Full title: Short- and long-term changes in corneal power are not correlated with axial elongation of the eye induced by orthokeratology in children.

Running head: Corneal power and axial length with orthokeratology

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ABSTRACT

Purpose: To assess the relationship between short- and long-term changes in power at different corneal locations relative to the change in central corneal power and the 2-year change in axial elongation relative to baseline in children fitted with orthokeratology contact lenses (OK).

Methods: Thirty-one white European subjects 6-12 years of age and with myopia -0.75 to -4.00DS and astigmatism ≤1.00DC were fitted with OK. Differences in refractive power 3 and 24 months post-OK in comparison to baseline and relative to the change in central corneal power were determined from corneal topography data in 8 different corneal regions (i.e. N (nasal)1, N2, T(temporal)1, T2, I(inferior)1, I2, S(superior)1, S2), and correlated with OK-induced axial length changes at 2-years relative to baseline.

Results: After two years of OK lens wear, axial length increased by 0.48±0.18mm ($p<0.001$); which corresponded to an increase of 1.94±0.74% ([2-years change in axial length/baseline axial length]*100). However, the change in axial elongation in comparison to baseline was not significantly correlated with changes in corneal power induced by OK relative to baseline for any of the corneal regions assessed (all $p>0.05$).

Conclusion: The reduction in central corneal power and relative increase in paracentral and pericentral power induced by OK over 2 years were not significantly correlated with concurrent changes in axial length of white European children.

Key words: cornea, power, topography, myopia progression, orthokeratology, contact lenses

INTRODUCTION

Myopia is globally recognized as a significant public health concern associated with increased ocular-related morbidity and considerable healthcare costs.[1-3] It is the most common refractive error; affects around 30% of the world's population; and its prevalence has been estimated a significant increase to affect around 50% of the world's population by 2050.[4] The prevalence of myopia in young adolescents has been increasing in recent decades to reach 10–25% in industrialized societies of the West and epidemic levels of 60–80% in East Asia.[4-6] Of particular concern is that there appears to have been a commensurate increase in high myopia (i.e. ≤ -6.00D)[7-10] leading to a higher risk of potentially blinding ocular pathologies such as glaucoma, macular degeneration and vitreous and retinal detachments.[11–14] That the myopic eye is, in terms of propensity to ocular pathology, a vulnerable eye[3] has prompted interest in therapies to ameliorate its progression. Several treatment options have been used in the past with limited success to eliminate or, at least, reduce myopia progression.[15-18] However, recent studies have reported orthokeratology contact lens wear (OK) to significantly reduce axial length growth by 30 to 50% in comparison to spectacle and soft contact lens wear.[19-24] In this regard, of the optical treatment options currently available OK is the method with the largest demonstrated efficacy in reducing myopia progression across different ethnicities.[25] Furthermore, OK lens wear has a relatively low rate of adverse events and discontinuations[26] and is well accepted by parents and children.[27]

Orthokeratology induces a flattening of central corneal curvature to temporarily correct myopia. In addition, there is a concurrent relocation of epithelial tissue or fluid within or between epithelial cells from the center to the mid-periphery that produces a decrease and increase in central and mid-peripheral corneal thickness, respectively.[28] Such induced changes in corneal curvature following OK lens wear can be precisely monitored with currently available corneal topographers and have important refractive implications.[29-31] In fact, a strong correlation has been previously reported between the amount of apical corneal power change and refractive power change following OK, although the change in power has been found to underestimate the change in manifest refractive error.[32] Furthermore, in myopic subjects, the change in central corneal thickness induced by OK has been shown to account for concomitant changes in refraction.[31] A number of animal studies have shown that peripheral refraction is important in the emmetropization process such that relative peripheral hyperopic and myopic defocus can induce and inhibit myopia progression, respectively.[33-41] Of relevance to myopia control in humans therefore is that relative peripheral hyperopic defocus is reduced in OK[42, 43] compared with the increase that occurs in single vision spectacle lens wear[44] and the neutral effect of bifocal soft or gas-permeable contact lens wear.[45, 46] Peripheral myopic defocus induced by OK has consequently been hypothesized in several studies as the basis for its efficacy in myopia control.[47]

Recently, Zhong et al. evaluated whether corneal power changes induced by a proprietary OK lens design (i.e. Hiline Optics, China) are predictive of myopia progression in 32 Chinese children aged from 9 to 14 fitted with OK for 2 years.[48] Using a TMS-4 corneal topographer instrument (Tomey Corporation, Japan), corneal apical refractive power was provided automatically and corneal sagittal powers were recorded manually at four locations along the nasal, temporal, and inferior corneal axes (i.e. 1, 2, 3 and 4 mm intervals from the apex).[48] The study compared the pre- and post-OK changes in peripheral corneal sagittal refractive powers (relative to the central apical power) and the 2-year change in axial length.[48] It was reported that the larger the relative post-OK change in relative positive peripheral corneal power along the nasal, temporal and inferior cornea the smaller the axial elongation after 24 months of lens wear.[48] In the Zhong et al. study, however, sagittal corneal power changes pre- and post-OK were measured manually and hence susceptible to human error.[48] Corneal topography sagittal maps measure corneal curvature at any given point on the cornea as the perpendicular distance from the corneal surface to the optical axis, which is then converted to sagittal power using the paraxial power formula for a single refracting surface.[49-51] Although sagittal maps provide useful measurements of the shape of the cornea in the form of curvature, their ability to represent corneal refractive power is limited.[49-51] Contemporary corneal topographers feature built-in software with refractive power difference maps that are able to measure directly changes in corneal power pre- and post-OK. Furthermore, difference refractive maps can provide mean changes in corneal power across certain regions of the cornea and are thus likely to better reflect corneal power changes following OK lens wear rather than assessing the change in corneal power at isolated corneal points (Figure 1). In addition, unlike sagittal maps, refractive maps account for spherical aberration and with reference to Snell's law describe how light is refracted through an aspheric surface such as the human cornea.[49-51] Therefore, difference refractive corneal topography maps offer particular advantages when assessing refractive changes following OK lens wear in comparison to no lens wear.

The present study examines the correlation between changes in axial length and short- (3 months post-OK) and long-term (24 months post-OK) changes in corneal power induced by OK with reference to data from our previous study, Myopia Control with Orthokeratology contact lenses in Spain (MCOS). MCOS evaluated, as the primary outcome measure, differences in growth of axial length over a 2-year period in white European children with myopia wearing OK contact lenses and distance single-vision spectacles.[23] Thirty-one children were prospectively allocated to OK and 30 to distance single-vision spectacles. No statistically significant differences were found in any of the baseline demographics and refractive and biometric data between groups, including central corneal power and corneal shape (p-value). However, we reported a statistically significant difference in axial length elongation relative to baseline between the OK (mean ± standard deviation, 0.47±0.18mm) and distance single-vision spectacles (0.69±0.32mm) groups ($p = 0.005$).[23]

METHODS

This study was part of a larger study designed to assess different aspects of OK lens wear specifically prescribed for the control of myopia progression in children.[23, 26, 27, 52-56] Normal, healthy, white European subjects 6 to 12 years of age with moderate levels of myopia [mean spherical equivalent (MSE) -0.75 to -4.00D] and astigmatism ≤1.00D) and free of systemic or ocular disease were fitted with Menicon Z Night contact lenses for overnight use (Menicon Co., Ltd, Nagoya, Japan). An OK fit was considered to be successful if the subject showed a CCLRU score regarding anterior eye segment signs of ≤1 unit,[57] a “bull’s eye” corneal topography pattern and unaided monocular and binocular visual acuities within ±1 line of the best-corrected spectacle decimal visual acuity. All patients underwent ocular examinations including slit-lamp examination, manifest refraction, and corneal topography at baseline and then following 1 day, 2 weeks, 3 months and 6-month intervals over a 2-year period. Axial length was measured at the time of enrolment and 6, 12, 18, and 24 months after the initiation of the treatment. Follow-up visits were scheduled to fall within 2 hours of awakening. A decrease in one line of visual acuity accompanied by a change in subjective refraction at any of the follow-up visits[58] was considered clinically significant and was remedied by supplying new contact lenses. Full informed consent and child assent was obtained from the parents/guardians prior to the start of all experimental work and data collection. Patient participation in the study could be discontinued at the examiner’s discretion should significant symptoms or slit-lamp findings occur. Subjects were instructed that they could withdraw from the study at anytime. The study was conducted in accordance with the Tenets of the Declaration of Helsinki and approved by the Institutional Ethical Committee Review Board of Novovision Ophthalmology Clinic.

Cycloplegic auto-refraction was performed following the instillation of three drops of cyclopentolate HCl 1% separated 10 min apart in each of the subjects' eyes using a multidose bottle (Alcon Cusí, Masnou, Barcelona, Spain). Ten minutes after the instillation of the third drop, three auto-refraction measurements were taken and a mean obtained (Topcon RM 8000B, CA, USA).

Measurements of axial length were taken with the Zeiss *IOLMaster* (Carl Zeiss Jena GmbH). Three separate measurements of axial length were recorded and a mean obtained.[59] The 2-year change in axial length relative to baseline was calculated as a percentage to normalize between-subjects differences in changes in axial length relative to the baseline axial length [(2-years change in axial length/baseline axial length)*100].

Corneal topography measurements were performed with the Wavelight Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The instrument incorporates a high resolution placido ring corneal topographer which detects 22,000 elevated data points of measurement evenly distributed from 22 ring edges with a accuracy and reproducibility of ±0.10D as claimed by the manufacturer. The instrument has been reported to display excellent reliability in measuring corneal power (i.e. an intraclass correlation coefficient ≥0.971).[60] The first measurement taken for each eye, which provided an optimum index value according to the manufacturer's recommendations, was used for the study. Baseline, 3- and 24-months topographic outputs were taken as representative of the pre-, short- and long-term post-OK treatment status, respectively.[28] Corneal topography was analyzed using Oculus Keratograph software (Version 1.76, Oculus Optikgeräte GmbH, Germany). Differences in refractive power between baseline and 3- and 24-months were quantified using the 'refractive compare' display map provided by the instrument software. The map displays average values of change in corneal power for 4 different quadrants (nasal, temporal, inferior and superior) and between the paracentral (i.e. 3 to 5mm ring diameters) and pericentral cornea (i.e. 5 to 8mm ring diameters). The map thus generates for analysis 8 discrete corneal regions N1, N2, T1, T2, I1, I2, S1, S2 and a single central corneal area, C (Figures 1 and 2). However, data from the superior pericentral cornea (i.e. S2) were not analyzed owing to intrusion by the upper lid and lashes. The change in corneal power induced by OK for each corneal region was measured relative to the change in central corneal power (e.g. $[N1_{post\text{-}OK} - N1_{pre\text{-}OK}] - [C_{post\text{-}OK} - C_{pre\text{-}OK}]$). Additionally, central and total multifocality were also calculated. Central multifocality was defined as the greatest difference in corneal power following subtraction of the change in central corneal power from the change in corneal power at any of the 7 different corneal regions measured (relative to the change in central corneal power). Total multifocality was defined as the greatest difference in corneal power between any two of the 7 different corneal regions assessed relative to the change in central corneal power.

Statistical analysis

A 1-way within-subjects analysis of variance (ANOVA) was used to assess whether OK lens wear induced differences in corneal power changes between different regions in the paracentral (i.e. N1, T1, I1 and S1) and pericentral (i.e. N2, T2 and I2) cornea separately. Equality of variances and sphericity were tested using the Levene and Mauchly tests, respectively. *Post-hoc* t-tests with Bonferroni correction were used to assess differences between pairs of comparisons. Differences in power at each individual corneal location relative to baseline between 3 and 24 months of OK lens wear as well as between central and total multifocality were assessed using a paired t-test. Simple linear regressions were used to demonstrate the relationship between the 2-years' change in axial elongation relative to baseline (i.e. the dependent variable) and the change in corneal power at each of the different corneal locations assessed as well as with central and total multifocality. Data from right eyes only were used for analysis and expressed as mean ± standard deviation. Statistical analyses were performed with *SigmaPlot* (Systat software Inc, California, USA). The level of statistical significance was set at 5%.

RESULTS

The subjects' demographic and baseline data have been reported elsewhere.[23, 52] In brief, thirty-one children were prospectively fitted with OK contact lenses, but two children discontinued the study; one due to discomfort with contact lens wear and another to unknown reasons.[26] One subject completed the study, but was excluded from the analysis as corneal topography data were unreliable. At the start of the study, the mean age of the remaining 28 subjects was 9.6 ± 1.6 years; 15 were male and 13 were female.

Three and 24 months of OK lens wear produced a significant reduction in myopia (MSE) from -2.20±1.13D to -0.19±0.23D and -0.33±0.29D, respectively (both $p<0.001$); the change in MSE between 3 and 24 months was also statistically significant ($p=0.005$). The cylindrical component of the refraction did not change significantly between any of the 3 pairwise comparisons (i.e. baseline vs. 3-months, baseline vs. 24-months and 3- vs. 24-months) (all $p>0.05$). Central corneal power decreased by -1.89±0.91D at 3 months and by -1.84 ±0.97 at 24 months in comparison to baseline; the difference in corneal power change relative to baseline between short- and long-term OK lens wear was not statistically significant ($p=0.710$). Axial length increased from 24.53±0.78mm at baseline to 25.01±0.82mm following 2-years of OK lens wear ($p<0.001$). The 2-years change in axial length (i.e. 0.48±0.18mm) corresponded to an increase of 1.94±0.74% (i.e. [2-years change in axial length/baseline axial length]*100).

Short- and long-term OK lens wear induced an asymmetric change in power in the paracentral cornea (p=0.003 and p<0.001, respectively) that was attributable to the difference in power between N1 and T1 at 3 months (p=0.001) and between T1 and N1, I1 and S1 at 24 months (all p<0.05) (Figure 3). Similarly, significant differences in power were found between different regions of the pericentral cornea at both 3 (p=0.021) and 24 months (p=0.02) relative to baseline that were attributable to the difference in power between N2 and T2 at both 3 and 24 months (both p<0.05) (Figure 3). Short- and long-term OK lens wear induced similar changes in corneal power relative to changes in central corneal power at each of the 7 corneal regions assessed (all p>0.05) with the exception of S1 where the change in corneal power was significantly more positive following long- in comparison to short-term OK lens wear (p=0.037).

After 3 and 24 months of OK treatment, the greatest differences in power between the central cornea and any other corneal region (i.e. central multifocality) were -2.69±1.16 D and -2.53±1.39 D, respectively; central multifocality was not statistically different between short- and long-term OK lens wear (p=0.474). After 3 and 24 months of OK treatment, the greatest differences in power between any two corneal regions (i.e. total multifocality) were -2.94±1.22 D and -2.70±1.41 D; total multifocality was not statistically different at 3 in comparison to 24 months (p=0.333). The difference between central and total multifocality was, however, statistically significant following both short- and long-term OK lens wear (both p<0.001).

The change in axial elongation over 2 years relative to baseline was not significantly correlated with changes in corneal power induced by OK over 3 or 24 months relative to baseline at any of the corneal regions assessed (all p>0.05) (Table 1). Similarly, the mean changes in corneal power at the nasal (i.e. mean of N1 and N2), temporal (i.e. mean of T1 and T2), inferior (i.e. mean of I1 and I2), horizontal (i.e. mean of N1, N2, T1 and T2), vertical (i.e. mean of I1, I2 and S1), paracentral (i.e. mean of N1, T1, I1 and S1) or pericentral corneal regions (i.e. mean of N2, T2 and I2) following either 3 or 24 months of OK lens wear were not significantly correlated with the 2-year change in axial length relative to baseline (all p<0.05) (Table 1 and Figures 4 and 5).

Neither central nor total multifocality following short- or long-term OK lens wear were significantly correlated with the 2-year change in axial length relative to baseline (all p<0.05) (Table 1).

DISCUSSION

The decrease in central corneal power and concomitant increase in paracentral and pericentral corneal power found in this study is consistent with previous reports of central corneal flattening and peripheral steeping following OK lens wear.[28-31] Following 3 months of OK lens wear, Zhong et al. reported significant increases (compared with baseline) in sagittal power at the nasal 2 and 3mm, temporal 3mm and inferior 2, 3 and 4mm corneal locations; peaking was evident at the 3mm location (i.e. 6mm corneal ring) compared with the apical center.[48] The present study found increases in corneal power at both the paracentral and pericentral locations but these were greater in the pericentral region (i.e. 5 to 8mm ring diameter) than in the paracentral region (i.e. 3 to 5mm ring diameter) following both 3 and 24 months of OK lens wear. That OK induced asymmetrical power changes along different areas of the cornea agrees with the results of Maseedupally et al.[61] The latter finding might be attributed to the fact that the normal corneal shape is not rotationally symmetric and exhibits some hemi-meridional variation.[62-64] Therefore, the wearing of a rotationally symmetric OK contact lens on the eye will result in asymmetrical power changes along different regions of the cornea. Additionally, the greater changes in corneal power found for the nasal cornea in comparison with the temporal cornea are in agreement with previous studies[48, 61, 65] and might be attributable to temporal decentration of the OK treatment leading to greater flattening and thus reduction of corneal power of the temporal cornea in comparison with the nasal cornea.[65] It should be noted that changes in central, paracentral and pericentral corneal powers following OK lens wear have important refractive implications which in turn are affected by pupil size. Incident light rays parallel to the visual axis will be susceptible to an increase in spherical aberration as pupil diameter increases.[66] The increase in spherical aberration is generally relatively moderate when the central area of corneal flattening following OK treatment encompasses the pupil. However, when light rays simultaneously pass through corneal regions of marked difference in refractive power (i.e. central and paracentral/pericentral corneal regions), which might occur with off-axis (i.e. oblique) incidence and/or in subjects with larger pupils, that would produce a peripheral astigmatic refraction (i.e. relative hyperopia and myopia for light rays passing through the central and paracentral/pericentral corneal regions, respectively). Although the resulting pattern of astigmatic refraction and the position of the sagittal and tangential image shells relative to the retina might have important implications in terms of regulating myopia progression, the physiological and optical mechanisms for modulating ocular growth are unclear.[67]

Hiraoka et al. reported an increase in corneal multifocality from 1.69±0.42 to 4.92±2.50 D (Δ=3.23D) following 12 months of OK lens wear,[68] whereas the present study found central and total multifocality to be 2.69±1.16 and 2.94±1.22D, respectively following 3 months of OK lens wear and 2.53±1.39 and 2.70±1.41D, respectively following 24 months of OK lens wear. Hiraoka et al. found a statistically significant negative correlation between changes in corneal multifocality and the 1-year change in axial elongation,[68] whereas in the present study neither central nor total multifocality were significantly associated with the 2-year change in axial length relative to baseline. The discrepancy might be attributable to differences between studies in the determination of multifocality as Hiraoka et al. measured corneal multifocality as the difference between the maximum and minimum corneal optical powers (in diopters) calculated within the central 4-mm pupillary.[68] The greater levels of multifocality found by Hiraoka over the central cornea could potentially be associated with changes in axial length. Furthermore, the finding that the changes in relative positive corneal power for the paracentral and pericentral cornea were not significantly correlated with the change in the axial length is in disagreement with the results of Zhong et al.[48] It is feasible that differences in OK lens designs and corneal topography between Caucasian and Chinese individuals[69] could produce different profiles of refraction in the peripheral cornea which, in turn, might differentially affect the axial elongation of the eye. The clear lack of correlation between changes in paracentral and pericentral corneal power and change in axial length found in this study was not anticipated given the well documented evidence from animal models that peripheral myopic and hyperopic defocus can modulate change in axial length.[33-41] However, the paracentral and relative pericentral myopic defocus induced by OK lens wear in children differs inherently from that produced by optically imposed defocus in animals where exposure to defocus is generally substantial in terms of both magnitude and duration.[33-41] Furthermore, large studies in humans have failed to find peripheral refraction to affect myopia progression.[70, 71] Other factors that could affect myopia progression and ultimately the correlation between changes in corneal power and axial length following OK treatment are ethnicity, family history and outdoor exposure. It is well established that certain ethnicities, such as those from Far East Asia (i.e.

Chinese, Hong Kongers, Taiwanese, South Korean, Japanese and Singaporean), are at higher risk of myopia development and progression.[4, 72, 73] However, all subjects recruited for this study were limited to White European ethnicity. Similarly, children with myopic parents are at higher risk of developing myopia, with the risk increasing with the number of myopic parents.[74-76] In fact, a previous analysis of the MCOS study showed smaller increases in axial length with lower levels of parental myopia in children wearing OK lenses in comparison to children wearing spectacles.[53] Higher levels of time spent outdoors have been shown to be protective for myopia development.[77, 78] Although time spent outdoors was not controlled in the MCOS study, it may be presumed that children participating in the study were exposed to similar levels of outdoor exposure.

In summary, we conclude that, based on the results of this study, the inhibition of axial length growth found in the MCOS study is a not consequence of a relative myopic shift in the peripheral retinal image induced by changes in corneal power following OK lens wear. It should be noted, however, that changes in corneal power give only an indirect estimate of changes in relative peripheral refractive error. We envisage that the findings of this study will contribute to the debate of the role of peripheral imagery in the etiology of human myopia.[47]

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TABLE LEGENDS

Table 1. Univariate regression analyses. The strength of association between the different factors is indicated by linear regression equations, R-squared values and p-values.

FIGURE LEGENDS

Figure 1. Refractive compare map of the Oculus Keratograph software displaying the post- to pre-OK change in corneal refractive up to a 8mm ring diameter for the right eye of an individual subject. The map on the top right shows data post-OK lens wear, the one on the bottom right data pre-OK lens wear, and the larger map on the left shows the difference in corneal power (i.e. post-OK – pre-OK). The right and left sides of each of the 3 maps correspond to nasal and temporal corneal regions, respectively. The color scale on the far right represents the absolute refractive power of the cornea, whereas the color scale on the far left represents the relative change in corneal power. Warmer (i.e. red) and darker colors (i.e. blue) indicate increases and decreases in corneal power, respectively. Average values of corneal power change for certain regions of the cornea are provided on the larger map on the left.

Figure 2. Areas of corneal power change (i.e. post-OK – pre-OK) for the right eye. The regions located between the 3- and 5-mm diameter rings are referred to as “paracentral” corneal regions (i.e. N1, T1, I1, S1), whereas the regions located between the 5- and 8-mm diameter rings are referred as pericentral corneal regions (i.e. N2, T2, I2, S2). C, central; N, nasal; T, temporal; I, inferior; S, superior. It has been estimated that the central region and each of the 4 regions of the paracentral (i.e. N1, T1, I1, S1) and pericentral (i.e. N2, T2, I2, S2) cornea assessed by the corneal topographer

encompass 3,094, 1,374 and 3,352 elevated data points of measurement, respectively.

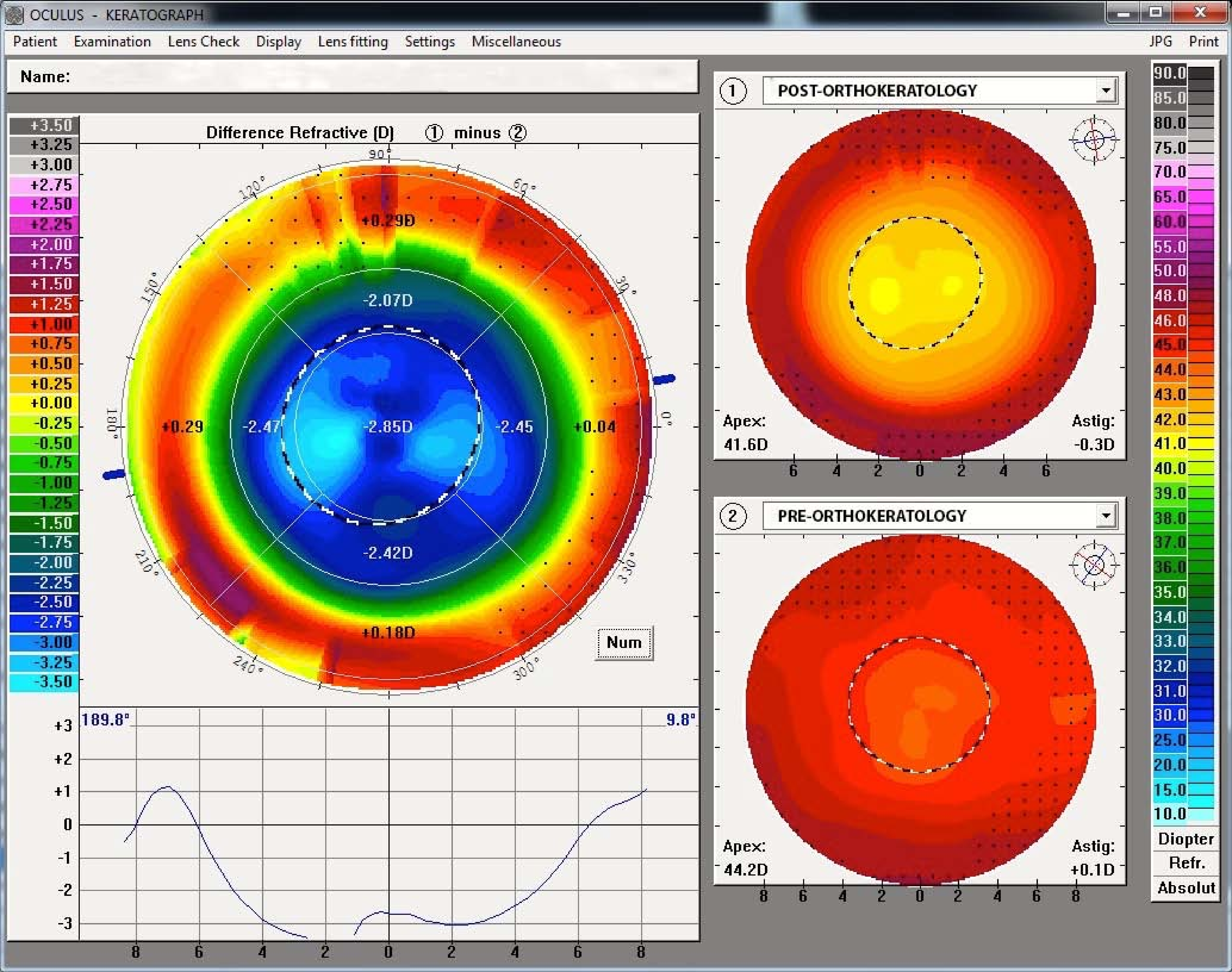
Figure 3. Mean changes in corneal power relative to the central corneal power at 3-months (left) and 24-months (right) relative to baseline for each of the 7 different corneal regions assessed. Data from the superior peripheral cornea (i.e. S2) were not analyzed as intrusion of the upper lid and lashes prevented reliable measurement.

Figure 4. Simple linear regressions between the 2-years change in axial length relative to baseline and the change in paracentral corneal power relative to central corneal power following 3- (solid triangles and line) and 24-months (open circles and dashed line) of OK lens wear.

Figure 5. Simple linear regressions between the 2-years change in axial length relative to baseline and the change in pericentral corneal power relative to central corneal power following 3- (solid triangles and line) and 24-months (open circles and dashed line) of OK lens wear.

	Short-term corneal power changes *vs.* changes in axial length		**Long-term corneal power changes *vs*. changes in axial length**	
Corneal areas	**Regression line equations**	**Statistical results**	**Regression line equations**	**Statistical results**
N1	y = -0.020x + 1.957	R^2=0.000, p=0.906	y = -0.026x + 1.958	R^2=0.000, p=0.919
N2	y = -0.102x + 2.184	R^2=0.000, p=0.392	y = -0.053x + 2.092	R^2=0.000, p=0.628
T1	y = -0.093x + 1.924	R^2=0.000, p=0.777	y = 0.226x + 1.936	R^2=0.000, p=0.639
T2	y = -0.003x + 1.947	R^2=0.000, p=0.980	y = 0.012x + 1.924	R^2=0.000, p=0.923
I1	y = -0.159x + 1.992	R^2=0.000, p=0.500	y = 0.050x + 1.924	R^2=0.000, p=0.895
I2	y = -0.006x + 1.957	R^2=0.000, p=0.951	y = -0.009x + 1.977	R^2=0.000, p=0.943
S1	y = -0.004x + 1.943	R^2=0.000, p=0.979	y = 0.022x + 1.931	R^2=0.000, p=0.902
Mean N: (N1+N2)/2	y = -0.108x + 2.111	R^2=0.000, p=0.514	y = -0.045x + 2.011	R^2=0.000, p=0.784
Mean T: (T1+T2)/2	y = -0.023x + 1.959	R^2=0.000, p=0.915	y = 0.043x + 1.909	R^2=0.000, p=0.848
Mean I: (I1+I2)/2	y = -0.044x + 1.998	R^2=0.000, p=0.784	y = 0.009x + 1.932	R^2=0.000, p=0.964
Mean H: (N1+N2+T1+T2)/4	y = -0.094x + 2.050	R^2=0.000, p=0.649	y = -0.017x + 1.962	R^2=0.000, p=0.934
Mean V: (I1+I2+S1)/3	y = -0.048x + 1.987	R^2=0.000, p=0.810	y = 0.031x + 1.913	R^2=0.000, p=0.892
Mean Para (N1+T1+I1+S1)/4	y = -0.044x + 2.032	R^2=0.000, p=0.734	y = 0.059x + 1.920	R^2=0.000, p=0.880
Mean Peri: (N2+T2+I2)/3	y = -0.077x + 1.967	R^2=0.000, p=0.766	y = -0.013x + 1.968	R^2=0.000, p=0.916
Central multifocality	y = 0.102x + 2.215	R^2=0.000, p=0.415	y = 0.047x + 2.060	R^2=0.000, p=0.656
Total multifocality	y = 0.146x + 2.372	R^2=0.023, p=0.212	y = 0.044x + 2.060	R^2=0.023, p=0.674

Table 1. Simple linear regressions between the change in axial length at 2-years relative to baseline and the change in corneal power at each of the corneal areas relative to baseline and the change in central corneal power following short- (3 months) and long-term (24 months) OK lens wear. N, nasal; T, temporal; I, inferior; S, superior; H, horizontal; V, vertical; Para, paracentral; Peri, pericentral.



Name: [redacted]

Difference Refractive (D) ① minus ②

① POST-ORTHOKERATOLOGY

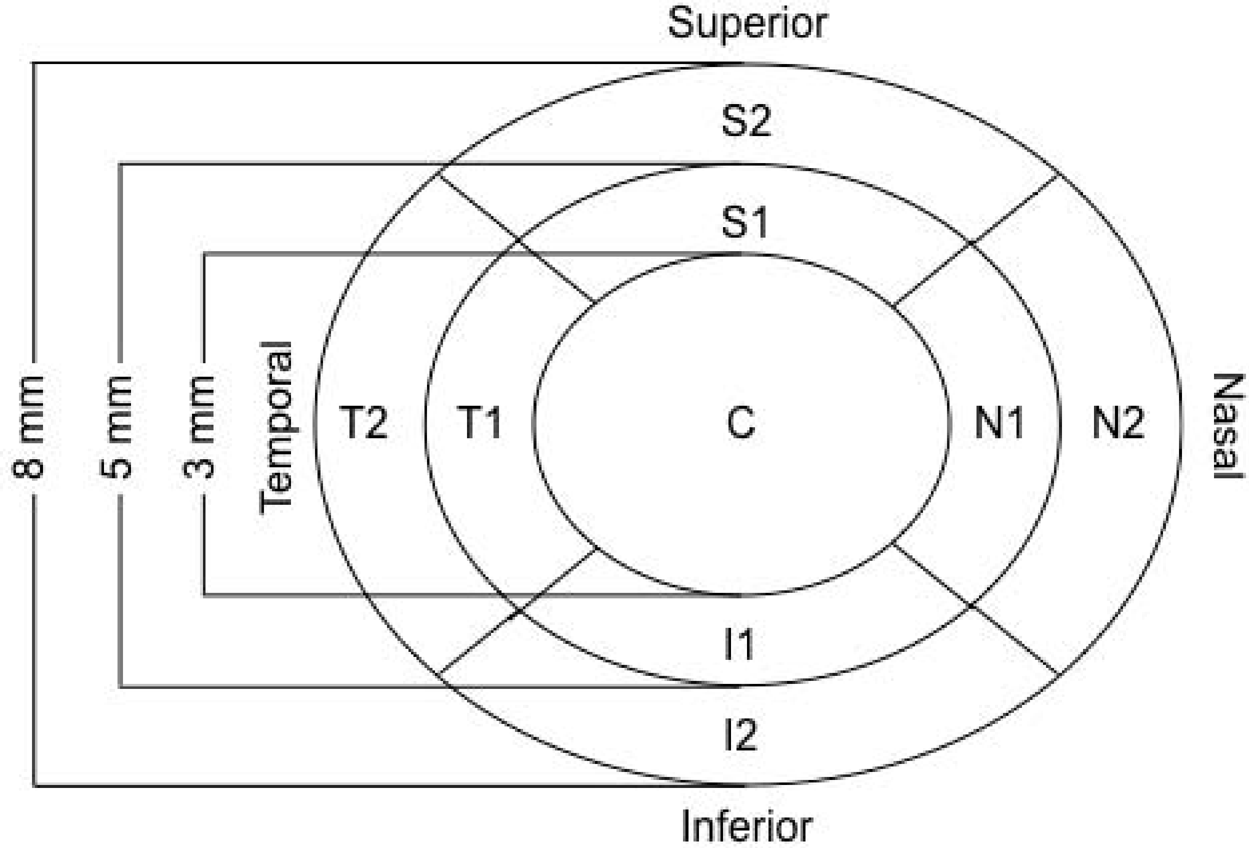
Apex: 41.6D

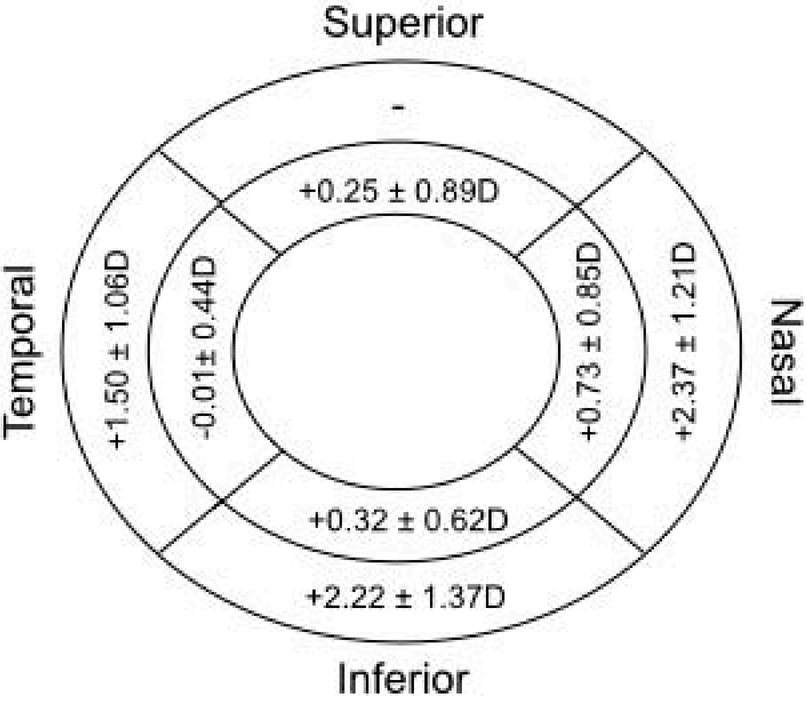
Astig: -0.3D

② PRE-ORTHOKERATOLOGY

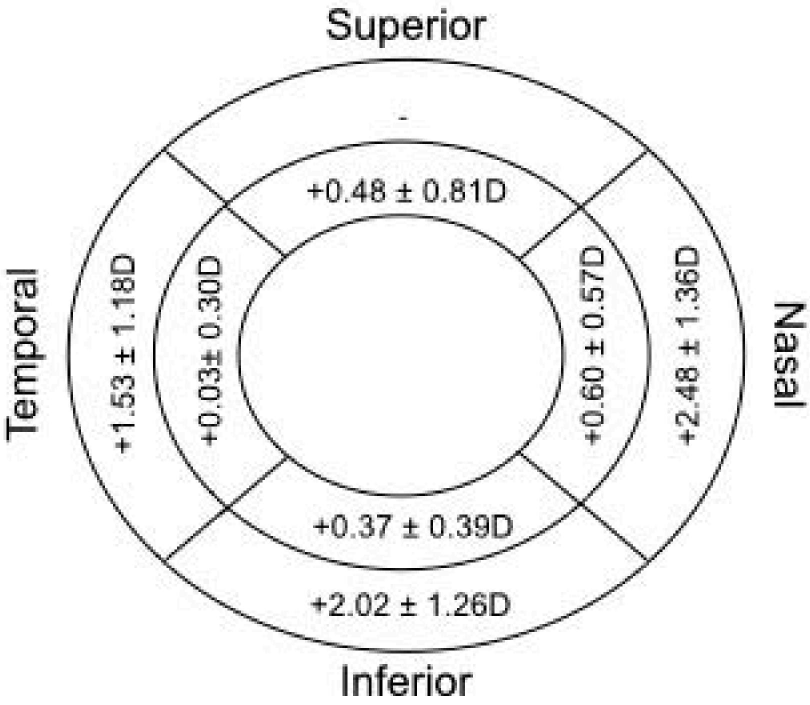
Apex: 44.2D

Astig: +0.1D

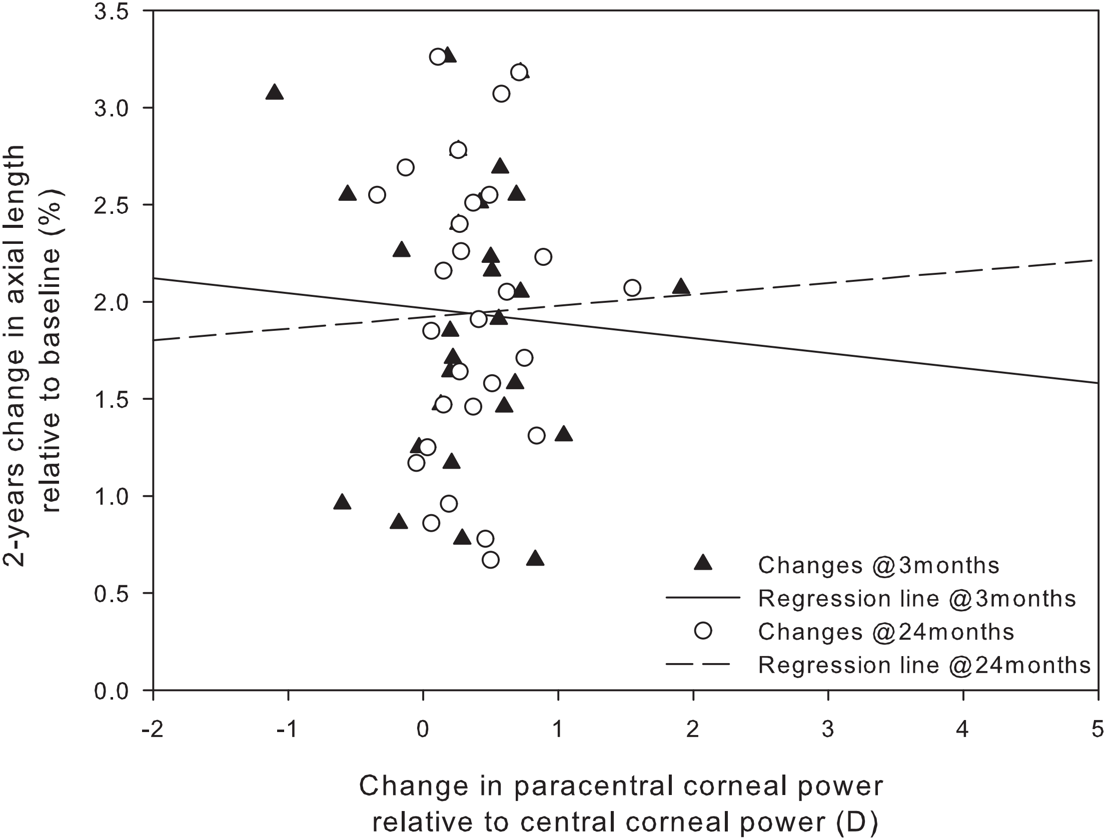

Superior
S2
S1
8 mm
5 mm
3 mm
Temporal
T2
T1
C
N1
N2
Nasal
I1
I2
Inferior

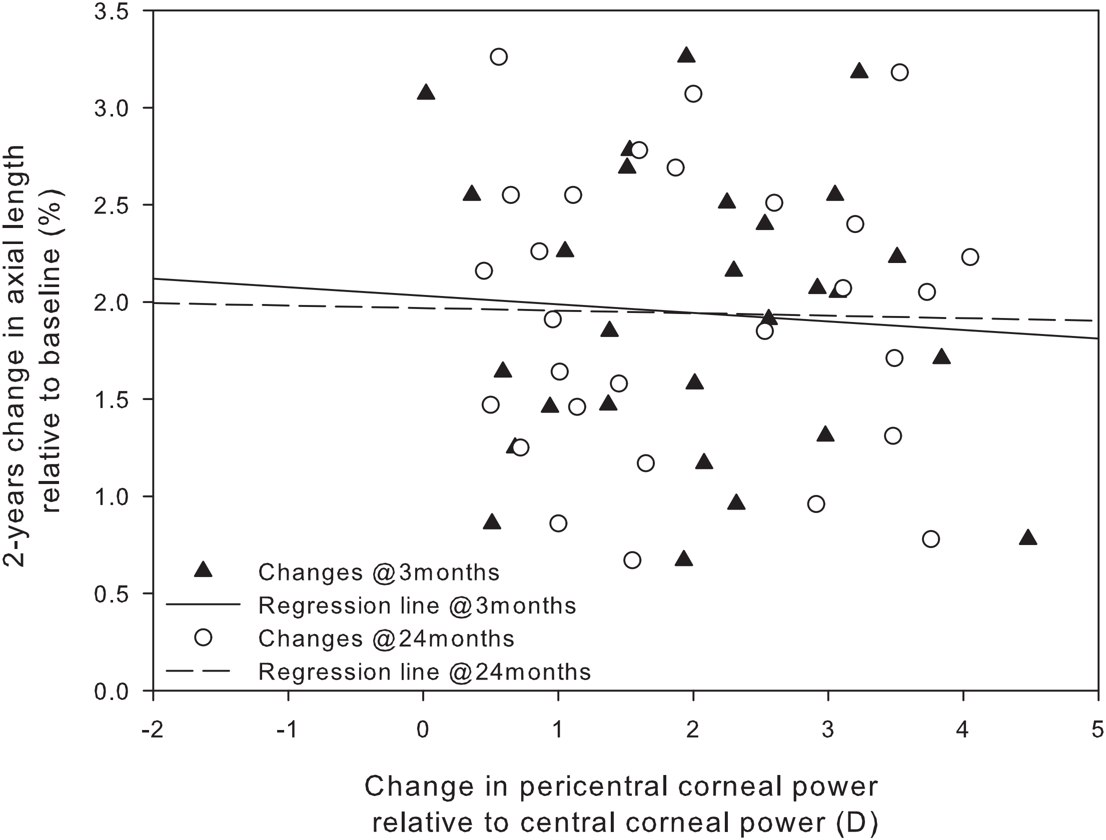


3-month vs. baseline



24-month vs. baseline


2-years change in axial length relative to baseline (%)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-2
-1
0
1
2
3
4
5
Change in paracentral corneal power relative to central corneal power (D)
▲ Changes @3months
Regression line @3months
○ Changes @24months
Regression line @24months


2-years change in axial length relative to baseline (%)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-2
-1
0
1
2
3
4
5
Change in pericentral corneal power relative to central corneal power (D)
Changes @3months
Regression line @3months
Changes @24months
Regression line @24months