.03 (1.28)	-0.63 (1.39)	-0.48 (1.46)	-0.14 (0.96)
J_{180} (Diopters)	OD	-0.03 (0.15)	-0.03 (0.14)	-0.05 (0.11)	0.01 (0.13)	0.01 (0.16)
	OS	-0.01 (0.11)	0.01 (0.13)	-0.01 (0.09)	0.01 (0.13)	-0.03 (0.11)
J_{45} (Diopters)	OD	0.02 (0.19)	-0.01 (0.20)	0.05 (0.27)	0.04 (0.19)	0.04 (0.16)
	OS	0.01 (0.13)	0.03 (0.14)	0.03 (0.13)	0.04 (0.19)	0.00 (0.06)
logMAR VA	OD	0.81 (0.25)	0.63 (0.27)	0.25 (0.32)	0.32 (0.42)	0.36 (0.47)
	OS	0.80 (0.26)	0.61 (0.27)	0.23 (0.30)	0.31 (0.40)	0.37 (0.47)

Table 4: Overall means and standard deviations (in parentheses) of CH, CRF, central corneal thickness, M, J_{180}, J_{45} and LogMAR Visual Acuity for all patients at each time point in the study.

There was also no statistically significant difference between mean CH and CRF for patients that discontinued the study due to visual reasons and those that discontinued for all other reasons (all p-values > 0.01 for CH and CRF, right and left eyes).

Corneal Characteristics and Lens Re-Fitting

Several patients required lens re-fitting during the study for various reasons including poor fit during overnight wear as evidenced by topography, incomplete refractive correction and halos. There was no statistically significant difference in CRF for patients requiring re-fittings (n=23) compared to patients who did not need lens re-fitting (n=18) for the duration of the study (p=0.40 and 0.067 for right eyes and left eyes respectively). There was also no statistically significant difference in CH for those patients requiring lens re-fittings compared to patients who did not need to change lenses during the study period (p=0.41 and 0.93 for right and left eyes respectively). Figure 8 demonstrates the CH and CRF for patients who required lens changes and those who did not. Baseline CH and CRF values were averaged between right and left eyes for this graph. Table 5 lists the reasons given for lens changes during the study.

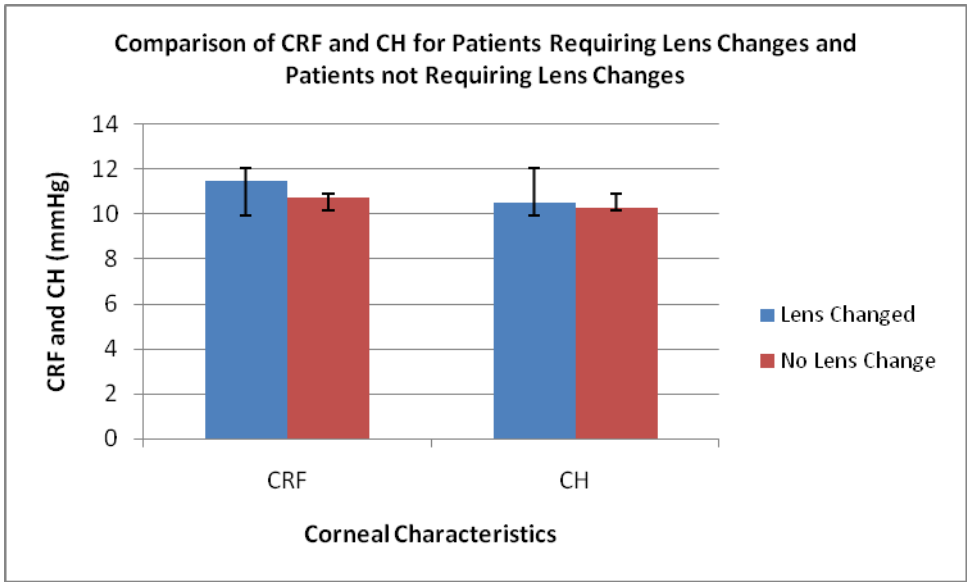


Figure 8: Averaged baseline CRF and CH of patients who had lens changes during the study compared to the values for the patients that did not change lenses. X axis – corneal measurements (averaged baseline CRF and CH), Y axis – CRF and CH in mmHg.

Reasons for Lens Changes	Frequency
Full Correction not Achieved	38.71%
Patient Perception of Halos	16.3%
Decentration During Sleep (Closed Eye)	12.9%
Over-Correction	9.68%
Lens Fit too Tightly	6.45%
Decentration on Open Eye	6.45%
Residual Astigmatism	6.45%
Poor Fit Causing Corneal Staining	3.23%

Table 5: Frequency of reasons for lens changes during the study.

Table 6 shows the total number of lens changes needed during the study and the total number of adults and children requiring lens changes.

Number of Lens Changes	Number of Patients		
	Total	Adults	Children
0	18	3	15
1	17	10	7
2	4	3	1
3	1	1	0
4	1	1	0

Table 6: Total number of patients requiring 0, 1, 2, 3 and 4 lens changes throughout the study. Shown overall and broken down by adults compared to children.

Change in CH and CRF over the Study Period

A statistically significant change in CRF was noted at the one week and three month time points for right eyes only ($p=0.000003$ and 0.001 for one week and three months respectively). There was also a trend noted in the data for the right eye change in CRF at the three week time point, although statistical significance was not reached ($p=0.0145$). There was no statistically significant change noted for left eyes (all p-values > 0.01). There was no statistically significant difference in CH values for right or left eyes. Figure 9 illustrates the overall average CH and CRF values during the study period for right and left eyes.

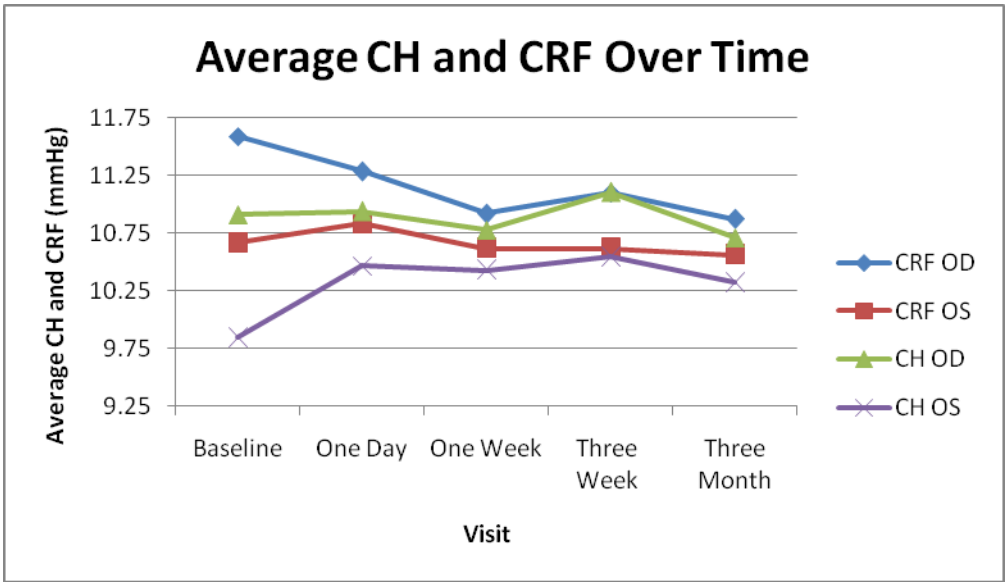


Figure 9: Overall average CH (OD – green, OS – purple) and CRF (OD – blue, OS – red) over each time point in the study. X axis – study visit, Y axis – average CH and CRF values in mmHg.

Simple linear regression analyses examined the relationship between corneal properties (CH and CRF) and change in corneal apical power, visual acuity and refractive error. Analyses were run using baseline CH and CRF values as well as with the average of all CH and CRF measurements taken throughout the study for each individual patient. Because of the finding showing some change in CH and CRF throughout the course of the study, baseline corneal properties were used in the analyses and are presented in this study. Analyses using the averaged corneal property values were also run and showed very similar results to those presented here.

Overall Results – CH and CRF vs. Apical Power

Baseline CH and CRF values were examined for correlations with change in corneal apical power at the one day, one week and three week time points. There was no statistically significant relationship between baseline CH and change in corneal apical power found in this study for either right or left eyes (p-values > 0.01 and R^2 values < 0.146). There was also no statistically significant relationship between baseline CRF and change in corneal apical power found for either right or left eyes (p-values > 0.01 and R^2 values < 0.167). Figures 10 and 11 include scatterplots showing these relationships. Three month time points were not analyzed due to previous findings that the majority of all changes due to orthokeratology have taken place after one to two weeks of lens wear.

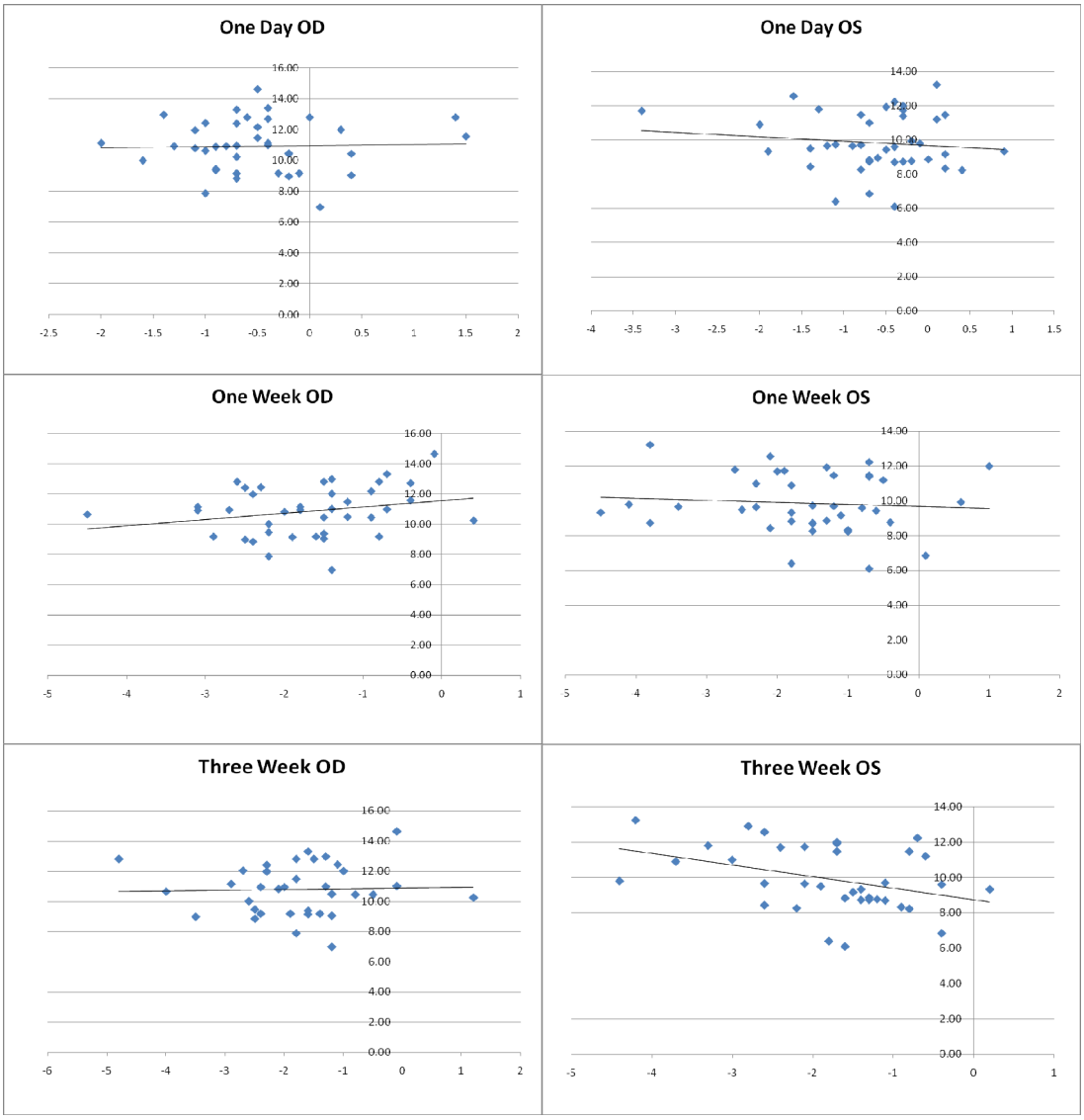


Figure 10: Relationship between baseline CH and corneal apical power change (calculated as apical power at given time point – baseline apical power) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in apical power (D), Y axis – baseline CH (mmHg).



Figure 11: Relationship between baseline CRF and corneal apical power change (calculated as apical power at given time point – baseline apical power) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in apical power (D), Y axis – baseline CRF (mmHg).

Overall Results – CH and CRF vs. Visual Acuity

Analysis of the relationship between baseline CH and change in visual acuity at one day, one week and three week time points showed no statistically significant correlation for either right or left eyes (p-values > 0.01 and R^2 values < 0.076). Analysis of baseline CRF and change in visual acuity showed similar results (p-values > 0.01 and R^2 values < 0.088). Figures 12 and 13 illustrate these relationships. Means and standard deviations for visual acuity at each time point in the study are shown in Table 4.

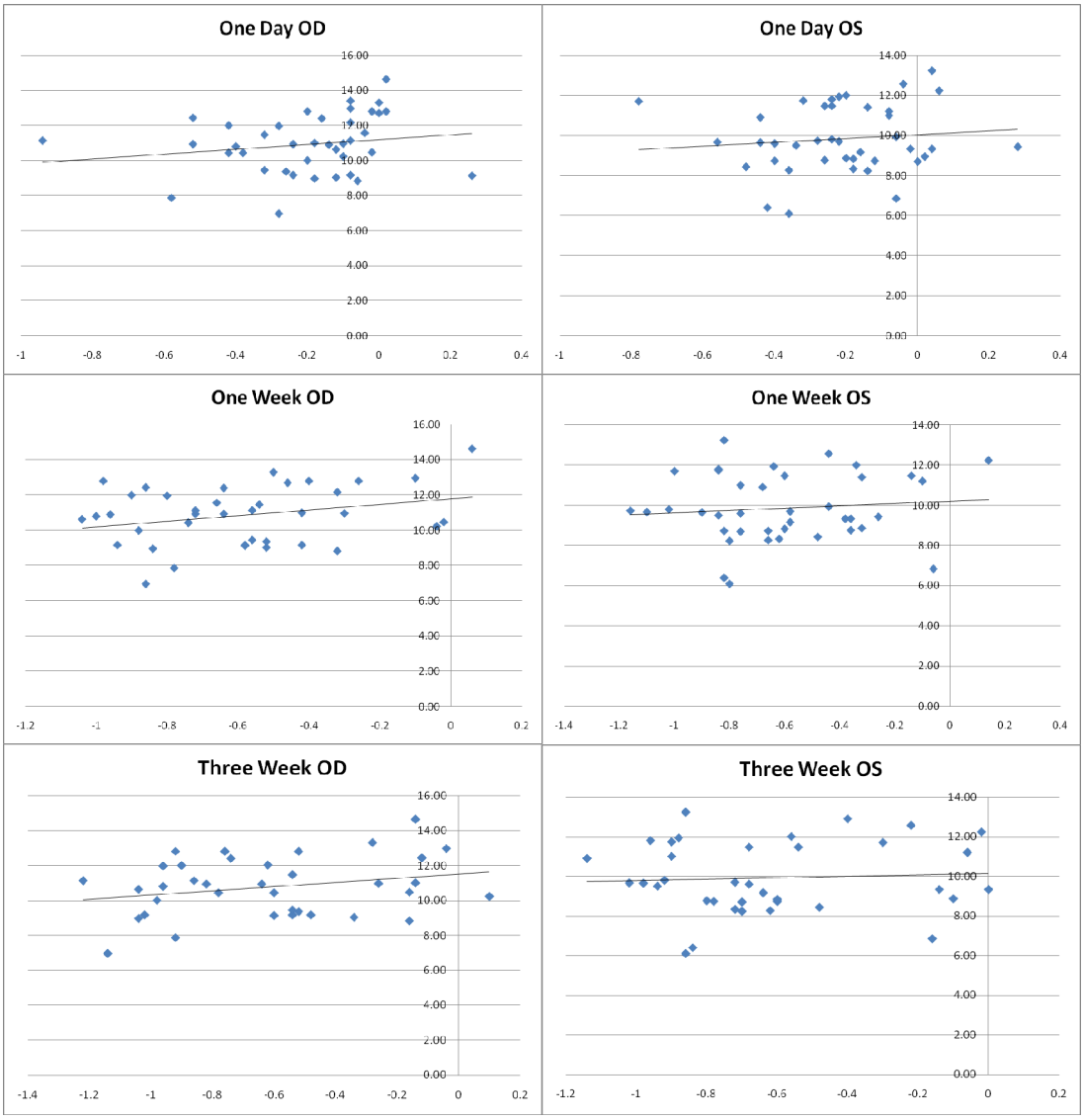


Figure 12: Relationship between baseline CH and uncorrected LogMAR visual acuity change (calculated as VA at a given time point – baseline VA) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in visual acuity (LogMAR), Y axis – baseline CH (mmHg).



Figure 13: Relationship between baseline CRF and uncorrected LogMAR visual acuity change (calculated as VA at a given time point – baseline VA) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in visual acuity (LogMAR), Y axis – baseline CRF (mmHg).

Overall Results – CH and CRF vs. Refractive Error

CRF and CH was also examined for relationships with refractive error values at each of the time points used in the above analyses. Refractive error was broken down into M, J_{180} and J_{45} values for these analyses. No statistically significant correlations were found between baseline CH or CRF and any aspect of refractive error measure at one day, one week or three weeks for either right or left eyes (p-values > 0.01 and R^2 values < 0.222). Figures 14-19 show the scatter plots used in these analyses. Mean and standard deviation data for refractive error are given in Table 4.

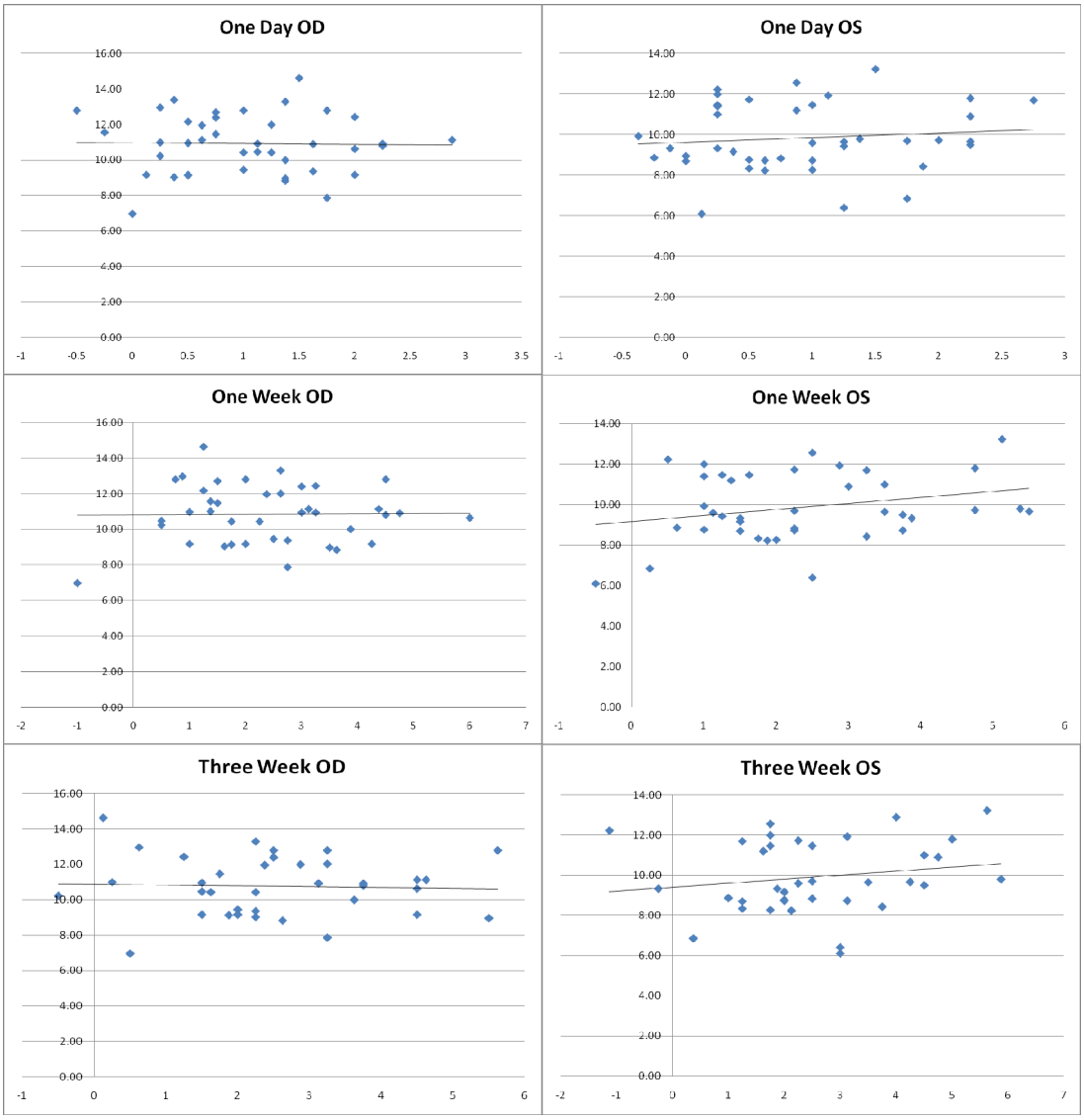


Figure 14: Relationship between baseline CH and M change (calculated as M value from a given time point – baseline M) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in M (D), Y axis – baseline CH (mmHg).



Figure 15: Relationship between baseline CRF and M change (calculated as M value from a given time point – baseline M) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in M (D), Y axis – baseline CRF (mmHg).

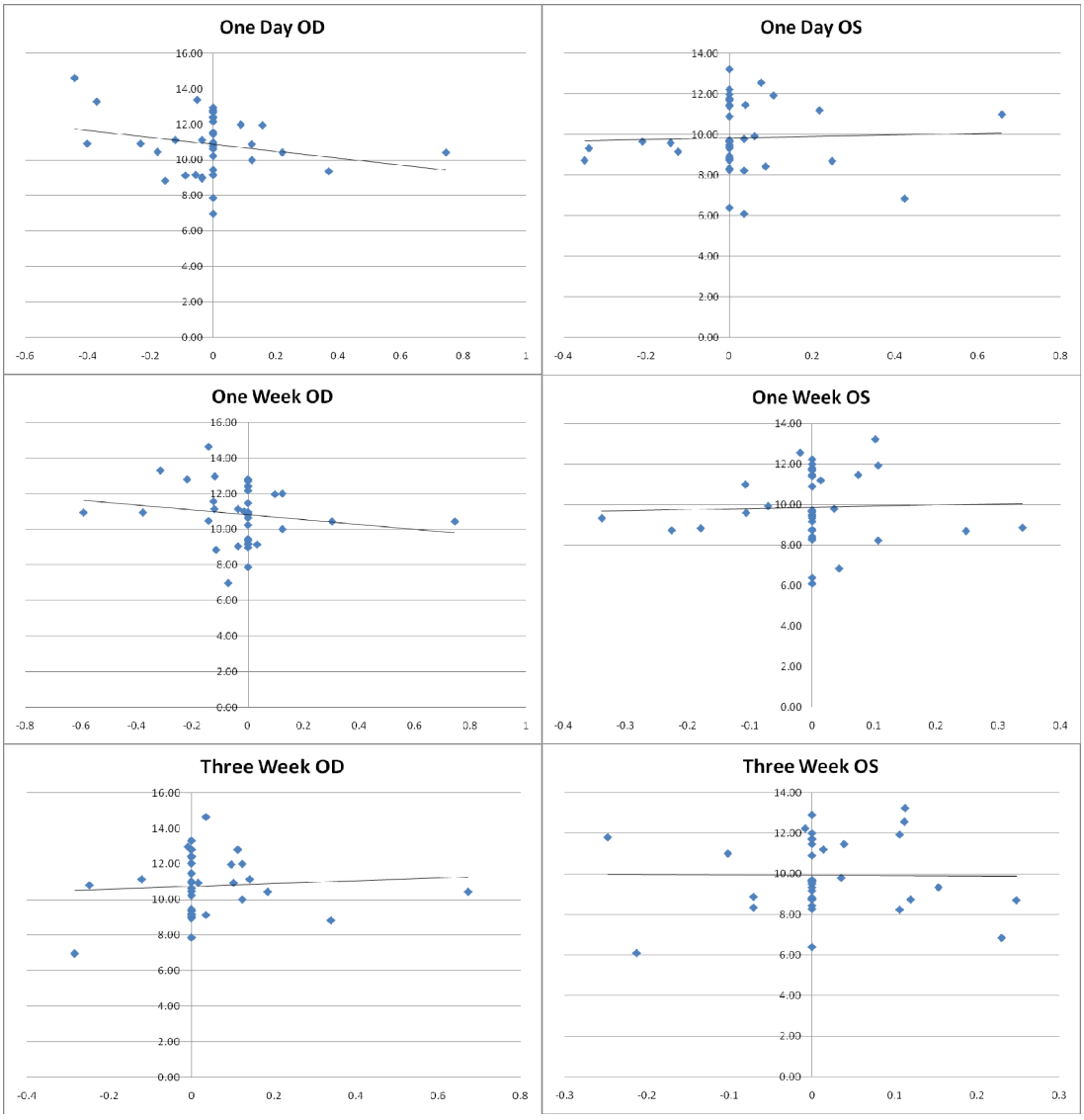


Figure 16: Relationship between baseline CH and J_{180} change (calculated as J_{180} value from a given time point – baseline J_{180}) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in J_{180} (D), Y axis – baseline CH (mmHg).

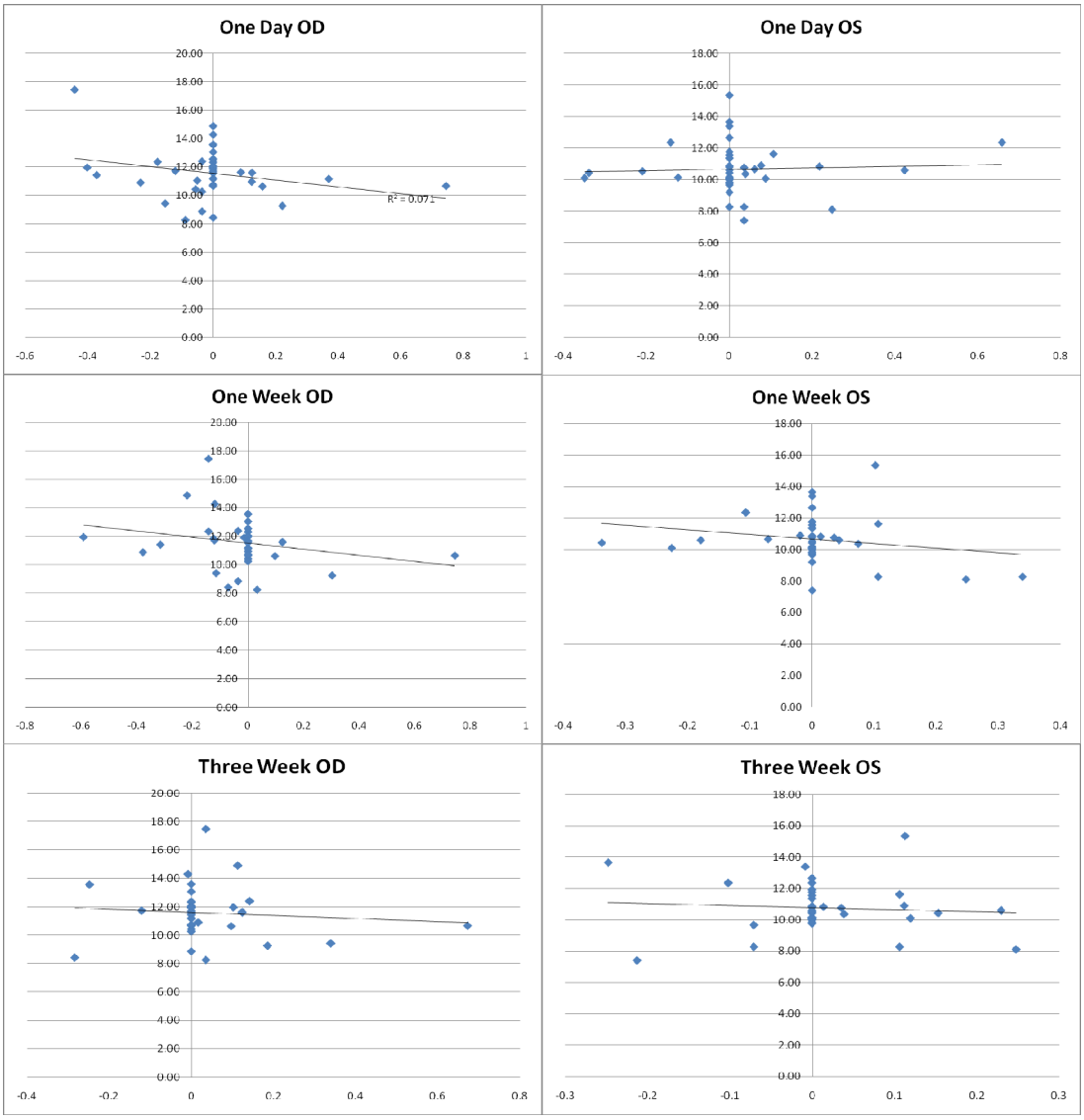


Figure 17: Relationship between baseline CRF and J_{180} change (calculated as J_{180} value from a given time point – baseline J_{180}) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in J_{180} (D), Y axis – baseline CRF (mmHg).

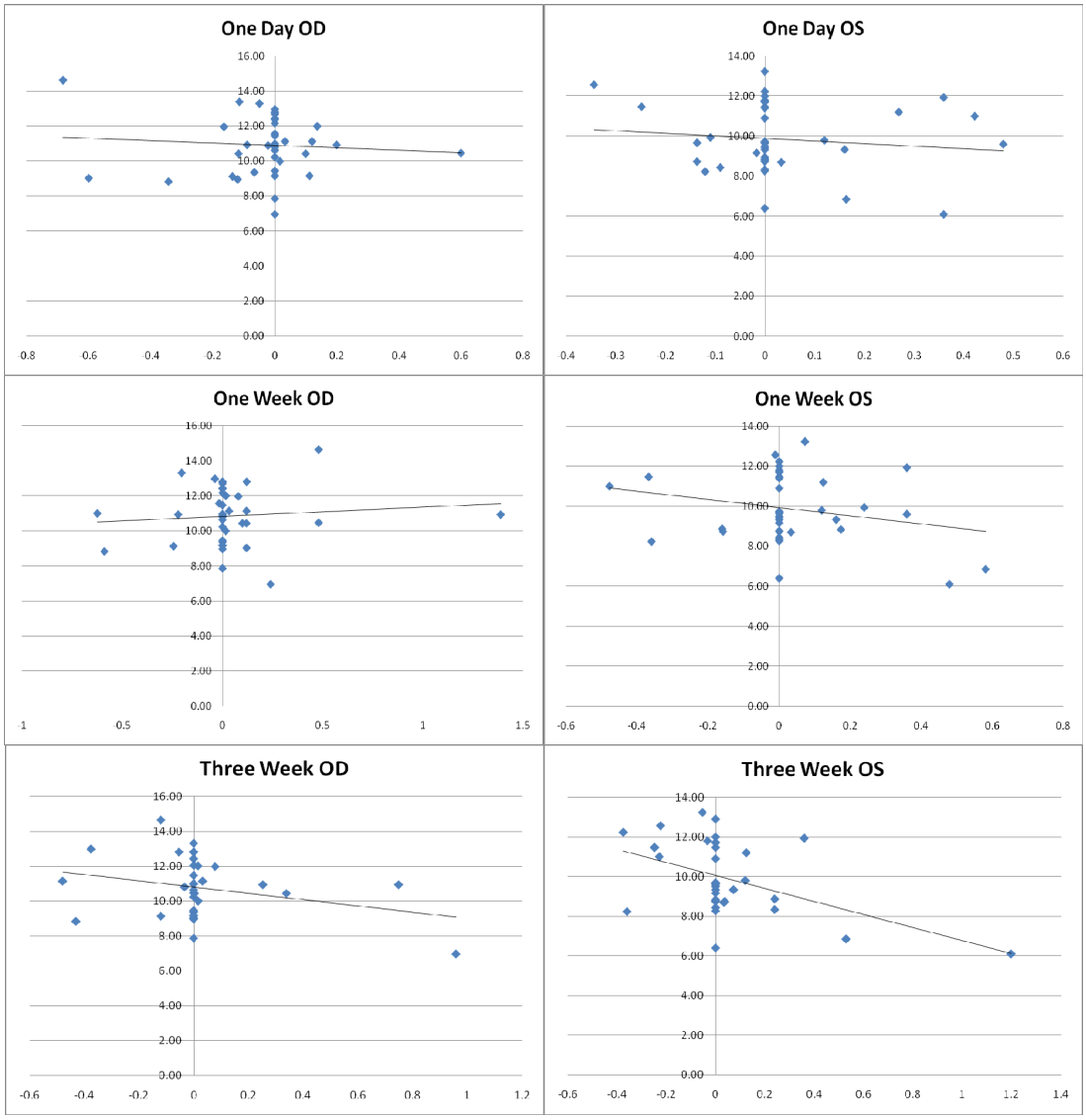


Figure 18: Relationship between baseline CH and J_{45} change (calculated as J_{45} value from a given time point – baseline J_{45}) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in J_{45} (D), Y axis – baseline CH (mmHg).

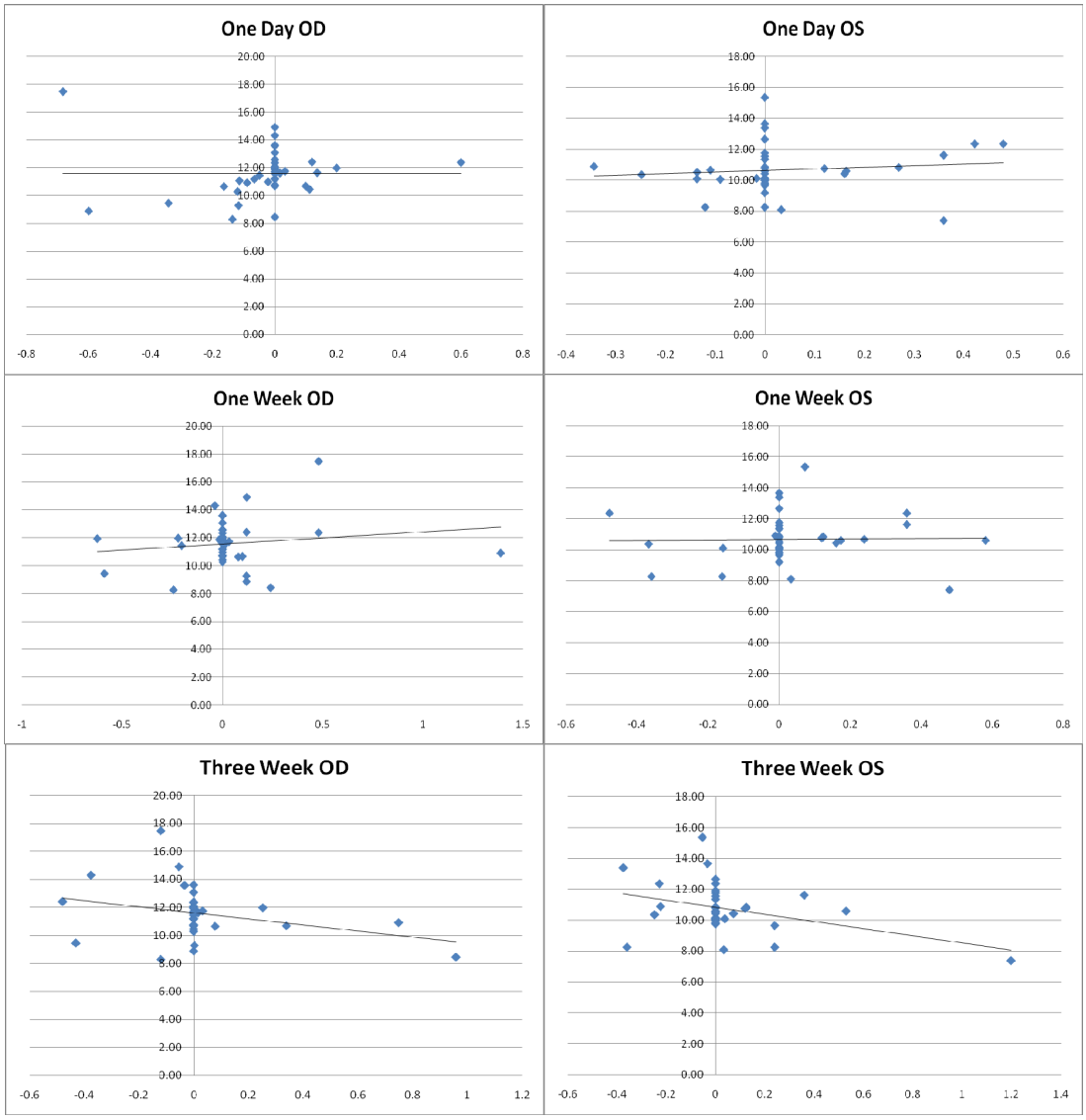


Figure 19: Relationship between baseline CRF and J_{45} change (calculated as J_{45} value from a given time point – baseline J_{45}) at one day, one week and three weeks for right and left eyes. For all scatterplots: X axis – change in J_{45} (D), Y axis – baseline CRF (mmHg).

Grouping of Data for Analyses

Because it is known that larger changes in corneal apical power are needed for larger refractive errors, patients were grouped for further analysis based on refractive error to eliminate a potential confounding factor in the analysis. Ideally, the data would have been broken into four groups (baseline M values of -1.00 to -1.75, -2.00 to -2.75, -3.00 to -3.75 and -4.00 to -5.00). However, there is not a separate group for patients with baseline M values between -3.00 and -3.75D in this study. This is because only four right eyes and four left eyes fell into this category. Since these numbers were not large enough to draw sound statistical conclusions, different groupings were done.

In this study, patients were grouped according to initial refractive error expressed as M values, creating three balanced groups. Group 1 had an initial refractive error (M) of -1.00 to -2.00D, Group 2 had -2.25 to -3.88D and Group 3 had -4.00 to -5.38D. Patient data was grouped in this manner to balance the number of data points in each group as well as to control for the confounding factor of baseline refractive error as much as possible. Table 7 shows the number of subjects in each refractive error group for right and left eyes.

	Refractive Error Groupings (M)		
Follow-Up Visit	-1.00 to -2.00	-2.25 to -3.88	-4.00 to -5.38
One Day	OD: n = 11 OS: n = 13	OD: n = 15 OS: n = 13	OD: n = 14 OS: n = 14
One Week	OD: n = 11 OS: n = 12	OD: n = 15 OS: n = 14	OD: n = 14 OS: n = 14
Three Weeks	OD: n = 8 OS: n = 9	OD: n = 15 OS: n = 14	OD: n = 13 OS: n = 13

Table 7: Number of right eyes and left eyes in each refractive error group throughout the study time points.

Multiple linear regression analyses were also run to control for the effect of baseline refractive error on amount of corneal change. Baseline CH and CRF values were used as independent variables along with baseline refractive error in the analyses. An overview of the results of the regression analyses using CH and baseline refractive error as independent variables is presented in Table 8. An overview of the results of the regression analyses using CRF and baseline refractive error as independent variables is presented in Table 9. According to these analyses, baseline M is a significant predictive factor for the treatment outcome. As seen in the following tables, many of the p-values for M are statistically significant.

	Dependent Variable	Apical Power Change		Refractive Error Change		Visual Acuity Change	
	Independent Variables	CH	M	CH	M	CH	M
One Day	OD	0.041 (0.541)	0.143 (0.094)	-0.047 (0.516)	-0.190 (0.040)	0.029 (0.168)	0.035 (0.181)
	OS	-0.036 (0.615)	0.194 (0.038)	0.033 (0.658)	-0.225 (0.020)	0.015 (0.452)	0.018 (0.469)
One Week	OD	0.138 (0.089)	0.307 (0.005)	0.025 (0.834)	0.499 (0.003)	0.047 (0.063)	0.051 (0.121)
	OS	0.0002 (0.998)	0.467 (0.001)	0.144 (0.249)	-0.545 (0.002)	0.044 (0.103)	0.073 (0.041)
Three Weeks	OD	0.071 (0.493)	0.287 (0.046)	-0.088 (0.512)	-0.455 (0.015)	0.059 (0.072)	0.078 (0.074)
	OS	-0.165 (0.076)	0.321 (0.015)	0.041 (0.772)	-0.506 (0.014)	0.033 (0.278)	0.059 (0.162)
Three Months	OD	0.117 (0.380)	0.438 (0.017)	-0.071 (0.589)	-0.856 (<0.0001)	-0.009 (0.756)	0.104 (0.012)
	OS	-0.075 (0.540)	0.548 (0.002)	-0.030 (0.824)	-0.856 (<0.0001)	0.053 (0.056)	0.132 (0.001)

Table 8: Results of multiple regression analysis using CH and baseline M values as independent variables. Data expressed as coefficient followed by associated p-value in parentheses.

	Dependent Variable	Apical Power		Refractive Error		Visual Acuity	
	Independent Variables	CRF	M	CRF	M	CRF	M
One Day	OD	-0.025 (0.697)	0.125 (0.137)	0.048 (0.489)	-0.165 (0.068)	0.015 (0.459)	0.029 (0.261)
	OS	0.013 (0.874)	0.203 (0.035)	0.074 (0.374)	-0.209 (0.033)	0.017 (0.432)	0.021 (0.415)
One Week	OD	0.138 (0.096)	0.328 (0.003)	-0.022 (0.857)	-0.503 (0.003)	0.059 (0.022)	0.061 (0.062)
	OS	0.048 (0.674)	0.278 (0.059)	0.113 (0.421)	-0.530 (0.003)	0.062 (0.041)	0.086 (0.018)
Three Weeks	OD	0.011 (0.917)	0.278 (0.059)	-0.062 (0.647)	-0.460 (0.017)	0.047 (0.157)	0.083 (0.069)
	OS	-0.153 (0.156)	0.294 (0.033)	0.131 (0.418)	-0.462 (0.028)	0.009 (0.809)	0.056 (0.214)
Three Months	OD	0.131 (0.307)	0.461 (0.014)	-0.026 (0.839)	-0.845 (<0.0001)	0.010 (0.719)	0.112 (0.009)
	OS	0.116 (0.409)	0.651 (0.001)	-0.165 (0.286)	-0.947 (<0.0001)	0.084 (0.007)	0.163 (<0.001)

Table 9: Results of multiple regression analysis using CRF and baseline M values as independent variables. Data expressed as coefficient followed by associated p-value in parentheses.

Corneal Characteristics and Corneal Apical Power

Change in apical power was measured as the difference between baseline and one day, one week and three week measures for each eye of each patient. These measurements were plotted according to baseline CRF and CH values for each eye of each patient. Simple linear regression analyses were run using this data. Analyses for the three month time points were not run due to small sample size in most groups.

No statistically significant trend was found in corneal apical power change when plotted against baseline CH for either eye at the one day and three week follow-up time points (p-values > 0.01 and R^2 values < 0.192 for all groups). However, there was a statistically significant relationship found between CH and apical power change at the one week time point for right eyes in group 1 only (p=0.004, R^2 value = 0.631). Figure 20 illustrates this relationship. There were no other statistically significant relationships found between these variables for left eyes in group one or for either eye in groups two or three at the one week time point (all p-values > 0.01; all R^2 values < 0.130). There was also no statistically significant relationship found for these parameters after adjusting for baseline M values (p-values > 0.01 for all study time points, Table 8).

No statistically significant correlations were noted for these measures when using CRF in place of CH for all groups (p-values > 0.01 and R^2 values < 0.299). No evaluations for the three month follow-up time point were conducted due to small sample sizes. There were also no statistically significant relationships found between CRF and change in corneal

apical power after adjusting for baseline M values (p-values > 0.01 for all study time points, Table 9).

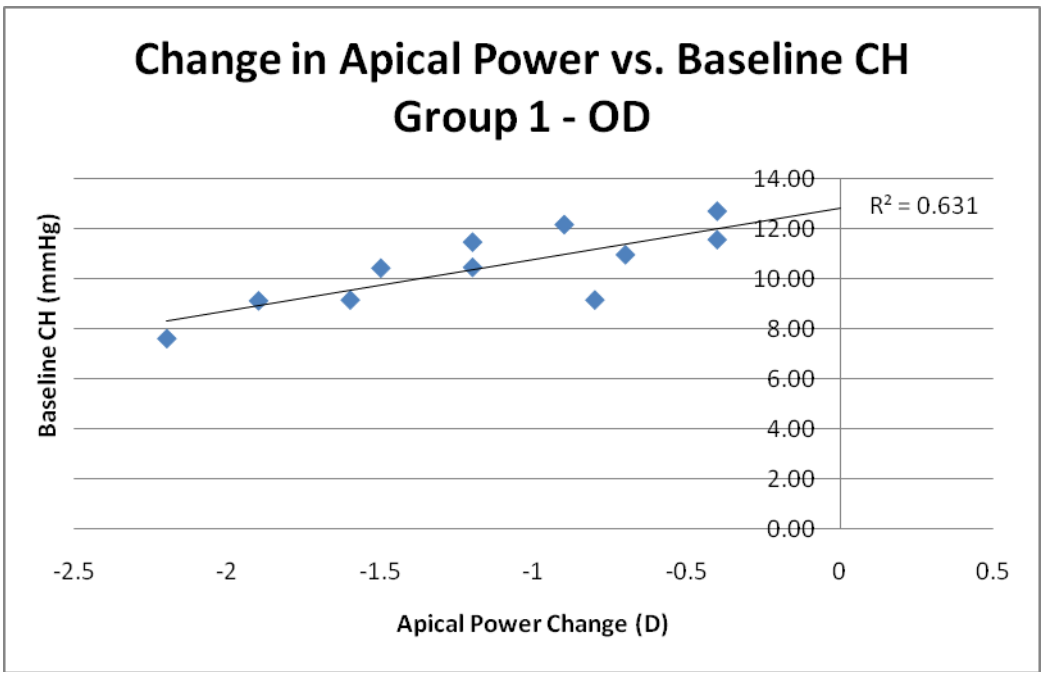


Figure 20: Relationship between change in corneal apical power and baseline CH for patients in group 1 (baseline M values between -1.00 and -2.00D) at the one week time point. Graph represents values for right eyes only. X axis – Corneal apical power change in D, Y axis – Baseline CH in mmHg.

Corneal Characteristics and Refractive Error

Refractive error was also examined for correlations with CRF and CH values at each of the time points used in the apical power analysis. Refractive error was again broken down into M, J_{180} and J_{45} values for accurate analysis. No statistically significant relationships were

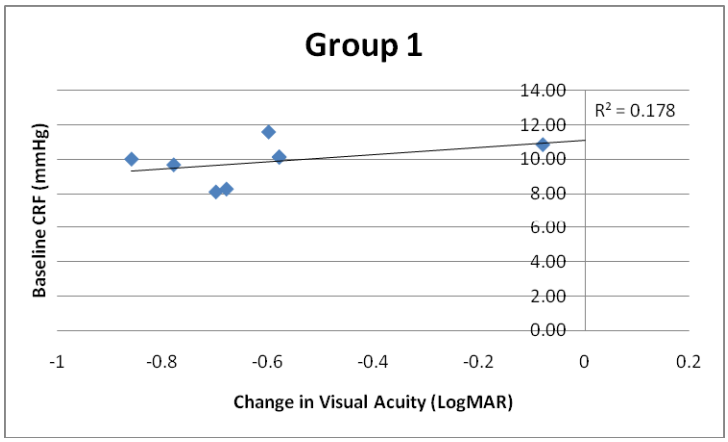
found for any aspect of refractive error measure for CRF or CH at any time point (p-values > 0.01 and R^2 values < 0.337 for all groups).

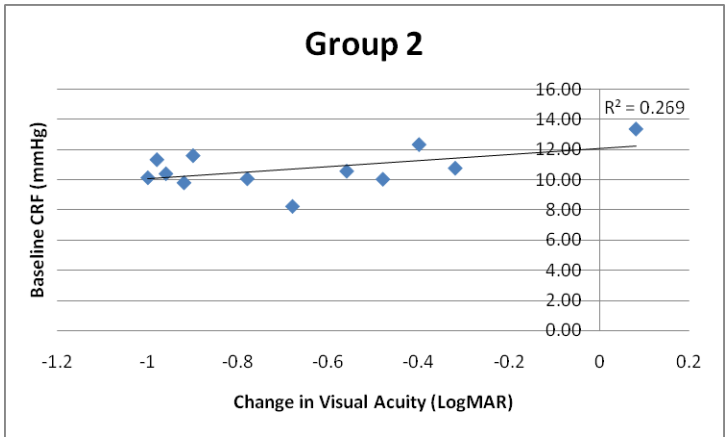
In addition, multiple linear regression analyses showed no statistically significant relationship for the data points above, for CH or CRF (p-values > 0.01 for all time points, Tables 8 and 9 for CH and CRF respectively).

Corneal Characteristics and Visual Acuity Outcomes

Uncorrected visual acuity as measured by logMAR was also examined for correlations with CH and CRF at each follow up visit. Using simple linear regression analyses, there were no statistically significant correlations between change in visual acuity and CH in this study (p-values > 0.01 and R^2 values < 0.169 for all groups). There were also no statistically significant correlations seen for CRF when compared to change in visual acuity when using simple linear regression analyses (p-values > 0.01 and R^2 values < 0.214 for all groups).

Multiple linear regression analysis of the above data showed a statistically significant relationship between baseline CRF and change in visual acuity for left eyes at the three month time point (p = 0.007, Table 9). Although simple linear regression analyses were not run on three month data due to small sample sizes, to further evaluate this finding, these analyses were run for the above data. Using these analyses, there were no statistically significant relationships shown between baseline CRF and change in visual acuity for left eyes at the three month time point (p-values > 0.01 and R^2 values < 0.269 for all groups). Figure 21 illustrates the relationships for these data points.





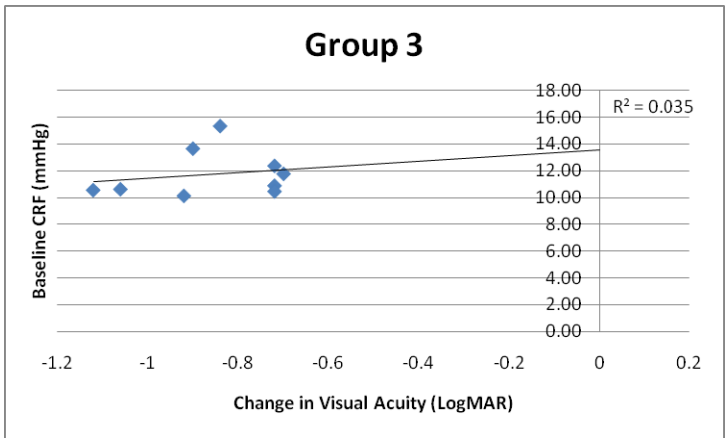


Figure 21: Relationship between baseline CRF and change in visual acuity at the three month time point for left eyes of each group. X axis – change in visual acuity measured in LogMAR, Y axis- baseline CRF in mmHg.

Differences in CH and CRF with Age

There did not appear to be a relationship between corneal characteristics and age in this study. There was no statistically significant difference in baseline CH between patients under 18 years of age and patients over 18 years of age (p = 0.09, 0.22 OD, OS respectively). There was also no statistically significant difference in baseline CRF between these two groups (p = 0.45, 0.97 OD, OS respectively). Figure 22 illustrates the mean CH and CRF for adults and children in this study. Since there was no statistically significant difference for either right or left eyes, the baseline values for CH and CRF were averaged between the eyes for the figure.

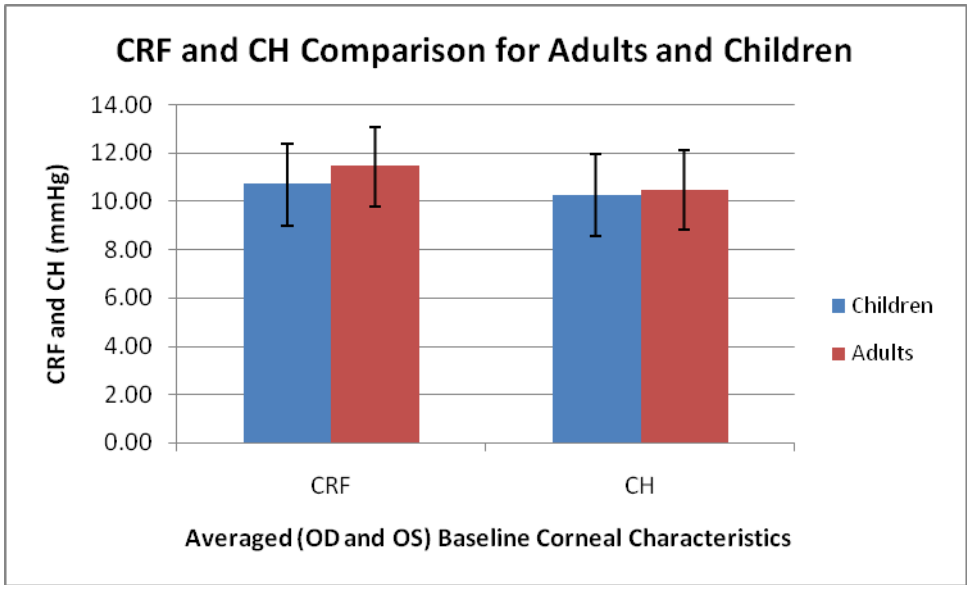


Figure 22: Averaged baseline (OD combined with OS) CRF and CH comparison for children (under 18, blue) and adults (18 and over, red). X axis – average baseline corneal measurements, Y axis – CRF and CH in mmHg.

There was also no statistically significant relationship between either baseline CH or baseline CRF and age in this study ($p > 0.01$ and R^2 values < 0.074). Figure 23 illustrates these relationships.

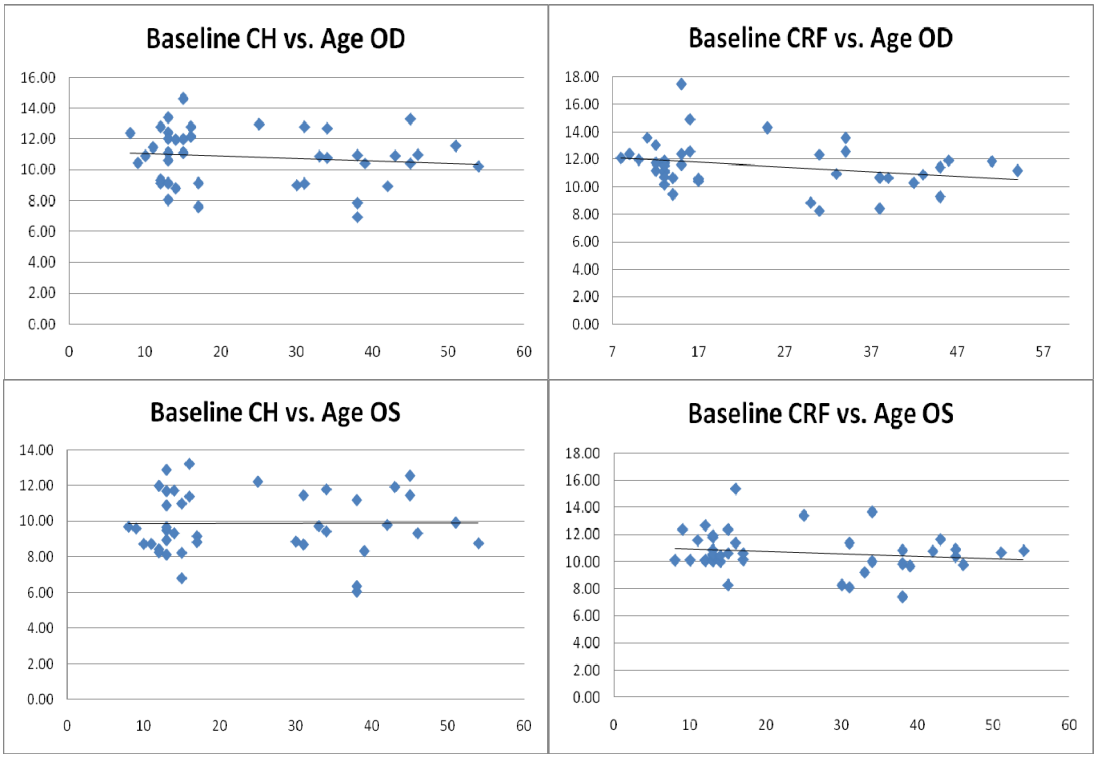


Figure 23: Relationship between age and baseline CH and CRF. For all graphs: X axis – age in years, Y axis – baseline corneal characteristic (CH or CRF).

Successful Completion of the Study and Patient Age

The ages of patients successfully completing the study and those discontinuing from the study were examined. There was a statistically significant difference in the average age for these two groups of patients ($p = 0.005$). On average, patients completing the study were significantly younger than those patients who dropped out (average age 20.87 yrs and 34.09 yrs for patients completing the study and patients discontinued from the study respectively). Figure 24 illustrates the number of adults and children that completed the study and those that did not.

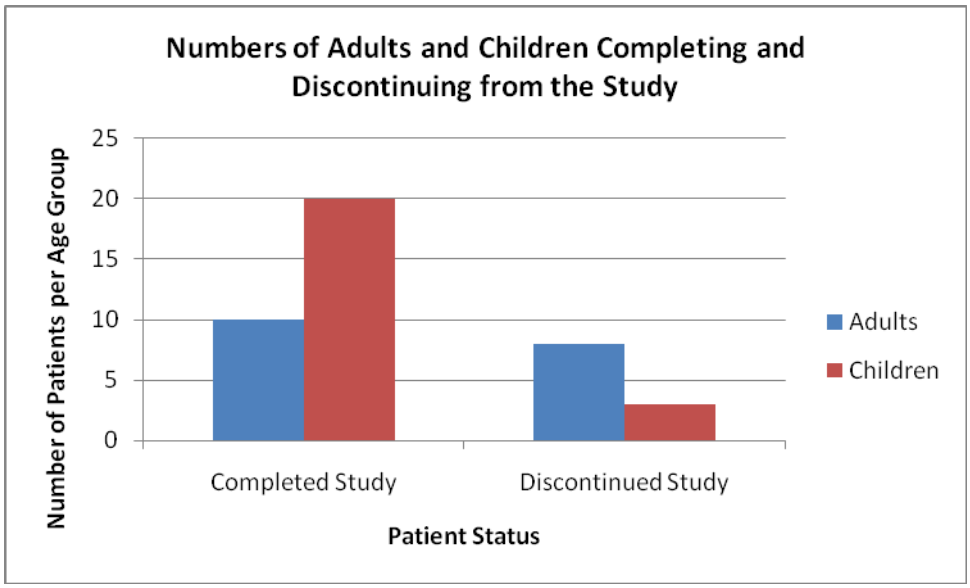


Figure 24: Number of patients completing the study and discontinuing from the study broken down by age group, adults (18 and over, blue) and children (under 18, red). X axis – patient status (Completed or Discontinued), Y axis – number of adult and child patients in each group.

Lens Changes and Patient Age

The ages of patients who required one or more lens changes during the study were also examined for differences from patients who wore the same lenses throughout the study. There was a statistically significant difference in these groups ($p = 0.003$). The average age of patients who did not require lens changes during the study was significantly lower than the average age of those patients that did change lenses (17.444 yrs for no lens changes and 29.869 yrs for lens changes). Figure 25 illustrates the difference in age between patients requiring lens changes and patients not requiring lens changes. Table 10 lists reasons for lens changes broken down by age.

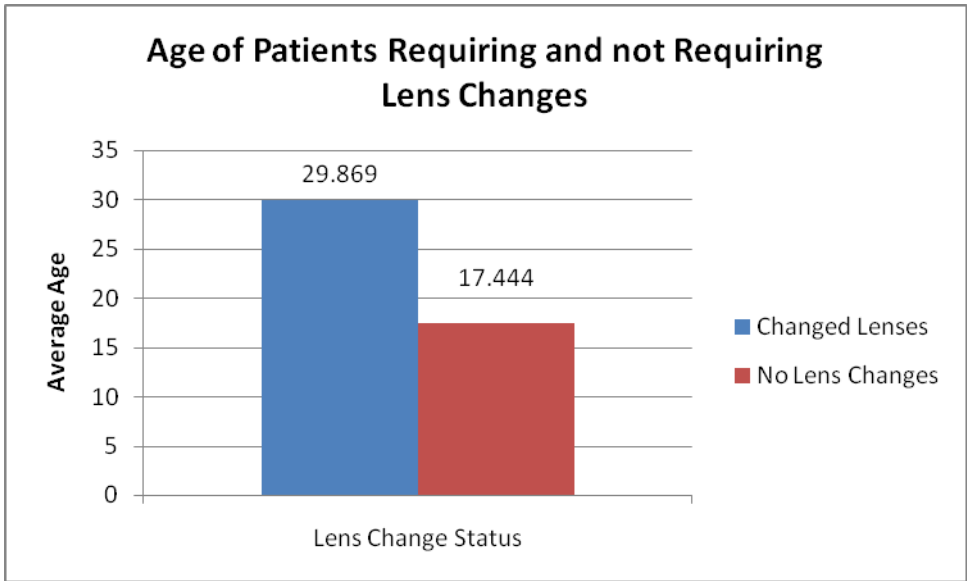


Figure 25: Comparison of average age of patients who had lens changes during the study (blue) and those who did not (red). X axis – Lens change status, Y axis – average age (years).

Reasons for Lens Changes	Frequency Children	Frequency Adults
Decentration During Sleep (Closed Eye)	25%	8.7%
Full Correction not Achieved	12.5%	47.83%
Patient Perception of Halos	12.5%	17.39%
Over-Correction	12.5%	8.7%
Lens Fit too Tightly	12.5%	4.35%
Decentration on Open Eye	12.5%	4.35%
Poor Fit Causing Corneal Staining	12.5%	-
Residual Astigmatism	-	8.7%

Table 10: Frequency of reasons given for lens changes expressed in percentages and broken down by age.

Corneal Shape Changes and Age

Amount of corneal change as measured by corneal apical power was also examined for differences based on patient age. The data was again grouped by baseline refractive error to minimize confounding factors. There was no statistically significant correlation between amount of corneal apical power change and patient age for either eye at any time point ($p > 0.05$ and R^2 values < 0.241). The three month follow-up data was not examined due to the lack of an adequate sample size for that time point. There was no statistically significant difference in baseline M values for adults or children in either right or left eyes in this study ($p=0.954$ and 0.699 for right and left eyes respectively).

Patients' Perception of Vision at Follow-Up Visits

The results of the patient satisfaction surveys are shown in Table 11. The majority of patients felt vision was fair or poor (41% and 26% for fair and poor respectively) at the one day follow-up visit. This is in contrast to the three month visit where the majority of patients felt that the uncorrected vision was good or excellent (48% and 45% for good and excellent respectively).

Rating of Overall Uncorrected Vision				
	One Day	One Week	Three Weeks	Three Months
Excellent	13%	18%	39%	48%
Good	20%	63%	42%	45%
Fair	41%	16%	11%	4%
Poor	26%	3%	8%	3%

Table 11: Patients' rating of overall uncorrected vision at each follow-up visit.

Slightly more than half of patients felt that the uncorrected vision had improved greatly or somewhat at the one day follow up visit (8% and 54% for improved greatly or improved somewhat respectively) when compared to baseline best-corrected vision. However, 28% felt that the vision had not changed significantly and 10% felt it was slightly worse. At the three month visit, most patients felt that uncorrected vision had improved greatly or somewhat from baseline (83% and 7% for improved greatly and improved somewhat respectively). Table 12 summarizes the patient responses for the quality of vision portion of the surveys.

Perception of How Vision has Changed from Baseline				
	One Day	One Week	Three Weeks	Three Months
Greatly Improved	8%	64%	72%	83%
Somewhat Improved	54%	23%	17%	7%
No Change	28%	8%	3%	3%
Somewhat Worse	10%	5%	8%	7%

Table 12: Patients' perception of change in uncorrected vision at each follow-up visit.

Comfort Ratings at Follow-Up Visits

Patients' reports of eye comfort improved over the span of the study with only 33% reporting very comfortable eyes at the one day follow up compared to 79% at the three month visit. Reports of eyes being somewhat uncomfortable showed a decline from the one day follow up through the three month follow up (16% at one day and 4% at three months). Interestingly, no patients reported that their eyes felt very uncomfortable at any visit in the study. Table 13 summarizes the responses for eye comfort over the follow-up visits.

Rating of Overall Eye Comfort				
	One Day	One Week	Three Weeks	Three Months
Very Comfortable	33%	59%	72%	79%
Somewhat Comfortable	51%	33%	22%	17%
Somewhat Uncomfortable	16%	8%	6%	4%
Very Uncomfortable	0%	0%	0%	0%

Table 13: Patient reports of eye comfort at each follow-up visit.

Overall Patient Satisfaction with Treatment

The majority of patients reported being very satisfied or somewhat satisfied with the treatment at the first day visit (43% and 46% respectively). All patients remaining in the study at three months rated themselves as very satisfied or somewhat satisfied (79% and 21% for very satisfied or somewhat satisfied respectively). Table 14 summarizes satisfaction ratings.

Overall Satisfaction with Orthokeratology Treatment				
	One Day	One Week	Three Weeks	Three Months
Very Satisfied	43%	54%	71%	79%
Somewhat Satisfied	46%	41%	23%	21%
Somewhat Unsatisfied	11%	5%	3%	0%
Very Unsatisfied	0%	0%	3%	0%

Table 14: Overall patient satisfaction with orthokeratology treatment at each follow-up visit.

Results of Patient Surveys by Age

The results of the patient surveys broken down by age are shown in Table 15. More children rated their uncorrected vision as excellent or good (24% and 19% for excellent or good respectively) at the one day visit when compared to the same rankings in adults (0% excellent and 22% good). At the three month visit, the percentages of patients rating their vision as good or excellent was similar for both age groupings (32% good and 63% excellent for children, 70% good and 20% excellent for adults).

Comparison of Survey Responses Between Children and Adults								
Overall Vision	One Day		One Week		Three Weeks		Three Months	
	Child	Adult	Child	Adult	Child	Adult	Child	Adult
Excellent	24%	0%	30%	6%	48%	27%	63%	20%
Good	19%	22%	60%	67%	43%	40%	32%	70%
Fair	29%	56%	10%	22%	5%	20%	5%	0%
Poor	29%	22%	0%	6%	5%	13%	0%	10%

Change in Vision	One Day		One Week		Three Weeks		Three Months	
	Child	Adult	Child	Adult	Child	Adult	Child	Adult
Greatly Improved	14%	0%	76%	50%	86%	53%	95%	60%
Somewhat Improved	57%	50%	24%	22%	10%	27%	0%	20%
No Change	24%	33%	0%	17%	0%	7%	0%	10%
Somewhat Worse	5%	17%	0%	11%	5%	13%	5%	10%

Overall Comfort	One Day		One Week		Three Weeks		Three Months	
	Child	Adult	Child	Adult	Child	Adult	Child	Adult
Very Comfortable	33%	33%	67%	50%	81%	60%	84%	70%
Somewhat Comfortable	57%	44%	29%	39%	14%	33%	16%	20%
Somewhat Uncomfortable	10%	22%	5%	11%	5%	7%	0%	10%
Very Uncomfortable	0%	0%	0%	0%	0%	0%	0%	0%

Overall Satisfaction	One Day		One Week		Three Weeks		Three Months	
	Child	Adult	Child	Adult	Child	Adult	Child	Adult
Very Satisfied	55%	29%	62%	44%	81%	54%	89%	56%
Somewhat Satisfied	30%	65%	38%	44%	19%	31%	11%	44%
Somewhat Unsatisfied	15%	6%	0%	11%	0%	8%	0%	0%
Very Unsatisfied	0%	0%	0%	0%	0%	8%	0%	0%

Table 15: Results of patient satisfaction surveys broken down by patient age. Child = Under 18 years old, Adult = 18 and over. Number of children: n=20, 21, 21 and 19 for one day, one week, three week and three months respectively. Fewer patients at the one-day visit are seen because one patient did not complete a one-day visit. Number of adults: n = 18, 18, 13 and 9 for one day, one week, three weeks and three months respectively.

Variability in Corneal Characteristic Measurements

For several subjects in the study, it was noted that there was considerable variability in the CH and CRF measurements between visits. For most of these patients, this variability was noted for both eyes and for both corneal measures. Because of this finding, an analysis of the variability of corneal measurements was done.

There was an expected level of variability seen in the CH measurements between subjects at baseline (SD = 1.66, 1.69 OD, OS respectively) There was also an expected level of variability in the CRF measurements between subjects at baseline (SD = 1.72, 1.51 OD, OS respectively). For most subjects, the within subjects variability for CH was also within what was expected when the measures were compared over time (SD < 1.09, 1.27 OD, OS respectively). The within subjects variability for CRF showed a similar pattern (SD < 1.33, 1.12 OD, OS respectively). However, some subjects showed much larger within subjects variabilities when compared to the between subjects values.

To determine if this variability had an impact on the analyses and conclusions in this study, the data for patients with large within subjects variabilities was examined to determine if there was a significant relationship between CH or CRF with the outcome measures of corneal apical power, visual acuity and refractive error. There were no statistically significant relationships between either CH or CRF with any outcome measure for either eye of these select patients (all p-values > 0.01).

The absolute range in corneal property measurements was also examined. When examining the range between maximum and minimum values for corneal measurements over

visits, 11 right eyes and 21 left eyes showed a range of 2 mmHg or more for CH. Of these, 4 right eyes and 6 left eyes showed ranges above 3 mmHg and 3 right eyes and 3 left eyes showed a range above 4 mmHg. For CRF, 11 right eyes and 11 left eyes showed ranges above 2 mmHg. Of these, 4 right eyes and 4 left eyes showed ranges above 3 mmHg and 3 right eyes and 3 left eyes showed ranges above 4 mmHg. These ranges were compared with several repeatability coefficients from previous studies and are covered further in the discussion.

Discussion

Pattern of Corneal Change

Most patients in the study showed a characteristic pattern in corneal apical power change. This pattern can be described as little to no change in apical power at the one day follow-up visit and significant flattening of the central apical power at the one week visit. The three week and three month visits showed little to no change in corneal apical power from the one week time point.

These findings are similar to the data from previous studies on corneal shape changes in orthokeratology treatment. An initial rapid change in corneal curvature was observed in a 100 day randomized controlled study comparing orthokeratology to standard RGP wear (Lui and Edwards, 2000). The most change occurred during the first ten days of orthokeratology lens wear and more gradual changes were observed through the one month follow-up point. The majority of corneal changes were observed during the first month of treatment. Another study followed orthokeratology patients for sixty days and found that the most corneal change occurred between the one day and seven day follow-up points (Nichols, Marsich, Nguyen, Barr and Bullimore, 2000).

Several (n=12) patients in this study did not show the characteristic pattern of corneal change during this study. The major reason for this deviation in most of these patients was due to non-compliance with treatment. Several patients (n=6) showed increases in apical power at follow-up visits, but revealed that they had not been wearing the lenses or had missed wearing the lenses the night before the visit. Several patients (n=3) also showed non-

characteristic apical power patterns due to the fact that the lenses were not providing enough correction. In these cases, the lenses were changed and some amount of corneal apical power flattening was seen at the following visit.

Change in Central Corneal Thickness

There was a significant change observed in central corneal thickness (CCT) in this study. Specifically, average central corneal thickness decreased significantly over the course of the study. The greatest change in average thickness was seen between baseline and three months, however, there was also a significant change in average thickness observed at the three week time point.

This finding agrees with previous studies showing thinning of the central cornea with different time courses of orthokeratology treatment. In one study, after just one hour of lens wear, a statistically significant central corneal thinning was noted in all subjects (Jayakumar et al., 2005). However, there was significantly less central corneal thinning on average for patients over the age of 36 compared to younger patients in that study. In a histological study on primates, significant central corneal thinning was seen as early as four hours after lens wear (Cheah et al., 2008). The thinning was found to occur both in the epithelium and stroma in that study. Another study on humans did not find a statistically significant decrease in central corneal thickness overall, but did find a significant change when looking at epithelial thickness separately (Swarbrick et al., 1998). Specifically, there was a significant thinning of the central corneal epithelium after 28 days of lens wear.

As mentioned in the introduction, histological studies have shown changes in both the corneal epithelial cells and stroma as a result of orthokeratology treatment. These changes appear clinically as central corneal thinning and mid-peripheral thickening. It is not yet clear which forces contribute to these changes and what corneal properties influence the rate of change.

The average thinning of the central cornea was more pronounced in left eyes than in right eyes in this study. This could have been due to several reasons, such as a difference in baseline CH and CRF between the right and left eyes or a difference in baseline refractive error (M) between the two eyes. It was found that there was a significant difference between baseline CH for right and left eyes in the study. There was also a significant difference in baseline CRF between right and left eyes. Specifically, baseline CH and CRF values were lower for left eyes when compared to right eyes. It is reasonable to hypothesize that since these measures are indications of corneal biomechanical properties, they may have some influence on changes in corneal shape and thickness.

One previous study did find a statistically significant relationship between CH and change in central corneal thickness (CCT) after three hours of lens wear. Specifically, as CH decreased, a faster change in central corneal thickness was noted (Gonzalez-Meijome et al., 2008). The previous study also found a trend in the data for the relationship between CRF and change in CCT, but this did not reach statistical significance. In the present study, no statistically significant relationship was found between CCT and CH or CRF for either right

or left eyes. These relationships were examined at the three week and three month time points, given the significant changes found in CCT at these points for left eyes.

There are several important differences between the current study and the study done by Gonzalez-Meijome et al. First, the current study followed patients over a three month time period. In the previous study patients wore the lenses for a total of three hours. Next, the current study included a larger number of patients (n = 30 for the three month time point) when compared to the previous study (n = 8). Lastly, patients in the current study had baseline refractive errors (M value) ranging from -1.00 to -5.38D. Patients in the previous study all started with a baseline refractive error of -4.00D. Given the differences between this study and the previous study, it is difficult to make comparisons on the conclusions for the relationship between baseline CH, baseline CRF and central corneal thickness change. It appears from this study that although there was a significant difference in baseline CH and CRF between right and left eyes, there was no statistically significant relationship between these variables and change in CCT. Given that CH and CRF do not appear to be related to change in CCT, the finding that change in CCT was more pronounced in left eyes in this study does not appear to be due to the baseline differences in CH or CRF between right and left eyes.

Another possible explanation for the discrepancy in CCT change between right and left eyes in this study could be a difference in baseline refractive error (M) between the two eyes. The relationship between central corneal thinning, corneal curvature change and reduction of myopic refractive error has been noted previously (Swarbrick et al., 1998). Eyes

with higher baseline refractive errors require greater corneal change than eyes with lower baseline refractive errors. Therefore, it could be expected that greater corneal thinning would be seen for eyes with greater baseline refractive errors. However, there was not a statistically significant difference in baseline refractive error (M) between right and left eyes in this study. Therefore, there is no strong evidence supporting the theory that the difference in CCT change between right and left eyes is due to differences in baseline refractive error between the two eyes.

Corneal Characteristics and Successful Completion of the Study

One of the initial aims of the current study was to use corneal characteristics to predict success with orthokeratology treatment. Success in this study was defined as completion of all three months of the study. There did not seem to be a significant difference in either mean CH or mean CRF for patients successfully completing the study and for patients who discontinued from the study. This suggests that CH and CRF cannot be used as effective predictors of success (defined as completion of the study) with orthokeratology treatment.

Corneal Characteristics and Lens Re-Fitting

The number of lens changes required by individual patients throughout the course of the study was also examined. Most lens changes were made because full correction was not achieved with the first lens prescribed. One possible explanation for under-treatment could have been that the cornea was more resistant to change. In other words, a higher CRF or CH value could have been present. However, there was no significant difference in either

baseline CRF or baseline CH values between patients requiring lens changes and patients not requiring lens changes. This indicates that baseline CRF and baseline CH were not likely factors in under-treatment or other reasons for lens changes given in the study.

Change in CH and CRF over the Study Period

A previous study had noted a statistically significant change in CRF over a six month study period (Chen et al., 2008). These changes were noted to occur after about one month of lens wear. This same study did not note a significant change in CH throughout the same study period. The current study showed a statistically significant change in CRF at the one week and three month time points for right eyes only. The change in CRF at the three week time point for right eyes showed a trend but did not reach statistical significance. There was no significant change in CRF for left eyes or for CH with either eye in this study.

There are several differences in these two studies. The current study only followed patients for three months, while the previous study followed patients for a total of six months. Also, the current study broke data analyses down into right and left eyes while the previous study combined data from right and left eyes to make conclusions. Despite these differences in study design, the current study is in agreement with previous data that the CH values did not change significantly over the study periods. It is also mostly in agreement that the CRF value changed significantly over time with orthokeratology treatment.

The reasons for the more pronounced change in CRF for right eyes compared to left eyes in this study are unclear. As previously noted, there was a statistically significant difference in baseline CRF between right and left eyes. However, the mean CRF for right

eyes was larger than that for left eyes in this study. Given that CRF is defined as a measure of overall corneal rigidity, it might be expected that the corneas with lower CRF would show greater change over time, as they could be considered to be more moldable. In this study, the opposite was the case, with corneas having higher CRF values showing more change over time. Whether or not this change in CRF represents an overall reduction in corneal rigidity brought about by orthokeratology treatment remains to be investigated.

Overall Results – CH and CRF vs. Apical Power

The data in this study was analyzed in several different ways, the first being an evaluation of the overall relationship between baseline CH, CRF and change in corneal apical power. This analysis included all subjects, not broken into baseline refractive error (M) groups. No significant relationships were found between these variables for either eye and at any time point in the study. However, these findings are derived from overall data and thus the confounding factor of baseline refractive error may be contributing to the results.

Overall Results – CH and CRF vs. Visual Acuity

Another overall analysis was made between baseline CH, baseline CRF and visual acuity change. Again, no significant relationships were found for either eye at any time point in the study. These findings also suggest no relationship between corneal characteristics and visual acuity change with orthokeratology treatment, but no strong conclusions can be made considering the possible confounding effect of baseline refractive error.

Overall Results – CH and CRF vs. Refractive Error

Refractive error was broken down into M, J_{180} and J_{45} values for analysis in this study. This is a standard way of analyzing refractive data because it allows for the data to be put in a format that can be analyzed statistically (Thibos, Wheeler & Horner, 1997). No significant relationships were found between baseline CH or CRF and change in any refractive error parameter in this study. Again, this was overall data and strong conclusions cannot be made until it is analyzed with baseline refractive error being controlled.

Corneal Characteristics and Corneal Apical Power

In a previous study, a statistically significant relationship between CH and the rate of corneal change has been shown (Gonzalez-Meijome et al., 2008). There was also a trend in the data showing a relationship between CRF and corneal curvature change, but it did not reach statistical significance. The study specifically suggested that corneas with lower CRF and CH values and thus more "pliable" corneas showed a faster treatment and recovery effect when compared to corneas with higher CRF and CH values.

In the current study, patient data was broken down into refractive error groupings for analysis as mentioned previously. A statistically significant relationship was found between baseline CH and corneal apical power change at the one week time point only. This result was found in only one refractive error group (group 1: -1.00 to -2.00D baseline M) and only for right eyes within this group. This significant result was noted with simple linear regression but not with multiple linear regression analysis when adjusting for the effect of

baseline M. There were no other statistically significant relationships found between corneal characteristics and change in apical power in the current study.

One statistically significant relationship was found in the analyses adjusting for baseline M values. However, this was significant for only one eye and at one time point and is not enough to support the theory that CH and CRF can be used to predict corneal apical power change. As a whole, these findings suggest that there is no relationship between either baseline CH or CRF and corneal apical power change with orthokeratology treatment.

Several key differences between the Gonzalez-Meijome (2008) study and the current study have been discussed previously. Given that only one statistically significant result was found in this study among many analyses, there was no strong evidence in the data indicating that a significant relationship exists between corneal properties and apical power change with orthokeratology treatment. Although a characteristic pattern of corneal apical power change was seen for most patients in our study, corneal biomechanical properties could not be successfully used to predict these changes.

Although it was shown in a prior study (Gonzalez-Meijome et al., 2008) that CRF and CH were predictive of rates of corneal change over short term wear with a small number of patients, it appears that the predictive value of these measurements cannot be applied over longer follow-up periods and over a larger patient sample population, as demonstrated by the current study. The current study more clearly illustrates the usefulness of these measures in an ordinary clinical setting.

Corneal Characteristics and Refractive Error

Another possible method of measuring progress with orthokeratology treatment is assessment of change in refractive error. In orthokeratology treatment, the biggest change in refractive error has been shown to be between the one day and one week period of lens wear (Nichols et al., 2000). Changes in refractive error can be linked to the corneal changes that occur with lens wear (Nichols et al., 2000). Thus, change in refractive error was compared with baseline corneal properties in this study. Subjective refractive error measurements were again converted in to M, J_{180} and J_{45} values for these analyses and patient data was grouped by baseline refractive error (M) as described previously.

There were no statistically significant relationships found between baseline CH or CRF and change in refractive error values for any time point in this study, for both eyes in all groups. This was true for both simple regression analysis by group and for multiple regression analysis controlling for baseline refractive error (M). It appears from this data that corneal characteristics cannot be used to reliably predict change in refractive error in orthokeratology patients.

Corneal Characteristics and Visual Acuity Outcomes

Uncorrected visual acuity is another measurement that was used in this study to assess success with treatment. Like refractive error, visual acuity change was found to be greatest between one day and one week time points of lens wear in previous studies (Nichols et al., 2000). A relationship between refractive error reduction, as measured by subjective refraction, and visual acuity improvement with orthokeratology treatment has been shown

previously (Swarbrick et al., 1998). However, corneal aberrations induced by orthokeratology treatment may have an affect vision.

Several previous studies have shown changes in corneal aberrations with orthokeratology treatment. In one study, a statistically significant increase in both spherical aberration and coma were noted with eight nights of orthokeratology lens wear (Stillitano, Chalita, Schor, Maidana, Lui, Lipener and Hofling-Lima, 2007). The authors of this study note that while not all aberrations can negatively affect visual performance, low contrast visual acuity could be affected (Stillitano et al., 2007). Another study on induced corneal aberrations with orthokeratology found an increase of irregular astigmatism, spherical-like aberration and coma-like aberration with a minimum of three months of lens wear (Hiraoka, Okamoto, Kaji and Oshika, 2006). These authors concluded that the optical quality of the cornea was reduced with orthokeratology treatment and that visual function may or may not be affected by this (Hiraoka et al., 2006).

Given these induced aberrations, it is reasonable to consider that visual acuity testing may be affected. However, a study on visual performance after orthokeratology treatment showed that visual acuity in different contrast conditions and contrast sensitivity did not seem to be affected by lens wear (Johnson et al., 2007). The authors conclude that although orthokeratology treatment induces higher order corneal aberrations, they are not large enough to affect visual function (Johnson et al., 2007). Therefore, visual acuity is a reasonable measure of progress with orthokeratology treatment.

In the current study, uncorrected visual acuity change was examined for relationships with baseline corneal measurements. Patient data was again broken into groups based on baseline refractive error (M). For the simple regression analyses, there were no significant relationships found in this data at any time point in the study, for either eye, in any group. Three month time points were not examined initially due to small sample sizes in some groups. However, multiple linear regression analysis, controlling for baseline refractive error (M), showed a statistically significant relationship at the three month time point for left eyes only. In light of this finding, additional simple regression analyses were done on three month data points, despite the small number of subjects in some refractive error groupings. These analyses did not show statistically significant relationships, however. From these analyses, it can be concluded that there is not likely a true relationship between change in visual acuity and corneal characteristics in orthokeratology treatment. Therefore, CH and CRF cannot be used to predict changes in visual acuity with lens wear.

Differences in CH and CRF with Age

Given recent studies that have shown differences in orthokeratology treatment results for different age groups (Subramaniam et al., 2007; Jayakumar et al., 2005), differences in treatment outcomes were investigated for these groups in the current study as well. A previous study showed that there was no correlation between age and corneal hysteresis (CH) (Kirwan et al., 2006). The current study also found that there was no statistically significant difference in CH for adults (18 years and over) and children (under 18 years). There was also no significant difference in CRF between adults and children in this study. Simple regression

analyses were also run for the age and corneal characteristic data in this study. No significant relationships were found between age and CH or CRF.

Successful Completion of the Study and Patient Age

In previous studies, children showed faster corneal response to orthokeratology treatment and better refractive outcomes when compared to adults (Subramaniam et al., 2007; Jayakumar et al., 2005). In the current study, there was a statistically significant difference in the mean age of patients completing the study and the mean age of patients discontinued from the study. Children were far more likely to successfully complete the three month study when compared to adults. This finding is in agreement with the previous studies.

Lens Changes and Patient Age

There was also a statistically significant difference in mean age for patients requiring lens changes and patients not requiring lens changes throughout the study. Patients requiring lens changes were, on average, older than those patients requiring no lens changes. Lenses were changed in the study due to several reasons including under-correction, perception of halos and lens decentration. Lens changes can indicate that the patient is having difficulties with the orthokeratology treatment and can be used to infer less successful outcomes. Interestingly, the majority of adults required lens changes because of under-correction, while the majority of children requiring lens changes were experiencing lens decentration. This finding is in agreement with a previous study where it was shown that adult's corneas are less responsive than children's corneas to orthokeratology treatment (Jayakumar et al., 2005).

Corneal Shape Changes and Age

Given the findings in this study showing differences in treatment outcomes between adults and children, possible reasons for these differences were investigated. Amount of corneal apical power change, as measured by corneal apical power at a certain time point minus baseline corneal apical power, was examined for relationships with patient age in this study. Although previous analysis suggested that children may have responded to orthokeratology treatment more quickly, no statistically significant relationships were found in this data. This finding does not agree with the previous study that showed older patients' corneas responding less or more slowly to treatment when compared to younger patients' corneas (Jayakumar et al., 2005). This study is different from the current study in that patients wore the lenses for only one hour. The shortest follow-up time for the current study was one day. Therefore, it seems that it may be possible, in at least the short term that older patients' corneas respond more slowly to orthokeratology treatment. This same outcome cannot be applied to long term data, at least based on the findings of the current study.

The difference in treatment outcomes between adults and children in this study are not likely due to differences in baseline refractive error (M values). There was no significant difference in baseline M found for either eye between adults and children. The difference in success between older and younger patients in this study also cannot be explained by corneal properties. There was no statistically significant difference in CH or CRF between older and younger patients in this study, indicating that there are most likely other explanations for the differences in treatment outcomes. At this point, it is unclear what factors may be involved.

Patients' Perception of Vision at Follow-Up Visits

Patient satisfaction surveys were administered at each visit in this study to assess patient perceptions of orthokeratology treatment. In a previous study assessing patients' experiences with orthokeratology, the most common patient complaint was blurred vision (Cheung and Cho, 2004). The authors conclude that this complaint was most likely due to residual astigmatism or due to the fact that some regression in treatment effect takes place during the first week of lens use (Cheung and Cho, 2004). A large number of patients in this study also reported glare as a significant side effect of the treatment (Cheung and Cho, 2004).

There are a few differences in the methods of the previous study when compared to the current study. The surveys in the previous study were given to patients who were already using orthokeratology lenses for at least twelve months before the study. The patients in the previous study were also all children. The surveys in the current study were given at each follow-up visit and patients included almost equal numbers of adults and children. Like the previous study, the surveys in the current study examined both patient reports of vision and comfort.

At the one day follow-up visit, most patients reported that the uncorrected vision was fair or poor. This finding makes sense given the fact that regression of treatment effect is occurring over the course of the day during this time point. Patients seemed to have a more positive assessment of the uncorrected vision as time went on in the study, with most patients reporting excellent or good vision at the three week and three month time points. This finding is likely due to the fact that the full treatment effect had already been reached at these time

points. Potentially confounding these findings is the fact that there were fewer patients at the later time points compared to the earlier ones. It is reasonable to assume that patients who were having difficulty with uncorrected vision were more likely to discontinue the study and are thus their opinions were not represented in the later surveys.

The same logic and conclusions can be applied to the findings on patient reports of change in vision from baseline uncorrected vision. Early on in the treatment, patients were less likely to report that the vision had improved from baseline. However, by the three month time point, the vast majority of patients had reported that the vision was either somewhat or greatly improved over the baseline uncorrected vision.

Comfort Ratings at Follow-Up Visits

Patients' eye comfort also appeared to improve over the course of the study. At the later follow up visits, slightly more patients reported that their eyes were either somewhat or very comfortable compared to the earlier visits. Again, these results may be confounded due to the fact that patients having eye comfort problems may have discontinued from the study before the later follow-up points and are not represented in the overall final totals.

Overall Patient Satisfaction with Treatment

The same trend seen in the previous survey measures was noted overall satisfaction data. More patients reported that they were either somewhat or very satisfied with orthokeratology treatment towards the end follow-up points compared to the beginning. No

patients reported being unsatisfied with the treatment at the three month visit. However, this data could again be confounded by patients who discontinued from the study.

Overall, it appears that patients are more likely to have difficulties with treatment during the early period when most corneal change and vision fluctuation is taking place. This suggests that patient education and frequent follow-up care is especially important in this time frame for successful use of orthokeratology lenses.

Results of Patient Surveys by Age

There were some key differences in patient responses to the surveys based on patient age. Children seemed more likely than adults to report that their vision was good or excellent earlier on in the study time frame. This same trend was seen with reports of perception of a change in vision. Children also seemed to have less overall problems with comfort when compared to adults in the earlier follow-up time points. Children also rated higher than adults in their satisfaction with treatment at all study time points.

This is interesting considering that children seemed to be more successful than adults with orthokeratology treatment in this study. This finding is perhaps due to the fact that children experience fewer side effects from treatment than adults, based on information from the surveys. However, another explanation for these findings could be that children may be less likely to complain about side effects compared to adults. Given this consideration, it is not clear whether or not the experience of side effects is a reason for the difference in success based on age.

Limitations of the Current Study

There were several important limitations to this study. Among these, patient compliance was one of the most important limitations. The study design was based on several predetermined follow-up time points. These time points were defined upon the basis of an average of eight hours lens wear per night and upon lens wear every night between follow-up visits with no skipped nights. Every effort was made to educate patients about the importance of wearing the lenses each night for an average of eight hours per night with the exception of adverse events outlined in the informed consent documents. However, not all patients were able to comply with this lens wearing regimen for various reasons. Compliance was good for the one day follow up visits. All patients wore the lenses on the previous night for six to ten hours. Compliance was again fairly good for the one week visit, with most patients wearing the lenses the night before the visit for six to ten hours. However, two patients were only able to wear the lenses three hours the night before the visit and another patient only wore the lenses for five hours. Additionally, three patients reported missing a few nights of wear during the previous week. At the three week visit, most patients wore the lenses close to the recommended number of hours the night before the visit. However, three patients did not wear the lenses at all the night before the visit. Also, two patients reported missing a few nights of wear during the previous two weeks between study visits. At the three month visit, only one patient did not wear the lenses for the recommended amount of time the night before the visit. However, several patients reported missing nights of lens wear during the previous months before the study visit.

Because the lenses were not worn on the same schedule by all patients, some of the data points collected could have been affected. Corneal apical power, refractive error, uncorrected visual acuity and central corneal thickness were the main data points that may have been skewed by a different schedule of lens wear.

Another limitation of this study is the time points at which data was collected. Because of the work and academic schedules of the principal investigator and research assistant, most patient appointments had to be scheduled in the afternoon and evening hours. Variable amounts of regression in treatment effect may have occurred between the time of lens removal upon awakening and the time at which measurements were taken in the afternoon. All patients were seen at the same time of day, within a two hour window, for each visit of the study. This was one of the important factors in reducing the variability in the corneal characteristic measurements.

Several studies have investigated both the sustainability of treatment during the day and reversibility of the treatment effects after discontinuation of lens wear and provide some information about how the data in this study may have been affected. One large study investigated the treatment effects of orthokeratology in patients both in the morning and in the afternoon for a period of twelve weeks (Kang, Kim and Byun, 2007). The time points where measurements were taken were similar to the follow-up points in this study. At the one day follow-up visit, large fluctuations in uncorrected visual acuity and corneal apical power were observed. Specifically, uncorrected visual acuity was best in the morning and had regressed significantly in the afternoon. The same pattern was seen with corneal apical

power, with most flattening seen in the morning and a large regression demonstrated in the afternoon. The amount of change noted between same day visits seemed to vary with each patient. The difference in measurements between morning and afternoon visits gradually decreased over time, with almost no difference observed at the one-month follow up point.

A different study on the reversibility of orthokeratology treatment after discontinuation of lens wear also provided some information of interest in the current study (Soni et al., 2004). In that study, patients wore orthokeratology lenses for one month and then discontinued lens wear. Uncorrected visual acuity, refractive error and corneal curvature all showed variable recovery periods after discontinuation. Most importantly, central corneal thickness had completely recovered to baseline values just one day after discontinuing lens wear. However, this measure was reported as an average of all patients and does not necessarily represent the exact changes seen in an individual patient.

These studies suggest that there may have been some variability introduced in the data for the current study. It is unclear how much regression in treatment may have occurred for each individual patient between the time of lens removal and each follow-up visit. Adding to this, there were different time periods between lens removal and study visits for each patient, with some visits occurring at noon and others occurring as late as 6pm. Both of these factors could have influenced the data to some extent, especially when making comparisons between patients.

There was much less variability when monitoring for corneal change within a single patient. Each study visit was at the same time of day for each patient in the current study. By

doing this, the time between lens removal and the study visit was approximately the same for each data point. Therefore, the change in corneal properties between follow-up visits for individual patients was likely less affected by regression.

Variability in Corneal Characteristic Measurements

Overall, the variability in CH and CRF measurements in this study were comparable to previous studies. All between and most of within subjects varaibilities were similar to what was found a previous study, with standard deviations (between subjects) of 1.90 mmHg for CH and 2.08 mmHg for CRF (Luce, 2005).

For those patients with high within subjects varaibilities in CH or CRF measurements, the relationship between these values and all outcome measures were examined. There were no significant relationships found between either CH or CRF with corneal apical power, visual acuity or refractive error values. Due to the small number of patients, small number of data points for each patient and lack of statistically significant associations seen, there is no strong evidence that the variability seen in CH and CRF measurements for these patients correlated with treatment outcomes in this study.

In a recent study on the repeatability of measurements taken by the Reichert Ocular Response analyzer, it was found that the coefficient of repeatability for CH was 2.61 mmHg (Kynigopoulos, Schlote, Kotecha, Tzamalis, Pajic & Haefliger, 2008). This means that the difference in two successive measurements of CH on the same eye of the same patient should fall within this range 95% of the time with this instrument. There are also some studies on the variability of several standard non-contact tonometers as well. In one study, the repeatability

coefficient for one non-contact tonometer was found to be 3.59 mmHg for right eyes and 3.51 mmHg for left eyes (Regine, Scuderi, Cesareo, Ricci, Cedrone and Nucci, 2006). In another study with a different non-contact tonometer, the coefficient of repeatability was found to be 3.1 mmHg (Ogbuehi and Almubrad, 2008). Given this information, very few of the maximum to minimum measurement ranges in this study fell outside of the ranges given for previous studies (4 right eyes and 6 left eyes for CH and 3 right eyes and 3 left eyes for CRF).

Conclusions

Overall Findings

This study found few significant relationships between corneal properties and measures of corneal change over time with orthokeratology lens treatment. Given these findings, it appears unlikely that corneal characteristics can be used to reliably predict corneal change in orthokeratology, at least in a clinical setting.

There were significant changes in central corneal thickness and CRF values seen over the study period. The change in central corneal thickness noted in this study was in agreement with several previous studies. The change in thickness can be linked to changes in refractive error and uncorrected visual acuity. The change in CRF was noted in one previous study and it is unclear whether or not this change represents an overall reduction in corneal rigidity brought about by orthokeratology treatment.

It appeared that children were more successful than adults with orthokeratology treatment in this study. This finding was not due to differences in baseline corneal properties between children and adults. It is possible that age is an important consideration when predicting the success of treatment for a potential orthokeratology patient.

Patients in this study were less satisfied with their vision and had more discomfort problems during the first few weeks of treatment. Therefore, patient education and frequent follow-up during this initial period of lens wear may be a very important factor in patient success.

Suggestions for Future Studies

Future work should focus on investigating other factors that may be predictive of corneal change including lid elasticity and tear film properties. Other future studies should examine the change in CRF over time with orthokeratology treatment and try to determine if this represents an overall reduction of corneal rigidity. Another area of possible study is the differences between children and adults with outcomes of treatment. Investigation into the possible reasons for these differences may provide good predictive measures for success with treatment.

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Appendices

Appendix A – Patient Take Home Information Sheet

Contact Lens Care and Cleaning Information

Contact Lens Solutions

Your contact lens solution is Boston SimPlus Multi Purpose Solution. You also have a bottle of Boston Rewetting Drops for use with your lenses. Never put contact lenses in your mouth to rewet them. The bacteria that normally live in your mouth can cause serious eye infections.

Why should I take good care of my lenses?

Contact lenses are classified as a medical device and should be used as recommended by your doctor. Proper lens cleaning is important in keeping your eyes healthy. With all contact lenses, there is a risk for serious and sometimes sight-threatening complications such as ulcers and infections. These risks are greatly reduced if your lenses are cleaned and handled correctly.

Insertion and nightly cleaning of your ortho K lenses

Notes: *Always* wash your hands before touching your lenses or your eyes. Mild soaps are the best ones to use and heavily scented soaps should be avoided. Insert your lenses at bedtime. Using a mirror that is placed flat on a table or surface is recommended for lens insertion.

1. Wash your hands.
2. Remove your lens from the case by placing your finger on the lens and lifting straight up. Scooping the lens from the case may scratch it.
3. Place the lens in the palm of your hand "bowl up" (see diagram on page 3) and put 4 drops of fresh SimPlus Solution in it. Rub the lens with the index finger of your other hand for 20 seconds. Rub from side to side and up and down to ensure you have cleaned the whole surface of the lens. Rubbing your lenses removes protein and lipid deposits from them.
4. Rinse the lens on both sides for 5 seconds with fresh SimPlus Solution. Rinsing your lenses washes away the pieces of protein and lipid deposits that you have just rubbed off the lenses.
5. Dry the index finger of your dominant hand with a lint free towel. Place the lens "bowl up" on your index finger. Place a small drop of SimPlus Solution in the lens.

6. With the index or middle finger of your non-dominant hand, pull up the upper lid of your eye and hold it in place.
7. With the middle finger of your dominant hand, pull down the lower lid of your eye and hold it in place.
8. Looking straight ahead, place the lens gently onto your cornea (colored part). It helps to keep both eyes open during lens insertion. It is not necessary to press hard on your eye to get the lens to stay in place.
9. Remove your finger from the lens and slowly release your eyelids.
10. Repeat steps 2-9 for your other eye.
11. Rinse your lens case with hot tap water and place it upside down on a lint free towel to air dry overnight.

Lens Removal and Daytime Storage

Notes: Always handle lenses over a table top or counter to minimize the risk of dropping them in/down the sink or on the floor. This is especially important during removal, as the lens may "pop" off the eye.

1. Wash your hands.
2. Check to see that your lens is moving on your eye. This is very important and you should be sure the lens is moving before you attempt to remove it. If the lens is not moving, follow the procedure for a "stuck" lens on page number 3.
3. When the lens is moving, there are two methods you can use to remove the lens:
    a. Method 1 – Pull and blink:
        i. Tilt your head down parallel to the counter top or table. To remove the right lens, cup your left hand under the right eye to catch the lens.
        ii. Place the tip of your right index finger at the outer corner of your right eye. Open your eye wide.
        iii. Pull the lids with your right hand toward your ear. Blink. Catch the lens as it falls out of the eye.
        iv. Repeat this procedure for the left eye.
    b. Method 2 – Scissor method:
        i. Place the index finger of either hand at the edge of the lower lid and place the index finger of the other hand at the edge of the upper lid.
        ii. Using your fingers, open your eye wider than the diameter of the contact lens.
        iii. Using gentle but adequate pressure on the eye, push your eyelids towards each other (so that the eye closes) slowly. The lens should come off of the eye.
        iv. Repeat this procedure for the other eye.
4. Place the lenses in a dry lens case and fill the wells with SimPlus Solution making sure the lenses are adequately covered.

5. Store the lenses in the solution for at least 4 hours before wearing again. Soaking your lenses allows the solution to kill bacteria and other microorganisms that can cause infections in your eyes.

Procedure for removing a "stuck" lens

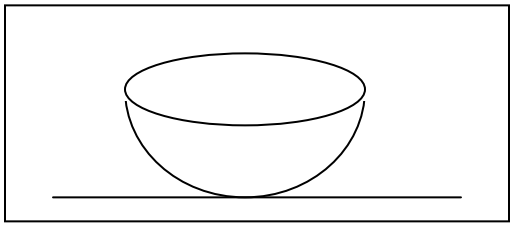
Sometimes, during overnight wear, an ortho K lens can adhere to the eye. This can be due to many factors, but it is easily loosened in most cases. If your lens is not moving freely on your eye, follow these steps:

1. Place one or two drops of rewetting solution in each eye. Wait a few minutes, blinking normally and looking up and down and side to side. In many cases, the lenses will begin to move on their own after doing this.
2. If your lenses are not moving after a few minutes:
    a. Look down and place your index finger on your upper lid. Feel for the edge of the lens through the lid. Apply gentle pressure to your eye just above the edge of the lens (not on the lens directly!!) for a few seconds.
    b. Look up and place your index finger on your lower lid. Again, feel for the edge of the lens through the lid. Apply gentle pressure to your eye just below the edge of the lens (not on the lens directly) for a few seconds.
    c. Look up and down and side to side and recheck the lens for movement.
    d. Repeat this procedure as necessary until the lens begins to move. You may also put in more rewetting drops as needed.
3. If your lenses still are not moving after 30 minutes, call Dr. Rah or the New England Eye Institute emergency line and come in to see us immediately. We will help you remove the lens.

Recentering a lens

Sometimes a lens can "decenter" on to the white part of the eye. This happens especially during insertion and removal. DON'T PANIC! Contact lenses cannot be "lost" behind your eye. Although it may be a bit uncomfortable, a decentered lens can be easily and safely moved back into position by following these steps:

1. Locate the lens by looking in a mirror.
2. Look in the opposite direction of where the lens is on the eye (if the lens is more towards your ear, look towards your nose.
3. Place your index fingers on your upper and lower lids (using both hands) near the edge of the lid. Hold the lens in place (gently!) and look towards the lens. The colored part of your eye will move under the stabilized lens and will cause the lens to be recentered.



“Bowl Up”

Problems with contact lens wear

If you experience any of the following symptoms, remove your lenses and call us. You may or may not need to come in for an appointment.

- Continuous or severe redness of one or both eyes
- Continuous or excessive tearing/watery eyes
- Changes in sensitivity to light, especially an increase in sensitivity
- Inability to keep your eyes open
- Continuous or severe pain in one or both eyes
- Sudden decreases in vision
- Unusual eye secretions

Remember:

- Always wash your hands before handling your lenses or touching your eyes
- Don’t handle your lenses over a sink. Handle them over a table or counter top.
- The **R**ed lens goes in the **R**ight eye and the ye**L**low lens goes in the **L**eft eye.
- Remove your lenses immediately if you have a problem.
- Wear your lenses 6-8 hours every night and don’t wear them during the daytime.

Contact Information

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Appendix B – Patient Satisfaction Surveys

Quality of Vision and Eye Comfort Survey - Baseline

Please answer all of the following questions by circling the answer that is most true for you.

1. Do you currently wear glasses?
□1 Yes (go on to question 1a)
□2 No (go on to question 2)

1a. How would you rate your vision with your glasses?
□1 Excellent
□2 Good
□3 Fair
□4 Poor

1b. How comfortable are your eyes when you wear your glasses?
□1 Very comfortable
□2 Somewhat comfortable
□3 Somewhat uncomfortable
□4 Very uncomfortable

1c. Overall, how satisfied are you with your glasses?
□1 Very satisfied
□2 Somewhat satisfied
□3 Somewhat dissatisfied
□4 Very dissatisfied

2. Do you currently wear soft contact lenses?
□1 Yes (go on to question 2a)
□2 No (go on to question 3)

2a. How would you rate your vision with your contacts?

□1 Excellent

□2 Good

□3 Fair

□4 Poor

2b. How comfortable are your eyes with your contacts?

□1 Very comfortable

□2 Somewhat comfortable

□3 Somewhat uncomfortable

□4 Very uncomfortable

2c. Overall, how satisfied are you with your contacts?

□1 Very satisfied

□2 Somewhat satisfied

□3 Somewhat dissatisfied

□4 Very dissatisfied

3. In general, how would you rate your everyday vision?

□1 Excellent

□2 Good

□3 Fair

□4 Poor

Quality of Vision and Eye Comfort Survey

Visit: □1 One day □2 One week □3 Three weeks □4 Three months

Please answer all of the following questions by circling the answer that is most true for you.

1. What was your previous method of vision correction?

□1 Glasses
□2 Soft contact lenses
□3 Glasses and contacts
□4 None
□5 Other (please specify)

2. How would you rate your vision *today*?

□1 Excellent
□2 Good
□3 Fair
□4 Poor

3. Thinking about how your vision was before starting ortho K treatment, would you say your vision has:

□1 Greatly improved
□2 Improved slightly
□3 Not changed significantly
□4 Become slightly poorer
□5 Become much poorer

4. How would you describe your vision *today* (check all that apply)?□1 Things are clear

□2 Things are sharp

□3 Things are blurry

□4 Things appear wavy

□5 I see things double

□6 Things appear cloudy

□7 Things are in focus

□8 Things are out of focus

□9 The world appears dim

□10 The world is bright

5. How do your eyes feel *today*?

□1 Very comfortable

□2 Somewhat comfortable

□3 Somewhat uncomfortable

□4 Very uncomfortable

6. Are you having any specific problems with your eyes *today*? □1 Yes (go on to question 6a)

□2 No (go on to question 7)

6a. Which problems are you having with your eyes *today*?

□1 They are dry

□2 They itch

□3 They are red

□4 They hurt

□5 They feel sticky

□6 They feel "sandy"

7. Overall, how satisfied are you with ortho k treatment?

□1 Very satisfied

□2 Somewhat satisfied

□3 Somewhat dissatisfied

□4 Very dissatisfied