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Full title: The effects of entrance pupil centration and coma aberrations on myopia progression following orthokeratology.

Running title: Effect of pupil centration and coma in orthokeratology

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ABSTRACT

Background: To assess the potential association between entrance pupil location relative to the coaxially-sighted corneal light reflex (CSCLR) and the progression of myopia in children fitted with orthokeratology (OK) contact lenses. Additionally, whether coma aberration induced by decentration of the entrance pupil centre relative to the CSCLR as well as following OK treatment is correlated with the progression of myopia was also investigated.

Methods: Twenty-nine subjects 6-12 years of age and with myopia -0.75 to -4.00DS and astigmatism ≤1.00DC were fitted with OK contact lenses. Measurements of axial length and corneal topography were taken at 6-month intervals over a 2-year period. Additionally, baseline and 3-month topographic outputs were taken as representative of the pre- and post-OK treatment status. Pupil centration relative to the CSCLR and magnitude of associated corneal coma were derived from corneal topography data at baseline and after 3 months of lens wear.

Results: The entrance pupil centre was located superior-temporally to the CSCLR both pre- $(0.09 \pm 0.14 \text{ and } -0.10 \pm 0.15 \text{mm}$, respectively) and post-OK $(0.12 \pm 0.18 \text{ and } -0.09 \pm 0.15 \text{mm}$, respectively) (p>0.05). Entrance pupil location pre- and post-OK lens wear was not significantly associated with the 2-year change in axial length (p>0.05). Significantly greater coma was found at the entrance pupil centre compared with CSCLR both pre- and post-OK lens wear (both p≤0.05). A significant increase in vertical coma was found with OK lens wear compared to baseline (p≤0.001) but total RMS coma was not associated with the change in axial length (all p>0.05).

Conclusion: Entrance pupil location relative to the CSCLR was not significantly affected by either OK lens wear or an increase in axial length. Greater magnitude coma aberrations found at the entrance pupil centre in comparison to the CSCLR might be attributed to centration of OK treatments at the CSCLR.

Key words: pupil centration; decentration; myopia progression; orthokeratology, coma

BACKGROUND

The eye has numerous optical aberrations that increase as the pupil dilates.¹ Furthermore, the location of the entrance pupil relative to the cornea has optical implications in the refractive status of the eye as corneal curvature varies across the cornea. The latter is particularly relevant with orthokeratology (OK) contact lens wear where myopia is temporarily corrected through changes in corneal shape. Successful OK treatment should produce a well-centred even treatment zone that encompasses the pupil.² In fact, a decentred treatment zone has been shown to be associated with significant reductions in contrast sensitivity function.³

Orthokeratology induces changes in both central and peripheral corneal optics: central myopic error is temporarily corrected by a flattening of the central cornea, usually over a 5 to 6 mm central region, and peripheral corneal optics are modified by a redeployment of epithelial tissue or fluid within or between epithelial cells to produce an increase in mid-peripheral corneal thickness.2 Corneal curvature changes following OK lens wear, which are limited to the anterior cornea, can be precisely monitored with currently available corneal topographers. 4-6 Ideally, corneal topography measurements should be centred on the location of the cornea intersecting the entrance pupil of the eye. However, topography measurements are centred on the coaxially-sighted corneal light reflex (CSCLR), also known as corneal vertex, which is the corneal position intersected by the optical axis of the corneal topographer, also known a vertex normal or videokeratographer axis, and marks the centre of the reflection of the placido rings. 7,8 The CSCLR is normally displaced with respect to the entrance pupil (i.e. normally nasally) due to the special characteristics of ocular alignment and the eccentric foveal position (Figure 1).9

Reports demonstrating control of myopia progression in children by 30 to 50% with OK compared with conventional spectacle and soft contact lens wear have attracted much interest. The aetiological basis for the efficacy of OK in the control of myopia progression is, however, unclear. It has been shown that peripheral hyperopic defocus has significance in the development of myopia in animal models and recent work in humans has shown OK to reduce

peripheral hyperopic defocus¹⁸ compared with some designs (i.e. non-aspheric) of single vision spectacle lens wear, which increases peripheral hyperopic defocus, 19 and over the naked eye of gas-permeable contact lens wearers, in which no effect upon peripheral refraction was found.²⁰ Furthermore, a recent study has found corneal power changes induced by OK lens wear to be predictive of myopia progression.²¹ More specifically, the latter study found that the larger the magnitude of relative positive peripheral corneal power change along the nasal, temporal and inferior cornea after OK treatment the slower the axial elongation following 24 months of lens wear. Furthermore, maximum corneal power changes along the three axes were negatively correlated with the 2-year axial length growth. Orthokeratology also significantly affects corneal and ocular aberrations, 22-26 and of interest is a recent report on myopic children treated with OK over a 1-year period that found axial elongation to be significantly correlated with OK-induced changes in spherical defocus, secondorder, coma-like, spherical-like and total higher-order aberrations, but not with changes in spherical aberration.²⁷ The change in coma-like aberration was found to have the strongest correlation with the increase in axial elongation. Although how changes in ocular aberrations induced by OK lens wear may be associated with changes in axial length elongation is unknown, the authors of the latter study indicated that asymmetric corneal shapes, rather than concentric and radially symmetric shapes, have a considerable effect on retardation of axial elongation, suggesting that the inhibitory effect of OK on myopia progression might be caused by mechanisms other than the reduction in peripheral hyperopic defocus.²⁷

To the best of our knowledge, the location of the entrance pupil centre relative to the CSCLR before and after OK lens wear has not been previously assessed as well as whether such location is associated with the progression of myopia. Furthermore, it is well established OK contact lens wear causes increases in higher-order wavefront aberrations including spherical aberration and coma, ²²⁻²⁶ and increases in spherical aberration generate third-order coma as a linear function of pupil decentration. ²⁸ The primary purpose of this study is to assess the potential association between entrance pupil location relative to the CSCLR and the progression of myopia in children fitted with OK contact lenses.

Additionally, whether coma aberration induced by decentration of the entrance pupil centre relative to the CSCLR as well as following OK treatment is correlated with the progression of myopia was also investigated.

METHODS

This study was part of a larger study designed to assess the safety, efficacy, subjective acceptance and discontinuation effects of OK lens wear for control of myopia progression in children. 14, 29-33 The methods have been described in detail elsewhere. 14, 29 In brief, normal, healthy white European subjects 6 to 12 years of age with moderate levels of mean spherical myopia (-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 using Menicon Easy Fit Software (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 ≤ 1 unit, 34 a "bull's eye" corneal topography pattern and monocular and binocular visual acuities within ±1 line of the best-correct spectacle visual acuity. All patients underwent ocular examinations including slit-lamp examination, manifest refraction, and corneal topography at baseline and after 1 day, 2 weeks, 3 months and at 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 visits³⁵ 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 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).³⁶ Three separate measurements of axial length were recorded and a mean obtained. 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 from 22 ring edges with a claimed accuracy and reproducibility of ± 0.10D according to the manufacturer. 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 and 3-month topographic outputs were taken as representative of the pre- and post-OK treatment status as it is well established OK treatment is normally completed and stabilized following the first 7 to 10 days of lens wear.² Corneal topographies were analysed using Oculus Keratograph software (Version 1.76, Oculus Optikgeräte GmbH, Germany). The software provides an automatic measurement of the cartesian coordinates of the centration of the entrance pupil relative to the CSCLR (Figure 1).

Insert Figure 1 around here

Individual corneal topography images were visually inspected to ensure the software had correctly identified the entrance pupil for all subjects. Additionally, vertical and horizontal coma aberrations (i.e. C_3^{-1} and C_3^{-1} , respectively) of the anterior cornea were derived from anterior cornea elevation data. Corneal height data were calculated with reference to a spherical surface with a radius

of curvature equal to the subject's central corneal radius and for a 8mm diameter. Subsequently, data were divided by the appropriate normalization factor *Fnm*, where *n* is the order of the Zernike monomial and *m* is the frequency of the term, and multiplied by the pupil radius as recommended by the Optical Society of America³⁷ and ANSI.³⁸ The normalization factors were determined as follows:

- If $n-2m \neq 0$ then Fnm = square root (2[n+1])
- If n-2m = 0 then Fnm = square root (n+1)

Normalized height data were imported to an analysis software program (Zemax, Redmond, WA, USA) to reconstruct the corneal surface for both the CSCLR and entrance pupil centres and ray tracing was performed to establish the Zernike aberration coefficients for a 5 mm entrance pupil following previously described methodology by Gifford et al.²⁵ To calculate coma aberrations for the entrance pupil centre, the cornea's location and tilt for the entrance pupil relative to the CSCLR was input into Zemax software. Pupil centration was automatically provided by the corneal topographer whereas tilts around the x and y axes were calculated as the angles of the horizontal and vertical location of the entrance relative to the CSCLR divided by a set distance of 148.3 mm representative of the distance between the cornea and the fixation target.³⁹ The entrance pupil was positioned at a distance of 3.60 mm from the anterior corneal surface.²⁵ A wavelength of 546 nm was used to match the wavelength used by the Wavelight Allegro Topolyzer instrument for ocular aberrations. Coma aberrations were expressed by Zernike expansion (i.e. C_3^{-1} and C_3^{-1}) and the total root-mean-square (RMS) coma aberration was also assessed (i.e. total RMS coma aberration = $\sqrt{[(C_3^{-1})^2 + (C_3^{-1})^2]}$). Additionally, coma angles of orientation of the combined coma terms were calculated as described by Kosaki et al.40 as follows:

If
$$C_3^1 \neq 0$$

$$axis = tan^{-1} \left(\frac{c_3^{-1}}{c_3^1} \right) (c_3^1 < 0)$$

$$axis = tan^{-1} \left(\frac{c_3^{-1}}{c_3^1} \right) + 180(c_3^1 > 0)$$

If $C_3^1 = 0$

$$angle = 90(c_3^{-1} < 0)$$

$$angle = 270(c_3^{-1} > 0)$$

The location of the entrance pupil centre relative to the CSCLR as well as coma aberrations at the CSCLR and entrance pupil centres were measured at both baseline and following 3-months of OK lens wear. The correlation between the latter variables and the magnitude of axial elongation over two years was also assessed.

Statistical analysis

Sphero-cylindrical refractions were converted from dioptres into a vector representation for analysis⁴¹: a spherical lens of power M (mean spherical equivalent refraction = sphere + [cylinder/2]); Jackson cross cylinder at axis 0° with power J0 (= -[cylinder/2] cos[2 X axis]); and Jackson cross cylinder at axis 45° with power J45 (= -[cylinder/2] sin[2 X axis]).

Differences between visits (i.e. pre- vs. post-OK) were tested using a paired ttest or Wilcoxon signed rank test depending on normality of the data
distribution. Similarly, correlations between pairs of variables were performed
with Pearson product moment correlation or Spearman Rho tests depending on
normality of the data distribution. Simple linear regressions were used to assess
the potential association between the 2-year change in axial length relative to
baseline and the centration of the pupil and coma aberrations. Data from right
eyes only were used for analysis. Statistical analyses and graphing were
performed with SigmaPlot (Systat software Inc, California, USA). The level of
statistical significance was set at 5%.

RESULTS

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 one due to unknown reasons. Subjects who discontinued the study were not included in the data analysis. A total of 8 subjects required OK lens refitting to compensate for changes in refraction throughout the study. In two subjects, the corneal topography software was unable to correctly identify the entrance pupil centres both pre- and post-OK and in one additional subject the software was unable to identify the entrance pupil post-OK; in all the cases, entrance pupil centres were manually identified. The subjects' demographic and baseline data have been reported elsewhere. In brief, subjects had a mean age of 9.6 \pm 1.6 years; 15 were male and 16 were female. Over two years of OK lens wear, axial length increased from 24.49 \pm 0.78 mm to 24.96 \pm 0.86 mm (p < 0.001). Table 1 shows the mean (\pm SD) refractive components, entrance pupil centration and coma aberrations at baseline and after 3 months of OK lens wear.

Three months of OK lens wear produced a significant reduction in mean spherical equivalent myopia (p<0.001) as well as significant changes in the J45 refractive component (p=0.021) compared to baseline. However, no significant changes were found in the J0 refractive component following OK lens wear in comparison to baseline (p=0.225) (Table 1).

Insert Table 1 around here

On average, the entrance pupil centre was located superior-temporally with regards to the CSCLR both pre- and post-OK lens wear (Table 1 and Figure 2). Furthermore, OK lens wear did not significantly change the horizontal (p=0.71) or vertical (p=0.75) location of the entrance pupil centre relative to the CSCLR.

Insert Figure 2 around here

Of note is that greater vertical, horizontal and total RMS coma aberrations were found at the entrance pupil centre in comparison to the CSCLR both pre- and post-OK lens wear (Figure 3, all p \le 0.05). Orthokeratology lens wear induced a positive shift in vertical coma measured at both the CSCLR and entrance pupil centre in comparison to baseline (Figure 3, both p \le 0.001). However, no significant differences were found pre- vs. post-OK in horizontal or total RMS coma at either the CSCLR or entrance pupil centre (Figure 3, both p \ge 0.05).

Insert Figure 3 around here

Coma angle of orientation measured at the CSCLR changed significantly pre-(mean axis: 120°; range: 5 to 357°) in comparison to post-OK (mean axis: 271°; range: 4 to 358°) (p<0.001). However, coma angle of orientation measured at the entrance pupil did not change significantly pre- (mean axis: 194°; range: 4 to 295°) in comparison to post-OK (mean axis: 246°; range: 55 to 346°) (p>0.05).

Neither the horizontal nor the vertical locations of the entrance pupil centre relative to the CSCLR were significantly correlated with horizontal, vertical or total RMS coma aberrations measured at the CSCLR pre- or post-OK treatment (all p>0.05). However, the horizontal location of the entrance pupil centre relative to the CSCLR was significantly correlated with horizontal coma measured at the entrance pupil centre both pre- (r=-0.638, p<0.001) and post-OK lens wear (r=-0.553, p<0.001). The vertical location of the entrance pupil centre relative to the CSCLR was also significantly correlated with vertical coma pre- (r=0.731, p<0.001) and post-OK lens wear (r=0.893, p<0.001) as well as with post-OK RMS coma (r=0.829, p<0.001) when measured at the entrance pupil centre. No other statistically significant correlations were found between the location of the entrance pupil and coma aberrations (all p>0.05).

The horizontal and vertical displacements of the entrance pupil centre relative to the CSCLR at baseline were not significantly associated to the 2-year increase in the axial length relative to baseline (both p>0.05). The horizontal, vertical and total RMS coma aberrations measured at the entrance pupil centre at baseline were not significantly associated to the 2-year change in the axial length of the eye relative to baseline (all p>0.05). Coma angles of orientation at the entrance pupil centre at baseline were not significantly associated to the 2-year change in the axial length of the eye relative to baseline (p>0.05).

DISCUSSION

In this study, the entrance pupil centre was found to be located in the superiortemporal corneal quadrant relative to the CSCLR (Table 1 and Figure 2). Previous studies have reported the entrance pupil to be located nasally and superiorly; however, entrance pupil location was measured relative to the centre of the limbus or the geometrical centre of the cornea. 42, 43 Due to the alignment characteristics of corneal topographers, the entrance pupil is normally located temporally relative to the CSCLR and nasally relative to the limbus centre. 7, 42, 43 Therefore, our results are in relative good agreement with those previously reported. 42, 43 While previous studies have measured entrance pupil location relative to the limbus or geometrical centres of the cornea, the location of the entrance pupil centre was assessed relative to the CSCLR in our study because this is a useful reference point in clinical practice as OK patients are almost undisputedly monitored with a corneal topographer. Additionally, entrance pupil location relative to the CSCLR was measured automatically by the corneal topographer thus preventing any human error during measurements. Although large changes in pupil offset might be associated to significant changes in the refractive status of the eye, the pupil offset relative to the CSCLR was, however, negligible and that probably explains its lack of association with the rate of myopia progression in this study. It should be noted, however, that a significant correlation has been previously reported between hyperopic refractive errors and large positive pupil offsets. 44 As hyperopic subjects normally have larger pupil offsets in comparison to myopic subjects, the pupil offset might be more relevant to optical control of eye growth in hyperopic in comparison to myopic subjects.

Significantly greater horizontal, vertical and total RMS coma aberrations were found at the entrance pupil centre in comparison to the CSCLR (Figure 3). Furthermore, OK lens wear induced a significant shift from negative to positive in vertical coma measured at the CSCLR and a positive increase in vertical coma at the entrance pupil centre in comparison to baseline (Table 1 and Figure 3). The increase in vertical coma with OK lens wear in comparison to baseline might be attributed to decentration of the treatment zone (i.e. the area of central corneal flattening) as a previous study found treatment zone

decentration to be associated with RMS coma.³ Orthokeratology treatments are centred on corneal topography maps and thus on the CSCLR rather than on the entrance pupil centre. Therefore, OK treatments are likely to be slightly decentered relative to the entrance pupil centre and that could potentially result in an increase in coma aberrations measured at the entrance pupil centre in comparison to the CSCLR.

Although the absolute amounts of coma aberrations found in our study were relatively similar to those of previous studies, the shifts reported in coma aberrations following OK lens wear in comparison to no lens wear varies between studies.^{22, 24-26} Hiraoka et al. reported statistically significant shifts from positive to negative and vice versa in vertical and horizontal corneal coma, respectively measured at the CSCLR for a 6mm pupil diameter. 22 Anera et al. found a significant negative shift in vertical coma as well as a significant increase in third order RMS (i.e. coma-like) corneal aberrations, but no significant changes in horizontal corneal coma measured at the CSCLR for a 5mm pupil diameter.²⁴ Gifford et al. reported a significant increase in total RMS corneal coma, but no significant changes in corneal coma angle of orientation measured at the entrance pupil for a 5mm pupil diameter. 25 A very recent study by Lian et al. found a significant increase in total RMS and horizontal corneal coma, but no significant changes in vertical corneal coma measured at the CSCLR for a 6mm pupil diameter. ²⁶ Comparison of coma aberrations found in OK studies should be carried out with special as differences in lens designs and instruments and methods (i.e. selection of the reference surface, pupil diameter, wavelength and normalization factor) between studies to derive coma aberrations from corneal height data are all likely to affect the results of coma aberrations.

Although the coma angles of orientation measured at the entrance pupil both pre- and post-OK lens wear were different than those previously reported by Gifford et al.,²⁵ both studies found a no statistically significant increase in coma angle of orientation post- in comparison to pre-OK lens wear. Changes in angle of coma orientation might be attributed to how OK treatments are centred on the cornea.³

No significant correlations were found between entrance pupil location and coma aberrations measured at the CSCLR. However, the horizontal and vertical locations of the entrance pupil centre relative to the CSCLR were significantly correlated with horizontal and vertical coma both pre- and post-OK, respectively. The latter was expected as pupil offsets relative to the CSCLR were taken into account to calculate coma aberrations at the entrance pupil based on coma aberrations measured at the CSCLR. Furthermore, it is well known that coma aberrations change as a linear function of pupil decentration. Although one previous study reported that decentrations <0.10 mm in wavefront-guided refractive surgery treatments for myopia can induce significant amounts of aberrations, another study did not find significant differences in coma aberrations between subjects with small (i.e. ≤0.25mm) vs. large (i.e. ≥0.55mm) pupil offsets (defined as the distance in the corneal plane between the entrance pupil and the corneal vertex).

It has been suggested that higher order aberrations may play a role in the development of refractive errors by reducing retinal image quality.⁴⁷ Orthokeratology lens wear induce an increase in corneal spherical aberration, ²²⁻²⁶ which is balanced to a certain degree by a decrease in internal spherical aberration, ^{25, 48, 49} perhaps as a result of an increased accommodative response²⁵ due to steepening of the crystalline lens' posterior surface.⁴⁸ Decreases in ocular spherical aberration have been associated with myopia progression. 48, 50 It is also known that changes in spherical aberration generate third-order coma as a linear function of pupil decentration.²⁸ Furthermore, changes in coma-like aberrations have been reported to be associated with corneal multifocality, suggesting that increases in corneal multifocality could reduce accommodative effort (i.e. mechanical tension of the ciliary muscle and crystalline lens) and/or accommodative lag (i.e. axial hyperopic blur) during near work and thus potentially slow myopia progression.²⁷ In our study, however, no significant associations were found between the change in coma aberrations following OK lens wear and the 2-years change in axial elongation, results which are in agreement with a previous study which investigated the influence of ocular wavefront aberrations on axial length elongation in myopic children

treated with overnight OK over 1-year period.²⁷ The latter study did not find statistically significant correlations between the change in axial length and horizontal and vertical coma aberrations, although the change in third order RMS (i.e. coma-like) ocular aberrations showed a strong association with the increase in axial elongation.

A limitation of this study might be that coma aberrations were solely derived from corneal topographies taken at the 3-month follow-up visit as representative of the corneal shape following OK treatment stabilization.² Although 8 subjects required refitting throughout the study to compensate for changes in refraction, which might induce different corneal coma in comparison to that found at the 3-month follow-up visit, the potential change in corneal shape induced by refitting was likely to be small (to compensate for small changes in refraction e.g., 0.50D) in comparison to corneal shape changes induced at the 3-month follow-up visit (to compensate for a mean baseline mean spherical equivalent refraction of -2.33D). In fact, corneal shape (i.e. corneal p-value) did not change significantly at follow-up visits after contact lens dispensing. More specifically, the mean corneal p-value changed by ≤0.02 units throughout the study in the eight subjects which required refitting.¹⁴

Another limitation of this study was that anterior corneal aberrations were measured. However, corneal changes induced by OK lens wear are limited to the anterior cornea.² It has been reported anterior corneal aberration components to be generally higher than the overall ocular aberrations but balanced to a considerable degree by internal ocular aberrations.⁴⁹ Although one previous study found the change in corneal aberrations to be partially neutralized by the internal aberrations of the eye with 7 days of OK lens wear,²⁵ a more recent study found almost identical anterior corneal and ocular aberrations at baseline and following 1 year of OK lens wear.²⁷

In summary, pupil offset relative to the CSCLR is negligible in our group of young, healthy children. Furthermore, entrance pupil location is not affected by OK lens wear and is not associated with the magnitude of axial elongation over a 2-year period. Similarly, coma aberrations measured at the entrance pupil

centre were not significantly correlated with the 2-years change in axial elongation. The higher coma aberrations found at the entrance pupil centre in comparison to the CSCLR might be attributed to centration of OK treatments at the CSCLR.

REFERENCES

- 1. Charman WN. Wavefront technology: past, present and future. Contact Lens Ant Eye 2005;28:75-92.
- 2. Swarbrick HA. Orthokeratology review and update. Clin Exp Optom 2006;89:124-143.
- 3. Hiraoka T, Mihashi T, Okamoto C, Okamoto F, Hirohara Y, Oshika T. Influence of induced decentered orthokeratology lens on ocular higher-order wavefront aberrations and contrast sensitivity function. J Cataract Refract Surg 2009;35:1918-1926.
- 4. Swarbrick HA, Wong G, O'Leary DJ. Corneal response to orthokeratology. Optom Vis Sci 1998;75:791-799.
- 5. Nichols JJ, Marsich MM, Nguyen M, Barr JT, Bullimore MA. Overnight orthokeratology. Optom Vis Sci 2000;77:252-259.
- 6. Alharbi A, Swarbrick HA. The effects of overnight orthokeratology lens wear on corneal thickness. Invest Ophthalmol Vis Sci 2003;44:2518-2523.
- 7. Mandel RB. Apparent pupil displacement in videokeratography. CLAO J 1994;20:123-127.
- 8. Applegate RA, Thibos LN, Twa MD, Sarver EJ. Importance of fixation, pupil center, and reference axis in ocular wavefront sensing, videokeratography, and retinal image quality. J Cataract Refract Surg 2009;35:139-152.
- Salmon TO, Thibos LN. Videokeratoscope-line-of-sight misalignment and its effect on measurements of corneal and internal ocular aberrations. J Opt Soc Am A 2002;19:657–669.
- 10. Cho P, Cheung SW, Edwards M. The longitudinal orthokeratology research in children (LORIC) in Hong Kong: a pilot study on refractive changes and myopic control. Cur Eye Res 2005;30:71-80.
- 11. Walline JJ, Jones LA, Sinnott LT. Corneal reshaping and myopia progression. Br J Ophthalmol 2009;93:1181–1185.
- 12. Kakita T, Hiraoka T, Oshika T. Influence of overnight orthokeratology on axial length elongation in childhood myopia. Invest Ophthalmol Vis Sci 2011;52:2170-2174.
- 13. Hiraoka T, Kakita T, Okamoto F, Takahashi H, Oshika T. Long-term effect of overnight orthokeratology on axial length elongation in childhood myopia: a 5-year follow-up study. Invest Ophthalmol Vis Sci 2012;53:3913-3919.

- 14. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Myopia control with orthokeratology contact lenses in Spain: refractive and biometric changes. Invest Ophthalmol Vis Sci 2012;53:5060-5065.
- 15. Cho P, Cheung SW. Retardation of Myopia in Orthokeratology (ROMIO) Study: a 2-year randomized clinical trial. Invest Ophthalmol Vis Sci 2012;53:7077-7085.
- 16. Smith EL, Kee CS, Ramamirtham R, Qiao-Grider Y, Hung LF. Peripheral vision can influence eye growth and refractive development in infant monkeys. Invest Ophthalmol Vis Sci 2005;46:3965–3972.
- 17. Smith EL 3rd, Ramamirtham R, Qiao-Grider Y et al. Effects of foveal ablation on emmetropization and form-deprivation myopia. Invest Ophthalmol Vis Sci 2007;48:3914-3922.
- 18. Queirós A, González-Méijome JM, Jorge J, Villa-Collar C, Gutiérrez AR. Peripheral refraction in myopic patients after orthokeratology. Optom Vis Sci 2010;87:323-329.
- 19. Lin Z, Martinez A, Chen X et al. Peripheral defocus with single-vision spectacle lenses in myopic children. Optom Vis Sci 2010;87:4-9.
- 20. Kang P, Swarbrick H. Peripheral refraction in myopic children wearing orthokeratology and gas-permeable lenses. Optom Vis Sci 2011;88:476-482.
- 21. Zhong Y, Chen Z, Xue F, Zhou J, Niu L, Zhou X. Corneal power change is predictive of myopia progression in orthokeratology. Optom Vis Sci 2014;91:404-411
- 22. Hiraoka T, Matsumoto Y, Okamoto F, Yamaguchi T, Hirohara Y, Mihashi T, Oshika T. Corneal higher-order aberrations induced by overnight orthokeratology. Am J Ophthalmol 2005;139:429-436.
- 23. Hiraoka T, Okamoto C, Ishii Y, Kakita T, Oshika T. Contrast sensitivity function and ocular higher order aberrations following overnight orthokeratology. Invest Ophthalmol Vis Sci 2007;48:550-556.
- 24. Anera RG, Villa C, Jiménez JR, Gutierrez R. Effect of LASIK and contact lens corneal refractive therapy on higher order aberrations and contrast sensitivity function. J Refract Surg 2009;25(3):277-284.
- 25. Gifford P, Li M, Lu H, Miu J, Panjaya M, Swarbrick HA. Corneal versus ocular aberrations after overnight orthokeratology. Optom Vis Sci 2013;90:439-447.

- 26. Lian Y, Shen M, Huang S, Yuan Y, Wang Y, Zhu D, Jiang J, Mao X, Wang J, Lu F. Corneal reshaping and wavefront aberrations during overnight orthokeratology. Eye Contact Lens 2014;40:161-168.
- 27. Hiraoka T, Kakita T, Okamoto F, Oshika T. Influence of ocular wavefront aberrations on axial length elongation in myopic children treated with overnight orthokeratology. Ophthalmology 2014;15:S0161-6420.
- 28. Mahajan VN. Optical imaging and aberrations, I: ray geometrical optics. SPIE 1998;1:438–442.
- 29. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortéga R. Myopia control with orthokeratology contact lenses in Spain (MCOS): study design and general baseline characteristics. J Optom 2009;2:215-2.
- 30. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Orthokeratology vs. Spectacles: Adverse Events and Discontinuations. Optom Vis Sci 2012;89:1133-9.
- 31. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Myopia Control with Orthokeratology contact lenses in Spain (MCOS): a comparison of vision-related quality-of-life measures between orthokeratology contact lenses and single-vision spectacles. Eye Contact Lens 2013;39:153-7.
- 32. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Factors Preventing Myopia Progression with Orthokeratology Correction. Optom Vis Sci 2013;90:1225-36.
- 33. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Short-term changes in ocular biometry and refraction after discontinuation of long-term orthokeratology. Eye Contact Lens 2014;40:84-90.
- 34. Terry RL, Schnider CM, Holden BA et al. CCLRU standards for successful daily wear and extended wear contact lenses. Optom Vis Sci 1993;70:234-243.
- 35. Lovie-Kitchin JE, Brown B. Repeatability and intercorrelations of standard vision tests as a function of age. Optom Vis Sci 2000;77:412-420
- 36. Santodomingo-Rubido J, Mallen EA, Gilmartin B et al. A new non-contact optical device for ocular biometry. Br J Ophthalmol 2002;86:458-2.
- 37. Thibos LN, Applegate RA, Schweigerling JT, Webb R. Standards for reporting the optical aberrations of the eye. J Refract Surg 2002;18:652–60.
- 38. ANSI American National Standards. American National Standard for

- Ophthalmics—methods for reporting optical aberrations of eyes. ANSI Z80.28; 2004.
- 39. Barbero S, Marcos S, Merayo-Lloves JM, Moreno- Barriuso E. Validation of the estimation of corneal aberrations from videokeratography: a test on keratoconus eyes. J Refract Surg 2002;18:263–270.
- 40. Kosaki R, Maeda N, Bessho K et al. Magnitude and orientation of Zernike terms in patients with keratoconus. Invest Ophthalmol Vis Sci 2007;48:3062-3068.
- 41. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. Optom Vis Sci 1997;74:367-75.
- 42. Yang Y, Thompson K, Burns SA. Pupil location under mesopic, photopic, and pharmacologically dilated conditions. Invest Ophthalmol Vis Sci 2002;43:2508–2512.
- 43. Tabernero J, Atchison DA, Markwell EL. Aberrations and pupil location under corneal topography and Hartmann-Shack illumination conditions. Invest Ophthalmol Vis Sci 2009;50:1964-1970.
- 44. Basmak H, Sahin A, Yildirim N, Papakostas TD, Kanellopoulos AJ. Measurement of angle kappa with synoptophore and Orbscan II in a normal population. J Refract Surg 2007;23:456-460.
- 45. Bueeler M, Mrochen M, Seiler T. Maximum permissible lateral decentration in aberration-sensing and wavefront-guided corneal ablation. J Cataract Refract Surg 2003;29:257-263.
- 46. Reinstein DZ, Gobbe M, Archer TJ. Coaxially sighted corneal light reflex versus entrance pupil center centration of moderate to high hyperopic corneal ablations in eyes with small and large angle kappa. J Refract Surg 2013;29:518-525.
- 47. Charman WN. Aberrations and myopia. Ophthal Physiol Opt 2005;25:285–301.
- 48. Marcos S, Barbero S, Llorente L. The sources of optical aberrations in myopic eyes. Invest Ophthalmol Vis Sci 2002; 43(suppl.): Abstract 1510.
- 49. Artal P, Guirao A, Berrio E, Williams DR. Compensation of corneal aberrations by the internal optics in the human eye. J Vis 2001;1: 1–18.
- 50. Philip K, Sankaridurg P, Holden B, Ho A, Mitchell P. Influence of higher order aberrations and retinal image quality in myopisation of emmetropic eyes. Vision Res 2014;105:233-43.

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FIGURE LEGENDS

Figure 1. Corneal topography image of a right eye showing pupil centration relative to the coaxially-sighted corneal light reflex (CSCLR). The red circle and the cross denote the CSCLR and the centration of the pupil, respectively. Right and left sides of the image represent nasal and temporal locations, respectively.

Figure 2. Pupil centration relative to the CSCLR before (black circles) and after (white circles) OK lens wear. Cartesian coordinates are expressed in mm. 0°, 90°, 180° and 270° denotes nasal, superior, temporal and inferior locations, respectively. CSCLR, coaxially-sighted corneal light reflex; OK, orthokeratology.

Figure 3. Coma aberrations before and after orthokeratology lens wear measured at both the CSCLR (black bars) and entrance pupil (white bars). Error bars represent 1 standard deviation of the mean. *, denotes statistically significant changes in comparison to baseline. CSCLR, coaxially-sighted corneal light reflex.

TABLE LEGENDS

Table 1. Mean (± SD) pre- and post-OK refractive components, pupil centration relative to the CSCLR and coma aberrations at the CSCLR and pupil centres. Negative signs in the X- and Y-axes of pupil centration relative to the CSCLR denote temporal and inferior locations, respectively. OK, orthokeratology; CSCLR, coaxially-sighted corneal light reflex. The post-OK refractive components were those measured at the 3-month follow-up visit. M, mean spherical equivalent refraction; J0, Jackson cross cylinder at axis 0°; J45, Jackson cross cylinder at axis 45°; Data in bold denotes statistically significant changes in comparison to baseline.

Table 1.

	Refractive components (D)			Entrance pupil centration relative to CSCLR (mm)		Coma aberrations (µm)					
						Vertical (C ₃ ⁻¹)		Horizontal (C ₃ ¹)		Total (RMS)	
	М	J0	J45	X-coordinate	Y-coordinate	CSCLR	Pupil	CSCLR	Pupil	CSCLR	Pupil
Pre-OK	-2.33 ± 1.10	-0.01 ± 0.15	0.00 ± 1.10	-0.10 ± 0.15	0.09 ± 0.14	-0.030 ± 0.035	0.018 ± 0.099	0.018 ± 0.107	0.071 ± 0.136	0.080 ± 0.085	0.150 ± 0.102
Post-OK	-0.34 ± 0.13	0.02 ± 0.13	0.08 ± 0.15	-0.09 ± 0.15	0.12 ± 0.18	0.035 ± 0.057	0.115 ± 0.165	-0.001± 0.074	0.052 ± 0.117	0.082 ± 0.055	0.178 ± 0.157



