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CLINICAL COMMUNICATION

Toric orthokeratology: a case report

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Spherical reverse geometry lens (RGL) designs used in orthokeratology (ortho-k) have been shown to be effective in correcting low to moderate levels of myopia, however, they are ineffective for the correction of astigmatism,¹ although there are reports of some effect.² Lens decentration is the most common problem with spherical ortho-k lenses on patients with corneal astigmatism, as poor lens centration can lead to induced astigmatism, glare and poor vision.

The number of ortho-k wearers, most of whom are children, has been increasing in Hong Kong in recent years due to the promising results in retarding myopic progression.³ Ortho-k is particularly popular in Hong Kong, where the prevalence of myopia is high in children. Most children undergo this treatment for control of myopia^{1,4} and this is mainly restricted to those with low to moderate corneal toricity (less than 1.50 D, with-the-rule). High corneal

toricity (greater than 1.50 D, with-the-rule) is considered to be a contraindication for the treatment.

Toric RGL designs (toric reverse and/or alignment zone) have been developed for patients with high corneal toricity and promising results have been reported.⁵ The current report presents the case of a young female subject whose parents were concerned about her myopic progression. She also had high corneal astigmatism and was successfully prescribed a pair of toric peripheral design RGL (toric alignment zone).

The tenets of the Declaration of Helsinki as revised in 2002 were followed and ethics approval was obtained from the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University before commencing the treatment.

CASE REPORT

A 13-year-old female subject presented at the university clinic for ortho-k with a current spectacle correction of -4.25/-1.50 × 165 (OD) and -4.25/-2.50 × 180 (OS) and visual acuity of 1.0 (decimal notation) in each eye. Her mother reported a history of myopic progression that had not been arrested by the use of progressive lenses. She was interested in investigating the prospects of ortho-k as a means of vision correction and myopic control, even though she was informed of the likelihood of significant residual refractive errors that

may have required her daughter to wear spectacles after the procedure. The subject had no contraindication for contact lens wear. Corneal topographical data from the Medmont E300 corneal topographer (version 3.90, Medmont Pty Ltd, Camberwell, Australia) showed the presence of corneal astigmatism of 2.40 D (OD) and 3.60 D (OS). The axial length as measured with the IOLMaster (Zeiss Humphrey System, CA, USA) before ortho-k was 23.87 mm (OD) and 24.21 mm (OS).

The patient was fitted with Menicon Z night toric RGL (NKL Contactlenzen, Netherlands) of Menicon Z material (Menicon Co, Ltd, Nagoya, Japan), for overnight wear. The Menicon Z night toric lens is a peripheral toric ortho-k lens design. The back optical zone (diameter six millimetres) and reverse zone of the lens is of spherical design. The advantage of using spherical design in the optical zone of a toric cornea is that the flattest meridian of the lens creates a normal ortho-k effect, whereas the steepest meridian creates greater ortho-k effect leading to the correction of the corneal cylinder. To achieve a toric effect, the periphery of the lens has two different tangent angles and lens heights, and together they give an optimal fitting and centration on a toric cornea. The tangent is calculated from the apical radius values of the steep and flat meridians, as well as the elevation along each meridian. Depending on these values, the Menicon Easy Fit software was used to determine whether a toric design

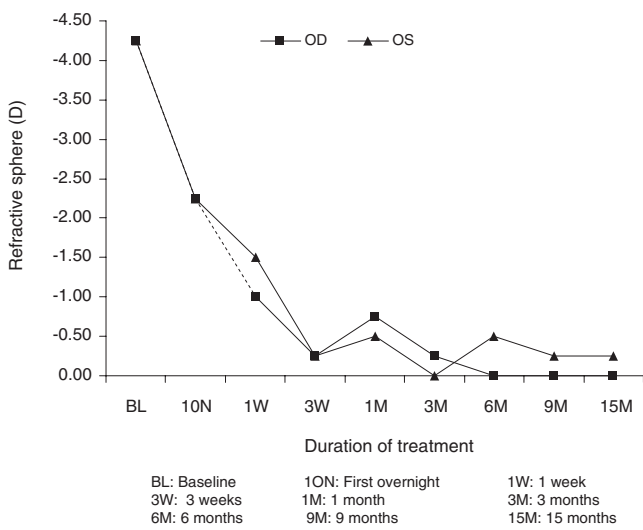


Figure 1. Refractive sphere during the course of ortho-k treatment

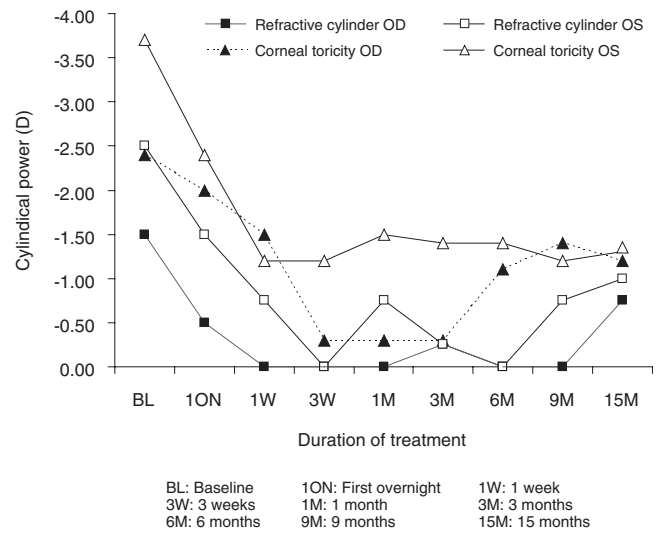


Figure 2. Cylindrical power during the course of ortho-k treatment

	UVA (decimal)	
	Right eye	Left eye
Baseline	—	—
1st overnight (early morning)	0.1	0.1
1 week (pm)	0.5	0.5
3 weeks (pm)	0.9	0.9
1 month (am)	0.8	0.9
3 months (pm)	1.0	0.9
6 months (pm)	1.0	1.0
9 months (pm)	1.0	1.0
15 months (pm)	1.0	1.0

Table 1. Changes in unaided visual acuity (UVA) during the course of treatment

was necessary or a spherical design ortho-k lens was sufficient.

The lens parameters required were determined using the software provided by NKL incorporated in the Medmont topographer. The lens parameters were sent to the laboratory for lens fabrication. The subject was fitted with the following lenses:

Menicon Z Nachtlens 2 Toric

OD: BC 8.25, tangent 57°, 56°, height 0.58, 0.61 and diameter 10.2 mm

OS: BC 8.40, tangent 58°, 55°, height 0.56, 0.65, and diameter 10.2 mm

As the corneal astigmatism and spectacle astigmatism did not match, the desired result was to correct the myopia and spectacle astigmatism, leaving 1.00 D corneal astigmatism in both eyes. Table 1 presents a summary of the unaided visual acuity (UVA) and Figures 1, 2 and 3 illustrate the refractive changes and axial length respectively over 15 months of lens wear.

At the delivery visit, lens fittings were assessed using the slitlamp with the aid of fluorescein. The fitting of both lenses was good (Figure 4), so the lenses were delivered after instructions on lens insertion/removal techniques and care of lens and accessories. The lens care system prescribed included Menicare Plus (Menicon Co, Ltd, Nagoya, Japan), Bausch & Lomb sensitive eye saline (Bausch & Lomb, Inc, Rochester, NY, USA) and Progent A + B (Menicon Co, Ltd, Nagoya, Japan). The subject was instructed to wear the lenses for one night and to return early the next morning.

The first after-care visit was scheduled in the morning with lenses *in situ*, within two

hours after awakening. The subject wore the lenses during sleep for eight hours the night before. No lens binding was observed and lens fittings were similar to those observed at the delivery visit. UVA was 0.1 (decimal notation) in both eyes, with residual refractive error (non-cycloplegic) of -2.25/-0.50 × 135 (OD) and -2.25/-1.50 × 170 (OS). The subtractive topographical plot (tangential map) showed a bull's eye pattern in both eyes with axial power changes of 2.50 D (OD) and 1.80 D (OS) and changes in corneal toricity of 0.40 D (OD) and 1.30 D (OS). Corneal health was unremarkable except for some mild foreign body tracks (less than Grade 1, Efron's scale⁶) at the superior corneal area. She was advised to use her old spectacles with a lower prescription (-3.00 D, OU) as a transient visual aid and to continue lens wear and return for review in two days.

The second after-care visit was arranged in the late afternoon without the lenses *in situ*. UVA was 0.4 (decimal) in both eyes and the residual refractive errors were -0.50/-0.75 × 130 (OD) and -1.00/-1.00 × 175 (OS). Subtractive plots showed a Bull's eye pattern in each eye with axial power changes of 2.80 D (OD)

and 2.60 D (OS), and changes in corneal toricity of 0.70 D (OD) and 1.20 D (OS). Trace (less than Grade 1) punctate corneal staining was observed in the right eye.

The one-week after-care visit was arranged in the late afternoon. UVA showed little improvement (0.5 in both eyes) and the residual refractive errors were -1.00 (OD) and -1.50/-0.75 × 100 (OS). Subtractive topographical plots

again showed a bull's eye pattern in each eye with axial power changes of 3.20 D (OD) and 2.80 D (OS) and changes in corneal toricity of 0.90 D (OD) and 2.40 D (OS). Trace central corneal staining (less than Grade 1) was observed in the right eye. Since the progression of the treatment was satisfactory, she was instructed to continue lens wear for another two weeks.

The three-week after-care visit was scheduled in the morning. The subject

came without wearing the lenses. UVA and residual refractive errors were 0.9 and -0.25 D, respectively, in both eyes. Subtractive topographical plots showed a bull's eye pattern in the right eye and a slight 'frowning' face pattern in the left eye (Figure 5). Axial power changes were 3.80 D (OD) and 2.80 D (OS), and changes in corneal toricity were 2.10 D (OD) and 2.50 D (OS). Slitlamp examination showed no abnormal findings in either cornea. She was instructed to continue lens wear and return in one week.

The one-month after-care visit was scheduled in the morning. She came to our clinic without wearing her lenses. UVA were 0.8 (OD) and 0.9 (OS) and the residual refractive errors were -0.75 (OD) and -0.50/-0.75 × 165 (OS). Subtractive topographical plots were similar to those at the last visit. Axial power changes were 3.30 D (OD) and 3.50 D (OS) and changes in corneal toricity were 2.10 D (OD) and 2.20 D (OS). Both corneas appeared normal. The patient was instructed to continue lens wear and return for regular after-care every three months.

At the 15-month after-care visit, the residual refractive errors were plano/-0.50 × 170 (OD) and -0.50/-0.75 × 180 (OS). Subtractive topographical plots again showed a bull's eye pattern in both eyes (Figure 6). Axial power changes were

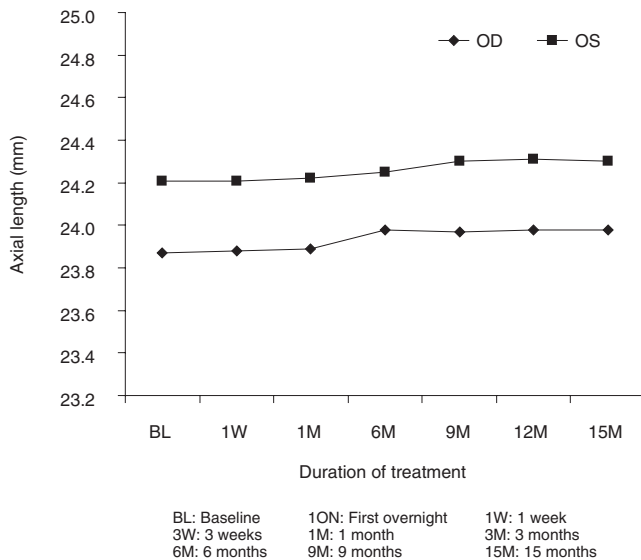


Figure 3. Axial length measurement during the course of ortho-k treatment

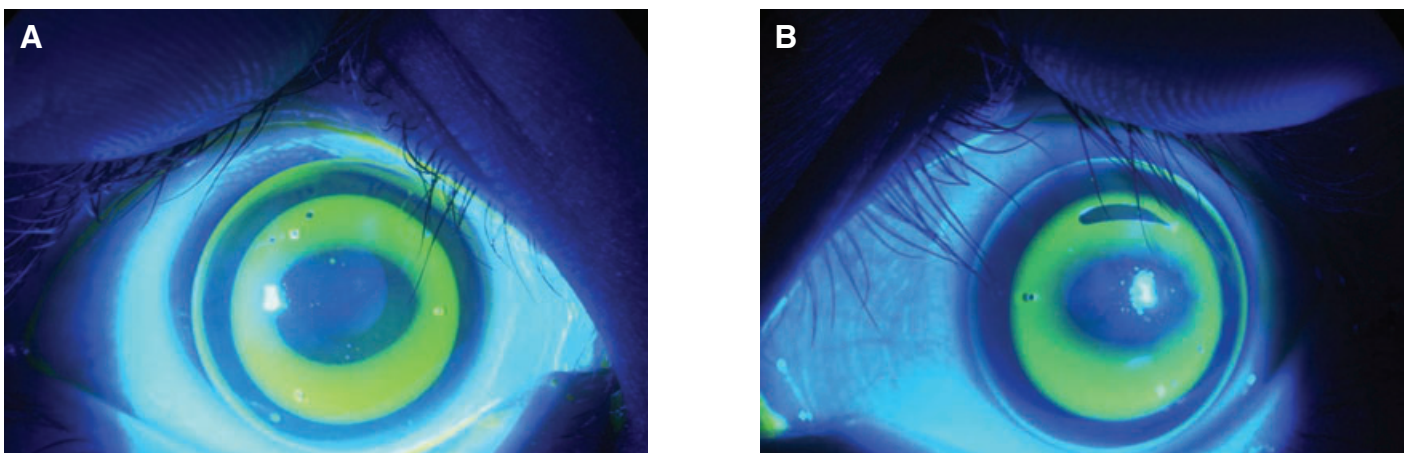


Figure 4. Fluorescein patterns of the lens fit; A: right eye, B: left eye

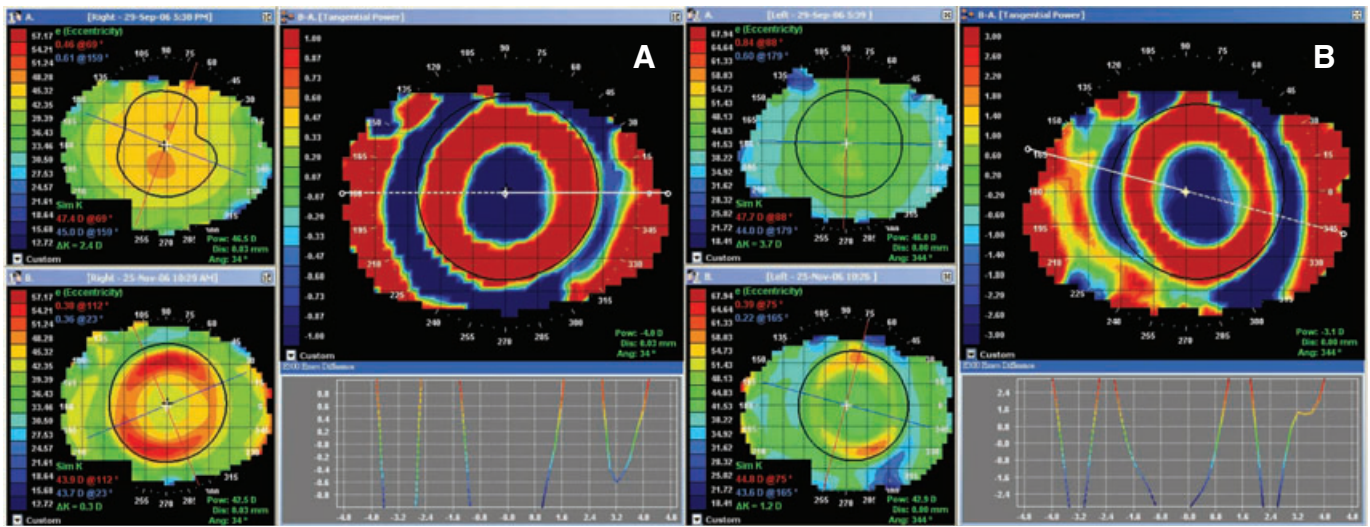


Figure 5. Three-week tangential difference maps; A: right eye, B: left eye

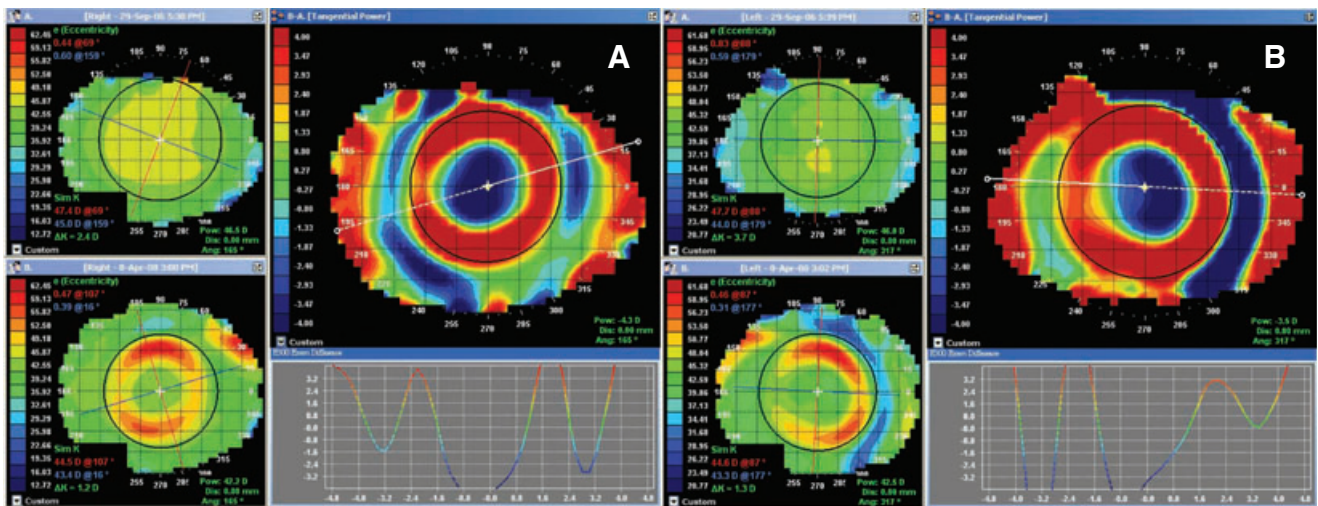


Figure 6. Tangential difference maps at the 15 months visit; A: right eye, B: left eye

4.00 D (OD) and 3.30 D (OS) and changes in corneal toricity were 1.20 D (OD) and 2.40 D (OS). Axial length showed no significant increase in either eye (0.11 mm and 0.09 mm in OD and OS, respectively, equivalent to less than 0.30 D progression in each eye) during the 15 months of lens wear (Figure 3). In addition, the patient had no undesirable corneal responses and was very happy with her 'glasses-free' unaided vision during

the daytime. She was advised to change her lenses yearly and is waiting for her second pair of lenses.

DISCUSSION

This report shows that toric peripheral RGL can be used effectively for correcting high corneal astigmatism. We observed a significant reduction of corneal toricity in the left eye (35 per cent) with the toric

peripheral RGL after a single night of lens wear. The effect was slower for the right eye (about 17 per cent reduction after one night of wear). The effect of the reduced astigmatism continued with lens wear and reached optimum levels in three weeks, with a reduction of myopia of 94.1 per cent in the right and left eyes and reductions in corneal toricity of 87.5 per cent in the right eye and 67.6 per cent in the left eye. Although mild inferior lens decentra-

tion was observed in some of the visits, based on the subtractive topographical maps in the left eye, there was no clinically significant corneal complication during the treatment and the patient was satisfied with the uncorrected vision during the daytime. Her parent was satisfied with the treatment as no significant change was observed in the axial length during the period of lens wear, indicating no myopic progression during the year.

Correction of astigmatism has been one of the major limitations in current ortho-k practice with spherical RGL design. Mountford and Pesudovs² reported that, at the central two-millimetre chord, about 50 per cent of with-the-rule corneal astigmatism of not more than 1.50 D, may be reduced with a spherical RGL design, however, they found no statistically significant reduction of corneal astigmatism, if the central three-millimetre chord length was used. To achieve an optimum refractive change with ortho-k, the lens should be located centrally on the cornea. Hence, limbus-to-limbus corneal astigmatism is contraindicated for spherical ortho-k as the lens is more likely to decentre on such a cornea, leading to a poor corneal curvature change. The decentred lens on such a cornea may even induce corneal astigmatism. Poor corneal curvature change will result in poor unaided vision and this problem has been reported to be one of the main reasons for discontinuation of the treatment.¹ In view of the increasing demand for ortho-k in Hong Kong in recent years, some manufacturers have developed toric RGL designs (toric reverse and/or alignment zone). A multi-centre retrospective study using toric RGL design has been evaluated in Switzerland with a reported 82.5 per cent successful fitting rate.⁵ Beerten and co-workers⁷ reported that toric RGL can successfully correct astigmatism up to 3.50 D and can be used for against-the-rule astigmatism. They also reported that 70 per cent of their patients achieved an UVA of 6/9 in both eyes. Though presented at conferences, none of these reports has been published.

The lens used in the current case is a back peripheral toric design, where the

BOZR and reverse curve are spherical over the optical zone, while the sag heights and tangent angles at the alignment zone of the lens are different with respect to the two principle meridians. Toric peripheral lens design, similar to that in the toric rigid gas permeable lens, facilitates lens stabilisation and centration on the toric cornea. Interestingly, in this case, the initial astigmatic reduction was slower in the right eye, which had less corneal astigmatism. The astigmatic reduction was only 17 per cent compared to 35 per cent in the left eye after treatment for one night. This may be due to the smaller sagittal difference between the steep and flat meridians of the right lens (30 µm) compared to that of the left lens (90 µm), that is, a greater sagittal difference can lead to greater reduction.

We also observed a regression in the reduction in corneal toricity with lens wear after three months without a reciprocal change in subjective astigmatism. The reduction in corneal toricity regressed from 87.5 per cent at the three-month visit to 54.2 per cent at the six-month visit in the right eye. There was no residual refractive cylindrical power and the UVA was 1.0. The regression in the right eye continued, with only a 41.7 per cent reduction of corneal toricity at the nine-month visit. In contrast in the left eye, the reduction of corneal toricity stabilised after three weeks of lens wear, leaving a 1.00 D residual refractive cylindrical power, which persisted until the 15-month after-care visit. The discrepancy in the changes of corneal toricity and manifest refraction indicates that topographical changes do not necessarily reflect the manifest refractive cylindrical power change in ortho-k. The implication is that other factors, other than anterior corneal change, may play a role in the refractive changes in ortho-k. Further investigation is warranted to investigate factors affecting changes in subjective refraction in ortho-k.

It is important to recognise that this is an anecdotal report on a single patient, which cannot be taken as representing proof of the efficacy of toric orthokeratology for the reduction of large amounts of

corneal astigmatism. This case report does provide a positive indication, and further research in the form of controlled, randomised clinical trials will be required to fully validate this approach to refractive error correction.

CONCLUSION

This report presents a successful case of a child with high corneal astigmatism who was fitted with a pair of toric peripheral RGL. Close to full correction of myopia and astigmatism were achieved with good unaided visual acuity of 1.0 in both eyes after 15 months of lens wear. The patient was very satisfied with this treatment and is waiting for annual replacement of her toric peripheral RGL.

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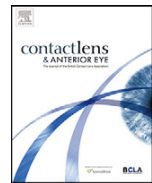
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Clinical performance of an orthokeratology lens fitted with the aid of a computer software in Chinese children

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ABSTRACT

Purpose: To report the clinical performance of the orthokeratology (ortho-k) lens fitted with computer assisted system after 1-month of lens wear, in a group of children undergoing ortho-k treatment in a 2-year randomized myopic control study.

Method: Children aged 6–11 years old were fitted with the ortho-k lenses using computerized fitting. The initial myopia was 4.00–0.50 D and the initial refractive astigmatism was within 1.25 D. Lens performance, in terms of centration, myopic reduction, vision, ocular health status and lens binding incidence, was evaluated at one night, one week and one month after lens wear. Only data from the right eye was presented.

Results: The initial spherical equivalent refraction (SER) for the 51 subjects was -2.29 ± 0.81 D. The first fit success rate was 90%. The reduction of SER after one night and one week aftercare visit were 57% and 81%, respectively. At the one month visit, the mean reduction in SER was 89% with unaided logMAR visual acuity of 0.03 ± 0.11 . Mild central corneal staining was found in 9–20% of the subjects at the aftercare visits. The incidences of lens binding at one night, one week and one month aftercare visits were 17%, 39% and 30%, respectively.

Conclusions: Computer assisted system for Menicon Z Night lens fitting gave a high first fit success rate. Menicon Z Night lens was effective in myopic reduction and provided stable vision after one week of lens wear. Ocular health of the subjects after lens wear was generally unremarkable.

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1. Introduction

Overnight orthokeratology (ortho-k) has been shown to have potential in slowing eyeball elongation in children with low to moderate myopia [1–3]. The use of ortho-k on children is increasing [4] in places with high prevalence of myopia such as Hong Kong [5]. The efficacy of overnight ortho-k on myopic reduction has been well studied and it has been proven to be effective in improving unaided visual acuity in both children and adults [6–11].

Like conventional rigid lens fitting, ortho-k fitting may require a diagnostic set provided by the manufacturer. Since the fitting of ortho-k requires information of the peripheral profile of the cornea, parameter other than the back optics zone radius and lens diameter, such as the sagittal depth, is also required for a successful ortho-k fitting. With the numerous possible combinations of lens parameters involved, many trial lenses are needed and this may pose a problem of storage. Chair time is also increased if a number of attempts are required to achieve the optimal fitting. As

computerized fitting approach is becoming more popular, it is necessary to evaluate the clinical performance of ortho-k fitted using this fitting method.

Some contact lens manufacturers have put a lot of effort to simplify ortho-k lens fitting by importing corneal profile information into the computer software to reduce the dependency of the diagnostic lens kit. Tahhan et al. [12] compared the efficacy of four brands of reverse-geometry lenses and Maldonado-Codina et al. [13] compared the clinical performance of a brand of ortho-k lenses fitted empirically and with another brand which employed a trial set. Tahhan et al. [12] reported that all four brands of lenses performed similarly in myopic reduction while Maldonado-Codina et al. [13] concluded that lenses fitted by trial set system were more effective in myopic reduction. El Hage et al. [10] studied the efficacy of ortho-k lenses ordered empirically using corneal topographical data and concluded that myopic reduction could be achieved by one week of lens wear. In these studies, the attention was only on myopic reduction and ocular health after lens wear.

This paper presents the 1-month data of children who are undergoing ortho-k treatment in a 2-year randomized myopic control study (Retardation of Myopia in Orthokeratology (ROMIO) study). The aim of this paper was to report the clinical performance of

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Table 1
Entry criteria.

Inclusion	
Age	6–11 years
Refractive errors (cycloplegic autorefraction)	
Myopia	0.50–4.00 D
Astigmatism	Within 1.25 D
Anisometropia	Not more than 1.50 D in myopia or astigmatism
Best corrected visual acuity (LogMAR)	Not worse than 0.10
Exclusion	
Abnormal ocular and general health	
History of rigid contact lens wear	
History of myopic control therapy i.e. progressive add spectacles	

the ortho-k lens fitted with computer assisted system, in terms of centration, myopic reduction, vision, ocular health status and lens binding incidence.

2. Methods

Fifty-one subjects were randomly assigned to ortho-k group and fitted with ortho-k lenses in the ROMIO study. The entry criteria of the study are shown in Table 1. Data collected at each visit included non-cycloplegic subjective refraction, ocular health, and unaided visual acuity (UVA) (Computerized LCD LogMAR acuity chart). Topographic data (Medmont E300 topographer (Medmont Pty Ltd., Australia)), manifest refractive errors and horizontal visible iris diameter were imported into the computer installed with the Easyfit software (NKL Contactlinsen, Netherlands). Lens parameters for the optimum Menicon Z Night (NKL Contactlinsen, Netherlands) of Menicon Z material (Menicon Co. Ltd., Nagoya, Japan) was determined by the Easyfit software. The lens design of Menicon Z Night lens is described in Table 2.

Contact lens solutions were provided to the subjects to ensure that all subjects used the same solutions and were compliant with the replacement schedule. Subjects were instructed not to switch to other solutions unless advised by the practitioners. Proper procedures in lens handling were taught before the delivery of the lenses. At the delivery visit, fluorescein pattern of each lens on the eye was examined and the lens was not dispensed if the fluorescein pattern was deemed unacceptable. Lenses with excessive central clearance, inadequate edge lift or inadequate bearing at the alignment curve were regarded as unacceptable fit.

The subjects were required to wear the lenses every night for at least 6 h. They were examined in the mornings after the first night of lens wear (1-overnight visit), one week (1-week visit) and one month (1-month visit) after lens wear. The subjects were required to attend the 1-overnight visit without removing their lenses, within 2 h after awakening. At the subsequent visits, they were required to remove their lenses before attending. Refraction, corneal topography, visual acuity and external ocular health assessment were performed at each of these visits. At the 1-overnight aftercare, if corneal topography revealed a decentered treatment

Table 2
Lens design of Menicon Z Night lens.

Fitting philosophy	Jessen factor (+0.50 D)
Fitting method	Computer assisted system – Easyfit software
Material	Menicon Z
Dk	163×10^{-11}
Design	Spherical lens
BOZR (mm)	7.20–9.50 (in 0.05 mm step)
Lens diameter (mm)	10.20/10.60/11.00
Tangential angle (°)	50–65 (in 1° step)
Sagittal depth (mm)	0.50–0.99 (in 0.01 mm step)
Fenestration	Three, located in the reverse curve, 120° apart

Table 3
Grading scale of lens binding.

Grade	Definition
0	No binding observed. Lens moving freely
1	Lens bound and loosens up spontaneously after ≤ 5 forced blinks
2	Lens bound and loosens up after one episode of pressure on the upper lid, then repeated on the lower lid and ≤ 5 forced blinks
3	As Grade 2, but two pressure pushes on the lids and ≤ 5 forced blinks
4	As Grade 2, but with three pressure pushes and ≤ 5 forced blinks

zone, the subject would be instructed to continue lens wear only if the fluorescein pattern of the decentered lens was acceptable and the corneal condition was unremarkable. Refit was indicated if both centration and the fluorescein pattern were not acceptable and or if the centration worsened at the 1-week visit. The lens performance was reviewed at the 1-month visit and refit was indicated only if lens decentration persisted or if the cornea under-responded (i.e. residual myopia was more than half a dioptre or UVA was worse than 0.20 (1-month visit)).

Subjects were required to cease lens wear in case of adverse general or ocular condition (e.g. fever or significant central corneal staining), the former monitored by parents, and the latter determined by the practitioner. Resumption of lens wear was indicated only after the adverse condition had subsided. Medical referral was indicated if the subject presented with significant or/persistent ocular problems (e.g. >Grade 3 corneal staining).

The level of severity of corneal staining was graded using the Efron scale [14]. Incidence of lens binding was graded by the subjects themselves, except at the 1-overnight visit which was evaluated by the practitioner (as the subjects were required to wear the lenses to this visit). The subjects were told to grade from Grade 0 to Grade 4 (Table 3). Incidences of corneal indentation ring and dimple veiling were determined by the practitioners at each visit. Data of the both eyes were measured but only results from the right eyes are reported in this paper.

2.1. Statistical analysis

The distributions of the SER at all visits were not statistically different from normal (Kolmogorov–Smirnov tests, $P > 0.05$). Repeated measures analysis of variance (ANOVA), followed by paired *t*-tests with Bonferroni corrections for multiple comparisons, where appropriate, were used to evaluate the effect of ortho-k on myopic reduction after wearing the lenses for one night, one week, and one month.

3. Results

3.1. Centration

Forty-six subjects (90%) had good lens centration at the 1-overnight visit, giving a first fit success rate of 90% (Fig. 1). Five subjects had laterally displaced treatment zone at the 1-overnight visit and refits were performed for these subjects at this or subsequent visits. However, their data were excluded from the following analyses.

3.2. SER reduction and vision

The SER and UVA of each visit are shown in Tables 4 and 5. The baseline mean \pm standard deviation (SD) SER was -2.29 ± 0.81 D.

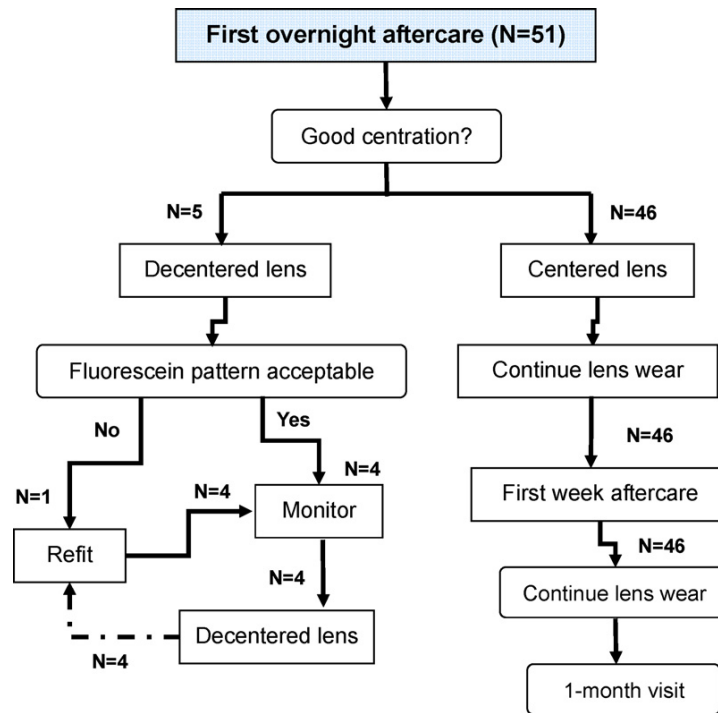


Fig. 1. Flowchart showing the progression of subjects through the first month of lens wear.

Table 4

Spherical equivalent refraction (SER) (mean ± standard deviation) and percentage reduction at each visit during first month of lens wear.

	SER (D)	SER reduction (%)	P values		
			Baseline	First overnight	First week
Baseline	-2.29 ± 0.81	-	-	-	-
First overnight	-0.98 ± 0.68	57	<0.001	-	-
First week	-0.45 ± 0.41	81	<0.001	<0.001	-
First month	-0.26 ± 0.40	89	<0.001	<0.001	<0.001

P=probability value (repeated measures ANOVA followed by paired t tests with Bonferroni corrections for multiple comparisons) for differences of SER between baseline visit and subsequent visits.

Significant differences in SER were found between baseline visit and the other three aftercare visits ($P < 0.001$). At the 1-overnight visit, 57% of SER reduction (i.e. SER at this visit minus SER at baseline as a percentage of absolute baseline SER) was achieved. The reduction in SER was 81% after wearing the lenses for a week. The mean ± SD SER after one month of lens wear was -0.26 ± 0.40 D and 89% of SER reduction was achieved. The UVA was logMAR 0.22 ± 0.26 after the 1-overnight visit and further improved to logMAR 0.03 ± 0.11 at the 1-month visit ($P < 0.001$). At the 1-month visit, the lenses of all forty-six subjects demonstrated good lens

centration but five subjects required refitting (to increase target reduction) at this visit (for the main myopic control study) due to under-responding.

3.3. Ocular health

One subjects (2%) had mild central corneal staining at the baseline visit. The incidences of central corneal staining were 22% and 17% at the 1-overnight and 1-week visits, respectively, and reduced to 11% at the 1-month visit. Almost all staining found was Grade 1 level of severity (Table 6). Staining was persistently observed in five subjects, but none of them was clinically significant.

Table 5

Unaided logMAR visual acuity (UVA) (mean ± standard deviation) at each aftercare visit.

	UVA	P values	
		First overnight	First week
First overnight	0.22 ± 0.26	-	-
First week	0.08 ± 0.12	<0.001	-
First month	0.03 ± 0.11	<0.001	0.01

P=probability value (repeated measures ANOVA followed by paired t tests with Bonferroni corrections for multiple comparisons) for differences of UVA between first overnight visit and subsequent visits.

Table 6

Incidences of central corneal staining and lens binding at each visit during the first month of lens wear.

	Central staining (%)		Binding (%)			
	Grade1	Grade 2	Grade1	Grade 2	Grade 3	Grade 4
Baseline	2	0	-	-	-	-
First overnight	20	2	13	2	2	0
First week	17	0	33	2	4	0
First month	11	0	24	2	2	2

3.4. Lens binding, corneal indentation ring and dimple veiling incidences

Lens binding was reported by eight subjects (17%) at the 1-overnight visit but only two of them (4%) had lens indentation mark on the cornea. The incidences of reported lens binding increased to 39% and 30% at the 1-week and 1-month visits, respectively, but no corneal indentation ring was observed at these two visits. Dimple veiling was observed in 20 subjects (43%) at the 1-overnight visit only. No dimple veiling was found in the subsequent visits.

4. Discussion

Fitting systems of different commercially available ortho-k lenses vary from empirical lens order to trial lens fitting or computer-assisted determination. Despite the differences in the fitting methods, the goal is the same: the lens that will give a good clinical performance, i.e. good lens centration, comfort, and good corneal health. Inadequate lens fitting may affect corneal health and refractive correction if the lens does not centre properly, hence the main criterion in ortho-k lens fitting is good lens centration. Considering the fact that each cornea responds differently to ortho-k regardless of the use of trial lenses or not, residual refractive error was not taken into account when evaluating the first fit success rate. Only lenses giving good lens centration was considered. The first fit success rate of the study lens was 90%. At the 1-month visit, 89% (41/46) of these subjects had achieved good unaided vision with well centered lens. Although the remaining five subjects also had good lens centration, they had poor unaided vision due to significant residual refractive errors (i.e. under-responding to target). They were refitted with higher target lenses and all subjects proceed with the main myopic control study. Our results showed that high success rate can be achieved with Menicon Z Night lenses ordered with the aid of the computerized program without the use of a trial lens set. Computer assisted system for ortho-k lens ordering is important to enhance the efficiency of ortho-k fitting to the practitioner and reduce the chair time of the patients. Although diagnostic trial set has the merit that the practitioners can assess the fluorescein pattern in the office and patients can experience the lens in the eye before ordering, practitioners are required to keep a set of trial lenses which could exceed 100 lenses for a full set of ortho-k diagnostic set. Trial lens maintenance and storage can be problematic to the practitioners as these lenses, particularly in wet storage, required regular disinfection/cleaning. Possible lens contamination or transmission of pathogens may result if the lenses were not maintained properly. Without trial lenses, time and effort spent on lens maintenance can be saved. In the United Kingdom, the outbreak of the variant Creutzfeldt-Jakob disease drew the attention of the eye care practitioners to the potential transmission route of prion [15]. Prion is a proteinaceous infectious agent which could be transmitted by fitting contact lens with re-useable trial lenses. Some researchers suggested that the risk of transmission of prion via contact lenses is negligible [16] while some believed that it is theoretically possible [17,18]. In view of the uncertainties, practitioners in the UK have to execute clinical judgment of a benefit/risk consideration towards the use of trial lenses and minimizing the use of trial lenses is considered to be beneficial to patients as the chance of exposure towards pathogens could be minimized. The high success rate of ortho-k fit with computer assisted lens ordering system will therefore be ideal for ortho-k practitioners as the worry of disease transmission would be removed.

Menicon Z Night lens demonstrated very good centration in 90% of the subjects at the 1-overnight visit. Five subjects required refit and refitting of the lenses did not improve the centration. Corneal topography revealed that all five subjects had the corneal

Table 7
Clinical performance of orthokeratology lenses reported in the previous and current studies.

Authors (years)	Lens (material)	Fitting method	No. of eyes	Baseline			First overnight			First week			First month		
				SER/[myopia] (D)	Reduction (%)	SER/[myopia] (D)	SER/[myopia] (D)	Reduction (%)	SER/[myopia] (D)	Reduction (%)	SER/[myopia] (D)	Reduction (%)			
Nichols et al. (2000) [7]	Contex OK Series (Airperm)	Determined empirically and given a day trial	8	-1.84 ± 0.81	25	-1.37 ± 1.12	-0.40 ± 0.90	78	-0.03 ± 0.49	98					
Rah et al. (2002) [8]	Fargo 6 lens and Paragon CRT	Empirical	46	-2.37 ± 0.93	-	-	-	-	-0.18 ± 0.82	92					
Maldonado-Codina et al. (2005) [13]	BE (Boston XO)	Trial fit	18	[-2.22 ± 0.63]	76	[-0.53 ± 0.83]	[0.67 ± 0.86]	130	-	-					
Maldonado-Codina et al. (2005) [13]	No. 7 (Paragon HDS)	Empirical	18	[-2.40 ± 0.59]	57	[-1.03 ± 0.45]	[-0.17 ± 0.50]	93	-	-					
El Hage et al. (2007) [10]	Lenses calculated using the CKR fitting program (Boston Equalens II)	Computer-assisted	20	-2.51	69	-0.77	-0.39	84	-0.23	91					
Current (2011)	Menicon Z Night lens (Menicon Z)	Computer-assisted	46	-2.29 ± 0.81	57	-0.98 ± 0.68	-0.45 ± 0.41	81	-0.26 ± 0.40	89					

apex either nasally or temporally displaced. These subjects were still recruited as they satisfied the recruitment criteria (displaced corneal apex was not the exclusion criteria) for the myopic control study. The fluorescein pattern of the lenses in these subjects was optimal. The lens centration did not improve significantly even when a larger diameter lenses was used. Our result suggested that displaced corneal apex may cause lateral lens displacement and spherical ortho-k may not work as well in such corneas in terms of lens centration. Further study is warranted to verify this observation.

Menicon Z Night lens also showed good reduction of myopia. The subjects achieved 57% of SER reduction after wearing the lenses for the first night and up to 81% achieving logMAR 0.10 or better UVA at the 1-week visit. Spectacles wear were no longer required by the first week of lens wear. The reduction was almost 90% at the 1-month visit. Although we found significant differences in SER and UVA between the 1-week and 1-month visits, the differences were clinically insignificant. In comparison of the results with previous studies (Table 7), Menicon Z Night lens ordered by the computer assisted system can obtain similar performance in terms of myopic reduction compared to other lens designs fitted empirically or with the use of trial lens set.

Mild level of central corneal staining has been reported after ortho-k lens wear [7,8,11–13]. Rah et al. [8] reported that up to 80% of subjects had corneal staining at the 1-month visit but the location of the staining was not mentioned. Tahhan et al. [12] found mild central staining in 42% of the subjects at the 1-overnight visit and the staining was reduced to 3% and 7% at 1-week and 1-month visits, respectively. Chan et al. [11] found central corneal staining in 30% of the subjects at the 1-overnight visit and most of them were Grade 1 or less. In this study, the incidences of corneal staining were 9–20% at different visits during the first month of lens wear. The rate was not high and the severity of the staining was mild; hence no cessation of lens or medical referral was required. No adverse event other than corneal staining was found during the first month of lens wear.

Lens binding was reported by 17% of the subjects at the 1-overnight visit. The incidence appeared to increase at the 1-week and 1-month visits. Since the subjects were asked to wear the lenses in situ to the office at the 1-overnight visit, the lenses may have been loosened up due to normal blinking on the way to our clinic. By the time the practitioner assessed the level of binding, the lenses may have been loosened for some time and this may explain the lower incidence rate of binding at the 1-overnight visit. Possible error may also be introduced as the practitioners graded the binding level at the 1-overnight visit based on corneal indentation ring while the subjects graded at the 1-week and 1-month visits based on their own observations. Also, subjects may have difficulty assessing the level of binding themselves and classifying them into different grades even though they were given the assessment criteria beforehand.

Although the rate of lens binding is quite high, the subjects were asymptomatic and corneal indentation ring was only observed at the 1-overnight visit and not in the subsequent visits. A high incidence of dimple veiling was also found at the 1-overnight visit probably due to bubbles trapped under the lens from blinking with lenses on.

In this study, the discontinuation rate of lens wear within the first month was 12% and subjects who failed the lens handling were already excluded and no lenses were dispensed to them. No subjects were excluded due to adaptation problem after commencing

lens wear and the five subjects who discontinued from the treatment were so advised by the practitioner due to inadequate lens fit. No subjects were required to cease lens wear due to undesirable ocular health condition during the one month study.

In conclusion, this study showed that the Easyfit software, computer assisted system for Menicon Z Night lens fitting, gave comparable success rate as lenses fitted with the use of diagnostic lens set. The first fit success rate with Menicon Z Night lens was 90% and the lens was effective for myopic reduction in subjects with low and moderate myopia. A stable vision could be achieved after first week of lens wear with good lens centration. Vision and ocular health of subjects were generally good within the first month of lens wear.

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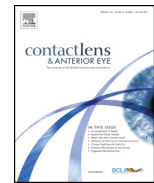
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Case report

Orthokeratology for slowing myopic progression in a pair of identical twins



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ABSTRACT

Purpose: To compare the axial length elongation and change in refractive errors in a pair of identical twins wearing orthokeratology (ortho-k) and single vision lenses (SVLs), respectively.

Case report: Identical Twin A and B, who were 8 years of age, with the same amount of near activities, were assigned to wear ortho-k and SVLs randomly and they were monitored for two years for myopic progression. Twin A and B were assigned to wear ortho-k and SVLs, respectively. Myopic progression was evaluated by the change in axial length and in refractive errors. A faster axial length elongation was observed in each eye of Twin B during the two-year study period. The overall change in axial length was 0.52 mm (OD) and 0.70 (OS) in Twin A and 0.77 mm (OD) and 0.82 mm (OS) in Twin B. In terms of cycloplegic refractive errors (SER), one month after ceasing lens wear (after completion of the two-year study), the increase (from baseline) were 11% (OD) and 48% (OS) in Twin A and 87% (OD) and 67% (OS) in Twin B.

Conclusions: Ortho-k is more effective in controlling myopic progression in terms of axial elongation than wearing SVLs in this pair of identical twins.

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1. Introduction

Overnight orthokeratology (ortho-k) has been shown to be able to correct low to moderate myopia and to retard myopic progression in children by 32%–55% [1–6]. It is becoming popular in countries where the prevalence of myopia is high like Hong Kong [7]. Clinical results of the early longitudinal studies [1–5] have shown the potential of ortho-k to slow axial elongation and a recent randomized clinical trial has confirmed the effectiveness of ortho-k for myopic control in children [6]. However, variability was found in the response to ortho-k treatment among subjects, indicating that there are other factors affecting the response, e.g. visual habits, environmental factor. The limitations and the confounding factors may affect the effect of ortho-k on myopic control. A case report of a pair of identical twins may give some insight of ortho-k on myopic control with these confounding factors minimized. In this report, the data of a pair of identical twins who were randomly assigned to wear ortho-k and single vision lenses (SVLs) for vision correction in a 2-year myopic control study were compared and presented.

2. Case report

The twins were eight years old when they enrolled in the myopic control study. At the baseline examination, both of them fulfilled the inclusion criteria of the myopic control study [6]. The twins were randomly assigned to wear ortho-k lenses (Twin A) and SVLs (Twin B) and were monitored for 24 months. Ethics approval for the project was obtained from the Departmental Research Committee of the School of Optometry, The Hong Kong Polytechnic University, and all the procedures in the study followed the tenets of Declaration of Helsinki in 2002. Informed consent was obtained from the subjects and their parent prior to the commencement of the study. Neither of them had worn contact lenses or had any myopic control treatment before. The twins have a family history of high myopia (–10 D for mother). Both of them attended the same class of the same school and spent equal time on extra-curricular activities. The two subjects were studying at primary school during the study period. School started early in the morning and finished after three o'clock in the afternoon and went to tutorial class right afterwards. They returned home usually after dark in the school day.

An insertion and removal training was arranged for Twin A after the randomization for the myopic control study. The performance of lens handling of both the subject and the parent was reviewed by a practitioner. Ortho-k lenses were ordered and delivered only after the practitioner was satisfied with their performance on lens handling. The ortho-k lenses fitted on Twin A was Menicon Z Night

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Table 1
Contact lens solutions and accessories delivered to Twin A.

	Solution	Replacement frequency	Remarks
Cleaner	O ₂ Care Daily Cleaner	Every 2 months	Rub each lens surface for 10 s
Soaking	MeniCare Plus	Every month	–
Rinsing	Bausch + Lomb Saline	Every month	Rub and rinse lens before insertion and after cleaning with cleaner
Enzymatic cleaner	Menicon Progent	–	Perform once a week after cleaning lenses as per routine
Artificial tears	Uni-dose Alcon Tears Naturale Free	–	For lens insertion and also before lens removal
Menicon cylindrical case	–	Replace with every new bottle of MeniCare Plus solution	Pour away MeniCare Plus; rinse and fill to the mark with fresh soaking solution after lens insertion, Store in a cool, dry place
Menicon SP vial	–	Annually	Clean vial after use; air dry and store in a cool, dry place

Table 2

Cycloplegic spherical equivalent refraction (SER) and LogMAR visual acuity (VA) of the twins in the baseline, 24- and 25-month visits. (Twin A – orthokeratology (*residual myopia); Twin B – single vision spectacles).

		Baseline		24-month			25-month (after ceasing orthokeratology treatment)		
		SER (D)	Best corrected VA	SER (D)	Percentage increase in SER (%)	Best corrected VA	SER (D)	Percentage increase in SER (%)	Best corrected VA
Twin A	OD	–3.08	–0.02	–0.62*	–	–0.04	–3.42	11	–0.06
	OS	–2.44	–0.08	–1.08*	–	0.00	–3.60	48	–0.14
Twin B	OD	–1.97	–0.10	–3.69	87	0.00	–	–	–
	OS	–2.81	0.04	–4.70	67	–0.02	–	–	–

(NKL Contactlinsen, Netherlands) and made from Menicon Z material (Menicon Co. Ltd, Nagoya, Japan). The initial lens parameters were determined with the Easyfit software (NKL Contactlinsen, Netherlands) based on imported corneal topographic data, horizontal visible iris diameter and the manifest subjective refraction of the subject. Contact lens care products (Table 1) were provided for the subjects during the study period. Deliveries of the ortho-k lenses and spectacles to the twins were arranged on the same day. Twin A was required to wear the ortho-k lenses every night for at least six hours and he was also instructed to return for aftercare after the first overnight, one week and one month of lens wear, to ensure good correction of refractive errors and ocular health.

The target of the ortho-k lenses was increased if unaided visual acuity (VA) was worse than logMAR 0.20 or if residual myopia was more than 0.50 D after stabilization of the treatment. The spectacles prescription of Twin B was also updated if there was more than 0.50 D difference with the habitual spectacles at any of the data collection visits. Cycloplegic examination was arranged every 6 months for both subjects. VA measurement was performed before cycloplegia using the high contrast ETDRS chart (Precision Vision, La Salle, IL, USA). Anterior corneal power (average of the SimK) was also measured using Medmont E300 (Medmont Pty Ltd, Melbourne, Victoria, Australia) and the central corneal thickness (CCT) and the posterior corneal power were measured using the Pentacam (Oculus, Wetzlar, Germany). Auto-refraction using the Shin-Nippon SRW-5000 open-field auto-refractor (Shin-Nippon Commerce Inc., Tokyo, Japan) and axial length (AL) measurement using the IOL Master™ (Zeiss Humphrey System, CA, USA) were performed by a masked examiner after cycloplegia.

During the study period, the ortho-k lenses and the spectacles of the subjects were updated once (at 12 month) and twice (at 6 and 18 month) for Twin A and Twin B, respectively, during the study period due to increased refractive errors.

2.1. Changes in refractive errors

The pre-treatment cycloplegic auto-refraction spherical equivalent refraction (SER) of Twin A were –3.08 D (OD) and –2.44 D (OS) and of Twin B were –1.97 D (OD) and –2.81 D (OS). At the end of the study period, Twin A was asked to return for a re-stabilization (RS)

visit every week, after stopping ortho-k lens wear, to review the stabilization of the refractive errors and the corneal topography. One month after cessation of lens wear (25-month), less than 0.25 D difference in SER and corneal topography from the previous RS visit (1 week before) and the refractive status of his eyes in that visit was considered stabilized. In terms of manifest refractive errors, the changes over the two years in Twin A were –0.34 D (OD) and –1.16 D (OS) and –1.72 D (OD) and –1.89 D (OS) in Twin B. Table 2 shows the percentage increase in SER and the best corrected VA of the two subjects over the 2-year study period.

2.2. Changes in corneal parameters

CCT decreased in Twin A during ortho-k wear but returned to original after cessation of ortho-k, whereas CCT slightly increase in Twin B after 24-month. The posterior corneal powers did not change significantly in both subjects during the study period. The anterior corneal power of Twin B at the baseline and 24-month visit remained the same while a decrease of 0.40 D (OD) and 0.60 D (OS) in anterior corneal power was observed in Twin A one month after cessation of ortho-k lens wear (Table 3).

2.3. Changes in AL

Increases in AL were observed in both eyes of each subject during the study period as shown in Fig. 1. The increase in AL was significantly larger in Twin B than in Twin A. The overall increases in AL were 0.52 mm (OD) and 0.70 mm (OS) in Twin A; 0.77 mm (OD) and 0.82 mm (OS) in Twin B. Fig. 1 shows the AL progression of the twins during the two years. For Twin A, AL measured at the end of the study period was not different from those measured one month after cessation of ortho-k lens wear.

3. Discussion

This is the first case report to present a comparison of the myopic control effect of ortho-k on twins. With two genetically identical twins who shared the same amount of daily activities attempting two different myopic control treatments, the confounding factors which may affect the responses can be minimized. Although the

Table 3
Ocular parameters of the twins at baseline and after the completion of the study.

	Eye	Visit	Axial length (mm)	Anterior corneal power (D)	Posterior corneal power (D)	Central corneal thickness (μm)
Twin A	OD	Baseline	24.83	43.1	-6.0	565
		25 month	25.35	42.7	-6.0	561
		Difference	0.52	-0.4	0.0	-4
	OS	Baseline	24.64	43.1	-6.3	553
		25 month	25.34	42.5	-6.4	541
		Difference	0.70	-0.6	-0.1	-12
Twin B	OD	Baseline	24.65	42.8	-5.9	542
		24 month	25.42	42.8	-5.9	548
		Difference	0.77	0.0	0.0	6
	OS	Baseline	24.77	43.1	-6.3	549
		24 month	25.59	43.2	-6.4	564
		Difference	0.82	0.1	-0.1	15

genetic variation and the environmental difference were well controlled in this twins report, patient compliance and the time lag between visits may still affect the results. These were however, kept to a minimum by stringent instructions and monitoring. During the study period, Twin A achieved full correction with ortho-k lenses worn at night and did not have to wear spectacles in the daytime. Twin B required full time spectacle correction to fulfill the requirement of daily activities. Because of the necessity to see clearly in the daytime, the compliance of the twins was reported to be good. The unaided VA of the left eye of Twin A was reduced at the 24-month visit compared to that taken at the 18-month visit. This was likely to be due to the residual refractive error which was -1.08 D SER. A delay in updating the correction of the refractive errors can occur in any treatment as subjects may not report or be aware of blurred vision (especially if it is only in one eye) until they returned for examination and the subject only returned every three months. Indeed, the axial length of Twin A showed relatively higher increase between 18 and 24 months of lens wear, compared to the first and second six months of lens wear.

In terms of both refractive errors and AL elongation after the completion of the study, a faster myopic progression was observed in Twin B who wore SVLs for visual correction. There was 11% (OD) and 48% (OS) increase in SER in Twin A, whereas there are 87% and 67% increase in SER in Twin B. The ortho-k treated eyes showed a slower increase in SER. A faster AL elongation was also observed in both eyes of Twin B than in Twin A.

Since the manifest refractive errors of Twin A, who wore ortho-k lenses, were not revealed at the 24-month visit, measurements of the refractive status of the eyes were not possible and the progression of myopia can only be based on the increases in axial elongation of the eyeballs. Currently, infra red interferometer like IOL MasterTM is considered the gold standard for AL measurements and the repeatability of AL measurements with the IOL MasterTM has been found to be very good in both children wearing ortho-k and spectacles [8].

In order to reveal the refractive errors of Twin A, the stabilization of the refractive errors and corneal topography was monitored every week after lens wear had ceased until the corneal power and refractive errors between the two last consecutive visits did not differ by more than 0.10 D and 0.25 D, respectively. Previous studies have found that the refractive errors and corneal curvature can return to the baseline within two weeks. [9,10] However, they only studied the refractive and corneal recovery of short-term ortho-k wearers. In this case report, corneal powers and refractive errors were considered to have stabilized after one month of cessation of lens wear. Decrease in the anterior corneal power and a thinning of CCT, compared with the baseline, were observed in both eyes of Twin A at the 25-month visit. A discrepancy was also found when the effect of myopic control was evaluated in terms of AL elongation and refractive errors. A previous study has shown that ortho-k not only affected anterior corneal power, but may also affect other ocular components [11]. Thus a change in manifest refractive power may not necessarily be reflected by changes in axial length. This may explain the deviation of the predicted refractive power from AL and the actual refractive power of the ortho-k treated eyes after the cessation of treatment. Since there would be changes in the anterior corneal power and CCT, it would be better to evaluate the AL elongation, instead of refractive errors, to monitor the progression of myopia in ortho-k treated eyes. However, AL measurement is not commonly available in private optometric practice, the efficacy of ortho-k evaluated by the manifest refraction after lens cessation may underestimate the rate of myopic progression. This case report indicates that AL measurement is particularly important in evaluating myopic progression in ortho-k wearers as the manifest refractive errors are not a good indicator to monitor myopic increase. In view of this, practitioners who did not measure the AL should remain alert of the risk of retinal degeneration in ortho-k treated eyes even though the manifest refractive errors appeared to be low.

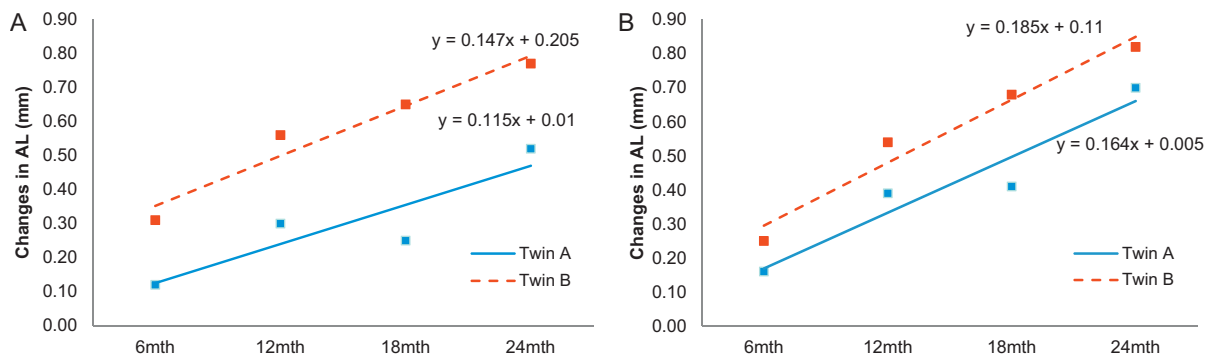


Fig. 1. Changes in axial length (AL) in the right eye (a) and left eye (b) of the twins during two years of monitoring (Twin A – orthokeratology; Twin B – single vision spectacles).

This identical twins case report presents the potential effect of ortho-k on myopic control when genetic variation and environmental factors are minimized. This is in agreement with previous studies of ortho-k on myopic control [1–3,6]. The different rate of myopic progression between the two eyes in Twin A may be due to the higher residual myopia in one eye than the other. Practitioners should note the importance of AL increase, instead of manifest refractive errors, in myopia development.

Acknowledgements

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ORIGINAL ARTICLE

High Myopia—Partial Reduction Ortho-k: A 2-Year Randomized Study

Jessie Charm* and Pauline Cho†

ABSTRACT

Purpose. To investigate if the combination of partial reduction (PR) orthokeratology (ortho-k) and spectacles for residual refractive errors in the daytime was effective to slow myopic progression in high myopic children.

Methods. High myopic children (aged 8 to 11 years) with spherical equivalent refraction at least -5.75 diopters (D) and myopia -5.00 D or more myopic were recruited and randomly assigned into PR ortho-k and control groups. Subjects in the PR ortho-k group were fitted with custom made four-zone ortho-k lenses with target reduction of 4.00 D for both eyes, and the residual refractive errors were corrected with single-vision spectacles for clear vision in the daytime. Control subjects were fully corrected with single-vision spectacles. Axial length of each eye of all subjects was measured with the IOLMaster at 6-month intervals by a masked examiner. This study was registered at www.clinicaltrials.gov with the identifier NCT00977236.

Results. Fifty-two subjects were recruited and randomized to the PR ortho-k and control groups. Twelve PR ortho-k and 16 control subjects completed the study. Compared with the residual refractive errors at the 1-month visit (after stabilization of ortho-k treatment), the median increase in noncycloplegic residual myopia at the 24-month visit was 0.13 D. In the control group, the median increase in myopia was 1.00 D at the end of the study. The mean \pm SD increases in axial length were 0.19 ± 0.21 mm in the PR ortho-k group and 0.51 ± 0.32 mm in the control group (95% confidence interval, -0.55 to -0.12 ; unpaired *t* test, $p = 0.005$).

Conclusions. This single-masked randomized study showed that PR ortho-k effectively slowed myopic progression in high myopes. Axial length elongation was 63% slower in PR ortho-k–treated children compared with children wearing spectacles. (*Optom Vis Sci* 2013;90:530–539)

Key Words: myopia control, orthokeratology, high myope, myopic progression, partial correction

Myopic progression in children is of great concern in Asian countries, such as Hong Kong, China, Japan, and Singapore, because of the high prevalence of myopia in these populations. Fan et al.¹ reported that the prevalence of severe myopia (spherical equivalent refraction of -6.00 diopters [D] or more myopic) was 1.19% in Hong Kong. The annual myopic shifts were -0.63 D and -0.71 D for low (-0.50 to -2.99 D)- and high myopic groups, respectively. High myopes have also been reported to show faster myopic progression.^{1–3} Degenerative changes of the vitreous, glaucoma, and myopic degeneration are complications associated with high myopia,^{4,5} and many researchers are still investigating ways to slow myopic progression.

Single-vision spectacles and contact lenses of conventional designs have been shown to be ineffective for myopic control,^{6,7} and treatments using progressive spectacle lenses/bifocals had not been successful.^{8,9} Pharmaceutical agents (atropine and pirenzepine) have been reported to reduce myopic progression,^{10,11} but side effects such as accommodation insufficiency and dilated pupils can affect daily activities.¹¹

Orthokeratology (ortho-k) was shown to have a potential to reduce myopic progression in a number of nonrandomized clinical studies.^{12–15} The LORIC study¹² and CRAYON study¹³ used A-scan biometry to measure axial length progression, whereas Santodomingo-Rubido et al.¹⁴ and Kakita et al.¹⁵ used the Zeiss IOLMaster (Carl Zeiss Meditec, Inc., Dublin, CA). These studies reported that axial length elongation in subjects wearing ortho-k lenses were 36 to 56% slower when compared with that of subjects wearing spectacles.^{12–15} A recent randomized single-mask study has however confirmed the efficacy of ortho-k for myopic control

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in children.¹⁶ This study reported a 43% slower increase in axial length in children wearing ortho-k lenses compared with those wearing single-vision glasses.

Most ortho-k lenses available commercially and used in published reports are for low to moderate myopes only. However, there is little information about the safety and success rate in correcting higher refractive errors. Clinically, attempts at high myopic reduction using commercially available ortho-k lenses could result in corneal staining, heavy lens binding, and lens decentration.¹⁷ In view of these potential problems and until lenses designed for high myopes are available, a more conservative approach for high myopes is to target for 4.00 D reduction and to correct the residual refractive errors with single-vision spectacles to allow good visual acuity in the daytime.

OBJECTIVE

The objective of this study was to investigate the efficacy, based on axial length elongation, of a combination of partial reduction (PR) overnight ortho-k and single-vision spectacles to correct the residual refractive errors in the daytime on myopic control in high myopic children.

METHODS

This was an intervention study using a stratified, randomized, parallel-group, and single-masked design to investigate axial elongation of the eyeball in myopic children wearing ortho-k lenses overnight and single-vision spectacles for residual refractive error in the daytime (PR ortho-k group) and single-vision spectacles (control group) for a period of 2 years. The subjects were stratified by age and sex to minimize systematic bias. Randomization was performed in blocks of two using a commercial spreadsheet random number generator (Excel, Microsoft, Redmond, WA). The randomization list was generated and inspected by an independent project member who was not involved in subject recruitment or data collection to ensure equal numbers of subjects assigned to each group. This project member revealed the random allocation sequence to the unmasked examiner after eligibility of subjects was confirmed (by the unmasked examiner). The unmasked examiner would then proceed to prescribe the assigned treatment to the subjects accordingly.

Subjects were recruited via advertisements posted in local newspapers and leaflets in the Optometry Clinic of the School of Optometry, The Hong Kong Polytechnic University. Eligible subjects and guardians were informed verbally and in writing about the nature, benefits, and risks of the study. Ethics approval for this study was obtained from the Departmental Research Committee of the School of Optometry at The Hong Kong Polytechnic University. All procedures were performed following the tenets of the Declaration of Helsinki, as revised in 2002, and written informed consent was obtained from the subjects and parents (and/or guardians) before commencing the study.

Subjects who were lost to follow-up, noncompliant with test procedures/schedule, contraindicated to continue ortho-k treatment (PR ortho-k group) were excluded from the study. The first and last subjects were recruited in June 2008 and January 2010, respectively, and the last data collection visit was in January 2012.

This study was registered in clinical trial at www.clinicaltrial.gov with the identifier NCT00977236.

Inclusion Criteria

Table 1 lists the inclusion criteria for this study. Only children aged 8 to 11 years with spherical equivalent refraction of at least 5.75 D and myopia of -5.00 D or more myopic (cycloplegic subjective refraction) were recruited.

Sample Size

To estimate the sample size of this study, we aimed for 80% power based on the SDs reported in the LORIC study¹² and to detect a 0.3-mm (~ 0.75 D) difference in axial length between the two groups. With the significant level of 0.05 (two-tailed), the sample size calculated was 14 in each group. To allow for 30% dropouts, at least 40 subjects should be recruited in total.

Lenses and Solutions Used

For the PR ortho-k subjects, the lens parameters for each eye were determined using the manufacturer's computer software (EyeLite, Procornea Ltd, The Netherlands).

The initial target of all lenses was 4.00D to attempt 4.00D myopic reduction. Once stabilization was confirmed (i.e. when changes in myopia and corneal curvatures at two consecutive visits (one week apart) were not more than 0.50D), if the myopic reduction achieved was less than 3.25D, a lens with a higher target was ordered and fitted until there was no further improvement. The subject would then continue to wear the previous lens with the lower target (i.e. the lowest target lens which gave the maximum myopic reduction).

The lens specifications and solutions used are shown in Table 2. A second pair of lenses with the same parameters as the stabilized

TABLE 1.
Inclusion criteria

Age	8–11 yr of age on the date of recruitment
Refractive errors	Cycloplegic manifest ocular refraction in either eye Spherical equivalent refraction ≤ -5.75 D AND Myopia -5.00 D or more myopic
Visual acuity	Monocular Snellen 6/7.5 or better
Ocular health	No binocular vision problems No ocular conditions that might affect vision or vision development No contraindications for overnight orthokeratology lens wear
General health	No systemic conditions that might affect vision or development of the refractive errors
Others	No previous experience in myopic treatment (e.g., refractive surgery) Willing to wear orthokeratology lenses in accordance with instructions if assigned to partial reduction orthokeratology group Available for monthly follow ups at the PolyU Optometry Clinic for 24 mo after treatment commences Willing to comply with the prescribed aftercare/data collection visits

TABLE 2.
Specifications of orthokeratology lens and solutions

Orthokeratology lens (Procornea Ltd., Netherlands)	
Material	Boston XO
Design	4-zone (BOZR, RC, AC, and PC) Spherical or toric (toric reverse curve and/or alignment curve), depending on corneal parameters
Jessen factor	0.75 D
Oxygen permeability	100 Barrer
Back optic zone radius	7.20–9.50 mm (0.05-mm step)
Optic zone diameter	6.0 mm
Total diameter	10.5 mm
Lens central thickness	0.22 mm
Wearing modality	Overnight orthokeratology
Replacement period	1 yr
Remarks	Manufacturer's recommendation for this lens design is for target up to 4.50 D myopia
Solution used (Menicon Co., Ltd., Japan)	
Soaking and disinfecting	MeniCare Plus
Daily cleaning	Menicon O ₂ Care
Weekly enzymatic cleaning	Menicon Progent
Replacement period	1 month

lenses was ordered for each subject after the desired myopic reduction was achieved. This pair of lenses acted as a spare pair in case of damage or loss or as an annual replacement pair where appropriate. All subjects had to learn how to insert and remove their lenses using their fingers without the aid of a suction holder (lens remover) and without any assistance from their parents. All subjects were prescribed a pair of single-vision spectacles for the correction of residual refractive errors for daytime wear after stability of the ortho-k treatment.

Spectacles

For the control subjects, single-vision spectacles were prescribed with maximum plus, which gave maximum visual acuity, and subjects were asked to wear the spectacles in the daytime during waking hours.

For PR ortho-k subjects, residual refractive errors were corrected with a pair of single-vision spectacles to be worn during daytime.

After the commencement of the study, the spectacle prescription would be updated at any subsequent visit for either group of subjects if there was an increase of more than 0.50 D in refractive error (sphere or astigmatism) at that visit compared with the baseline (control group) or the stabilized refractive errors (PR ortho-k group).

Examination Schedules and Procedures

All subjects were required to attend noncycloplegic and cycloplegic examinations at the baseline and every 6-month visits for 2 years. Partial reduction ortho-k subjects had to attend three extra noncycloplegic visits (first morning after commencing lens wear [1-overnight], 1 week [1-week], and 1 month [1-month]) after lens delivery to assess/confirm lens performance (Fig. 1). Extra aftercare consultations were provided as required during the study period.

All measurements, excluding axial length measurements, were performed by the same examiner throughout the study. Axial length measurements were made by a masked examiner. All measurements were made on both eyes, but only data from the right eye were analyzed and presented in this report.

Masking

This study was a single-masked design to eliminate any examiner bias on myopic progression. The masked examiner (not involved in patient care) only measured and recorded the axial length.

Ophthalmic Examination

Cycloplegic assessments included objective and subjective refraction, axial length measurement, and fundus examination. These assessments were made at the baseline and at every 6-month visit following the noncycloplegic examination at each visit (Table 3). One drop of 0.5% proparacaine (Alcaine; Alcon-Couvreur, Puurs, Belgium) was first instilled, followed 1 minute later by one drop of 1.0% tropicamide (Mydracil; Alcon-Couvreur), and

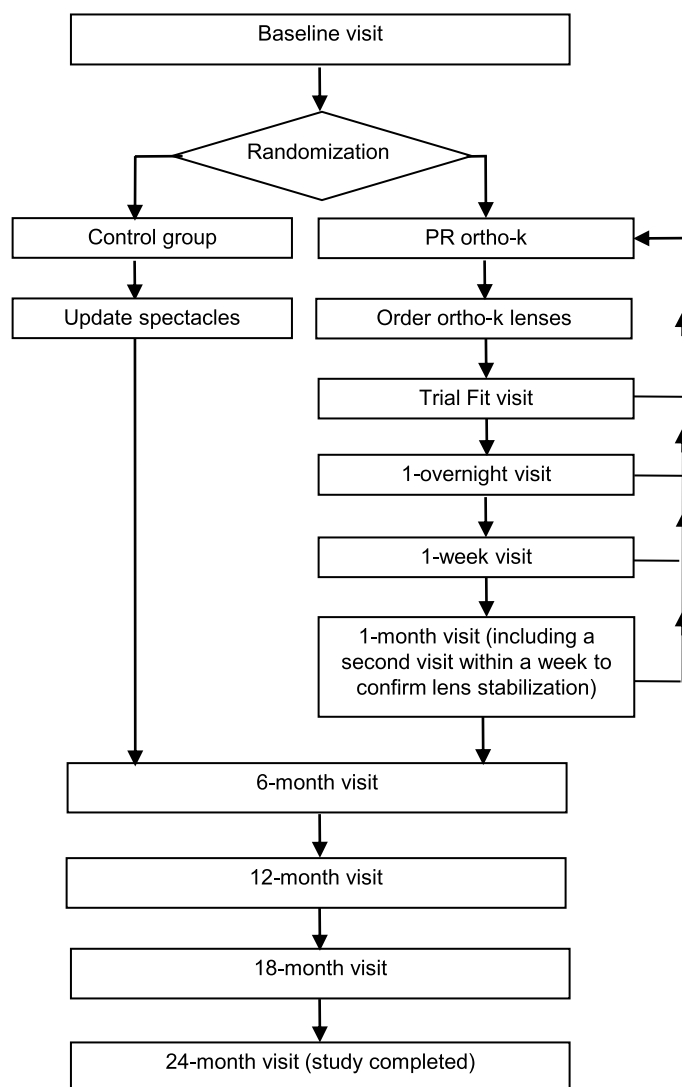


FIGURE 1.
Schedule of visits.

5 minutes later by one drop of 1.0% cyclopentolate (Cyclogy; Alcon-Couvreur). After 30 minutes, when no pupillary response was confirmed and the amplitude of accommodation was measured to be less than 2.00 D, cycloplegic measurements were made.

Objective refraction was performed with the Shin-Nippon Open field 5500K autorefractor (Ajinomoto Trading Inc., Japan). The autorefractor provided mean values of sphere and cylinder powers. Three measurements with any intermeasurement difference (of sphere and cylinder powers) of not more than 0.25 D were taken. The average value was calculated and used for analysis. Subjective refraction was measured in an examination room with lighting of 400 Lux, and the maximum plus maximum acuity was taken as the end point of refraction. Early Treatment Diabetic Retinopathy Study (ETDRS) chart series 2000 (Precision Vision, LaSalle, IL) were used to measure high (>90%) and low (10%) contrast visual acuity (VA). Three high-contrast (one for right eye, one for left eye, and one for binocular acuity) and one low-contrast charts were used. Both habitual VA and best-corrected VA (BCVA) were measured, with the high-contrast chart first, followed by the low-contrast chart. Habitual VA for the right eye was always assessed first, then the left eye, and finally both (binocular) eyes.

The anterior segment of the eyes of all subjects and lens-fitting evaluation of PR ortho-k subjects were performed using Topcon SL7 and Topcon IMAGEnet (Topcon Corporation, Japan). All corneal signs were graded using Efron grading scale where appropriate with photodocumentation.

Measurements of axial length were performed with Zeiss IOLMaster (Carl Zeiss Meditec, Inc.) by masked examiners after cycloplegia at baseline and at every 6-month visit. At each of these visits, the masked examiner was instructed to take the first five axial length readings with between-reading difference within 0.02 mm (as recommended by the manufacturer). The average data were used for analysis.

Corneal topography was performed with the Medmont E300 (Medmont International Pty Ltd, Australia) at baseline and at every 6-month visit for all subjects. Four corneal profiles, each with a score of 98 or above (as recommended by the manufacturer), were saved for each eye at each visit.

TABLE 3.
Data collection schedule

Data taking visits		Baseline	1-mo visit	Every 6 mo
Refraction (subjective and objective)	Precycloplegic	X	X	X
	Cycloplegic	X		X
BCVA (precycloplegic)	High contrast	X	X	X
	Low contrast	X	X	X
Photobiomicroscopy	Ocular health	X	X	X
	Lens assessment	-	X	X
Topography	Prefitting	X	-	-
	Postfitting	-	X	X
Corneal thickness	Precycloplegic	X	-	X
Pupillary response		X	-	X
Axial length	Postcycloplegic	X	-	X

Treatment of Data

Because data on age, pretreatment and posttreatment subjective spherical refractive error (myopia), and habitual VA were not normally distributed, nonparametric tests were used to analyze the data. Data for corneal thickness, axial length, flat K, and steep K were normally distributed, so parametric tests were used for analysis. The significance level was set at 0.05 with Bonferroni corrections, where multiple tests were performed. Medians and ranges were reported for data showing non-Gaussian distributions and mean \pm SD for data that were normally distributed.

RESULTS

A total of 79 subjects were screened, and 52 eligible subjects were randomly assigned to the PR ortho-k ($n = 26$) and control ($n = 26$) groups at the baseline visit. After the first month of lens wear, only 19 subjects in each group continued in the study. At the end of the study, 16 control and 12 PR ortho-k subjects completed the study (Fig. 2).

No significant differences (Mann-Whitney U tests, $p > 0.05$) were found in the baseline demographic and ocular characteristics between subjects who completed the study and subjects who did not (Table 4).

Power of the Study

The power of this study, based on the sample size and axial length results, was 85% (95% confidence interval [CI], -0.55 to -0.12 ; unpaired t test, $p = 0.005$) (G*Power 3.0).

Baseline Data (of Completed Cases)

Table 4 also shows a summary of the baseline data of the two groups of subjects who completed the study. The median (range) age of the subjects was 10 (9 to 11) years and 10 (8 to 11) years in PR ortho-k and control groups, respectively. No significant differences in axial length, flat and steep K, and central corneal thickness were found between the two groups of subjects (unpaired t tests, $0.49 < p < 0.86$). Also, no significant between-group differences in age, precycloplegic subjective myopia and postcycloplegic subjective myopia and astigmatism, high- and low-contrast BCVA were found (Mann-Whitney U tests, $0.10 < p < 0.73$).

Ocular health presentation was comparable between the two groups (Table 5) (Fisher exact test, $0.175 < p < 1.000$). Corneal staining was found in four subjects (two in each group), but the severity was not more than grade 1.

Changes in Refractive Errors

Changes in myopia and astigmatism during the 2 years of monitoring are shown in Table 6 and Fig. 3. In the control group, five subjects were required to change their spectacles once during the study period (two at the 6-month visit, two at the 12-month visit, and one at the 18-month visit). In the PR ortho-k group, no change in lens target or daytime spectacles was necessary during the study period.

The myopia in the control group increased significantly over time (Friedman tests, $p < 0.001$). At the end of the study period, the median increase in myopia in the control group was -1.00 D (-2.50 to 0.50 D).

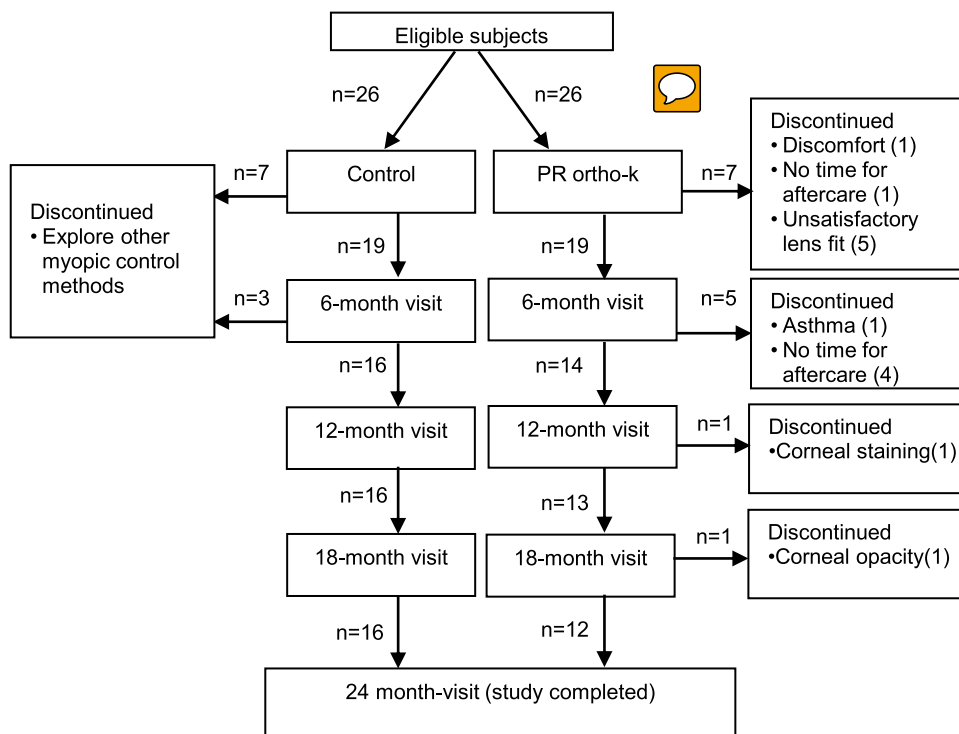


FIGURE 2. Progression of subjects during the study period.

Compared with the residual refractive errors at the noncycloplegic 1-month visit (i.e., after stabilization of treatment), the median change (i.e., increase) in residual noncycloplegic myopia at the 24-month visit was -0.13 D (-0.75 to 1.00 D).

No significant increase in astigmatism in either group of subjects was observed during the 2-year study period (Mann-Whitney U tests with Bonferroni correction, $0.041 < p < 0.290$).

TABLE 4. Baseline data of subjects who completed the study and those who did not

	All		Completed cases		Dropouts	
	PR ortho-k (n = 26)	Control (n = 26)	PR ortho-k (n = 12)	Control (n = 16)	PR ortho-k (n = 14)	Control (n = 10)
Age, yr	10 (8–11)	10 (8–11)	10 (9–11)	10 (8–11)	10 (8–11)	10 (8–11)
High-contrast BCVA (logMAR)	0.02 (-0.08 to 0.08)	0.04 (-0.10 to 0.16)	-0.04 (-0.08 to 0.06)	-0.05 (-0.20 to 0.14)	0.04 (-0.04 to 0.12)	0.04 (-0.08 to 0.18)
Low (10%)-contrast BCVA (logMAR)	0.25 (0.12–0.38)	0.22 (0.10–0.48)	0.25 (0.12–0.38)	0.17 (0.10–0.48)	0.36 (0.16–0.36)	0.22 (0.12–0.38)
Precycloplegic subjective Myopia, D	6.41 (5.00–8.00)	6.22 (5.00–8.00)	6.50 (6.00–8.30)	6.13 (5.00–8.30)	6.17 (5.25–7.50)	6.08 (5.25–9.00)
Postcycloplegic subjective Myopia, D	6.34 (5.00–8.00)	6.08 (5.00–8.00)	6.38 (5.75–8.25)	6.00 (5.50–8.00)	6.06 (5.00–7.50)	6.00 (5.25–9.00)
Postcycloplegic subjective Astigmatism, D	-0.68 (-1.75 to 0.00)	-1.09 (-2.00 to 0.00)	-0.63 (-1.50 to 0.00)	-1.00 (-1.50 to -1.00)	-0.69 (-2.00 to 0.00)	-1.10 (-1.75 to -0.50)
Axial length, mm	26.02 ± 0.57	25.93 ± 0.54	26.05 ± 0.80	25.97 ± 0.53	26.08 ± 0.64	25.73 ± 0.94
Flat corneal curvature, mm	7.78 ± 0.17	7.87 ± 0.16	7.78 ± 0.30	7.84 ± 0.13	7.82 ± 0.16	7.80 ± 0.31
Steep corneal curvature, mm	7.55 ± 0.18	7.60 ± 0.18	7.56 ± 0.29	7.58 ± 0.15	7.55 ± 0.16	7.51 ± 0.33
Central corneal thickness, μm	573 ± 46	573 ± 37	573 ± 56	581 ± 34	569 ± 35	560 ± 39

Values are presented as median (range) or mean ± SD.

TABLE 5.

Ocular signs (incidence [%]) observed in the two groups of subjects

		Baseline		6-mo		12-mo		18-mo		24-mo	
		PR ortho-k	Control	PR ortho-k	Control	PR ortho-k	Control	PR ortho-k	Control	PR ortho-k	Control
Corneal staining	Central	0	0	16.7	0	16.7	8.3	0	16.7	8.3	0
Grade 1	Inferior	16.7	12.5	8.3	18.8	25	16.7	25	25	16.7	25
Efron Grading	Nasal	0	6.3	8.3	0	8.3	16.7	6.3	8.3	16.7	6.3
Scale	Superior	0	0	8.3	0	0	0	0	0	0	0
	Temporal	0	0	8.3	0	0	0	0	0	0	0
Pigmented arc	Inferior	0	0	92	0	100	0	100	0	100	0

No significant differences between the two groups of subjects at any visit (Fisher exact test, $0.175 < p < 1.000$), excluding pigmented arc.

High- and low-contrast BCVAs were not significantly different over time within-group (Friedman tests, $0.099 < p < 0.585$) or between groups at each visit (Mann-Whitney *U* tests, $0.093 < p < 0.586$).

Ocular Health

Corneal staining was observed in some subjects in both groups at each visit, but the incidence was generally higher in the PR ortho-k subjects (Table 5). However, all stainings observed were not significant (all were grade 1) between the two groups of subjects during the 2-year study (Fisher exact tests, $0.175 < p < 1.000$) (Table 5). No other adverse events were reported in either group of subjects who completed the study.

The incidence of pigmented arc among the PR ortho-k subjects at the 6-month visit was 92%. After 1 year of lens wear, the pigmented arc was found in all PR ortho-k subjects. The intensity of the pigmented arc increased with lens wear during the monitoring period.

Significant differences in central corneal thickness were found between the two groups at the 6-month, 18-month, and 24-month visits (Mann-Whitney *U* tests, $p = 0.011$, 0.026 , and 0.026 , respectively) (Fig. 4). No significant within-group differences were found at different visits during the study period (Friedman tests, $p = 0.359$ [PR ortho-k]; $p = 0.474$ [control]).

Len Binding and Lens Replacements

None of the PR ortho-k subjects reported lens binding at and after the 6-month visit. All subjects had a lens replacement at the 12-month visit (annual replacement) except for one subject who reported lens damage at the 6-month visit. Because a pair of spare lenses was ordered for each subject after the stabilization of treatment, this subject had an extra lens replacement (no change in lens parameters) during the study period without ceasing lens wear.

Axial Length Changes

Both groups of subjects showed increases in axial length during the 2-year monitoring period but at different rates (Fig. 5). Increases in axial length in the PR ortho-k group were significantly slower (by 63%) compared with increases in the control subjects (95% CI, -0.55 to -0.12 ; unpaired *t* test, $p = 0.005$). At the end of the 2-year monitoring period, the mean \pm SD increases in axial length were 0.19 ± 0.21 mm in the PR ortho-k group and 0.51 ± 0.32 mm in the control group.

DISCUSSION

Compared with previous studies on low to moderate myopes^{12–16} (Fig. 6), the current study showed the highest myopic retardation rate (63%). Although the number of subjects in each of group was small, this study has a power of 85% at 0.05% level of significance. To our knowledge, this study is the first randomized and single-blind study on the efficacy of PR ortho-k for myopic control in high myopic children. The high level of myopic control observed in this study may be caused by a relatively high magnitude of myopic reduction in PR ortho-k subjects, that is, the median myopic reduction in this group of subjects was about 4.00 D throughout the study period (Fig. 3).

It has been proposed that relative peripheral hyperopic defocus in myopes may trigger axial elongation.^{18,19} The hypothesis is that, because peripheral retina shows greater relative hyperopia with respect to axial refraction in myopes (compared with emmetropes and hyperopes), this peripheral hyperopic defocus may promote axial myopia. In ortho-k, the central cornea is flattened, reducing the myopia, whereas the midperipheral cornea is steepened, leading to a ring of increased peripheral myopia in myopic eyes. The peripheral ring of myopia created on the corneal surface will lead to a reduction of peripheral hyperopic defocus, and this may reduce the visual feedback for eye elongation, leading to slower myopic progression.^{18–23}

In the current study, all PR ortho-k subjects wore ortho-k lenses of target 4.00 D. Midperipheral corneal changes in these subjects were therefore more significant compared with low to moderate myopic subjects in previous studies^{12–16} and the greater corneal

TABLE 6.

Changes (median [range]) in postcycloplegic subjective myopia and astigmatism (D) in the two groups of subjects at the end of the study

Change in	PR ortho-k (n = 12)	Control (n = 16)	<i>p</i> *
Myopia	4.50 (2.75–6.25)	−1.00 (−2.50 to 0.50)	<0.001
Astigmatism	−0.50 (−1.50 to 0.50)	0.00 (−0.75 to 0.75)	0.153

*Probability values for differences between groups using Mann-Whitney *U* tests (positive value indicates reduction in power; negative value indicates increase in power).

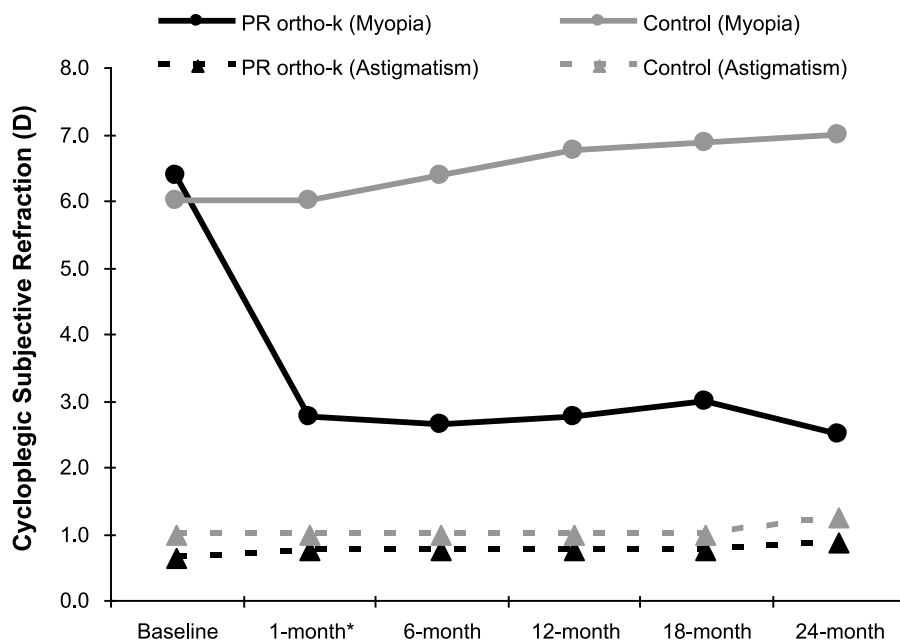


FIGURE 3. Changes (median) in the refractive components of the subjects during the study period. *Noncycloplegic.

change (hence, greater increase in peripheral myopia) may have resulted in a better control of myopic progression. Further investigation in this area is warranted to confirm the role of peripheral refraction in myopic progression and in ortho-k.

The increase in axial length in the spectacle-wearing control subjects during the 2-year monitoring period was relatively small compared with that in control subjects in previous studies on myopic control in Chinese children.^{12,15,16} This may be because the subjects in the current study were relatively older (mean age was 10 years).

In the LORIC study,¹² a weak relationship was reported between baseline spherical equivalent refraction and increases in vitreous chamber depth. The more myopic ortho-k subjects showed greater

slowing in terms of changes in vitreous chamber depth ($R^2 = 0.30$), whereas the more myopic spectacle-wearing control subjects showed faster progression in terms of changes in vitreous chamber depth ($R^2 = 0.34$) after 2 years of lens wear. Kakita et al.¹⁵ observed an association between changes in the axial length and the initial myopia only in higher myopic ortho-k subjects. Cho and Cheung,¹⁶ however, reported no association between changes in the axial length and the initial myopia in the ROMIO study. In the current study, no relationships were observed between the baseline spherical equivalent refraction and increases in axial length in the control group ($R^2 = 0.08$) and the PR ortho-k ($R^2 = 0.06$). The amount of change in axial length cannot be predicted based on the individual's baseline spherical equivalent refraction.

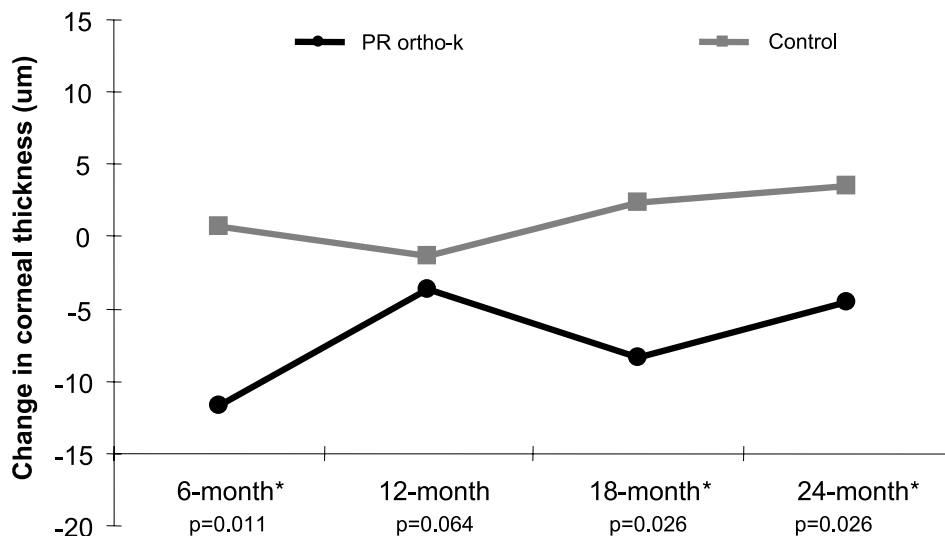


FIGURE 4. Changes (median) in central corneal thickness between two groups during the study period. *Significant differences were found between the two groups of subjects.

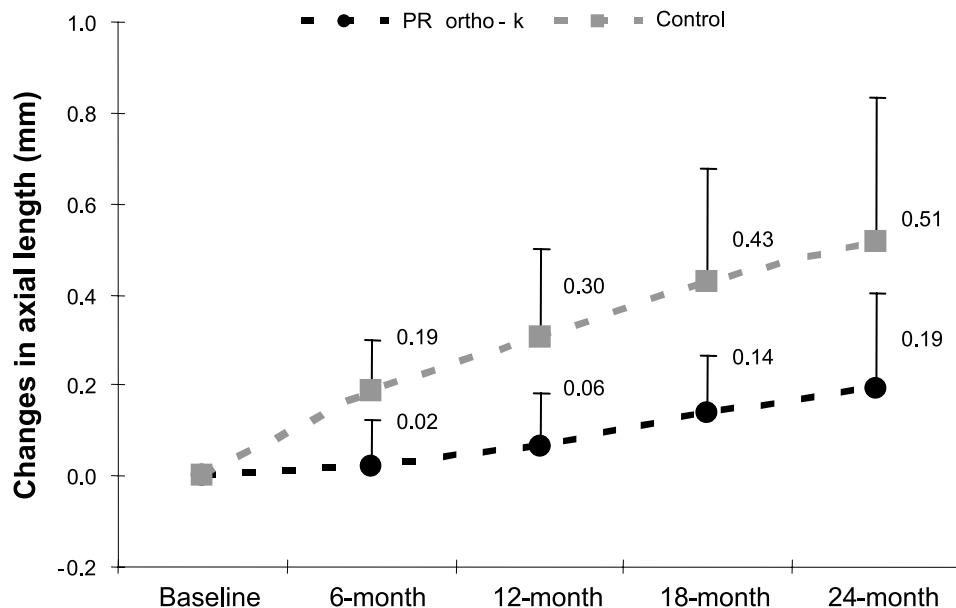


FIGURE 5. Changes in axial length (mean ± SD) in the subjects.

After 1 month of lens wear, only 12 and 16 subjects in the PR ortho-k and control groups, respectively, completed the study. The dropout rates were 37% and 16% in the PR ortho-k and spectacle-wearing groups, respectively. There were no significant differences in the baseline parameters of those who completed the study and those who dropped out. The dropout rate in the study group was higher than those reported in other studies.^{12,13,15,16} Cho et al.¹² reported complication (50%) such as corneal staining as the main reason for dropouts, whereas Walline et al.¹³ reported that loss to follow-up contributed to 30% of the dropouts in their ortho-k group. Kakita et al.¹⁵ reported only three dropouts in their study on 45 ortho-k subjects, and the reason for the dropout was caused by insufficient improvement in the uncorrected visual acuity and loss to follow-up in two subjects and one subject, respectively. Cho and Cheung¹⁶ reported 27% dropout in their

ortho-k group, and the main reason was lost to follow-up (10%). In the current study, the dropout in the PR ortho-k group was mainly caused by the inability of the subjects (parents) to comply with the intensive follow-up/data collection schedule. Because a higher frequency of corneal staining, although not clinically significant, was found in subjects undergoing ortho-k treatment, a number of unscheduled visits had to be arranged to ensure safe ortho-k lens wear. Four of these subjects withdrew as they were not able to attend the follow-up visits. The dropout subjects were offered extra visits to follow up the myopic progression after the completion of the study. However, all of them sought ortho-k from private practitioners and refused to attend the extra visits. A traditional intent-to-treat analysis was therefore not conducted.

During the study period, two subjects in the PR ortho-k group presented with undesired ocular signs, and they were withdrawn

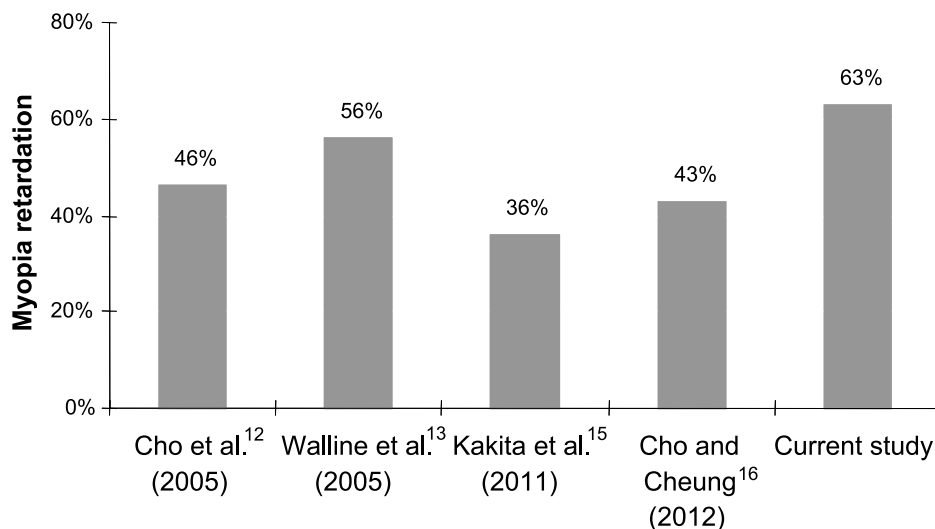


FIGURE 6. Myopia retardation in orthokeratology subjects compared with those in the control groups in published myopic control studies and the current study.

from the study. One subject had grade 2 (coverage) peripheral corneal staining at the 12-month visit. The staining was epithelial, and the cornea recovered the next day. However, the parents were worried and decided to terminate participation in the study. Another subject was found to have corneal opacities in both eyes at the 18-month visit. He was referred for immediate medical consultation, but his parents were too busy to take him until about 2 months later. His ophthalmologist confirmed that the opacities were probably caused by allergy, which was not ortho-k related. During the 2 months before he consulted the ophthalmologist, his ocular health was monitored, and no changes (including the corneal opacities) were noted. Corneal curvatures returned to baseline values within 2 months, and there were no associated complications. Although the ophthalmologist advised that the subject may resume ortho-k treatment, the subject did not return and missed both 18- and 24-month data collection). Hence, he was excluded from the study.

Some studies have reported a tendency for increased corneal staining with increasing ortho-k lens wear in low to moderate myopes,^{24–27} but the severity of the staining was mild (grade 1). Our results were in agreement with these reports^{24–27} but only before lens stabilization. In contrast to these reports,^{24–27} we found no significant differences in the incidences of staining between our ortho-k and control subjects in subsequent visits during the study period.

Pigmented arc was found in 32% of the PR ortho-k subjects at the 1-month visit and the incidences reached 92% and 100% after 6- and 12-month of lens wear respectively in the current study. Cho et al.²⁸ first reported the observation of pigmented arc in ortho-k Chinese children. They reported the presence of pigmented arcs in their subjects with high refractive errors after 1 week of lens wear. In a later study, Cho et al.²⁹ reported that the incidence of corneal pigmented arc was 27% after 3 months of lens wear in low myopic subjects. They reported that the incidence and the intensity of the arc were related to the baseline myopia, spherical equivalent refraction, the target myopia reduction, the amount of myopic reduction, and changes in central corneal curvatures. It was suggested that the pigmented arc was formed in the midperipheral cornea because the area of the reverse curve of the lens coincides with the area of abrupt corneal curvature change, where deep reservoirs of tears were formed under the lens.²⁹ In the current study, because all subjects were fitted with target 4.00 D lenses compared with lower targets for low myopes, a deeper tear reservoir was formed at the reverse curve region. This led to substantial steepening of the midperipheral cornea, giving a more significant change in topography within a relatively shorter period. This may explain the high incidence of pigmented arc found in the current study.

We found no significant differences in either high- or low-contrast BCVA between the two groups of subjects at any visit in this study. Previous ortho-k studies^{30,31} have reported that unaided VA was significantly worse at the low-contrast level. The current study did not aim at complete reduction of the refractive errors of subjects randomized to wear ortho-k lenses, and all PR ortho-k subjects had to wear spectacles to correct their residual refractive errors in the daytime. Our results showed that both high- and low-contrast BCVAs were stable and comparable between visits after lens stabilization in these subjects, and VAs were comparable to those in the control group.

The combination of PR ortho-k and spectacles offered stable vision for the high myopic subjects throughout the 2 years of monitoring. Although we did not conduct a formal survey, all children and parents preferred to continue with this wearing mode at the end of the study. The parents appreciated the results of the study because they were not required to change the prescription of the ortho-k lenses and spectacles for 2 years, except for one subject who had to update his spectacle prescription at the 18-month visit (myopia increased by 0.75 D). All the ortho-k subjects in our study were required to handle the ortho-k lenses themselves, including insertion, removal, and cleaning, and all were capable and diligent in these respects, although there was one report of lens damage. This subject was not required to cease lens wear as a spare pair of lenses was ordered for each subject after stabilization for such incidents.

Limitations

A limitation of the current study was the relatively small sample size, leading to an apparently high dropout rate in the PR ortho-k group. Although run-in period and other incentives may be considered in future studies to minimize dropouts, they may not work as most of the subjects dropped out either because of adverse events and inability of the subjects (parents) to comply with the intensive follow-up/data collection schedule (PR ortho-k group) or parents seeking myopic control treatment for their children (control group). Notwithstanding this limitation, the result of this study supports the confirmation by Cho and Cheung¹⁶ that ortho-k can control myopic progression. If a new ortho-k lens design for high myopes is available, full correction using ortho-k could be recommended because subjects will find it even more convenient if they do not have to wear spectacles in the day time.

CONCLUSIONS

The results of this randomized, single-masked study suggested that the combination of PR ortho-k and spectacles is a safe and feasible option for myopic reduction and control for high myopic children. Elongation of axial length compared with subjects wearing spectacles was slower by 63% during a 2-year monitoring period.

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High myopia-partial reduction orthokeratology (HM-PRO): Study design



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ABSTRACT

Purpose: To report the study design and preliminary results of a pilot study, High Myopia-Partial Reduction Orthokeratology study.

Methods: Children with myopia of 6.00D or above and who satisfied the recruitment criteria were randomly assigned to partial reduction orthokeratology (PR ortho-k) and spectacle-wearing control groups. The myopia of the PR ortho-k children were partially reduced using custom made 4-zone ortho-k lenses of target 4.00D. Residual refractive errors were corrected with single vision spectacles. Control subjects were fully corrected with single vision spectacles. PR ortho-k subjects were also required to return for assessment after the first overnight lens wear, and one week and one month after lens wear.

Results: Fifty-two eligible subjects were randomly assigned to PR ortho-k group ($n=26$) and control group ($n=26$). The median age of each group was 10.00 years. The median (range) subjective myopia of the right eye at baseline was 6.41D (5.00–8.00D) and 6.22D (6.00–8.00D) for PR ortho-k and spectacle groups, respectively ($p>0.05$). Nineteen (79%) PR ortho-k subjects achieved successful lens fit at the one month visit and the median myopic reduction was 3.75D in the right eye. The incidence of (mild) corneal staining in PR ortho-k subjects reduced from 30% at the first overnight lens wear to 16% at the 1-month visit. Corneal pigmented arc was observed in 32% of PR ortho-k subjects at the 1-month visit.

Conclusions: PR ortho-k was successfully applied to high myopic children with no significant changes in ocular health/best corrected visual acuity after one month of lens wear.

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1. Introduction

Myopic progression in children is of great concern in Asian countries because of the high prevalence of myopia [1–6]. For decades, researchers have investigated ways to control myopic progression, but have not come up with a clinically acceptable and effective method. However, in recent years, orthokeratology (ortho-k) has been shown to have a potential for myopic control, and the interest in this treatment is on the increase, particularly in Asian countries [7–9].

Ortho-k is effective for correcting myopia under 4.00D [10,11]. Many studies have reported that at least 80% myopic reduction can be achieved for low to moderate amount of myopia [10–15]. Ortho-k has been shown to have a potential to retard myopic progression in non-randomized clinical studies [7,9]. Cho et al. showed that the increase in axial length (AL) in ortho-k subjects was about 46% slower compared to a spectacle-wearing control group [7]. Walline

et al. reported 56% slower increase in AL in children wearing ortho-k lenses compared to those wearing soft contact lenses [9].

Ortho-k alters the corneal profile to achieve myopic reduction. Hence the refractive errors measured during the treatment do not reflect the actual amount of myopia. Since change in AL is closely related to myopic progression, comparison of AL before and after myopic control treatment is the gold standard for determining myopic progression, especially in orthokeratology studies [16–21]. Ortho-k is becoming increasingly popular for myopic reduction and control in children with low to moderate myopia and astigmatism. For children with higher myopia, it may not be possible to achieve full reduction and clinicians and researchers are cautious about the safety associated with the use of high targets. A pilot study (unpublished data) at the School of Optometry, The Hong Kong Polytechnic University, evaluated the effectiveness of ortho-k on high myopes. With increasing target (above 4.00D), significant corneal staining and lens decentration tend to occur. This was in agreement with other published reports that severity of corneal staining would increase when attempting to fully correct high myopes [22,23]. In view of these problems, partially reducing high myopes using target 4.00D with single vision spectacles to correct the residual refractive errors to obtain good visual acuity in the daytime may be a more conservative approach for high myopes [14].

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Table 1
Inclusion criteria.

Age	8–12 years of age on the date of recruitment
Refractive errors	(Cycloplegic manifest ocular refraction either eye) SER>5.50DS
Spherical refractive error (-ve, D)	
Astigmatism	≤1.50DC for axis 180±30
Visual acuity	Monocular Snellen 6/7.5 or better
Ocular health	No binocular vision problems No abnormal ocular health No ocular conditions which might affect vision or vision development (for example, cataract and ptosis)
General health	No contraindications for overnight orthokeratology lens wear No systemic conditions which might affect vision or development of the refractive errors
Others	No previous experience in myopic treatment (e.g. refractive surgery, progressive add lens wear, orthokeratology wear) Willing to wear orthokeratology lenses in accordance with instructions if assigned to PR orthokeratology group Available for the monthly follow up at the PolyU Optometry Clinic for 12 months after treatment commences Willing to comply with the prescribed aftercare/data collection visits

Axial elongation in myopic eye has been suggested to be associated with the visual feedback due to peripheral defocus in myopes [24,25]. The hypothesis is that, since there is greater relative hyperopia in the periphery with respect to axial refraction in myopes compared to emmetropes and hyperopes, peripheral hyperopic defocus may promote axial myopia in humans. In ortho-k, the reshaped cornea, flattened in the central with steeper mid-periphery, leads to a reduction of relative peripheral hyperopia in myopic eyes and this may retard the visual feedback for eye elongation which was reported to retard myopia. Different from spectacles which induced hyperopic defocus at peripheral, partial reduction using ortho-k would induce a certain amount of myopic defocus. It remains a question if partial reduction would help to slow down myopia progression.

The HM-PRO (High Myopia – Partial Reduction Orthokeratology) study is a single-blind randomized study with the aim of evaluating the effectiveness of partial reduction (PR) ortho-k in slowing myopic progression in the children. This study is registered in clinical trial at www.clinicaltrials.gov with the identifier NCT00977236. This report describes the study design, methods, eligibility criteria, and one-month partial reduction of high myopia changes secondary to ortho-k.

2. Methodology

Subjects were recruited via advertisements posted on local newspapers and leaflets in the Optometry Clinic of the School of Optometry, The Hong Kong Polytechnic University. Parents who were interested in the study would contact the researchers by phone and baseline (BL) visits would be arranged to determine eligibility and to collect baseline data. Ethics clearance for this study was obtained from the Departmental Research Committee of the School of Optometry at The Hong Kong Polytechnic University. All procedures were performed under the tenets of the

Table 2
Specifications of DreamLite lens.

Manufacturer	Procornea Ltd, The Netherlands
Material	Boston XO
Design	4 zone reverse geometry
Oxygen permeability (Barrer)	100
Back optic zone radius (mm)	7.20–9.50 (0.05 mm step)
Optic zone diameter (mm)	6.0
Total diameter (mm)	10.50
Lens central thickness (mm)	0.22
Wearing modality	Overnight orthokeratology
Replacement period	1 year

Declaration of Helsinki, as revised in 2002, and written informed consent was obtained before commencing the study. Eligible subjects and guardians were informed verbally and in writing about the nature, benefits and risks of the study. Subjects were randomized to receive PR ortho-k treatment or wear single vision spectacles in a 1:1 ratio (Microsoft office Excel 2003 spreadsheet). Once assigned to the designated group, subjects were not allowed to change group during the study.

2.1. Sample size

This myopic control study was designed to achieve 80% power to detect a minimum difference 0.30 mm (about 0.75 D) difference in AL in two years at the 5% level of statistical significance, using group standard deviation of 0.27 mm from our previous report [7]. A sample size of 14 subjects would be required. To allow for 30% dropouts, about 20 subjects should be recruited in each group.

2.2. Inclusion criteria

Table 1 lists the inclusion criteria for this study. Only children aged 8–11 years old, with spherical equivalent refractive error (SER (negative)) of more than 5.50D and astigmatism not more than 1.50D, were recruited. Eligible subjects were randomly assigned to wear spectacles or PR ortho-k lenses with spectacles to correct residual refractive errors. Those who refused to comply with the grouping were excluded (see Table 1).

2.3. Lenses and solutions

PR ortho-k subjects were fitted with ortho-k lenses (DreamLite, Procornea Ltd, The Netherlands) of target 4.00D. DreamLite (Procornea Ltd, The Netherlands) lens parameters were determined using the computer software (EyeLite) provided by the manufacturer. The software utilized sagittal height data imported from the corneal topography, and the spectacle prescription to calculate the parameters of the lens required. Back optic zone radius (BOZR) required was determined based on the Jessen factor philosophy (Jessen factor of 0.75) (i.e. the BOZR ordered will be 0.75D flatter than the attempted target). Lens parameters could be modified if necessary to improve fit using the software. The study lens is 4-zone (back optic zone curve, fitting curve, alignment curve and peripheral curve) reverse geometry. All lenses were made of Boston XO material. In the current study, the lens diameter of 10.5 mm was selected to cover about 90% of the corneal diameter. The lens parameters generated could be spherical or toric (toric reverse

curve and/or alignment curve), depending on corneal parameters. Spherical trial lenses were available from an inventory set provided by the manufacturer. Back surface toric design lenses had to be ordered and shipped from The Netherlands. Stabilization was confirmed when changes in myopia and corneal curvatures at two consecutive visits (within one week) were not more than 0.50D. A second pair of lenses would be ordered after confirmation to act as a spare pair in case of damage or loss or as an annual replacement pair where appropriate. The lens specifications are shown in Table 2. Residual refractive errors were corrected by a pair of single vision spectacles to be worn during daytime. All subjects had to learn how to insert and remove their lenses using their fingers and without any assistance from their parents. No suction holder (lens remover) was prescribed.

PR ortho-k subjects were prescribed with Menicon O2 Care, MeniCare Plus, Menicon Progent (Menicon Co. Ltd, Japan) were used for daily cleaning, soaking and disinfecting, and weekly enzymatic cleaning respectively. Complimentary Menicon O2 Care was given to the subjects to encourage all subjects to use this daily cleaner (instead of MPS) for cleaning the lenses. All solutions and lens cases were replaced monthly. Ortho-k lenses were replaced yearly.

For control subjects, single vision spectacles were prescribed and subjects were asked to wear the spectacles in the daytime during waking hours.

After the commencement of the study, spectacle prescription would be updated at any subsequent visit for either group of subjects if difference in residual refractive errors (sphere or astigmatism) obtained at that visit exceeded 0.50D.

2.4. Examination schedules and procedures

All subjects who enrolled in this study were required to attend non-cyclopegic and cyclopegic examinations every six months over two years. PR ortho-k subjects had to attend three extra visits (first morning after lens wear (1-ON), one week (1-week) and one month (1-month)) after lens delivery to assess/confirm lens performance (Fig. 1). Extra aftercare consultations would be provided as required during the study period (e.g. in case of adverse events such as significant lens binding leading to corneal staining).

2.4.1. Masking

This study was a single-masked design to eliminate any examiner bias on myopic progression. The masked examiner only measured and recorded the AL which was the primary outcome of the study.

2.4.2. Ophthalmic examination

Two types of examinations were conducted during the study period: non-cyclopegic and cyclopegic examinations. Cyclopegic measurements included objective and subjective refraction, and AL measurement and fundus examination. These measurements were made at every 6-month visit and after the non-cyclopegic examination at the same visit (Table 3). One drop of 1.0% Alcaine (Alcon-Couvreur, Puurs, Belgium) was first instilled, followed one minute later by one drop of 1.0% Mydracil (Alcon-Couvreur, Purrs, Belgium) and five minutes later by one drop of 1.0% Cyclogyl (Alcon-Couvreur, Purrs, Belgium). Pupillary response and the amplitude of accommodation were evaluated after 30 min, and every 10 min thereafter if necessary. Cyclopegic measurements were performed only when there was no pupillary response and the amplitude of accommodation was less than 2.00 D.

2.4.3. Objective refraction

The Shin-Nippon Open field 5500K autorefractor (Ajinomoto trading Inc., Japan) was used to measure distance objective

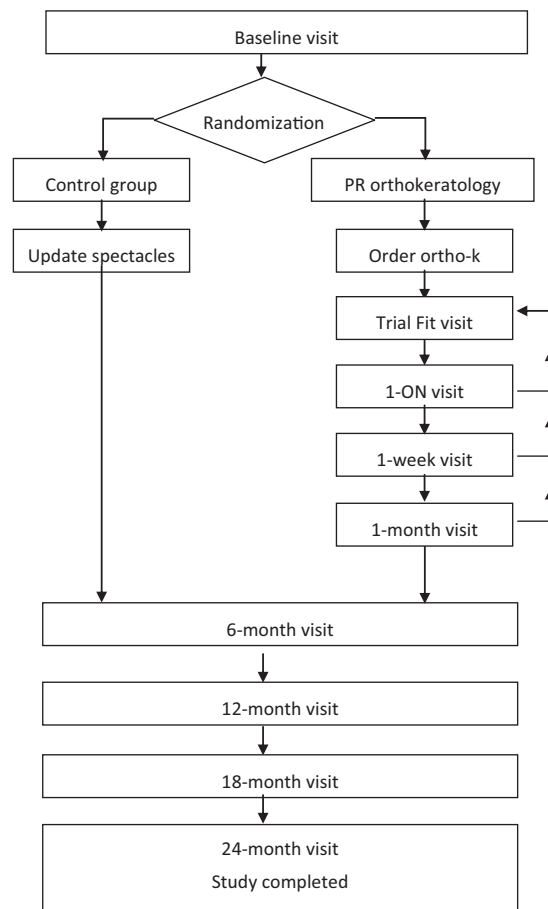


Fig. 1. Flow chart presenting the HM-PRO study design.

refraction at all visits. Three average readings, each from a set of three measurements of difference within 0.25D in sphere and cylinder, were recorded for analysis.

2.4.4. Subjective refraction

Subjective refraction was measured in an examination room with lighting 400 Lux. The same room was used throughout the study. The refraction endpoint was considered as maximum-plus-to-maximum-acuity.

2.4.5. Visual acuity (VA)

Early Treatment Diabetic Retinopathy Study (ETDRS) charts series 2000 (Precision Vision, IL, US) were used to measure the high (>90%) contrast and low (10%) contrast VA. Three high contrast and one low contrast charts were used. Both habitual visual acuity (VA) and best corrected VA (BCVA) were measured, with the high contrast chart first, followed by the low contrast chart. VA for the right eye was always assessed first, then the left eye, and finally both (binocular) eyes.

2.4.6. Slit-lamp examination

Topcon SL7 and Topcon IMAGEnet (Topcon Corporation, Japan) were used to examine the anterior segment of the eyes of all subjects and to evaluate the lens fitting for subjects in the PR ortho-k group. Photodocumentation was made for all corneal signs which were graded using Efron grading scale (Efron 2000) [26] where appropriate.

Table 3
Data collection schedule.

Data taking visits		Baseline	1-month visit	Every 6 months
Lens wear in situ			x	
Consent		x		
History taking		x		
Refraction (Subjective and objective)	Pre-cycloplegic	x	x	x
	Post-cycloplegic	x		x
VA (best corrected)	High contrast	x	x	x
	Low (10%) contrast	x	x	x
Photo-bi microscopy	Lens assessment		x	x
Topography	Pre-fitting	x		
	Post-fitting		x	x
Pupillary response		x		x
Axial length	Post-cycloplegic	x		x

2.4.7. Axial length (AL)

Measurements of AL were performed with the Zeiss IOLMaster (Carl Zeiss Meditec, Inc., USA) by masked examiners after cycloplegia at baseline and every 6-month visits. Five AL measurements, between-measurement difference not more than 0.02 mm, were recorded and averaged for analysis [18,19].

2.4.8. Corneal topography

Corneal topography was performed with the Medmont E300 (Medmont International Pty Ltd, Australia) at baseline and every 6-month visits for all subjects. At each visit, for each eye, four corneal profiles, each of score not less than 98 (as recommended by the manufacturer), were saved for evaluation and monitoring purposes. This procedure was also performed on PR ortho-k subjects at the 1-ON, 1-week, and 1-month visits.

2.5. Statistical analysis

Since this was a pilot study with small sample size, non-parametric tests were used to analyze the results (baseline (both groups) and one month (only PR-ortho-k group)). The significance level was set at 0.05, with Bonferroni correction where multiple tests were performed. Only the data from the right eyes are presented in this report. Median and range were reported for data showing non-Gaussian distributions (age, pre-cyclo subjective myopia, post-cyclo subjective myopia and VA) and mean ± SD for data which were normally distributed (AL, flat K and steep K).

3. Results

A total of 79 subjects were screened and 52 eligible subjects were randomly assigned into the PR ortho-k (n = 26) and control (n = 26) groups (Fig. 2).

3.1. Baseline data (n = 26 per group)

Table 4 shows a summary of the baseline data of the two groups of subjects. The median cycloplegic subjective myopia was 6.34D (5.00D–8.00D) and 6.08D (5.00D–8.00D) for the PR ortho-k and control subjects respectively, and the mean ± SD AL were 26.02 ± 0.57 mm and 25.93 ± 0.54 mm respectively. No significant differences in age, baseline pre- and post-cycloplegic subjective myopia, high and low contrast BCVA ((Mann–Whitney tests, 0.19 < p < 0.83) were found between the two groups. The AL, steep and flat K were comparable between the two groups of subjects (Unpaired t-tests, 0.23 < p < 0.65). Ocular health condition was similar between the two groups of subjects (Pearson Chi-square, p > 0.99). Staining was found in six subjects (three in

each group) but the severity of all staining was not more than Grade 1.

3.2. Lens performance (PR ortho-k group)

Of the 26 subjects, two subjects were terminated before one week of study (see Dropouts below). For the remaining 24 subjects, lens performance was determined after at least one week of lens wear. Optimum fit was achieved in 11 subjects (46%) with the first pair of lenses. Of the remaining 13 subjects, five (21%) and three (13%) subjects required two and three pairs of lenses respectively before achieving optimum lens fits. Five subjects (21%) did not manage to achieve satisfactory fit even after three pairs of lenses. Only 19 subjects continued the study.

3.3. Dropouts (both groups)

Seven subjects in the control group decided to quit the study after baseline examination. One PR ortho-k subject quitted after two days of lens wear due to lens discomfort, five were terminated due to poor lens fitting despite repeated lens modifications, and another was terminated after one week of lens wear due to non-compliance with aftercare schedule.

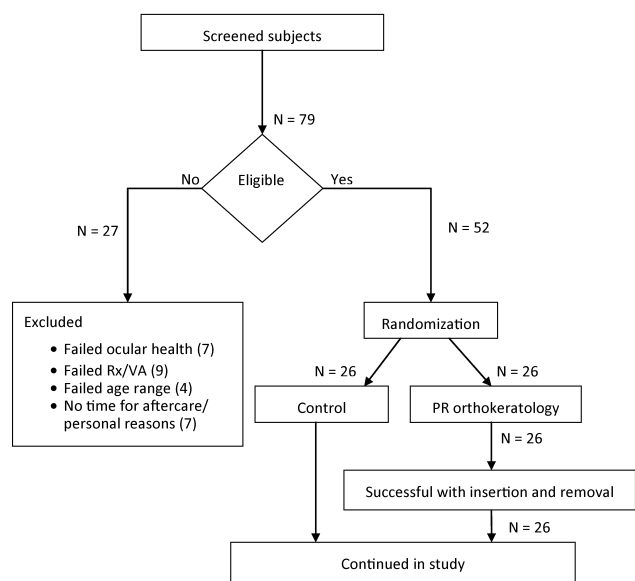


Fig. 2. Flowchart showing recruitment of HM-PRO subjects.

Table 4
Baseline data [median (range)] or mean \pm SD of subjects.

	PR ortho-k (n = 26)	Control (n = 26)	p Value
Age (years)	[10 (8–11)]	[10 (8–11)]	0.19 [*]
High contrast BCVA (logMAR)	[0.02 (–0.08–0.08)]	[0.04 (–0.10–0.16)]	0.22 [*]
Low (10%) contrast BCVA (logMAR)	[0.25 (0.12–0.38)]	[0.22 (0.10–0.48)]	0.83 [*]
Pre-cycloplegic subjective Myopia (D)	[6.41 (5.00–8.00)]	[6.22 (5.00–8.00)]	0.25 [*]
Post-cycloplegic subjective Myopia (D)	[6.34 (5.00–8.00)]	[6.08 (5.00–8.00)]	0.20 [*]
Axial length (mm)	26.02 \pm 0.57	25.93 \pm 0.54	0.65 [#]
Flat K (mm)	7.78 \pm 0.17	7.87 \pm 0.16	0.23 [#]
Steep K (mm)	7.55 \pm 0.18	7.60 \pm 0.18	0.42 [#]

PR ortho-k: Partial reduction orthokeratology.

BCVA: best corrected visual acuity.

^{*} Probability values for differences between groups using Mann–Whitney tests.

[#] Probability values for differences between groups using Unpaired t tests.

3.4. One-month results (PR ortho-k group)

Nineteen subjects who achieved lens stabilization returned after one month of lens wear. The median (range) in myopic reduction and residual myopia were 3.75D (2.25–5.00D) and 2.75D (1.50–5.25D) respectively at the 1-month visit. All subjects wore single vision spectacles to correct their residual refractive errors. No significant difference was found in high and low contrast BCVA among visits (i.e. baseline, 1 overnight, 1 week and 1 month) (Friedman tests, High: $p = 0.148$; Low: $p = 0.192$). Changes in refractive components are shown in Fig. 3.

No significant differences were noted in ocular health (corneal staining and lens binding) between visits in the first month after commencement of lens wear (Chi square tests, $p > 0.068$), except for the formation of a pigmented arc (Chi square test, $p = 0.001$). The incidence of a pigmented arc among the PR ortho-k subjects at the 1-month visit was 32%. Although about 30% of the PR ortho-k subjects reported lens binding at the beginning of the study, they were able to loosen their lenses in a safe manner as per instructions given. There were no reports of damage or loss of lenses during the first month of lens wear.

4. Discussion

HM-PRO study is a pilot study on myopic progression on high myopes using PR ortho-k. It is a single-masked, randomized clinical trial. Double-masked study design is not possible as subjects would know whether or not they were wearing ortho-k lenses. Since the examiner would know from the refraction and topography assessments whether or not a subject was wearing ortho-k lenses, the masked examiner was restricted to take AL measurements only. In

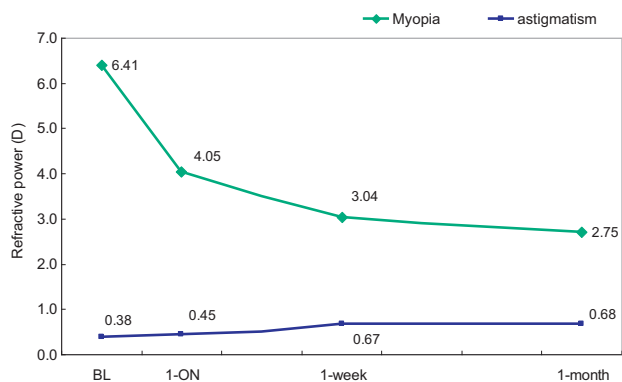


Fig. 3. Changes (median) in refractive components during lens stabilization in PR orthokeratology group ($n = 19$).

this study, the masked examiner was involved in the study, but not in patient care.

In the current study, 34% ($n = 27$) of subjects screened were ineligible. All 27 ineligible subjects had no experience with contact lenses wear. Among them, 16 subjects were not suitable for spherical/toric ortho-k contact lens wear due to high astigmatism (> 1.50 D cyl) and poor ocular health (e.g. such as Grade 3 corneal staining and trichiasis). Four subjects were out of the age range for this study and they sought ortho-k treatment in private practices. Five subjects were excluded because the parents were not able to comply with the required aftercare/data collection visits. Two subjects refused to join the study due to personal reasons – one was going overseas to study and the other worried about lens handling.

For the eligible subjects, no significant differences were found in the pertinent baseline data between the control and PR ortho-k groups (Tables 4 and 5). The first-fit success rate was about 46% (11 subjects) and five subjects (21%) were unable to achieve satisfactory fit even after three modifications. Since the lenses used in this study were actually designed for use on low myopes, the low first-fit success rate may be because these lenses were fitted on high myopic eyes. Further study is necessary to determine if this is in fact the case.

Most published ortho-k studies [7,27–31] recruited subjects with low spherical equivalent refractive errors (average myopia, 2.50D) and low astigmatism (< 1.50 D cyl). As mentioned earlier, we found that corneal health may be compromised when higher target lenses were used. Hence, we only targeted for 4.00D reduction for our high myopic subjects, and the median myopic reduction was 3.75D within one month (Fig. 3) in the current study. The myopic reduction profile, in terms of percentage of reduction achieved with lens wear, in this study was similar to those reported in previous studies for low myopes [11,13–15,32]. About 65% of the target attempted (i.e. 4.00D) was achieved after one night of lens wear, 90% after 1 week and about 99% after 1 month of lens wear. High and low contrasts BCVA were comparable between visits during lens stabilization in the PR ortho-k subjects.

The most common ocular finding in the PR ortho-k subjects was corneal staining (Table 5). Although the incidence of corneal staining tended to increase with lens wear, the severity of the staining was mild (Grade 1). Our results were in agreement with previous reports on low myopes [29–31,33]. None of the staining episodes required any clinical intervention.

Pigmented arc was found in 32% of subjects after one month of lens wear, but there were no associated complications. The high incidence of pigmented arc found in this study may be because all subjects were targeted for 4.00D reduction. Cho et al. first reported the observation of pigmented arc in Chinese ortho-k children [34]. Cheung et al. reported that incidence of corneal pigmented arc of the pigmented arc was 27% after 3-month lens wear in their low myopic subjects [35]. In ortho-k, pigmented arc may be formed in

Table 5Ocular signs (Efron's Grading scale) and symptoms reported during orthokeratology lens wear ($n = 19$).

		Baseline (%)	First overnight visit (%)	One week (%)	One month (%)	<i>p</i> -Value*
Corneal staining (Grade 1)	Central	0	31.6	15.8	15.8	0.068
	Inferior	15.8	0	21.1	26.3	0.136
	Nasal	0	5.3	0	10.5	0.550
	Superior	0	5.3	10.5	5.3	0.282
	Temporal	0	10.5	0	0	0.104
Pigmented arc (Grade 1)	Inferior cornea	0	0	5.3	31.6	0.001*
Lens binding		0	31.6	21.1	15.8	0.073

* Probability values using Chi Square tests.

the mid-peripheral cornea where is an abrupt corneal curvature change leading to deep reservoirs of tears when the lens is in the eye. In the current study, all subjects were high myopes who were fitted with target 4.00D lens. The 4.00D target lens creates deeper tear reservoirs, compared to those targeting lower reduction, at the reverse curve region, leading to substantial steepening of the midperipheral cornea, leading to more significant changes in the topography within a relatively shorter period of time. This may explain why an incidence of 32% was observed in the current study after only 1-month lens wear.

The combination of PR ortho-k and spectacles offered a stable vision for high myopic subjects. Although we did not conduct a formal survey, all children and parents indicated that they liked this mode of correction. The children appreciated the opportunity of wearing thinner (weaker) glasses as well as the option of relatively clear vision even without glasses to correct their residual errors, which allowed them to enjoy outdoor activities, such as dancing, playing football, singing competition. The children in our study were required to handle their contact lenses on their own, including insertion, removal and cleaning, and all subjects were capable and diligent in these respects. No subjects reported lens damage or loss within the first month of lens wear.

This pilot study showed that PR ortho-k with spectacles for correcting residual refractive errors can be offered to high myopic children who wish to undergo ortho-k treatment for myopic control. It remains to be determined whether or not this mode of treatment is able to slow myopic progression in these children.

5. Conclusion

The results of this pilot study indicate that the combination of PR ortho-k and spectacles is a safe and feasible option for correcting high myopic children.

Acknowledgements

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The authors have no proprietary interest in any of the products used in the study.

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ORIGINAL ARTICLE

Toric Orthokeratology for Highly Astigmatic Children

Chia Chi Chen*, Sin Wan Cheung†, and Pauline Cho‡

ABSTRACT

Purpose. To determine the efficacy of toric orthokeratology (ortho-k) in correcting myopia and astigmatism in myopic children with moderate to high astigmatism.

Methods. Asymptomatic subjects aged 6 to 12 years with myopia of 0.50 to 5.00 D and astigmatism of 1.25 to 3.50 D of axes $180 \pm 20^\circ$ were fitted with Menicon Z Night Toric Lens (NKL Contactlinsen B.V., Emmen, The Netherlands). Data collection was performed at baseline and 1 night, 1 week, and 1 month after the commencement of lens wear. The results from the right eye or the eye with higher astigmatism were reported.

Results. The first lens fit success rate was 95%. Two subjects had to be refitted due to lens decentration and inadequate central clearance after one overnight lens wear and were successfully fitted with a second pair of lenses. Toric ortho-k significantly reduced the manifest myopia from 2.53 ± 1.31 D to 0.41 ± 0.43 D and astigmatism from 1.91 ± 0.64 D to 0.40 ± 0.39 D (paired t-tests, $p < 0.02$) after 1 month of lens wear. The unaided visual acuity (logMAR) was 0.11 ± 0.13 after 1 month of lens wear. No significant lens binding, corneal staining, or other adverse events were observed during this period of lens wear.

Conclusions. This toric lens design lens, with a first lens fit success rate of 95%, was effective in correcting low-moderate myopic children who had moderate-high astigmatism. It has the potential to be used in myopic control studies for myopic children who have high astigmatism.

(Optom Vis Sci 2012;89:849–855)

Key Words: toric design, orthokeratology, astigmatism, myopia, myopia control

Myopia is a common ocular disorder especially in Asian countries such as Hong Kong, Singapore, Korea, Taiwan, and China.^{1–6} Orthokeratology (ortho-k) uses specially designed rigid contact lenses to temporarily reduce myopia.^{7–11} Recent reports have shown ortho-k to be effective in slowing the progression of myopia in children.^{10,12,13} The rate of axial elongation of the eyeball in children wearing ortho-k lenses was reported to be at least 40% slower compared with those wearing spectacles¹⁰ or soft contact lenses.¹²

Most myopic children are also astigmatic.^{14,15} Kleinstein et al.¹⁵ reported that the prevalence of astigmatism was 33.6% in Asian children aged 5 to 17 years. In their article, astigmatism was defined as at least 1.00 D difference between the two principal meridians. Although it has been shown that spherical design ortho-k lenses are effective in correcting low-moderate myopia, they can-

not adequately reduce moderate refractive astigmatism^{16–18} and hence ortho-k for myopia control is not indicated for children with refractive or corneal astigmatism more than 1.50 D.

The most common problem with spherical ortho-k lenses on patients with a significant amount of corneal astigmatism is poor lens centration which can lead to induced astigmatism and poor vision.^{17,19} Toric reverse geometry designs have been developed to improve lens centration as well as for astigmatic correction. However, apart from some case reports^{20,21} and some conference abstracts,^{22,23} to our knowledge, there are no published research reports on the efficacy of toric ortho-k for correcting astigmatism or for myopia control in moderate to high astigmatic children.

In our case reports,^{20,21} good lens centration, using toric ortho-k lenses, was obtained in all the three children, aged 10 to 13 years, who had high refractive astigmatism. While significant reductions of refractive myopia and refractive astigmatism were observed in two of the subjects, only a modest response was found in the other subject. Yet, despite the differences in response, during the 1-year ortho-k lens wear, all the three subjects did not show any significant increase in axial length. The results suggested the potential of

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myopia control on myopes with significant amount of refractive astigmatism with this lens design.

The Toric Orthokeratology-Slowing Eyeball Elongation (TO-SEE) study is a 2-year longitudinal study investigating the efficacy of toric ortho-k for myopic and astigmatic reduction in myopic children who had moderate to high astigmatism and for myopia control. This report presents the clinical performance of the toric ortho-k lens used for the correction of myopia and astigmatism in these subjects after 1 month of lens wear.

MATERIALS AND METHODS

Study Design

Subject recruitment was conducted between April 2008 and December 2009. Eligible subjects were given a comprehensive vision examination at the beginning of the study. A pair of ortho-k lenses was prescribed based on the manifest refraction and the corneal topography. Lens performance was reviewed after 1 night, 1 week, and 1 month after commencement of lens wear. All procedures followed the Declaration of Helsinki, and the protocol was reviewed and approved by the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University. Informed consent was obtained from the parents of each subject before commencement of the study.

Subjects

The subjects were between 6 and 12 years and had manifest myopia of 0.50 to 5.00 D (inclusive) and refractive astigmatism of 1.25 to 3.50

D of axes $180 \pm 20^\circ$ (Table 1). All subjects had unremarkable ocular health and did not have any ocular or general health problems which could affect the normal development of refractive status of the eye. They had no contraindication for ortho-k lens wear and did not have any previous myopia control treatment. Each eye had a best-corrected visual acuity (VA) of 0.10 logMAR or better.

The subjects and parents were trained to insert, remove, and care for the lenses. Subjects and their parents were also taught about the possibility of lens binding (adherence) on eye opening and how to remove a bound lens properly. Table 2 shows the grading scale of lens binding given to the subjects. The subjects were required to wear the lenses for 8 to 10 h every night unless instructed otherwise by the examiner and to attend aftercare visits which were scheduled after first overnight, 1 week, 1 month, (each visit within 2 h after waking up in the morning), and every 3 months after commencing lens wear. Un-scheduled visits were also arranged when necessary in case of adverse events. They were also required to record their lens wearing and lens removal time as well as the incidence and severity of lens binding in the ortho-k diary provided.

Any subjects who presented with significant adverse events or failed to comply with the prescribed procedures despite reminders (three times) were required to withdraw from the study. All prescribed lenses and solutions had to be returned to the examiner upon completion or withdrawal from the study.

Sample Size

For the main myopia control study, the sample size required was determined to be 40 to achieve a power of 80%.

Lenses and Solutions

Lenses used were the Menicon Z Night Toric Reverse Geometry Lens (RGL) (NKL Contactlinsen B.V., Emmen, The Netherlands). The Menicon Z night toric lens is a peripheral toric ortho-k lens design (both sagittal height and tangent) with spherical back optic and reverse zones. The back optic zone diameter is 6.0 mm, center thickness is 0.24 mm, and the available diameters are 10.2, 10.6, and 11.0 mm. The back vertex power of the lens is plano. Each lens has three fenestrations at 120° intervals in the area of the reverse curve. All lenses are made in Menicon Z material [ISO Dk

TABLE 1.

Inclusion and exclusion criteria for subject recruitment in TO-SEE project

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> Age: between 6 and 12 yr Chinese children Myopia from 0.50 to 5.00 D With-the-rule astigmatism from 1.25 to 3.50 D of axes $180 \pm 20^\circ$ Anisometropia not more than 1.50 D in myopia Best-corrected monocular visual acuity equal to or better than 0.10 logMAR Available for follow-up for at least 2 yr 	<ul style="list-style-type: none"> Strabismus at distance or near Contraindication for contact lens wear and orthokeratology (e.g., limbus to limbus corneal cylinder and dislocated corneal apex) Prior experience with the use of rigid lenses (including orthokeratology) or with myopia control Systemic or ocular conditions which may affect contact lens wear (e.g., allergy and medication) or affect refractive development (e.g., Down syndrome, ptosis)

TABLE 2.

Grading scale for lens binding

Grade (lens binding)	Definition
0	No binding observed. Lens move freely.
1	Lens bound and loosens up spontaneously after less than five forced blinks.
2	Lens bound and loosens up after one episode of pressure on the upper lid, then repeated on the lower lid and less than five forced blinks.
3	Similar to grade 2, but two pressure pushes on the lids and less than five forced blinks.
4	Similar to grade 2, but with three pressure pushes and less than five forced blinks.

163×10^{-11} (cm²/sec) (ml O₂/(ml · mm Hg)) ISO 9913-1]. All lenses used in this study were replaced every 12 months.

The lens parameters were determined with the NKL Easy Fit Software (version VIP 2006, NKL Contactlinsen B.V., Emmen, The Netherlands). Pertinent data, including the manifest refractive error, the horizontal visible iris diameter (HVID), and four corneal topographic maps, were required for the computer program to calculate the initial lens parameters for the eye. The software calculates the back optic zone radius according to the refractive power and simulated keratometry reading. HVID was used to determine the lens diameter (about 90% of the HVID) and the software also determined the tangent angle and the lens height based on the corneal topography. If an ordered lens produced an adverse response²⁴ such as displacement, smiley face, or frowny face topographic pattern after one night of lens wear, a new lens was ordered for the eye using the software.

The lens care system prescribed included Menicon O₂ Care cleaner, MeniCare Plus, Progent A+B (Menicon, Nagoya, Japan), Alcon Tears Naturale Free (Alcon Laboratories, Fort Worth, TX), and Bausch & Lomb sensitive eye saline (Bausch & Lomb, Rochester, NY). Subjects were required to rinse the lenses thoroughly with saline after rubbing with Menicon O₂ daily cleaner, disinfect their lenses in MeniCare Plus, and rinse their lenses again with saline before lens insertion. Artificial tears were used before lens insertion to minimize the formation of air bubbles and before lens removal to loosen the lenses. Protein removal was performed weekly. All accessories were disinfected every week, and all bottle solutions and lens cases were replaced every month. Tap water and suction were not allowed for lens handling to minimize the risk of infection. All lenses and solutions used were complimentary to ensure that all subjects used the same solutions and complied with the replacement schedule.

Assessment/Measurements

All examinations were carried out by the examiner (CC). The right eye was always measured first followed by the left eye at each visit.

Clinical performance of the lenses during the first month of lens wear, in terms of the anterior ocular health, VA, and subjective refraction, was assessed.

Orthokeratology Lens Fitting

At the delivery visit, the ortho-k lens fitting assessment was first performed by assessing the fluorescein pattern with the lens in situ with the slitlamp. The targeted ideal fluorescein pattern was characterized by a central zone of light touch (3.0 to 3.5 mm diameter), surrounded by a wide deep doughnut-shaped tear reservoir, a zone of peripheral light touch, and peripheral clearance, with lens movement of 1 to 2 mm on blink. Lenses demonstrating the described fluorescein pattern for an acceptable fit were delivered. If the corneal response showed a bull's eye pattern²⁵ at the first overnight visit, the subject would continue lens wear. First, fit success rate was determined by the percentage of subjects who achieved satisfactory fitting and continued lens wear with the first pair of lenses after first overnight visit. If the cornea showed a poor response (e.g., displacement, smiley face, and frowny face topographic pat-

tern), lens wear was ceased and a new lens with adjusted parameters, as suggested by the Easy Fit Software (based on topographical response of first lens), for each eye was ordered and the above procedures repeated. Subjects who could not achieve satisfactory fits despite repeated modifications (three pairs of lenses) were terminated from the study. For an eye with myopia not more than 4.00 D, the target reduction would be the amount of myopia of the eye. For an eye with myopia 4.25 to 5.00 D, the first lens ordered was targeted for 4.00 D reduction.

VA and Subjective Refraction

At each visit, the LCD logMAR VA chart in the same examination room was used when taking the entrance VA and subjective refraction. Distance subjective monocular refractive error for each eye was determined at every visit using trial frame and trial lenses. High (close to 100% contrast) and low contrast (10% contrast) unaided VA (UVA) and best-corrected VA were taken with the ETDRS charts (Precision Vision, La Salle, IL) at cycloplegic visits. The procedures for VA measurement were reported in a previous study.¹¹

Anterior Ocular Health

Anterior ocular health assessment was performed at each visit using Topcon TRC-NW6S photographic slitlamp (Topcon, Tokyo, Japan) after VA assessment. Corneal staining, taking into account type, depth, and extent, was graded from 0 to 4 using Efron grading scales.²⁶ The location (superior, inferior, nasal, temporal, and central) of the corneal staining was also recorded. Presence of lens binding and corneal pigmented arc was assessed at every visit after commencement of lens wear.

Corneal Topography

After slitlamp biomicroscopy, corneal topography was measured using the Medmont E300 corneal topographer (version 3.9.3, Medmont, Camberwell, Australia). All subjects were asked to blink normally to avoid the disruption of tear film, open the eyes wide after the last blink, and fixate on the internal target during the image acquisitions. Images were automatically captured and four images, each with score higher than 98, were accepted. The subtractive maps between pre- and post-lens wear were used to determine lens centration and size of treatment zone (tangential maps) and the amount of corneal flattening (refractive maps).

Outcome Measures

The primary outcomes for the clinical performance of the toric ortho-k lenses were the first lens fit success rate and the amount of myopic and astigmatic reductions in subjective refraction. The amount of myopic reduction at each subsequent visit was determined by subtracting the residual myopia from baseline myopia. Changes in astigmatism were determined by comparing changes in refractive astigmatism as well as power vectors: $J_0 = (-C/2) \cos(2\theta)$ and $J_{45} = (-C/2) \sin(2\theta)$, where C denotes the amount of astigmatism at axis θ and J_0 and J_{45} are the horizontal or vertical and oblique components of astigmatism, respectively.²⁷ Changes in corneal toricity were also analyzed and presented.

Data Analysis

Statistical package used was SPSS version 18 (SPSS, Chicago, IL). Because the distribution of data were not significantly different from normal (Kolmogorov-Smirnov tests, $p > 0.05$), parametric tests were used to compare myopia, astigmatism, J0 and J45, and VA data between baseline and the subsequent visits. Repeated measures analysis of variance (ANOVA) was used to study the change in the parameters after ortho-k lens wear and paired t-tests, with Bonferroni correction, were used for post hoc analysis. Data from the right eye, if the two eyes had the same amount of refractive astigmatism, or the eye with higher refractive astigmatism were analyzed in this report.

RESULTS

Subjects

A total of 83 subjects were screened and 43 subjects (22 males and 21 females), who satisfied the recruitment criteria (Table 1), were enrolled and fitted with the toric lenses. The mean \pm SD age was 9.4 ± 1.4 years, and Table 3 presents the demographic data and the baseline characteristics of the subjects. Fig. 1 presents a flowchart of subject recruitment and progress of the subjects.

First Fit Success Rate

Lens fittings with the first pair of lenses were satisfactory for all subjects at the delivery visit. At the first overnight visit, only two subjects were refitted with a second pair of lenses due to poor lens decentration and inadequate central clearance. The first lens fit success rate without the use of trial lenses was 95%.

Visual Acuity

Mean \pm SD UVA was 0.37 ± 0.24 at the first overnight and improved to 0.11 ± 0.13 logMAR after 1 month of lens wear (paired t-test, $p < 0.001$) (Fig. 2). UVA at 1 month was significantly different from baseline best-corrected VA (0.00 ± 0.07 logMAR) (paired t-test, $p < 0.001$). Best-corrected VA at the 1-month visit (0.00 ± 0.04 logMAR) was not significantly different from that at baseline (paired t-test, $p = 0.628$).

TABLE 3.

Baseline data (mean \pm SD) of subjects recruited ($n = 43$) (right eye or the eye with higher astigmatism)

Age (yr)	9.4 ± 1.4
Myopia (D)	2.53 ± 1.31
Astigmatism (D)	1.91 ± 0.64
Steep K (D)	45.70 ± 1.54
Flat K (D)	43.20 ± 1.31
High contrast BCVA (logMAR)	0.00 ± 0.07
Central corneal thickness (μm)	563 ± 32
Intraocular pressure (mm Hg)	13.8 ± 2.1
Axial length (mm)	24.32 ± 0.89
Anterior chamber depth (mm)	3.61 ± 0.22

BCVA, best-corrected visual acuity.

Changes in Refractive Errors and Corneal Toricity

Fig. 3 shows the changes in myopia and refractive astigmatism during the 1-month ortho-k lens wear. There were significant changes in myopia and refractive astigmatism after 1 month of lens wear (repeated measures ANOVA, $p < 0.05$). The mean \pm SD baseline myopia was 2.53 ± 1.31 D. Myopia was significantly reduced to 1.33 ± 0.80 D (42% reduction) at the first overnight visit and to 0.41 ± 0.43 D (81% reduction) at the 1-month visit (paired t-tests, $p < 0.001$) (Fig. 3).

Refractive astigmatism (mean \pm SD) reduced from 1.91 ± 0.64 D to 0.88 ± 0.59 D (54% reduction) and to 0.40 ± 0.39 D (79% reduction) at the first overnight and 1-month visits, respectively (paired t-tests, $p < 0.001$) (Fig. 3). Corneal toricity reduced from 2.30 ± 0.51 D at baseline to 2.01 ± 0.61 D (13%) at the first overnight visit and to 1.28 ± 0.53 D (44%) at 1-month visit (paired t-tests, $p < 0.001$). Fig. 4 shows changes in both refractive astigmatism and corneal toricity, J0 and J45 before and after ortho-k treatment. Significant reductions at subsequent visits were observed for J0 of both refractive astigmatism and corneal toricity (repeated measures ANOVA, $p < 0.001$). No significant changes were observed for J45 of both refractive astigmatism and corneal toricity over the 1-month period (repeated measures ANOVA, $p = 0.168$).

Effect on Anterior Ocular Health

At the first overnight visit, corneal staining was observed in 23% of subjects, only in one of the five corneal zone in each eye [central (5%), inferior (9%), superior (2%), nasal (2%), and temporal (5%)]. No significant corneal staining (all staining $<$ grade 2) was observed in the subsequent visits during the 1-month lens wear, although mild (grade 1) staining was observed at different corneal locations in some subjects at different visits.

Dimple veiling was observed in 70% of the subjects (30/43) at the first overnight visit. No dimple veiling was observed at subsequent visits. During the 1-month lens wear, no pigmented arc was observed and no adverse events were noted in any subject.

Lens Binding

Grade 1 lens binding was reported by 14% of subjects at the first overnight visit and by about 5% of subjects before they removed their lenses at the 1-week visit. No lens binding was reported at the 1-month visit.

DISCUSSION

Toric design ortho-k can be used not just for reduction of refractive astigmatism but also for improving lens centration on toric corneas. In this study, no subjects had been excluded because of poor lens centration. Currently, a few manufacturers (e.g., NKL Contactlinsen B.V., Emmen, The Netherlands; Paragon Vision Sciences, Mesa, AZ) have developed toric RGL design (toric reverse and/or alignment zones). No trial lenses were used in this study. The NKL Easy Fit Software (NKL Contactlinsen B.V., Emmen, The Netherlands) allows empirical lens ordering, hence reducing chair time which would otherwise be needed for trial lens fitting, and practitioners do not need to store or maintain a large set

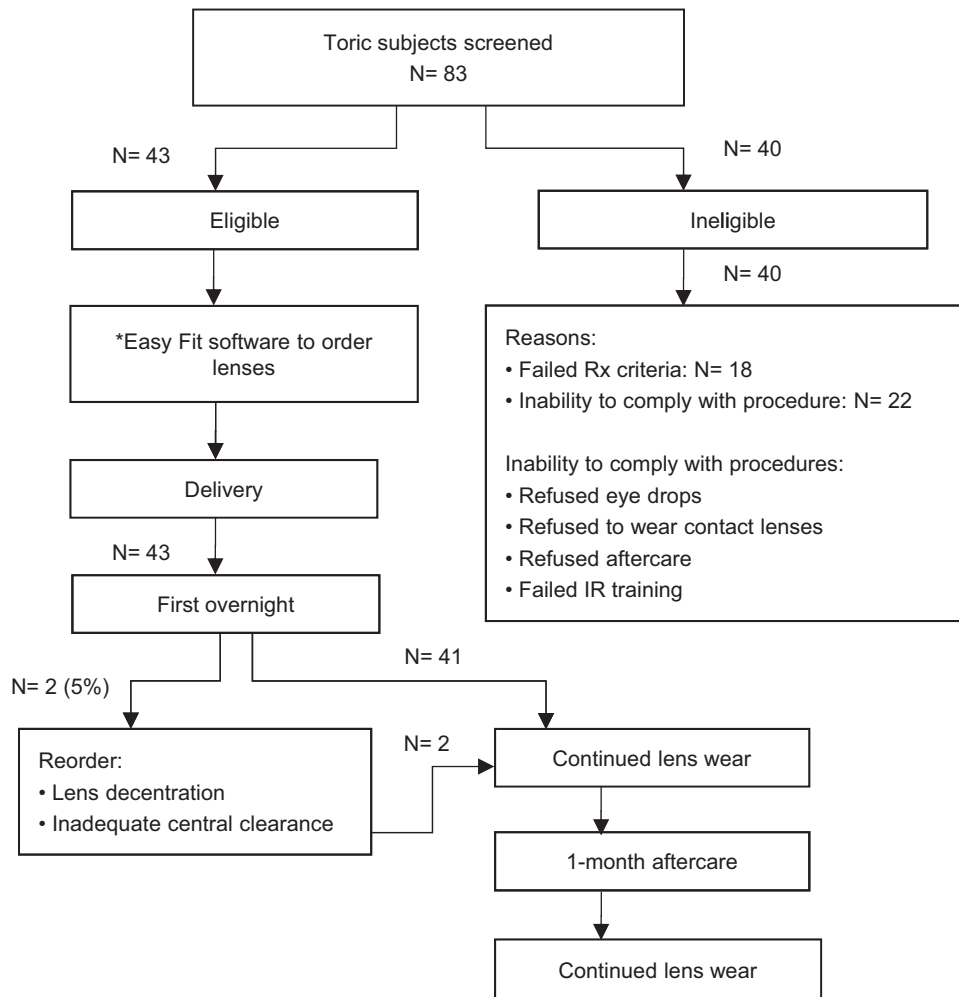


FIGURE 1.

Subject recruitment and clinical performance of the lenses at 1-month visit [*NKL Easy Fit Software (version VIP 2006, NKL Contactlenzen B.V., Emmen, The Netherlands)]. IR, Insertion and removal.

of trial lenses. This is ideal for those who are concerned with cross-contamination or transmission of prion disease from trial lenses.²⁸ The first lens fit success rate with Night Toric RGL was 95%, which was better than the rate with trial lens fitting reported in our clinic (73.5%).¹⁷ The Easy Fit Software also allows practitioners to modify parameters as they see fit, which is an added advantage to experienced practitioners.

Our results show that toric ortho-k could reduce myopia by 81% and refractive astigmatism by 79% after 1 month of lens wear with one pair of lenses. The mean \pm SD myopia reduction after 1 month of lens wear in our subjects was 2.03 ± 1.26 D (81%), whereas previous studies have reported reduction in spherical equivalent of 1.50 to 3.50 D.^{10,29,30} While these previous studies have reported no significant change in refractive astigmatism with spherical ortho-k lens wear, our subjects achieved 79% reduction in refractive astigmatism with the toric design lenses after 1 month of lens wear. At the 1-month visit, mean \pm SD UVA was 0.11 ± 0.13 logMAR which was satisfactory to all subjects. However, the UVA was significantly poorer compared with baseline best-corrected VA due to significant residual myopia (0.41 ± 0.43 D) and/or refractive astigmatism (0.40 ± 0.39 D). Twelve of the subjects had residual myopia or refractive astigmatism

>0.75 D due to underresponding at the 1-month visit. Reordering of lenses with higher targets were made for these subjects as they did not achieve the endpoint criteria (i.e., myopia >0.75 D or UVA worse than 0.18 logMAR) to continue in the myopia control study.

Corneal staining associated with ortho-k lens wear is a common finding, and mechanical trauma and hypoxia have been proposed to be likely causes.^{17,31,32} Mild corneal staining of about 40% had been reported after first overnight wear of ortho-k lenses.^{17,32} In this study, grade 1 cornea staining was observed in only 23% of subjects at the first overnight visit. In agreement with previous reports,^{12,31} none of the subjects presented any adverse events that required them to cease lens wear or seek medical intervention. The low incidence of staining observed in this study may be due to improved lens centration with the toric design ortho-k, the lens material used, and the lower incidence of lens binding associated with the use of lens fenestrations.

Dimple veiling occurs when air bubbles are trapped between the lens and the cornea. The lens mechanically compresses the bubbles which indent the corneal epithelium, producing transient depressions on the corneal surface, observed as dimple veiling in the fluorescein-stained eye.³³ Most of the “staining” usually recovers

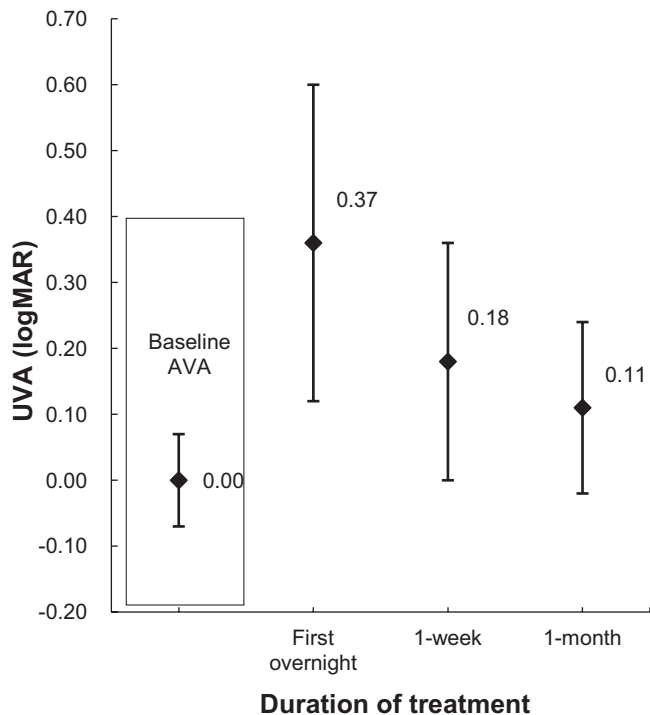


FIGURE 2. Best-corrected aided and unaided logMAR visual acuity before and after orthokeratology lens wear. BL, baseline; AVA, aided visual acuity; UVA, unaided visual acuity.

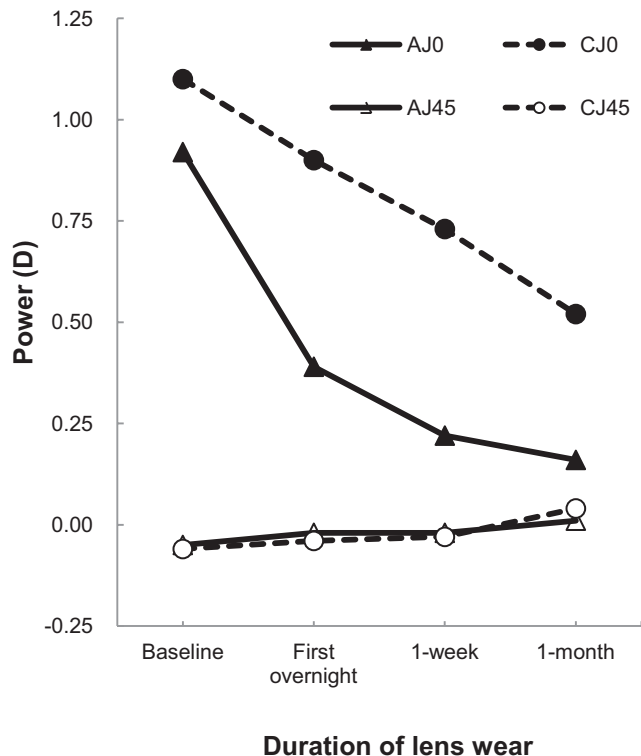


FIGURE 4. Refractive astigmatism (AJ0), corneal toricity (CJ0), refractive astigmatism (AJ45), and corneal toricity (CJ45) before and after orthokeratology lens wear.

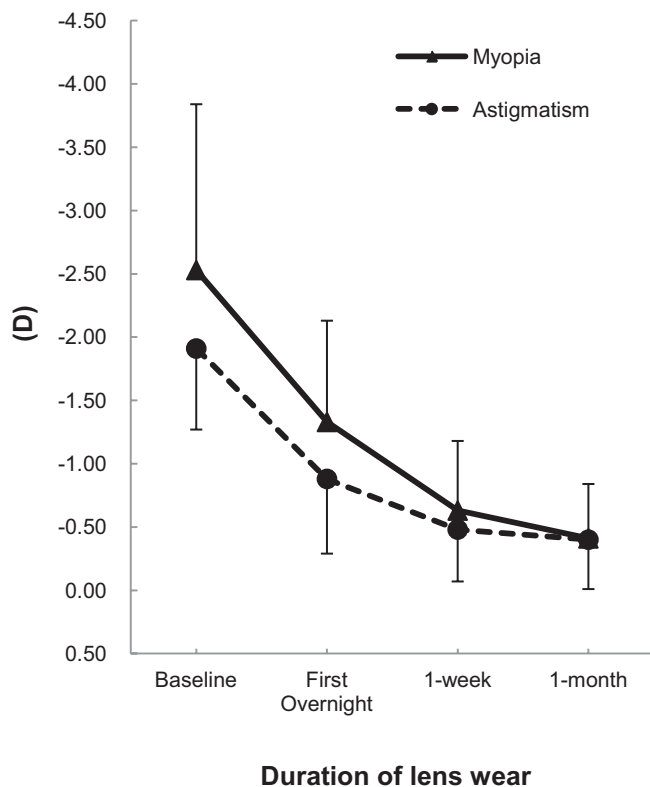


FIGURE 3. Changes in myopia and refractive astigmatism after orthokeratology lens wear.

after 1 to 2 h of lens removal.³⁴ In this study, dimple veiling was observed in 70% of the subjects at the first overnight visit. This was likely because of the requirement for subjects to return for this visit without removing their lenses. Air bubbles may have been trapped during blinking with the lenses in situ on the way to our clinic. The presence of fenestrations on the lenses used may also facilitate trapping of bubbles behind the lenses on blinking. Five of the subjects forgot the instruction and attended the first overnight visit after removing their lenses and no dimple veiling was observed in their eyes. For about 10% of the subjects, some distortions of the topographical mire image during measurements of corneal topography were observed and the situation was resolved by the use of artificial tears. Subjects were required to return with their lenses in situ at the first overnight visit to allow assessment of lens binding.

For the 40 ineligible subjects at the screening visit, 18 subjects failed the refractive criteria and 22 subjects were excluded due to inability to comply with test procedures (Fig. 2). The latter included those who refused to have cycloplegic refraction, wear ortho-k lenses (i.e., parents wanted ortho-k but not the subjects themselves), attend the frequent aftercare consultations, and those (i.e., both the subject and their parent) who failed lens insertion and removal (IR) training after multiple attempts. In this study, all subjects had to learn IR using their fingers. No suction (lens) holder was used or prescribed as this item has been reported to be frequently and heavily contaminated.^{35,36} All subjects were taught IR and if they failed to demonstrate safe IR after multiple attempts (up to five), especially for those younger than 9 years, their parents were taught how to do it for them. Each IR attempt lasted for about 30 min. All parents were taught how to recenter a dislocated lens. Lens and accessory care procedures were taught to both subjects

and parents. If care procedures were carried out by the subject, the parent had to agree to monitor compliance. These steps were taken to ensure safe ortho-k lens wear. At the 1-month visit, more than 70% of IR and care procedures were performed by the subjects themselves.

Our preliminary data showed that Night Toric RGL can be used safely, with stringent aftercare and instructions, and effectively for reductions of myopia and astigmatism in children. However, further investigation is warranted to address the issues of long-term safety and efficacy of myopia control and the results will be available after the completion of this 2-year study.

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Myopia Control Using Toric Orthokeratology (TO-SEE Study)

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PURPOSE. This nonrandomized clinical study aimed to investigate the effectiveness of toric orthokeratology (ortho-k) for myopia control in myopic children with moderate-to-high astigmatism

METHODS. We enrolled 80 subjects (aged 6-12 years; ortho-k, 43; control, 37) with myopia of 0.50 to 5.00 diopters (D), and with-the-rule astigmatism of -1.25 to -3.50 D, and unremarkable ocular and general conditions. Data collection, including visual acuity, subjective and objective refraction, axial length, corneal topography, and biomicroscopy examination, was performed every 6 months during the 24-month study period. Results from the right eye or the eye with higher astigmatism were reported.

RESULTS. A total of 35 ortho-k and 23 control subjects completed the study successfully. Subjects in both groups demonstrated axial elongation ($P < 0.001$). The average axial elongation at the end of study was 0.31 ± 0.27 and 0.64 ± 0.31 mm in the ortho-k and control groups, respectively ($P < 0.001$). At the end of 24 months, axial elongation in ortho-k subjects was 52% slower than that in the control group. Axial elongation was correlated significantly with the initial age of the subjects ($P = 0.02$) and treatment assigned ($P = 0.04$), but not with sex, initial myopia, initial refractive cylinder, or initial corneal toricity ($P > 0.08$).

CONCLUSIONS. Toric ortho-k lenses can slow axial elongation effectively in myopic children with moderate-to-high astigmatism. (ClinicalTrials.gov number, NCT00978692.)

Keywords: toric design, orthokeratology, astigmatism, myopia, myopia control

The prevalence of myopia is high in East Asia (Hong Kong, China, Taiwan, Japan, and Korea).¹⁻⁷ Vitale et al.⁸ also have reported increasing prevalence of myopia in the United States in recent decades. Hence, preventing or slowing myopic progression has attracted the interest of many clinicians and researchers. For years, researchers have been trying to find an effective method to retard or control the progression of myopia in children.⁹⁻²⁷ These myopia control treatments include bifocal spectacle lenses,^{9,25} progressive spectacle lenses,^{10,11,20} undercorrection of myopia,¹² rigid contact lenses,^{18,19,21} soft bifocal contact lenses,¹³ and pharmaceutical agents, such as atropine¹⁴ and pirenzepine.¹⁵⁻¹⁷

The potential of modern orthokeratology (ortho-k), which uses reverse geometry rigid contact lenses worn overnight to reshape the cornea and, thus, temporarily reducing myopia,^{22,24,26-31} for myopia control^{22-24,26,27,32} has been confirmed via a 24-month randomized clinical trial.³² The rate of axial elongation of the eyeball in children wearing ortho-k lenses has been reported to be 32% to 55% slower compared to those wearing single-vision spectacles or soft contact lenses.^{22-24,26,27,32} All of these studies used ortho-k lenses of spherical design on low myopes (<6.00 diopters [D]) with low astigmatism. Clinically, corneal astigmatism greater than 1.50 D (with-the-rule) is regarded as unsuitable for spherical ortho-k lenses, because of problems with poor lens centration, and limited or no correction of astigmatism.³³⁻³⁵ In patients with high corneal astigmatism (>1.50 D), lens decentration is the most common problem with spherical ortho-k lenses, and it can lead to induced astigmatism and poor vision.^{34,36} Hence,

spherical ortho-k is not indicated for children with refractive (corneal) astigmatism more than 1.50 D. However, most myopic children also are astigmatic, and the prevalence of astigmatism has been reported to be approximately 21%,³⁷ and 34%^{37,38} in Asian children 3 to 6 and 15 to 17 years old, respectively. Previous myopia control studies using various methods focused mainly on myopic children with no or low amounts of astigmatism. Considering the high prevalence of astigmatism in myopic children, there is a need for a myopia control treatment for myopic children with astigmatism to control progression of myopia, while providing clear unaided vision in the daytime.

Therefore, toric reverse geometry ortho-k designs have been developed and introduced to improve lens centration, as well as for astigmatic correction. While a number of case reports exist on the effectiveness of toric design ortho-k lenses for astigmatic correction,³⁹⁻⁴¹ to our knowledge there is no published study on the use of toric ortho-k for myopia control in children with moderate-to-high astigmatism.

At the time when this myopia control study using toric ortho-k was planned, children with moderate-to-high astigmatism were considered contraindicated for ortho-k (spherical design), and there was little evidence on the safety and effectiveness of toric ortho-k for myopic correction in astigmatic children. Without supporting evidence, a randomized study was not warranted and, hence, a nonrandomized study was conducted where parents were allowed to decide which treatment they preferred for their children, the conventional treatment (spectacles) or a new treatment (toric

TABLE 1. Inclusion and Exclusion Criteria

Inclusion criteria	
Age	6–12 y
Ethnicity	Chinese
Myopia	0.50–5.00 D
With-the-rule astigmatism	1.25–3.50 D, axis 180 ± 20
Anisometropia	: not more than 1.50 D in myopia
Best-corrected monocular visual acuity	equal to or better than 0.10 logMAR
Available for follow-up	for at least 2 y
Exclusion criteria	
Strabismus	at distance or near
Contraindications for contact lens wear and orthokeratology	(e.g., limbus to limbus corneal cylinder, dislocated corneal apex)
Prior experience with the use of soft or rigid lenses, including orthokeratology, or with myopic control	
Systemic or ocular conditions that may affect contact lens wear	(e.g., allergy and medication) or affect refractive development (e.g., Down syndrome, ptosis)

ortho-k). Therefore, the objective of this study was to determine the effectiveness of toric ortho-k lenses for myopia control, in terms of axial elongation, in myopic children with moderate-to-high astigmatism.

METHODS

This was a nonrandomized clinical study, in that parents of eligible children were allowed to select the treatment option for their children, on a first-come, first-served basis. Subjects were assigned to the other treatment group when the quota for their preferred treatment was filled up. Subjects, aged 6 to 12 years, who satisfied the inclusion criteria (Table 1), with myopia (spherical component) of 0.50 to 5.00 D (inclusive), and with-the-rule refractive astigmatism of 1.25 to 3.50 D were recruited at approximately the same time of the year. All subjects had unremarkable ocular and general health. They were fitted either with ortho-k lenses (study group) or single-vision spectacles (control group). All subjects were followed up biannually for a period of two years. This study was registered at ClinicalTrials.gov, number NCT00978692.

Subjects in the ortho-k group were fitted with Menicon Z Night Toric lenses (NKL Contactlinsen B.V., Emmen, The Netherlands) made of a material of high oxygen permeability (Table 2). All lenses used in this study were replaced annually. Details of the complimentary care solutions, ortho-k fitting, and evaluation procedures have been reported previously.⁴² Subjects in the control group were fitted with single-vision spectacles made of CR39 material with refractive index of 1.56 (Hong Kong Optical Lens Co., Hong Kong, China). For all subjects, at each subsequent 6-month visit after baseline visit, ortho-k lenses/spectacles were updated if habitual visual acuity (HVA; for the ortho-k subjects, HVA referred to the unaided visual acuity [VA]) was found to be worse than 0.18 logMAR, or if refractive error (either myopia or astigmatism) increased by 0.50 D or more compared to the previous visit. Ortho-k subjects whose HVA was worse than 0.18 logMAR and could not be improved despite lens modification ($\times 3$) were discontinued. For all subjects, those presenting significant adverse events, or failing to comply with the prescribed procedures despite repeated reeducation or reminders were terminated from the study.

The study complied with the tenets of the Declaration of Helsinki in 2002 and ethics clearance was approved by the Departmental Research Committee of School of Optometry of

TABLE 2. Parameters of Z Night Contact Lens Used in This Study

Manufacturer	NKL
Material name	Siloxanylstyrene fluoromethacrylate (tisifilcon A)
Design	Parallel reverse geometry
Dk, barrer	163
Back optic zone radius, mm	7.2–9.50 (0.05 step)
Basic optic zone diameter, mm	6
Overall lens diameter, mm	10.2/10.6/11.0
Tangential angle, deg	50–65 (1 step)
Sagittal depth, mm	0.50–0.99 (0.01 step)
Central thickness, mm	0.24

The Hong Kong Polytechnic University. Consent and assent from parents and subjects, respectively, were obtained after a detailed explanation of the examination procedures and a complete disclosure of the effects of the topical cycloplegic used. Upon completion or withdrawal from the study, ortho-k subjects were required to return all the prescribed ortho-k lenses and solutions to the examiner.

Examination Procedures

Each subject received a detailed eye examination to confirm normal ocular condition before the commencement of the study. Cycloplegic eye examination was performed at the baseline visit and once every 6 months over a period of 2 years. Before the cycloplegic examination at each data collection visit, high contrast (100%) and low contrast (10%) HVA, and best corrected VA (BCVA) were measured with the Early Treatment Diabetic Retinopathy Study (ETDRS) charts (Precision Vision, La Salle, IL) under normal room lighting condition. Anterior ocular health assessment was performed and any abnormality, if observed, was graded using Efron grading scales.⁴² Corneal topography was measured using the Medmont E300 corneal topographer (Version 3.9.3; Medmont Pty. Ltd., Camberwell, Australia) for monitoring changes in the corneal profile during the study period.

Axial length measurements (Zeiss IOLMaster; Zeiss Humphrey Systems, Dublin, CA) were performed by a masked examiner at least 30 minutes after the administration of 1 drop of 0.5% Alcaine, 1 drop of 1% tropicamide, and 1 drop of 1% cyclopentolate, at 5 minutes apart. Axial length measurements were performed according to the manufacturer's instructions. Five consecutive readings were recorded and averaged for analysis.

Sample Size

This myopia control study was designed to achieve 80% power to detect a minimum difference 0.18 mm (0.50 D) difference in axial length in 2 years at 5% level of statistical significance, using the within group SD of 0.27 mm from our previous report.²² Based upon these calculations, a sample size of at least 20 subjects would be required for each group.

Treatment of Data

Statistical analyses were performed using SPSS (ver 18.0; SPSS, Inc., Chicago, IL). Data from the eye with higher astigmatism of each subject were analyzed in this study. Data from the right eye were used if the amount of astigmatism was the same in both eyes. Since all data were distributed normally (Kolmogorov-Smirnov test, $P > 0.05$), parametric tests were used for data analysis. For comparison of baseline data between the two

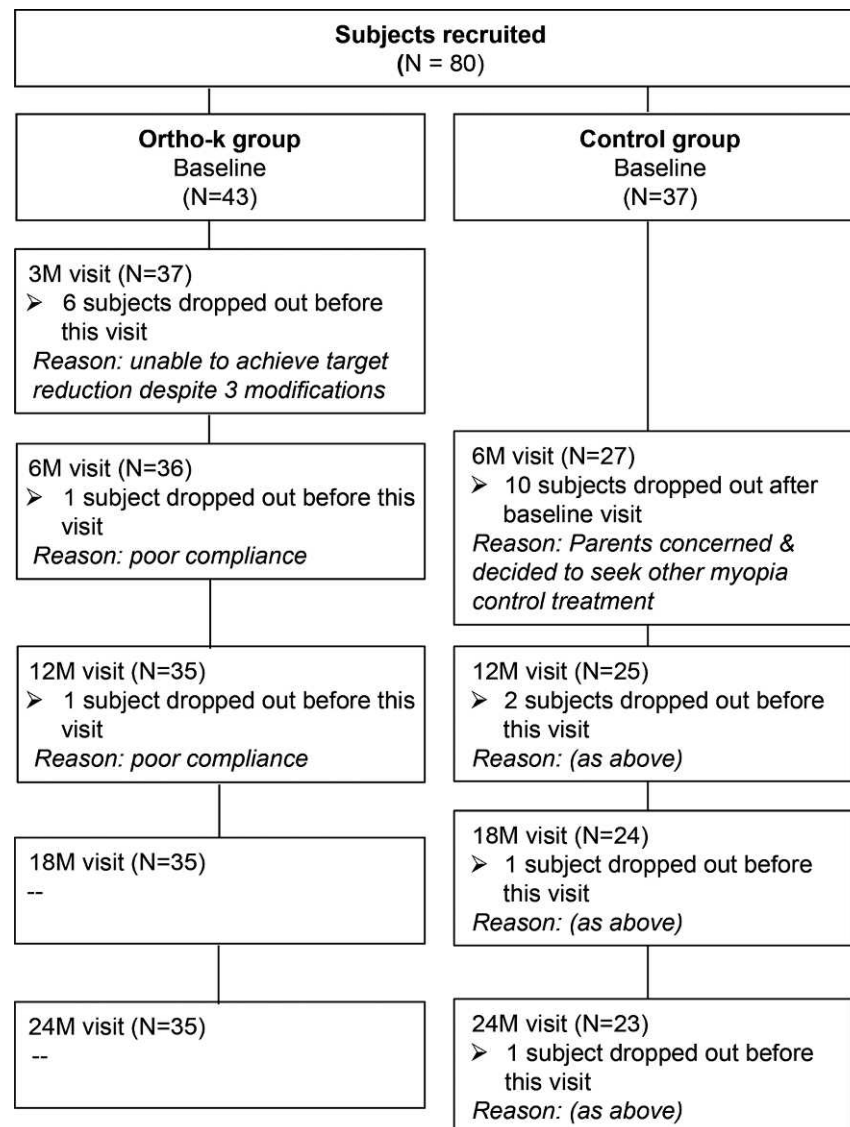


FIGURE 1. Number of subjects (and reasons for) dropping out at different visits.

groups, unpaired *t*-tests were used. Repeated measures ANOVA with post hoc tests were used to compare axial length obtained from the baseline and the 6-monthly visits in the two groups of subjects. Unpaired *t*-tests with Bonferroni correction ($\alpha \leq 0.01$) were used to test for differences between groups. To obtain further insight into the observed treatment effect, crosstab analyses were used to compare the proportions of fast myopia progressors (>1.00 D per year) in the ortho-k and control groups, although each subgroup sample size in these analyses was small. Factors affecting axial elongation, including age, initial myopia, astigmatism, corneal toricity, and treatment, were investigated using stepwise multiple linear regression analysis.

RESULTS

We fitted 43 subjects with ortho-k lenses and 37 control subjects with single-vision spectacles. **Only 35 subjects (18 males and 17 females) in the ortho-k group successfully completed the 24-month study** (Fig. 1). Of the eight subjects who dropped out, six could not achieve the target reduction in

HVA after 3-month lens wear despite lens modifications (3 times) and two subjects showed poor compliance during the study period, one before the 6-month visit and one before the 12-month visit.

Only 23 subjects (eight males and 15 females) in the control group completed the study; 10 subjects dropped out after the baseline visit, two after the 6-month visit, one after the 12-month visit, and one after the 18-month visit. The main reason for dropout was parental anxiety about the myopic progression in their children. None of the dropouts in either group of subjects was due to ocular adverse events.

No statistically significant differences in baseline values (age, myopia, astigmatism, corneal astigmatism, BCVA, and axial length) were found between those who completed and those who dropped out of the study (unpaired *t*-tests, $0.14 < P < 0.43$). The mean \pm SD ages of the ortho-k and control subjects who completed the study were 9.4 ± 1.4 and 8.9 ± 1.6 years, respectively, when they commenced this study, and their baseline data are shown in Table 3.

Figures 2A and 2B show the high and low contrast HVA and BCVA of the subjects, respectively. There were no significant differences in the high and low contrast HVA and BCVA during

TABLE 3. Baseline Characteristics of Subjects Who Completed the 2-Year Study

	Ortho-k Group, <i>n</i> = 35, 18 Male/ 17 Female	Control Group, <i>n</i> = 23, 8 Male/ 15 Female
Age, y	9.4 ± 1.4	8.9 ± 1.6
Myopia, D	-2.46 ± 1.32	-2.04 ± 1.09
Refractive astigmatism, D	-1.86 ± 0.64	-2.07 ± 0.56
Corneal astigmatism, D	-2.28 ± 0.53	-2.43 ± 0.62
Best-corrected VA, logMAR	0.00 ± 0.05	-0.02 ± 0.03
AL, mm	24.37 ± 0.88	24.18 ± 1.00

Values are mean ± SD. AL, axial length.

the study period in both groups of subjects (repeated measures ANOVAs with post hoc tests, $P > 0.05$). Changes in high and low contrast HVA and BCVA were not significantly different between the two groups of subjects at any visit during the study (unpaired t -tests, $P > 0.01$). At the 24-month visit, in the ortho-k and control groups, the mean ± SD high contrast logMAR HVA values were 0.08 ± 0.11 and 0.08 ± 0.13 , respectively, and high contrast logMAR BCVA values were -0.03 ± 0.05 and -0.04 ± 0.03 , respectively.

Mean ± SD low contrast HVA values for the ortho-k and control groups were 0.36 ± 0.15 and 0.27 ± 0.14 , respectively, and low contrast BCVA values were 0.20 ± 0.08 and 0.14 ± 0.05 , respectively.

Figure 3 shows the refractive errors of the subjects at different visits during the study period. For the ortho-k

subjects, there was a significant change in myopia and astigmatism over time (repeated measures ANOVA; myopia, $P < 0.001$; astigmatism, $P < 0.001$), but this was only due to significant decreases at the 6-month visit. Myopia reduced from 2.46 ± 1.32 D (baseline) to 0.18 ± 0.37 D (6-month, paired t -tests, $P < 0.001$) while astigmatism reduced from -1.86 ± 0.64 D (baseline) to -0.37 ± 0.39 D (6-month, paired t -tests, $P < 0.001$). Myopia and astigmatism at subsequent visits were not significantly different in the ortho-k group (repeated measures ANOVA (6-, 12-, 18-, 24-month; myopia, $P = 0.06$; astigmatism, $P = 0.83$). For the control subjects, the amount of myopia increased with time at every 6-month visit (repeated measures ANOVA, $P < 0.001$). Myopia increased gradually from 2.04 ± 1.09 D at baseline to 3.17 ± 1.22 D at the 24-month visit (paired t -tests, $P < 0.001$). Astigmatism remained unchanged during the study period (repeated measures ANOVA, $P = 0.07$). It was 2.07 ± 0.56 D at baseline and 2.10 ± 0.51 D at the 24-month visit (Fig. 3).

Changes in axial length during the study period are shown in Figure 4. Subjects in both groups demonstrated significant axial elongation (repeated measures ANOVA; ortho-k, $P < 0.001$; control, $P < 0.001$). Axial elongation was significantly slower in the ortho-k group than in the control group at every 6-month visit (unpaired t -tests, $0.01 < P < 0.001$). The mean ± SD increase in axial length in ortho-k subjects was 0.33 ± 0.05 mm less than the control subjects at the end of the 24-month study period (Table 4). The levels of reduction of myopia progression compared to the spectacle-wearing control group were 61%, 58%, 53%, and 52% after 6, 12, 18, and 24 months of ortho-k lens wear.

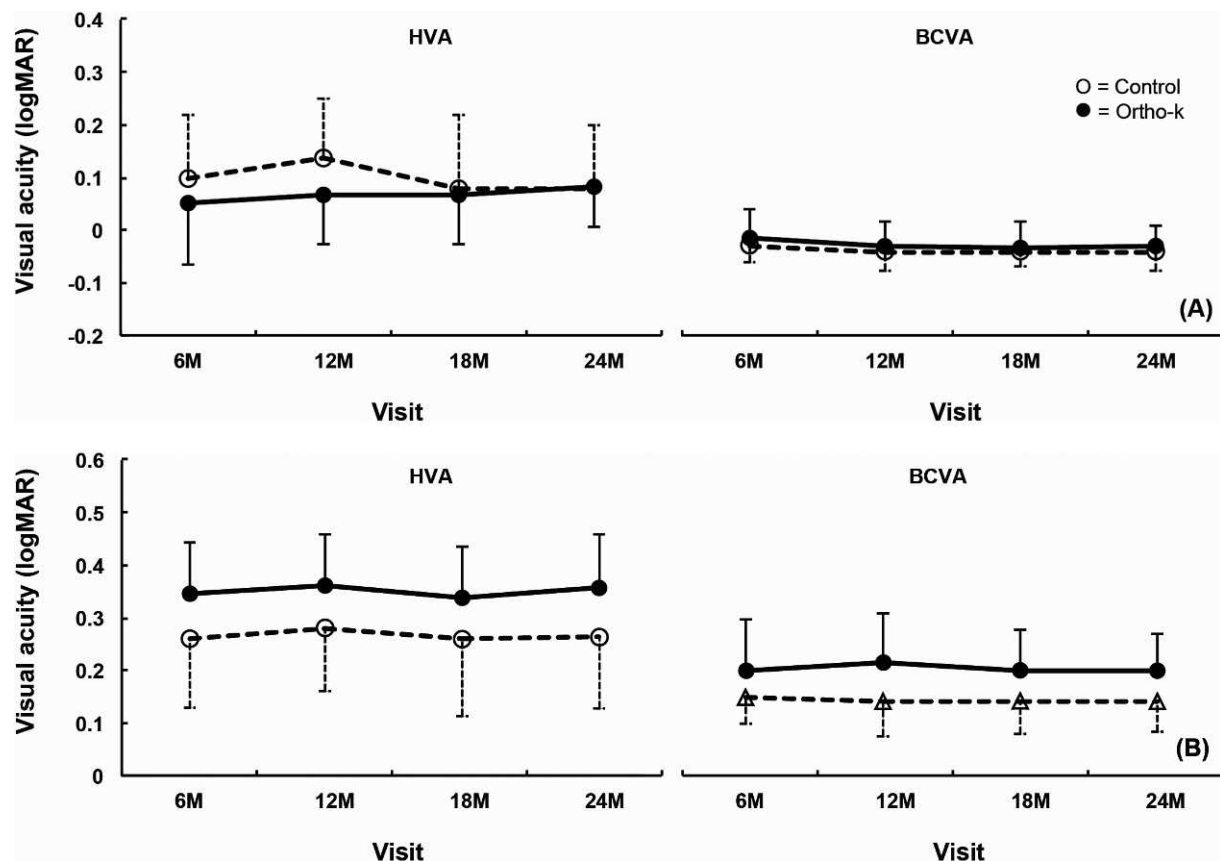


FIGURE 2. High contrast (A) and low contrast (B) HVA and BCVA logMAR visual acuities at different visits during the study period (HVA logMAR VA in orthokeratology subjects = unaided VA). Each error bar represents 1 SD. M, month.

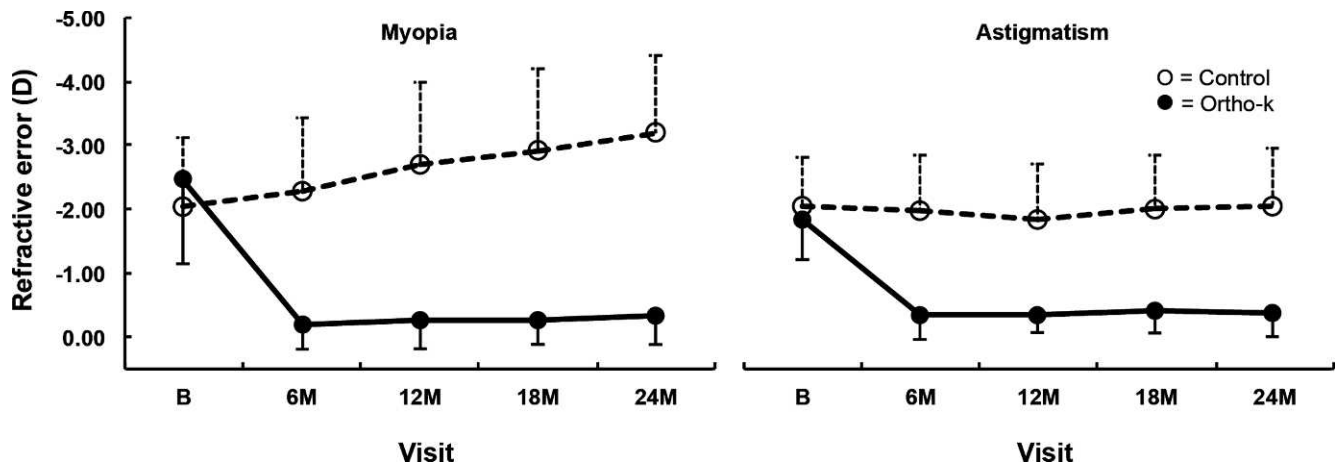


FIGURE 3. Cycloplegic subjective refractive error changes at different visits during the study period. Each error bar represents 1 SD. B, baseline.

At the end of the 24-month monitoring period, seven subjects in the control group demonstrated fast myopic progression (myopic progression exceeding 1.00 D per year or axial elongation > 0.36 mm per year), while only one subject in the ortho-k group had fast myopic progression. The odds of becoming fast progressors was 14.9 times greater in children wearing single-vision spectacles than those wearing ortho-k lenses (95% confidence interval [CI], 1.7–131.3; Fisher's exact test, $P = 0.005$). Stepwise multiple linear regression analysis showed that among the predicting factors, axial elongation was correlated significantly with the initial age of the subjects (standardized $\beta = -0.30$, $P = 0.02$) and treatment assigned (standardized $\beta = -0.36$, $P = 0.04$). However, axial length elongation was not affected by sex, initial myopia, initial refractive cylinder, or initial corneal toricity (partial r , -0.36 – 0.22 , $P > 0.08$).

No significant adverse event was observed in either group of subjects. Only mild corneal staining (grade 1) was observed in both groups of subjects at different visits (Table 5) and most were in the inferior cornea. There were no changes in the incidence of inferior corneal staining over time in the ortho-k group (17%–23%). However, in the control group, the incidence of inferior corneal staining was lower at the 24-month visit (baseline to 18 month visits, 14%–20%; 24 month visit, 9%). The incidence of mild central corneal staining was not common in either group of subjects; two observations in the control group and five observations in the ortho-k group over the 24-month study period. Superior and nasal corneal

staining in the control group was rare, and no corneal staining was observed in the temporal cornea of the control subjects. Incidences of mild corneal staining in the peripheral corneal regions appeared to increase after ortho-k lens wear, especially in the inferior cornea. No lens binding was reported after 1 month of lens wear.

DISCUSSION

To our knowledge, this is the first longitudinal clinical study to investigate the effectiveness of toric design ortho-k for controlling myopic progression in myopic children with moderate-to-high amounts of astigmatism. Our results showed that toric design ortho-k effectively corrected myopia and astigmatism, providing the ortho-k subjects with high and low contrast unaided visual acuities comparable to the HVA of the control subjects after stabilization of ortho-k treatment. There have been reports of consistent reductions in contrast sensitivity, including low contrast BCVA, and the area under the log contrast sensitivity function after the commencement of ortho-k lens wear.^{43–45} These researchers also have reported significant increases in higher-order aberrations with ortho-k lens wear, which was consistent with the reduced contrast sensitivity finding. However, our results did not agree with their findings, as we observed consistently no changes in low contrast BCVA over time (Fig. 2B). The differences in findings between studies may be due to different methodologies (e.g., different charts used, dilated versus nondilated pupil, lighting) used, and our subjects were children, whereas previous reports were on adults. Toric design ortho-k lenses also can slow myopic progression in children with myopia and moderate-to-high astigmatism.

Reports discussing the relationship between myopia and astigmatism are scarce.^{37,46} Saw et al.⁴⁶ reported no difference in the increase in myopia between astigmats (astigmatism > 0.50 D) and nonastigmats in children 6 to 11 years old, but they did not investigate the association between initial astigmatism and myopic progression. Fan et al.³⁷ reported an association between astigmatism and myopic progression among Asian children aged 3 to 6 years old, but it appeared that their subjects were mostly hyperopes. Unfortunately, they did not provide further information about the myopic and astigmatic progression in their subjects.

The relationship between the baseline astigmatism and axial elongation of our subjects was analyzed, and our result showed no correlation between these two factors. Since the current study did not include children with low astigmatism, to have

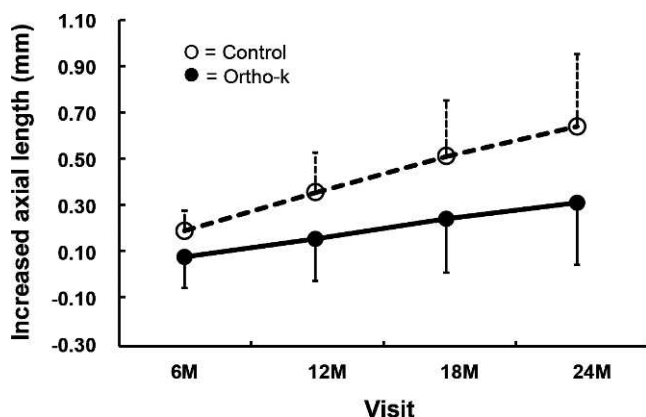


FIGURE 4. Changes in axial elongation (mean \pm SD) at different visits during the study period. Each error bar represents 1 SD.

TABLE 4. Increases in Axial Length in Orthokeratology and Control Subjects at Different Visits During the Study Period

	Orthokeratology, mm, <i>n</i> = 35	Control, mm, <i>n</i> = 23
6 mo	0.07 ± 0.13	0.19 ± 0.08
12 mo	0.15 ± 0.18	0.36 ± 0.16
18 mo	0.24 ± 0.23	0.51 ± 0.24
24 mo	0.31 ± 0.27	0.64 ± 0.31

Values are mean ± SD.

better understanding of the effect of astigmatism on myopic progression in children, we compared our results to those obtained from the ROMIO study,⁵² which was a randomized clinical trial on the use of ortho-k for myopia control in myopic children with no or low astigmatism. TO-SEE and ROMIO studies were conducted concurrently at the same location by the same research group. The inclusion criteria of the two studies differed in age (up to 10 years old in ROMIO and up to 12 years old in TO-SEE) and refractive astigmatism (“low astigmats,” refractive [corneal] astigmatism of less than 1.25 D in ROMIO study; “moderate-high astigmats,” refractive [corneal] astigmatism 1.25 D or more in the TO-SEE study). There were no significant differences in the initial myopia among the four groups of subjects (low or moderate-high astigmats fitted with ortho-k or spectacles, 1-way ANOVA, $F_{3,132} = 1.30$, $P = 0.28$). We used analysis of covariance to adjust the effect of age and initial myopia, and to test for differences between low astigmats and moderate-high astigmats wearing ortho-k lenses or single-vision spectacles. There were no differences in the axial elongation between the low and moderate-high astigmats wearing single-vision spectacles (1-way ANCOVA, $F_{1,60} = 0.20$, $P = 0.66$) or ortho-k lenses (1-way ANCOVA, $F_{1,68} = 0.28$, $P = 0.60$). The 24-month axial elongations were 0.63 ± 0.26 and 0.65 ± 0.31 mm in low astigmats and moderate-high astigmats, respectively, wearing single-vision spectacles, and were 0.36 ± 0.24 and 0.33 ± 0.28 mm in low astigmats and moderate-high astigmats, respectively, wearing ortho-k lenses. That is, myopic progression was not affected by the initial refractive astigmatism of the eye, but by the method of vision correction given to the subjects.

Corneal complications associated with any contact lens wear can lead to vision impairment and potential blindness.⁴⁷ Many clinicians/researchers are concerned with the potentially increased risk involving overnight wear of contact lenses.^{48–50} Microbial keratitis in ortho-k lens wear has been reported in case studies,^{51,52} but not in clinical studies, which usually require and may involve a higher standard of care given to the subjects. Clinical studies on ortho-k for myopia control published to date, including the current study, have shown no severe adverse events that left permanent damage to the eye or vision.^{23,24,26,32} That is, with stringent management protocol (e.g., proper education and review on lens handling, and lens care products and procedures, frequent aftercare visits, education, and reeducation of patients and parents, and delivery of written and verbal instructions), complications associated with ortho-k lens wear can be minimized. Santodomingo-Rubido et al.⁴⁸ reported adverse events, such as contact lens-induced peripheral ulcer and conjunctivitis, but they also reported that the conditions “are not considered to be serious, are similar to those reported with other contact lens types, and can be managed easily in clinical practice.”

In the current study, we found no significant adverse events in both groups of subjects. Although ortho-k lens wear tended to increase the incidence of corneal staining in the peripheral cornea, the staining observed was considered to be mild, as depth of staining was mostly superficial (grade 1) and the

TABLE 5. Percentages of Mild Corneal Staining (Not More Than Grade 2) at Different Corneal Locations in Orthokeratology and Control Subjects at Different Visits

Location	Baseline, %	6-mo, %	12-mo, %	18-mo, %	24-mo, %
Ortho-k, <i>n</i> = 35					
Central	0	0	2.9	5.7	5.7
Inferior	22.9	17.2*	17.2*	17.1	17.1
Superior	2.9	5.7	8.6	14.3	8.6
Nasal	0	5.7	0	2.9	5.7
Temporal	0	2.9	5.7	2.9	0
Control, <i>n</i> = 23					
Central	2.9	0	0	2.9	0
Inferior	20.0	20.0	14.3†	17.1	8.6
Superior	2.9	0	0	5.7	2.9
Nasal	0	2.9	0	0	0
Temporal	0	0	0	0	0

Grading is based on Efron's scale.⁴³

* One subject showed grade 2 corneal staining.

† Two subjects showed grade 2 corneal staining.

average incidence was less than 10%. The situation was similar to wearing any other types of daily wear soft contact lenses.⁵³ Such minor ocular problems can be monitored and managed easily by early detection and treatment, such as use of artificial tears for lubrication.

Poor lens cleaning procedure and poor lens hygiene may increase the risk for infection in ortho-k patients as lenses are worn overnight. Therefore, providing careful and specific education in the care of ortho-k lenses to parents and children is important to minimize complications in ortho-k lens wear.

Lens binding has been reported to be the most common nonvisual problem in ortho-k lens wear^{33,54,55} and is a risk factor for corneal staining. However, in the current study, no lens binding was reported after 1 month of lens wear. The low incidence of lens binding may be due to the use of fenestrated lenses⁵⁶ and application of artificial tears to the eye before lens removal. All ortho-k subjects were required to remove the lens from each eye using their fingers instead of a lens remover. These steps may have aided lens mobility after waking up and minimized lens binding.

In ortho-k, the reshaped cornea changed relative peripheral refraction of the myopic eyes from relative hyperopia to relative myopia, and this appears to be consistent with the suggestion that relative peripheral hyperopia drives myopic progression.⁵⁷ However, further evidence is required before any firm conclusion can be made on the mechanism of myopia control in ortho-k. The effectiveness of ortho-k for myopia control, in terms of axial elongation, has been reported to range from 32% to 55%.^{22,23,26,27,32} To our knowledge, the only randomized longitudinal clinical trial published to date on ortho-k for myopia control reported 43% effectiveness.³² Axial elongation of subjects wearing toric ortho-k lenses was 52% slower compared to subjects wearing spectacles in our study. However, as this was a nonrandomized study, systematic bias cannot be ruled out. In our study, the odds of children having fast progression in myopia (more than 1.00 D per year) were reduced with the use of ortho-k lenses. However, no conclusive evidence can be drawn on this issue from this study, as only eight subjects demonstrated fast progression. Our results also may be affected by selection bias, since the number of subjects with faster progression may not have been balanced at the beginning of the study without randomization. A randomized clinical trial would have provided better evidence on the effectiveness of using toric ortho-k for myopia control in myopic children with significant astigmatism.

Another potential limitation is that it is unknown if the treatment effect continues after year 2. We believe that a randomized clinical trial now is warranted, in light of the evidence from this study, to confirm the effectiveness of toric ortho-k for myopia control.

Apart from being effective and safe, a good myopia control treatment also should provide convenience for children's daily activities. If the treatment is causing inconvenience or problems, a high dropout rate would be expected. The dropout rates in ortho-k ranged from 6%²⁷ to 30%²³ in previous studies. In our study, the dropout rates were 19% (8/43) and 38% (14/37) in the ortho-k and control groups, respectively. The reasons for dropouts in the two groups of subjects differed. All dropouts in the control group were initiated by the parents. They were concerned and worried about the myopic progression in their children, and decided to withdraw from the study to seek myopia control treatment for their children. On the other hand, dropouts in the ortho-k group were initiated by the investigators, either because of the unsatisfactory ortho-k lens wear that affected the daytime vision (six of eight subjects) or noncompliance to the study protocol (stopped lens wear from time to time without notifying the investigator), which affected the daytime vision and, therefore, the results of myopia control (two subjects). The dropout results may be an indication that parents in Hong Kong are very concerned about myopic progression in their children, and are eager to seek effective treatment to slow myopia. However, not all children are suitable to wear ortho-k lenses and even those who had good response in the beginning may not continue to show good or satisfactory responses with continued lens wear. Good ocular and visual responses require combined efforts from the practitioners, the children, and their parents. Subjects wearing ortho-k lenses who completed the study had comparable visual quality to those wearing single-vision spectacles, but enjoyed the additional benefit of convenience from spectacle-free vision in the daytime.

CONCLUSIONS

This nonrandomized study has provided evidence that toric ortho-k lenses can provide clear unaided vision for myopic children with moderate-to-high astigmatism, and can slow axial elongation effectively in these children.

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CLINICAL COMMUNICATION

Toric orthokeratology for high myopic and astigmatic subjects for myopic control

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Spherical reverse geometry lens (RGL) designs used in orthokeratology (ortho-K) are effective in correcting low to moderate myopia^{1–3} but ineffective in correcting moderate to high astigmatism.^{1,3,4} Tahhan and colleagues found no significant change in the refractive astigmatism of 46 subjects who had been on ortho-K treatment for three months.² Their observation was confirmed by another study on 30 subjects who had been wearing ortho-K lenses for more than 12 months.¹ The most common problem with ortho-K lenses of spherical designs on patients with corneal astigmatism is lens decentration, which can lead to induced astigmatism and poor vision.³

Clinically, corneal toricity greater than -1.50 DC (with-the-rule) is regarded as unsuitable for spherical ortho-K, although some authors^{4,5} have reported limited correction of astigmatism using spherical ortho-K lenses. Hence, toric reverse geometry lens designs have been developed for moderate to high corneal astigmatism, although there are no published papers on these designs.

The current report presents the findings for two young subjects whose parents were concerned about their myopic progression and who wanted to enrol in our toric ortho-K project with Menicon Z Night Toric lens (NKL Contactlinsen BV, Emmen, the Netherlands). Both subjects had high myopia and high astigmatism and failed the refraction criteria for that project. Although this lens design is recommended by the manufacturer for myopia up to 4.00 D, we decided to try this lens design on these two high myopic and astigmatic subjects. The main objective was to limit myopic progression and to correct the initial astigmatism. As full reduction in myopia was not deemed possible, the subjects would be required to wear spectacles during the day to correct their residual refractive errors. All procedures followed the tenets of the Declaration of Helsinki revised in 2002 and ethics approval was obtained from the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University. Both the parents and subjects were fully informed of the risks and benefits of the procedure and agreed to the treatment protocol.

The parents of both subjects signed informed consent before commencement of the study. All lenses used were complimentary from the manufacturer.

Menicon Z Night Toric lens of toric design were fitted to the two subjects using stepwise reduction (Figure 1). This lens has a toric alignment curve and a spherical back optical zone radius and reverse

curve. The fitting philosophy used was the Jessen Factor⁶ with a compression factor of 0.50, that is, to achieve the desired amount of myopic reduction, the eye is fitted with a lens of back optic zone radius, which is flatter than the flattest K by the same amount +0.50 (Figure 1). [Corrections added after online publication 22 September 2011: 'without' is replaced by 'with' in '... was the Jessen Factor with ...'; 'of 0.50' is added after '... a compression factor ...'; '+0.50' is added before '(Figure 1)'] If the cornea under-responds (that is, fails to achieve the targeted reduction in myopia) even though the topographic map shows a bull's eye pattern, a lens with increased target (by 1.00 D) will be used to try to achieve further reduction. If no significant reduction is achieved with the higher target lens, lens wear will be continued with the previous lens of lower target.

No trial lens set is necessary for this lens design. Pertinent data including refractive power and horizontal visible iris diameter are entered into the computer (NKL Easy Fit Software, Emmen, The Netherlands) with imported corneal topographic maps and the software calculates the initial lens parameters for the eye.

Corneal topography was performed using the Medmont E300 corneal topographer (Version 3.90, Medmont Pty Ltd, Melbourne, VIC, Australia) and the axial length was monitored with the IOLMaster (Zeiss Humphrey System, Dublin, CA, USA). Each axial length measurement was the average of five consecutive readings,

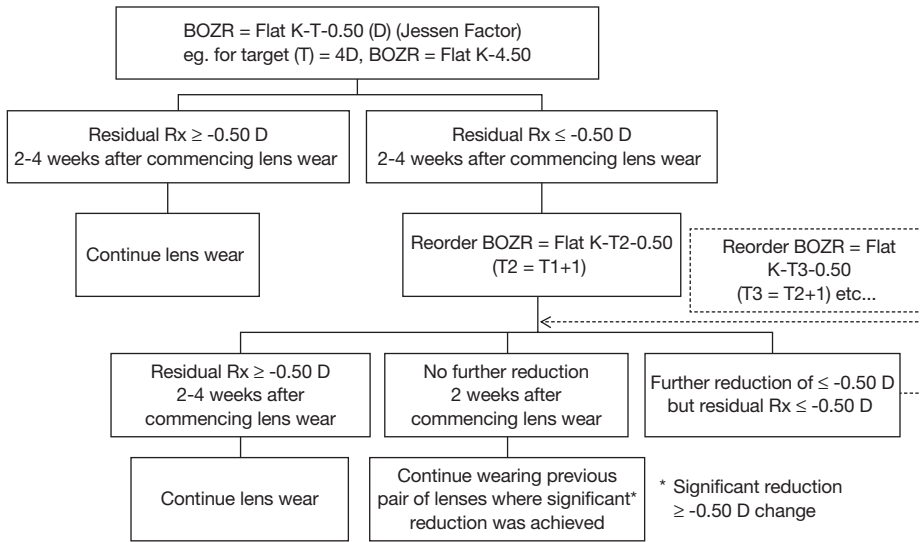


Figure 1. Fitting philosophy of the lens design used and stepwise correction procedures for highly myopic eyes [Corrections added after online publication 22 September 2011: ‘-0.50’ is added to and ‘4’ is amended to ‘4.50’ in the topmost box; ‘-0.50’ is added to the middle and right boxes in the third row.]

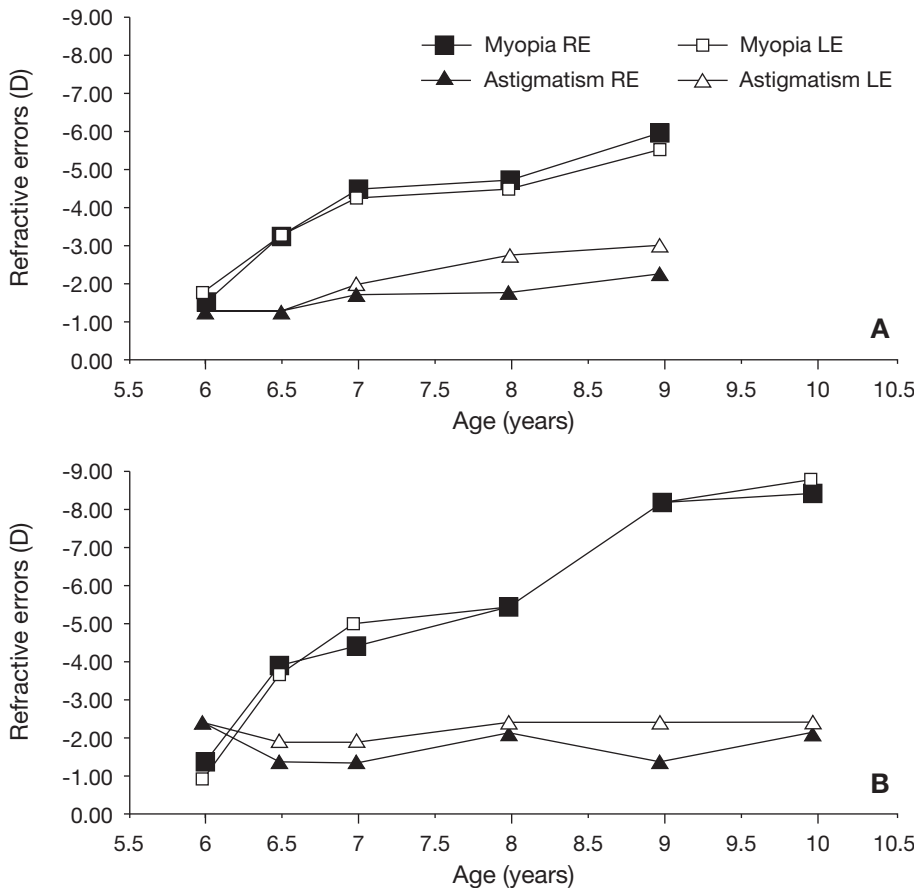


Figure 2. History of refractive status of (A) Subject 1 and (B) Subject 2 before commencing orthokeratology treatment. LE, left eye; RE, right eye.

which were within 0.02 mm of one another as recommended by the manufacturer.

The lens care system prescribed included O₂ care cleaner, Menicare Plus and Progent A+B by Menicon Co., Ltd, Nagoya, Japan and B & L sensitive eye saline (Bausch & Lomb, Inc., Rochester, NY, USA). All solutions were complimentary to the subjects. Follow-up visits included first overnight, one week, one, three and six months and every three months thereafter. At the first overnight, one-week and one-month visits, both subjects were required to return to the clinic within two hours of waking in the morning. The subjects were required to wear their lenses at the first overnight visit to ensure that there was no significant lens binding.

Both subjects achieved only partial reduction of myopia and, while one achieved close to full reduction of astigmatism, the other only achieved 30 to 40 per cent reduction. These two subjects demonstrate differences in corneal and refractive responses to toric ortho-K lenses; however, myopic progression (axial length change) was retarded in both subjects during the 12-month monitoring period.

CASE REPORTS

Subject 1

Subject 1 was a nine-year-old girl. Refractive errors (in the spectacle plane) at the baseline visit were -6.00/-2.25 × 5 R and -5.50/-3.00 × 180 L with logMAR (Snellen) visual acuities of 0.10 (6/7.5) and 0.00 (6/6), respectively. Figure 2A shows the refractive history before the subject commenced ortho-K treatment as determined from previous spectacles and the subjective refraction measured at the first visit before fitting ortho-K lenses (baseline).

The subject had no contraindications for contact lens wear. Corneal astigmatism for the right and left eyes was 2.70 DC and 3.40 DC, respectively, and axial lengths were 25.01 mm and 24.77 mm, respectively.

Table 1 shows the lenses ordered for this subject and Figure 3A shows changes to the refractive sphere (in the corneal

(A) Subject 1					
Baseline K-readings					
Eye	Flat K (mm)	Steep K (mm)			
R	7.82	7.36			
L	7.86	7.31			
Lens parameters					
First pair of lenses					
Eye	Target (D)	BC (mm)	Tangent (°)	Height (mm)	Diameter (mm)
R	-4.00	8.6	56/53	0.70/0.80	10.6
L	-4.00	8.6	56/52	0.70/0.82	10.6
Second pair of lenses					
R	-5.00	8.8	56/53	0.71/0.81	10.6
L	-5.00	8.8	56/52	0.71/0.83	10.6
Third pair of lenses					
R	-6.00	9.0	56/53	0.73/0.83	10.6
L	-6.00	9.0	56/52	0.72/0.84	10.6
(B) Subject 2					
Baseline K-readings					
Eye	Flat K (mm)	Steep K (mm)			
R	7.33	6.83			
L	7.29	6.8			
Lens parameters					
First pair of lenses					
Eye	Target (D)	BC (mm)	Tangent (°)	Height (mm)	Diameter (mm)
R	-4.00	7.9	57/54	0.58/0.66	10.2
L	-4.00	7.85	57/53	0.58/0.68	10.2
Second pair of lenses					
R	-5.00	8.1	57/54	0.59/0.67	10.2
L	-5.00	8.05	55/52	0.59/0.69	10.2
Third pair of lenses					
R	-6.00	8.3	57/54	0.60/0.68	10.2
L	-6.00	8.25	57/53	0.60/0.71	10.2

Table 1. K-readings and parameters of lenses ordered for (A) Subject 1 and (B) Subject 2 during the 12-month lens wear

plane) and Figure 4A shows the refractive astigmatism (in the corneal plane) and corneal toricity with ortho-K lens wear.

At the early morning visit after the first overnight lens wear (8.5 hours), no lens binding or significant corneal staining was observed. The residual subjective

refractive errors (in the spectacle plane) were $-5.50/-2.25 \times 175$ R and $-5.25/-2.50 \times 180$ L and the objective refraction from a Shin-Nippon autorefractor (Shin-Nippon Commerce Inc., Tokyo, Japan) showed similar results. Visual acuities were 0.04 (6/6⁻²) R and 0.04 (6/6⁻²) L. Subtrac-

tive tangential maps showed a bull's eye pattern^a in both eyes. Due to significant residual refractive errors (Figure 3A), the subject was advised to wear an old pair of spectacles (refractive powers $-4.50/-1.75 \times 180$ R and $-4.50/-2.75 \times 180$ L) in the daytime and to continue lens wear every night.

At the three-month visit, the residual refractive errors (in the spectacle plane) were $-4.00/-2.00 \times 180$ (0.10 [6/7.5]) R and $-4.00/-2.00 \times 180$ (0.06 [6/6⁻³]) L. Due to the slow myopic reduction, a new pair of lenses (target: 5.00 D) was ordered (Table 1).

One week after wearing the new pair of lenses, binocular unaided vision was 0.24 and the residual refractive errors were $-2.50/-0.75 \times 15$ R and $-1.75/-1.25 \times 15$ L. Spectacles with a lower prescription ($-2.50/-0.75 \times 15$ R and $-1.75/-1.25 \times 15$ L) were prescribed to correct the residual refractive errors. No significant improvement was found in the topography and refractive errors when the subject returned three weeks later. A third pair of lenses was ordered with target increased by a further 1.00 D (Table 1). After wearing these lenses for one month, further myopic reductions of 0.50 D R and 0.25 D L were observed and the subject was allowed to continue wearing the lenses. Two months later, at the 12-month visit, although the corneal topography of both eyes still presented bull's eye patterns, the residual refractive errors had increased (worsened) to $-3.50/-1.50 \times 180$ R and $-2.75/-1.75 \times 175$ L.

Figure 5 shows the axial length elongation of 0.09 mm (equivalent to approximately 0.25 D⁷) during the 12-month ortho-K lens wear. Central corneal thickness decreased by 0.007 mm in the right eye and 0.001 mm in the left eye. Although full reduction was not achieved, both the subject and parents were happy with the achieved myopic reduction and the low degree of myopic progression during the 12-month lens wear.

a. In ortho-K, the bull's eye pattern is an indication of good centration with good alignment at the peripheral cornea. The subtractive topographical map shows a 'red ring' centred with respect to the pupil.

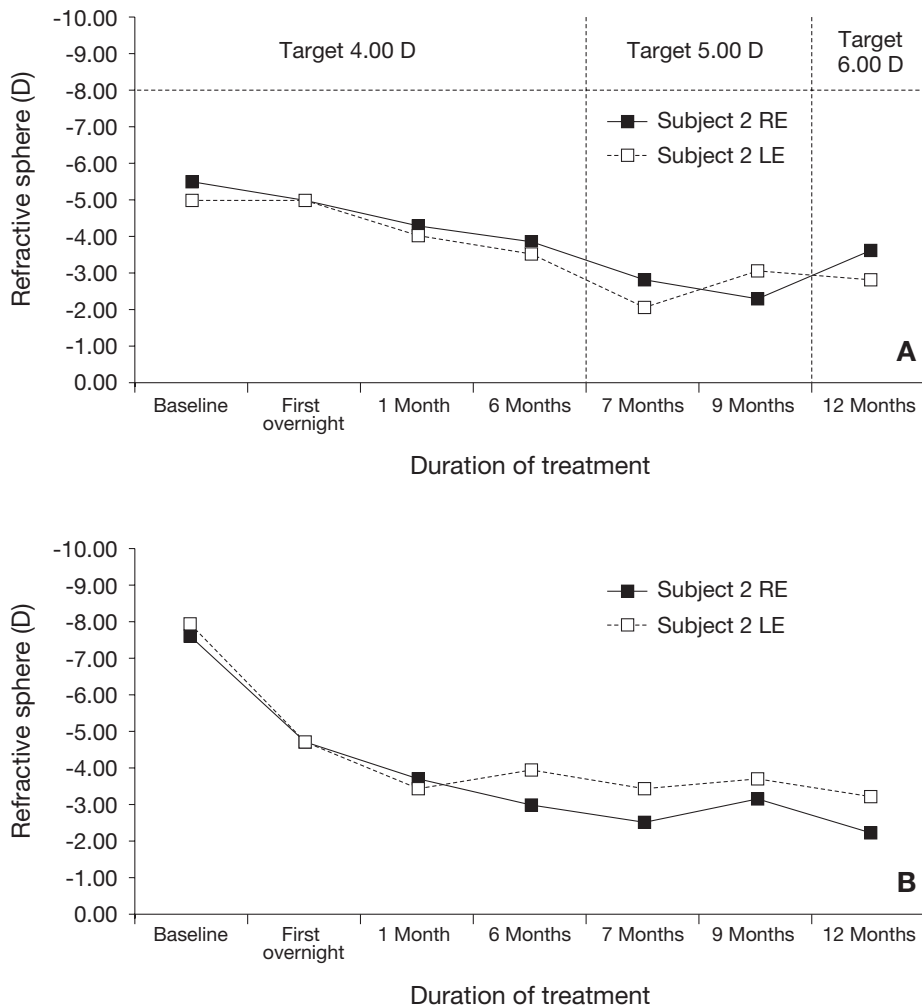


Figure 3. Changes in refractive sphere (corneal plane) of (A) Subject 1 and (B) Subject 2 during the 12-month orthokeratology treatment. LE, left eye; RE, right eye.

The subject was asked to continue lens wear with the previous pair of ortho-K lenses (target 5.00 D) and spectacles (-2.50/-0.75 × 15 R and -1.75/-1.25 × 15 L) and to return after one week. The subject did not return and was lost to further follow-up.

Subject 2

This 10-year-old subject had been a patient of The Hong Kong Polytechnic University's Optometry Clinic for five years. Figure 2B shows the refractive history and subjective refraction measured at the first

visit before the subject commenced ortho-K treatment. The former was determined from the clinical record. Baseline manifest refractive errors (in the spectacle plane) were -8.50/-2.25 × 180 (0.00 [6/6]) R and -8.75/-2.50 × 180 (0.00 [6/6]) L. Corneal astigmatism was 3.40 D in each eye and the subject had no contraindication for contact lens wear. Baseline axial lengths were 24.22 mm R and 24.51 mm L.

Table 1 shows the parameters of the lenses ordered for this subject. A summary of the changes to the refractive errors

(corneal plane) and corneal toricity during the 12 months of ortho-K lens wear is shown in Figures 3B and 4B.

At the first visit (early morning) after wearing the lenses overnight for eight hours, no lens binding or significant corneal staining was observed. The residual refractive errors were -5.00/-0.75 × 170 (0.00 [6/6]) R and -5.00/-1.25 × 10 (0.00 [6/6]) L and subtractive tangential maps showed a bull's eye pattern in each eye. At the one-month after-care visit, the residual refractive errors were -3.75 DS (0.00 [6/6]) R and -3.50 DS (0.00 [6/6]) L and no significant ocular adverse reaction was observed. The subject was instructed to continue lens wear.

At the three-month visit, the residual refractive errors were -3.25 DS (0.00 [6/6]) R and -3.50 DS (0.10 [6/7.5]) L with no significant corneal staining. A second pair of lenses (target: 5.00 D) were ordered (Figure 3B).

At the six-month visit, the residual refractive errors were -3.00/-0.75 × 160 (0.04 [6/6²]) R and -4.25/-1.00 × 180 (0.04 [6/6²]) L. New spectacles were prescribed to aid vision for the daytime and the subject was asked to continue wearing the new lenses targeting 5.00 D. One month later, the residual refractive errors were -2.50/-0.50 × 160 (0.00 [6/6]) R and -3.50/-0.25 × 180 (0.00 [6/6]) L.

At the nine-month visit, no further myopic reduction was observed compared with the previous visit, so a third pair of lenses (target 6.00 D) was ordered for the subject and delivered at the 10-month visit. At 12 months, the residual refractive errors were -2.25/-0.50 × 170 (0.00 [6/6]) R and -3.25/-0.25 × 165 (0.04 [6/6²]) L. The subject was instructed to continue lens wear and to wear the prescribed glasses (-2.00 DS R and -3.00 DS L) in the daytime. At the time of writing, the subject is still on the treatment with new lenses of the same parameters as the third pair of lenses.

No increase in axial length was observed for this subject during the 12-month ortho-K lens wear (Figure 5). For this subject, central corneal thickness decreased by 0.013 mm and 0.021 mm in the right and left eyes, respectively. Both

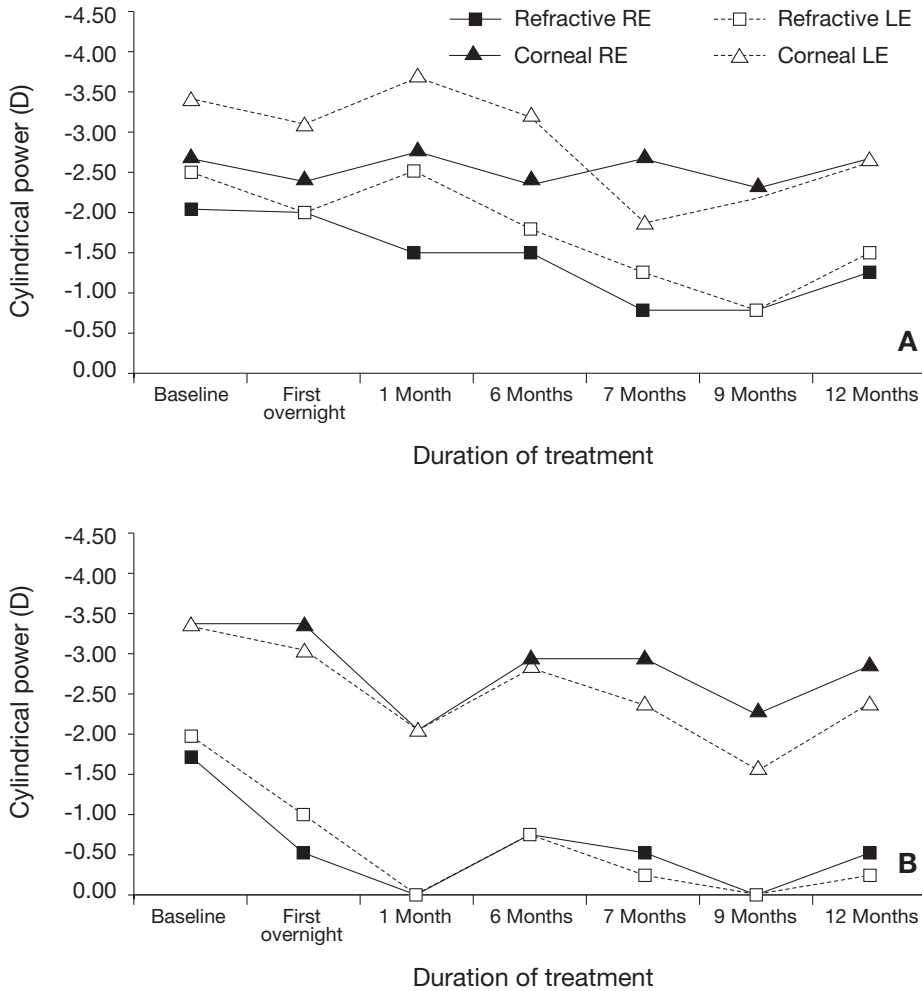


Figure 4. Changes in refractive cylindrical power (corneal plane) and corneal toricity of (A) Subject 1 and (B) Subject 2 during the 12-month orthokeratology treatment

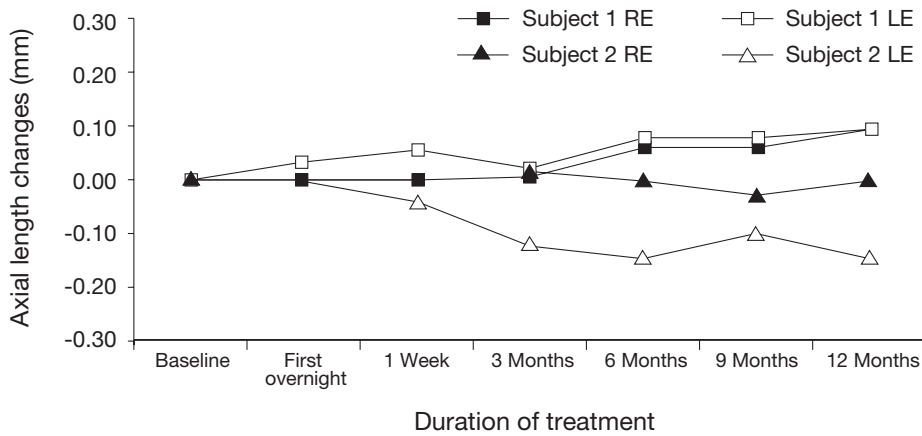


Figure 5. Changes in axial length in the eyes of the two subjects during the 12-month orthokeratology treatment. LE, left eye; RE, right eye.

the subject and parents were happy with the achieved myopic and astigmatic reduction and the retardation of myopic progression.

DISCUSSION

Toric design ortho-K can be used not only for reduction of astigmatism but also for improved lens centration. Currently, a few manufacturers (for example, NKL Contactlinsen BV; Paragon Vision Sciences, Arizona, USA) have developed toric reverse geometry lens designs (toric reverse and/or alignment zones). Both subjects in this report had good lens centration but demonstrated different responses to the toric lens design used. Significant reductions of refractive myopia and astigmatism were observed in Subject 2 (Figures 3B and 4B), whereas only a modest response was found in Subject 1 (Figures 3A and 4A). It is of interest to note that central corneal thickness showed practically no change (0.007 mm R, 0.001 mm L) in Subject 1 compared with those (0.013 mm R, 0.021 mm L) observed in Subject 2. It is unclear whether there is a relationship between changes in central corneal thickness and myopic reduction in ortho-K and further study is warranted in this area.

The changes in both subjective and objective refractive astigmatism (in the corneal plane) were not reflected in the changes in corneal toricity, as previously reported by Cheung, Cho and Chan.⁴ For Subject 1, refractive astigmatism reductions were approximately 37.5 per cent R and 40 per cent L, whereas reductions in corneal toricity were zero per cent R and 21 per cent L (Figure 4A). For Subject 2, reductions were approximately 71 per cent R and 87.5 per cent L in refractive astigmatism and only 15 per cent R and 29 per cent L in corneal toricity (Figure 4B). Mountford and Pesudovs⁵ reported approximately 50 per cent reduction of with-the-rule corneal astigmatism of not more than 1.50 D with a spherical design if the central 2.0 mm chord was considered. In the current two subjects, when the central 2.0 mm chord was considered, corneal toricity reductions were only one

to two per cent in Subject 1 and 19 to 40 per cent in Subject 2.

Similar results (percentage reductions of J_0) were obtained if changes to astigmatism (refractive and corneal) were analysed using power vectors; that is, $J_0 = (-C/2) \cos(\theta)$ and $J_{45} = (-C/2) \sin(\theta)$, where C denotes the amount of astigmatism at axis θ , and J_0 and J_{45} are the horizontal/vertical and oblique components of astigmatism, respectively.⁶ Slight changes in J_{45} were observed in both subjects but the observed changes were not clinically significant. Our results suggest that the normal relationship between refractive astigmatism and corneal toricity in non-reshaped eyes might not apply in ortho-K and some other factors might be effecting the change in refractive astigmatism in post-ortho-K subjects. Further study is warranted to investigate the relationship between post-ortho-K refractive astigmatism and corneal toricity.

Subject 1 also showed less reduction in myopia (36 per cent R, 45 per cent L) compared with Subject 2 (70 per cent R, 60 per cent L). Clinically, if the eye under responds but achieves good lens centration (bull's eye presentation), lenses with higher targets can be used to increase the amount of myopic reduction. Although Subject 1 was less myopic (ocular refraction -5.50 D R, -5.00 D L) than Subject 2 (ocular refraction -7.75 D R, -8.00 D L), smaller amounts of myopic reduction were achieved despite increases in the target of ortho-K lenses up to 6.00 D during the 12-month lens wear.

During the one-year ortho-K lens wear, neither of the subjects showed a significant increase in axial length (Figure 5). This is in agreement with previous reports that ortho-K has the potential for myopic control in children^{7,8} and is despite the differences in responses (amount of myopic reduction) in the two subjects. It is also of interest to note that the axial length of the left eye of Subject 2 continued to decrease during ortho-K treatment. It is unclear why this particular eye demonstrated such a trend, although such an observation has also been reported clinically in some eyes undergoing ortho-K (unpublished data).

The parents of these two subjects were happy with the results as myopic progression was apparently retarded with ortho-K lens wear. Although disappointed that full reduction was not achievable, both subjects (and parents) were happy to wear glasses to correct the residual refractive errors. Both also commented on the comparatively good vision (compared with pre-ortho-K treatment) at waking time even without the spectacles and the lenses were much thinner than the original full correction. Partial reduction ortho-K might play an important role in the management of myopia if it not only allows patients to wear thinner, lower-power glasses but also can help to retard myopic progression.

This is an anecdotal report on two highly myopic and highly astigmatic subjects, demonstrating different responses to toric ortho-K treatment and effective slowing of axial length change. Further investigation is necessary to investigate why responses to the same ortho-K treatment can be very different between individuals and whether partial reduction ortho-K can indeed retard myopic progression.

CONCLUSION

This report presents two highly myopic astigmatic subjects with histories of myopic progression, who were fitted with toric ortho-K lenses using a stepwise fitting protocol. One subject responded very well to the treatment, while the other demonstrated modest and small amounts of myopic reduction and incomplete astigmatic reduction. Axial length did not show a significant increase during the one-year ortho-K treatment in both subjects.

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Validity of Axial Length Measurements for Monitoring Myopic Progression in Orthokeratology

Sin-Wan Cheung and Pauline Cho

PURPOSE. To investigate the short-term effect of orthokeratology (ortho-k) lens wear on the anterior segment length for validating the use of axial length for monitoring myopic progression after ortho-k treatment.

METHODS. Thirty-seven and 39 subjects (ages: 7–10 years) were randomly assigned to wear ortho-k and single-vision spectacles, respectively. Central corneal thickness (CCT), anterior chamber depth (ACD), crystalline lens thickness (LT), and anterior segment length (ASL: summation of CCT, ACD, and LT) were measured before and 6 months after the treatment under cycloplegia. Changes in these parameters were evaluated and compared between the two groups of subjects.

RESULTS. There were no significant between-group differences in the baseline data ($P > 0.37$). After 6 months of lens wear, in the ortho-k group, CCT was significantly reduced by 0.009 ± 0.009 mm ($P < 0.001$), whereas ACD and LT remained unchanged ($P > 0.15$). In the spectacle group, ACD was significantly increased by 0.01 ± 0.03 mm ($P = 0.008$), whereas CCT and LT remained unchanged ($P > 0.06$). In both groups of subjects, ASL did not appreciably change but axial length was significantly increased by 0.10 ± 0.10 mm and 0.20 ± 0.11 mm in the ortho-k and the spectacle groups, respectively ($P < 0.001$).

CONCLUSIONS. Eyeball elongation occurred in children wearing both ortho-k and single-vision spectacles. Since ASL was not affected by ortho-k treatment, axial length measured reflects the true growth of the eyeball and is a valid parameter for monitoring myopic progression in ortho-k treated eyes. (ClinicalTrials.gov number, NCT00962208.) (*Invest Ophthalmol Vis Sci.* 2013;54:1613–1615) DOI:10.1167/iovs.12-10434

Orthokeratology (ortho-k) has been shown to be effective in slowing myopic progression in children.^{1–6} Because the refractive error is reduced after ortho-k treatment, myopic progression after ortho-k is commonly evaluated by change in axial length (AL). AL is the distance from the anterior cornea to

the retina, that is, the anterior segment length (ASL) plus the vitreous chamber depth (VCD) and ASL is the summation of central corneal thickness (CCT), anterior chamber depth (ACD), and crystalline lens thickness (LT). In ortho-k, CCT is thinned and central corneal curvature is flattened.^{7,8} These have led to some concerns that ortho-k may affect ACD, which in turn may affect the AL measurements.^{9,10} It may imply that axial elongation in ortho-k-treated eyes may be underestimated (or the efficacy of myopic control may be overestimated) due to a possible decrease in ACD from ortho-k lens wear, and thus shorter AL, and misinterpreted as a slower myopic progression compared with non-ortho-k-treated eyes. However, since ACD is only one component of ASL, to investigate if AL measurements are affected by ortho-k lens wear, investigation should focus on the change in ASL rather than the change in ACD alone. The current short-term study aimed at investigating the validity of using AL for monitoring myopic progression after ortho-k treatment by comparing the changes in individual components of and the overall change in ASL in subjects undergoing ortho-k and those wearing single-vision spectacles over a period of 6 months.

METHODS

The short-term effect of ortho-k lens wear was analyzed by evaluating the changes in CCT, ACD, LT, ASL, and AL before and after the stabilization of the treatment, which is usually within 3 months after lens wear. We used the first 6 months of data from 78 subjects (ages: 7–10 years) participating in a randomized clinical trial on myopic control using ortho-k (ClinicalTrials.gov number, NCT00962208).⁹ These subjects, who had a low to moderate amount of myopia (0.75–4.00 diopters [D]) and with-the-rule astigmatism (≤ 1.25 D), were randomly assigned to wear either ortho-k lenses or single-vision spectacles. For the ortho-k subjects, their refractive error was close to full correction such that they had good unaided vision (monocular unaided visual acuity better than 0.18 logMAR) and low refractive error (residual myopia/astigmatism not exceeding 0.50 D) after the stabilization of the treatment. The myopic control study followed the Declaration of Helsinki and was approved by the ethic committee of The Hong Kong Polytechnic University. Consent was obtained from all subjects and their parents when they enrolled in the myopic control study.

CCT, ACD, and LT were determined using an anterior segment tomographer (Pentacam, software version 1.14; Oculus, Wetzlar, Germany) after cycloplegia. The 25-scan mode was selected to facilitate image capturing in children. The first three good images captured were saved and the average data from the three images were used for data analysis. AL was determined using a commercial optical biometer (IOLMaster; Zeiss Humphrey, Dublin, CA). The first five readings with a difference of < 0.02 mm and with signal-to-noise ratio above 3.5 were saved. The average was used for data analysis. All measurements were taken 30 minutes after instillation of one drop of 0.5% proparacaine, followed by one drop of 1.0% tropicamide, and one drop of 1.0% cyclopentolate, each drop 5 minutes apart. Pupil reaction and accommodation were checked prior to the tests to ensure full pupil

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TABLE 1. Demographic Data and the Ocular Parameters of the 76 Subjects at the Baseline Visit

Variable	Ortho-k, <i>n</i> = 37	Control, <i>n</i> = 39
Age, y (range)	9 (7-10)	9 (7-10)
Sex	18F/19M	17F/22M
Spherical equivalent, D	-2.29 ± 0.74	-2.47 ± 0.94
Axial length, mm	24.52 ± 0.71	24.41 ± 0.87
Central corneal thickness, mm	0.576 ± 0.024	0.577 ± 0.032
Anterior chamber depth, mm	3.39 ± 0.21	3.36 ± 0.20
Lens thickness, mm	3.29 ± 0.19	3.31 ± 0.17
Anterior segment length, mm	7.25 ± 0.24	7.25 ± 0.26

dilation and relaxation of the ciliary muscles. Only data from the right eyes were reported.

Statistical Analysis

Except for age, distributions of the initial refractive error (spherical equivalent), CCT, ACD, LT, ASL, and AL and their changes were not significantly different from normal (Kolmogorov-Smirnov tests, $P > 0.41$). Therefore, nonparametric tests (χ^2 or Mann-Whitney U tests) were used to compare the differences in age and sex between the two groups at the baseline, whereas parametric tests (independent t -tests) were used to compare the initial refractive errors and ocular parameters in the two groups. Two-way repeated-measures ANOVAs were used to compare CCT, ACD, LT, ASL, and AL at baseline and the 6-month visits in the two groups of subjects. Independent t -tests were used if any significant main effect or interaction was found.

RESULTS

Data were excluded from two subjects in the control group because of poor image quality ($n = 1$) and missing data ($n = 1$). A total of 37 subjects (18 females and 19 males) and 39 participants (17 females and 22 males) were in the ortho-k and control groups, respectively. Table 1 shows the demographic data and the ocular parameters of these subjects. There were no significant differences in age, sex, refractive errors, or the ocular parameters between the two groups of subjects at the baseline visit ($P > 0.37$). The median age was 9 years and the initial mean ± SD spherical equivalent was -2.38 ± 0.84 D. Table 2 shows changes in CCT, ACD, LT, ASL, and AL during the study period. In the ortho-k group, CCT was significantly reduced by 0.009 ± 0.009 mm ($P < 0.001$), whereas ACD and LT remained unchanged ($P > 0.15$). In the control group, ACD was significantly increased by 0.01 ± 0.03 mm ($P = 0.01$), whereas CCT and LT remained unchanged ($P > 0.06$). However, ASL showed no changes ($P > 0.05$) in either group of subjects. AL significantly increased in both groups of subjects ($P < 0.001$) and the rate of axial elongation was faster in the control group (0.20 ± 0.11 mm) compared with that in the ortho-k group (0.10 ± 0.10 mm). Significant between-group differences in the changes in CCT, ACD, LT, and AL ($P < 0.02$) were observed, but not in ASL ($P = 0.92$).

DISCUSSION

Our results agreed with previous studies that CCT was thinned,^{7,8} whereas ACD remained unchanged after ortho-k.^{11,12} However, these studies did not investigate the effect of ortho-k on ASL. We found that ASL remained unchanged during 6 months of wearing ortho-k lenses compared with wearing single-vision spectacles. Previous studies on ocular biometry in

TABLE 2. Changes in the Anterior Segment Components and Eyeball Length after 6 Months

Variable	Ortho-k, <i>n</i> = 37	Control, <i>n</i> = 39	<i>P</i>
Central corneal thickness, mm	$-0.009 \pm 0.009^*$	0.001 ± 0.008	<0.001
Anterior chamber depth, mm	-0.01 ± 0.04	$0.01 \pm 0.03^*$	0.025
Lens thickness, mm	0.01 ± 0.06	-0.02 ± 0.05	0.018
Anterior segment length, mm	0.00 ± 0.07	0.00 ± 0.06	0.917
Axial length, mm	$0.10 \pm 0.10^*$	$0.20 \pm 0.11^*$	<0.001

P: statistical significance on between-group difference using independent t -tests. Regular: statistically insignificant; italic: statistically significant.

* Changes were significantly different from zero (one-sample t -tests, $P < 0.05$).

children mainly focused on corneal power, ACD, LT, VCD, and AL.¹³⁻¹⁸ Although these studies have reported changes in each component of ASL, to our knowledge none actually analyzed overall change in ASL.

It is well known that changes in CCT, ACD, LT, and VCD in children can be related to the normal growth of the eyeball and, thus, affect the refractive status of the eye. Among these parameters, change in CCT stabilizes at the age of 3 years.^{17,18} From the ages of 6 to 14 years, there is a mean increase of 0.73, 0.19, and 0.61 mm in AL, ACD, and VCD, respectively, and a mean decrease of 0.06 D, 0.07 mm, and 2.11 D in corneal power, LT, and crystalline lens power, respectively, in emmetropes.¹³ That is, during emmetropization in young children, the eyeball continues to grow and the refractive status of the eye is compensated by change in the crystalline lens power rather than the change in corneal power to allow the eyes to remain emmetropic. Myopes tend to have longer AL, ACD, and VCD, but shorter LT than emmetropes and hyperopes.^{14,15}

By deriving ASL from adding ACD to LT or subtracting VCD from AL using data available from previous literature,^{1,2,13-16} we found that there was a small increase in ASL in children over time and longer ASL was associated with age, refractive error, and sex. Cross-sectional studies showed that ASL increased by 0.11 mm from 6 to 14 years of age.¹⁶ The extent of change in ASL over time was minimal compared with the change in AL (1.15 mm). ASL was 0.2 mm longer in myopic children when compared to hyperopic children¹⁴ and 0.1 mm longer in boys compared to girls.^{15,16} Data from longitudinal studies also showed minimal increase in ASL over 2 years, from 0.02 mm in emmetropic children¹³ to 0.06 mm in myopic children wearing single-vision spectacles¹ and 0.11 mm in those wearing single-vision soft lenses.² The effect of ortho-k on change in ASL was insignificant. The 2-year changes in ortho-k subjects were +0.06 mm in the LORIC study¹ and -0.01 mm in the CRAYON study.² In the current study, we found no significant changes in ASL in both the ortho-k and control subjects over a period of 6 months.

In this study, subjects in both groups showed axial elongation but they had a small but significantly different behavior in the change in ACD. The behavior in the changes in ACD and AL in the spectacle-wearing subjects followed normal growth in myopic eyes (i.e., ACD increased with axial elongation; ACD increased by 0.01 mm, whereas AL increased by 0.20 mm in 6 months). However, there was no change in ACD in ortho-k subjects despite the increase in AL.

It should be noted that a change in any individual component of ASL may affect the refractive power of the

eye. In theory, a 1-mm forward displacement of the crystalline lens into the anterior chamber can increase the myopia of the eye by 1.40 D, if all the other ocular components remain unchanged.¹⁹ In an ortho-k-treated eye, the overall refractive change can be complicated because the treatment appears to affect all components of AL, including ASL. Thus, a change in corneal power in an ortho-k-treated eye may not necessarily reflect the overall change in the refractive power of the eye.²⁰ The current study focused only on the change in dimension and did not consider ocular power. Further studies are warranted to investigate the effect of the change in the ocular biometry on the refractive system of the eye after ortho-k. Future research on myopic control treatment based on axial elongation may also consider including the assessment of ASL and its individual components.

As mentioned earlier, there are concerns that myopic control effect using ortho-k may be overestimated due to the shortening of ACD, because of the backward displacement of the cornea or thinning of CCT with rigid lens wear leading to an apparent shortening of AL.^{9,10} Despite the thinning of CCT, our results rejected this speculation in that we did not find any associated changes in ACD, LT, and ASL after the treatment.

In conclusion, our study showed that although ortho-k lens wear affected CCT, the change was negligible compared with the change in AL. The treatment itself did not affect the ACD, LT, and ASL; thus, AL is a valid parameter for monitoring myopic progression. Changes in ocular biometry during eyeball elongation are the result of the modification of growth in response to ortho-k lens wear.

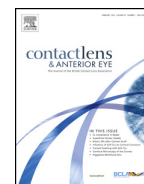
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Long-term effect of orthokeratology on the anterior segment length



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ABSTRACT

Purpose: To compare the effects of normal growth and longer term use of orthokeratology (ortho-k) on ocular biometric parameters in the anterior segment, including central corneal thickness (CCT), anterior chamber depth (ACD), crystalline lens thickness (CLT), and anterior segment length (ASL).

Methods: Baseline and six monthly data were retrieved from 78 subjects (aged 7–10 years, with myopia ≤ 4.00 D and astigmatism ≤ 1.25 D) who had completed a two-year randomized clinical trial using ortho-k for myopia control. They were randomly assigned to wear ortho-k lenses or single-vision spectacles (control). Anterior segment parameters were measured with the Pentacam after cycloplegia.

Results: No significant changes in CLT and ASL over time were observed in either group of subjects (37 ortho-k; 38 control). In the control group, CCT remained unchanged during the study period but in the ortho-k group, it was significantly reduced by an average of 0.009 mm by the 6-month visit ($p < 0.001$) and remained unchanged thereafter. No significant changes in ACD was found in the ortho-k group but it was significantly increased by an average of 0.04 mm ($p = 0.001$) in the control group.

Conclusion: CLT nor ASL did not change over time in either control or ortho-k subjects. Although ACD significantly increased in the control subjects and CCT significantly reduced in the first six months of ortho-k lens wear, these changes were small and did not affect the overall ASL.

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1. Introduction

The human eye grows from infancy to childhood leading to changes in refractive power during childhood. Infants are usually hyperopic with short axial length (AL). This refractive error of the eye reduces when the eye starts to grow accompanied by change in shape of the cornea and the crystalline lens [1,2]. Central corneal thinning generally stabilizes at the age of three years [3,4]. During childhood, the eye becomes longer resulting in deeper vitreous chamber depth, whereas the crystalline lens becomes flatter and thinner [3–9]. Crystalline lens thickness tends to remain stable after reaching 10 years of age but may be influenced by refractive errors of the eye [1,8]. Decrease in crystalline lens thickness (CLT) is accompanied by an increase in anterior chamber depth (ACD) [3,5,8,9]. These changes are usually small in hyperopes and emmetropes, but are more significant in myopes. The more myopic the eye, the larger the magnitude of change [5,8].

Orthokeratology (ortho-k) can slow axial elongation of the eye [10–13]. Our previous study determining the short-term effects

(six months) of ortho-k treatment on refractive correction revealed that there was thinning of central corneal thickness (CCT) which did not affect ACD, CLT and the overall anterior segment length (ASL) [14]. A different pattern of change in ACD in children on ortho-k treatment compared to those using spectacles was observed. While ACD increased with time in subjects using single-vision spectacles, ACD remained unchanged in subjects on ortho-k treatment. This implies that ortho-k not only modifies axial elongation, but may also affect the growth pattern of the interior structure. The effect of ortho-k on AL has been reported elsewhere [11]. This paper focused on the longer term effects of ortho-k lens wear on ocular parameters in the anterior segment.

2. Methods

Data were retrieved from subjects who had completed the ROMIO study, a two-year randomized clinical trial evaluating the effectiveness of myopia control using ortho-k [11]. The study was registered at ClinicalTrials.gov, number NCT00962208. It followed the tenets of Declaration of Helsinki and was approved by the Ethics Committee of the School of Optometry of The Hong Kong Polytechnic University. Informed consent was obtained from the subjects and their parents prior to the commencement of the

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study. Biometric measurements performed at the 6 monthly cycloplegic visits (i.e., baseline, 6 months, 12 months, 18 months and 24 months) were retrieved.

Seventy-eight subjects, who had been randomly assigned to the two treatment groups, completed the ROMIO study. Of these, 37 received ortho-k and 41 were in the control (single-vision spectacles) group. The subjects were aged from seven to 10 years, with low-to-moderate myopia (-0.50 to -4.00 DS) and low refractive astigmatism (≤ 1.25 DC) in the test eyes. The right eye was selected as the test eye if both eyes were eligible. Refractive error (Shin-Nippon NVision K5001, Shin-Nippon Commerce Inc., Tokyo, Japan), anterior segment dimensions (CCT, ACD and CLT) (Pentacam, ver 1.14; Oculus, Wetzlar, Germany) and AL (IOLMaster; Zeiss Humphrey, Dublin, CA) were determined after cycloplegia with 1 drop of 0.5% proparacaine, followed by 1 drop of 1% tropicamide, and 1 drop of 1% cyclopentolate, administered five minutes apart. The effectiveness of cycloplegia was checked at least 30 min after instillation of all eyedrops and the tests were performed when residual accommodation was found not to exceed 2.00 D. The operation procedures and data retrieval for Pentacam and IOLMaster were as previously reported in the previous short-term study [10]. In order to differentiate the refractive correction effect of ortho-k on corneal thickness from the myopia control effect on AL, ACD was defined as the distance from the posterior corneal surface to the anterior crystalline lens surface and ASL was the distance from the anterior cornea to the posterior crystalline lens, i.e. ASL was derived as the summation of CCT, ACD and CLT obtained from Pentacam.

2.1. Statistical analysis

Statistical analyses were performed using the SPSS software (ver. 18.0; SPSS Inc., Chicago, IL). The distributions of the ocular biometric values and their changes were not significantly different from normal (Kolmogorov–Smirnov tests, $p > 0.05$), therefore, parametric tests were used for data analysis. Repeated-measures ANOVAs were used to evaluate the effect of time on CCT, ACD, CLT, and ASL in the two groups of subjects. Post-hoc analyses were performed (paired and unpaired t tests with Bonferroni corrections) where appropriate.

3. Results

Data from three subjects were excluded due to missing Pentacam data, one at baseline, one at the 12-month visit and one at the 18-month visit. Table 1 shows the demographic data of the remaining 75 subjects (37 ortho-k; 38 control). There were no significant differences in the initial age, gender, refractive error and ocular parameters between the two groups of subjects at baseline

Table 1

Demographic data and ocular parameters of the 75 subjects at the baseline visit.

	Ortho-k (n=37)	Control (n=38)
Age (years)	8.86 ± 0.95	8.74 ± 1.06
Sex	18F/19M	17F/21M
Refractive sphere (D)	-2.05 ± 0.72	-2.16 ± 0.80
Refractive cylinder (D)	-0.23 ± 0.30	-0.27 ± 0.35

visit ($0.92 \geq p \geq 0.42$). The two-year changes in ocular parameters are shown in Tables 2 and 3.

Two-way repeated measures ANOVA analyses revealed no significant changes in CLT and ASL over time ($0.42 \geq p \geq 0.25$) in all subjects and no significant interaction between time and treatment ($0.48 \geq p \geq 0.30$). However, there was significant effect of time ($p \leq 0.004$) and significant interaction of time and treatment ($p \leq 0.005$) on CCT and ACD. Therefore, the effect of time on the ocular parameters was assessed for each group using repeated measures ANOVA.

In the ortho-k group, CCT significantly reduced by 0.009 mm at the 6-month visit ($p < 0.001$) and remained unchanged thereafter ($p = 0.53$). ACD, CLT and ASL showed no significant changes ($p > 0.64$) over time. In the control group, ACD was significantly increased with time ($p < 0.001$) whereas no significant changes ($p > 0.28$) were found in CCT, CLT and ASL during the study period. However, changes observed in these parameters did not affect the overall ASL.

4. Discussion

The current study was an extension of our previous study on the short-term changes in ocular biometric parameters after ortho-k [14]. We confirmed a different pattern of change in ACD with time in subjects wearing ortho-k lenses and single-vision spectacles (Table 3). The increase in ACD with time observed in subjects wearing single-vision spectacles was not observed in those wearing ortho-k lenses. CLT and ASL remained unchanged in both groups of subjects. Different pattern of change in CCT was observed in the two groups of subjects (Table 3). However, it was only due to the initial reduction in CCT during the refractive correction effect of ortho-k treatment. CCT on ortho-k subjects then remained stable once maximum refractive correction has been achieved (Table 2).

This study is the first report on the long-term changes in the anterior components of the eye in subjects receiving myopia control treatment. Refractive error and axial length are the most commonly reported parameters in myopia control studies [10–13,15–19]. We found three myopia control studies, using three different active and control interventions, which reported the results of changes in ACD and CLT over time [10,15,17]. However,

Table 2

Ocular parameters (mm) of the 75 subjects at different visits.

	Baseline	6 months	12 months	18 months	24 months
Ortho-k					
Central corneal thickness	0.577 ± 0.025	0.568 ± 0.024	0.570 ± 0.023	0.568 ± 0.027	0.569 ± 0.024
Anterior chamber depth	3.39 ± 0.21	3.38 ± 0.21	3.39 ± 0.21	3.39 ± 0.20	3.39 ± 0.21
Crystalline lens thickness	3.29 ± 0.20	3.30 ± 0.19	3.30 ± 0.17	3.28 ± 0.20	3.30 ± 0.21
Anterior segment length	7.25 ± 0.25	7.25 ± 0.24	7.26 ± 0.22	7.24 ± 0.24	7.25 ± 0.24
Axial length	24.52 ± 0.71	24.61 ± 0.70	24.72 ± 0.70	24.82 ± 0.70	24.88 ± 0.72
Control					
Central corneal thickness	0.578 ± 0.032	0.579 ± 0.030	0.578 ± 0.030	0.578 ± 0.031	0.580 ± 0.030
Anterior chamber depth	3.38 ± 0.19	3.40 ± 0.20	3.41 ± 0.20	3.41 ± 0.20	3.42 ± 0.20
Crystalline lens thickness	3.31 ± 0.16	3.30 ± 0.17	3.30 ± 0.16	3.29 ± 0.17	3.30 ± 0.17
Anterior segment length	7.27 ± 0.25	7.27 ± 0.28	7.28 ± 0.26	7.29 ± 0.26	7.30 ± 0.26
Axial length	24.37 ± 0.84	24.57 ± 0.86	24.75 ± 0.90	24.89 ± 0.89	25.02 ± 0.90

Table 3

Changes in the ocular parameters (mm) after 24 months.

	Ortho-k (n=37)	Control (n=38)	p-value
Central corneal thickness	-0.008 ± 0.010 ^a	0.003 ± 0.009	<0.001
Anterior chamber depth	0.001 ± 0.049	0.040 ± 0.042 ^a	<0.001
Crystalline lens thickness	0.010 ± 0.061	-0.014 ± 0.066	0.103
Anterior segment length	0.004 ± 0.070	0.029 ± 0.077	0.141

p-value: probability values for between-group difference using unpaired t-test. Italic: statistically significant.

^a Changes were significantly different from baseline for individual group (repeated measures ANOVAs, $p < 0.001$).

change in overall ASL has not been reported before. Whilst there is a general agreement on the effects of myopia control, reports of changes in other ocular parameters differed between studies (Table 4). The active interventions in Table 4 included ortho-k, atropine, and multifocal soft contact lenses, all of which may affect the anterior segment (CCT, ACD, or CLT). These three studies [10,15,17] used ultrasound biometry whereas the current study used optical tomography for measuring ACD and CLT. ACD was defined from the anterior corneal surface with ultrasound rather than the posterior corneal surface as in the current study. However, this would not affect the comparison made in Table 4 as mean changes rather than the actual ACD values were compared.

Shih et al. [15] reported that a combined therapy of 0.5% atropine with multifocal spectacles slowed axial elongation by 63% in children aged six to 13 years. In this randomized study, subjects were stratified by age, gender and initial myopia. The authors did not report the changes in ACD and CLT over time. Instead, they compared the changes in ACD and CLT among the three study groups. They reported no significant differences in changes in ACD among the three study groups but significantly greater increase in CLT in the groups receiving single interventions compared to the active treatment group receiving combined therapy. Walline et al. [10] showed that ortho-k could slow axial elongation by 55% in children aged eight to 11 years. Their results showed that while CLT remained unchanged during the study period, ACD did not change

in ortho-k subjects but increased significantly by 0.10 mm in control subjects wearing single-vision soft lenses. In another study, using data from historic control subjects using soft lenses [20], Walline et al. [17] investigated the potential of using multifocal soft lenses for myopia control by fitting new subjects who were age and gender matched with the historic control subjects [20]. They found that axial elongation was slowed by 29% in subjects wearing multifocal soft lenses. In their study, CLT did not change with time in both groups of subjects. While ACD remained unchanged in the single-vision group, it was significantly increased by 0.04 mm in the multifocal group. Subjects in the current study has been shown to have slower axial elongation by about 44% [11]. CLT remained unchanged in both groups of subjects. ACD did not change significantly in subjects on ortho-k treatment but increased by 0.04 mm in those wearing single-vision spectacles.

The changes in ACD and CLT reported in these studies were so small and may not be clinically significant. For instance, in the current study, the average changes in ACD, CLT, ASL and AL in the control subjects (who showed greater changes than in the ortho-k subjects) were 0.040 mm, 0.014 mm, 0.029 mm and 0.645 mm, respectively. The percentage changes in AL contributed by ACD, CLT and ASL were only 6%, 2% and 4%, respectively. The magnitudes of changes in ACD, CLT and ASL were much smaller than the change in AL. Despite the small magnitudes of changes, the different pattern of changes in ACD and CLT reported for subjects receiving different interventions were of interest.

Our results agreed with the two non-randomized studies reported by Walline et al. [10,17] that there were no significant changes in CLT over time in both the study and control subjects. In terms of ACD, our study showed a different pattern of change which may be due to the use of different interventions. However, it is also of interest to note that changes in ACD in subjects not receiving any interventions in these studies were not all in agreement. The current study and the studies reported by Walline et al. [10,17] investigated the effect of optical methods (contact lenses) for myopia control whereas the study reported by Shih et al. [15] investigated the use of ophthalmic eyedrops for myopia

Table 4

Changes in anterior chamber depth (ACD) and crystalline lens thickness (CLT) reported by the current and other myopia control studies.

Authors	Shih et al. [15]	Walline et al. [10]	Walline et al. [17]	Current study
Year	2001	2009	2013	–
Age	6–13 yo	8–11 yo	8–11 yo	7–10 yo
Treatment	(1) Atropine + MF spectacles (2) MF spectacles (3) SV spectacles	(1) Ortho-k (2) SV SCL	(1) MF SCL (2) SV SCL	(1) Ortho-k (2) SV spectacles
Change in ACD (mm)	(1) 0.005 (2) -0.006 (3) -0.015	(1) -0.01 (2) 0.1	(1) 0.04 (2) -0.01	(1) 0.001 (2) 0.04
p value				
Change from baseline	–	(1) 0.63 (2) 0.0005	(1) 0.0299 (2) >0.05	(1) 0.64 (2) <0.001
Between group difference	>0.05	0.004	0.0204	<0.001
Change in CLT (mm)	(1) -0.01 (2) 0.033 (3) 0.042	(1) -0.01 (2) 0.01	(1) -0.007 (2) 0.008	(1) 0.01 (2) -0.014
p value				
Change from baseline	–	(1) 0.43 (2) 0.43	(1) 0.05 (2) 0.05	(1) 0.25 (2) 0.25
Between group difference	0.01	>0.47	0.42	0.103

MF: multifocal.; SV: single-vision; Ortho-k: orthokeratology; SCL: soft contact lenses.

control. The use of drugs may explain the discrepancy in the results as they affected different components of the anterior segment.

The results obtained in the current study may be affected by the relatively small sample size and possibly different accommodative demands between the two groups of subjects. Although cycloplegia was employed to paralyze accommodation, measurements of ACD and CLT may be affected if the ciliary muscles were not fully paralyzed resulting in residual accommodation.

In view of the limited reports, variety of treatments involved, and small changes observed, no conclusion can be drawn about the effect of ortho-k and other myopia control treatments on anterior segment changes at the moment. Further studies are warranted on the effect of myopia control treatment on the anterior segment parameters. In summary, the current study shows that ortho-k for myopia control has no effect on ASL and CLT compared to the control subjects.

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Protective Role of Orthokeratology in Reducing Risk of Rapid Axial Elongation: A Reanalysis of Data From the ROMIO and TO-SEE Studies

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PURPOSE. To determine the relative risk of rapid progression and number needed to treat (NNT) in younger and older children using combined data from the retardation of myopia in orthokeratology (ROMIO) and toric orthokeratology-slowing eye elongation (TO-SEE) studies.

METHODS. Data from 136 subjects of two studies, ROMIO and TO-SEE, were retrieved (72 orthokeratology [ortho-k]: 37 ROMIO, 35 TO-SEE; 64 control: 41 ROMIO, 23 TO-SEE) and the myopia control effect on younger (6–8 years) and older (9–12 years) subjects evaluated. The rate of axial elongation was classified as not rapid (axial elongation = <0.36 mm/year) or rapid (axial elongation >0.36 mm/year).

RESULTS. Cumulative frequency curves showed that the younger subjects in the control group had the greatest and most rapid axial elongation at the end of 24 months. In the younger subjects, ortho-k lens wear significantly reduced the risk of rapid progression by 88.8% ($P = 0.002$). The 2-year NNT for the younger ortho-k subgroup was 1.8, suggesting that treating just two younger subjects with ortho-k would prevent one subject from experiencing rapid progression over a 2-year period of treatment. The 2-year NNT for the older ortho-k subgroup was 11.8, which was statistically insignificant ($P = 0.197$).

CONCLUSIONS. Orthokeratology significantly reduced risk of rapid progression in younger subjects. Treating just two 6- to 8-year-old subjects with ortho-k instead of single-vision spectacles could prevent one subject from developing rapidly progressing axial elongation during this critical 2-year period.

Keywords: orthokeratology, myopia control, younger children, rapid progression, NNT, relative risk

Myopia, the most frequent cause of distance impairment, is a major concern^{1–2} as children who become myopic earlier are more likely to later develop high myopia.¹ Axial elongation, associated with progression of myopia, can lead to adverse mechanical stretching and thinning of the retina, resulting in retinal degenerative changes.³ For decades, researchers studying myopia have searched for effective ways to slow its progression in children.^{4–12} In the last decade, a number of reports have been published on the effectiveness of orthokeratology (ortho-k) for myopia control in children.^{9,11,13–18} These studies have been subjected to meta-analysis by two groups of researchers^{19,20} who both confirmed the effectiveness of ortho-k for myopia control. However, Si et al.¹⁹ suggested that, since five of the seven studies included in the meta-analysis were from Asia, further work would be required. Two main limitations of meta-analyses are the frequent unavailability of raw data and problems with different methodologies of the studies included in the analysis, which restrict the amount of further statistical analysis that can be performed with the combined data from the studies. However, two of the studies listed in the meta-analyses, retardation of myopia in orthokeratology (ROMIO)¹¹ and toric orthokeratology-slowing eye elongation (TO-SEE),¹⁷ were prospective cohort studies conducted around the same period of time by

the same research team in Hong Kong using the same methodology, with the exception that the former was a randomized study on children with low myopia and low astigmatism, whereas the latter was a nonrandomized study on children with low myopia but moderate to high astigmatism. Raw data from both were available for combined analyses (Table 1). Respectively, the ROMIO¹¹ and TO-SEE¹⁷ studies reported 46% and 56% slower increases in axial length of children aged 6 to 12 years wearing ortho-k lenses compared to children wearing spectacles. The retardation of myopia in orthokeratology¹¹ study also reported a significantly lower percentage of younger subjects (age 7–8 years) with rapid axial elongation (>0.36 mm per year [i.e., equivalent myopic progression >1.00 diopter [D] per year]) in the ortho-k group (20%) compared to control subjects wearing single vision spectacles (65%). The toric orthokeratology-slowing eye elongation¹⁷ study reported that the odds of becoming a rapid progressor was 14.9 times greater in subjects wearing single-vision spectacles than those wearing ortho-k lenses, but only eight subjects (ortho-k: $n = 1$; control groups: $n = 7$) in this study demonstrated rapid myopic progression.

The number needed to treat (NNT), an average number of patients needed to be treated to prevent one adverse event or one specified clinical endpoint, is a statistical metric that can



TABLE 1. Details of ROMIO¹¹ and TO-SEE¹⁷ Studies

	ROMIO Study	TO-SEE Study
Study design	Randomized	Nonrandomized
Masking	Examiners masked to axial length measurements	
Ethnicity	Chinese	
Age, y	6–10	6–12
Myopia, D	0.50–4.00	0.75–5.00
WTR	Up to 1.25 (other axes:	1.25–3.00
astigmatism, D	<0.75)	
Study group	Menicon Z Night	Menicon Z Night Toric
Control group	Single-vision spectacles	
Data collection	Baseline and every 6 months after start of lens or spectacle wear for 2 years	
Axial length measurement	IOLMaster (Zeiss Humphrey, Dublin, CA, USA)	

WTR, with-the-rule.

help decision making between treatment options. It is treatment-time specific and takes into account both absolute risk and relative treatment effects, allowing the translation of research data into clinical practice.²¹ It is a simple way to demonstrate the clinical benefit or impact of a treatment. For example, a 2-year NNT of 100 suggests that 100 subjects would need to be treated for 2 years to prevent one specified (adverse) outcome.

Although the calculated powers to detect a statistically significant difference for both the ROMIO¹¹ and TO-SEE¹⁷ studies were over 85%, subgroup sample sizes in each study were small. Combining data from these two studies offers the potential to extract further meaningful results with improved statistical power. Specifically, combining these data allows determination of the relative risk (RR) of rapid progression in subjects not using ortho-k treatment. To our knowledge, findings in terms of benefit analysis have not been previously presented for ortho-k.

The purpose of this study was to reanalyze the combined data from the ROMIO and TO-SEE studies to determine the RR of rapid progression in younger and older children, and to determine the NNT, that is, the number of children needed to be fitted with ortho-k to prevent one rapid progressor. Results obtained offer a new perspective on myopia control using ortho-k, specifically on the benefit of this treatment that can be applied in clinical decision making.

METHODS

Data from two studies, ROMIO¹¹ and TO-SEE,¹⁷ were pooled for analysis. Both studies were approved by the Departmental

Research Committee of the School of Optometry of The Hong Kong Polytechnic University and written consent was obtained from both subjects and their parents before study participation. Both studies were registered at ClinicalTrials.gov (ROMIO: NCT00962208; TO-SEE: NCT00978692). No significant adverse effect was reported in either study.^{11,17}

TREATMENT OF DATA

We used commercial software (SPSS 23.0; IBM Corp., Armonk, NY, USA) for statistical analysis. Parametric tests were used for the analysis of refractive sphere and axial length that followed Gaussian distributions, while nonparametric tests were used for the analysis of age and initial cylinder. A linear multiple regression model was utilized to study factors affecting axial elongation. Due to the differences in subject assignments (randomization) in the ROMIO and TO-SEE studies, and moderate to high astigmatism in TO-SEE subjects, one-way analysis of covariance (ANCOVAs) controlled for age, initial sphere, and astigmatism was used to investigate the axial elongation in children with and without ortho-k. Relative risk of rapid progression and NNT were determined for subjects treated with ortho-k and single-vision spectacles.

RESULTS

Data from 136 subjects were retrieved (72 ortho-k: 37 ROMIO, 35 TO-SEE; 64 control: 41 ROMIO, 23 TO-SEE). Table 2 shows the demographic data and axial elongation during the course of the 2-year studies. No significant differences in initial age (Kruskal-Wallis, $P = 0.81$), initial refractive sphere (1-way ANOVA, $F_{3,132} = 1.30$, $P = 0.28$), and initial axial length (1-way ANOVA, $F_{3,132} = 1.30$, $P = 0.59$) were present between subjects from the ROMIO and TO-SEE studies, and between those wearing single-vision spectacles and ortho-k lenses in the two studies. The data from the two studies were pooled and further analyses performed.

Stepwise multiple regression analysis revealed that of the factors investigated, axial elongation was significantly associated with the use of ortho-k (standardized $\beta = -0.48$, $P < 0.001$) and initial age (standardized $\beta = -0.32$, $P < 0.001$), but not with initial refractive sphere, initial refractive cylinder, or initial corneal toricity (part r : -0.04 to 0.09 , $P > 0.29$). The regression model was fair in predicting axial elongation based on initial age and the use of ortho-k (adjusted $R^2 = 0.35$) and statistically significant ($F_{2,133} = 35.21$, $P < 0.001$). Axial elongation was negatively associated with age in both groups (control: Pearson $r = 0.44$, $P < 0.001$; ortho-k: Pearson $r = 0.30$, $P = 0.01$).

TABLE 2. Demographic Data and Axial Elongation of the 136 Subjects That Completed the ROMIO¹¹ and TO-SEE¹⁷ Studies

	Study	Age, y	Initial Sphere, D	Initial Axial Length, mm	Axial Elongation >2 y, mm
Control	ROMIO, $n = 41$	8.9 ± 1.6	-2.23 ± 0.84	24.40 ± 0.84	0.63 ± 0.26
	TO-SEE, $n = 23$	8.7 ± 1.0	-2.04 ± 1.09	24.18 ± 1.00	0.64 ± 0.31
	<i>P</i> value				0.72*
Ortho-k	ROMIO, $n = 37$	8.9 ± 0.5	-2.05 ± 0.72	24.48 ± 0.71	0.40 ± 0.25
	TO-SEE, $n = 35$	9.0 ± 1.5	-2.46 ± 1.32	24.37 ± 0.88	0.31 ± 0.27
	<i>P</i> value				0.15*
Control	Combined, $n = 64$	8.77 ± 1.27	-2.16 ± 0.93	24.32 ± 0.90	0.63 ± 0.28
	Ortho-k	8.92 ± 1.22	-2.25 ± 1.07	24.45 ± 0.79	0.35 ± 0.25
	<i>P</i> value	0.805†	0.278‡	0.593‡	<0.001*

* *P* value from 1-way ANCOVA controlled for age, and initial Rx and initial cylinder.

† *P* value from Kruskal-Wallis test.

‡ *P* value from 1-way ANOVA.

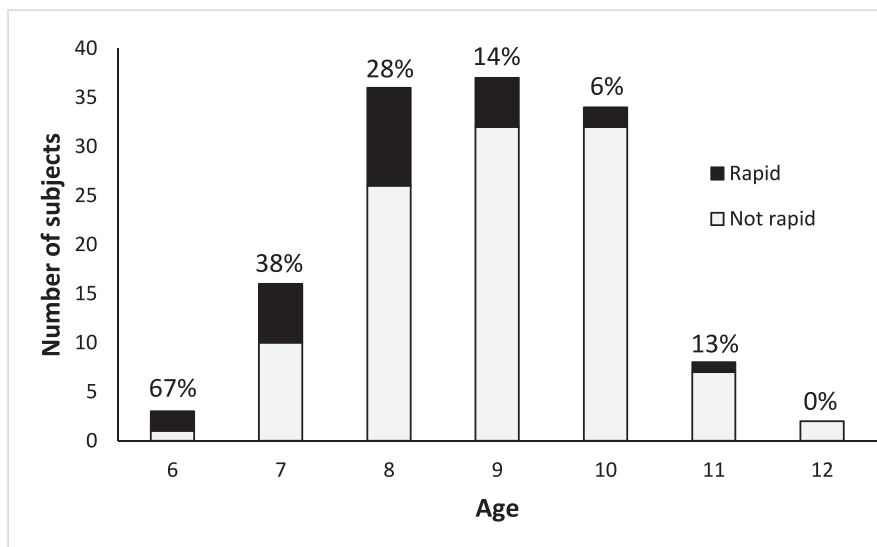


FIGURE 1. Percentage of subjects with rapid progression (axial elongation >0.36 mm/year; black).

Figure 1 shows the overall number and percentage of subjects with rapid progression. The percentage of subjects with rapid progression reduced from 67% at the age of 6 to 28% at the age of 8. The percentage of subjects with rapid progression was rather low (range, 0%–14%) for those aged 9 to 12 years. Therefore, to determine the myopia control effect on younger and older children, the subjects were divided into two age groups: 6 to 8 and 9 to 12 years. The average axial elongations over 2 years

were 0.46 ± 0.22 mm and 0.81 ± 0.27 mm, respectively, in the ortho-k and control subjects aged 6 to 8 years and were 0.28 ± 0.26 mm and 0.52 ± 0.22 mm, respectively, in the ortho-k and control subjects aged 9 to 12 years.

Figure 2 shows the cumulative percentage frequencies of subjects with specified axial elongation at the end of 24 months. The graph indicates that ortho-k lens wear led to reduced axial elongation over 2 years of lens wear (curves for

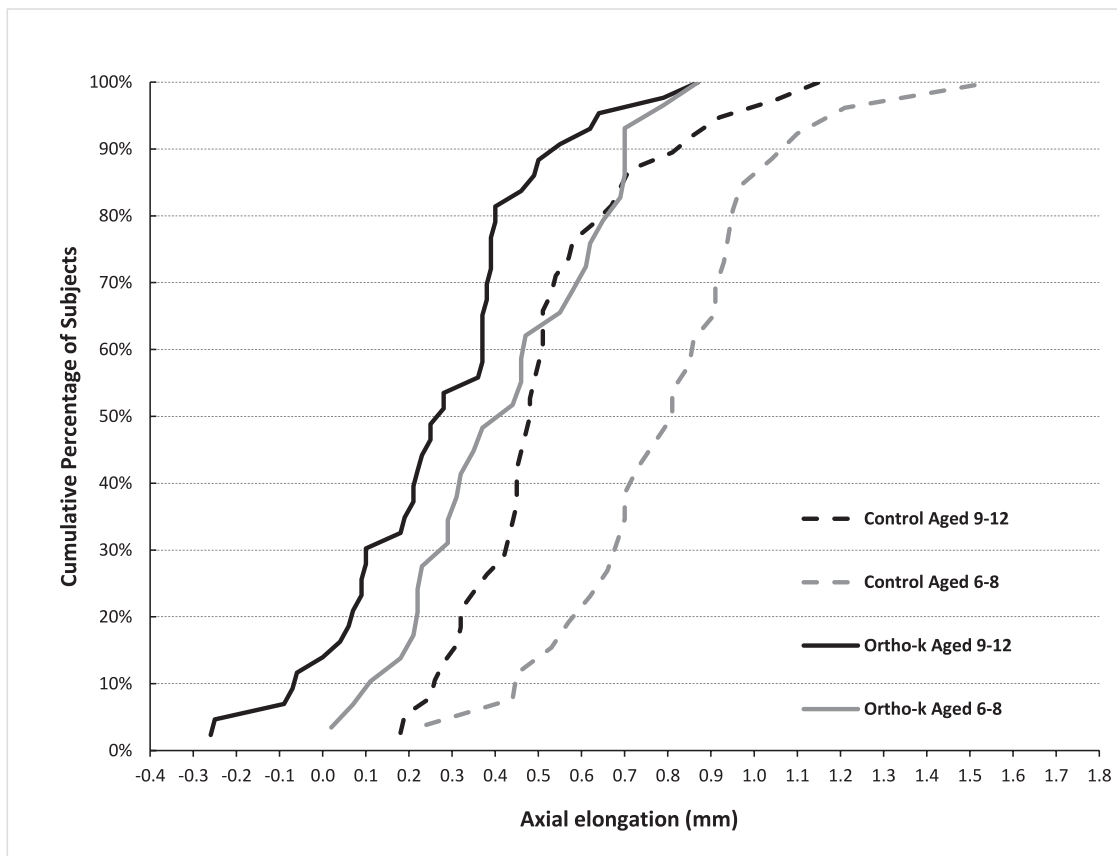


FIGURE 2. Cumulative percentage frequencies of subjects by age group and axial elongation at the end of 24 months.

TABLE 3. Relative Risk of Rapid Progression in Relation to the Use of Ortho-k and Initial Age

	Ortho-k	Control	RR (95% CI)	NNT (95% CI)	P Value
All					
Rapid	4	21	0.17 (0.06-0.47)	3.67 (2.53-6.65)	<0.001
Not rapid	68	43	-	-	-
Aged 6-8 y					
Rapid	2	16	0.11 (0.03-0.44)	1.83 (1.33-2.90)	0.002
Not rapid	27	10	-	-	-
Aged 9-12 y					
Rapid	2	5	0.35 (0.07-1.72)	11.76 (4.85-27.67)	0.197
Not rapid	41	33	-	-	-

Italics indicate statistically significant. RR, relative risk; NNT number needed to treat.

ortho-k subjects shifted toward the left for both subgroups compared to curves for control subjects). Older subjects tended to have smaller axial elongation compared to younger subjects. This is true for both ortho-k and control subjects: 50% of subjects in the ortho-k and control groups had axial elongations ranging from 0.27 to 0.86 mm and 0.48 to 1.15 mm, respectively; and interestingly, 14% of older ortho-k subjects displayed a shortening of axial length after 2 years of lens wear. Myopia control effect was more pronounced in the younger ortho-k subjects, with 50% of subjects showing axial elongations of 0.40 to 0.88 mm, compared to 0.81 to 1.55 mm in the younger control subjects. Orthokeratology also increased the percentage of subjects with slow progression (annual axial elongation <0.18 mm (i.e., equivalent myopic progression <0.25 D per year) especially in the younger age group. The percentage of slow progressors was 46% in the older control subjects compared to 56% in the older ortho-k subjects, and 5% in the younger control subjects compared to 25% in the younger ortho-k subjects.

The overall RR of rapid axial elongation was reduced by ortho-k treatment (RR: 0.17; 95% confidence interval [CI]: 0.06-0.47; $P < 0.001$). Considering all subjects, the 2-year NNT was 3.87 (95% CI: 2.5-6.7). In other words, ortho-k can prevent one out of four subjects (aged 6-12 years) from having rapid progression after 2 years of treatment. However, the effect reached statistical significance only for the younger subjects (Table 3). Only 2 of 29 younger subjects in the ortho-k group displayed rapid progression, as compared with 16 of 26 subjects in the control group (RR: 0.11; 95% confidence interval: 0.03-0.44; $P = 0.0018$). This suggested an 88.8% reduction in risk of rapid progression if younger subjects were treated with ortho-k for myopia control. For older subjects, although fewer subjects showed rapid progression compared to the control subgroup, the RR did not reach statistical significance (RR: 0.35; 95% CI: 0.07-1.72, $P = 0.1973$). The 2-year NNT for the younger ortho-k subgroup was 1.8 (95% CI: 1.3-2.9), implying that treating two younger subjects with ortho-k for myopia control would prevent one subject from having rapid progression over a 2-year period of treatment. Although the RR for the subgroup of older ortho-k subjects did not reach statistical significance, the direction of risk remains protective. For this sub-group, the NNT (11.8; 95% CI: 4.85-27.67) was considerably higher. This may be because older subjects tended to have smaller axial length changes compared to the younger subjects (rapid progressors: younger age group = 18/55; older age group = 7/81).

DISCUSSION

Our results confirmed that ortho-k slows axial elongation. It significantly decreased the number of subjects with rapid

progression and increased the number of subjects with slow progression over the 2-year treatment period.

Younger subjects showed more rapid axial elongation than older subjects, hence use of ortho-k displayed a more pronounced myopia control effect even though the percentage control was similar in both subgroups. The finding that axial elongation in younger myopic children is more rapid is not new, having been previously reported by several studies.²²⁻²⁵ In their study, Hyman et al.²⁵ reported that the baseline age of the children was the "strongest factor independently associated with faster myopic progression." Strong evidence of control of axial elongation, especially in younger children, can justify targeting this age group. Starting ortho-k or other myopia control treatment at age 6 coincides with commencement of primary education, when it is common to implement vision screening²⁶⁻³⁰ to ensure that vision problems are addressed early to prevent adverse effects. Children at this age are usually able to accept the required testing procedures. Current knowledge of effectiveness and benefits of ortho-k and other myopia control treatments does question the use of conventional correction with single-vision spectacles or single-vision contact lenses alone for managing early childhood myopia. Practitioners may be prudent to reconsider the routine prescription of such optical aids and take myopia control into consideration, and fully inform parents of the options and the potential benefits and advantages of early implementation.

Most of the previous studies for myopia control, including our work, mainly presented the percentage reduction in axial elongation without actually determining the risk and benefits of the particular treatment. In the current study, although the percentage of reduction in axial elongation was similar in younger and older subjects (around 43%-46%), the RR and NNT of rapid axial elongation with ortho-k were different in the two subgroups. Hence, reporting the overall percentage reduction of myopia or axial elongation alone may not represent adequate information on the effectiveness of any myopia control intervention.

The current study has reported reduced risk and low NNT of rapid axial elongation with ortho-k treatment. The treatment was more effective in reducing rapid axial elongation in younger children; in this subgroup, the risk was reduced by 88.8% with ortho-k treatment. For the older age group, the NNT of rapid progression did not reach statistical significance, but a lower percentage of subjects had rapid axial elongation in the ortho-k group compared to the controls (see Fig. 2). The 2-year NNT metric indicated a substantial benefit of ortho-k treatment for myopia control in younger children by reducing rapid progression in these subjects, as treating just two children for 2 years would prevent one subject from experiencing rapid axial elongation.

It is of interest to note that about 14% of the older ortho-k subjects showed a reduction, instead of an increase in axial length at the end of 2 years of lens wear. None of the younger subjects exhibited this reduction. The cause of this apparent shortening of axial length remains unclear. No other studies have reported prolonged shortening of axial length over the course of treatment, although a shortening of axial length has commonly been observed at the initiation of ortho-k lens wear, attributed at least in part to central corneal thinning^{9,11,12,17,18} and choroidal thickening.³¹⁻³³ Central corneal thinning reflects the redistribution of corneal tissue and this change usually stabilizes within a few weeks, once the optimal refractive correction has been achieved.³⁴⁻³⁵ Compared to reports on the effect of ortho-k on corneal thickness, few studies have investigated changes in choroidal thickness. However, choroidal thickening with ortho-k has been reported in two separate studies.^{31,33} One was a short-term study,³³ lasting no more than 4 weeks, and the other was a longer term study,³¹ investigating changes 1 to 9 months after lens wear. If the choroid is responding to the change in retinal defocus experienced initially with ortho-k, this adaptation would be expected to end when refractive status correction stabilized (i.e., no uncorrected myopia remains). This explanation is consistent with findings of one of the two above studies that changes in choroidal thickness did not persist beyond the initial stabilization period.³¹ However, controlled clinical trials with a larger sample size and of longer duration are warranted to investigate the association between choroidal thickness changes and axial elongation in ortho-k.

As explained above, ROMIO and TO-SEE used the same methodology, with the exception that ROMIO was a randomized control trial whereas TO-SEE allowed self-selection of treatments. Analyses showed that there were no significant differences in the baseline values of pertinent parameters between subjects except for astigmatism, which was shown to have no interaction with axial elongation. The pooled data analyses confirmed previous findings and provided further insight into benefits of ortho-k for myopia control in children. A high prevalence of myopia has until recently been assumed to be a predominantly East Asian problem. Countries, such as China, Singapore, and Japan have voiced concerns about myopia progression in children for many years.³⁶⁻⁴¹ However, recent studies have revealed that myopia should be considered a worldwide problem.⁴²⁻⁴³ Parents who are concerned about myopia progression in their children tend to be more proactive in searching for a treatment for its control and ortho-k is a popular option.⁴⁴ A common question asked is the optimal timing for ortho-k treatment for their children. The results of this study suggest that ortho-k treatment should be started in younger myopic children (6-8 years).

It is recognized that results from clinical research are performed under optimal conditions and care in the real-world community may not be as successful due to issues of compliance and practice.⁴⁵ Notably, our results are based on analysis of data from a cohort study (TO-SEE) and a randomized control trial (ROMIO) performed by the same group of researchers in Hong Kong, both reporting encouraging outcomes. However, further confirmation should be obtained from studies performed in other settings as cultural factors can affect success of interventions.

In conclusion, ortho-k treatment significantly reduces risk of rapid progression in younger (6-8 years) subjects and is predicted to protect one in two of these subjects from rapid axial elongation. Thus, its use should be seriously considered for young children exhibiting rapid myopia progression.

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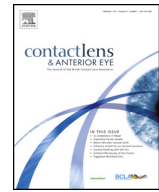
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Discontinuation of orthokeratology on eyeball elongation (DOEE)

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ABSTRACT

Purpose: To evaluate and compare changes in axial elongation, over a 14-month period, in subjects who discontinued and then resumed ortho-k lens wear with those who continued to wear their lenses or spectacles following a 2-year myopia control study.

Method: This single masked, prospective study recruited subjects who had just completed a 2-year myopia control study. Ortho-k subjects were classified as Group OKc, in which subjects continued ortho-k lens wear for the duration of the study; or Group OKd in which subjects discontinued lens wear for seven months and wore single-vision spectacles (Phase I) and then resumed ortho-k lens wear for another seven months (Phase II). Spectacle-wearing control subjects from the initial myopia control study continued wearing spectacles as control subjects. Axial lengths were measured at scheduled visits using the IOLMaster.

Results: Thirteen, 16, and 15 Control, OKc, and OKd subjects, aged 8–14 years, respectively completed the study. Significant increase in axial elongation was found in OKd subjects only in Phase I but not in Phase II. On resuming lens wear, in Phase II, the rate of axial elongation was no longer significantly different from those of the Control or OKc subjects.

Conclusion: Stopping ortho-k lens wear at or before the age of 14 years led to a more rapid increase in axial length; comparable to those wearing spectacles during the initial 2-year myopia control study, but greater than the Control and OKc group in this study. Axial elongation slowed again with resumed lens wear after six months.

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1. Introduction

Orthokeratology (ortho-k), shown to be effective in slowing the progression of myopia [1–8], is now popular for myopia control in children, particularly in East Asian countries where the prevalence of myopia is high [9–12]. Toric ortho-k lenses have also been shown to be effective in reducing high astigmatism [7] and a pilot study using partial correction ortho-k (targeting 4.00D reduction for all high myopic subjects) demonstrated a higher level of myopia control, compared to treatment for low myopes [8], giving improved prognosis for children with high myopia and whose myopia is still progressing.

A survey, conducted in Hong Kong and soliciting parents' perspective on optical methods for myopia control, revealed that ortho-k was the most recognised method for myopia control. When parents were asked about their preferred option if all three optical treatments – ortho-k, soft contact lenses, and spectacles, were equally effective for myopia control, more parents chose

ortho-k over the other treatments [13]. Although safety was a crucial concern, confidence in the treatment and convenience offered were also important considerations when the parents decided on the myopia control method for their children. Children undergoing ortho-k treatment could achieve >50% of myopia reduction after only one overnight lens wear [14–16], which boosted parents' confidence in ortho-k. For most children, the correction of refractive error, after stabilization of treatment, is sufficient to allow freedom from the need of vision correcting aids during the day. Wide publicity of ortho-k treatment in East Asia, including Hong Kong, also reassured parents of its effectiveness for myopia control. While many studies on the effectiveness of ortho-k for myopia control have been published [1–8] less emphasis has been placed on the clinical aspects of this treatment. Common queries from many parents included at what age could their children stop ortho-k lens wear and what would happen when lens wear was ceased. This information is necessary and important as parents do have concerns about permanent dependency on ortho-k once their children had commenced the treatment. It is unknown whether the myopic control effect would dissipate upon discontinuation of the treatment leading to a rebound effect to where the refraction or eyeball length would have been if they had not

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received the treatment (i.e. assuming their myopia was progressing) or, worse still, increased even faster than if they had never had the treatment.

This study aimed to evaluate and compare changes in axial elongation, over a 14-month period, in subjects who continued or discontinued and then resumed ortho-k lens wear following two years of ortho-k lens wear. Axial elongation was compared with control subjects wearing spectacles who had also been monitored over the previous two years.

2. Methods

This study was a single masked, prospective study of 14-month duration. Parents with children participating in the ROMIO [6] and TO-SEE [7] myopia control studies were invited to enroll in this study immediately after their children had completed the myopia control study. The study was approved by the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University and registered at ClinicalTrials.gov, number NCT01236742. Written consent was obtained from both subjects and their parents before study participation. Ortho-k subjects from the initial 2-year myopia control studies who agreed to participate were assigned mainly by randomizing them into two ortho-k groups but due to a few refusals to be randomized, four subjects were allowed to transfer to the group they preferred. The two ortho-k groups were Group OKc where subjects continued ortho-k lens wear for the duration of the study; and Group OKd where subjects discontinued lens wear for seven months and wore single-vision spectacles (Phase I) and then resumed ortho-k lens wear for another seven months (Phase II). All spectacle-wearing control subjects were also invited to continue as control subjects (Group C) and to continue wearing spectacles during the study.

2.1. Group OKd

At the beginning of Phase I (Spectacle-wear phase), in the RS (Refraction Stabilization) period, subjects were required to wear single-vision spectacles to aid distance vision. They could use their old spectacles from before ortho-k use if the prescription was within ± 0.50 DS and ± 0.50 DC from the refraction determined at the time of visit, otherwise, a new pair of spectacle lenses was

ordered. They were required to return weekly until stabilization of refractive errors was achieved. Refraction was considered stabilized when changes in refractive sphere and refractive cylinder in manifest refraction and change in apical radius in corneal topography between two consecutive visits was 0.25 D or less. Refraction measured after stabilization was used to prescribe a new pair of spectacles which were delivered at Visit I-1 (baseline of Phase I, see Table 1). All subjects were required to wear the fully-corrected spectacles in the daytime during Phase I. They were excluded if they used any contact lenses during Phase I. New ortho-k lenses for these subjects were ordered one month before the end of Phase I (ie. at Visit I-6) and dispensed at the end of Phase I (Visit I-7) before commencing Phase II (Table 1) (Ortho-k phase), in which the subjects were required to wear the lenses every night unless otherwise instructed by their examiner, for example, in cases of illness, sore eyes, or presence of corneal insult. Refractive correction with ortho-k was considered stabilized when changes in manifest refractive sphere and refractive cylinder and change in apical radius in corneal topography between two consecutive visits was not more than 0.25 D. Baseline of Phase II was performed at Visit II-1 and the examination was repeated six months later at Visit II-7.

2.2. Group C and Group OKc

Subjects were required to wear their habitual spectacles (Group C) or ortho-k lenses (Group OKc) at the commencement of Phase I, before Visit I-1. New glasses were prescribed based on the prescription determined at Visit I-0 and new spectacles were delivered at Visit I-1 and if indicated (based on data collected at Visit I-6), at Visit I-7 before commencing Phase II. There was no RS period for these two groups of subjects, but, similar to Group OKd, cycloplegic and non-cycloplegic data correction visits were scheduled accordingly.

All subjects were required to use the prescribed spectacles/ortho-k lenses every day/night unless otherwise instructed. Regular ortho-k aftercare visits (Table 2) were arranged for all ortho-k subjects upon delivery of ortho-k lenses to ensure healthy and safe ortho-k lens wear. The ortho-k effect was reviewed one night, one week, two weeks, three weeks, one month, and every 2–3 months after commencing lens wear. Complimentary contact

Table 1
Data collection visits.

Cycloplegic	Non-cycloplegic	Description	Remark
<i>Phase I</i>			
I-0		Baseline	End of the initial 2-year myopia control study
<i>[RS period: Weekly visits (for Group OKd subjects) to determine stabilization of refraction. Order new orthokeratology lenses/spectacles for the 3 groups of subjects for delivery at Visit I-1 (Prescription for Group C and OKc should not be more than 1 month old)]</i>			
I-1		End of RS period in Phase I for OKd; or 28 (± 3 days) after I-0 for OKc and control and for subjects in OKd if RS period was less than 4 weeks	Delivery of glasses for control and OKd and ortho-k lenses for OKc
	I-3	2 (± 1 week) after I-1	
	I-6	5 months (± 1 week) after I-1	Order new ortho-k lenses/spectacles based on updated Rx for the 3 groups of subjects for Visit I-7 where indicated
I-7		6 months (± 1 week) after I-1	Delivery of glasses for control and OKc, and ortho-k lenses for OKd and OKc (if deemed necessary)
<i>Phase II</i>			
II-0		Equivalent to Visit I-7	
II-1		End of RS period for OKd or 28 (± 3 days) after II-0 for OKc and control and for subjects in OKd if RS period was less than 4 weeks	
	II-3	2 (± 1 week) after II-1	
	II-6	5 months (± 1 week) after II-1	
II-7		6 months (± 1 week) after II-1	

RS – Refraction-Stabilization.

Group OKc – Orthokeratology subjects who continued orthokeratology lens wear for the whole experiment period.

Group OKd – Orthokeratology subjects who discontinued orthokeratology lens wear in Phase I and resumed orthokeratology lens wear in Phase II.

Table 2

Scheduled aftercare visits for orthokeratology subjects.

Commencement of lens wear	The night when the ortho-k treatment commenced or resumed. Within 14 days after the last data collection visit, if applicable.
First overnight visit	The following morning after commencing lens wear. Within 2 h after awakening in the morning.
One-week visit	Seven days (± 3 days) after commencing lens wear. Within 2 h after awakening in the morning.
Two-week visit	Fourteen days (± 3 days) after commencing lens wear. Within 2 h after awakening in the morning.
Three-week visit	Twenty-one days (± 3 days) after commencing lens wear. Within 2 h after awakening in the morning.
One-month visit	Twenty-eight days (± 3 days) after commencing lens wear. Can be in the morning or in the afternoon.
Three-monthly visit	Coincided with data collection visits

lens solutions and lens accessories were also supplied to OKd and OKc subjects during the treatment to ensure compliance with replacement. They also had to complete a daily compliance check list in an ortho-k journal provided. Subjects using ortho-k with residual refractive error more than -0.75 DS would be prescribed with a pair of spectacles to be used in the daytime when indicated. They were required to return the ortho-k lenses at the completion of study at Visit II-7. Weekly review on the regression of refraction and corneal topography would be performed and subjects would be dismissed from the study upon stabilization of changes in refractive error and corneal topography.

2.3. Data collection visits

Cycloplegic (0.5% atropine followed by 1% tropicamide and 1% cyclopentolate) data collection visits were conducted at the beginning of each phase, after one month, and at the end of each phase. Non-cycloplegic data was collected after three and six months into each phase. To minimize the effect of diurnal variation, data collection visits were scheduled at about the same time of the day for each visit.

Subjective and objective refraction were measured; the latter using the Shin-Nippon NVision-K 5001 open field autorefractor (Shin-Nippon Commerce Inc, Tokyo, Japan). Corneal topography was performed with Medmont E300, Australia) and ocular integrity assessed using a slitlamp (Topcon SL-D7; Topcon Corp., Tokyo, Japan). Axial length measurements were performed by a masked examiner using the IOLMaster (Zeiss Humphrey, Dublin, CA, USA).

2.4. Ortho-k lenses, solutions and spectacles lenses

Menicon Z Night and Night Toric lenses (NKL Contactlinsen BV, Emmen, The Netherlands) were used. Lenses were ordered using the Easy Fit software from NKL. Complimentary solutions (Menicon O2 Care for daily cleaning, Menicare Plus for daily disinfection and Menicon Progent for protein removal, Menicon Co. Ltd, Japan; Tears Naturale Free for eye lubrication, Alcon Hong

Kong Ltd) were prescribed to the ortho-k subjects, but subjects had to purchase preserved saline for lens rinsing. All solutions had to be replaced monthly.

Complimentary spectacles lenses (refractive index 1.56 spherical lenses; Founder Optical Company, Hong Kong) were provided, if indicated during the RS period. Once the refraction had stabilized at the end of the RS period, new complimentary spectacle lenses were prescribed. For the Control and OKc subjects, spectacles and new ortho-k lenses, respectively were provided at the commencement of the study.

2.5. Statistical analysis

Statistical analyses were performed using SPSS version 23. Data were first tested to check if they deviated from normality. Oneway ANOVA or Kruskal-Wallis test, as appropriate, was used to test for differences between groups. Changes in axial length between groups, controlled for age and initial axial length, were evaluated using analysis of covariance (ANCOVA), and within groups using repeated measures ANCOVA.

3. Results

A total of 64 ortho-k and 72 control subjects from ROMIO [6] and TO-SEE [7] studies were invited to participate but only 53 agreed. A total of 16, 19 and 18 subjects were recruited for the Control, OKc, and OKd groups, respectively but only 13, 16, and 15 subjects, respectively completed the study. Subjects were 8–14 years old when they commenced this study.

All subjects were able to comply with the instruction on lens wear, i.e. at least eight hours a day and at least five hours a week, either using spectacles or ortho-k lenses.

The baseline refractive errors of the subjects before they commenced ROMIO/TO-SEE studies and before and during this study are shown in Table 3. All OKd subjects achieved stabilization of refraction within six weeks after ceasing lens wear in Phase I and within five weeks after commencement of lens wear in Phase II.

Table 3

Demographic data of the three groups of subjects.

	Control (N = 13)	Okc (N = 16)	Okd (N = 15)	P value
<i>Baseline (before commencing initial 2-year myopia control studies[#])</i>				
<i>(retrospective data)</i>				
SER (D)	-2.12 ± 0.81	-2.42 ± 0.92	-2.36 ± 1.06	0.676*
Axial length (mm)	24.07 ± 0.79	24.26 ± 0.89	24.61 ± 0.90	0.255*
<i>Baseline (before commencing current study)</i>				
Age (years, median (range))	11.0 (9–13)	11.0 (9–12)	10.0 (10–14)	0.479**
Axial length (mm)	24.69 ± 0.88	24.72 ± 0.90	24.94 ± 0.89	0.704*

P value – probability values from * One-way ANOVA; **Kruskal-Wallis test.

[#] ROMIO⁶/TO-SEE⁷ studies.

At Visit I-0, all pertinent data, except for age, were normally distributed ($p > 0.05$). No significant differences in age, initial Rx, initial axial length and axial length were found among the three groups of subjects (age: Kruskal-Wallis test, $p = 0.479$; AL: one-way ANOVA, $0.255 < p < 0.704$). At the end of Phase I, after adjusting for age and initial axial length before commencing this study, significant differences in axial elongation were found among the three groups of subjects (ANCOVA, $p = 0.041$). However, these differences were not observed in Phase II (ANCOVA, $p = 0.945$) (Table 4). Post hoc with LCD tests indicated that the differences in Phase I were between OKd and the other two groups of subjects (Control vs OKd, $p = 0.027$; OKc vs OKd, $p = 0.030$). Axial elongation in OKd group was faster than those of Control and OKc subjects in this phase. Changes in axial length (unadjusted) during the different phases of the study are shown in Fig. 1. The graph shows wide and overlapping standard deviations at each visit within groups, indicating large variations.

4. Discussion

This is the first study to investigate the effects of discontinuation and resumption of ortho-k lens wear in children. The results of this study showed a faster axial elongation in OKd group compared to those of OKc and Control in Phase I of the study. We believe that this is the first longitudinal study to address the concerns of dependency on ortho-k once children commenced treatment and effect on refraction after discontinuation of lens wear. Although

the sample sizes were relatively small and therefore the power of the study was limited, some interesting observations were noted.

In Phase I, axial elongation of OKd subjects was faster when lens wear was terminated after two years of ortho-k lens wear. The rate appeared to be similar to that of progression of control subjects wearing spectacles during the initial myopia control studies (ROMIO [6]/TO-SEE [7]) (see Fig. 2). Since OKd subjects were aged 10 to 14 years when they commenced participation in this study, the results of this study suggested that ortho-k treatment should not stop at the age of 14. So, if termination of treatment at 14 years old is not recommended, when should it be terminated? The COMET group (COMET study [17]) evaluated the age of myopia stabilization of children of different ethnic groups. They monitored the refraction of the subjects over 11 years and, based on seven refraction assessments, they reported that the age of stabilization of myopia for Asian subjects was 16 years old. However, it should be noted that at age 16, the proportion of their Asian subjects with estimated stable myopia was about 60%, that is to say, the myopia of 40% of the subjects were still progressing, albeit at a slower rate.

Another interesting observation that may be observed in Fig. 2 is that axial elongation after resuming lens wear in Phase II (month 31–38) was slower than the rate before stopping lens wear (before month 24). It appears that after stopping lens wear for six months, resuming lens wear led to much slower axial elongation, although it is unclear why. Possibly, the myopia progression mechanism was disrupted due to the interrupted lens wear pattern. Nevertheless, if the rate continued to be slower, with continued lens wear for another 12 months, OKd subjects may eventually have a much lower increase in axial length than if they did not stop lens wear.

The results of this study indicated that taking short break of limited period from lens wear did not adversely affect axial elongation if lens wear was later resumed. This information is important for practitioners and parents; they can be assured that allowing their child to take a break from lens wear in case of illness or travelling, may not affect the overall outcome of the treatment.

Table 4
Six-monthly increases (mean (SE)) in axial length (mm), adjusted for age and axial length before commencing the study.

	Control (N=13)	OKc (N=16)	OKd (N=15)	P value
Phase I	0.082 (0.022)	0.087 (0.020)	0.153 (0.021)	0.041
Phase II	0.064 (0.015)	0.068 (0.013)	0.059 (0.014)	0.901

P value – probability values from ANCOVA.

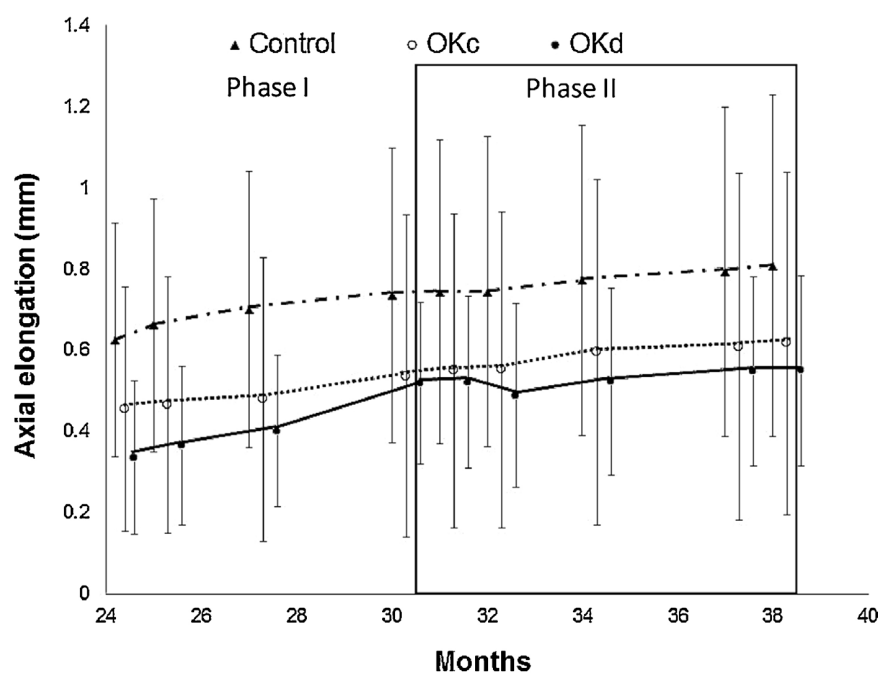


Fig. 1. Axial elongation of the subjects at each visit over 14 months (starting at month 24, as current study commenced following completion of a 2-year myopia control study). Control – continued to wear single vision spectacles in both Phases of the study; OKc – continued to wear orthokeratology lenses in both Phases of the study; OKd – ceased orthokeratology lens wear for 6 months (Phase I) and then resumed lens wear in Phase II. Data points shown in the graph are staggered to allow easier view of the error bar. Each error bar represents one standard deviation.

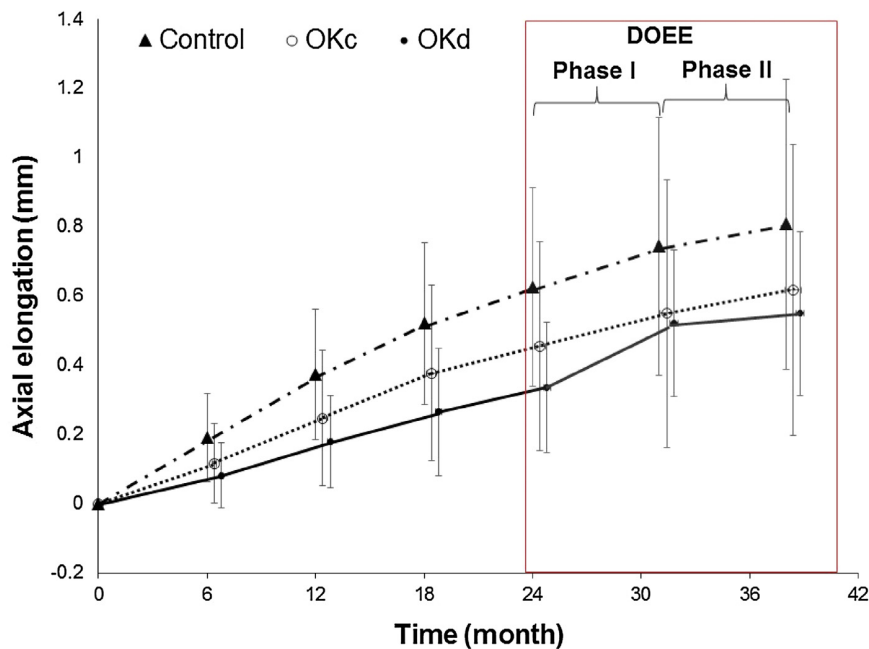


Fig. 2. Axial elongation of the subjects at each visit, including data (retrospective) from subjects' initial 2-year myopia control study. Control – continued to wear single vision spectacles in both Phases of the study; OKc – continued to wear orthokeratology lenses in both Phases of the study; OKd – ceased orthokeratology lens wear for 6 months (Phase I) and then resumed lens wear in Phase II.

Data collection visits for the three groups of subjects were the same but data points shown in the graph are staggered to allow easier view of the error bar. Each error bar represents one standard deviation.

The results of this study suggest a potential option for parents who ask if their children could stop lens wear after two years of myopia control. Practitioners could suggest ceasing lens wear for six months, and monitor eyeball elongation every three months. If the axial elongation rate increased, then they should resume lens wear after six months.

Randomisation of subjects into OKd and OKc groups was initially attempted but abandoned after a few parents refused to participate in the study if their children were assigned to OKd group. Although clinical trials involving children often encounter difficulties with subject recruitment and retention, this study encountered more difficulties than most in enrolling subjects for several reasons. The most important reasons for refusal of subjects to stop ortho-k lens wear were fears of losing the benefits of the initial 2-year myopia control treatment and the need for vision correction in the daytime once they stopped lens wear. Many subjects were reluctant to participate in this study because of the need to attend frequent scheduled visits and the necessity of cycloplegic examination as the drug used affected their near work for at least a day; about 16–19% of subjects dropped out of the study for these reasons.

Compliance with lens wear and care was carefully monitored throughout the study. Subjects were requested to withdraw from the study if any of the following occurred: persistent corneal staining (>Grade 2 in Efron's scale [18]); non-compliance with study protocol (e.g. wearing contact lenses during the discontinuation period or rarely use ortho-k lenses during the lens wear period).

Clearly there are problems both with recruitment of subjects leading to a small sample size and inability to completely randomize subjects into different groups. However, the study does show a significant different in rates of axial elongation during the period of discontinuation of lens wear, which can be reversed by resumption. We believe that any other study including similar groups of subjects is likely to encounter similar difficulties.

From experience, once children are undergoing successful ortho-k treatment, parents are reluctant to stop as the treatment because, apart from being effective in slowing myopia progression, it also allows their children to be free from the need to wear any vision correction in the daytime, bringing convenience to daily activities for their children. The major concern of parents commencing ortho-k treatment is not knowing when they can discontinue the treatment. About 50% of the ortho-k subjects continued to wear ortho-k lenses after the study. It is hoped that these subjects and those who have discontinued can be contacted at a later date for assessment of their ocular parameters.

In summary, axial elongation appeared to speed up when ortho-k lens wear was terminated after two years of ortho-k lens wear, before or at the age of 14. The rate of elongation was similar to those wearing spectacles during their 2-year myopia control study, but more rapid than either the control and OKc group in this study.

The results of this study suggest that early termination of ortho-k treatment may not be recommended and, in case of discontinuation, it would be prudent to continue to monitor axial elongation after stopping lens wear for at least 6 months and to resume lens wear if rapid axial elongation was observed during the discontinuation period.

Conflicts of interest

None.

Acknowledgements

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Retardation of Myopia in Orthokeratology (ROMIO) Study: A 2-Year Randomized Clinical Trial

Pauline Cho and Sin-Wan Cheung

PURPOSE. This single-masked randomized clinical trial aimed to evaluate the effectiveness of orthokeratology (ortho-k) for myopic control.

METHODS. A total of 102 eligible subjects, ranging in age from 6 to 10 years, with myopia between 0.50 and 4.00 diopters (D) and astigmatism not more than 1.25D, were randomly assigned to wear ortho-k lenses or single-vision glasses for a period of 2 years. Axial length was measured by intraocular lens calculation by a masked examiner and was performed at the baseline and every 6 months. This study was registered at ClinicalTrials.gov, number NCT00962208.

RESULTS. In all, 78 subjects (37 in ortho-k group and 41 in control group) completed the study. The average axial elongation, at the end of 2 years, were 0.36 ± 0.24 and 0.63 ± 0.26 mm in the ortho-k and control groups, respectively, and were significantly slower in the ortho-k group ($P < 0.01$). Axial elongation was not correlated with the initial myopia ($P > 0.54$) but was correlated with the initial age of the subjects ($P < 0.001$). The percentages of subjects with fast myopic progression (>1.00 D per year) were 65% and 13% in younger (age range: 7–8 years) and older (age range: 9–10 years) children, respectively, in the control group and were 20% and 9%, respectively, in the ortho-k group. Five subjects discontinued ortho-k treatment due to adverse events.

CONCLUSIONS. On average, subjects wearing ortho-k lenses had a slower increase in axial elongation by 43% compared with that of subjects wearing single-vision glasses. Younger children tended to have faster axial elongation and may benefit from early ortho-k treatment. (ClinicalTrials.gov number, NCT00962208.) (*Invest Ophthalmol Vis Sci.* 2012;53:7077–7085) DOI:10.1167/iovs.12-10565

The prevalence of myopia is high in Hong Kong and other East Asian countries.^{1–9} It is well documented that significant axial elongation of the eyeball in high myopia can be associated with higher risk of sight-threatening complications such as maculopathy and retinal detachment.^{10,11} Thus,

early preventative treatment in children for retardation of axial elongation is important to prevent the development of high myopia.

Orthokeratology (ortho-k), an optical correction mainly for correcting low-to-moderate myopia, has been shown to have potential in slowing myopic progression in myopic children.^{12–15} Lenses are worn during sleep and removed after waking up. Successful treatment allows users to see clearly in the daytime, provided that they continue to wear the lenses regularly at night to maintain the reshaping effect.

Five quasi-experimental studies using historical or self-selecting controls have reported slower myopic progression (by 32–55%) in low-to-moderately myopic children wearing ortho-k lenses compared with those wearing conventional eyeglasses^{12,14–16} or single-vision soft contact lenses.¹³ The treatment was well received by both children and parents, and there were no significant adverse effects reported with proper instruction and proper care given. The primary objective of the current study was to confirm if ortho-k can retard myopia in children with low-to-moderate myopia using a randomized clinical trial (ClinicalTrials.gov number, NCT00962208).

The importance of myopic control is to prevent the development of high myopia, that is, to reduce the number of children with fast progression in myopia. The average increase in myopia in myopic Chinese children in Hong Kong is approximately 0.50 diopter (D) per year.^{17–19} Children with an average increase of more than 1.00D per year in myopia can therefore be regarded as fast progressors.^{20–22} The secondary objective of this study was to determine and compare the percentages of subjects with slow, moderate, and fast progression of myopia in the two groups of subjects.

METHODS

Study Design

This was an interventional study using a stratified, randomized parallel group and single-masked design to investigate axial elongation of the eyeball in myopic children wearing ortho-k lenses (study group) and single-vision spectacles (control group) for a period of 2 years. Subject recruitment was stratified by age, sex, and manifest refractive error to minimize systematic bias. Randomization was performed in blocks of two using a commercial spreadsheet random number generator (Excel; Microsoft, Redmond, WA). The randomization list was generated and inspected by a project member who was not involved in subject recruitment or data collection, to ensure equal numbers of subjects assigned to each group. The random allocation sequence was revealed to the unmasked examiner who would proceed to prescribe the assigned treatment to the subjects accordingly.

Myopic progression was estimated from changes in axial length in both groups and the primary outcome measure (i.e., the axial length) was masked in the study. Double-masking could not be achieved because of the unique characteristics of the ortho-k treatment. Subjects in the study group knew that they were wearing ortho-k lenses because they needed to wear the lenses to sleep and had improved unaided

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TABLE 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • 6 to 10 years old (inclusive) • Myopia: between 0.50D and 4.00D in at least 1 eye • Astigmatism: <1.50D; with-the-rule astigmatism (axes 180 ± 30) ≤ 1.25D; astigmatism of other axes ≤ 0.50D in both eyes • Spherical equivalent (SE): >0.50D and ≤ 4.50D in both eyes • Anisometropia: ≤ 1.50D • Best-corrected logMAR visual acuity 0.10 or better in both eyes • Symmetrical corneal topography with corneal toricity <2.00D in either eye • Agreed to randomization 	<ul style="list-style-type: none"> • Strabismus at distance or near • Previous experience in contact lens wear or myopia control treatment (e.g., refractive therapy or progressive spectacles) • Contraindication for contact lens wear and orthokeratology (e.g., limbus to limbus corneal cylinder and dislocated corneal apex) • Previous history of ocular surgery, trauma, or chronic ocular disease • Concurrent use of medications that may affect tear quality • Systemic or ocular conditions that may affect tear quality or contact lens wear (e.g., allergy and concurrent medication) or that may affect refractive development (e.g., Down syndrome, ptosis) • Poor compliance to tests (e.g., poor fixation in noncontact tonometry or intolerance of lens wear) • Not willing to comply with the allocated treatment and follow-up schedule

vision in the daytime. The unmasked examiners knew if a subject was on ortho-k treatment from the good unaided vision, the low (residual) refractive error, the typical topographic maps, and ocular signs (i.e., pigmented arc) observed in slit-lamp biomicroscopy. However, ortho-k did not present any particular identifying features during axial length measurement (IOLMaster; Zeiss Humphrey, Dublin, CA) and the examiner performing the measurement could be masked.

The study was approved by the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University. Written consent was obtained from both subjects and their parents before study participation. This study was registered at ClinicalTrials.gov, number NCT00962208.

Subjects

Subject recruitment was advertised in local newspapers and on the campus of The Hong Kong Polytechnic University from March 2008 to June 2009. Telephone interview was performed to screen out ineligible subjects using a checklist. Children, ranging in age from 6 to 10 years, with low-to-moderate myopia (0.50–4.00D) in at least one eye, and low refractive astigmatism (≤ 1.25 D) and spherical equivalent not more than 4.50D in both eyes, and low anisometropia (≤ 1.50 D) (based on manifest refraction), were recruited (Table 1). Ortho-k subjects were fitted with spherical 4-zone lenses (Menicon Z Night lenses; NKL Contactlinsen B.V., Emmen, The Netherlands) made of gas-permeable lens material (Menicon Z material, DK 163 ISO; central lens thickness: 0.24 mm). Lens fitting was performed according to the manufacturer's instructions (Easy Fit Software, v. 2006; NKL Contactlinsen B.V.) based on corneal topography, noncycloplegic manifest refraction, and the horizontal visible iris diameter. The use of a computer program helped to reduce subjective bias in lens selection. Complimentary lenses, solutions, and accessories were provided to facilitate compliance with regular replacement. Lenses were removed by manipulating the lens edge with the eyelid margins using fingers to reduce risk of contamination associated with the use of suction holder.²³ Control subjects were corrected with single-vision lenses made of plastic lens material, with refractive index of 1.56 (CR-39 material; Hong Kong Optical Lens Co., Hong Kong, China). They were given complimentary spectacle frames and lenses. Unless otherwise instructed, all subjects were required to wear the assigned treatment item on a daily basis. Full correction was targeted for all subjects. Habitual prescription was updated if the monocular VA was worse than 0.18 (logMAR) (Snellen 6/9) or residual myopia/astigmatism exceeded 0.50D at any visit after stabilization of treatment.

Subjects who were lost to follow-up, noncompliant with test procedures/schedule, contraindicated to continue ortho-k treatment (study group only), or could not achieve the desired myopic reduction (study group only) after modification of lens parameters were excluded

from the study. The first and last subjects were recruited in March 2008 and November 2009, respectively, and the last data collection visit was in November 2011.

Procedures

All subjects were required to attend 6-monthly cycloplegic examinations (data collection visits) at the Optometry Clinic of the School of Optometry of The Hong Kong Polytechnic University after the initial visit for 2 years. Ortho-k subjects were also required to attend routine ortho-k aftercare visits (1 day, 1 week, 1 month, and every 3 months after lens delivery) and unscheduled visits where necessary, to ensure good ocular response and health. Clinical care was provided by the same practitioner throughout the study period.

At each data collection visit, habitual and best-corrected logMAR VA, manifest subjective refractive error (trial frame and trial lenses), anterior segment of the eye (TOPCON slit-lamp SL7 and TOPCON IMAGENet system, ver. 2000; Topcon Corp., Tokyo, Japan), corneal topography (Medmont E300 topographer; Medmont Pty Ltd., Vermont, VIC, Australia), and intraocular pressure (NIDEK NT-2000; Nidek Co., Ltd., Aichi, Japan) were assessed by the unmasked examiner before cycloplegia. Maximum plus maximum VA was used in the assessment of subjective refraction. For corneal topography, at each data collection visit, the first four good corneal topographic maps with image score above 98 were saved. For ocular tonometry, the first three measurements (between measurement differences not more than 3 mm Hg) were saved.

Axial length measurement of the eyeball (IOLMaster) was performed by a masked examiner 30 minutes after cycloplegia with 1 drop of 0.5% proparacaine, followed by 1 drop of 1% tropicamide, and 1 drop of 1% cyclopentolate, administered 5 minutes apart. The first five axial length readings with signal-to-noise ratio above 3.5 and a maximum difference of 0.02 mm between any two readings were saved and the average was used for data analysis.

Subjects were classified into different myopic progression groups for further analysis. Those with myopic progression not exceeding the average annual growth (i.e., 0.50D per year or axial elongation ≤ 0.18 mm per year²⁴) were regarded as slow progressors, whereas those showing myopic progression exceeding 1.00D per year (i.e., axial elongation >0.36 mm per year) were regarded as fast progressors. The remaining subjects who fell between the two categories (i.e., >0.50 and ≤ 1.00 D per year or >0.18 and ≤ 0.36 mm per year) were regarded as moderate progressors.

Sample Size Calculation

The efficacy of myopic control of ortho-k was determined by dividing the difference in mean axial length changes in the two groups after 2

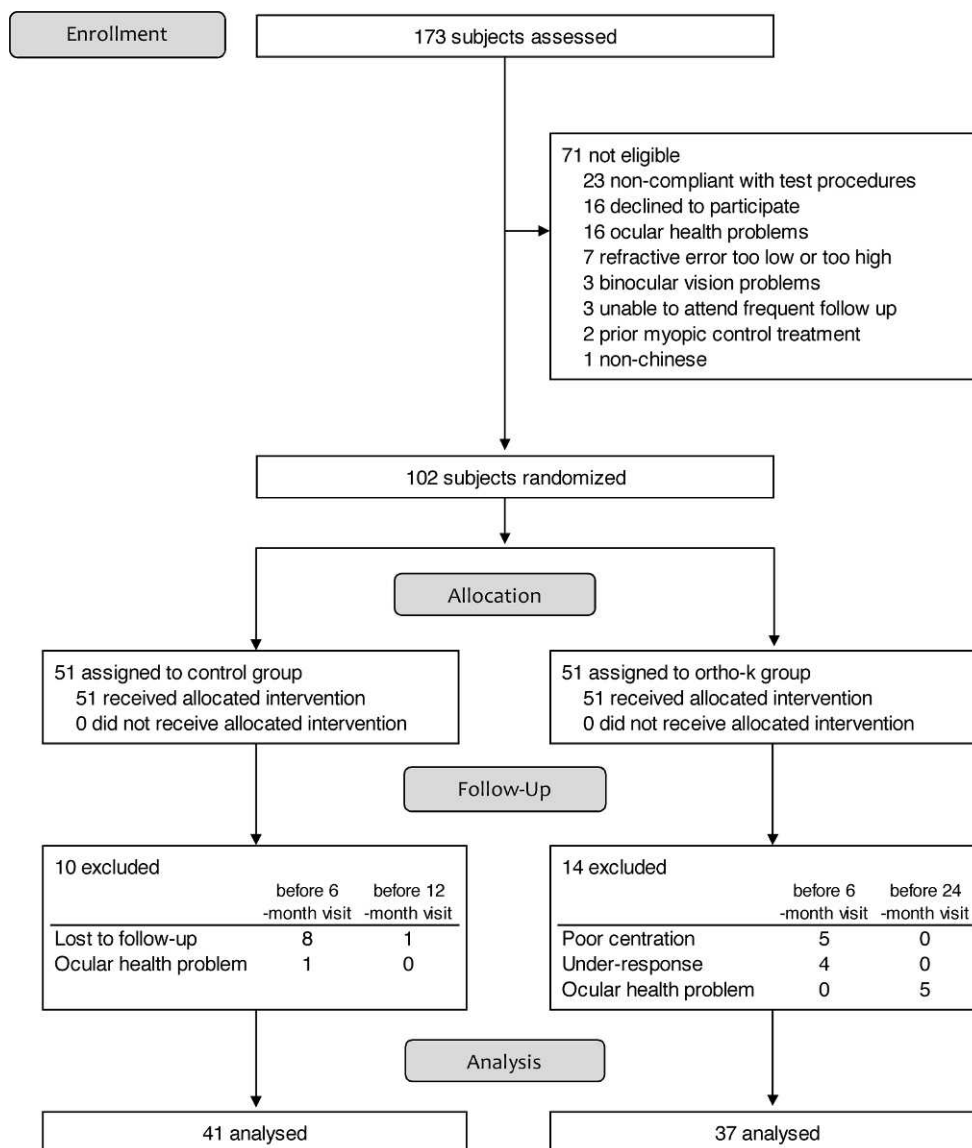


FIGURE 1. Study flow chart and dropouts.

years with the mean axial length change in the control subjects times 100%. We sought 80% power to detect a 0.18 mm (SD 0.27 mm)¹² (equivalent to 0.50D change in refraction)²⁴ difference in eye elongation between the two groups (over 2 years) with a significance level of 0.05 (two-tailed); the minimum number of subjects required to complete the study in each group was 20.

Statistical Analysis

Because all right eyes satisfied inclusion criteria, only data from the right eye were used for data analyses. Statistical analysis (SPSS software ver. 18.0; SPSS Inc., Chicago, IL) was performed by the principal investigator. Only completed cases were analyzed. Intention-to-treat analysis was not used in this study because subjects lost to follow-up in both groups and ortho-k subjects who were deemed not suitable to continue the treatment were not motivated or were reluctant to return for cycloplegic examinations. Mann-Whitney *U* tests and unpaired *t*-tests were used to compare the baseline characteristics between the two groups of subjects. Repeated-measures ANOVA tests (and paired *t*-tests with Bonferroni correction where appropriate) were used to compare changes in axial length during the study period. Since interim

analyses (12- and 18-month axial length data between groups) on the primary outcome (i.e., axial elongation) were made during the study period, the level of significance used was adjusted accordingly where appropriate. Factors affecting axial elongation including age, sex, treatment, initial myopia, and initial corneal topography were investigated using stepwise multiple linear regression analysis. To obtain further insight into the observed treatment effect, cross-tab analyses were used to compare the proportions of fast progressors in the ortho-k and control groups, although each subgroup sample size in these analyses was small.

RESULTS

In all, 173 subjects passed the phone screening and 102 subjects were eligible at the baseline visit; 50% were randomly assigned to the ortho-k group and 50% to control group (Fig. 1). No significant differences in age, sex, refractive errors, and corneal shape were found between the two groups of subjects ($P > 0.05$) (Table 2). Ten control subjects and 14 ortho-k subjects were excluded at different stages of the study (Fig. 1). Nine control subjects were lost to follow-up (eight and one

TABLE 2. Demographic Data (Mean ± SD or Median [Range]) of the 102 Subjects in the Ortho-k and the Control Subjects

	All		Completed Cases		Dropout	
	Ortho-k, n = 51	Control, n = 51	Ortho-k, n = 37	Control, n = 41	Ortho-k, n = 14	Control, n = 10
Age, y	9 [6, 10]	9 [7, 10]	9 [7, 10]	9 [7, 10]	8 [6, 10]	9 [7, 10]
Sex	25F; 26M	25F; 26M	18F; 19M	19F; 22M	7F; 7M	6F; 4M
Myopia, D	2.12 ± 0.87	2.29 ± 0.87	2.05 ± 0.72	2.23 ± 0.84	2.32 ± 1.19	2.53 ± 1.00
Astigmatism, D	0 [0, 1.25]	0.25 [0, 1.25]	0 [0, 1.00]	0 [0, 1.25]	0.38 [0, 1.25]	0.25 [0, 0.75]
Flat keratometry reading, D	42.93 ± 1.21	43.12 ± 1.37	42.85 ± 1.18	43.21 ± 1.46	43.16 ± 1.32	42.74 ± 0.86
Eccentricity	0.65 ± 0.09	0.62 ± 0.09	0.66 ± 0.08	0.62 ± 0.09	0.63 ± 0.10	0.64 ± 0.09
Axial length, mm	24.46 ± 0.75	24.46 ± 0.79	24.48 ± 0.71	24.40 ± 0.84	24.42 ± 0.88	24.70 ± 0.53
Habitual logMAR VA	0.25 ± 0.22	0.21 ± 0.22	0.24 ± 0.22	0.22 ± 0.22	0.27 ± 0.24	0.18 ± 0.25
Best-corrected logMAR VA	0.00 [-0.10, 0.10]	-0.04 [-0.20, 0.08]	-0.04 [-0.10, 0.06]	-0.04 [-0.20, 0.08]	0.00* [-0.06, 0.10]	-0.01 [-0.10, 0.04]

* Significantly different from the completed subjects in the corresponding group ($P = 0.014$).

before 6- and 12-month visits, respectively) and one was excluded before the 6-month visit due to recurrent eye inflammation. Nine ortho-k subjects could not achieve the desired myopic correction despite lens modifications and another five were contraindicated to continue ortho-k treatment due to general conditions (Fig. 1; see subheading Adverse Events in the following text) affecting the ocular health (four and one before the 18- and 24-month visits, respectively). There were no significant differences in the baseline characteristics in the completed and dropout cases for both groups ($P > 0.20$), except that in the ortho-k group, the best-corrected VA of the completed subjects was significantly better than that of the dropouts ($P = 0.014$); however, the difference was clinically insignificant (Table 2).

A total of 37 (18 females, 19 males) ortho-k subjects and 41 (19 females, 22 males) control subjects completed the 2-year study. There were no significant differences in the baseline data between the two groups of subjects ($P > 0.05$). The mean ± SD age was 9.23 ± 1.06 years in the ortho-k group and 9.39 ± 1.00 years in the control groups. The mean ± SD of initial myopia was 2.05 ± 0.72 D in the ortho-k group and 2.23 ± 0.84 D in the control group. At the 24-month visit, the habitual logMAR VA was 0.02 ± 0.10 in the ortho-k subjects and 0.07 ± 0.11 in the control subjects and the best-corrected logMAR VA was -0.06 ± 0.04 in the ortho-k subjects and -0.04 ± 0.05 in the control subjects. The habitual logMAR VA was slightly better (by 2–3 letters) in the ortho-k group than that in the control group ($P = 0.03$), but there was no significant difference in the best-corrected VA between the two groups of subjects ($P = 0.11$) (Table 3).

Efficacy of Myopic Control

Figure 2 shows that axial length increased with time in both groups of subjects. The increase with time was statistically significant (repeated-measures ANOVA, $P < 0.01$) and significantly faster in the control groups (repeated-measures ANOVA, $P < 0.01$). The rate of axial elongation was significantly slower in the ortho-k group compared with that in the control group at all follow-up visits (unpaired t -tests, $P < 0.001$) (Table 3). The mean increase in axial length in ortho-k subjects was 0.27 mm less than that in control subjects after 2 years.

The 6-monthly axial elongation was significantly slower in the ortho-k group than that in the control group at all visits (unpaired t -tests, $P < 0.05$) (Fig. 2). In the ortho-k group, the 6-monthly change in axial length was rather consistent during the study period and was only significantly higher between the second and fourth 6-month periods (mean difference ± SD: 0.05 ± 0.09 mm, 95% confidence interval [CI]: 0.02 to 0.08, paired t -test, $P = 0.003$) (Fig. 2). In the control group, a gradual slowing of axial elongation with age was observed. Axial elongation was significantly faster in the first 6-month period compared with the third and fourth 6-month periods (mean difference ± SD [first–third 6-month period]: 0.06 ± 0.12 mm, 95% CI: 0.03 to 0.10 mm, paired t -tests, $P = 0.002$; mean difference ± SD [first–fourth 6-month period]: 0.07 ± 0.11 mm, 95% CI: 0.04 to 0.11 mm, paired t -tests, $P < 0.001$) (Fig. 2). As a result, the efficacy of myopic control varied at different stages of the study period: 55%, 32%, 29%, and 54% in the first, second, third, and fourth 6-month periods. On average, at the end of the study period, axial elongation was slower by 43% in the ortho-k subjects compared with the control subjects.

Stepwise multiple linear regression analysis showed that among all the predicting factors, axial elongation was significantly correlated with the treatment (standardized beta = -0.45 , $P < 0.001$) and initial age (standardized beta = -0.39 , $P < 0.001$) of the subjects but not with sex, initial myopia, or the initial corneal shape of the subjects (partial r : -0.21 to

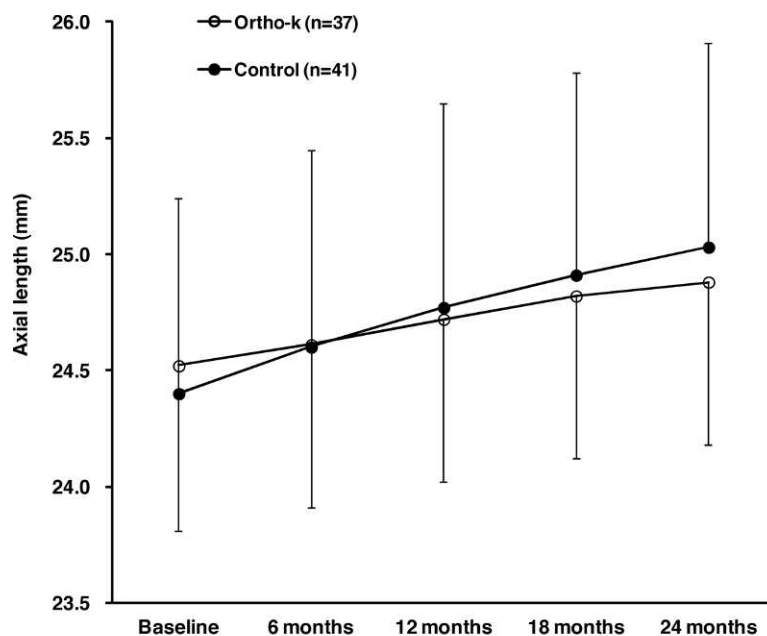
TABLE 3. Changes (Mean ± SD) in Axial Length in Subjects Who Completed the 2-Year Study and Differences (Mean ± SE) in Axial Elongation between the Two Groups at Each Visit

	Orthokeratology, n = 37	Control, n = 41	Difference	95% CI
6 months	0.09 ± 0.10	0.20 ± 0.11	0.10 ± 0.02	0.07 to 0.15
12 months	0.20 ± 0.15	0.37 ± 0.16	0.16 ± 0.04	0.09 to 0.24
18 months	0.30 ± 0.20	0.50 ± 0.21	0.20 ± 0.05	0.11 to 0.30
24 months	0.36 ± 0.24	0.63 ± 0.26	0.27 ± 0.06	0.16 to 0.38

0.09, $P > 0.08$). The regression of the model using treatment and initial age to predict axial elongation was fair (adjusted $R^2 = 0.37$) but significant ($F_{2,75} = 23.49$, $P < 0.001$). Since axial elongation was significantly affected by treatment, linear regression of axial elongation and initial age was performed for each group. Figure 3 shows significant negative correlations between axial elongation and the initial ages in both group of subjects (ortho-k group: Pearson $r = 0.33$, $F_{1,35} = 4.28$, $P = 0.046$; control group: Pearson $r = 0.54$, $F_{1,39} = 15.90$, $P < 0.001$). Figure 4 shows the lack of association between changes in the axial length and the initial myopia in either group of subjects ($P > 0.05$).

The ortho-k group had fewer fast progressors compared with the control group (χ^2 , $P = 0.006$). The percentage of fast progressors reduced from 34% in the control group to 15% in the ortho-k group, whereas the percentage of slow progressors increased from 14% in the control group to 46% in the ortho-k

group. Because the myopic control effect was affected by age, subjects were further divided into younger and older subjects to study the effect of age on the percentage of fast progressors. The median age of 9 years was arbitrarily selected as the cutoff value. Subjects younger than 9 years of age (i.e., range, 7–8 years) were considered as younger subjects, whereas subjects ranging in age from 9 to 10 years were considered as older subjects. As shown in Figure 5, the percentages of older subjects with fast myopic progression were 9% and 13% in the ortho-k and control groups, respectively. However, the percentages of younger subjects with fast myopic progression were 65% in the control group compared with 20% in the ortho-k group. The proportion of younger subjects with faster myopic progression was significantly higher when compared with older subjects in the control group (χ^2 , $P = 0.002$) but not in the ortho-k group (χ^2 , $P = 0.61$).



Duration of study			
6-monthly increase	Ortho-k	Control	p-value #
First	0.09±0.10	0.20±0.11	<0.001
Second	0.11±0.09	0.16±0.09	0.004
Third	0.10±0.08	0.14±0.09 *	0.043
Fourth	0.06±0.08 ^	0.13±0.08 *	0.001

statistical significance of the between group difference (unpaired t tests)
 ^ significantly different from the second 6-monthly increase in the ortho-k group, paired t test, $p=0.003$
 * significantly different from the first 6-monthly increase in the control group, paired t tests, $p<0.002$

FIGURE 2. Means and SD of axial length in the ortho-k and control groups over 2 years.

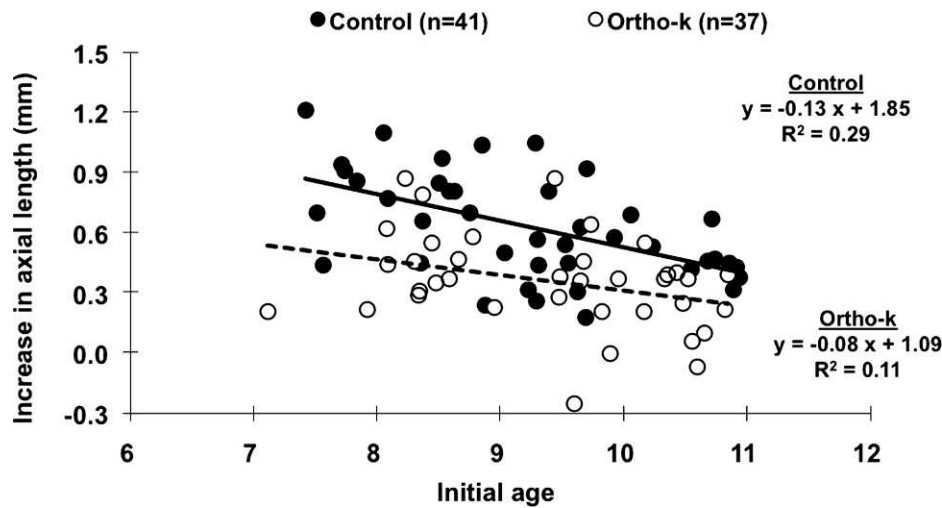


FIGURE 3. Changes in axial length after 2 years of monitoring versus the initial age in the two groups of subjects.

Adverse Events

One recurrent corneal inflammation was reported in the control group and the subject was excluded from the study. The five dropouts due to ocular health issue in the ortho-k group were excluded because they were not deemed suitable to continue contact lens wear; three had mild rhinitis, resulting in persistent and significant inferior-nasal corneal staining, one had increased conjunctival hyperemia after failing to comply with care procedures despite reeducation, and the remaining subject developed chalazion in the right eye after 21 months of lens wear. Ocular conditions and vision of these ortho-k subjects were not affected after cessation of ortho-k treatment.

DISCUSSION

The current study is the first long-term randomized clinical trial to confirm that ortho-k can effectively slow myopic progression by 43% in children with low-to-moderate myopia compared with those wearing single-vision glasses. Table 4 compares the study designs and the 2-year results obtained from published reports¹²⁻¹⁶ on myopic control using ortho-k and the current study. Study design varies in the ethnicity and

the initial age of the targeted subjects, the method of assignment of intervention, and the treatment for control subjects. All studies showed a positive myopic control effect of 32% to 55% slower axial elongation with ortho-k.

In a review paper on treatment for myopia, Gwiazda²⁵ commented that the myopic control effect using pharmaceutical agents and bifocal/progressive glasses reduced after the initial treatment period. The study by Hiaroka et al.¹⁵ also showed an apparent reduced efficacy on myopic control using ortho-k. Their study was an extension of the 2-year study by the same group¹⁴ on selected subjects fulfilling their inclusion criteria (Table 4). They reported no additional beneficial effect for myopic control using ortho-k after 3 years of lens wear.

However, although their data showed an apparent reduction in efficacy of ortho-k with time, the reduction was not due to reduced efficacy of ortho-k but due to the gradual slowing of myopic progression in the control group with age, which may be expected. Literature has reported that myopic progression in children slowed with age.^{17,26-30} Meta-analysis performed by Donovan et al.²⁶ showed that myopic progression was faster in younger children and in subjects of Asian than that in subjects of European descent. Myopia in Caucasian children was reported to increase in age from 6 to 14 years,²⁷ but the rate of myopic progression decreased with age²⁸ and stopped after

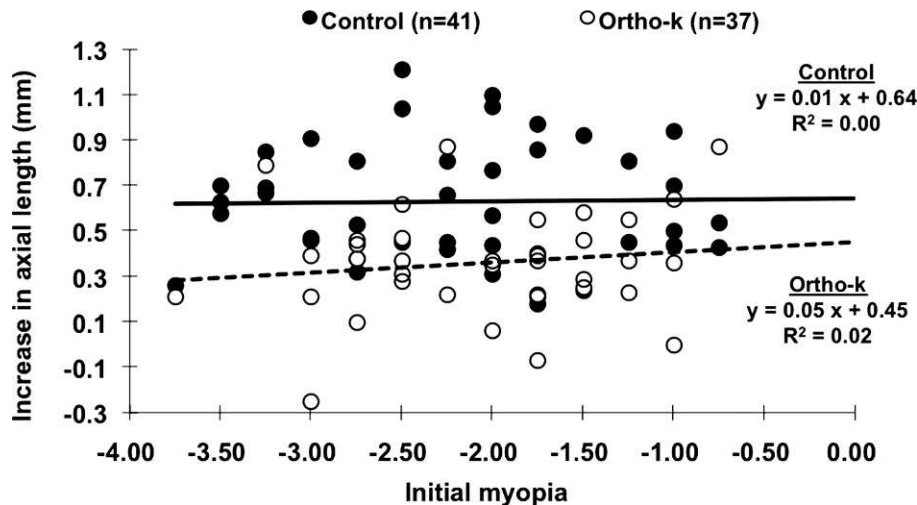


FIGURE 4. Changes in axial length after 2 years of monitoring versus the initial myopia.

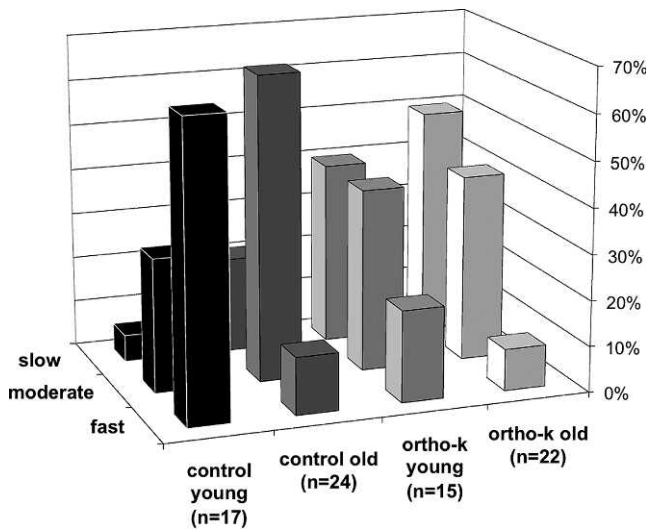


FIGURE 5. Percentages of subjects demonstrating slow (0.18 mm/y), moderate (>0.18 and ≤0.36 mm/y), and fast (>0.36 mm/y) myopia progression in younger (6–8 years old) and older (9–10 years old) children in the ortho-k and control groups.

the age of 15 years in males and 14 years in females.²⁹ The greatest change in myopia in Chinese children was reported in those ranging in age from 9 to 11 years.¹⁷

The subjects in the study reported by Hiraoka et al.¹⁵ started with a mean age of 10 years and would be 14 to 15 years old after 4 to 5 years (study period), which may explain the slower myopic progression in the control group. In their study, except for the second year, the annual axial elongation in their ortho-k subjects was rather consistent (0.16–0.19 mm) during the 5-year monitoring period. On the contrary, the annual axial elongation in their control subjects reduced from an average of 0.33 and 0.38 mm in the first 2 years to 0.17 and 0.24 mm in year 4 and year 5, respectively, and the latter was comparable to the average increase in their ortho-k subjects in that year.

The annual axial elongation in the current study was 0.36 and 0.27 mm in the first and second years, respectively, in the control subjects, and was 0.20 and 0.16 mm, respectively, in the ortho-k subjects. Our results were similar to the annual growth in the first 2 years as reported by Hiraoka et al.¹⁵ Our results showed relatively better myopic control in the first 6-months of the study period (55%) compared with the other 6-month periods (Fig. 2). The reduced myopic control effect may be due to the slowing of myopic progression in the control group and this was also observed and reported by Hiraoka et al.¹⁵ The apparent decline in axial elongation in control subjects may have offset the myopic control effect with ortho-k and narrowed the differences between the two groups, thus leading to an impression of reduced efficacy of myopic control treatment with time. Another possible explanation may be the adaptation of subjects to the signal that slows myopic progression in the ortho-k group. Our results also showed accrual of effect with continuation of ortho-k after 1 year.

Our results suggested that ortho-k has the potential to reduce the development of high myopia by reducing the proportion of fast progressors. Among all the currently available methods, 1% atropine is the most effective treatment reported for myopic control in myopic children in Asia.^{20–22} Shin et al.²⁰ showed that the proportions of fast progression were 33%, 17%, and 4% in children on 0.1%, 0.25%, and 0.5% atropine, respectively. However, they did not have control subjects in their study. Chua et al.²¹ showed that the

TABLE 4. Studies on Controlled Clinical Treatment on Myopic Control Using Ortho-k

	Cho et al. ¹² (2005)	Walline et al. ¹³ (2009)	Kakita et al. ¹⁴ (2011)	Hiraoka et al. ¹⁵ (2012)	Santodomingo-Rubido et al. ¹⁶ (2012)	Current Study (2012)
Age, y	7 to 12 (mean 9.6)	8 to 11 (mean 10.5)	8 to 16 (mean 12)	8 to 12 (mean 10)	6 to 12 (mean 10)	7 to 10 (median 9)
Race	Chinese	Caucasian	Japanese	Japanese	White European	Chinese
Duration of study, y	2	2	2	5	2	2
With control group	Yes	Yes	Yes	Yes	Yes	Yes
Method of assignment	Historic data	Historic data	Self-selection	Self-selection	Self-selection	Randomized
Control treatment	Glasses	Soft lenses	Glasses	Glasses	Glasses	Glasses
Initial SER (Ortho-k, D)	-2.27 ± 1.09	—	-2.55 ± 1.82	-1.89 ± 0.82	Myopia: -2.20 ± 1.09	-2.16 ± 0.77
Initial SER (Control, D)	-2.55 ± 0.98	—	-2.59 ± 1.66	-1.83 ± 1.06	Myopia: -2.35 ± 1.17	-2.36 ± 0.86
Increase in axial length in 2 y (Ortho-k, mm)	0.29 ± 0.27	0.25 ± 0.27	0.39 ± 0.27	0.45 ± 0.21	0.47	0.36 ± 0.24
Increase in axial length in 2 y (Control, mm)	0.54 ± 0.27	0.57 ± 0.27	0.61 ± 0.24	0.71 ± 0.40	0.69	0.63 ± 0.26
Myopic control effect	46%	55%	36%	37%	32%	43%
Dropout rate (Ortho-k)	19% (8/43)	30% (12/40)	7% (3/45)	24% (7/29)*	6% (2/31)	27% (14/51)
Dropout rate (Control)	—	—	17% (10/60)	30% (9/30)*	20% (6/30)	20% (10/51)

* Between 3rd and 5th years.

proportion of fast progressors reduced from 64% in the placebo-treated eyes to 14% in 1% atropine-treated eyes, whereas the proportion of slow progressors increased from 16% in the placebo-treated eyes to 66% in the 1% atropine-treated eyes. Our results showed that 15% of subjects (age range: 7–10 years) demonstrated fast myopic progression, which is comparable to the effect of the use of atropine.²¹ Our results also showed that younger subjects (age range: 7–8 years) tended to show faster axial elongation (Fig. 3) and ortho-k would be more beneficial to this age group, given that the percentage of younger subjects with fast myopic progression reduced from 65% in the control group to 20% in the ortho-k group (Fig. 5). Therefore, early initiation of ortho-k treatment may be necessary to reduce the prevalence of high myopia.

The LORIC (longitudinal orthokeratology research in children [in Hong Kong]) study reported slower axial elongation in higher myopic (2.00–4.00D) subjects undergoing ortho-k when compared with higher myopic subjects wearing single-vision glasses and no between-group difference in axial elongation when initial myopia was <2.00D.¹² Walline et al.¹³ and Santodomingo-Rubido et al.¹⁶ did not investigate the relationship between eyeball elongation and initial refractive errors. Kakita et al.¹⁴ reported an association between eyeball elongation and initial refractive error only in the higher myopic ortho-k subjects, but they did not define high myopia in their study. Using ANCOVA to control the covariances, Hiraoka et al.¹⁵ showed that axial elongation was associated with age but not with initial refractive errors and the findings in the current study supported their results. Again, the results suggest that myopic control treatment would be more beneficial to younger than that to older myopic children.

A good myopic control treatment, apart from being effective, should be well received by the targeted population without causing significant adverse effect or inconveniences to daily activities. Not everybody can wear contact lenses and not every child is suitable for ortho-k treatment. A treatment with high dropout rate would not be useful even if it is effective and high dropout rates could affect the results. The dropout rate reported in previous studies with ortho-k varies from 6%¹⁶ to 30%.¹³ The dropout rate of the current study was 27% and 20% in the ortho-k and control groups, respectively. Fourteen ortho-k subjects were withdrawn from the study. Nine were withdrawn from the study because of unsatisfactory myopic reduction, five due to poor lens centration, and the other four due to undercorrection. The five subjects with poor lens centration were refitted with toric ortho-k lenses and four were successfully fitted. The four undercorrected subjects were prescribed with spectacles to correct their residual refractive errors for daily activities. All eight subjects continued ortho-k lens wear outside the study. Thus, if other lens designs were included (see the following text), the dropout rate would have been lower. Five ortho-k subjects were withdrawn from the study due to contraindication to continued ortho-k treatment. Termination of ortho-k treatment was essential to ensure good ocular integrity. For safe ortho-k treatment, there is a need for good compliance from the practitioners, the wearers, and parents (if children are involved). Careful patient selection and monitoring during the course of the treatment are essential to minimize risk and development of serious complications (e.g., microbial keratitis) in ortho-k treatment. With proper and regular eye examination, ortho-k can slow myopic progression in children and provide clear unaided vision for well-adapted wearers without affecting ocular health.

Only one lens design (spherical 4-zone lens) was used in the current study and the current result applies only to children with low-to-moderate myopia and low astigmatism and who could achieve satisfactory ortho-k response. As mentioned

earlier, eight of the nine subjects who could not achieve the desired ortho-k response using the designated lens design and were excluded from the current study due to deviation from protocol, continued ortho-k treatment after they were successfully refitted with other lens design or with the use of low prescription eye glasses to aid daytime vision. There are a number of different lens designs currently available in the market aiming at improving the performance of ortho-k lenses, for example, toric ortho-k designs.³¹ A number of research studies are currently under way to investigate the potential of these lenses for refractive correction as well as myopic control. Results of these studies would be helpful toward the application of ortho-k for myopic control to a wider population with different degrees of myopia and astigmatism, thereby allowing more children to benefit from the myopic control treatment using ortho-k.

In conclusion, this randomized clinical trial confirmed that ortho-k slowed axial elongation (by 43%) and reduced the percentage of fast progressors in younger subjects (from 65% to 20% in subjects ranging in age from 7–8 years). Our results suggested that it would be beneficial to commence ortho-k treatment in younger myopic children.

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Does a two-year period of orthokeratology lead to changes in the endothelial morphology of children?

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ABSTRACT

Purpose: To compare changes in endothelial morphology in the central and superior cornea in subjects wearing single-vision spectacles and orthokeratology lenses over two years.

Methods: Endothelial images of the two locations of 99 subjects (6–12 years) from completed myopia control studies were analysed. Endothelial cell density (ECD), coefficient of variation in cell size (CV), and hexagonality (HEX) before and two years after treatment were compared between the two groups of subjects.

Results: Baseline ECD and CV in the central cornea were slightly lower than those in the superior cornea, but no significant difference in HEX was found in the two corneal locations. After two years, reduction in ECD and increase in CV were only significant in the central cornea, but not in the superior cornea. Reduction in HEX was significant in both corneal locations. Subjects receiving orthokeratology had smaller reduction in ECD in the central cornea compared to the controls (orthokeratology: 56 ± 94 cells/mm²; control: 98 ± 91 cells/mm², $p = 0.024$), otherwise, there were no significant differences in the changes in endothelial morphology in the two corneal locations between the two groups of subjects.

Conclusions: The current study confirmed that there were differences in endothelial morphology of central and superior cornea of Chinese children aged 6–12 years. The morphological response to normal ageing differed between the two corneal locations as reduction in cell density and polymegathism were found only in the central cornea whilst pleomorphism was found in both locations. Orthokeratology lens wear had minimal effect on the developmental changes in endothelial morphology.

1. Introduction

Clinical evidence has shown that orthokeratology (ortho-k) is an effective and safe treatment to slow axial elongation in children [1–9]. One of the indicators for safety in ortho-k lens wear is corneal endothelial morphology. A few longitudinal studies have evaluated the long term effects of ortho-k on the corneal endothelium [10–14]. Three of these studies [10–12] did not find any significant change in endothelial cell density (ECD), pleomorphism in terms of percentage of hexagonal cells (HEX), and polymegathism in terms of coefficient of variation in cell size (CV) 1–7 years after treatment. Hiraoka et al. [10] reported no changes in ECD, CV, and HEX in 52 eyes of 31 subjects aged 10–44 years (mean \pm SD: 17 ± 9 years) before and after one year of ortho-k lens wear. Zhong et al. [11] conducted a cross-sectional study to compare corneal thickness and morphology in subjects after one night and five years of ortho-k lens wear (mean \pm SD age: one night = 23 ± 4 years; 5 years = 19 ± 5 years). Data collected 8 h prior to lens wear from subjects on one-night treatment were used as

control. The authors used data collected from the two eyes and reported no significant difference in ECD and HEX after either one night or 5 years of lens wear. In the retrospective study conducted by Guo and Xie [12], there were no significant changes in ECD, CV, and HEX in 30 subjects aged 8–20 years before and after seven years ortho-k lens wear. In contrast, Cheung and Cho [13] found a significant reduction in ECD without any changes in polymegathism or pleomorphism in children aged 7–17 years (median: 10 years) after two years of lens wear. On the other hand, Nieto-Bone et al. [14] observed an increase in polymegathism without any changes in ECD or pleomorphism after one year of lens wear in 15 adults aged 18–30 years. These studies varied with respect to study designs, age of subjects, duration of study, and lack of proper control subjects. Thus, there is a need to confirm if ortho-k leads to changes in corneal endothelium.

It is known that ECD reduces with age, starting at birth [15–22]. The rate of reduction is most rapid in the first five years of age, slows down during childhood and the adolescent period, and finally becomes stable in adulthood. Of the five studies on the effect of ortho-k on the

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Table 1
Demographic data and baseline ocular and corneal endothelial parameters of the subjects.

	All (N = 99)	Orthokeratology (N = 50)	Control (N = 49)	Between groups p-value ⁺
Age (y), median (range)	9 (6–12)	9 (6–12)	9 (6–12)	0.367 ^a
Gender, female	57%	56%	57%	0.909 ^b
Sphere (D)	−2.13 ± 0.99	−2.25 ± 1.05	−2.00 ± 0.92	0.221
Cylinder (D)	−0.90 ± 0.93	−0.82 ± 0.88	−0.98 ± 0.98	0.437 ^a
Spherical equivalent (D)	−2.58 ± 1.12	−2.66 ± 1.22	−2.49 ± 1.02	0.465
Axial length (mm)	24.3 ± 0.8	24.4 ± 0.7	24.2 ± 0.9	0.162
Central cornea				
ECD (cells/mm ²) [#]	3271 ± 215	3241 ± 178	3302 ± 246	0.160
CV (%) [#]	24.49 ± 1.92	24.67 ± 1.96	24.31 ± 1.88	0.346
HEX (%)	71.47 ± 7.11	71.06 ± 7.34	71.90 ± 6.92	0.560
Superior cornea				
ECD (cells/mm ²)	3475 ± 287	3461 ± 226	3488 ± 341	0.648
CV (%)	26.70 ± 3.26	26.95 ± 2.89	26.45 ± 3.62	0.451
HEX (%)	71.07 ± 7.45	69.24 ± 6.48	72.94 ± 7.97	0.013

ECD: endothelial cell density; CV: coefficient of variation in cell size; HEX: hexagonality.

⁺ Probability values for between group differences using unpaired *t*-tests (unless otherwise specified); bold for p-values < 0.05.

^a Mann-Whitney *U* tests.

^b Pearson Chi-square.

[#] Significant differences in ECD and CV between the central and superior cornea using paired *t*-tests, p-values < 0.001.

endothelium, three were longitudinal studies. Hiraoka et al. [10] and Nieto-Bone et al. [14] included adults in their studies and they did not find significant change in ECD, whereas Cheung and Cho [13] reported ECD reduction in the children. As ECD can be affected by normal ageing in children, without information from control subjects, the change or lack of change in corneal endothelial morphology after ortho-k can be due to ageing or ortho-k lens wear, or both.

Previous studies mainly focused on changes in the central cornea, but little is known about the effects on the peripheral cornea. As the ortho-k lens is large and covers over 90% of the cornea, its use may lead to changes in the peripheral cornea which may differ from those observed in the central cornea. The primary objective of the current study was to compare the changes in endothelial morphology in the central and superior cornea over two years in children wearing ortho-k and controls wearing single-vision spectacles. The secondary objectives were to determine the morphological differences between the central and superior locations, and to determine factors affecting the endothelial morphology.

2. Methods

Endothelial images of subjects who had completed the Retardation Of Myopia In Orthokeratology (ROMIO) [4] and Toric Orthokeratology – Slowing Eye Elongation (TO-SEE) [7] studies were evaluated. These two studies investigated the effectiveness of orthokeratology for myopia control in children. The lenses and solutions used in these studies have been described elsewhere [4,7]. Endothelial images for the central and four peripheral corneal locations were captured using a specular microscope, TOPCON SP-2000P, but only images from the central and superior cornea were analysed. The superior cornea was selected as the peripheral site because pilot results showed a significantly highest ECD in this corneal location whereas there were no significant differences in ECD in the inferior, temporal and nasal cornea compared to the central cornea [13]. This may be related to the increased coverage of this part of the cornea by the upper eyelid in Asian eyes. For each subject, at least three images were captured for each corneal location and the clearest image was selected for analysis. The first image was selected if the image quality was similar for all the three captures [23]. Data from eyes with poor image quality or in which the cell count was less than 100 were excluded. Endothelial cells were manually retraced by one masked examiner (JW) trained to use the TOPCON IMAGEnet software (version 1.54). Endothelial cell morphology of the right eyes, including

ECD, HEX, and CV, captured at baseline and after two years of the myopia control studies were compared between the ortho-k and control groups.

2.1. Statistical analysis

Commercially available software (SPSS 23.0; IBM Corp., Armonk, NY, USA) was used for statistical analysis. Paired *t*-tests were used to compare the baseline endothelial morphology in the two corneal locations for all subjects. Stepwise multiple linear regression was used to evaluate the association between baseline endothelium morphology and demographic data and baseline ocular parameters.

The baseline characteristics between the ortho-k and control subjects were evaluated to ensure that there was no between-group difference at the beginning of the study. The comparisons were performed using unpaired *t*-tests, Mann-Whitney *U* tests, or Pearson Chi-Squares, depending on the type of the data and the normality of the distribution of data. Repeated measures ANOVAs (or ANCOVAs) were used to compare the endothelial morphology at the baseline and the 24-month visits in the two study groups after controlling for covariates identified in the multiple linear regression models for the baseline characteristics. Unpaired *t*-test for between-group comparison of changes in the endothelial morphology was performed if significant interaction was found between time and study group. Factors affecting changes in the endothelial morphology were evaluated for the two study groups using stepwise multiple linear regression.

3. Results

Of the 136 participants who completed the two studies, data from 37 subjects were excluded (16 missing baseline; 21 poor image quality). For the remaining 99 subjects, approximately 50% had used ortho-k. There were no significant differences in the demographic data, including initial age and gender, and baseline ocular parameters, including refractive error and axial length, between the two groups of subjects (Table 1).

3.1. Baseline endothelial morphology

Baseline endothelial morphology for all subjects showed a higher ECD and CV in the superior cornea compared to the central cornea (unpaired *t*-tests, *p* < 0.001), but no significant difference in HEX

Table 2
Factors affecting baseline endothelial morphology.

Factors	Standardized beta			Adjusted R ²	F	p-value ⁺
	Age	Gender	Axial length			
Central cornea						
ECD	-0.246	0.245	-	0.109	6.988	0.001
CV	-	-	-	-	-	-
HEX	-	-0.238	-	0.047	5.816	0.018
Superior cornea						
ECD	-	0.308	-	0.086	10.187	0.002
CV	-	-	-0.231	0.044	5.474	0.021
HEX	-	-	-	-	-	-

ECD: endothelial cell density; CV: coefficient of variation in cell size; HEX: hexagonality.

⁺ Probability values for the multiple linear regression; other excluded variables: initial sphere, initial cylinder; bold for p-values < 0.05.

between the two locations (unpaired *t*-tests, $p = 0.647$) (Table 1). The baseline morphology was weakly associated with age, gender, and initial axial length at both corneal locations (Table 2). For instance, 11% of variance in central ECD could be explained by age and gender. In this model, ECD reduces by 42 cells/mm² for each year increase in age after controlling for gender. ECD in females was 106 cells/mm² higher than males after controlling for age. The mean \pm SD ECD in the central cornea was 3208 \pm 209 cells/mm² and 3320 \pm 209 cells/mm² for male and female subjects, respectively, and this difference was statistically significant (unpaired *t*-test, $p = 0.010$). Baseline endothelial morphology in the central cornea was not associated with initial sphere or cylinder or axial length.

3.2. Effect of time and use of orthokeratology on endothelial morphology

At the beginning of the study, except for a significantly lower HEX in the superior cornea in ortho-k subjects (unpaired *t*-test, $p = 0.013$), there were no differences in the baseline endothelial morphology between the ortho-k and control subjects at the two corneal locations (unpaired *t*-tests, $p > 0.160$) (Table 1). Changes in the endothelial morphology over two years at the central and superior cornea in the two groups were shown in Table 3. Time was shown to have significant effect on ECD and CV at the central cornea and HEX at both corneal locations (repeated measures, $p < 0.044$), but not on ECD and CV at the superior cornea (repeated measures, $p > 0.489$). That is, for the central cornea, all the three parameters were significantly changed over time; but for the superior cornea, only HEX changed with time. Except for the central ECD with significant interaction (repeated measures, $p = 0.032$), there were no significant interactions found between time and study groups in the endothelial morphological parameters (repeated measures, $p > 0.105$). That is, except for the central ECD, the change or lack of change in endothelial morphology was not significantly different between the two groups. For the central ECD, *post-*

hoc analysis comparing the changes between the two study groups showed that the reduction in central ECD was significantly greater in the control group (mean \pm SD: 98 \pm 91 cells/mm²) than in the ortho-k group (mean \pm SD: 56 \pm 94 cells/mm²) (unpaired *t*-test: $p = 0.024$) (Table 3).

At the central cornea, changes in ECD were not associated with the demographic data, baseline ocular parameters, or the baseline values in both groups of subjects (multiple linear regressions, $p > 0.05$). Changes in CV and HEX were weakly and negatively associated with their baseline values (CV controls: adjusted R² = 0.079, $p = 0.028$; CV ortho-k: adjusted R² = 0.100, $p = 0.015$; HEX controls: adjusted R² = 0.094, $p = 0.018$; HEX ortho-k: adjusted R² = 0.134, $p = 0.006$). At the superior cornea, changes in ECD and CV were not associated with the demographic data, baseline ocular parameters or its baseline value in both groups of subjects (multiple linear regressions, $p > 0.05$). Changes in HEX were negatively associated with the baseline value in the control subjects (adjusted R² = 0.240; $p < 0.001$) and associated with both gender (standardized beta = -0.287) and the baseline value (standardized beta = -0.279) in the ortho-k subjects (adjusted R² = 0.140; $p = 0.012$).

4. Discussion

The corneal endothelium has limited regenerating capacity. It consists of a single layer of cells which regulates ion transport of the cornea to maintain corneal health and transparency [15,16]. Most cells are in the shape of a hexagon and this structure is disturbed in the presence of cell loss or chronic stress [15]. The human cornea has up to 500,000 cells, with ECD up to 7500 cells/mm² at birth [15]. ECD reduction is most rapid in the first five years of age, dropping from about 4000 cells/mm² at the age of one year to 3500 cells/mm² at the age five years, and 3000 cells/mm² by age 20 [17–21]. The reduction in ECD before adolescence is mainly due to hypertrophy, as there are no remarkable changes in total cell counts [24]. ECD was negatively correlated with corneal diameter, but the association is significant only before the age of two, as the size of the cornea stabilizes in children aged between five and 14 years [17,21]. The current results agree with previous studies which reported that age-related reduction in ECD is accompanied by a reduction in HEX and an increase in CV in both normal children and adults [19,20,24,25]. As central ECD, CV, and HEX change with time in the control group (3.0% reduction in ECD, 2.2% increase in pleomorphism, and 0.4% increase in polymegathism), it was expected to find an association between these parameters with time. However, the changes in ECD were not associated with demographic or ocular parameters identified in the current study (*i.e.* age, refractive error, axial length and baseline ECD) in both corneal locations. This may suggest that the reduction of ECD in normal children is a natural process not influenced by external factors.

In addition to reduced ECD in older children, the current study also found that girls had higher ECD than boys. A few studies have reported

Table 3
Mean changes in the endothelial morphology over two years in the two groups of subjects.

	Effect of time [#]	Time*Group [#]	Orthokeratology (N = 50)	Control (N = 49)	Between groups p-value ⁺
Central cornea					
ECD (cells/mm ²)	0.017	0.032	-55.5 \pm 94.0	-98.4 \pm 91.5	0.024
CV (%)	0.030	0.105	0.69 \pm 1.76	0.10 \pm 1.84	ns
HEX (%)	0.044	0.949	-1.52 \pm 6.06	-1.59 \pm 6.18	ns
Superior cornea					
ECD (cells/mm ²)	0.803	0.998	-13.7 \pm 169.4	-13.8 \pm 151.0	ns
CV (%)	0.489	0.247	1.24 \pm 2.72	0.54 \pm 2.81	ns
HEX (%)	0.001	0.183	-1.58 \pm 7.77	-3.71 \pm 8.06	ns

ECD: endothelial cell density; CV: coefficient of variation in cell size; HEX: hexagonality.

[#] Probability values for the repeated measures ANOVA/ANCOVA for the within subject effect and interaction; bold for p-values < 0.05.

⁺ Probability value of the unpaired *t*-test to compare changes in central ECD between the ortho-k and control subjects.

no differences in ECD between males and females in young adolescents and young adults [20,25,27] but it is known that ocular parameters change before adulthood. In children, girls have smaller corneas than boys [26]. If the corneal diameter plays a role in ECD, then higher ECD would be expected in girls than in boys and this was observed in the current study. However, corneal diameter was not measured and could not be used to explore the effect of gender and corneal diameter on ECD.

Some researchers have found significant association between ECD and refractive error, that is, high myopia is associated with lower ECD [25,27,28]. Again, age and gender were not considered in their analyses. Sheng and Bullimore [29] investigated the effects of age, refractive error, ethnicity, and years of contact lens wear on ECD, CV, and HEX in adults aged between 19 and 71 years using multiple linear regression model. They found that ECD was negatively associated with age and positively associated with Asian ethnicity, whereas CV was positively associated with age and contact lens wear, and HEX was negatively associated with age and myopia. The current results agreed with their findings with respect to ECD not being associated with refractive error. However, the current study did not find any significant effect of age on CV and HEX, or any association between HEX and refractive error. In view of the limited number of reports, further study is warranted to investigate the effect of age, gender, and refractive error on endothelial morphology.

The current study shows that endothelial morphological changes were not associated with ortho-k lens wear. One of the concerns in ortho-k lens wear is hypoxia due to the overnight wear modality. Direct injury or chronic disorder of the corneal endothelium can lead to cell loss resulting in reduction in ECD, and increases in pleomorphism and polymegathism. Physiologically, the cornea suffers from hypoxia during sleep as eye closure reduces the oxygen supply to the eyes. Corneal oedema induced during sleep dissipates within minutes of waking up. The level of oedema during sleep and recovery upon awakening is affected by the presence of a contact lens. Sleeping with contact lenses made from low oxygen permeable material thus retards the recovery of hypoxia, resulting in chronic corneal oedema when the lenses are worn every night. Lens materials with oxygen transmissibility (Dk/t) of 87 and 125 units are recommended to avoid 3% and 4% oedema, respectively [30,31].

Most current ortho-k lenses are made of highly oxygen permeable materials with Dk 100 or above. With lens thickness ranging from 0.15 to 0.20 mm, the Dk/t of ortho-k lenses varies from around 60 to 79. Unlike soft lenses covering both cornea and limbus, the lens diameter of an ortho-k lens is smaller than the corneal diameter, allowing some degree of oxygen supply in the limbal area. Although Dk/t for most of the ortho-k lenses is lower than the recommended value to avoid corneal oedema during sleep, these recommended values are more meaningful for extended wear modality of soft lenses. In extended wear, the lenses cover both the cornea and limbus and remain on the eyes after eye opening, such that lower Dk/t lenses will have slower corneal recovery. Unlike conventional contact lenses that correct vision with lenses *in situ*, ortho-k corrects vision by molding the cornea during sleep. Patients are required to remove their lenses after waking and thus, ortho-k will have minimal effect on recovery from hypoxia. The recommended Dk/t value for avoiding oedema, derived from *in vitro* conditions, is less crucial and serves better as a guideline for lens selection. Dk/t of the ortho-k lenses used in this study was 79 and results show that it exerted minimal corneal stress to the endothelium after two years of lens wear resulting in insignificant effects on polymegathism and pleomorphism, as there were no differences between the two groups of subjects. One issue left unanswered is the slower reduction in ECD in ortho-k subjects compared to the controls. Further study is warranted to confirm this observation.

Because of the limited regenerating power, endothelial cells in the peripheral cornea serve as a 'physiologic reserve and storage region' especially in wound healing [32]. Although the limbus is spared in

ortho-k lens wear, little is known about the physiological response towards ortho-k in the peripheral cornea, as previous studies have mainly focused on the effect in the central region [10–14]. Results from *in vivo* studies on endothelial morphology in humans vary with respect to characteristics of the subjects (*e.g.* age, contact lens experience *etc.*), instrumentation and method of cell analysis, and locations of peripheral cornea examined [22,23,32–35]. Wiffen *et al.* [33] reported a higher ECD in the central cornea compared to the temporal location in 84 non-contact lens wearers, aged 46 ± 18 years, but observed no difference in ECD in 43 contact lens wearers, aged 35 ± 9 years, who had been using contact lenses for over five years. Zheng *et al.* [22] did not find any difference in ECD and HEX between the central and inferior cornea in 80 normal Chinese aged 0 to 79 years. However, despite the differences in the methodology, most studies reported an increase in ECD in para-central and peripheral cornea either in children [23] or in adults [32,34,35]. Only two *in vivo* studies examined topographic difference in ECD [23,32], both reporting highest ECD in the superior cornea compared to the other three peripheral locations, but reasons for the differences were not suggested. The ECD in the inferior, nasal, and temporal cornea was similar. The current study selected the superior cornea for the investigation of changes in the peripheral cornea, because the results of pilot study on ortho-k showed highest ECD in the superior cornea [13]. Eyelid position may be a possible reason accounting for the difference. Whilst the cornea in the nasal, temporal, and inferior regions is usually exposed to the atmosphere, the superior cornea is usually covered by the upper eyelids, especially in Asian eyes, with small vertical palpebral aperture height, causing chronic hypoxia in the superior cornea, resulting in lower HEX and higher CV. If upper eyelids do play a role, it is expected that morphology in the nasal, temporal, and inferior cornea would be similar, thus, these areas were not investigated in the current study.

Topographic *in vivo* assessment of polymegathism and pleomorphism are less well studied. If the upper lid does affect endothelial morphology, the superior cornea would be expected to have higher CV and lower HEX than the central cornea. This hypothesis is supported by a histological study by Holley *et al.* [36] but no conclusion can be drawn from *in vivo* studies [22,32,33]. Wiffen *et al.* [33] found lower HEX in the central cornea with no significant difference in CV. Amann *et al.* [32] did not find any significant difference in HEX and CV between central and peripheral locations. Zheng *et al.* [22] found lower HEX in the peripheral cornea. In the current study, higher CV in the superior cornea was observed, but no significant difference in HEX was found. The honeycomb geometry of the endothelium is the most stable structure in nature for distributing stress. High HEX is essential to maintain endothelial function and the lack of difference in central and peripheral locations in the current study may suggest that homeostasis of the endothelium is maintained in the healthy cornea in children aged 6–12 years. Change in HEX in the superior cornea was similar to that observed in the central area, but the changes in ECD and CV in the superior cornea did not reach statistical significance. Considering the variability of the endothelial cell evaluation of CV and HEX, the effects of normal ageing on polymegathism and pleomorphism in the central and superior cornea indicate a need for further investigation of these parameters in children.

In summary, ortho-k had a minimal effect on the endothelial morphology of children after two years of lens wear. The changes in endothelial morphology observed over the two years period were primarily driven by the normal ageing process.

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ORIGINAL ARTICLE

Orthokeratology vs. Spectacles: Adverse Events and Discontinuations

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ABSTRACT

Purpose. To assess the relative clinical success of orthokeratology contact lenses (OK) and distance single-vision spectacles (SV) in children in terms of incidences of adverse events and discontinuations over a 2-year period.

Methods. Sixty-one subjects 6 to 12 years of age with myopia of -0.75 to -4.00 DS and astigmatism ≤ 1.00 DC were prospectively allocated OK or SV correction. Subjects were followed at 6-month intervals and advised to report to the clinic immediately should adverse events occur. Adverse events were categorized into serious, significant, and non-significant. Discontinuation was defined as cessation of lens wear for the remainder of the study.

Results. Thirty-one children were corrected with OK and 30 with SV. A higher incidence of adverse events was found with OK compared with SV ($p < 0.001$). Nine OK subjects experienced 16 adverse events (7 significant and 9 non-significant). No adverse events were found in the SV group. Most adverse events were found between 6 and 12 months of lens wear, with 11 solely attributable to OK wear. Significantly more discontinuations were found with SV in comparison with OK ($p < 0.05$).

Conclusions. The relatively low incidence of adverse events and discontinuations with OK is conducive for the correction of myopia in children with OK contact lenses.

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Key Words: myopia control, orthokeratology, adverse events, discontinuations, drop out, spectacles, rates

Orthokeratology (OK) concerns the fitting of specially designed contact lenses to reshape the corneal contour to temporarily modify refractive error. The most common clinical application of OK is the reduction of myopic error through corneal flattening.¹ Although studies in the late 70s and early 80s did not find significant adverse events associated with the use of OK contact lenses, their application proved to be unpopular owing to incomplete treatment effects and transient, unpredictable reductions in refractive error.²⁻⁶ The subsequent development of innovative materials, lens designs, and instrumentation to depict changes in corneal topography has facilitated assessment of OK safety and efficacy in correcting low to moderate levels of myopia in adult individuals.⁷⁻⁹

Following an earlier retrospective study¹⁰ and case report,¹¹ longitudinal studies have provided evidence for the efficacy of OK

contact lens wear in slowing myopia progression in children, although prospective randomized clinical trials are required to ascertain this.¹²⁻¹⁵ Furthermore, it has been recently reported that orthokeratology represents a large proportion of all contact lens wear fits undertaken in children worldwide.¹⁶ Although OK in children has been associated with adverse ocular effects, including microbial keratitis,¹⁷ severe complications have generally been restricted to regions where regulation is limited such as east Asia and, in particular, countries such as China and Taiwan. The complications have been attributed to inadequately trained practitioners, lack of appropriate clinical equipment, the use of non-gas-permeable materials, and tap water as multipurpose contact lens care solution.¹⁸ Where regulation and monitoring are optimum, several studies have shown OK to be effective and safe in reducing low to moderate levels of myopia in children.¹⁹⁻²¹ However, all the latter studies have not been specifically designed to assess the incidence of adverse events and complications; have been carried out over short period; and have not employed adequate control groups. Although case reports and case series of observations of overnight OK have been presented for undefined populations, there are no formal prospective reports that have assessed the incidence of adverse events associated with the long-term use of OK for the treat-

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ment of myopia progression control in children.²² Furthermore, subject compliance with the treatment schedule is important when assessing the effectiveness of a treatment option: high discontinuation rates might suggest that the treatment is unlikely to be successful, irrespective of its clinical outcome. The relationship between the incidence of adverse events and discontinuation rates has been advocated as an alternative methodology for assessing the clinical success or failure of a visual correction method.^{23,24} The purpose of this study is therefore to compare the incidence of adverse events and discontinuations of orthokeratology contact lenses (OK) and distance single-vision spectacles (SV) in children during a 2-year period.

METHODS

This study was part of the Myopia Control with Orthokeratology contact lenses study (MCOS) designed to assess the safety, efficacy, and subjective acceptance of OK vs. SV in white European myopic children during a 2-year period.^{15,25}

Methods have been described in detail elsewhere.²⁵ In brief, normal, healthy, white European subjects 6 to 12 years of age with moderate levels of myopia (-0.75 to -4.00 D) and astigmatism (≤ 1.00 D) and free of systemic or ocular disease affecting ocular health were recruited for the study and prospectively allocated OK or SV correction. Parent(s) or guardian(s) were allowed to choose one of two treatment modalities offered (i.e., SV or OK), after they were given a balanced account of their respective advantages and disadvantages.

Spectacles or contact lenses, contact lens care solutions (for the OK group only), and full ocular examinations were provided free of charge to all subjects throughout the study. Fully informed parental consent and child assent was obtained before 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 any time. 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.

At the recruitment session, all subjects underwent a full anterior eye biomicroscopy, indirect fundus microscopy, binocular vision, and refractive evaluation to elucidate whether they were eligible to participate in the study; baseline study measurements were then recorded for eligible subjects.

Subjects in the SV group were prescribed distance single-vision spectacles having the highest positive spherical power consistent with optimum visual acuity and asked to wear the spectacles at all times. Subjects from the OK group were fitted with Menicon Z Night contact lenses using the Menicon Professional Easy Fit Software (Menicon Co., Ltd, Nagoya, Japan). After initial contact lens fitting, subjects were instructed on the first day on procedures for insertion, removal, and cleaning/disinfection, and instructions were reinforced at subsequent visits. Subjects were provided with MeniCare Plus multipurpose solution for the daily cleaning, rinsing, and disinfecting of their contact lenses, and Menicon Progent intensive cleaner for use once a week (Menicon Co., Ltd, Nagoya, Japan). Additionally, subjects were provided rewetting drops for

instillation before lens removal during the first 2 weeks of lens wear (TheraTears, Advanced Vision Research, IL). At subsequent visits, subjects presenting with corneal staining ≥ 1 CCLRU unit were recommended to instill rewetting drops before lens removal.²⁶

Subjects in the OK trial were informed that contact lenses should be inserted everyday just before going to sleep and removed immediately on waking the following morning. Subjects were requested to attend the clinic no later than 2 hours after lens removal on the morning following the first night of lens wear; the stipulation applied to all subsequent visits. A visit was scheduled 3 weeks later to ascertain whether the contact lens fitting was clinically acceptable; otherwise, new contact lens specifications were calculated and ordered. Subjective refraction was undertaken to check whether changes in contact lens' back surface contact lens design were required to correct a change in refraction. A successful OK fit was considered to be one which after 3 weeks of lens wear showed CCLRU anterior eye signs ≤ 1 unit,²⁶ a "bull's eye" corneal topography pattern, and monocular and binocular spectacle visual acuities within ± 1 line of the best-corrected decimal acuity.

All OK subjects were informed that contact lenses should be removed if any problems were experienced. Subjects and their parent/guardians were instructed on steps to take in the event of an adverse reaction and on the importance of adherence to the study protocol; compliance was monitored closely by one of the authors (C.V.-C.). Subjects from both study groups were instructed to report to the clinic immediately should a reaction appear to be abnormal (e.g., red eye, pain, unusual discomfort, or eye secretions).

After initial enrollment, subjects were followed at 1, 6, 12, 18, and 24-month intervals. 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 refraction²⁷ at any of the follow-up visits was considered clinically significant and was remedied by supplying contact lenses or spectacles made to the new prescription.

Adverse Events

The classification of adverse events and discontinuations was adapted from Morgan et al. (2005).²³ Adverse events were classified into "serious," "significant," or "non-significant" according to Table 1.^{23,24} Although Table 1 shows most of the ocular adverse events that could occur as a result of contact and spectacle lens wear, all adverse events, additional to those shown in Table 1, were recorded. For obscure adverse reactions, the opinion of the ophthalmologist on duty at the clinic was sought and the condition treated in collaboration with the MCOS clinician. In all cases, an appropriate classification of an adverse reaction was determined. Recurrences of the same adverse event(s) in the same or fellow eye at any of the subsequent study visits were classified as separate events; bilateral events were counted as two separate events. For the purposes of comparison, the incidence of adverse events was calculated as a percentage of eyes per annum.^{23,24}

Corneal Staining

The extent and depth of corneal staining were measured in both eyes of subjects wearing OK lenses using the CCLRU grading

TABLE 1.Classification of adverse events. The table is adapted from Morgan et al. (2005)²³

Classification Symptomatology	Serious Symptomatic	Significant Commonly Symptomatic	Non-significant Asymptomatic
Description	An adverse event that produces or has the potential to produce significant visual impairment and might warrant permanent discontinuation from lens wear	An adverse event of sufficient clinical concern to warrant clinical intervention and perhaps temporal discontinuation from lens wear	An adverse event which is of no immediate clinical concern and does not warrant discontinuation from lens wear
Condition	Central corneal opacity Corneal warpage Epithelial wrinkling Hypopyon Microbial keratitis Penetration of Bowman's membrane Persistent epithelial defect Corneal abrasion requiring medical intervention	3 and 9 o'clock staining Disorders of the eyelids and lashes (e.g. blepharitis, meibomitis, hordeolum) Conjunctival epithelial flaps Conjunctivitis Contact lens-induced acute red eye Contact lens-induced papillary conjunctivitis Contact lens-induced peripheral ulcer Corneal scarring Epithelial microcysts Epithelial arcuate lesion Infiltrative keratitis Keratoconjunctivitis Ptosis Vascularized limbal keratitis Corneal abrasion requiring no medical intervention	Asymptomatic infiltrates Asymptomatic infiltrative keratitis Blinking disorders Deep stromal opacities Epithelial vacuoles Localized allergic reaction Corneal white lines Corneal epithelial iron lines

scales at baseline and after 1 night, 3 weeks, and 1, 6, 12, 18, and 24 months of wear.²⁶ Additionally, the location (i.e., superior, inferior, nasal, temporal, and central) of the staining was recorded. A cobalt blue filter and a fluorescein enhancement filter (Kodak Wratten no. 12; Eastman Kodak, Rochester, NY) placed respectively in the illumination system and over the objective lens were used to facilitate assessment of corneal staining.²⁸ Corneal staining was graded approximately 2 hours after lens removal, and staining with an extent and/or depth grade ≥ 2 was classified as an adverse event.

Discontinuations

Discontinuation was defined as cessation of lens wear for the duration of the remainder of the study.²³ Discontinuation may occur for a number of reasons: adverse events, ocular discomfort, visual problems, lack of motivation, failure to follow instructions, unacceptable visual acuity, and other logistic or personal reasons that may or may not have been directly related to lens wear. Temporary suspension of lens wear of up to 2 weeks was allowed (at the investigator's discretion) should significant symptoms or slit-lamp findings occur. Although temporarily discontinued, in these cases subjects were examined at frequent intervals until resolution of the condition, and attempts were made to limit the duration of discontinuation to as short a period as possible. Some subjects discontinued the study as result of "lost to follow-up"—defined as a

situation whereby a subject did not present for the next follow-up visit (despite active efforts to encourage attendance). The incidence of discontinuations was calculated as a percentage of subjects per annum.^{23,24}

Statistical Analysis

The difference in incidence of adverse events and discontinuations between OK and SV was tested with Fisher exact test. The Friedman test was used to test differences in the extent and depth of corneal staining over time. Differences between single pairs of visits were further explored with the Wilcoxon signed rank test. The correlation between the extent of corneal staining and its depth was tested using the Spearman rho test. Statistical analyses were conducted using SPSS 15.0 (SPSS, Inc., Chicago, IL). The level of statistical significance was taken as 5%.

RESULTS

Between March 2007 and March 2008, 69 subjects enrolled in the study with 8 failing to meet the inclusion criterion for participation for the following reasons: corneal staining (1), high spherical refractive error (3), hypermetropic refractive error (1), and high cylindrical refractive error (3). Thirty-one children were subsequently and prospectively allocated OK and 30 SV lenses. The baseline demographics and refractive and biometric data of the two groups were found to be similar.²⁵

Adverse Events

A higher incidence of adverse events was found with OK compared with SV ($p < 0.001$). Nine OK subjects experienced 16 adverse events, whereas no adverse events were found in the SV group (Table 2). Two male subjects experienced 2 adverse events each at different time points (i.e., contact lens–induced peripheral ulcer, dimple veiling, corneal abrasion, and hordeolum) and 1 female subject experienced 3 adverse events (corneal abrasion, papillary conjunctivitis, and corneal staining). Two female and 1 male subjects experienced bilateral adverse events at the same time points (i.e., papillary conjunctivitis, blepharitis, and bacterial conjunctivitis). None of the adverse events resulted in a reduction of best-corrected visual acuity. Most adverse events were found between 6 and 12 months of lens wear, but 5 significant adverse events could not be solely attributable to OK lens wear (i.e., blepharitis [2], hordeolum [1], and bacterial conjunctivitis [2]) (Table 2, Fig. 1).

Corneal Staining

Considering both eyes of subjects across all time points, 101 eyes (22%) showed some degree of corneal staining. Some eyes (numbers in parenthesis) showed corneal staining at baseline (0), 1-night (5), 2-week (13), and 1- (5), 6- (8), 12- (3), 18- (3), and 24-month (8) visits. Significant differences in the extent of corneal staining were found over time ($p = 0.008$), and this was attributed to the significant increase in corneal staining from baseline to 1-night, 2-week, and 1- and 24-month visits, as well as the increase from the 1-night to 2-week visit (all $p < 0.05$).

The extent of corneal staining decreased significantly from 2 weeks to 12 and 18 months (all $p < 0.05$). No significant changes were found in the extent of corneal staining between any of the other pairs of visits ($p > 0.05$). Depth of corneal staining changed significantly over time ($p = 0.009$), owing to the significant increase in corneal staining observed between the baseline visit and all other visits and the increase at the 2-week visit in comparison with the 1-night and the 1-, 12-, and 18-month visits (all $p <$

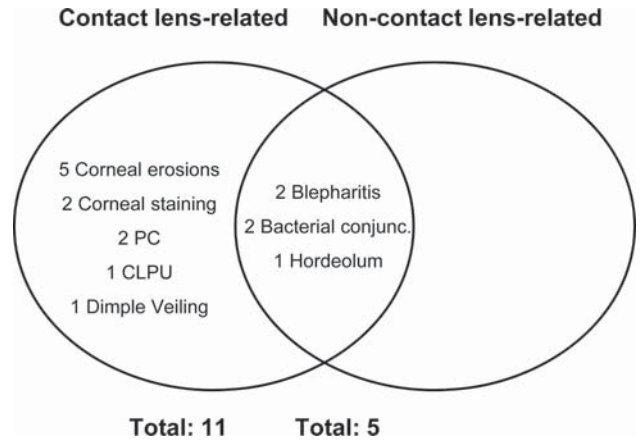


FIGURE 1.

Contact lens and non-contact lens-related adverse events. PC indicates papillary conjunctivitis; CLPU, contact lens-induced peripheral ulcer.

0.05). No significant changes were found in depth of corneal staining between any of the other pairs of visits ($p > 0.05$).

The extent and depth of corneal staining across all time points as well as at 1-night, 2-week, and 6-, 12-, and 24-month visits were strongly correlated (all $p < 0.001$) (Fig. 2). No significant correlations were found between extent and depth of corneal staining at baseline and 1- and 18-month visits ($p > 0.05$).

Discontinuations

Two and 6 subjects from the OK and SV groups, respectively, discontinued the study; this difference was not statistically significant ($p = 0.15$). Two discontinuations occurred between 3 and 6 months and the remaining between 12 and 24 months (see Table 2).

DISCUSSION

To the authors’ knowledge, MCOS is the first prospective clinical study specifically designed to compare the relative clinical suc-

TABLE 2.
Type and time line of adverse events and discontinuations

Time (month)	Orthokeratology		Single vision spectacles	
	Adverse events	Discontinuations	Adverse events	Discontinuations
0 to ≤ 1	1 Corneal abrasion ♀ 2 Corneal staining ♀♀	—	—	—
>1 to ≤ 3	2 Papillary conjunctivitis ♀♀	—	—	—
> 3 to ≤ 6	1 Contact lens–induced PU ^a ♂	Unknown reason ♀	—	1 Soft contact lenses ♀ 1 Orthokeratology ♀
> 6 to ≤ 12	3 Corneal abrasion ♀♀♂ 1 Corneal abrasion ^a ♀ 2 Blepharitis ^a ♀♀ 2 Bacterial conjunctivitis ^a ♂♂ 1 Hordeolum ^a ♂	—	—	—
> 12 to ≤ 18	1 Dimple veiling ♂	1 Discomfort ♀	—	1 Lost to follow-up ♂
> 18 to 24	—	—	—	3 Lost to follow-up ♂♂♀
Total	16 (7 significant^a)	2	—	6

^aSignificant adverse events.

PU indicates peripheral ulcer; ♀, female; ♂, male.

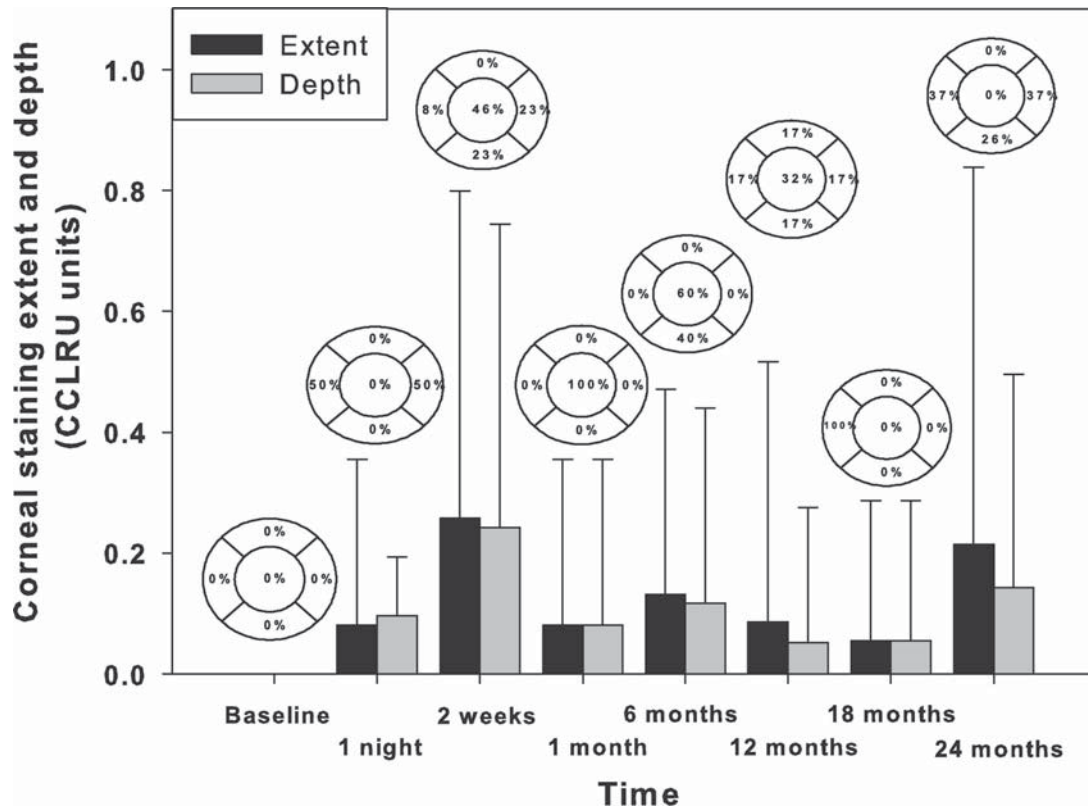


FIGURE 2. Corneal staining extent and depth for the orthokeratology group. Error bars represent 1 standard deviation of the mean.

cess of OK vs. SV in children in terms of incidence of adverse events and discontinuations during a 2-year period. Subjects and parents engaged enthusiastically in the study and responded well to the study protocols.

Adverse Events

The greater incidence of adverse events found with OK vs. SV was expected as this has typically shown to be the case for all contact lens types (Table 3). The adverse events found with OK in this study are not considered to be serious, are similar to those reported with other contact lens types, and can be managed straightforwardly in clinical practice (Tables 2 and

3).^{23,24,29} Furthermore, although some of the adverse events found were anticipated they are not exclusively attributable to contact lens wear (Fig. 1).

That the adverse events found in this study were limited in severity is likely to be a consequence of how OK affects the morphology and biometry of the cornea. In thinning and re-shaping the corneal epithelium, OK reduces epithelial cell size without affecting epithelial permeability and is therefore considered not to exert any changes in the corneal stroma or endothelium.^{30–32}

In the present study, most adverse events were found between 6 and 12 months of lens wear, which is consistent with previous

TABLE 3. Incidence of adverse events as a percentage of eyes per annum (95% confidence intervals)

Type of adverse event	Orthokeratology	EW RGP ²³	EW SiHy ²³	DW Hydrogels ²⁹	Spectacles	Spectacles (other study) ²⁹
Serious	0.0 (0.0–3.1)	0.0 (0.0–3.7) 0.2 (0.0–0.9)	1.0 (0.2–5.4) 0.2 (0.1–0.7)	0.0 (0.0–1.6)	0.0 (0.0–3.1)	0.0 (0.0–1.6)
Significant	5.8 (2.9–11.6)	5.0 (2.2–11.2) 3.8 (2.6–5.6)	16.0 (10.1–24.4)	5.4 (2.9–9.6)	0.0 (0.0–3.1)	0.0 (0.0–1.6) 8.0 (6.6–9.6)
Non-significant	9.2 (5.2–15.7)	3.0 (1.0–8.5) 0.2 (0.0–0.9)	1.0 (0.2–5.4) 1.1 (0.7–1.9)	22.0 (16.7–28.5)	0.0 (0.0–3.1)	11.4 (8.0–16.1)
Total	13.3 (8.4–20.6)	8.0 (4.1–15.0) 4.1 (2.8–5.9)	18.0 (11.7–26.7) 9.3 (7.9–11.0)	19.0 (14.3–25.6)	0.0 (0.0–3.1)	11.4 (8.0–16.1)

EW indicates extended wear; DW, daily wear; RGP, rigid gas-permeable contact lenses; SiHy, silicone hydrogel contact lenses.

studies that have shown adverse events to peak at the beginning of contact lens wear and reduce thereafter.^{23,24,29}

Corneal Staining

The incidence of corneal staining found in this study was lower^{19,20} and similar³³ to previous reported studies, which might be attributed to differences in lens design, lens material, and lens surface properties. Some of the corneal staining found in this study might be partly attributable to subjects failing to instill rewetting drops before lens removal. Nevertheless, it should be noted that the levels of corneal staining found in this study are below what would be considered clinically significant.²⁶

Corneal staining occurred most commonly in the central cornea, reaching a maximum extent within the first few weeks of lens wear and reducing thereafter, which again is in agreement with previous studies.^{19,20,33,34} This observation was to be expected because myopia reduction after OK treatment is achieved by flattening of the central cornea and redistribution of epithelial tissue from central to peripheral regions of the cornea.³⁰ Therefore, practitioners undertaking OK treatments should be especially vigilant during the first few weeks of lens wear with regard to the risk of potential complications associated with corneal staining.

Discontinuations

The lower incidence of discontinuations found with OK in comparison with SV agrees with that reported in a recent study (Table 4).¹⁴ Furthermore, the incidence of discontinuations with OK lens wear appears generally to be lower in comparison with other modalities of contact lens wear, including extended wear of gas-permeable,²³ extended wear of silicone hydrogel contact lenses,²³ and daily wear of hydrogel contact lenses²⁹ (Table 4).

The rate of discontinuations found with OK in the present study was lower^{12,13} and similar¹⁴ to those previously reported (Table 4), whereas the incidence of discontinuations found with SV was intermediate to rates previously reported (Table 4).^{14,29}

Comparisons of the incidence of adverse events and discontinuations between this study and historical controls shown in Tables 3

TABLE 4.
Incidence of discontinuations as a percentage of subjects per annum (95% confidence intervals)

Discontinuations			
Contact lenses	Orthokeratology MCOS	3.2 (0.9–11.0)	
	Orthokeratology (other studies)	9.3 (4.8–17.3) ¹² 15.0 (8.8–24.4) ¹³ 3.3 (1.1–9.3) ¹⁴	
	EW rigid gas-permeable	26.0 (15.9–39.6) ²³ 11.0 (8.0–15.0) ²³	
	EW silicone hydrogels	20.0 (11.2–33.0) ²³ 26.6 (23.4–30.1) ²³	
	DW hydrogels	33.1 (25.8–41.3) ²⁹	
	Spectacles	Spectacles MCOS	11.7 (5.8–22.2)
		Spectacles (other studies)	8.3 (4.6–14.7) ¹⁴ 16.9 (11.6–23.9) ²⁹

EW indicates extended wear; DW, daily wear.

and 4 should be interpreted with caution. Nevertheless, all the studies used to make these comparisons used a similar study design to MCOS in that they were prospective trials undertaken for at least a 1-year period and were designed to assess the incidence rate of adverse events and/or discontinuations. It should also be taken into account that some studies recruited adults,^{24,29} whereas others recruited children,^{12–14} and it is possible that the incidence of adverse events and discontinuations might differ between adults and children.³⁵

A limitation of this study is that it lacks an appropriate sample size to detect the absolute incidence rate of adverse events and discontinuations associated with OK and SV wear. However, the purpose of this study was to detect differences in the relative incidence of adverse events and discontinuations between OK and SV, rather than absolute incidence rates. Previous studies have used sample sizes similar to that used in the present study and were able to detect statistically significant differences in the incidence of adverse events and discontinuations between two different visual correction types.^{23,24}

In summary, the relatively low incidence of adverse events and discontinuations found in MCOS is conducive to the correction of myopia in children with OK contact lenses. Good clinical practice in the fitting these lenses in children is, of course, imperative,³⁶ and under these circumstances, OK appears to be a safe option for myopia correction in children.

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ORIGINAL ARTICLE

Factors Preventing Myopia Progression With Orthokeratology Correction

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ABSTRACT

Purpose. To examine which baseline measurements constitute predictive factors for axial length growth over 2 years in children wearing orthokeratology contact lenses (OK) and single-vision spectacles (SV).

Methods. Sixty-one children were prospectively assigned to wear either OK (n = 31) or SV (n = 30) for 2 years. The primary outcome measure (dependent variable) was axial length change at 2 years relative to baseline. Other measurements (independent variables) were age, age of myopia onset, gender, myopia progression 2 years before baseline and baseline myopia, anterior chamber depth, corneal power and shape (p value), and iris and pupil diameters as well as parental refraction. The contribution of all independent variables to the 2-year change in axial length was assessed using univariate and multivariate regression analyses.

Results. After univariate analyses, smaller increases in axial length were found in the OK group compared to the SV group in children who were older, had earlier onset of myopia, were female, had lower rate of myopia progression before baseline, had less myopia at baseline, had longer anterior chamber depth, had greater corneal power, had more prolate corneal shape, had larger iris diameter, had larger pupil sizes, and had lower levels of parental myopia (all $p < 0.05$). In multivariate analyses, older age and greater corneal power were associated with smaller increases in axial length in the OK group (both $p < 0.05$), whereas in SV wearers, smaller iris diameter was associated with smaller increases in axial length ($p = 0.021$).

Conclusions. Orthokeratology is a successful treatment option in controlling axial elongation compared to SV in children of older age, had earlier onset of myopia, were female, had lower rate of myopia progression before baseline, had lower myopia at baseline, had longer anterior chamber depth, had greater corneal power, had more prolate corneal shape, had larger iris and pupil diameters, and had lower levels of parental myopia.

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Key Words: myopigenic factors, myopia control, orthokeratology, axial length, myopia progression, eye elongation

Myopia is now recognized as a common condition with prevalence levels in young adolescents approaching 10% to 25% and 60% to 80% in industrialized societies of West and East Asia, respectively.^{1,2} Furthermore, high myopia (i.e., ≤ -6.00 D) is generally associated with a range of ocular pathologies, such as vitreous and retinal detachment, macular degeneration, and glaucoma.^{3–6} The rising prevalence of myopia has significant economic and social implications, resulting in interest in therapies to ameliorate its progression.^{7,8}

Several treatment options have been used in the past, with limited success to eliminate, or at least reduce, myopia progression.^{9–11} Recent studies have reported orthokeratology contact lens wear to significantly reduce axial length growth by 30% to 50% in comparison to spectacle and soft contact lens wear.^{12–17} However, an important clinical issue that is unresolved is the identification of those children where orthokeratology is likely to be most effective.

The development of effective treatment strategies for control of myopia onset and progression requires a clear understanding of what governs the underlying physiological and biological processes. Previous studies have reported the association of baseline age and refraction on the axial growth of the eye in orthokeratology and spectacle lens wearers. Cho et al.¹² reported smaller increases in axial length in children with higher and lower baseline myopia wearing orthokeratology contact lenses and spectacles, respectively. Similarly, Kakita et al.¹⁴ reported smaller increases in axial length in children with higher myopia at baseline wearing orthokeratology

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lenses, but they did not find baseline myopia to affect the rate of axial length growth in spectacles lens wearers. Hiraoka et al.¹⁵ extended the 2-year longitudinal study of Kakita et al. to follow up children for three additional years. The latter study also reported higher baseline myopia to be associated with smaller increases in axial length in orthokeratology lens wearers, but no association was found between baseline myopia and the rate of axial elongation in spectacle lens wearers.¹⁵ In addition, the latter study also reported smaller axial elongation with increasing age regardless of the treatment option assessed (i.e., orthokeratology or spectacles).¹⁵ More recently, Cho and Cheung¹⁷ also reported smaller axial elongation in children of older age wearing both orthokeratology contact lenses and spectacles, but no relationship was found between baseline myopia and the change in axial length in either of the study groups.

In addition to age and refractive error, other baseline demographics and refractive and biometric parameters as well as parents' refractive status might contribute to axial elongation.^{18–22} For example, myopia has been reported to progress as a function of age between 6 and 14 years,^{18–20} with earlier onset of myopia resulting in greater progression of myopia and higher levels of end point myopia.²⁰ Myopia has been shown to progress faster in females than in males.^{18–20} Anterior chamber depth, vitreous chamber depth, and axial length have been shown to increase with increasing myopia, although corneal power remains relatively stable.^{18,19} Children with parents who have myopia are at a higher risk of myopia development and progression, with the risk increasing with the number of parents with myopia.^{20–22}

We have recently reported the results of a prospective study, the Myopia Control with Orthokeratology contact lenses in Spain (MCOS), which evaluated, as the primary outcome measure, differences in growth of axial length over a 2-year period in White European children with myopia wearing orthokeratology contact lenses (OK) and distance single-vision spectacles (SV).^{16,23} Thirty-one children were prospectively allocated to OK and 30 to SV. We found a statistically significant difference in axial length elongation relative to baseline between the OK (mean [standard deviation {SD}], 0.47 [0.18] mm) and SV (0.69 [0.32] mm) groups ($p = 0.005$). A number of additional measurements were recorded as part of the MCOS study: age of myopia onset, gender, and parental refractive error as well as children's baseline age, refraction, anterior chamber depth, corneal power and shape, and iris and pupil diameters. The purpose of this study was to examine the degree to which these measurements affect the axial length growth over 2 years in children wearing OK and SV.

METHODS

This study was part of the MCOS study designed to assess the safety, efficacy and subjective acceptance of OK versus SV in White European children with myopia over a 2-year period.^{16,23–25}

Methods have been described in detail elsewhere.^{16,23–25} In brief, normal, healthy white European subjects 6 to 12 years of age with moderate levels of myopia (-0.75 to -4.00 D) and astigmatism (≤ 1.00 D) and free of systemic or ocular disease were recruited for the study and prospectively assigned to wear OK or SV. Spectacles or contact lenses, contact lens care solutions (for the OK group only), and full ocular examinations were provided free of charge to all subjects throughout the study. Full informed

consent and child assent were obtained from the parents/guardians before 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.

At the recruitment session, all subjects underwent a full anterior eye biomicroscopy, indirect fundus microscopy, binocular vision, and refractive evaluation to elucidate whether they were eligible to participate in the study; baseline study measurements were subsequently taken on eligible subjects (see below for full details of measurement procedures).

Subjects in the SV group were prescribed for constant wear distance single-vision spectacles having the highest positive/least negative power consistent with optimum visual acuity. Subjects from the OK group were fitted with *Menicon Z Night* contact lenses using Easy Fit Software (Menicon Co., Ltd., Nagoya, Japan). Contact lenses were ordered, and subjects from the OK group were rescheduled for an appointment approximately 2 weeks later. After initial contact lens fitting, all contact lens subjects were instructed on the first day on procedures for insertion, removal, and cleaning/disinfection and instructions were reinforced at subsequent visits. Subjects were provided with *MeniCare Plus* multipurpose solution for the daily cleaning, rinsing, and disinfecting of their contact lenses, and *Menicon Progent* intensive cleaner for use once a week (Menicon Co., Ltd).

After initial enrolment, subjects were followed at 1-, 6-, 12-, 18-, and 24-month intervals. 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 refraction²⁶ at any of the follow-up visits was considered clinically significant and was remedied by supplying contact lenses or spectacles made to the new prescription.

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

Measurements of axial length and anterior chamber depth were taken with the Zeiss *IOLMaster* (Carl Zeiss GmbH, Jena, Germany).²⁷ Three separate measurements of axial length were recorded, whereas a single shot automatically generated five measures of anterior chamber depth.

Corneal topography measurements were performed with the WaveLight Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The first measurement taken for each eye (which provided an optimum index value according to the manufacturer's recommendations) was used for the study. Mean corneal power was calculated by averaging the powers of the mean flatter and steeper corneal meridians. Also, the measurement generated a simulated central keratometry reading and the rate of peripheral corneal flattening/steepening with displacement from the corneal apex, the latter indicating the degree to which an aspheric surface differs from the spherical form (i.e., p value).²⁸

The p value was calculated over a 7-mm chord because this is the default setting of the instrument. In addition, iris and pupil diameters were also calculated automatically by the software.

Parental subjective refractions were taken at the baseline visit, and if required, parents provided estimates of the age of onset and progression of the child's myopia over the 2 years before the beginning of the study.

Statistical Analysis

Statistical analyses were conducted using SPSS 15.0 (SPSS, Inc., Chicago, IL). Data for the right eye only were used and expressed as mean (SD).

Differences in subjects' demographics and baseline data between groups were tested using unpaired sample *t*-tests for all variables, except for the male/female ratio that was tested using a χ^2 test.

The change in axial length at 2 years in comparison to baseline was taken as the dependent variable. Independent variables assessed as predictive factors for myopia progression were age, age of myopia onset, gender, myopia progression over the 2 years before the beginning of the study and baseline myopia, anterior chamber depth, mean corneal power and shape (i.e., p value), iris and pupil diameters, and parental refraction.

Simple linear regressions between the change in axial length and the different independent variables were calculated for each group separately and presented graphically (Figs. 1–11), with the exception of gender, which was assessed using a two-way analysis of variance. Differences between groups in the slopes of the regression lines were compared using analysis of covariance. Whenever analysis of covariance showed a significant interaction between independent and group variables, differences in the slopes of the

regression lines between groups were tested using aptitude-by-treatment interaction to take into account individual differences in the process of treatment evaluation (Table 2).²⁹ In addition, multivariate regression analysis was performed for each of the groups separately using the backward stepwise removal method. The F probability test was used to select each variable's enter and exit criteria for the model. Factors that were significant at $p < 0.2$ were considered for multivariate testing. The strength of association for significant factors is summarized using beta values ($\pm 95\%$ confidence intervals), corrected R^2 values, and p values (Table 3).

RESULTS

Sixty-nine children were initially examined for eligibility to participate in the study, but eight subjects could not be enrolled because they failed to meet the inclusion criteria for refraction. Thirty-one children were prospectively allocated to OK and 30 to SV. No statistically significant differences were found between groups in any of the variables assessed (Table 1; $p > 0.05$),^{16,23} with the exception of pupil diameter that was larger in the OK than the SV group ($p = 0.005$). Two and six children from the OK and SV groups, respectively, discontinued the study.²⁴ In the OK group, one child discontinued the study owing to discomfort with contact lens wear and another child owing to unknown reasons. In the SV group, four children were lost to follow-up and another two children sought contact lens correction.

Univariate Analysis

Generally, the older the age at baseline, the smaller the axial elongation at 2 years in both study groups, although the relationship was not statistically significant in either the OK ($R^2 = 0.119$,

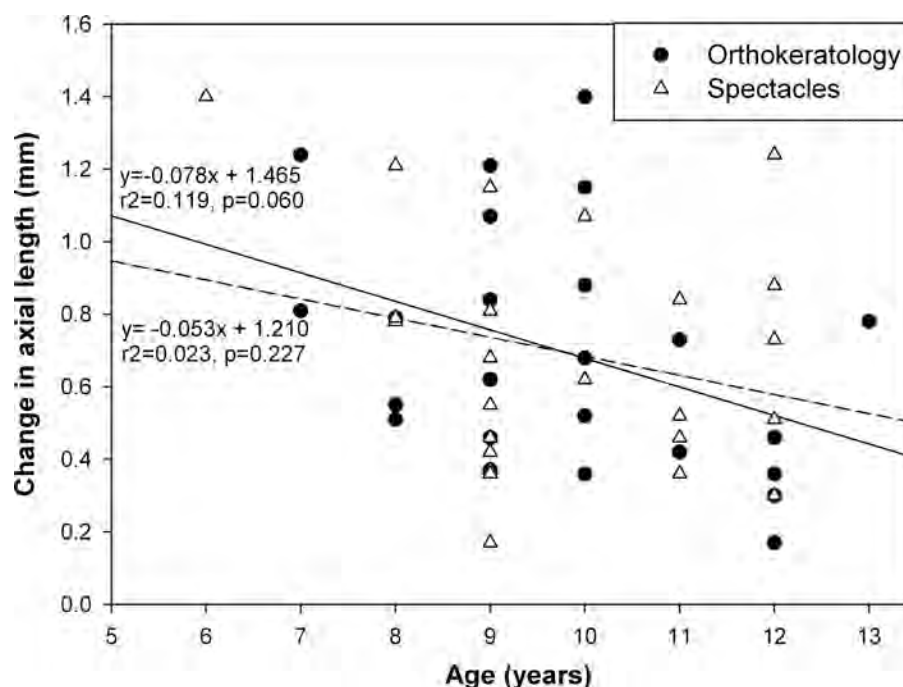


FIGURE 1.

Simple linear regressions between the change in axial length at 2 years relative to baseline and age for the orthokeratology (solid lines) and spectacle groups (dashed lines).

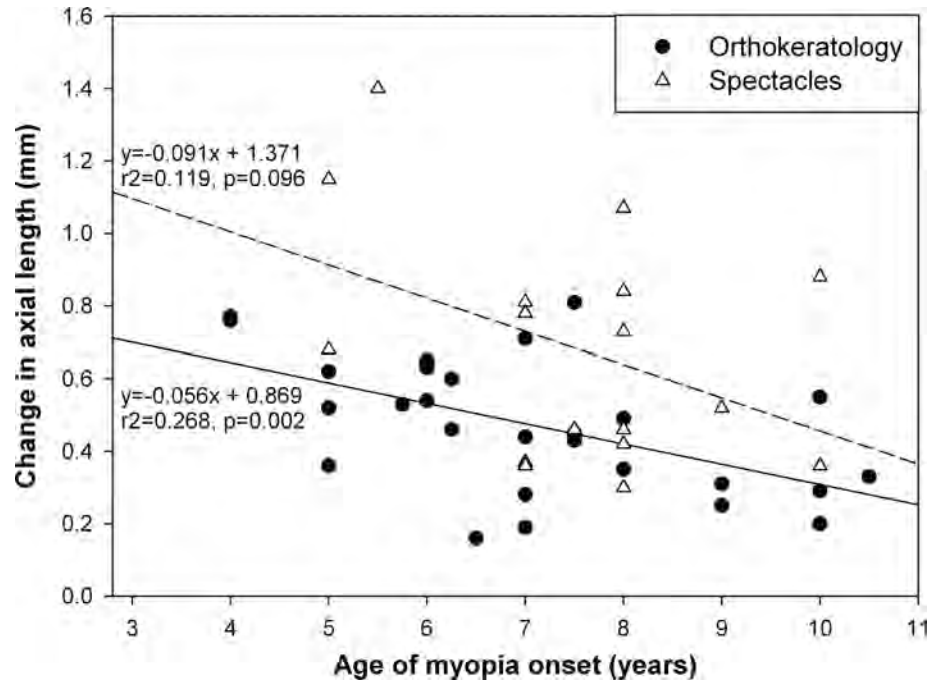


FIGURE 2.

Simple linear regressions between the change in axial length at 2 years relative to baseline and age of myopia onset for the orthokeratology (solid lines) and spectacle groups (dashed lines).

$p = 0.060$) or the SV group ($R^2 = 0.023$, $p = 0.227$). However, the effect of baseline age on axial elongation was greater in the OK group in comparison to the SV group (Fig. 1 and Table 2, $p = 0.001$). Similarly, the later the myopia onset, the smaller the axial elongation; regressions were statistically significant for the OK group ($R^2 = 0.268$, $p = 0.002$) but not for the SV group ($R^2 = 0.119$, $p = 0.096$). Age of myopia onset was found to have a

stronger effect in axial elongation in the SV group in comparison to the OK group (Fig. 2 and Table 2, $p = 0.007$).

Female gender was associated with smaller increases in axial length (0.52 [0.26] mm) in comparison to male gender (0.62 [0.29] mm) irrespective of the type of visual correction ($p = 0.002$). The interaction between gender and visual correction type was also statistically significant, indicating that female OK wearers were

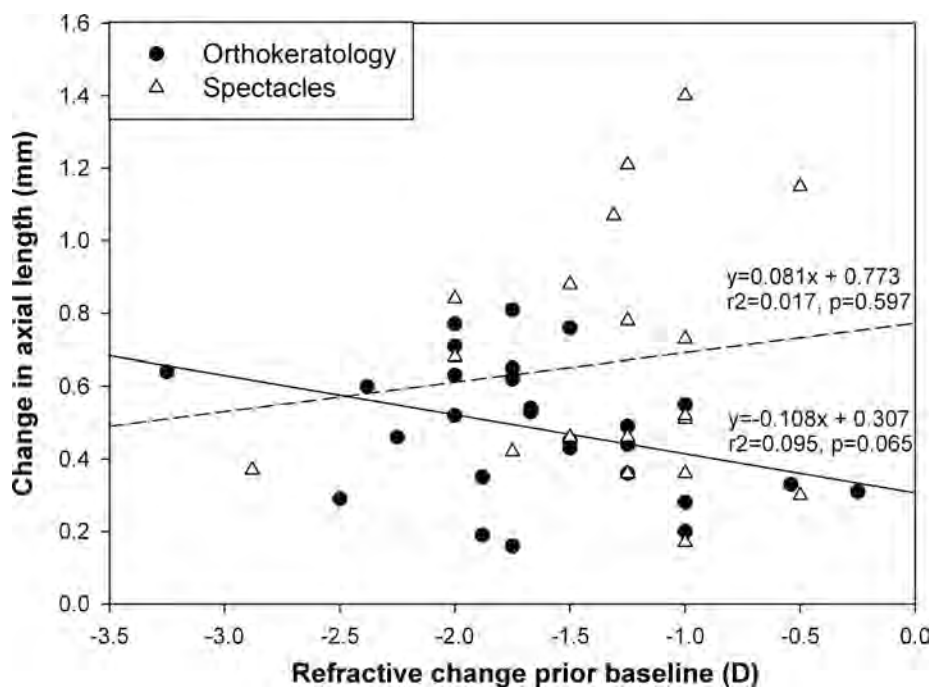


FIGURE 3.

Simple linear regressions between the change in axial length at 2 years relative to baseline and refractive change before baseline for the orthokeratology (solid lines) and spectacles groups (dashed lines).

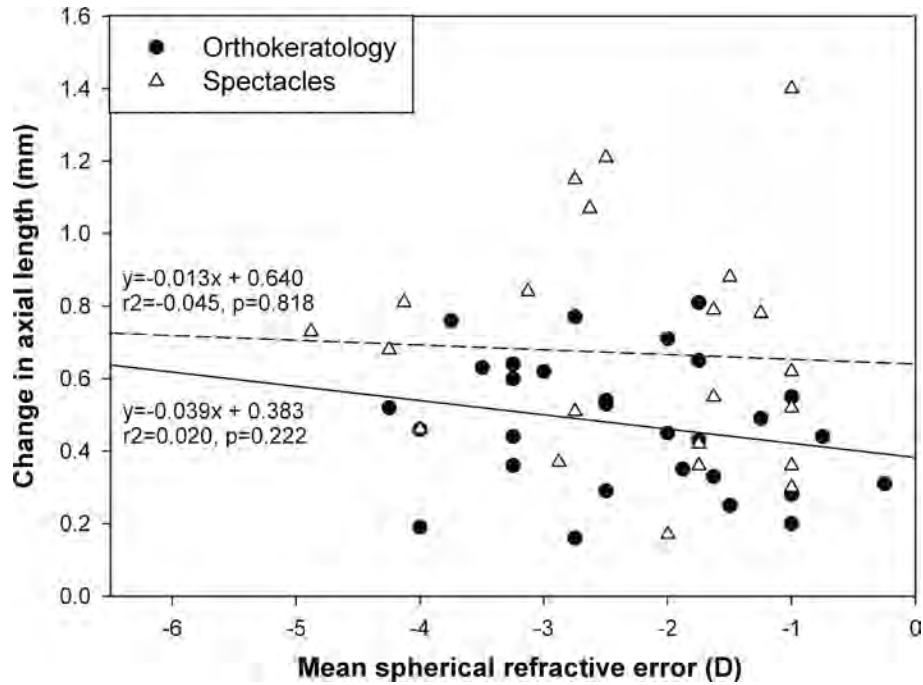


FIGURE 4.

Simple linear regressions between the change in axial length at 2 years relative to baseline and mean spherical equivalent refractive error for the orthokeratology (solid lines) and spectacle groups (dashed lines).

the subgroup that experienced smaller axial elongation at 2 years ($p = 0.001$).

Smaller myopic shifts 2 years before baseline were associated with smaller increases in axial length in the OK group, but the opposite was found in the SV group. Although these relationships were not statistically significant in either the OK ($R^2 = 0.095$,

$p = 0.065$) or the SV group ($R^2 = 0.017$, $p = 0.597$), statistically significant differences were found between groups in the slopes of the regression lines (Fig. 3 and Table 2, $p = 0.025$).

The smaller the baseline myopia the smaller the increase in axial length in both study groups, although none of the two relationships was found to be statistically significant (both $p > 0.05$).

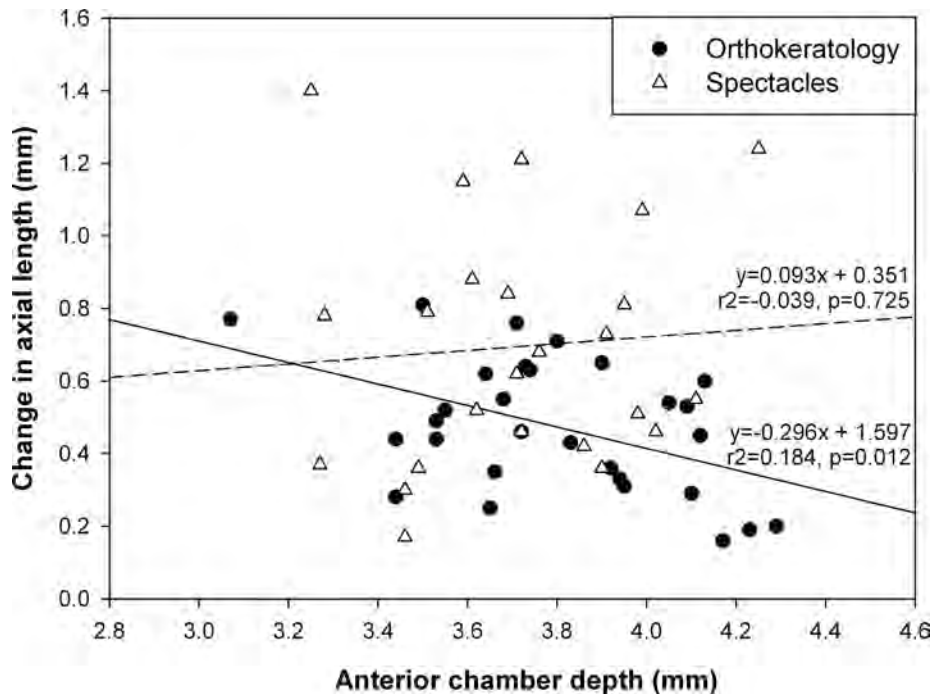


FIGURE 5.

Simple linear regressions between the change in axial length at 2 years relative to baseline and anterior chamber depth for the orthokeratology (solid lines) and spectacle groups (dashed lines).

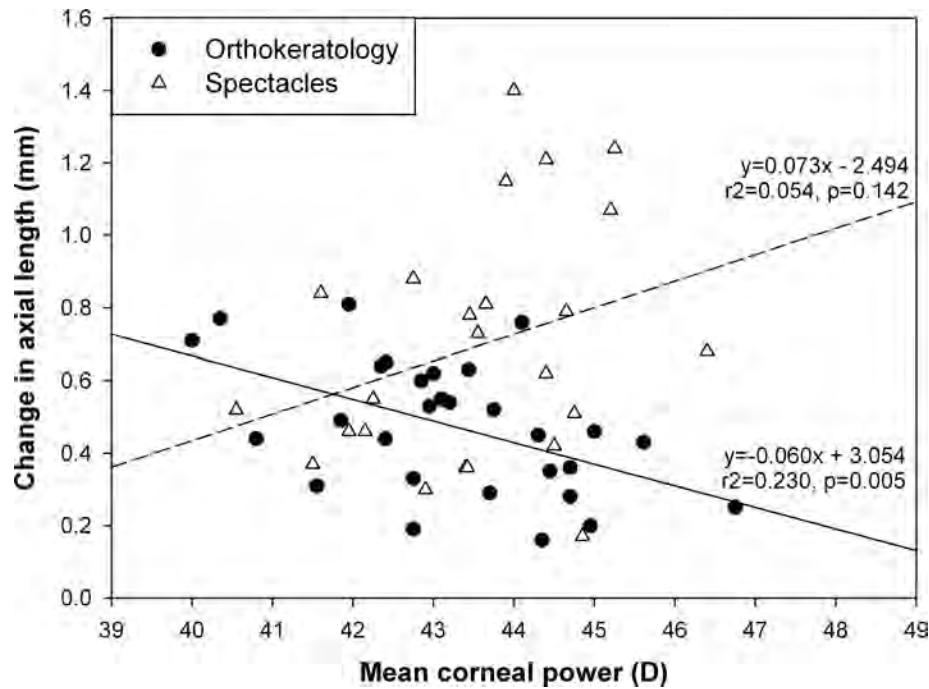


FIGURE 6.

Simple linear regressions between the change in axial length at 2 years relative to baseline and mean corneal power for the orthokeratology (solid lines) and spectacle groups (dashed lines).

However, a steeper regression line was found for the OK group in comparison to the SV group, indicating a greater effect in controlling axial elongation in subjects with lower baseline myopia in the OK group than in the SV group (Fig. 4 and Table 2, $p = 0.007$).

Longer anterior chamber depths were associated with smaller increases in axial length in the OK group ($R^2 = 0.184$, $p = 0.012$),

but the opposite was found in the SV group, although the latter relationship was not statistically significant ($R^2 = -0.039$, $p = 0.725$). Statistically significant differences were found between groups in the slopes of the regression lines (Fig. 5 and Table 2, $p = 0.003$).

Greater corneal powers were associated with smaller increases in axial length in the OK group ($R^2 = 0.230$, $p = 0.005$), but the

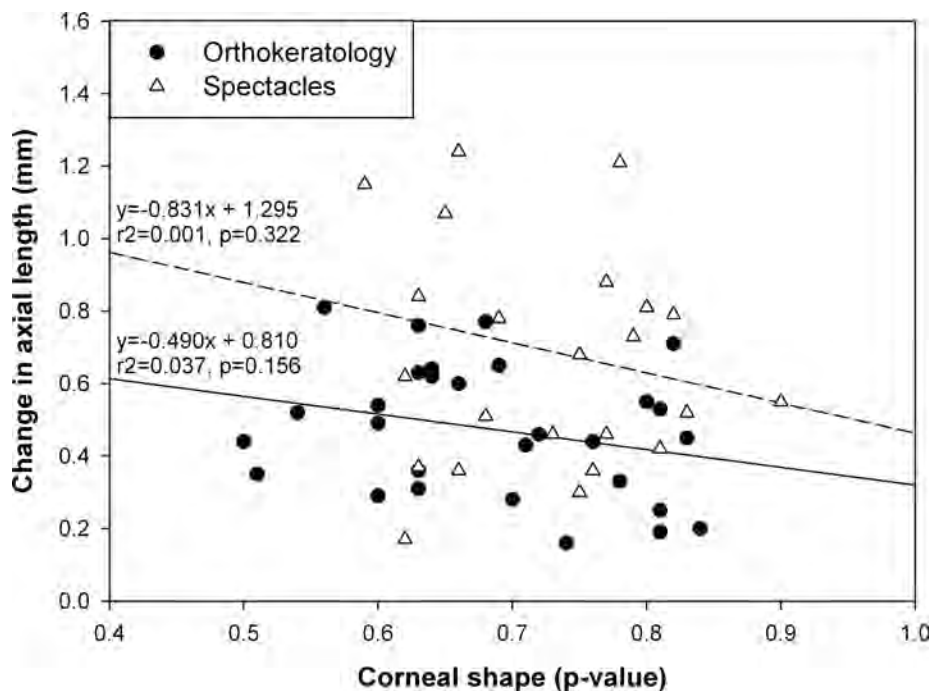


FIGURE 7.

Simple linear regressions between the change in axial length at 2 years relative to baseline and corneal shape for the orthokeratology (solid lines) and spectacle groups (dashed lines).

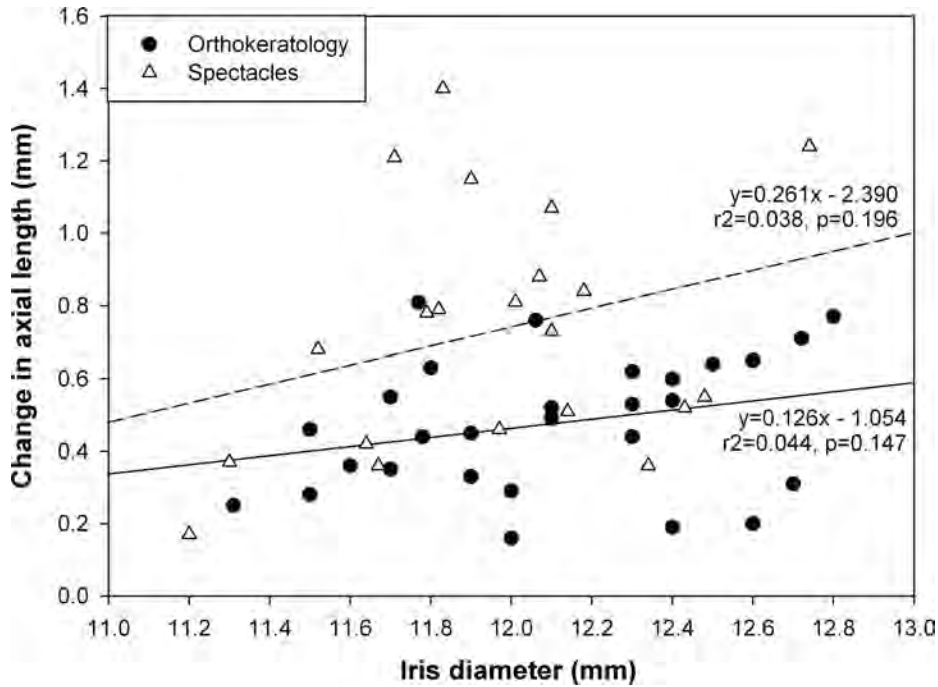


FIGURE 8.

Simple linear regressions between the change in axial length at 2 years relative to baseline and iris diameter for the orthokeratology (solid lines) and spectacle groups (dashed lines).

opposite was found in the SV group, although the latter relationship was not statistically significant ($R^2 = 0.054$, $p = 0.142$). Statistically significant differences were found between groups in the slopes of the regression lines (Fig. 6 and Table 2, $p = 0.004$).

The less prolate the corneal shape, the smaller the increase in axial length at 2 years in both study groups, although these such

relationships were not statistically significant in either of the groups (both $p > 0.05$). However, the effect of corneal shape on axial elongation was greater in the SV group in comparison to the OK group (Fig. 7 and Table 2, $p = 0.003$).

The smaller the iris diameter, the smaller the increase in axial length at 2 years in both study groups, although these relationships

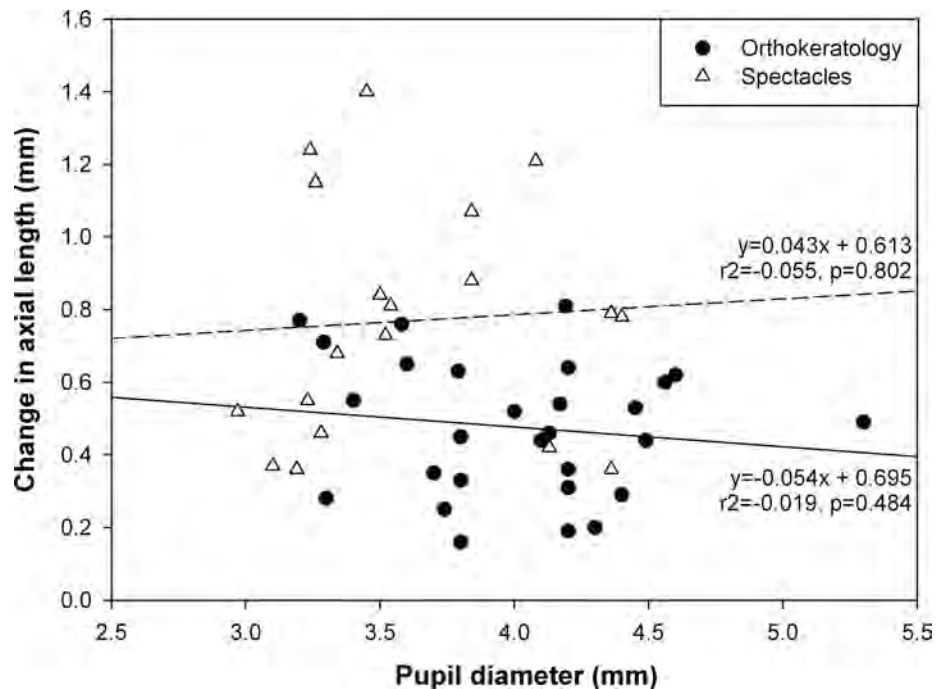


FIGURE 9.

Simple linear regressions between the change in axial length at 2 years relative to baseline and pupil diameter for the orthokeratology (solid lines) and spectacle groups (dashed lines).

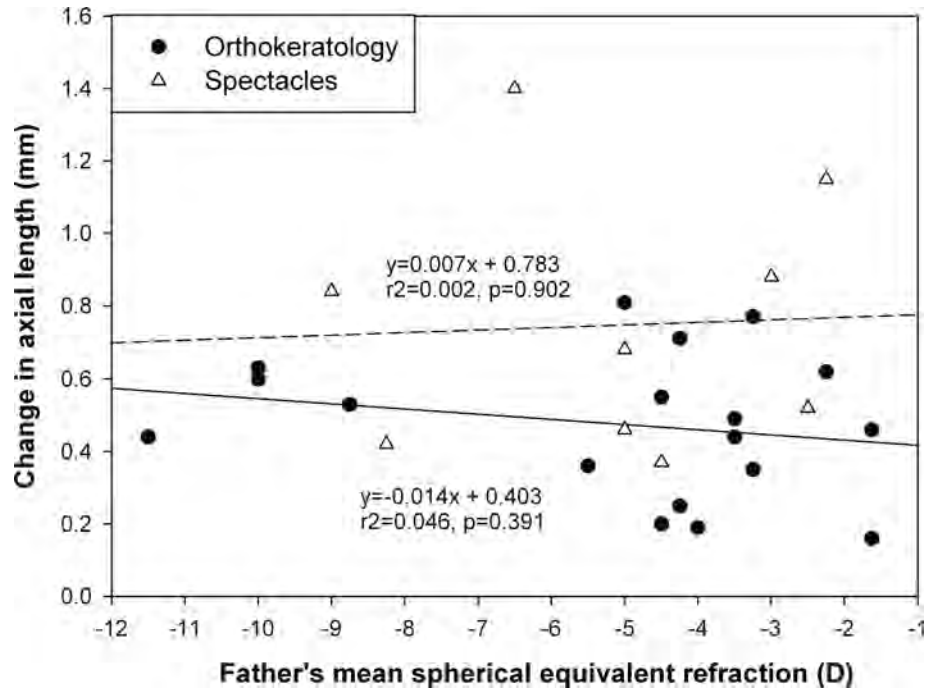


FIGURE 10.

Simple linear regressions between the change in axial length at 2 years relative to baseline and father's mean spherical refractive error for the orthokeratology (solid lines) and spectacle groups (dashed lines).

were not statistically significant in either the OK ($R^2 = 0.044$, $p = 0.147$) or the SV group ($R^2 = 0.038$, $p = 0.196$). However, the effect of iris diameter on the change in axial length was greater in SV group in comparison to the OK group (Fig. 8 and Table 2, $p = 0.002$).

The larger the pupil diameter in the OK group and the smaller the pupil diameter in SV group the smaller the increase in axial

length. Although the latter relationships were not statistically significant ($p > 0.05$), statistically significant differences were found between groups in the slopes of the regression lines (Fig. 9 and Table 2, $p < 0.001$).

Father's refraction did not affect axial length change in either the OK ($R^2 = 0.046$, $p = 0.391$) or the SV group ($R^2 = 0.002$,

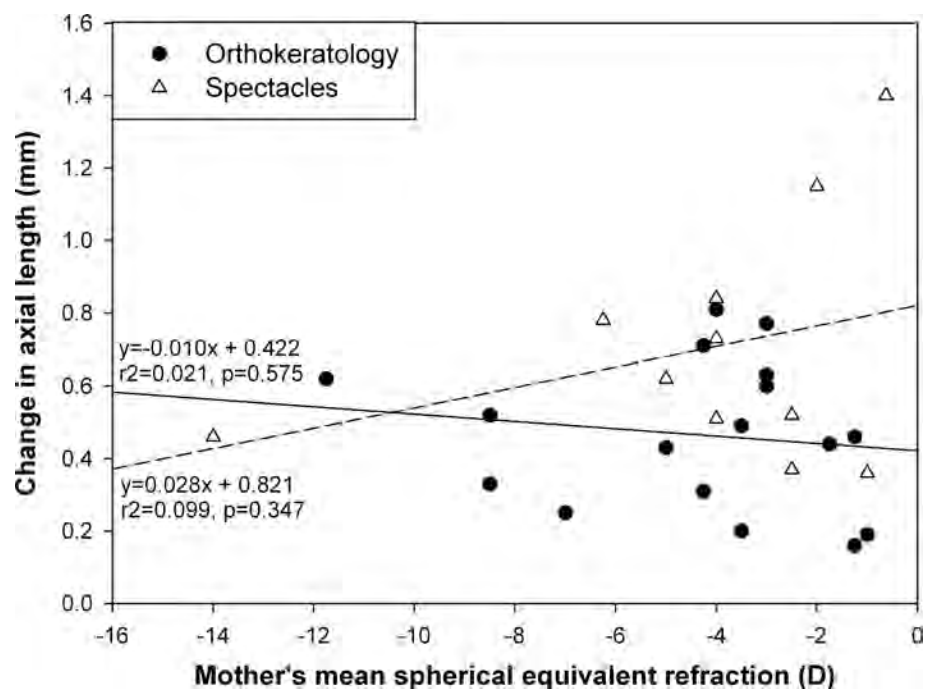


FIGURE 11.

Simple linear regressions between the change in axial length at 2 years relative to baseline and mother's mean spherical refractive error for the orthokeratology (solid lines) and spectacle groups (dashed lines).

TABLE 1. Subjects' baseline demographics, refractive and biometric parameters and parents' spherical equivalent refractions

	OK	SV	Statistical significance (p value)
Age (years)	9.6 (1.6)	9.9 (1.9)	0.76
Age of myopia onset (years)	7.3 (2.0)	7.6 (1.4)	0.60
Male/female ratio	15/16	15/15	0.55
Myopic shift 2 years before baseline (D)	-1.53 (0.65)	-1.79 (0.90)	0.22
Mean spherical equivalent refractive error (D)	-2.29 (1.11)	-2.34 (1.23)	0.86
Axial length (mm)	24.40 (0.81)	24.22 (0.91)	0.40
Anterior chamber depth (mm)	3.63 (0.55)	3.76 (0.38)	0.28
Mean corneal power (D)	43.33 (1.55)	43.82 (1.62)	0.12
Corneal shape factor (p value)	0.69 (0.10)	0.72 (0.08)	0.16
Iris diameter (mm)	12.09 (0.41)	11.95 (0.38)	0.20
Pupil diameter (mm)	4.02 (0.47)	3.61 (0.46)	0.005
Father's mean spherical equivalent refractive error (D)	-3.26 (3.42)	-2.53 (3.21)	0.46
Mother's mean spherical equivalent refractive error (D)	-2.70 (3.18)	-2.06 (3.24)	0.48

p = 0.902). However, statistically significant differences were found between groups in the slopes of the regression lines (Fig. 10 and Table 2, p = 0.016).

Lower levels of myopia in the mother were associated with smaller increases in axial length in the OK group, whereas the opposite was found for the SV group, although none of two relationships was found to be statistically significant ($R^2 = 0.021$ and $p = 0.575$; $R^2 = 0.099$ and $p = 0.347$, respectively). However,

statistically significant differences were found between groups in the slopes of the regression lines (Fig. 11, p = 0.026).

Multivariate Analysis

In the OK group, children of older age, later onset of myopia, greater corneal power, and larger iris and pupil diameters at baseline exhibited smaller increases in axial length at 2 years (Table 3),

TABLE 2. Univariate regression analyses

	OK	SV	Statistical differences between groups in the slopes of the regression lines (p value)
Age (years)	$\beta = -0.078 [-0.096/-0.018]$ $R^2 = 0.119, p = 0.060$	$\beta = -0.053 [-0.140/0.035]$ $R^2 = 0.023, p = 0.227$	p = 0.001
Age of myopia onset (years)	$\beta = -0.056 [-0.088/-0.019]$ $R^2 = 0.268, p = 0.002$	$\beta = -0.091 [-0.201/0.018]$ $R^2 = 0.119, p = 0.096$	p = 0.007
Gender	—	—	—
Myopic shift 2 years before baseline (D)	$\beta = -0.108 [-0.202/0.019]$ $R^2 = 0.095, p = 0.065$	$\beta = 0.081 [-0.157/0.210]$ $R^2 = 0.017, p = 0.597$	p = 0.025
Mean spherical equivalent refractive error (D)	$\beta = -0.039 [-0.104/0.025]$ $R^2 = 0.020, p = 0.222$	$\beta = -0.013 [-0.131/0.105]$ $R^2 = -0.045, p = 0.818$	p = 0.007
Anterior chamber depth (mm)	$\beta = -0.296 [-0.520/-0.071]$ $R^2 = 0.184, p = 0.012$	$\beta = 0.093 [-0.446/0.632]$ $R^2 = -0.039, p = 0.725$	p = 0.003
Mean corneal power (D)	$\beta = -0.060 [-0.100/-0.020]$ $R^2 = 0.230, p = 0.005$	$\beta = 0.073 [-0.026/0.173]$ $R^2 = 0.054, p = 0.142$	p = 0.004
Corneal shape factor (p value)	$\beta = -0.490 [-1.177/0.207]$ $R^2 = 0.037, p = 0.156$	$\beta = -0.831 [-2.519/0.882]$ $R^2 = 0.001, p = 0.322$	p = 0.003
Iris diameter (mm)	$\beta = 0.126 [-0.047/0.300]$ $R^2 = 0.044, p = 0.147$	$\beta = 0.261 [-0.147/0.669]$ $R^2 = 0.038, p = 0.196$	p = 0.002
Pupil diameter (mm)	$\beta = -0.054 [-0.212/0.103]$ $R^2 = -0.019, p = 0.484$	$\beta = 0.043 [-0.316/0.403]$ $R^2 = -0.055, p = 0.802$	p < 0.001
Father's mean spherical equivalent refractive error (D)	$\beta = -0.014 [-0.029/0.015]$ $R^2 = 0.046, p = 0.391$	$\beta = 0.007 [-0.060/0.043]$ $R^2 = 0.002, p = 0.902$	p = 0.016
Mother's mean spherical equivalent refractive error (D)	$\beta = -0.010 [-0.026/0.021]$ $R^2 = 0.021, p = 0.575$	$\beta = 0.028 [-0.037/0.057]$ $R^2 = 0.099, p = 0.347$	p = 0.026

The strength of association between the different factors is summarized using standardized beta values [\pm 95% confidence intervals], R^2 values, and p values for the model. The column on the far right shows statistical differences between groups in the slopes of the regression lines (p value).

TABLE 3.

Multivariate regression analyses

	OK	SV
Age (years)	$\beta = -0.365 [-0.082/-0.002]$ $p = 0.041$	—
Age of myopia onset (years)	$\beta = -0.292 [-0.064/0.005]$ $p = 0.092$	$\beta = -0.600 [-0.243/0.019]$ $p = 0.084$
Gender	—	—
Myopic shift 2 years before baseline (D)	—	—
Mean spherical equivalent refractive error (D)	—	—
Anterior chamber depth (mm)	—	$\beta = -0.592 [-1.557/0.071]$ $p = 0.068$
Mean corneal power (D)	$\beta = -0.560 [-0.112/-0.023]$ $p = 0.005$	$\beta = 0.062 [-0.057/0.230]$ $p = 0.202$
Corneal shape factor (p value)	—	—
Iris diameter (mm)	$\beta = -0.272 [-0.298/-0.047]$ $p = 0.146$	$\beta = 0.818 [0.152/1.438]$ $p = 0.021$
Pupil diameter (mm)	$\beta = -0.159 [-0.182/0.055]$ $p = 0.276$	—
Father's mean spherical equivalent refractive error (D)	—	—
Mother's mean spherical equivalent refractive error (D)	—	—
Final model	$R^2 = 0.506, p = 0.001$	$R^2 = 0.495, p = 0.047$

The strength of association between the different factors is summarized using standardized beta values [$\pm 95\%$ confidence intervals], R^2 values, and p values for the model. Only factors that provided the strongest model are shown. The bottom row shows the R^2 values and p values for the final models.

although age and mean corneal power were the only statistically significant factors in the model (both $p < 0.05$). In the SV group, later onset of myopia, longer anterior chamber depth, lower corneal power, and smaller iris diameter exhibited smaller increases in axial length (Table 3), but iris diameter was the only statistically significant factor in the model ($p < 0.05$).

DISCUSSION

We found subjects' demographics, baseline refractive and biometric data, and parental refraction to have a differential effect on the axial elongation occurring with OK and SV correction, indicating that myopia progression is a complex and multifactorial clinical phenomenon. Nevertheless, this study has attempted to identify those children where orthokeratology is likely to be most effective in controlling myopia progression.

After univariate regression analyses, smaller increases in axial length were found in the OK group compared to the SV group in children who were older, had earlier onset of myopia, were female, had lower rate of myopia progression before baseline, had less myopia at baseline, had longer anterior chamber depth, had greater corneal power, had more prolate corneal shape, had larger iris diameter, had larger pupil sizes, and had lower levels of parental myopia. In multivariate analyses, older age and greater corneal power were associated to smaller increases in axial length in OK wearers, whereas smaller iris diameter was associated to smaller increases in axial length in SV wearers.

It is well established that older age and later onset of myopia are associated with smaller increases in myopia regardless of the visual correction tested in this study.^{15,17–19} The mechanism whereby older age has a greater effect in controlling axial elongation with OK in comparison to SV group is unclear.

We did not find baseline myopia to be significantly associated with axial elongation of the eye when either univariate or multivariate regression analyses were used in each of the groups separately (Fig. 4). However, the steeper regression line found for the OK group in comparison to the SV group (Fig. 4 and Table 2) indicates a greater effect in controlling axial elongation in subjects with lower baseline myopia in the OK group than in the SV group. The latter result is consistent with that of a recent study that used the same contact lens design as that used in the current study.¹⁷ In contrast, other studies have reported smaller axial elongation in OK wearers with higher baseline myopia.^{12,14,15} The discrepancy might be related to differences in the contact lens designs used and how these affected the peripheral refraction of the eye^{30,31} as this, in turn, could affect myopia progression.³²

The OK group exhibited smaller increases in axial length, which were associated with longer anterior chamber depths, whereas no association between these two variables was found for the SV group (Fig. 5). However, the significant differences in the slope of the regression lines between groups (Fig. 5 and Table 2) indicate that longer anterior chamber depths might be conducive to myopia progression control in children fitted with OK in comparison to children prescribed SV. Small increases in anterior chamber depth are expected in children with myopia of around 10 years of age over a 2-year period.^{18,19} Therefore, children with shorter anterior chamber depths at baseline might be more likely to experience an increase in the depth of the anterior chamber concomitant with an axial elongation of the eye.

Greater corneal power was found to be associated with smaller axial elongation in OK wearers (Fig. 6). It is well established that corneal shape is one of the most determinant factors associated with successful OK lens wear.³³ A steeper cornea allows greater redistribution of corneal epithelial tissue from the central to the

peripheral cornea in OK lens wearers.³⁴ The redistribution could conceivably reduce the amount of peripheral hyperopic defocus,^{30,31} which is considered to be a putative stimulus for axial elongation.^{35,36} The SV group did not show a significant association between corneal power and axial elongation, which agrees with previous studies whereby little change in corneal power was found in children with progressing myopia.^{18,19}

We found that the larger the pupil diameter in the OK group, the smaller the increase in axial length, a finding in agreement with a recent study.³⁷ It is possible that a larger pupil diameter coupled with redistribution of corneal epithelial tissue from the central to the peripheral cornea³⁴ in the OK group produces a reduction in peripheral hyperopic defocus,^{30,31} leading to smaller increases in axial length.^{35,36}

The differences in slope between groups with regard to parental refraction indicate that the lower the parental myopia, the smaller the increase in axial length in the OK group, whereas the opposite was found for the SV group (Figs. 10 and 11, and Table 2). Children with parents who have myopia have been reported to be at a higher risk of myopia onset and progression, with the risk^{21,22} and amount of progression³⁸ increasing with the number of parents with myopia. However, the mechanism whereby, for OK versus SV wear, lower levels of parental myopia are associated with shorter increases in axial elongation is unclear.

A limitation of this study was that several variables were tested as contributory factors to the change in axial elongation despite the relatively small sample size used. Future studies with larger sample sizes should be undertaken to better understand factors affecting myopia progression in OK and SV wearers. Nevertheless, we have been able to identify a number of factors which affect significantly myopia progression, as measured by the axial elongation of the eye, in OK and SV wearers. Specifically, the data suggest that OK is a successful treatment option in controlling axial elongation in comparison to SV in children of older age, had earlier onset of myopia, were female, had lower rate of myopia progression before baseline, had lower myopia at baseline, had longer anterior chamber depth, had greater corneal power, had more prolate corneal shape, had larger iris and pupil diameters, and had lower levels of parental myopia. Although there are factors not assessed in this study, which could contribute to myopia progression such as near work,³⁹ time spent outdoors,⁴⁰ dietary intake,⁴¹ and peripheral refraction,^{30,31} it is envisaged that the results of this study will assist eye care practitioners in identifying children at greater risk of myopia progression when corrected with OK and SV as well as those children who are likely to benefit most from OK for controlling myopia progression.

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Long-term Efficacy of Orthokeratology Contact Lens Wear in Controlling the Progression of Childhood Myopia

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ABSTRACT

Purpose: The primary outcome of this study is to compare the axial length growth of white European myopic children wearing orthokeratology contact lenses (OK) to a control group (CT) over a 7-year period.

Methods: Subjects 6–12 years of age with myopia -0.75 to -4.00 DS and astigmatism ≤ 1.00 DC were prospectively allocated OK or distance single-vision spectacles (SV) correction. Measurements of axial length (Zeiss IOLMaster), corneal topography, and cycloplegic refraction were taken at 6-month intervals over a 2-year period. Subjects were invited to return to the clinic approximately 5 years later (i.e., 7 years after the beginning of the study) for assessment of their ocular refractive and biometric components. The CT consisted of 4 SV and 12 subjects who switched from SV to soft contact lens wear after the initial 2 years of SV lens wear. Changes in axial length relative to baseline over a 7-year period were compared between groups.

Results: Fourteen and 16 subjects from the OK and CT groups, respectively, were examined 6.7 ± 0.5 years after the beginning of the study. Statistically significant changes in the axial length were found over time and between groups (both $p < 0.001$), but not for the time*group interaction ($p = 0.125$). The change in the axial length for the OK group was 22% ($p = 0.328$), 42% ($p = 0.007$), 40% ($p = 0.020$), 41% ($p = 0.013$), and 33% ($p = 0.062$) lower than the CT group following 6, 12, 18, 24, and 84 months of lens wear, respectively.

Conclusion: A trend toward a reduction in the rate of axial elongation of the order of 33% was found in the OK group in comparison to the CT group following 7 years of lens wear.

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Introduction

Globally, uncorrected refractive errors represent the second major cause of vision loss¹ of which myopia is the most common and distinctive in that its prevalence has increased substantially in recent decades. To date, it has been estimated that myopia currently affects approximately 30% of the world's population,^{2,3} although a significant increase to affect around 50% of the world's population by 2050 has been forecast.² The prevalence of myopia in young adolescents is also increasing and has approached around 25% and up to 98% in industrialized societies of the West and East Asia, respectively.³ Of particular concern is that relatively low degrees of myopia may be associated with increased risk of ocular complications, such as vitreous and chorioretinal detachment, macular degeneration, and glaucoma all of which can increase the risk of vision loss.^{4–7} Furthermore, myopia incurs substantial expenditure such that in the USA, the annual cost for eye examinations and corrections by spectacles and contact lenses has been estimated to be between \$2 and \$5 billion.^{8,9} Therefore, finding effective therapies to slow the progression of myopia could potentially benefit millions of individuals and save on substantial healthcare expenditure worldwide.

Several optical treatment options have been used in the past with limited success to eliminate or, at least, reduce myopia

progression in children.^{10–12} Of these, orthokeratology (OK) contact lens wear appears to be one of the most effective as it has consistently been shown to reduce the axial elongation of the eye by 30% to 50% in comparison with conventional distance single-vision spectacle (SV) and soft contact lenses (SCL).^{12–17} Most previous studies have demonstrated reduced rates in axial elongation over 2 years of OK lens wear. A recent meta-analysis study reported that the pooled reduction in axial elongation declined with time, with 55%, 51%, 51%, and 41% obtained after 6, 12, 18, and 24 months of OK lens wear, respectively.¹⁸ However, little is known about the efficacy of OK lens wear in reducing the rate of axial elongation for longer periods of lens wear. Two retrospective studies have shed some light on the latter.^{19,20} Kwok-Hei Mok and Sin-Ting Chung compared changes in myopia over a 7-year period between 34 children with a mean age at a baseline of 9 years wearing OK and 36 children with a mean age at a baseline of 10 years wearing SV.¹⁹ Determination of the final refractive error of the OK lens wearing subjects was conducted by the washout period method, whereby subjects were refracted after not wearing the lenses for a period of time until the flatter corneal meridian reverted to its pre-OK levels.¹⁹ It took a mean (\pm standard deviation) of 25.5 ± 1.0 (range 22–29) days for the central flat corneal curvature to return to pre-OK levels. The average myopic progression

for the OK group ($-0.37 \pm 0.49\text{D}$) was significantly lower than that found for the SV group ($-2.06 \pm 0.81\text{D}$) following 7 years of lens wear.¹⁹ Downie and Lowe compared the progression rate of manifest refractive prescription in myopic children under the age of 16 years between 26 OK lens wearers and 30 age- and refraction-matched SV wearers in 2 yearly intervals over a period up to 8 years.²⁰ The study found that OK wearers showed a significantly more stable myopic refractive prescription than SV over all of the 2-year treatment intervals, indicating that OK can reduce the rate of progression of childhood myopia over the long term.²⁰ Furthermore, a subpopulation of OK lens wearers (64%) demonstrated an apparent total arrest of manifest myopic refractive change.²⁰ Although the above two studies have provided preliminary evidence for the long-term efficacy of OK contact lens wear in reducing the progression of myopia, their limitations are retrospective study designs, non-randomization of subjects to study groups and the use of non-cycloplegic refractions as primary outcome measures. Furthermore, neither of the studies measured axial length, the key structural correlate of myopic progression in OK-treated eyes.²¹ Hiraoka et al. compared changes in axial length between 22 OK and 21 SV Japanese lens wearers with a mean age at a baseline of 10 years over a period of 5 years.²² The study found statistically significant reductions in the annual increases in the axial length in the OK group compared with the SV group for the first, second, and third years, but not for the fourth and fifth years.²²

We have previously reported the results of the Myopia Control with Orthokeratology contact lens in Spain (MCOS) study which evaluated differences in growth of axial length over a 2-year period in white European children with myopia wearing OK and SV.¹⁶ We found a statistically significant difference in axial length elongation relative to baseline between the OK ($0.47 \pm 0.18\text{mm}$) and SV ($0.69 \pm 0.32\text{mm}$) groups ($p = 0.005$).¹⁶ Approximately 5 years after completion of the MCOS study, subjects were contacted by telephone and invited to return to the clinic for evaluation of their ocular refractive and biometric parameters. The purpose of this study is to compare, as the primary outcome measure, differences in growth of the axial length over a 7-year period between white European myopic children wearing OK and a control group (CT) wearing SV or SCL. Additionally, refractive and biometric changes in subjects who switched corrections were also evaluated.

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.^{16,23–26} The methods employed in MCOS have been described in detail elsewhere.^{16,23} 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 ($\leq 1.00\text{D}$) 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 CCLR score regarding anterior eye segment signs ≤ 1 unit, a “bull’s eye” corneal topography pattern and monocular and binocular visual acuities within ± 1 line of the best-corrected spectacle visual acuity.

All subjects underwent ocular examinations including slit-lamp examination, manifest refraction, and corneal topography at baseline and at 6-month intervals over a 2-year period. Follow-up visits were scheduled to fall within 2 hours of awakening in order to measure subjective refraction and visual acuity without the lens on the eye. A decrease in one line of visual acuity accompanied by a change in subjective refraction at any of the follow-up visits was considered clinically significant and was remedied by supplying new contact lenses. Approximately, 5 years after completion of the MCOS study, subjects were contacted by telephone and invited to return to the clinic for evaluation of their ocular refractive and biometric parameters. 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 (Madrid, Spain). Full informed consent and child assent was obtained in writing 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 any time.

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 Cusi, 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).²⁷ Three separate measurements of axial length were recorded and a mean obtained.

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 $\pm 0.10\text{D}$ 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. The measurement generates a simulated central keratometry reading and the rate of peripheral corneal flattening/steepening that occurs with displacement from the corneal apex; the latter indicates the degree to which an aspheric surface differs from the spherical form (i.e., the p value). The p value was calculated over a 7-mm chord in accord with the default setting of the instrument.

Statistical analysis

Differences in subjects’ demographics and baseline data between groups were tested using unpaired sample t-tests for all variables, except for the male:female ratio which was tested using a chi-square test. Changes (from baseline) in refractive and biometric data over time and between groups (i.e., OK vs. CT) were tested using a general linear model (GLM) with repeated measures to test the statistical significance of differences in outcome variables (i.e., axial length, spherical and cylindrical refractive components, corneal power and corneal shape) for the between-subject

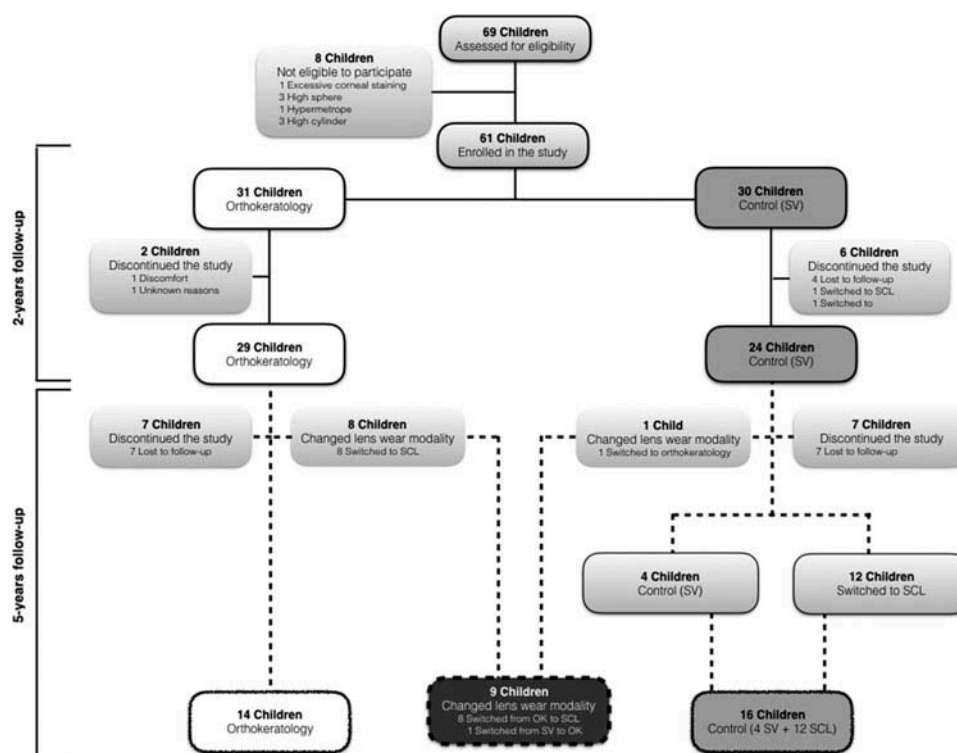


Figure 1. Flowchart of the subjects recruited for the study. SV, distance single-vision spectacles; SCL, soft contact lenses.

factor of refractive correction (two levels: OK and CT) and for the within-subject factor of time (five levels: 6, 12, 18, 24, and 84 months). The significance of the interaction between OK and CT with respect to time was then tested for all time intervals combined and then separately for each of the five time intervals following post hoc Bonferroni correction. GLM with repeated measures was also used to test the effect of switching treatments from OK to SCL. Additionally, an unpaired sample t-test was used to test, for each time point, differences between the groups in refractive and biometric variables. Equality of variances and sphericity were tested using the Levene and Mauchly tests, respectively, to select appropriate p values. Additionally, simple linear regressions between the change in axial length at 7 years relative to baseline and baseline age, mean spherical equivalent refractive error, axial length, mean central corneal power, and corneal shape factor were calculated for the OK and CT groups separately. Differences between groups in the slopes of the regression lines were compared using an analysis of covariance. The strength of association between the different factors is summarized using linear regression equations, R^2 squared values and p values. Data are expressed as mean \pm 1 standard error of the mean (SEM). Data from right eyes only were used for analysis. Statistical analyses were performed with *IBM SPSS Statistics* (IBM Corp., Ver. 22, Armonk, NY, USA) and graphing with *SigmaPlot* (Systat software Inc, San Jose, CA, USA). The level of statistical significance was set at 5%.

Results

At the inception of MCOS, 69 subjects were examined for eligibility: Eight subjects were not eligible to participate and

31 and 30 children were prospectively allocated to OK and SV, respectively (Figure 1). Twenty-nine and 24 subjects from the OK and SV groups, respectively, thus completed the initial 2 years of the MCOS study. Seven subjects were subsequently lost to follow-up in each group and no further information was able to be collected from these subjects leading to a total of 39 subjects of the original cohort available for review at the 7-year visit. Of these, 14 and 4 remained in their original OK and SV lens wear categories, respectively. In addition, twelve of the 39 subjects switched to standard SCL wear after 2 years of SV lens wear which thus constituted a control group (CT) of 16 subjects (i.e., 4 SV + 12 SCL). Nine subjects switched lens wear category the effect of which was assessed separately (see subheading below) (Figure 1).

Long-term effects in the OK and CT groups

The OK and CT groups were followed for 6.9 ± 0.1 and 6.5 ± 0.1 years, respectively; this difference was statistically significant ($p = 0.001$). Subjects reported inserting and removing their OK lenses every night and morning, respectively. None of the subjects from the OK group reported cessation of lens wear for any significant periods of time over the entire 7-year period of OK lens wear. Furthermore, all subjects reported ≥ 0.9 uncorrected decimal visual acuities (equivalent to 0.05 logMAR or $> 20/25$) at the 7-year visit. The incidence, type and timeline of adverse events found over the initial 24 months of the study have been previously reported.²⁴ At the 84-month visit, all subjects underwent a thorough ophthalmic examination and no remarkable adverse events were found. Furthermore, none of the subjects reported any significant complications in the last 5 years of lens

wear. The 12 subjects who switched to standard SCL wear after 2 years of SV lens wear and who became part of the CT group wore SCL for 2.5 ± 0.4 years prior to the 7-year visit. No statistically significant differences between the OK and CT groups were found in any of the baseline demographics and refractive and biometric data (Table 1).

Statistically significant changes were found in axial length both over time and between groups ($p < 0.001$), but not for the time*group interaction ($p = 0.125$) (Figure 2 and Table 2). Changes over time were statistically significant for all pairs of time points (all $p \leq 0.001$) (Figure 2 and Table 2). In comparison to the CT group, the change in axial length for the OK group was 22% ($p = 0.328$), 42% ($p = 0.007$), 40% ($p = 0.020$), 41% ($p = 0.013$), and 33% ($p = 0.062$) lower following 6, 12, 18, 24, and 84 months of lens wear, respectively (Figure 2 and Table 2).

Statistically significant differences were also found in the spherical component of the refraction over time, between groups and for the time*group interaction (all $p < 0.001$) (Table 2). Statistically significant differences between time points were found between 6- and 12-, 18-, 24-, and 84-months (all $p < 0.01$); between 12- and 84-months ($p = 0.002$); between 18- and 24-, and 84-months (both $p < 0.001$); and between 24- and 84-months ($p < 0.001$) (Table 2). Statistically significant differences were found between groups at all the different time

points ($p < 0.001$) (Table 2). However, no statistically significant differences were found in the cylindrical component of the refraction over time, between groups or for the time*group interaction ($p > 0.05$) (Table 2).

Statistically significant differences were found in corneal power over time (both $p < 0.001$) and between groups (both $p < 0.001$), but not for the time*group interaction (both $p > 0.05$) for both the flatter and steeper meridians (Table 2). Significant differences were found for pairs of time points between 6-, 12-, 18-, 24-, and 84-months for both meridians (all $p \leq 0.02$) (Table 2). Significant differences were also found between groups in corneal power at all time points for both meridians (all $p < 0.001$) (Table 2). However, no significant differences were found in the corneal shape (i.e., corneal p value) over time, between groups or for the time*group interaction (all $p > 0.05$) (Table 2).

Univariate linear regression analysis revealed that the older the age at baseline the smaller the axial elongation at 7 years in both study groups, although the relationship was statistically significant for the CT ($R^2 = 0.274$, $p = 0.022$), but not for the OK group ($R^2 = 0.142$, $p = 0.101$). The effect of baseline age on axial elongation was, however, similar between groups ($p = 0.208$) (Figure 3 and Table 3). Greater corneal powers at baseline were associated with smaller increases in axial length in the OK group ($R^2 = 0.290$, $p = 0.027$), but no significant relationship was found for the CT group ($R^2 = 0.000$, $p = 0.817$) (Figure 4 and Table 3). Furthermore, statistically significant differences were found between groups in the slopes of the regression lines ($p = 0.044$) (Figure 4 and Table 3). No significant relationships were found between the change in axial length at 7 years in comparison to baseline and baseline mean spherical equivalent refractive error, axial length and corneal shape for either the OK or CT groups (Table 3). In addition, no statistically significant differences were found between groups in the slopes of the regression lines for either spherical equivalent refractive error, axial length or corneal shape (all $p > 0.05$) (Table 3).

Table 1. Baseline demographics, refractive and biometric data for both treatment groups. Variables are expressed as mean \pm SEM.

	Orthokeratology	Control	p value
Age (years)	10.4 \pm 0.5	9.6 \pm 0.4	0.244
Male/female ratio	8/6	7/9	1.00
Sphere (D)	-2.27 \pm 0.31	-2.16 \pm 0.26	0.375
Cylinder (mm)	-0.25 \pm 0.09	-0.30 \pm 0.09	0.876
Axial length (mm)	24.39 \pm 0.23	24.08 \pm 0.27	0.621
Flatter meridian (D)	43.18 \pm 0.45	43.45 \pm 0.46	0.665
Steeper meridian (D)	43.82 \pm 0.41	44.11 \pm 0.54	0.667
Corneal shape factor (p value)	0.70 \pm 0.03	0.70 \pm 0.02	0.982

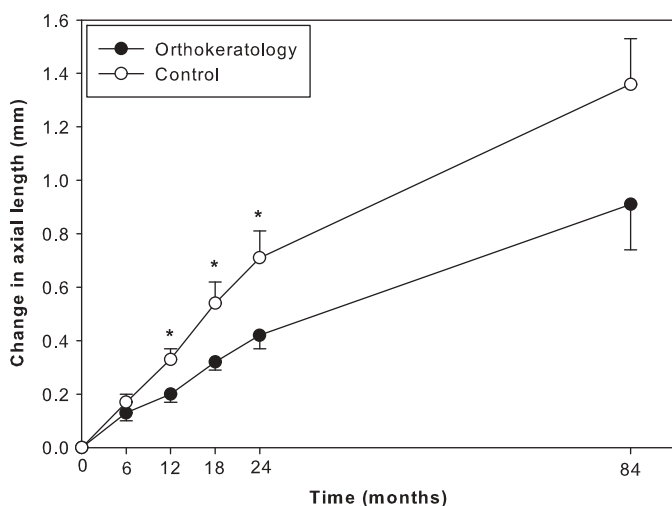


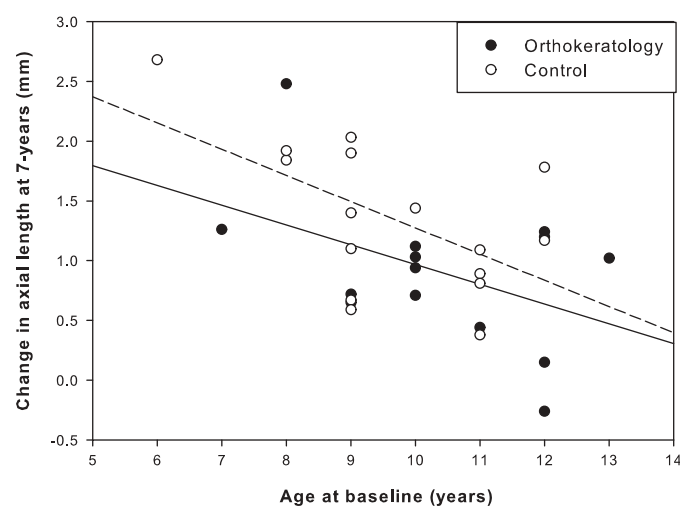
Figure 2. Changes (mean \pm SEM) in axial length (mm) from baseline over time for the OK (black, solid circles) and CT (white, open circles) groups. Error bars represent one standard error of the mean. Asterisks indicate statistically significant differences in the change in axial length between groups at 12-, 18-, and 24-month time intervals (all $p \leq 0.02$). OK, orthokeratology; CT, control.

The effect of switching treatments

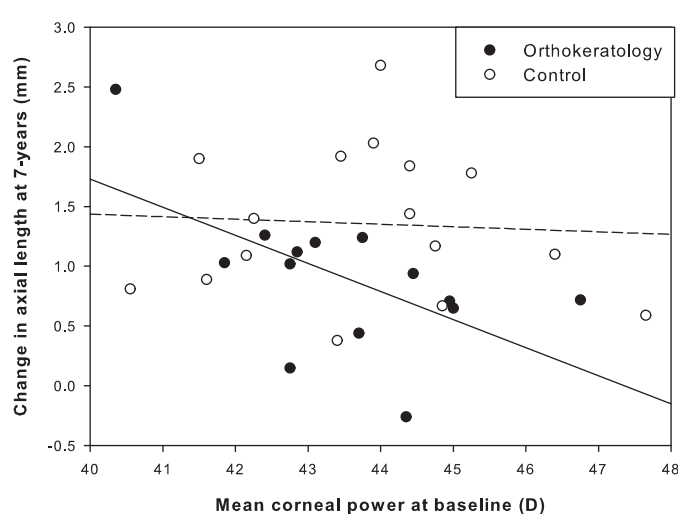
Following 2 years of OK lens wear, eight subjects (4 male and 4 female) switched from OK to SCL 1.7 ± 0.5 years (range 0.2 to 3.9 years) thereafter and wore SCL for the last 3.3 ± 0.5 years (range 1.3 to 5.3 years). A trend was found for increased time of SCL wear to be associated with shorter increases in axial length (Figure 5). The reasons for switching from OK to SCL were (number of subjects): expensive treatment (4), recurrent punctate keratitis (2) and concerns regarding regression (1) and efficacy (1). These subjects had mean ages of 9.3 ± 0.4 , 11.4 ± 0.4 and 16.4 ± 0.5 at baseline, following 2 years of OK lens wear and at the 7 year study visit, respectively. On average, axial length increased by 0.57 ± 0.06 mm during the initial 2 years of OK lens wear and by 0.80 ± 0.16 mm in the subsequent 5 years (Table 4), although there was large between-subject variability (Figure 6). As expected, the increase in axial length following cessation of OK lens wear was associated with an increase in myopia, a steepening of corneal curvature and a more prolate corneal shape (Table 4). In comparison to the CT group (Table 2), these

Table 2. Mean (\pm SEM) refractive and biometric values for the OK and CT groups who completed the 7-year study at each time interval.

	Baseline	6 months	12 months	18 months	24 months	84 months
Refractive components						
Sphere (D)						
Orthokeratology	-2.27 ± 0.31	-0.14 ± 0.07	-0.21 ± 0.07	-0.14 ± 0.07	-0.23 ± 0.06	-0.29 ± 0.10
Control	-2.16 ± 0.26	-2.39 ± 0.29	-2.74 ± 0.30	-3.07 ± 0.30	-3.37 ± 0.32	-5.00 ± 0.43
Cylinder (D)						
Orthokeratology	-0.25 ± 0.09	-0.38 ± 0.09	-0.27 ± 0.10	-0.30 ± 0.10	-0.29 ± 0.13	-0.30 ± 0.10
Control	-0.30 ± 0.09	-0.25 ± 0.08	-0.30 ± 0.08	-0.30 ± 0.11	-0.37 ± 0.10	-0.59 ± 0.10
Biometric components						
Axial length (mm)						
Orthokeratology	24.39 ± 0.23	24.52 ± 0.23	24.41 ± 0.23	24.71 ± 0.24	24.81 ± 0.25	25.30 ± 0.31
Control	24.08 ± 0.27	24.25 ± 0.27	24.46 ± 0.27	24.61 ± 0.26	24.78 ± 0.26	25.43 ± 0.27
Flatter corneal meridian power (D)						
Orthokeratology	43.18 ± 0.45	41.32 ± 0.46	41.36 ± 0.48	41.10 ± 0.44	41.36 ± 0.49	40.49 ± 0.41
Control	43.45 ± 0.46	43.51 ± 0.46	43.52 ± 0.46	43.45 ± 0.45	43.47 ± 0.48	42.69 ± 0.42
Steeper corneal meridian power (D)						
Orthokeratology	43.82 ± 0.41	42.23 ± 0.47	42.12 ± 0.48	41.99 ± 0.43	42.16 ± 0.47	41.35 ± 0.41
Control	44.11 ± 0.54	44.29 ± 0.51	43.36 ± 0.51	44.31 ± 0.52	44.18 ± 0.53	43.68 ± 0.45
Corneal shape factor (<i>p</i> value)						
Orthokeratology	0.70 ± 0.03	0.82 ± 0.05	0.79 ± 0.04	0.82 ± 0.04	0.76 ± 0.05	0.78 ± 0.05
Control	0.70 ± 0.02	0.70 ± 0.02	0.73 ± 0.02	0.71 ± 0.02	0.74 ± 0.02	0.69 ± 0.03

**Figure 3.** Simple linear regressions between the change in axial length at 7 years relative to baseline and age at baseline for the orthokeratology (black, solid circles and solid line) and control groups (white, open circles and dashed line).

subjects experienced mean reductions in the rate of axial elongation of 47%, 30%, 22%, and 19% following 6, 12, 18, and 24 months of OK lens wear, respectively (Tables 2 and 4). However, when these subjects switched from OK to SCL the rate of axial elongation observed at 84 months in comparison to the CT group was -1% , indicating the effect of OK lens

**Figure 4.** Simple linear regressions between the change in axial length at 7 years relative to baseline and mean central corneal power at baseline for the orthokeratology (black, solid circles and solid line) and control groups (white, open circles and dashed line).

wear in reducing the rate of axial elongation is negligible with discontinuation of lens wear (Tables 2 and 4). One male subject switched from SV to OK lens wear immediately after the initial 2 years of SV lens wear and wore OK lenses for the following 5 years. The reason for changing to OK was to

Table 3. Simple linear regressions between the change in axial length at 7 years relative to baseline and the different baseline variables for both the OK and CT groups. The strength of association between the different factors is summarized using linear regression equations, R^2 values and *p* values. OK, orthokeratology; CT, control; MSE, mean spherical equivalent.

	Orthokeratology	Control	Statistical differences between groups in the slopes of the regression lines (<i>p</i> value)
Age (years)	$y = -0.165x + 2.620$ $R^2 = 0.142, p = 0.101$	$y = -0.220x + 3.469$ $R^2 = 0.274, p = 0.022$	$p = 0.208$
MSE refractive error (D)	$y = 0.070x + 1.073$ $R^2 = 0.000, p = 0.669$	$y = -0.075x + 1.528$ $R^2 = 0.000, p = 0.653$	$p = 0.987$
Axial length (mm)	$y = 0.115x - 1.904$ $R^2 = 0.000, p = 0.591$	$y = -0.206x + 6.315$ $R^2 = 0.048, p = 0.207$	$p = 0.085$
Mean central keratometry (D)	$y = -0.235x + 11.131$ $R^2 = 0.290, p = 0.027$	$y = -0.021x + 2.282$ $R^2 = 0.000, p = 0.817$	$p = 0.044$
Corneal shape factor (<i>p</i> value)	$y = -1.541x + 1.982$ $R^2 = 0.000, p = 0.376$	$y = -1.868x + 2.659$ $R^2 = 0.005, p = 0.319$	$p = 0.058$

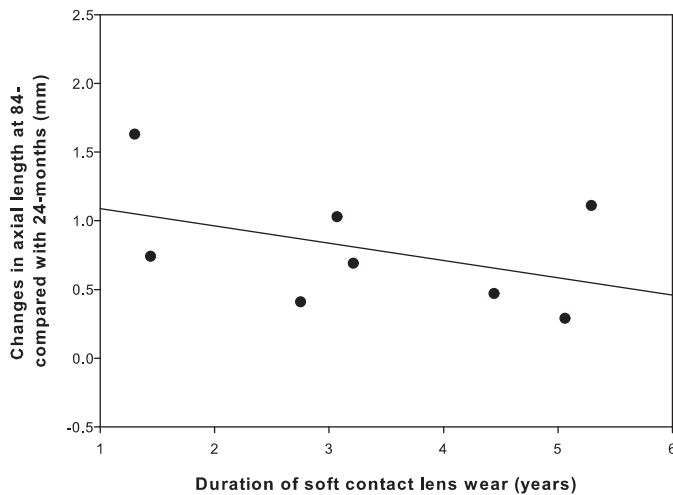


Figure 5. Simple linear regressions between the change in axial length at 84 months compared with 24 months and the duration of soft contact lens wear.

reduce the rate of myopia progression. In this subject, the axial length increased by 0.81 mm during the initial 2 years of SV lens wear, but only by 0.35 mm in the following 5 years of OK lens wear (Table 4).

Discussion

This study assessed the long-term efficacy of OK lens wear in reducing the rate of axial elongation over a period of as long as 7 years in White European subjects. The significant reduction in manifest myopia and the rate of myopia progression found in the OK group after initial lens wear remained throughout the 7-year period and is primarily attributed to the corneal reshaping effect induced by OK contact lens wear and the resultant change in corneal power and shape (Table 2). The CT group, however, showed an average increase in myopia of 2.84D accompanied by negligible changes in corneal power and shape (Table 2).

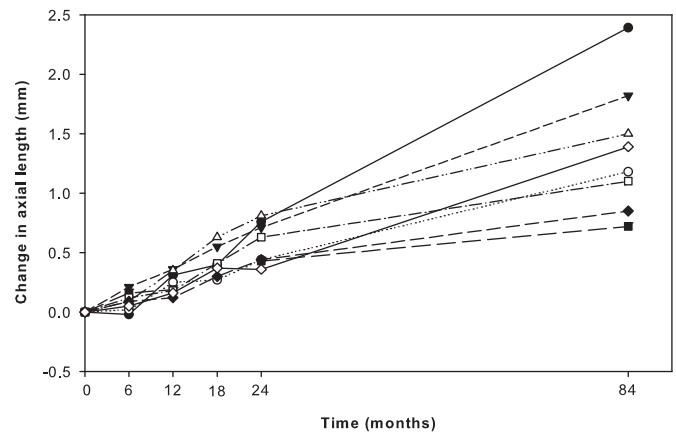


Figure 6. Changes in axial length (mm) from baseline over time for eight subjects who switched from OK to SCL after an initial phase of 2 years of OK lens wear. OK, orthokeratology; SCL, soft contact lens.

Of interest is the finding of a trend toward a reduction in the rate of axial elongation of the order of 33% in the OK group in comparison to the CT group following 7 years of lens wear (Figure 2 and Table 2). Interestingly, a study estimated that reducing the rate of myopia progression by 33% would lead to a reduction of 73% in the frequency of high myopia ($<-5.00D$);²⁸ such reduction could therefore have important implications in terms of reducing ocular-related morbidity⁷ and healthcare costs.⁸

Despite differences in corneal topography and contact lens-induced responses between Caucasian and Japanese ethnicities have been previously reported,^{29,30} our results are similar to those reported by Hiraoka et al.²² We found OK to reduce the rate of axial elongation by 33% after 7 years of lens wear, whereas Hiraoka et al. found OK to reduce the rate of axial elongation by 31% after 5 years of lens wear.²² The study of Hiraoka et al. was performed in Japanese subjects using one particular OK contact lens design (i.e., α Ortho-K; Alpha Corp., Nagoya, Japan),²² whereas the present study was undertaken in White European subjects using a different OK

Table 4. Mean (\pm SEM) refractive and biometric values for the eight subjects who switched from OK to SCL as well as for one single subject who switched from SV to OK at each time interval. OK, orthokeratology; SCL, soft contact lens; SV, single-vision spectacles.

	Baseline	6 months	12 months	18 months	24 months	84 months
Refractive components						
Sphere (D)						
OK to SCL	-2.31 ± 0.38	-0.31 ± 0.06	-0.25 ± 0.13	-0.33 ± 0.08	-0.50 ± 0.12	-4.81 ± 0.62
SV to OK	-3.75	-4.00	-4.00	-4.50	-5.00	-0.25
Cylinder (D)						
OK to SCL	-0.38 ± 0.08	-0.22 ± 0.07	-0.44 ± 0.11	-0.31 ± 0.09	-0.19 ± 0.09	-0.59 ± 0.16
SV to OK	-0.75	-0.75	-0.75	-0.75	-0.50	-0.75
Biometric components						
Axial length (mm)						
OK to SCL	24.66 ± 0.30	24.75 ± 0.30	24.90 ± 0.32	25.06 ± 0.32	25.23 ± 0.32	26.03 ± 0.41
SV to OK	25.00	25.39	25.39	25.72	25.81	26.16
Flatter corneal meridian power (D)						
OK to SCL	42.51 ± 0.75	40.74 ± 0.67	40.84 ± 0.62	40.71 ± 0.74	40.82 ± 0.82	41.54 ± 0.74
SV to OK	43.30	43.20	43.20	43.44	43.44	40.40
Steeper corneal meridian power (D)						
OK to SCL	43.24 ± 0.63	41.68 ± 0.70	41.69 ± 0.61	41.78 ± 0.77	41.76 ± 0.79	42.57 ± 0.67
SV to OK	44.00	43.90	43.90	43.95	44.12	41.5
Corneal shape factor (<i>p</i> value)						
OK to SCL	0.65 ± 0.04	0.87 ± 0.05	0.94 ± 0.02	0.85 ± 0.05	0.91 ± 0.04	0.68 ± 0.03
SV to OK	0.80	0.82	0.85	0.86	0.85	0.94

lens design (i.e., Menicon Z Night, Menicon Co., Ltd, Nagoya, Japan). Interestingly, our results also agree with those of Hiraoka et al. in that the benefit of OK in reducing the axial elongation of eye diminishes with longer periods of lens wear.

The reduced efficacy of myopia control with long periods of lens wear found in this study may be attributed to the natural history of myopia progression, in which there is a reduced rate of axial elongation with increased age, thereby making it more difficult to find significant differences between groups in axial length over longer periods of lens wear (Figures 2 and 3, and Table 2). In fact, the increases in axial length over the first 24 months of this study were remarkably similar to those found between 24 and 84 months for both the OK (0.42 ± 0.05 and 0.39 ± 0.04 mm, respectively) and the CT (0.71 ± 0.10 and 0.65 ± 0.11 mm, respectively) groups, clearly indicating a decrease in the rate of axial elongation regardless of the visual correction being worn (Figure 3 and Table 2). It is well established that older age is associated with smaller increases in myopia and axial elongation. Furthermore, it has been previously reported that myopia stabilizes at around 16 years of age.³¹ Subjects in this study had mean ages of 10 and 12 years at baseline and following 2 years of OK lens wear, respectively. Therefore, a reduced rate of myopia progression would be expected on these subjects during the subsequent 5 years of data collection.

Greater corneal power was found to be associated with smaller axial elongation in OK wearers (Figure 4). Following OK lens wear, a steeper cornea is likely to provide a smaller treatment zone of central corneal flattening³² and a wider peripheral ring of increased corneal power. Therefore, it is feasible that a steeper cornea facilitates corneal reshaping and reduction in axial elongation following OK lens wear.^{11,25}

The large variability in the increases in axial length found in the 8 subjects who discontinued OK lens wear at 2 years and switched to SCL wear could be attributed to the length of time that SCLs were worn after ceasing OK lens wear (Figure 5), individual differences and differences in the power profile between the different SCLs worn (Figure 6).³³ In any event, the results found on the effect of switching treatments appear to be consistent with those found in the OK and CT groups over the 7-year period in that the efficacy of OK diminishes and resumes with discontinuation and restoration of OK lens wear, respectively.

A limitation of this study is the potential bias introduced by subjects' self-selection to continue wearing OK, SV, or SCL. However, the major limitation concerns the relatively small sample size employed in this study. The overall power to detect between-subjects differences (i.e., OK vs. CT) in the general linear model employed in our study was $P = 0.68$ (*IBM SPSS Statistics*). However, the power varied at each of the different time points, being lowest at the 6- ($P = 0.16$) and 84-month visits ($P = 0.47$) and highest at the 12- ($P = 0.81$), 18- ($P = 0.76$), and 24-month visits ($P = 0.73$), indicating that the relatively low statistical power found at the 84-month visit is not only related to the sample size employed but also to the large variability in changes in axial length in both the OK (0.91 ± 0.63 mm) and CT (1.36 ± 0.63 mm) groups. Taking the standard deviation of the change in axial length (0.63) and the difference in axial length found between groups at the 84-month visit (0.45 mm), a

sample size of 32 subjects per group would be needed for a designated statistical power of 0.80 at $\alpha = 0.05$. Despite the above-mentioned limitations, our study offers notable features such as being the first study to assess the efficacy of OK lens wear in White European subjects in reducing the rate of axial elongation over a period of as long as 7 years. In addition, the study measures changes in axial elongation over the entire follow-up period with the *IOLMaster*, a partial coherence interferometer well known to provide excellent resolution and repeatability.²⁷ Nonetheless, randomized, controlled, clinical trials are warranted to confirm the findings of this study.

In summary, a trend toward a reduction in the rate of axial elongation of the order of 33% was found with long-term OK lens wear in comparison to SV and SCL wearers over a period of 7 years. The reduction observed over time in the efficacy of OK lens wear in slowing the axial elongation of the eye might be partly attributed to axial length (and myopia) stabilization as children approach the teenage years.³¹ Reducing myopia progression has important implications in terms of reducing ocular-related morbidity⁷ and healthcare costs.⁸

Acknowledgments

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Declaration of interest

Jacinto Santodomingo-Rubido and Keiji Sugimoto are full-time employees of Menicon Co., Ltd. The authors alone are responsible for the content and writing of the paper.

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Myopia Control with Orthokeratology Contact Lenses in Spain: Refractive and Biometric Changes

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PURPOSE. To compare axial length growth between white children with myopia wearing orthokeratology contact lenses (OK) and distance single-vision spectacles (SV) over a 2-year period.

METHODS. Subjects 6 to 12 years of age with myopia -0.75 to -4.00 diopters of sphere (DS) and astigmatism ≤ 1.00 diopters of cylinder (DC) were prospectively allocated OK or SV correction. Measurements of axial length (Zeiss IOLMaster), corneal topography, and cycloplegic refraction were taken at 6-month intervals.

RESULTS. Thirty-one children were fitted with OK and 30 with SV. Following 24 months, axial length increased significantly over time for both the OK group (0.47 mm) and SV group (0.69 mm; $P < 0.001$), with a significant interaction between time and group ($P = 0.05$) reflecting a greater increase in the SV group. Significant differences in refraction were found over time, between groups and for the interaction between time and group for spherical (all $P < 0.001$) but not cylindrical components of refraction (all $P > 0.05$). Significantly greater corneal flattening was evident in the OK group for the flatter and steeper corneal powers and for corneal shape factor (all $P \leq 0.05$).

CONCLUSIONS. Orthokeratology contact lens wear reduces axial elongation in comparison to distance single-vision spectacles in children. (*Invest Ophthalmol Vis Sci.* 2012;53:5060-5065) DOI:10.1167/iovs.11-8005

The prevalence of myopia in young adolescents has increased substantially in recent decades and has approached 10 to 25% and 60 to 80% in industrialized societies of the West and East Asia, respectively.^{1,2} Furthermore, high levels of myopia (i.e., ≤ -6.00 diopters [D]) are associated with a range of ocular pathologies, such as vitreous and retinal detachment, macular degeneration, and glaucoma.³⁻⁶ Therefore, myopia can incur significant ocular-related morbidity and substantial healthcare costs.^{7,8}

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Several treatment therapies have been used in the past with limited success to eliminate or, at least, reduce myopia progression.⁹⁻¹¹ Spectacle intervention does not appear to significantly affect the progression of human myopia.¹² Bifocal and progressive addition spectacle lens wear have shown very modest treatment effects in controlling myopia progression,¹³⁻¹⁷ although the effect is enhanced in children with larger accommodative lags in conjunction with near esophoria, short reading distances, and low baseline myopia.¹⁸ A recent study has compared the effect of progressive addition lenses and single-vision lenses on myopia progression in children with high accommodative lag and near esophoria.¹⁹ Whereas progressive addition lenses produced a slowing of progression that reached statistical significance, the effect was not considered to be clinically significant.¹⁹

Although it has been reported that soft single-vision spherical contact lenses do not affect the progression of myopia in children and young adolescents,^{20,21} a recent study has shown that dual-focus concentric, bifocal soft contact lenses can significantly reduce progression in children in comparison to soft single-vision paired-eye control lenses.²² The dual-focus lenses had a central zone that corrected refractive error and concentric treatment zones that created 2.00 D of simultaneous myopic retinal defocus during distance and near viewing. The basis for the reduced progression was considered to be the presence of sustained peripheral myopic defocus. This principle was further examined in a later study by Sankaridurg et al.²³; the study used a soft contact lens designed to reduce relative peripheral hyperopic defocus and demonstrated a significant (34%) reduction in myopia progression over a 1-year period in children in comparison to results with spherocylindrical spectacle lenses.

There have been reports over several decades that gas-permeable contact lenses can slow myopia progression in children.²⁴⁻²⁸ However, most of these studies have limitations in study design.²⁹ A well-conducted study showed that the control of myopia progression with gas-permeable contact lenses is attributable to the temporary reduction in myopia induced by corneal flattening.³⁰ At beginning of this decade, a retrospective study³¹ and a case report³² suggested that modern orthokeratology³³ has the potential to reduce myopia progression in children. These reports were followed by three prospective studies that assessed the effect of orthokeratology contact lens wear on myopia progression in children.³⁴⁻³⁶

Over a 2-year period, Cho et al.³⁴ assessed axial length changes in 35 Hong-Kong Chinese children 7 to 12 years of age fitted with orthokeratology lenses and compared the rate of change in axial length with a well-matched historical control group of 35 children wearing single-vision spectacles. At the end of 24 months, axial length increased 0.25 mm more in the spectacle lens group compared with the orthokeratology group.

A later study undertaken in the United States by Walline and coworkers³⁵ compared the growth of the eye in myopic

children 8 to 11 years of age wearing orthokeratology contact lenses to that of an historical control group wearing soft contact lenses. Over the 2-year period, the axial length of the soft contact lens group increased 0.32 mm more than that of the orthokeratology group.

More recently, Kakita et al. compared axial length growth in myopic children 8 to 16 years of age wearing orthokeratology contact lenses and single-vision spectacles.³⁶ After 2 years of follow-up, axial length increased 0.22 mm more in the spectacle lens group than in the orthokeratology group. The study involved children significantly older (i.e., 8–16 years) and with significantly higher refractive errors (i.e., -0.50 to -10.00 D) than previous studies (i.e., 7–12 years and -0.25 to -4.50 D, respectively).^{34,35} Childhood myopia has been shown to progress faster between 6 to 13 years of age and to stabilize thereafter.^{37–39} Furthermore, it appears that a proportion of subjects used in the Kakita et al. study may not have been optimally corrected as the manufacturer's recommended refraction limit for the orthokeratology lenses used is -5.00 D.³⁶

The above three studies differ in methodology and design. Cho et al.³⁴ and Walline et al.³⁵ did not recruit prospective control groups and, in both studies, different A-scan ultrasonography biometers were used to measure axial length in the prospective and historical control groups. In contrast, Kakita et al. used partial coherence interferometry (the Zeiss IOLMaster) to take noncontact measures of axial length with a dioptric resolution of 0.03 D (an order of magnitude better than 10 Hz ultrasound).⁴⁰

Cho et al.³⁴ and Kakita et al.³⁶ recruited Chinese and Japanese subjects, respectively, whereas the Walline et al. study took place in the United States and 86% of the subjects who completed the study were classified as white.³⁵ Since the baseline level and progression of myopia in East Asian children are generally significantly greater than those for children from Western countries,^{1,2} account needs to be taken of differences in ethnicities between studies. In addition, differences in contact lens-induced responses in the corneas of Asian and non-Asian subjects have also been previously observed.⁴¹

The purpose of the study (designated the Myopia Control with Orthokeratology Contact Lenses in Spain [MCOS] study) is to compare, as the primary outcome, differences in growth of axial length over a 2-year period for white European children with myopia wearing orthokeratology contact lenses (OK) and distance single-vision spectacles (SV).

METHODS

Methods have been described in detail elsewhere.⁴² In brief, normal, healthy white European subjects 6 to 12 years of age with moderate levels of myopia (-0.75 to -4.00 diopters of sphere [DS]) and astigmatism (≤ 1.00 diopters of cylinder [DC]) and free of systemic or ocular disease were recruited and prospectively allocated to OK or SV wear. The method of treatment allocation used was similar to that of Kakita et al.³⁶ Following an unbiased account of the advantages and disadvantages of OK and SV modes of vision correction, parent(s) or guardian(s) chose one of the two treatment modalities available. Spectacles or contact lenses, contact lens care solutions (for the OK group only), and full ocular examinations were provided free of charge to all subjects throughout the study. Full informed consent and child assent were 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 any time. 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.

At the recruitment session, all subjects underwent a full anterior eye biomicroscopy, indirect fundus microscopy, binocular vision, and refractive evaluation to determine whether they were eligible to participate in the study. Baseline study measurements of cycloplegic autorefractometry, axial length, and corneal topography were subsequently recorded for eligible subjects (see below for full details of measurement procedures).

Subjects in the SV group were prescribed for constant wear distance single-vision spectacles having the highest positive/least negative power consistent with optimum visual acuity.

Subjects in the OK group were fitted with Menicon Z Night contact lenses using Menicon Professional Easy Fit Software (Menicon Co., Ltd., Nagoya, Japan). Contact lenses were ordered following fitting, and an appointment for dispensing was arranged approximately 2 weeks later for the purpose of instruction in procedures for insertion, removal, and cleaning/disinfection. Subjective overrefraction with the contact lens in situ was undertaken to assess whether changes in the back surface design of the contact lens were required; the base curve of the lens was flattened or steepened by 0.05 mm for every 0.25 D of residual myopia or hypermetropia, respectively. An appointment was scheduled for the following morning, and subjects were asked not to remove their lenses on the morning of their appointment, to allow adequate lens removal to be verified. At all subsequent visits, subjects were instructed to attend no later than 2 hours after lens removal in order to assess subjective refraction and visual acuity without the lens on the eye. Following the first 3 weeks of lens wear, any residual refraction accompanied with a bull's eye corneal topography pattern was remedied by altering the base curve of the lens. An incorrect corneal topography pattern (i.e., decentered and central island patterns) was remedied by changing the contact lens specifications (i.e., base curve, reverse curve, and/or landing zone). Changes in lens parameters were made as many times as needed and at any follow-up visits, until a clinically acceptable fit was achieved. Subjects were provided with MeniCare Plus multipurpose solution for the daily cleaning, rinsing, and disinfecting of contact lenses and Menicon Progent intensive cleaner for use once a week (Menicon Co., Ltd., Nagoya, Japan).

After delivery of the lenses, subjects were followed up at 1-, 6-, 12-, 18-, and 24-month intervals. 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 refraction⁴³ at any of the follow-up visits was considered clinically significant and was remedied by supplying new contact lenses or spectacles.

Cycloplegic autorefractometry was performed following the instillation in both eyes of three drops of cyclopentolate hydrochloride 1% (multidose preparation, Alcon Cusí, Masnou, Barcelona, Spain), each separated by 10 minutes. Ten minutes later, three autorefractometry measurements were taken (Topcon RM 8000B, Tokyo, Japan) and a mean refraction obtained.

Measurements of axial length were taken with the Zeiss IOLMaster (Carl Zeiss Jena GmbH, Jena, Germany).⁴⁰ Three separate measurements of axial length were recorded and a mean obtained.

Corneal topography measurements were performed with the Wavelight Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The first measurement taken on each eye (which provided an optimum index value according to the manufacturer's recommendations) was used for the study. The measurement generates a simulated central keratometry reading and the rate of peripheral corneal flattening/steepening that occurs with displacement from the corneal apex; the latter indicates the degree to which an aspheric surface differs from the spherical form (i.e., the *P* value).⁴⁴ The *P* value was calculated over a 7-mm chord in accord with the default setting of the instrument.

Statistical Analysis

Statistical analyses were conducted using SPSS 15.0 (SPSS, Inc., Chicago, IL). The level of statistical significance was taken as 5%. Data for the right eye only were used. Differences in subjects' demographics

TABLE 1. Baseline Demographics and Refractive and Biometric Data for Both Treatment Groups

	OK	SV	<i>P</i> Value
Age (y)	9.6 ± 1.6	9.9 ± 1.9	0.76
M/F ratio	15/16	15/15	0.55
Sphere (D)	-2.15 ± 1.12	-2.08 ± 1.23	0.79
Cylinder (mm)	-0.28 ± 0.29	-0.31 ± 0.33	0.96
Axial length (mm)	24.40 ± 0.81	24.22 ± 0.91	0.40
Flatter meridian (D)	42.97 ± 1.65	43.41 ± 1.56	0.36
Steeper meridian (D)	43.69 ± 1.46	44.01 ± 1.77	0.50
Corneal shape factor (<i>P</i> value)	0.69 ± 0.10	0.72 ± 0.08	0.16

Variables are expressed as mean ± 1 SD. M/F, male/female.

and baseline data between groups were tested using unpaired sample *t*-tests for all variables, except for the male/female ratio, which was tested using a χ^2 test. Actual differences in refractive and biometric data between groups and the variation in differences over time were tabulated (Table 2) and tested using repeated measures ANOVA for those subjects who completed the study. Type of refractive correction (i.e., OK versus SV) was designated the factor of interest and time the repeated measure. A repeated measures ANOVA was also used to test differences in axial length relative to baseline between groups and for 6-, 12-, 18-, and 24-month time intervals (Table 3 and Fig. 1). Equality of variances and sphericity were tested using the Levene and Mauchly tests, respectively, to select appropriate *P* values. Standard contrasts available in the SPSS software were used to test the linearity and significance of the interaction between refractive correction and time for selected combinations of time intervals. Data are expressed as mean ± 1 SD.

RESULTS

Sixty-one subjects were recruited for the study between March 2007 and March 2008. Thirty-one children were prospectively allocated to OK and 30 to SV. No statistically significant differences were found in any of the baseline demographics and refractive and biometric data between groups (Table 1).⁴²

Two and six children from the OK and SV groups, respectively, discontinued the study. In the OK group, one

child discontinued the study at 6 months and another child at the 18-month follow-up visit. In the SV group, three children discontinued the study at the 6-month follow-up visit, two at the 18-month, and one at the 24-month follow-up visit.

The effect of refractive correction and time on the spherical component of refraction were found to be significant ($P < 0.001$) together with their interaction ($P < 0.001$), the latter reflecting a greater increase in negative spherical error over time in the SV group compared to the OK group (Table 2). In contrast, the effect of refractive correction and time on the cylindrical component, as well as their interaction, were not found to be statistically significant ($P > 0.05$).

The effect of time on actual axial length was found to be significant ($P < 0.001$), but the effect of refractive correction on axial length was insignificant ($P = 0.22$). However, the interaction between refractive correction and time was significant ($P = 0.05$), the latter reflecting a greater increase in length over time in the SV group compared to the OK group (Table 2). Of particular interest was the change in axial length relative to baseline (Fig. 1 and Table 3), and the effects of refractive correction ($P = 0.005$), time ($P < 0.001$), and their interaction ($P = 0.030$) were found to be significant. Standard contrasts indicated the interaction between refractive correction and time to be linear ($P = 0.027$) and significance levels for 6- versus 24-months, 12- versus 24-months and 18- versus 24-months to be $P = 0.027$, $P = 0.043$ and $P = 0.127$ respectively (Fig. 1).

TABLE 2. Mean (±SD) Refractive and Biometric Values for the Orthokeratology and Single-Vision Spectacle Groups Who Completed the Study at Each Time Interval

	Baseline	6 Months	12 Months	18 Months	24 Months
Refractive components					
Sphere (D)					
OK	-2.20 ± 1.09	-0.19 ± 0.23	-0.22 ± 0.27	-0.21 ± 0.27	-0.34 ± 0.29
SV	-2.35 ± 1.17	-2.58 ± 1.24	-2.97 ± 1.24	-3.26 ± 1.28	-3.60 ± 1.38
Cylinder (D)					
OK	-0.29 ± 0.29	-0.31 ± 0.29	-0.33 ± 0.33	-0.30 ± 0.31	-0.24 ± 0.37
SV	-0.35 ± 0.34	-0.30 ± 0.33	-0.32 ± 0.33	-0.32 ± 0.40	-0.38 ± 0.35
Biometric components					
Axial length (mm)					
OK	24.49 ± 0.78	24.61 ± 0.79	24.71 ± 0.81	24.91 ± 0.79	24.96 ± 0.86
SV	24.26 ± 1.01	24.44 ± 1.01	24.63 ± 1.02	24.79 ± 0.98	24.95 ± 0.99
Flatter corneal meridian power (D)					
OK	42.89 ± 1.66	41.11 ± 1.62	41.11 ± 1.63	40.81 ± 1.51	41.14 ± 1.82
SV	43.35 ± 1.59	43.37 ± 1.58	43.35 ± 1.56	43.31 ± 1.54	43.33 ± 1.61
Steeper corneal meridian power (D)					
OK	43.60 ± 1.47	41.99 ± 1.67	41.92 ± 1.62	41.77 ± 1.52	41.99 ± 1.74
SV	43.96 ± 1.87	44.15 ± 1.76	44.20 ± 1.73	44.30 ± 1.77	44.17 ± 1.93
Corneal shape factor (<i>P</i> value)					
OK	0.68 ± 0.10	0.84 ± 0.16	0.84 ± 0.17	0.82 ± 0.17	0.82 ± 0.19
SV	0.72 ± 0.09	0.72 ± 0.09	0.73 ± 0.08	0.73 ± 0.09	0.75 ± 0.06

TABLE 3. Differences in Growth in Axial Length with Time Compared to Baseline for Orthokeratology and Control Groups (mm)

Study	Intervention	6 Months	12 Months	18 Months	24 Months
Cho et al. ³⁹	OK vs. SV	0.21	0.18	0.28	0.25
Walline et al. ⁴⁰	OK vs. SCL	...	0.15	...	0.32
Kakita et al. ⁴¹	OK vs. SV	0.22
MCOS	OK vs. SV	0.06	0.15	0.11	0.22

OK, orthokeratology; SV, single-vision spectacles; SCL, soft contact lenses.

The effects of refractive correction and time on corneal power were found to be significant (for both flatter and steeper meridians, $P < 0.001$), together with their interactions ($P < 0.001$) (Table 2).

The effects of refractive correction ($P = 0.05$) and time ($P = 0.003$) on corneal shape were found to be significant, but their interaction was not significant ($P = 0.13$) (Table 2).

DISCUSSION

The introduction of reverse geometry contact lens designs, highly oxygen-permeable lens materials, and accurate clinical instrumentation for the measurement of corneal topography has made orthokeratology an effective and highly predictable procedure for the temporary reduction of up to -6.00 D of myopia.³³ It was not until the beginning of last decade, however, that data emerged suggesting that OK contact lens wear could reduce myopia progression in children.^{31,32} The earliest OK studies to show this effect were followed by others that, together with the MCOS study, consistently reported reduced axial elongation with OK lens wear compared to spectacle and soft contact lens wear in children.³⁴⁻³⁶

Significant differences in the spherical but not the cylindrical component of refraction were found over time, between groups and for the interaction between time and group. The differences were primarily attributed to the corneal reshaping effect induced by OK contact lens wear and the resultant change in corneal power and shape.^{33,45,46} In agreement with results of previous studies,³⁷⁻³⁹ the SV group showed an increase in myopia of over 1 D accompanied by negligible changes in corneal power and shape.

The difference in axial length growth found between the OK and SV groups is reasonably consistent with previously

reported studies (see Table 3), despite the fact that the variation in ethnicity and age between studies is likely to affect the rates of myopia progression.³⁴⁻³⁶ Recent work has shown that East Asians with moderate levels of myopia have a greater degree of relative peripheral hyperopia and, hence, a relatively more prolate ocular shape than do Caucasian subjects with similar central refractive error.⁴⁷ It has been proposed that the differences in retinal shape are the basis for a greater propensity for East Asians to develop myopia and progress in myopia compared to Caucasians.^{47,48}

Several studies have shown that chronic exposure to lens-induced hyperopic defocus accelerates the axial length growth of the eye in a predictable manner in various species, suggesting that foveal defocus influences eye growth.⁴⁹⁻⁵³ However, later investigations on the effect of hyperopic defocus on ocular growth have highlighted the importance of peripheral image formation in the etiology and progression of myopia. Specifically, peripheral hyperopic defocus has been suggested to play a significant role in the development of refractive error.^{54,55} It has been reported that myopes have greater relative peripheral hyperopia than emmetropes and hyperopes, at least in the lateral visual field, because of their relatively less oblate ocular shape.^{47,48,56} Two recent investigations have specifically assessed the effect of peripheral refraction on development of central refractive error. Measuring peripheral refraction at a single point 30° in the nasal visual field with A-scan ultrasonography, Mutti et al. did not find peripheral hyperopia to exert a significant influence on the risk of onset of myopia, its rate of progression, or on axial elongation.⁵⁷ However, Schmid reports steeper retinas to be associated with greater myopic shifts, supporting the hypothesis that eye shape at the posterior pole is one of the factors influencing visually guided axial eye growth, possibly through associated peripheral defocus.⁵⁸

Recent work also shows that OK contact lens wear reduces peripheral hyperopic defocus⁵⁹ compared with SV, which increases peripheral hyperopic defocus,⁶⁰ and gas-permeable contact lens wear, which has no effect in peripheral refraction.⁶¹ It is, therefore, hypothesized that the reduction in relative peripheral hyperopic defocus with OK contact lens wear underlies the reduction in axial elongation with this treatment.

A limitation of our MCOS study was that subjects were not randomly allocated to treatment groups. However, recently published studies have also employed nonrandom allocation.^{36,62} Future studies should consider randomization to allocate subjects to treatment groups.

In summary, the present study (and that of Kakita et al.³⁶) did not randomly allocate subjects to treatment groups; but, despite this limitation, the MCOS data provide further evidence that, compared with SV, OK contact lens wear is an effective method of controlling myopia progression in children. Clinical issues that will need to be addressed in future work are: identification of children in whom orthokeratology is likely to be most effective; the treatment durations that will optimize reduction in progression of myopia; and the effect of

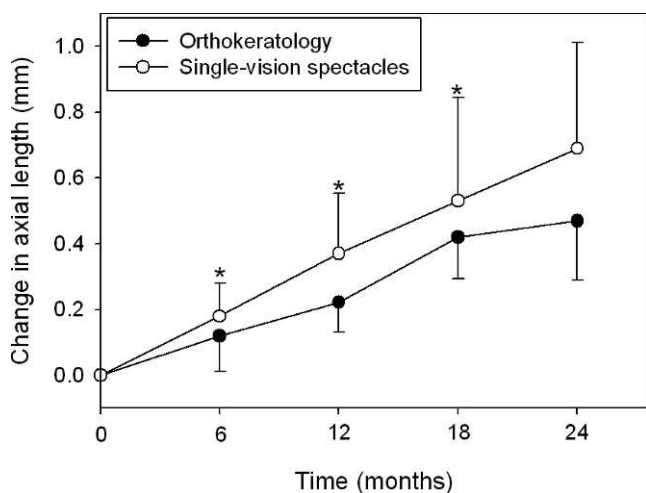


FIGURE 1. Changes (mean \pm SD) in axial length (mm) from baseline over time. Asterisk indicates statistically significant interactions between refractive correction and time at 6-, 12-, and 18- vs. 24-months (all $P < 0.05$).

discontinuation of long-term lens wear on subsequent progression of myopia.

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Short- and Long-Term Changes in Corneal Aberrations and Axial Length Induced by Orthokeratology in Children Are Not Correlated

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Purpose: To assess the correlation between changes in corneal aberrations and the 2-year change in axial length in children fitted with orthokeratology (OK) contact lenses.

Methods: Thirty-one subjects 6 to 12 years of age and with myopia -0.75 to -4.00 DS and astigmatism ≤ 1.00 DC were fitted with OK. Measurements of axial length and corneal topography were taken at regular intervals over a 2-year period. Corneal topography at baseline and after 3 and 24 months of OK lens wear was used to derive higher-order corneal aberrations (HOA) that were correlated with OK-induced axial length changes at 2 years.

Results: Significant changes in C_3^{-1} , C_4^0 , C_4^4 , root mean square (RMS) secondary astigmatism and fourth and total HOA were found with both 3 and 24 months of OK lens wear in comparison with baseline (all $P < 0.05$). Additionally, significant changes in C_3^3 and RMS tetrafoil were found at 3 months and in second-order RMS at 24 months of OK lens wear in comparison with baseline (all $P < 0.05$). However, none of the changes in corneal aberrations were significantly correlated with the 2-year change in axial elongation (all $P > 0.05$). Coma angle of orientation changed significantly pre-OK in comparison with 3 and 24 months post-OK as well as secondary astigmatism angle of orientation pre-OK in comparison with 24 months post-OK (all $P < 0.05$). However, coma, trefoil, secondary astigmatism, and tetrafoil angles of orientation pre-OK or post-OK were not significantly correlated with the 2-year change in axial elongation (all $P > 0.05$).

Discussion: Short-term and long-term OK lens wear induces significant changes in corneal aberrations that are not significantly correlated with changes in axial elongation after 2-years.

Key Words: Cornea—Aberrations—Topography—Myopia progression—Orthokeratology—Contact lenses—Axial length.

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The prevalence of myopia has increased substantially in recent decades and has been estimated to currently affect approximately 25% of the world population.^{1–3} Myopia has become an important health concern, as it is strongly associated with different ocular pathologies, such as vitreous and retinal detachment, macular degeneration, and glaucoma.^{4–7} As a result, myopia can incur significant ocular-related morbidity and health care costs.^{8–10}

It has been suggested that higher-order aberrations may play a role in the development of refractive errors by reducing retinal image quality.¹¹ In young adults, Marcos et al.¹² observed an increase in myopia to be associated with a significant positive increase in corneal spherical aberration and a negative increase in internal spherical aberration. Llorente et al.¹³ found ocular third-order total root mean square (RMS) aberration (i.e., coma-like), ocular spherical aberration, and corneal spherical aberration to be significantly greater in young hyperopic eyes than in young myopic eyes, whereas internal spherical aberration did not differ significantly between the two groups. Philip et al.¹⁴ found no differences in ocular or corneal horizontal, vertical or RMS coma aberrations and coma-like aberrations between hyperopic, emmetropic, and myopic adolescent eyes, although ocular spherical aberration was significantly less positive in low myopic, moderate myopic, and emmetropic eyes compared with low hyperopic eyes. Philip et al.¹⁵ monitored ocular aberrations in emmetropic children over a 5-year period and found that children who became myopic underwent an increase in negative spherical aberration or a decrease in positive spherical aberration together with an increase in RMS coma and coma-like aberrations, whereas eyes that remained emmetropic showed an increase in positive spherical aberration and a decrease in vertical coma. Furthermore, third-order RMS and coma RMS at baseline were found to be greater in the group that remained emmetropic in comparison with the group that became myopic.

Orthokeratology (OK) contact lens wear has consistently shown to be effective in reducing myopia progression by 30% to 50% in comparison with conventional spectacle and soft contact lens wear in children.^{16–21} It is well established that OK induces central corneal flattening and an increase in mid-peripheral corneal thickness,²² which significantly affect corneal and ocular aberrations.^{23–27} Of special interest is a recent report by Hiraoka et al.²⁸ performed in Japanese children over a 1-year period that found changes on spherical defocus, second-order aberration, coma-like aberration, spherical-like aberration, and total higher-order aberrations to be significantly correlated with changes in axial length. This study evaluated whether changes in corneal aberrations are correlated with axial

elongation in children wearing OK with reference to data from the Myopia Control with Orthokeratology contact lenses in Spain (MCOS) study.²⁰ The MCOS study found a statistically significant difference in axial length elongation relative to baseline over a 2-year period between white European children with myopia wearing OK (N=31) and distance single-vision spectacles (N=30).²⁰

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.^{20,29-35} The methods used in MCOS have been described in detail elsewhere.^{20,29-35} 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 (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, a “bull’s eye” corneal topography pattern and monocular and binocular visual acuities within ±1 line of the best-corrected spectacle visual acuity. All patients underwent ocular examinations including slitlamp examination, manifest refraction, and corneal topography at baseline and after 1 day, 2 weeks, 3-month 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 hr of awakening. A decrease in one line of visual acuity accompanied by a change in subjective refraction at any of the follow-up visits was considered clinically significant and was remedied by supplying new contact lenses. Full informed consent and child assent was obtained from the parents/guardians before 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 slitlamp findings occur. Subjects were instructed to 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.

Measurements of axial length were taken with the Zeiss IOLMaster (Carl Zeiss Jena GmbH, Jena, Germany).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-year 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- and 24-month topographic outputs were taken as representative of the pre-OK and the short and long-term post-OK treatment status, respectively. Corneal topographies were analyzed using Oculus Keratograph software (Version 1.76; Oculus Optikgeräte GmbH, Wetzlar, Germany). Corneal aberrations of the anterior cornea were derived from anterior cornea

elevation data following previously reported methodology.^{26,34} 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 8 mm 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 American National Standards Institute.³⁸ The normalization factors were determined as follows:

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

Normalized height data were imported to an analysis software program (Zemax, Redmond, WA) to reconstruct the corneal surface for the entrance pupil, and ray tracing was performed to establish the Zernike aberration coefficients for a 5-mm entrance pupil. To calculate corneal aberrations for the entrance pupil center, the location of the cornea and tilt for the entrance pupil relative to the coaxially sighted corneal light reflex (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.²⁶ The entrance pupil was positioned at a distance of 3.60 mm from the anterior corneal surface.³⁹ A wavelength of 546 nm was used to match the wavelength used by the Wavelight Allegro Topolyzer instrument for ocular aberrations. Corneal aberrations were expressed by Zernike expansion (i.e., C_2^{-2} up to C_4^4) and the RMS of coma aberration (i.e., $\sqrt{([C_3^{-1}]^2 + [C_3^1]^2)}$), trefoil (i.e., $\sqrt{([C_3^{-3}]^2 + [C_3^3]^2)}$), secondary astigmatism (i.e., $\sqrt{([C_4^{-2}]^2 + [C_4^2]^2)}$) and tetrafoil (i.e., $\sqrt{([C_4^{-4}]^2 + [C_4^4]^2)}$), as well as RMS of the second, third (i.e., coma-like), fourth (i.e., spherical-like), and total higher-order corneal aberrations (HOA) (i.e., third to fourth order) were calculated. Additionally, the angles of orientation of coma, trefoil, secondary astigmatism, and tetrafoil vectors of the combined Zernike terms were calculated using the formula shown below as described by Kosaki et al.,⁴⁰ where n is the order of the Zernike monomial and m is the frequency of the term (i.e., coma: $n=3$ and $m=1$; trefoil: $n=3$ and $m=3$; secondary astigmatism: $n=4$ and $m=2$; and tetrafoil: $n=4$ and $m=4$).

$$\text{If } C_n^m \neq 0,$$

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

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

$$\text{If } C_n^m = 0,$$

$$\text{angle} = 90 (C_3^{-1} < 0)$$

$$\text{angle} = 270 (C_3^{-1} > 0).$$

The changes in corneal aberrations and angles of orientation (i.e., post-OK – pre-OK) at the entrance pupil were correlated with changes in axial length over 2 years.

Statistical Analysis

Differences between visits (i.e., pre-K vs. post-OK) were tested using a paired *t* test or Wilcoxon signed rank test depending on normality of data distribution. Similarly, correlations between the 2-year change in axial length and changes in corneal aberrations and the orientation of combined asymmetric aberration components were determined with the Pearson product–moment correlation or Spearman Roh tests depending on normality of data distribution. Data from right eyes only were used for analysis. Statistical analyses and graphing were performed with *Sigma Plot* (Systat software Inc., San Jose, CA). 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 because of discomfort with contact lens wear and another due to unknown reasons.³⁰ The remaining subjects engaged enthusiastically in the study and were compliant with contact lens wear for the entire duration of the study. Subjects who discontinued the study were not included in the data analysis. The subjects' demographic and baseline data have been reported elsewhere.^{20,30} At the start of the study, subjects showed a mean age of 9.6±1.6 years; 15 were men and 16 were women. Over 2 years of OK lens wear, axial length increased from 24.49±0.78 mm to 24.96±0.86 mm ($P<0.001$).²⁰

Three months of OK lens wear induced statistically significant changes in vertical coma (i.e., C_3^{-1}), oblique trefoil (i.e., C_3^3), spherical aberration (i.e., C_4^0), vertical tetrafoil (i.e., C_4^4), RMS secondary astigmatism, RMS tetrafoil, spherical-like and total HOA (Fig. 1) (all $P<0.05$). Similarly, 24 months of OK lens wear induced statistically significant changes in vertical coma (i.e., C_3^{-1}), spherical aberration (i.e., C_4^0), vertical tetrafoil (i.e., C_4^4), RMS secondary astigmatism, second-order RMS, spherical-like and total HOA

(Fig. 1) (all $P<0.05$). Of special interest is, however, that neither short-term nor long-term changes in corneal aberrations were significantly correlated with the 2-year change in axial elongation (Table 1) (all $P>0.05$).

Coma angle of orientation changed significantly pre-OK (mean axis: 194°; range: 4–295°) in comparison with 3-month (mean axis: 246°; range: 55–346°) ($P=0.006$) and 24-month post-OK (mean axis: 232°; range: 29–288°) ($P=0.014$) (Fig. 2). Trefoil angle of orientation did not change significantly pre-OK (mean axis: 61°; range: 2–109°) in comparison with 3-month (mean axis: 88°; range: 1–115°) ($P=0.383$) or 24-month post-OK (mean axis: 75°; range: 6–116°) ($P=0.645$) (Fig. 3). Secondary astigmatism angle of orientation did not change significantly pre-OK (mean axis: 156°; range: 4–176°) in comparison with 3-month post-OK (mean axis: 112°; range: 14–175°) ($P=0.259$), but a statistically significant change was found pre-OK in comparison with 24-months post-OK (mean axis: 139°; range: 20–170°) ($P=0.009$) (Fig. 4). Tetrafoil angle of orientation did not change significantly pre-OK (mean axis: 7°; range: 1–89°) in comparison with 3-month (mean axis: 1°; range: 1–90°) ($P=0.248$) or 24-month post-OK (mean axis: 20°; range: 5–82°) ($P=0.290$) (Fig. 5). Coma, trefoil, secondary astigmatism, and tetrafoil angles of orientation pre-OK or post-OK were not significantly correlated with the 2-year change in axial elongation (all $P>0.05$).

DISCUSSION

Short-term and long-term OK lens wear induced significant changes in vertical coma, spherical aberration, vertical tetrafoil, RMS secondary astigmatism, and fourth and total HOA RMS. Additionally, significant changes in oblique trefoil and RMS tetrafoil at 3 months and in second-order RMS at 24 months of OK lens wear were found in comparison with baseline (Fig. 1). However, neither short-term nor long-term changes in corneal aberrations were significantly correlated with the 2-year change in axial elongation.

Philip et al.¹⁵ reported that children who remain emmetropic showed an increase in ocular positive spherical aberration and a decrease in vertical coma. This finding is consistent with the

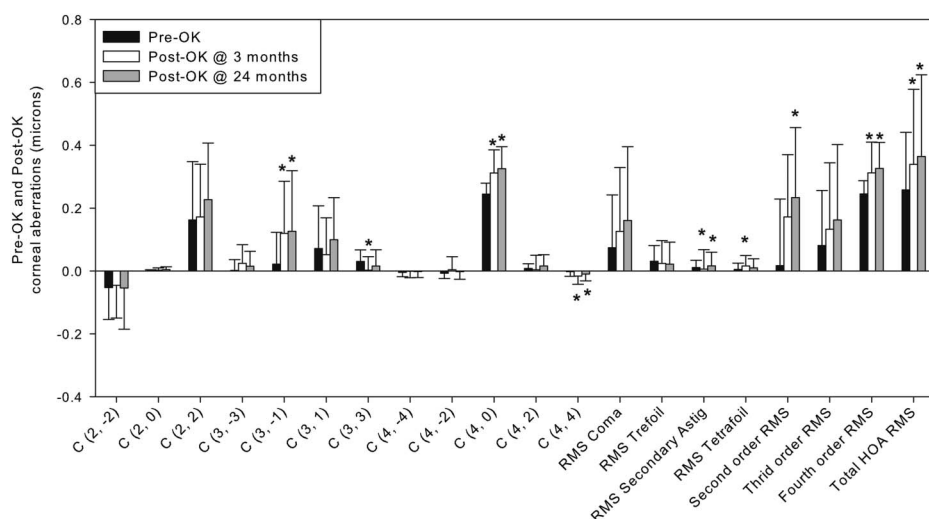


FIG. 1. Pre-OK (black bars) and 3-month (white bars) and 24-month (gray bars) post-OK lens wear corneal aberrations. *Statistically significant differences pre-OK in comparison with post-OK at $P<0.05$. Astig, astigmatism; HOA, higher-order aberrations; OK, orthokeratology; RMS, root mean square. Error bars represent one standard deviation of the mean.

TABLE 1. Statistical Results (i.e., *r* and *P* values) for the Simple Correlations Between the 2-Year Changes in Axial Elongation and the 3- and 24-Month Changes in Corneal Aberrations Following Orthokeratology Lens Wear

Zernike Coefficients	At 3 Months		At 24 Months	
	Correlation Coefficient (<i>r</i>)	<i>P</i>	Correlation Coefficient (<i>r</i>)	<i>P</i>
C (2, -2)	-0.019	0.925	-0.235	0.226
C (2, 0)	0.133	0.499	0.112	0.566
C (2, 2)	0.046	0.817	0.139	0.477
C (3, -3)	0.130	0.511	0.022	0.910
C (3, -1)	0.180	0.359	0.067	0.731
C (3, 1)	-0.293	0.131	-0.147	0.451
C (3, 3)	-0.045	0.821	-0.126	0.518
C (4, -4)	-0.085	0.667	-0.340	0.076
C (4, -2)	0.073	0.711	-0.099	0.615
C (4, 0)	0.188	0.338	0.150	0.443
C (4, 2)	0.030	0.881	0.082	0.675
C (4, 4)	-0.182	0.354	-0.273	0.159
RMS coma	0.309	0.110	0.151	0.438
RMS trefoil	0.046	0.817	0.225	0.247
RMS tetrafoil	0.061	0.758	-0.078	0.689
RMS secondary astigmatism	0.018	0.929	0.066	0.737
Second-order RMS	0.211	0.281	0.058	0.767
Third-order RMS	0.302	0.118	0.194	0.320
Fourth-order RMS	0.102	0.607	0.156	0.424
Total HOA RMS	0.316	0.102	0.215	0.269

HOA, higher-order aberrations; RMS, root mean square.

present study as an increase in corneal positive spherical aberration with OK lens wear was observed that might partly account for the significant reduction in axial elongation found over the 2 years of follow-up; albeit the increase in corneal positive spherical aberration was not significantly correlated with the 2-year change in

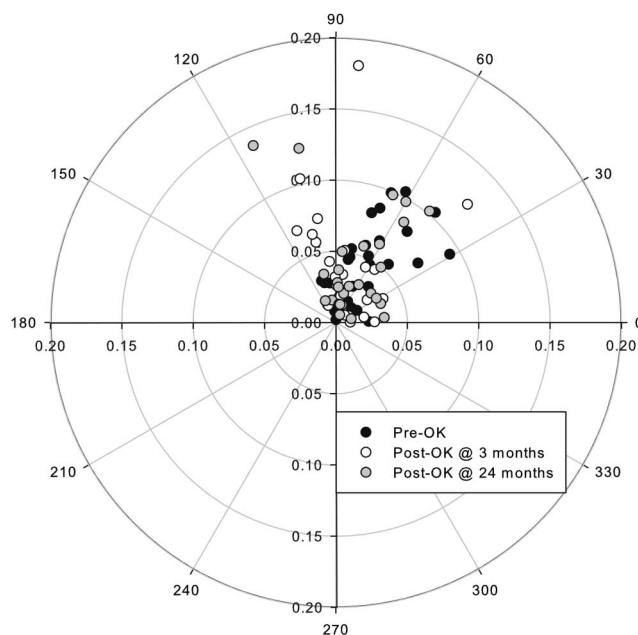


FIG. 3. Magnitude (i.e., $\sqrt{[C_3^{-3}]^2 + [C_3^3]^2}$ in μm) and orientation (i.e., angle in degrees) of the combined vertical and oblique trefoil components (i.e., C_3^{-3} and C_3^3) pre-OK (black circles) and 3-month (white circles) and 24-month (gray circles) post-OK lens wear. OK, orthokeratology.

axial elongation. In contrast to the study of Hiraoka et al.,²⁸ the present study could not demonstrate significant associations between the 3 and 24 months induced change in any of the corneal aberration components examined and the 2-year change in axial

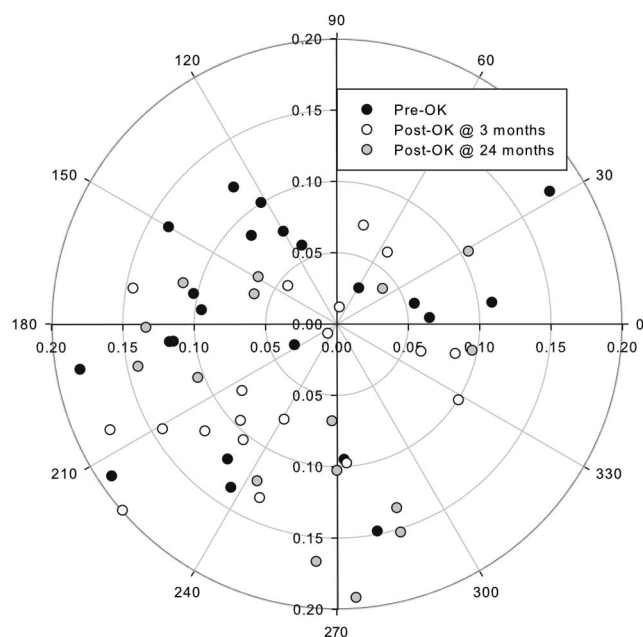


FIG. 2. Magnitude (i.e., $\sqrt{[C_3^{-3}]^2 + [C_3^3]^2}$ in μm) and orientation (i.e., angle in degrees) of the combined horizontal and vertical coma components (i.e., C_3^{-3} and C_3^3) pre-OK (black circles) and 3-month (white circles) and 24-month (gray circles) post-OK lens wear. OK, orthokeratology.

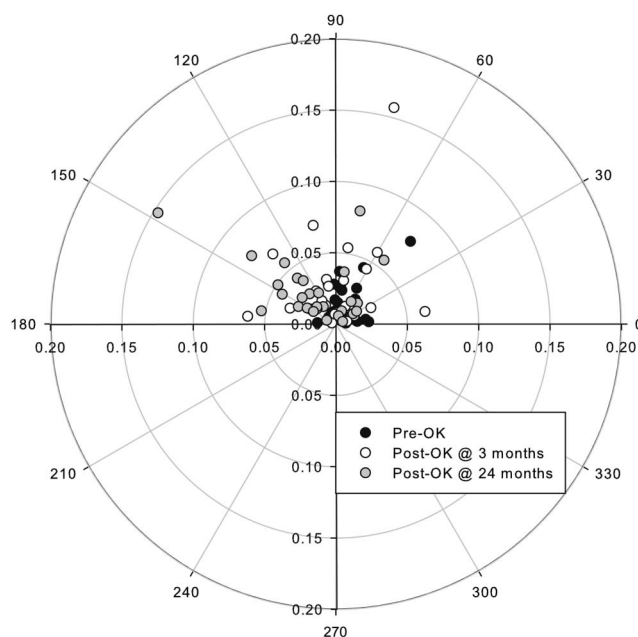


FIG. 4. Magnitude (i.e., $\sqrt{[C_4^{-2}]^2 + [C_4^2]^2}$ in μm) and orientation (i.e., angle in degrees) of the combined oblique and vertical secondary astigmatic components (i.e., C_4^{-2} and C_4^2) pre-OK (black circles) and 3- (white circles) and 24-month (gray circles) post-OK lens wear. OK, orthokeratology.

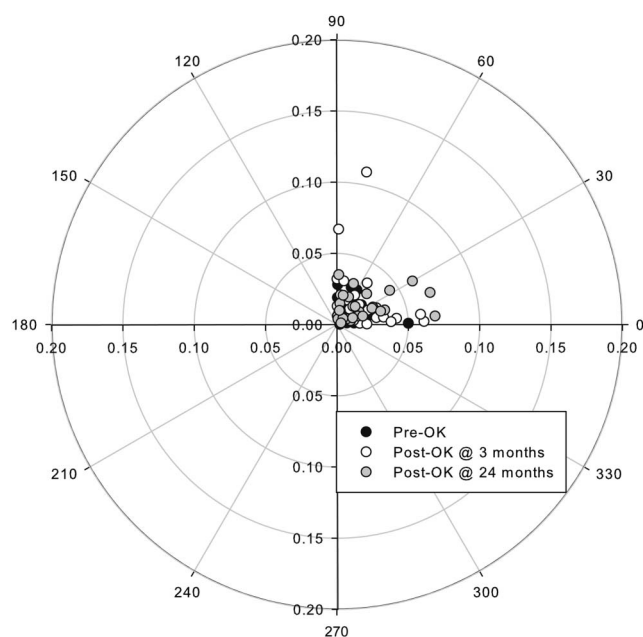


FIG. 5. Magnitude (i.e., $\sqrt{[C_4^{-4}]^2 + [C_4^4]^2}$ in μm) and orientation (i.e., angle in degrees) of the combined oblique and vertical tetrafoil components (i.e., C_4^{-4} and C_4^4) pre-OK (black circles) and 3-month (white circles) and 24-month (gray circles) post-OK lens wear. OK, orthokeratology.

elongation following OK lens wear. Our data are consistent with those reported by Hiraoka et al. in that coma-like, spherical-like, and total HOA increased with OK lens wear, although the increase in coma-like aberration was not statistically significant. It should be noted, however, that differences between the Hiraoka et al. study and this study might account for the discrepancy in the results of the correlations between changes in aberrations and changes in axial length found between the two studies. Hiraoka et al. opted to analyze ocular aberrations in Japanese subjects using one particular OK lens design (i.e., α Ortho-K; Alpha Corp., Nagoya, Japan), whereas in our study we measured only corneal aberrations in white European subjects using a different lens design (i.e., Menicon Z Night; Menicon Co., Ltd). In the present study, the effect of orientation of combined asymmetric corneal aberration components on axial elongation was also assessed. However, coma, trefoil, secondary astigmatism, and tetrafoil angles of orientation pre-OK or post-OK were not significantly correlated with the 2-year change in axial elongation.

A limitation of this study was that anterior corneal rather than total ocular aberrations were measured. However, corneal changes induced by OK lens wear are limited to the anterior cornea.²² Anterior corneal aberration components have been reported to be generally higher than the overall ocular aberrations but balanced to a considerable degree by internal ocular aberrations.⁴¹ 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,²⁶ a more recent study found almost identical anterior corneal and ocular aberrations at baseline and after 1 year of OK lens wear.²⁸

In summary, short-term and long-term OK lens wear induced significant changes in corneal aberrations measured at the entrance

pupil that are not significantly correlated with the 2-year change in axial length. Furthermore, as far as we are aware, this is the first study to report the lack of a significant correlation between the orientation of the combined asymmetric aberration components and change in axial elongation induced by OK. Nevertheless, OK has consistently shown to be effective in reducing myopia progression across different ethnic groups.¹⁶⁻²¹ However, further research should be undertaken to understand the etiological basis for the efficacy of OK in the control of myopia progression. We envisage that the findings of this study will contribute to the debate on the uncertainty concerning the role of changes in corneal aberrations induced by OK in the etiology of human myopia.²⁸

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Short-Term and Long-Term Changes in Corneal Power Are Not Correlated With Axial Elongation of the Eye Induced by Orthokeratology in Children

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Purpose: To assess the relationship between short-term 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 to 12 years of age and with myopia -0.75 to -4.00 DS and astigmatism ≤ 1.00 DC were fitted with OK. Differences in refractive power 3 and 24 months post-OK in comparison with baseline and relative to the change in central corneal power were determined from corneal topography data in eight 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 two years relative to baseline.

Results: After 2 years of OK lens wear, axial length increased by 0.48 ± 0.18 mm ($P < 0.001$), which corresponded to an increase of $1.94 \pm 0.74\%$ ($[2\text{-years change in axial length}/\text{baseline axial length}] \times 100$). However, the change in axial elongation in comparison with 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.

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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 to significantly 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% to 25% in industrialized societies of the West and epidemic levels of 60% to 80% in East Asia.^{4–6} Of particular concern is that there appears to have been a commensurate increase in high myopia (i.e., ≤ -6.00 D)^{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 eye³ 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 with 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 discontinuations²⁶ 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 after 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 after 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 wear⁴⁴ 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

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Recently, Zhong et al. evaluated whether corneal power changes induced by a proprietary OK lens design (i.e., Hiline Optics, Macro Vision, Taipei, Taiwan, 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, Nagoya, 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 post-OK to pre-OK changes in peripheral corneal sagittal refractive powers (relative to the central apical power) and the two-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 study of Zhong et al.⁴⁸, however, sagittal corneal power changes pre-OK and post-OK were measured manually and hence susceptible to human error. 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 post-OK in comparison to pre-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 after OK lens wear rather than assessing the change in corneal power at isolated corneal points (Fig. 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 after OK lens wear in comparison with no lens wear.

The present study examines the correlation between changes in axial length and short-term (three 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). Myopia Control with Orthokeratology contact lenses in Spain evaluated, as the primary outcome measure, differences in growth of axial length over a two-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 thirty 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 \pm standard deviation, 0.47 ± 0.18 mm) and distance single-vision spectacles (0.69 ± 0.32 mm) 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 -4.00 D) and astigmatism (≤ 1.00 D) 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 slitlamp examination, manifest refraction, and corneal topography at baseline and then followed up 1 day, 2 weeks, 3 months, and 6-month intervals over a two-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 hr of awakening. A decrease in one line of visual acuity accompanied by a change in subjective refraction at any of the follow-up visits⁵⁸ was considered clinically significant and was remedied by supplying new contact lenses. Fully informed consent and child assent were obtained from the parents/guardians before 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 slitlamp 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 after 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, Tokyo, Japan).

Measurements of axial length were taken with the Zeiss *IOL-Master* (Carl Zeiss Jena GmbH). Three separate measurements of axial length were recorded and a mean obtained.⁵⁹ The two-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 ($[2\text{-years change in axial length}/\text{baseline axial length}] \times 100$).

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 that detects 22,000 elevated data points of measurement evenly distributed from 22 ring edges with accuracy and reproducibility of ± 0.10 D 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 months and 24 months topographic outputs were taken as representative of the preterm, short-term, and long-term post-OK treatment status, respectively.²⁸ Corneal topography was analyzed using Oculus Keratograph software (version 1.76, Oculus Optikgeräte GmbH, Wetzlar, Germany). Differences in refractive power between baseline and 3 months and 24 months were quantified using the "refractive compare" display map provided by the

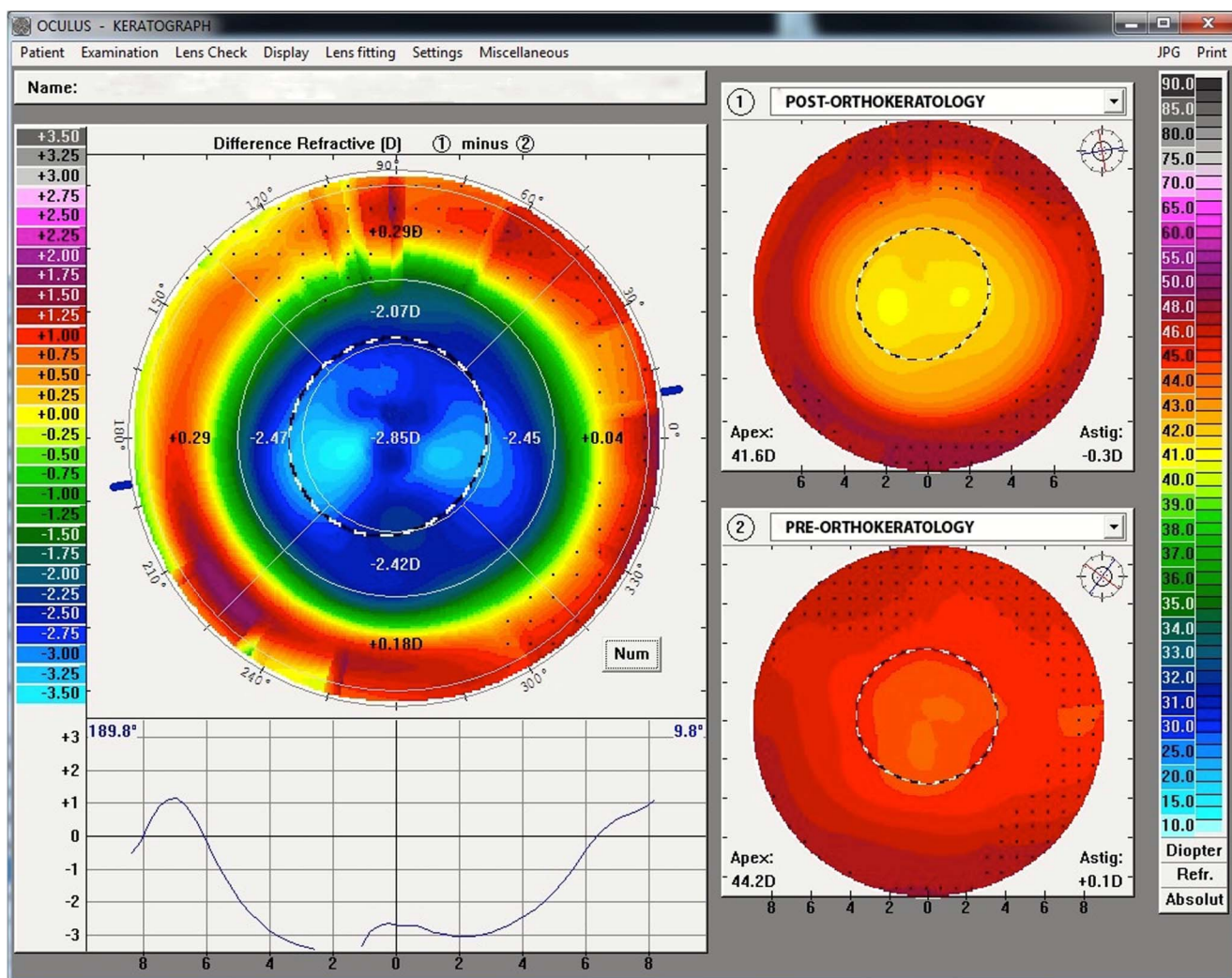


FIG. 1. Refractive compare map of the Oculus Keratograph software displaying the post-OK to pre-OK change in corneal refractive power up to a 8-mm diameter ring for the right eye of an individual subject. The map on the top right shows data of post-OK lens wear, the one on the bottom right shows data of 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.

instrument software. The map displays average values of change in corneal power for four different quadrants (nasal, temporal, inferior, and superior) and between the paracentral (i.e., 3 to 5 mm ring diameters) and pericentral cornea (i.e., 5 to 8 mm ring diameters). The map thus generates for analysis eight discrete corneal regions N1, N2, T1, T2, I1, I2, S1, S2 and a single central corneal area, C (Figs. 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., $[N1_{\text{post-OK}} - N1_{\text{pre-OK}}] - [C_{\text{post-OK}} - C_{\text{pre-OK}}]$). Additionally, central and total multifocality were also calculated. Central multifocality was defined as the greatest difference in corneal power after subtraction of the change in central corneal power

from the change in corneal power at any of the seven 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 seven different corneal regions assessed relative to the change in central corneal power.

Statistical Analysis

A one-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

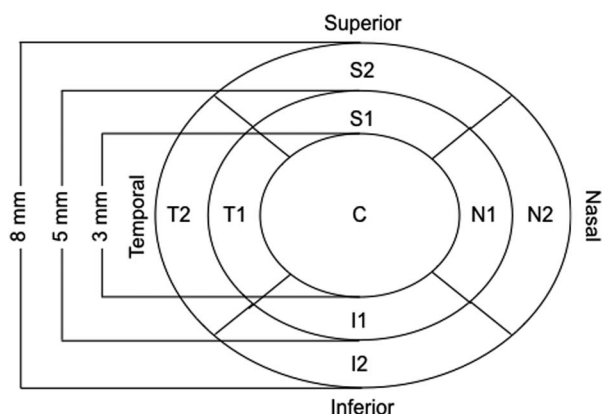


FIG. 2. Areas of corneal power change (i.e., post-OK-pre-OK) for the right eye. The regions located between the 3-mm and 5-mm diameter rings are referred to as “paracentral” corneal regions (i.e., N1, T1, I1, S1), whereas the regions located between the 5-mm and 8-mm diameter rings are referred to as 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.

pairs of comparisons. Differences in power at each individual corneal location relative to baseline between 3 and 24 months of OK lens wear and between central and total multifocality were assessed using a paired *t* test. Simple linear regressions were used to demonstrate the relationship between the two 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 and 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, San Jose, CA). The level of statistical significance was set at 5%.

RESULTS

The subjects’ demographic and baseline data have been reported elsewhere.^{23,52} In brief, 31 children were prospectively fitted with OK contact lenses, but two children discontinued the study; one

because of 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 boys and 13 were girls.

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

Short-term 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 three months (*P* = 0.001) and between T1 and N1, I1 and S1 at 24 months (all *P* < 0.05) (Fig. 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) (Fig. 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 after long-term OK lens wear in comparison with 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-term and long-term OK lens wear (*P* = 0.474). After 3 and 24 months of OK treatment, the greatest differences in power

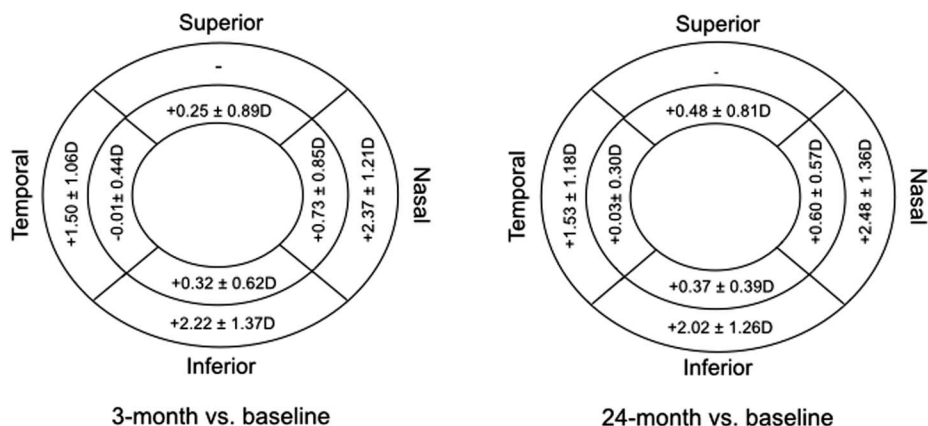


FIG. 3. Mean changes in corneal power relative to the central corneal power at 3 months (left) and 24 months (right) relative to baseline for each of the seven different corneal regions assessed. Data from the superior peripheral cornea (i.e., S2) were not analyzed as intrusion of the upper lid and lashes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

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 with 24 months ($P=0.333$). The difference between central and total multifocality was, however, statistically significant after both short-term and long-term OK lens wear (both $P<0.001$).

The change in axial elongation over two 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) after either 3 or 24 months of OK lens wear were not significantly correlated with the two-year change in axial length relative to baseline (all $P<0.05$) (Table 1 and Figs. 4 and 5).

Neither central nor total multifocality after short-term or long-term OK lens wear were significantly correlated with the two-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 after OK lens wear.²⁸⁻³¹ After three months of OK lens wear, Zhong et al.⁴⁸ reported significant increases (compared with baseline) in sagittal power at the nasal 2 and 3 mm, temporal 3 mm and inferior 2, 3 and 4 mm corneal locations; peaking was evident at the 3 mm location (i.e., 6 mm corneal ring) compared with the apical center. 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 8 mm ring diameter) than in the paracentral region (i.e., 3 to 5 mm ring diam-

eter) after 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 Masedupally 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 after 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 after 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 ($\Delta=3.23$ D) after 12 months of OK lens wear,⁶⁸ whereas the present study found central and total

TABLE 1. Simple Linear Regressions Between the Change in axial Length at two 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 After Short-Term (3 Months) and Long-Term (24 Months) OK Lens Wear.

Corneal Areas	Short-Term Corneal Power Changes vs. Changes in Axial Length		Long-Term Corneal Power Changes vs. Changes in Axial Length	
	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	$y = 0.146x + 2.372$	$R^2=0.023, P=0.212$	$y = 0.044x + 2.060$	$R^2=0.023, P=0.674$

The strength of association between the different factors is indicated by linear regression equations, R^2 values and P values.

H, horizontal; I, inferior; N, nasal; OK, orthokeratology; para, paracentral; peri, pericentral; S, superior; T, temporal; V, vertical.

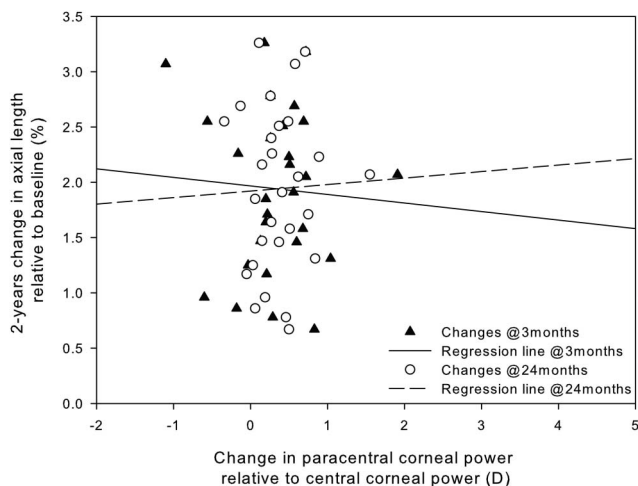


FIG. 4. Simple linear regressions between the two-year change in axial length relative to baseline and the change in paracentral corneal power relative to central corneal power after 3 months (solid triangles and line) and 24 months (open circles and dashed line) of orthokeratology lens wear.

multifocality to be 2.69 ± 1.16 and 2.94 ± 1.22 D, respectively, after three months of OK lens wear and 2.53 ± 1.39 and 2.70 ± 1.41 D, respectively, after 24 months of OK lens wear. Hiraoka et al.⁶⁸ found a statistically significant negative correlation between changes in corneal multifocality and the one-year change in axial elongation, whereas in the present study neither central nor total multifocality were significantly associated with the two-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.⁶⁸ measured corneal multifocality as the difference between the maximum and minimum corneal optical powers (in diopters) calculated within the central 4-mm pupillary area. 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 individuals⁶⁹ 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 after OK treatment are ethnicity, family history, and outdoor exposure. It is well established that

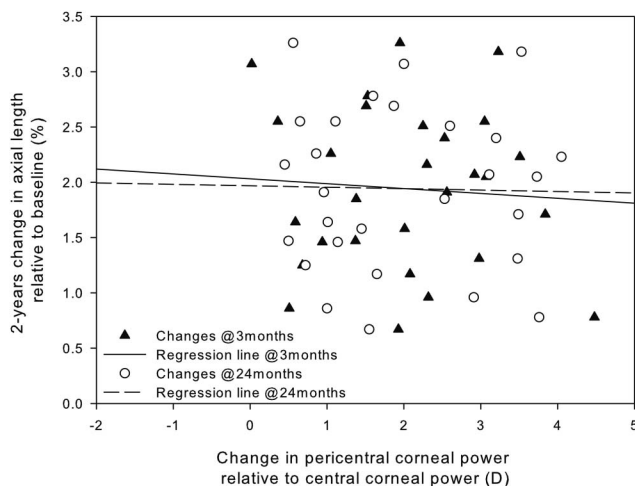


FIG. 5. Simple linear regressions between the two-year change in axial length relative to baseline and the change in pericentral corneal power relative to central corneal power after 3 months (solid triangles and line) and 24 months (open circles and dashed line) of orthokeratology lens wear.

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 with 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 not a consequence of a relative myopic shift in the peripheral retinal image induced by changes in corneal power after 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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Short-Term Changes in Ocular Biometry and Refraction After Discontinuation of Long-Term Orthokeratology

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Objective: To assess refractive and biometric changes 1 week after discontinuation of lens wear in subjects who had been wearing orthokeratology (OK) contact lenses for 2 years.

Methods: Twenty-nine subjects aged 6 to 12 years and with myopia of -0.75 to -4.00 diopters (D) and astigmatism of ≤ 1.00 D participated in the study. Measurements of axial length and anterior chamber depth (Zeiss IOLMaster), corneal power and shape, and cycloplegic refraction were taken 1 week after discontinuation and compared with those at baseline and after 24 months of lens wear.

Results: A hyperopic shift was found at 24 months relative to baseline in spherical equivalent refractive error ($+1.86 \pm 1.01$ D), followed by a myopic shift at 1 week relative to 24 months (-1.93 ± 0.92 D) (both $P < 0.001$). Longer axial lengths were found at 24 months and 1 week in comparison to baseline (0.47 ± 0.18 and 0.51 ± 0.18 mm, respectively) (both $P < 0.001$). The increase in axial length at 1 week relative to 24 months was statistically significant (0.04 ± 0.06 mm; $P = 0.006$). Anterior chamber depth did not change significantly over time ($P = 0.31$). Significant differences were found between 24 months and 1 week relative to baseline and between 1-week and 24-month visits in mean corneal power (-1.68 ± 0.80 , -0.44 ± 0.32 , and 1.23 ± 0.70 D, respectively) (all $P \leq 0.001$). Refractive change at 1 week in comparison to 24 months strongly correlated with changes in corneal power ($r = -0.88$; $P < 0.001$) but not with axial length changes ($r = -0.09$; $P = 0.66$). Corneal shape changed significantly between the baseline and 1-week visits (0.15 ± 0.10 D; $P < 0.001$). Corneal shape changed from a prolate to a more oblate corneal shape at the 24-month and 1-week visits in comparison to baseline (both $P \leq 0.02$) but did not change significantly between 24 months and 1 week ($P = 0.06$).

Conclusions: The effects of long-term OK on ocular biometry and refraction are still present after 1-week discontinuation of lens wear. Refractive change after discontinuation of long-term OK is primarily attributed to the recovery of corneal shape and not to an increase in the axial length.

Key Words: Myopia control—Orthokeratology—Axial length—Myopia progression—Eye elongation—Discontinuation—Recovery—Cornea—Rebound.

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Orthokeratology (OK) is a clinical technique that uses specially designed and fitted gas-permeable contact lenses to reshape corneal contour to temporarily modify refractive error. Today, the most common clinical application of OK is for the reduction of myopia. The introduction of reverse geometry contact lens designs, highly oxygen-permeable lens materials, and accurate clinical instrumentation for the measurement of corneal topography has made OK an effective and highly predictable procedure for the temporary reduction of up to -6.00 diopters (D) of myopia.¹

Refractive correction with OK is achieved by flattening and thinning of the corneal epithelium.²⁻⁴ One of the proposed benefits of OK for the overnight reduction of myopia is its reversibility upon discontinuation from lens wear. Unlike refractive surgery, after ceasing to wear reverse geometry lenses, the cornea and thus refractive error are expected to return to baseline levels.⁵⁻⁹

Soni et al.⁵ assessed refractive and corneal topography recovery after 2 weeks of discontinuation of lens wear in 10 subjects aged 19 to 33 years who wore reverse geometry lenses for 1 month. Central corneal thinning recovered after 1 night of no lens wear, corneal curvature after 1 week of no lens wear, and refractive correction and binocular uncorrected visual acuity after 2 weeks of no lens wear.⁵

Barr et al. assessed refractive error changes after 8, 24, 48, and 72 hours of lens wear discontinuation in 93 subjects who wore OK contact lenses for a period of 6 to 9 months. The authors reported refractive error to return to baseline levels within 72 hours, with the greater the magnitude of treatment, the more rapid the recovery to baseline refraction.⁶

Wu et al. assessed the effects of 50 months of OK lens wear on corneal curvature among 28 subjects, with a mean age of 10 years, after a mean lens wear discontinuation of 17 days. The authors found a residual but statistically significant corneal flattening in the flat (0.07 mm) and steep (0.02 mm) corneal meridians, indicating that corneal curvature may not necessarily return completely to baseline after discontinuation of 17 days in long-term OK lens wearers.⁷

Kobayashi et al. reported on the recovery after 1 year of OK lens wear in 15 young adults. Refractive error, visual acuity, contrast sensitivity, and corneal asymmetry and regularity indices returned to baseline values within 8 weeks of lens wear discontinuation.⁸

More recently, Chen et al. reported posterior corneal curvature recovery after 1 week, 2 weeks, 1 month, and 2 months of lens wear discontinuation in 28 young adults (age, 19–30 years) who wore reverse geometry lenses for 6 months.⁹ They found a steepening of the posterior cornea immediately after the lens removal, but it returned to its original shape within 2 hours after the cessation of lens wear and concluded that this change is in line with

recent reports of the diurnal variation in posterior corneal shape in non-contact lens wearers.⁹

Previous studies that assessed corneal recovery after OK had a small sample,^{5,8} a short period of OK lens wear⁵ and recovery assessment.^{5,6} Others limited assessments to refractive⁶ and/or corneal curvature changes.^{5,7,9} Additionally, previous studies on the topic of corneal recovery after OK lens wear have used adult subjects.⁵⁻⁹

Recent studies have reported OK contact lens wear to significantly reduce axial length growth by 30% to 50% in comparison to spectacle and soft contact lens wear in children.¹⁰⁻¹⁵ Although a previous prospective study reported complete recovery of refraction, uncorrected visual acuity, corneal aberrations, and contrast sensitivity after 1 week of lens wear discontinuation in 17 subjects aged 20 to 37 years who have been wearing OK lenses for 12 months,¹⁶ no previous studies have reported restoration to baseline levels of refractive and biometric variables after the long-term use of OK for the control of myopia progression in children. Therefore, the purpose of this study was to assess refractive and biometric changes after 1 week of lens wear discontinuation in children who have been wearing OK contact lenses for 2 years.

METHODS

This study was part of a larger study designed to assess the safety, efficacy, and subjective acceptance of OK lens wear for the control of myopia progression in children.^{14,17-20} Methods have been described in detail elsewhere.^{14,16} In brief, normal, healthy, white European subjects aged 6 to 12 years with moderate levels of myopia (-0.75 to -4.00 D) and astigmatism (≤ 1.00 D) 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). In addition to baseline, subjects were seen at 24 months and on the subsequent week of lens wear discontinuation. Follow-up visits were scheduled to fall within 2 hours of awakening. Full informed consent and child assent were obtained from the parents/guardians before 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 slitlamp findings occur. Subjects were instructed that they could withdraw from the study at any time. 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.

Measurements of axial length and anterior chamber depth were taken with the Zeiss IOLMaster (Carl Zeiss Jena GmbH, Jena, Germany).²¹ Three separate measurements of axial length were recorded, and a mean was obtained. The mean of three measurements of axial length using the IOLMaster has been reported to provide an impressive level of precision (i.e., 0.02 ± 0.32 mm when compared with ultrasound) and repeatability (i.e., 0.00 ± 0.04 mm).²¹ A single-shot, which automatically generated five measures of anterior chamber depth, was taken with the IOLMaster, and a mean obtained. The repeatability of anterior chamber depth measurements with the IOLMaster has been reported to be between 10 and 20 μm .^{21,22}

Corneal topography measurements were performed with the Wavelight Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The first measurement taken for each eye

(which provided an optimum index value according to the manufacturer's recommendations) was used for the study. The measurement generated a simulated central keratometry reading and the rate of peripheral corneal flattening/steepening with displacement from the corneal apex, the latter indicating the corneal shape (i.e., P value).²³ The P value was calculated over a 7-mm chord because this is the default setting of the instrument.

Subsequently, subjects were instilled 3 drops of cyclopentolate hydrochloride 1% (Alcon Cusi, Barcelona, Spain) separated 10 minutes apart in each of the subjects' eyes using a multidose bottle. Ten minutes after the instillation of the third drop, 3 autorefractometry measurements were taken (Topcon RM 8000B, West Sacramento, CA), and a mean was obtained.

Statistical Analysis

Spherocylindrical refractions and corneal curvatures were converted from diopters to a vector representation for analysis²⁴: a spherical lens of power M (mean spherical equivalent refraction or corneal power = sphere + [cylinder/2]); Jackson cross cylinder at axis 0° with power J_0 ($= -[\text{cylinder}/2] \cdot \cos[2 \times \text{axis}]$); and Jackson cross cylinder at axis 45° with power J_{45} ($= -[\text{cylinder}/2] \cdot \sin[2 \times \text{axis}]$).

Differences in refractive and biometric components between the baseline, 24-month, and 1-week discontinuation visits were assessed using a 1-way repeated measures analysis of variance. Equality of variances and sphericity were tested using the Levene and Mauchly tests, respectively, to select appropriate P values. Post hoc contrasts with bonferroni correction were used to determine differences between pairs of comparisons (i.e., baseline vs. 24 months, baseline vs. 1 week, and 24 months vs. 1 week). Additionally, the agreement between 24-month and 1-week visits were determined by plotting the differences between the 2 sets of data against their mean using Bland-Altman plots.²⁵ Pearson correlations were used to investigate the interrelationships of mean spherical equivalent refractive error and axial length changes with the mean corneal curvature and shape changes. Data for only the right eye are presented and expressed as mean \pm standard deviation. Statistical analyses were conducted using SPSS 15.0 (SPSS, Inc, Chicago, IL). The level of statistical significance was taken as 5%.

RESULTS

Thirty-one children were prospectively allocated to OK lens wear, but two children discontinued the study. The subjects' demographic and baseline data have been reported elsewhere.^{14,17}

The mean spherical refractive error changed significantly over time ($P < 0.001$), and this was attributed to a significant reduction in myopia at the 24-month visit in comparison to the baseline and 1-week visits (both $P < 0.001$) (Fig. 1). Mean spherical equivalent myopia was found to increase by as much as -3.50 D or decrease by as much as 0.00 D at the 1-week visit in comparison to the 24-month visit (Fig. 2). There was a significant mean difference (bias) in the change in mean spherical equivalent refractive error for the whole range of mean spherical refractive errors assessed in this study (i.e., -2.69 to 0.00 D); the greater the mean spherical equivalent myopia, the greater the myopic shift at 1-week visit in comparison to the 24-month visit (Fig. 2).

The J_0 cylindrical component of the refraction changed significantly over time ($P = 0.001$), and this was attributed to the

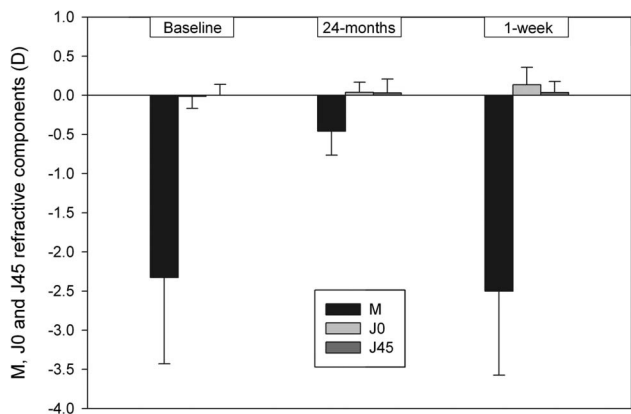


FIG. 1. Mean spherical equivalent, J0, and J45 refractive power components at baseline, 24-month, and 1-week discontinuation visits.

significant increase at the 1-week visit (0.13 ± 0.22 D) in comparison to baseline (-0.01 ± 0.15 D) ($P=0.002$) (Fig. 1). The J0 astigmatic component was found to increase by as much as 0.75 D or decrease by as much as -0.25 D at the 1-week visit in comparison to the 24-month visit. A slight bias was found in the change in J0 for the range of J0 components assessed in this study (i.e., -0.37 to 0.59 D); the greater the mean J0, the greater the change at 1 week in comparison to 24 months (Fig. 3). In contrast, no statistically significant differences were found over time in the J45 cylindrical component of the refraction ($P=0.25$) (Fig. 1). The J45 astigmatic component was found to increase by as much as 0.25 D or decrease by as much as -0.23 D at the 1-week visit in comparison to the 24-month visit. Again, a slight bias was found in the change in J0 for the entire range of J45 components assessed in this study (i.e., -0.24 to 0.29 D), with greater mean J45 components being associated to greater changes at 1 week in comparison to 24 months (Fig. 3).

Axial length increased significantly over time ($P<0.001$). Longer axial lengths were found at 24-month and 1-week discontinuation visits in comparison to baseline (both $P<0.001$), and a further increase of 0.04 mm was also observed at the 1-week discontinua-

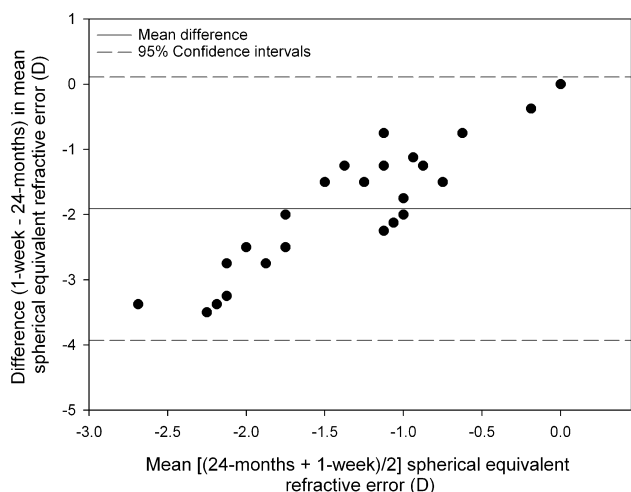


FIG. 2. Mean spherical equivalent refractive error: difference between 1-week and 24-month visits.

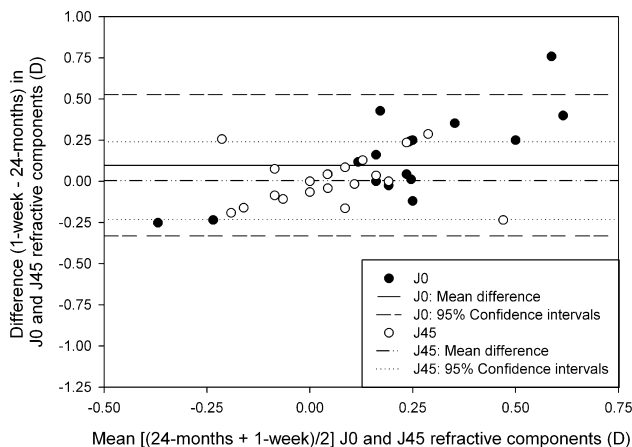


FIG. 3. Mean J0 and J45 refractive power components: difference between 1-week and 24-month visits.

tion visit relative to the 24-month visit ($P=0.006$) (Fig. 4). Axial length was found to increase as much as 0.18 mm and decrease as much as -0.06 mm at 1 week in comparison to 24 months (Fig. 5). There was no significant bias in the change in axial length for the whole range of axial lengths assessed in this study (i.e., 22.92 to 26.26 mm).

Anterior chamber depth did not change significantly over time ($P=0.31$) (Fig. 6). Mean anterior chamber depth was found to increase as much as 0.15 mm and decrease by as much as -0.03 mm at 1 week in comparison to 24 months, and there was no significant bias for the entire range of anterior chamber depths assessed in this study (i.e., 3.38 to 4.31 mm).

The mean corneal power component changed significantly over time ($P<0.001$) (Fig. 7). Mean corneal power was significantly reduced at 24 months in comparison to baseline ($P \leq 0.001$), followed by a partial recovery at 1 week in comparison to 24 months ($P \leq 0.001$). However, corneal power did not completely return to baseline levels (43.24 ± 1.55) after 1 week of lens wear discontinuation (42.81 ± 1.54) ($P \leq 0.001$) (Fig. 7). Mean corneal power was found to increase as much as 2.50 D and decrease as much as -0.21 D at 1 week in comparison to 24 months (Fig. 8). There was no significant bias in the change in mean corneal power for the

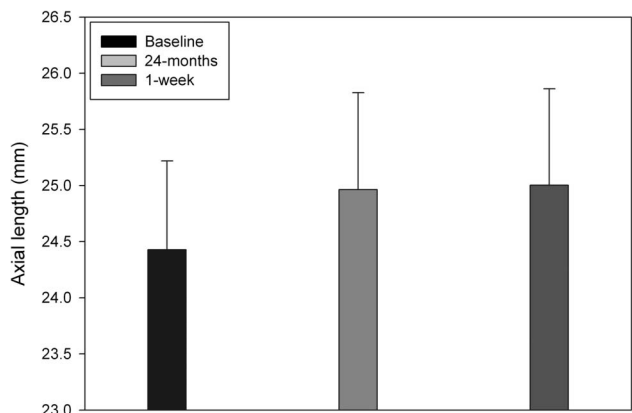


FIG. 4. Axial length at baseline, 24-month, and 1-week discontinuation visits.

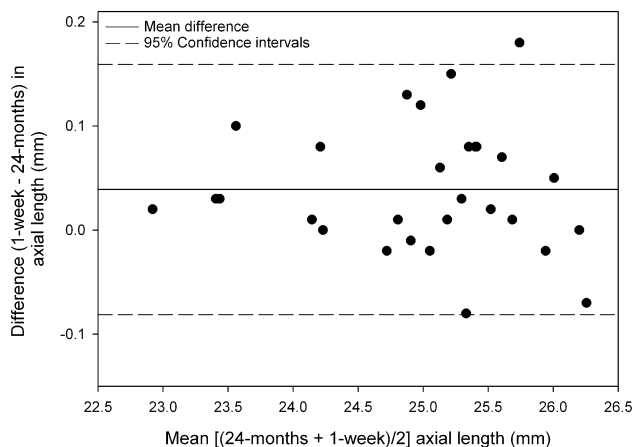


FIG. 5. Axial length: difference between 1-week and 24-month visits.

whole range of mean corneal powers assessed in this study (i.e., 39.00 to 45.62 D) (Fig. 8).

The J0 corneal power component changed significantly over time ($P=0.03$) (Fig. 9). However, no significant differences were found in any of the 3 individual paired comparisons ($P>0.05$). The J0 component was found to increase as much as 0.38 D and decrease as much as -0.57 D at 1 week in comparison to 24 months. There was a significant bias in the change of the J0 astigmatic component for the whole range of mean J0 components assessed in this study (i.e., -1.00 to 0.12 D); greater the mean J0 component, the greater the change at 1 week in comparison to 24 months (Fig. 10). In contrast, no statistically significant differences were found in J45 corneal power component over time ($P>0.05$) (Fig. 9). The J45 component was found to increase as much as 0.30 D and decrease as much as -0.43 D at 1 week in comparison to 24 months (Fig. 10). There was no significant bias in the change in mean J45 astigmatic component for the whole range of mean J45 components assessed in this study (i.e., -0.55 to 0.34 D) (Fig. 10).

Corneal shape changed significantly over time ($P=0.03$) (Fig. 11). The cornea changed from a more prolate into less prolate corneal shape at the 24-month and 1-week visits in comparison to baseline ($P=0.02$ and $P\leq 0.0001$, respectively). However,

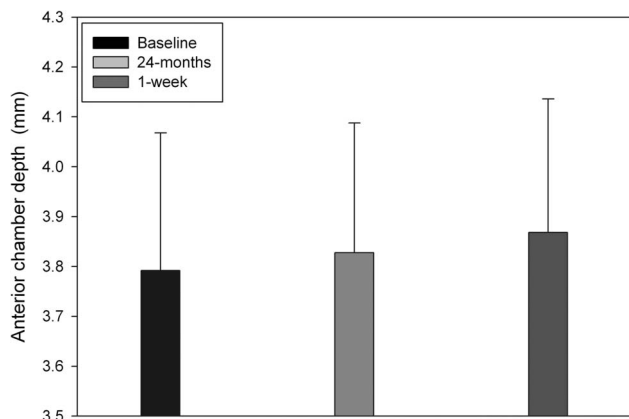


FIG. 6. Anterior chamber depth at baseline, 24-month, and 1-week discontinuation visits.

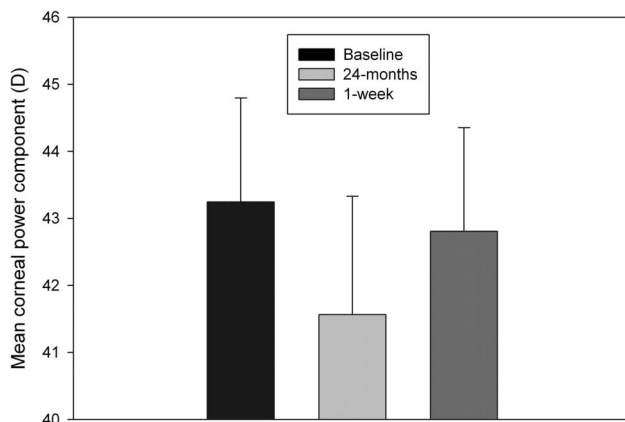


FIG. 7. Mean corneal power component at baseline, 24-month, and 1-week discontinuation visits.

no significant differences were found between 24-month and 1-week visits ($P=0.06$). Corneal shape was found to increase as much as 0.56 and decrease as much as -0.47 D at 1 week in comparison to 24 months. There was no significant bias in the change in corneal shape for the entire range of corneal shapes assessed in this study (i.e., 0.65 to 0.91 D).

The change in mean spherical equivalent refractive error at 24 months in comparison to baseline strongly correlated with the change in mean corneal power at 24 months in comparison to baseline ($r=-0.86$; $P<0.001$). Similarly, the change in mean spherical equivalent refractive error at the 1-week discontinuation visit in comparison to 24 months also strongly correlated with the change in the mean corneal power at the 1-week discontinuation visit relative to 24 months ($r=-0.88$; $P<0.001$; Fig. 12). The changes in J0 and J45 refractive components at 24 months in comparison to baseline also significantly correlated with the changes between these 2 visits in J0 and J45 corneal power components ($r=-0.41$; $P=0.03$ and $r=-0.51$; $P=0.005$, respectively). Similarly, the changes in J0 and J45 refractive components at 1 week in comparison to baseline also significantly correlated with the changes between these 2 visits in J0 and J45 corneal power components ($r=-0.55$; $P=0.003$ and $r=-0.49$; $P=0.008$, respectively).

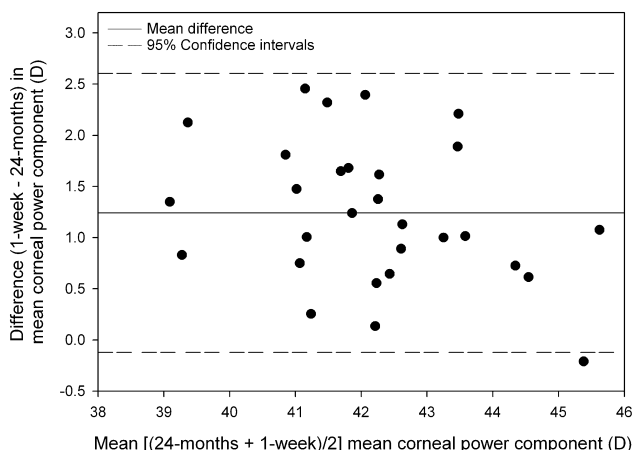


FIG. 8. Mean corneal power: difference between 1-week and 24-month visits.

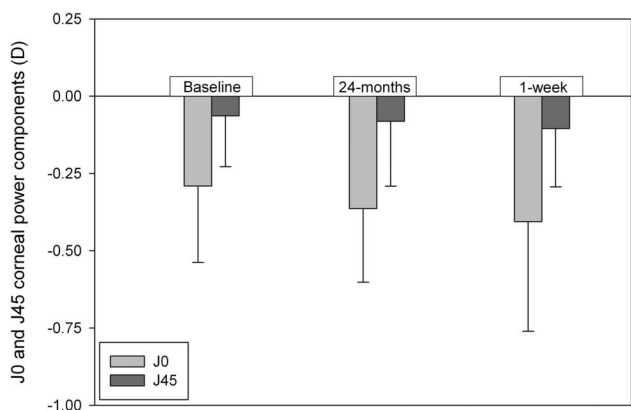


FIG. 9. J0 and J45 corneal power components at baseline, 24-month, and 1-week discontinuation visits.

The change in axial length at 24 months in comparison to baseline did not correlate with the change in mean refractive or mean corneal power components at 24 months in comparison to baseline ($r=0.14$; $P=0.47$ and $r=-0.34$; $P=0.08$, respectively). Similarly, the change in axial length at the 1-week discontinuation visit in comparison to 24 months did not correlate with the change in mean refractive or mean corneal power components at the 1-week discontinuation visit relative to 24 months ($r=-0.09$; $P=0.66$ and $r=0.12$; $P=0.55$, respectively) (Fig. 13).

The change in mean spherical equivalent refractive error at 24 months in comparison to baseline did not correlate with the change in corneal shape at 24 months in comparison to baseline ($r=-0.25$; $P=0.25$). However, the change in mean spherical equivalent refractive error at the 1-week discontinuation visit in comparison to 24 months significantly correlated with the change in corneal shape at the 1-week discontinuation visit relative to 24 months ($r=-0.47$; $P=0.01$).

The change in axial length at 24 months in comparison to baseline did not correlate with the change in corneal shape at 24 months in comparison to baseline ($r=0.18$; $P=0.39$). Similarly, the change in axial length at the 1-week discontinuation visit in

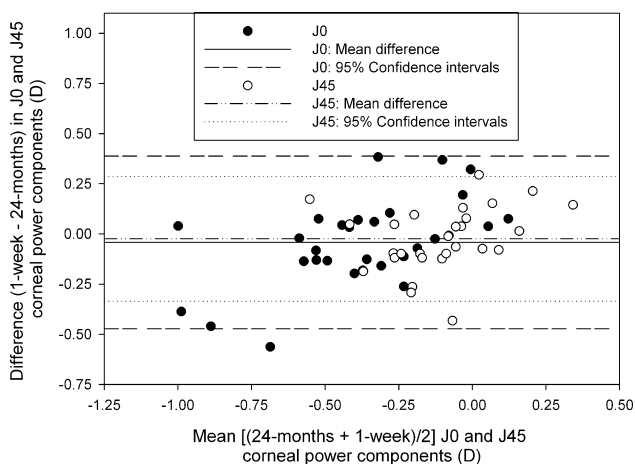


FIG. 10. J0 and J45 corneal power components: difference between 1-week and 24-month visits.

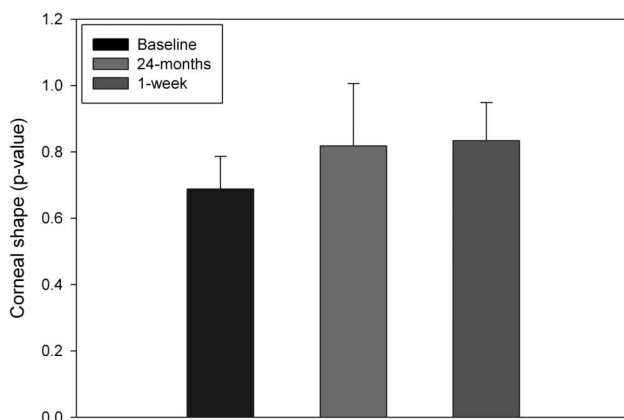


FIG. 11. Corneal shape (P value) at baseline, 24-month, and 1-week discontinuation visits.

comparison to 24 months did not correlated with the change in corneal power at the 1-week discontinuation visit relative to 24 months ($r=0.11$; $P=0.59$).

DISCUSSION

Recently, OK contact lens wear has been shown to be an effective¹⁰⁻¹⁵ and safe^{18,26} treatment option to reduce the axial elongation of the eye in children. However, little is known about the short-term discontinuation effects on refractive and biometric variables in children who undergo long-term OK. This is the first study to assess the effect of short-term discontinuation after long-term OK lens wear on a few refractive and biometric variables in children fitted with overnight OK specifically for the control of myopia progression.

As a result of the corneal flattening induced by OK lens wear, the mean spherical equivalent refraction experienced a significant hyperopic shift at 24 months of similar magnitude to that of the baseline mean spherical equivalent refraction (but in the opposite direction) in comparison to baseline, and this change was primarily attributed to the change in corneal power (Figs. 1 and 7). In fact,

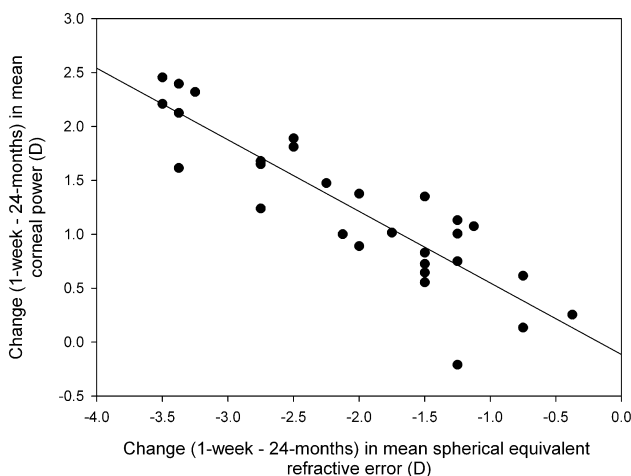


FIG. 12. Linear relationship between the change in mean spherical equivalent refractive error at the 1-week discontinuation visit in comparison to 24-month discontinuation visit and the change in the mean corneal power at the 1-week discontinuation visit relative to 24 months ($r=-0.88$; $P<0.001$).

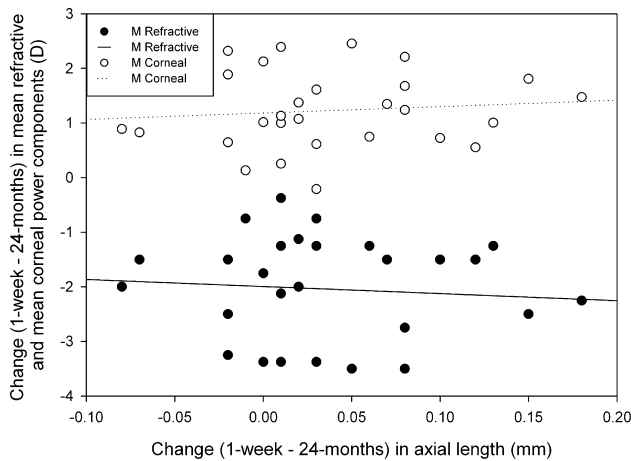


FIG. 13. Linear relationships between the change in axial length at the 1-week discontinuation visit in comparison to 24-month visit and the change in mean refractive and mean corneal powers components at the 1-week discontinuation visit relative to 24 months ($r = -0.09$; $P = 0.66$ and $r = 0.55$, respectively).

the change in corneal power highly correlated with the change in refraction, a finding in agreement with previous studies (Fig. 12).¹⁻³ A small decrease in mean spherical equivalent refractive error was found after 1 week of lens wear discontinuation in comparison to baseline (-0.17 ± 0.40 D), and this is partly attributed to the increase in myopia expected over the 24-month and 1-week period of follow-up of this study (Fig. 1). However, corneal power did not completely return to baseline levels after 1 week of lens wear discontinuation. In fact, the mean corneal power was -0.44 ± 0.32 D below the baseline mean corneal power (Fig. 7). Although most corneal and refractive changes (approximately 80% to 90%) are expected to return to baseline levels within 1 week of OK lens wear discontinuation, there are still some changes expected in the cornea with longer periods of lens wear discontinuation (i.e., a reversion of corneal flattening and concomitant increase in myopia).⁵⁻⁹ In fact, a previous study found a residual but statistically significant corneal flattening in the flatter and steeper corneal meridians after discontinuation for 17 days in subjects who worn OK contact lenses for a period of 50 months.⁷ Nevertheless, taking into account the additional increase in myopia expected from restoration to baseline levels of the mean corneal power component with longer periods of lens wear discontinuation (-0.44 ± 0.32 D) together with the mean spherical equivalent refraction at 1 week (-0.17 ± 0.40 D), the combined mean spherical equivalent refraction (-0.61 D) cannot predict the changes in axial length found in this study. The increase in axial length found at the 1-week visit in comparison to baseline was 0.51 mm (Fig. 4), which is estimated to be equivalent to an increase in myopia of -1.36 D using the conversion factor of $1 \text{ mm} = 2.67 \text{ D}$.²⁷ A mismatch in the change in refractive error, which can be predicted from axial length measurements, in comparison to the actual change in refractive error, has been previously reported with multifocal spectacles²⁸ and multifocal soft contact lenses.²⁹⁻³¹

Although a statistically significant increase in the J0 cylindrical component of the refraction was found at 1 week in comparison to baseline, the change was considered to be of limited clinical significance (0.15 ± 0.22 D). That the J45 astigmatic component of the refraction did not experience significant changes is expected as

subjects had to have ≤ 1.00 D of with-the-rule and/or against-the-rule astigmatism to participate in the study.

Axial length increased by 0.04 mm from 24 months to 1 week of lens discontinuation visits. Assessment of corneal changes together with the use of the Munnerlyn formula, commonly used to calculate the required ablation per diopter of refractive change in refractive surgery procedures, showed that half of the increase in axial length after OK lens wear discontinuation (i.e., 0.02 mm) could be attributed to a recovery of corneal shape.³² This later value agrees with previously reported reversible corneal epithelial thinning changes after OK treatment⁴ and with previous work undertaken using a novel study design similar to that employed in this study.³³ However, the mechanism responsible for the remaining increase in axial length (i.e., 0.02 mm) is unclear, but this might be attributed to choroidal thickness changes, which have been recently reported to occur in humans as a result of lens-induced defocus,³⁴ or to the instrument's between-visits repeatability.^{21,22} Nevertheless, the remaining increase in axial length, which could not be accounted for changes in corneal shape (i.e., 0.02 mm), is negligible and certainly clinically insignificant, as it is equivalent to approximately 0.06 D.²⁷ Furthermore, that refractive change at 1 week in comparison to 24 months strongly correlated with the changes in corneal power (Fig. 12) but not with axial length changes (Fig. 13) indicates that there was no rebound effect in the axial elongation of the eye over 1 week of lens wear discontinuation and that refractive change is primarily attributed to a recovery of corneal steepening. However, a case report found faster axial elongations in a girl when she worn spectacles in comparison to the time when she worn OK, but such faster axial elongations took place over a 6-month period.³⁵

That the anterior chamber depth did not change significantly over time agrees with a previous study.³⁶ It is well accepted that the effects of OK lens wear are limited to the front of the cornea and more specifically to the corneal epithelium.^{2-4,37} A previous study reported intraobserver and interobserver coefficients of variation in the measurement of anterior chamber depth with the IOLMaster of less than 1% (i.e., of the order of 0.03 mm).²² Another study reported the repeatability of anterior chamber depth measurements with the IOLMaster to be -0.01 ± 0.08 mm.²¹

That corneal shape at the 1-week visit remained similar to that found at the 24-month visit is an interesting finding. It is possible that the peripheral cornea takes longer periods to regress to baseline levels in comparison to the central cornea, thus affecting the recovery of the corneal *P* value assessed in this study.

Although it would have been interesting to assess restoration to baseline levels of refractive and biometric variables over longer periods in our study, the latter was not possible because subjects could not be followed for a longer period without lens wear. Another limitation is that additional biometric measurements such as corneal and choroidal thicknesses and posterior corneal curvature, which are likely to contribute to a better understanding of the changes in ocular biometry and refraction after discontinuation of long-term OK, were not taken in this study.

In summary, 1 week of lens wear discontinuation is not enough for the cornea to return to baseline levels in children who have been wearing OK contact lenses for a long term.¹⁻⁴ Refractive change after discontinuation of long-term OK contact lens wear is primarily attributed to the recovery of corneal shape and not to an increase in the axial length of the eye or recoveries in other ocular biometric components.

ACKNOWLEDGMENTS

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Myopia Control with Orthokeratology Contact Lenses in Spain (MCOS): Study Design and General Baseline Characteristics

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ABSTRACT

PURPOSE: Although previous studies suggest that orthokeratology contact lens wear slows eye growth in children with progressing myopia, some limitations in the methodology employed have become evident. Furthermore, the safety of this modality of visual correction has not been assessed. The study "Myopia Control with Orthokeratology Contact Lenses in Spain" (MCOS) is being conducted to compare axial length growth between white European myopic children wearing orthokeratology contact lenses (OK) and wearing distance single-vision spectacles (SV). Additionally, the incidence of adverse events and discontinuations is also recorded. We outline the methodology and baseline data adopted.

METHODS: Subjects aged 6 to 12, with myopia ranging from 0.75 to 4.00 D and astigmatism ≤ 1.00 D were prospectively allocated OK or SV correction. Measurements of axial length, anterior chamber depth, corneal topography, cycloplegic autorefractometry, visual acuity and corneal staining are performed at 6-month intervals. The incidence of adverse events and discontinuations are also recorded.

RESULTS: Thirty one children were fitted with OK and 31 with SV correction. Eight subjects did not meet the refraction-related inclusion criteria for enrollment. No significant differences were found in baseline mean age and refractive and biometric data between the two groups ($P > 0.05$). No adverse events were found in any of the two groups at baseline.

CONCLUSION: To the authors' knowledge, MCOS is the first prospective clinical trial to assess the safety and efficacy of orthokeratology contact lens wear to slow myopia progression vs. single-vision spectacle wear. The MCOS offers a number of notable features: prospective design; well-matched samples and high-resolution ocular biometry measures, which should collectively elucidate whether orthokeratology contact lens wear is a feasible and safe method for myopia-progression control.

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KEY WORDS: myopia control; orthokeratology; axial length; myopia progression; eye elongation.

RESUMEN

OBJETIVO: A pesar de que estudios previos sugieren que el uso de lentes de contacto para ortoqueratología ralentizan el crecimiento

ocular en niños con miopía progresiva, ha quedado de manifiesto algunas limitaciones en la metodología empleada en dichos estudios. Además, hasta la fecha no se ha evaluado la seguridad de esta modalidad de corrección visual. El estudio "Control de la miopía con lentes de contacto para ortoqueratología en España" (MCOS, según sus siglas en inglés) se está llevando a cabo para evaluar el aumento de la longitud axial ocular en niños miopes europeos de raza blanca, usuarios de lentes de contacto de ortoqueratología frente a usuarios de gafas monofocales. Además, también se está evaluando la incidencia de reacciones adversas y abandonos. En este artículo explicamos la metodología empleada, así como los datos iniciales del estudio.

MÉTODOS: Se asignó de manera prospectiva corrección OK o SV a sujetos de entre 6 y 12 años de edad, con una miopía comprendida entre 0,75 y 4,00 D y con astigmatismo $\leq 1,00$ D. Se llevan a cabo, inicialmente y cada 6 meses, medidas de la longitud axial, profundidad de la cámara anterior, topografía corneal, de autorrefracción cicloplégica, agudeza visual y tinción corneal. Además, se está evaluando la incidencia de reacciones adversas y abandonos.

RESULTADOS: A 31 niños se les adaptó corrección OK y a 30 corrección SV. Ocho sujetos no cumplían el criterio de inclusión relativo a la refracción. No se encontraron diferencias significativas entre los dos grupos en lo que respecta a edad media y a valores de refractivos y biométricos ($P > 0.05$). No se encontraron reacciones adversas en ninguno de los 2 grupos en la visita inicial.

CONCLUSIONES: Según el conocimiento de los autores, el MCOS es el primer ensayo clínico prospectivo en el que se evalúa la seguridad y eficacia del uso de lentes de contacto ortoqueratológicas para ralentizar el avance de la miopía, comparando los resultados con los obtenidos en un grupo de control compuesto por usuarios de gafas monofocales para miopía. El estudio MCOS tiene una serie de características destacables: diseño prospectivo; muestras bien emparejadas, medidas de biometría ocular de alta resolución; todo ello debería permitir dilucidar si el uso de lentes de contacto ortoqueratológicas es un método factible y eficaz para frenar la progresión de la miopía en niños.

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PALABRAS CLAVE: control de la miopía; ortoqueratología; longitud axial; progresión de la miopía; elongación ocular.

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INTRODUCTION

The prevalence of myopia in young adolescents has increased substantially over recent decades and is now approaching 10-25% and 60-80% in industrialized societies of Western and Eastern Asia, respectively;¹ worldwide, the condition is considered to be the leading cause of visual impairment.² In clinical terms, it is widely acknowledged that the myopic eye is a vulnerable eye, especially for myopia levels greater than 6.00 D, and one that is especially susceptible to a range of ocular pathologies.³⁻⁷ Several treatment therapies, including rigid contact lenses, bifocal and multifocal spectacle lenses as well as pharmaceutical agents, have been used in the past

with relatively modest success to eliminate or, at least, reduce myopia progression.^{8,9} More recently, modern orthokeratology has claimed to be effective in slowing the progression of myopia in children. This technique is an effective treatment for the temporary reduction of up to -6.00D of myopia with the overnight use of reverse-geometry gas-permeable contact lenses.¹⁰ Usually, studies evaluating the effect of orthokeratology lens wear on myopia progression measure changes in the eye's axial length, the principal structural correlate of refractive error,¹¹ due to the concomitant temporary reduction in myopia that occurs as a consequence of the corneal flattening induced by orthokeratology contact lens wear.¹²

Although a retrospective study¹³ and a case report¹⁴ on the subject were previously published, only two prospective studies have assessed the effect of orthokeratology contact lens wear on myopia progression in children.^{15,16}

Over a two-year period, Cho et al.¹⁵ monitored the increase in axial length in 35 Hong-Kong Chinese children aged 7 to 12 who were fitted with orthokeratology lenses, and compared the rate of change of axial length with that observed in a historical control group made up of 35 children wearing single-vision spectacles. Both groups were matched for age, gender and baseline spherical equivalent refractive error. At the end of the 24 months, the increase in axial length was 0.29 ± 0.27 mm and 0.54 ± 0.27 mm for the orthokeratology lenses and single-vision spectacle groups, respectively. However, the study failed to recruit a prospective control group. Furthermore, the baseline level and progression of myopia observed among Chinese children are reported to be significantly greater than among white European children.⁸ In addition, differences in contact-lens-induced responses in the corneas of Asian and non-Asian subjects have also been previously observed.¹⁷

More recently, a study undertaken in the USA by Walline and co-workers¹⁶ compared the growth of the eye observed among myopic children wearing orthokeratology contact lenses with that observed in a historical control group of children wearing soft contact lenses. The groups consisted of children aged 8 to 11 with myopia ranging from 0.75 to 4.00 D and having less than 1.00 D of astigmatism. Over the two-year period, the axial length for the soft-contact-lens group increased, on average, 0.32 mm more than for the orthokeratology-lens group. However, the Walline et al.¹⁶ study was unable to recruit a prospective control group. Since Cho et al.¹⁵ and Walline et al.¹⁶ employed historical prospective control groups, subjects were not randomized into one modality of visual correction vs. another. Additionally, these two previous studies measured axial-length growth using A-scan ultrasonography.^{15,16} An alternative measuring method (the Zeiss IOLMaster) uses partial coherence interferometry to carry out non-contact measures of axial length with a dioptric resolution of 0.03 D (an order of magnitude better than the 10 Hz ultrasound technique).¹⁸

As with any treatment regimen, both efficacy and safety need to be assessed. Although case reports and case series of observations on undefined populations of participants wearing overnight orthokeratology contact lenses have been presented, there are no formal prospective reports on the inci-

dence of adverse events associated with overnight orthokeratology contact lenses specifically used to treat myopia.¹⁹

This report introduces the study designated as MCOS (Myopia Control with Orthokeratology contact lenses in Spain) and outlines its design, methodology and baseline findings. The primary outcome measure of MCOS is to compare differences in axial length growth between white European myopic children wearing orthokeratology contact lenses (OK) and distance single-vision spectacles (SV) over a 2 year period. The secondary outcome is to record differences in the incidence of adverse events and discontinuations between the two study groups. To the authors' knowledge, the MCOS study is the first prospective clinical trial to assess the safety and efficacy of overnight orthokeratology contact lens wear.

METHODS

Sample size

The study's sample size was calculated using a statistical power analysis software (JMPIN 4.0.2, SAS Institute Inc., NC, USA) based on data from previous clinical trials.^{15,16} Assuming that the standard deviation of the change in axial length over a two-year period is 0.27 mm and taking a statistical power of 0.90, a sample size of 25 subjects per group is needed to be able to detect a difference of variation in axial length equal to 0.25 mm (equivalent to approximately 0.75 D)²⁰ at $P=0.05$. Previous studies have reported drop-out rates of approximately 17% among OK¹⁵ and SV²¹ subjects enrolled in clinical trials. Therefore, to account for attrition, the number of subjects to be recruited in this study was taken to be at least 29 per group.

Method of Recruitment

Subjects were sought through advertisements in local newspapers, among individuals attending the clinic where the study was to be undertaken, by word-of-mouth and by randomly mailing the area of Madrid.

Recruitment Session and Follow-up Visits

The objectives of the recruitment session were to determine whether or not the children met the inclusion and exclusion criteria for the study (*Table 1*) and to inform the child's parent(s) or guardian(s) verbally and in writing about the nature of the study. During this session, parent(s) or guardian(s) were given a balanced account of the advantages and disadvantages of the two vision correction modalities offered in the study (i.e. SV or OK). Particular care was taken not to suggest that one modality might perform better than the other or provide a better control over myopia progression. Parent(s) or guardian(s) were also informed that for the whole duration of the study (2 years) children would obtain visual correction (i.e. glasses or contact lenses) made to their prescription, contact lens care solutions (for the OK group only) and full ocular examinations free of charge. After parent(s) or guardian(s) chose one of the two modalities offered, full informed consent and child assent were obtained prior to the start of all experimental work and data collection. The informed consent also included detailed information regarding the potential adverse reactions that might occur as a result of contact lens wear (e.g. microbial

TABLE 1
Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Be 6 to 12 years of age, both ages inclusive	Systemic or ocular disease affecting ocular health
A low-to-moderate level of refractive error (between 0.75 and 4.00 D) and of astigmatism (≤ 1.00 D)	Use of any systemic or topical medications that could affect ocular physiology or contact lens performance
Neophyte contact lens wearer	Any lid or anterior segment abnormalities for which contact lens wear could be contraindicated
Be successfully fitted with spectacles or orthokeratology contact lenses	CCLRU grade ≥ 2 for any given anterior segment ocular clinical signs
Be able to achieve, through spherical refraction correction, a logMAR visual acuity of 0.8 or better in each eye	Aphakic, amblyopic, and atopic individuals
Be willing and able to follow the subject instructions and to meet the protocol-specified schedule of follow-up visits	Refractive astigmatism $\geq 1/2$ spherical refraction
White European ethnicity	Previous contact lens wear

D: diopters; CCLRU: Cornea and Contact Lens Research Unit.

TABLE 2
Menicon Z Night contact lens specifications

Name	Menicon Z Night
Manufacturer	Menicon
Material name	Siloxanylstyrene fluoromethacrylate (tisifilcon A)
Design	Parallel reverse geometry
Dk (Barrer)	163
BOZR (mm)	7.20 to 9.50 (0.05 mm steps)
Optic zone diameter (mm)	6
Total diameter (mm)	10.20/10.60 (standard)/11.00
Tangential angle (degrees)	50 to 65 (1° steps)
Sagittal depth (mm)	0.50 to 0.99 (0.01 mm steps)
Wearing modality	Overnight orthokeratology
Replacement	1 year

Dk: oxygen permeability; BOZR: back optic zone radius.

keratitis). 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 anytime. All measurements were obtained at Clinica Oftalmológica Novovision (Madrid, Spain). The study protocol was reviewed and approved by the Institutional Review Board. No Ethics Committee Approval was required; otherwise, the study followed the tenets of the Declaration of Helsinki.

At the recruitment session, all subjects underwent a full anterior segment examination, indirect fundus microscopy, binocular vision and refractive evaluations to elucidate whether or not they were eligible to participate in the study. Subsequently, baseline study measurements were performed in eligible subjects (see below for further details on the measurement procedures).

Subjects in the SV group were prescribed distance single-vision spectacles having the highest positive power consistent with optimum visual acuity and were asked to wear the spectacles at all times. Subjects in the OK group were fitted with Menicon Z Night contact lenses (Table 2) using the Menicon Professional Easy Fit Software (Figure 1) (Menicon Co., Ltd, Nagoya, Japan). Corneal topography and cycloplegic refraction data for both eyes of each subject were input into the software, which automatically calculated the specifications of the Menicon Z Night trial lens to allow orthokeratology fitting. Contact lenses were ordered and subjects from the OK group were rescheduled for an appointment approximately two weeks later. After the initial contact lens fitting, on the first day all contact lens subjects were instructed in the procedures for contact lens insertion, removal and cleaning/disinfection and these instructions were reinforced in subsequent visits. Subjects were provided with MeniCare Plus multipurpose solution for daily cleaning, rinsing and disinfecting of their contact lenses, and also Menicon Progent intensive cleaner, to be used once a week (Menicon Co., Ltd, Nagoya, Japan).

Subjects in the OK study group were informed that contact lenses had to be inserted every day, just before going to sleep, and removed the following morning. Subjects were requested to attend no later than two hours after lens removal on the morning following the first night of lens wear. A subsequent visit was scheduled for three weeks later to ascertain whether or not the contact lens fitting was clinically acceptable; otherwise, new contact lenses were calculated and ordered. An orthokeratology fit was considered to be successful if after three weeks of lens wear, the subject showed a CCLRU score regarding the anterior eye segment signs ≤ 1 unit,²² a "bull's eye" corneal topography pattern and monocular and binocular visual acuities within ± 1 line of the best-correct decimal spectacle visual acuity. Subjective over-refraction was undertaken to ascertain whether changes in the contact lens base curve were required. If so, new lenses were ordered for the subjects while maintaining the same design specifications for the con-

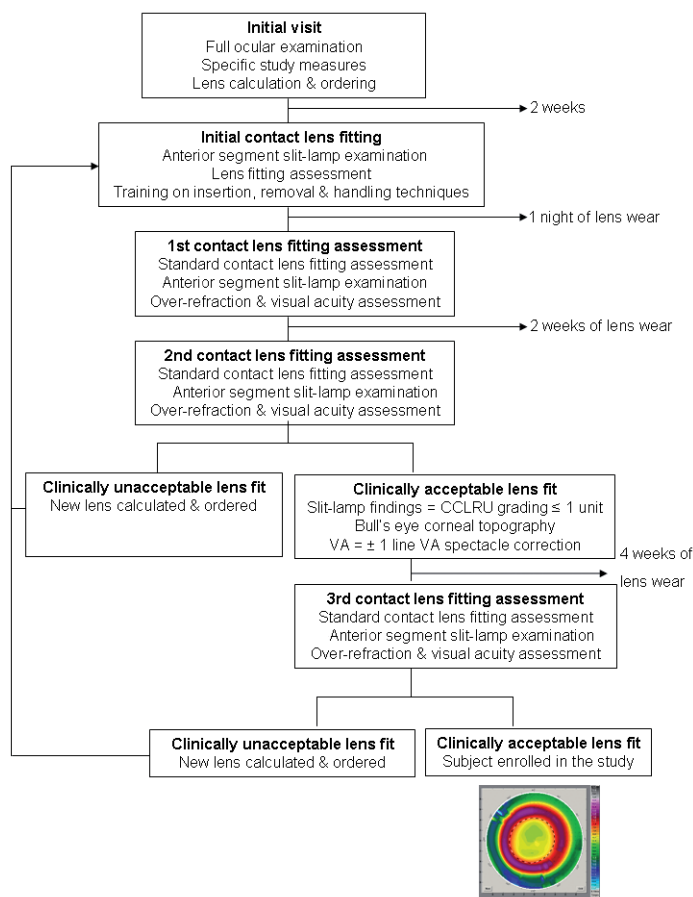


FIGURE 1 Contact lens fitting criteria. The colour image at the bottom shows a bull's eye corneal topography pattern required for a clinically acceptable lens fit. VA, visual acuity.

tact len's back surface. In the event of an unsuccessful fitting (i.e. flat- or steep-fitting lenses), the Menicon Professional Easy Fit Software was used to calculate alternative contact lenses that would constitute a successful lens fit; this tool is included in the Menicon software.

It was made clear to all OK subjects that they had to remove their contact lenses if they experienced any sort of problem. Subjects and their parent/guardians were instructed in the steps to take in the event of an adverse reaction, and were instructed to ensure adherence to the study protocol. Moreover, compliance was monitored closely by one of the authors (CV-C). Subjects from both study groups were advised to report/turn up at the clinic immediately should events not considered normal (e.g. red eye, pain, unusual discomfort, unusual eye secretions) occurred.

After initial enrolment, subjects are seen again at the scheduled 1-, 6-, 12-, 18- and 24-months follow-up visits. To prevent subjects from forgetting their follow-up appointments, all subjects receive a telephone reminder one day before their appointment. Follow-up visits are scheduled to fall within two hours of awakening. A decrease in one line of visual acuity accompanied by a change in subjective refraction²³ at any one of the follow-up visits was considered to be clinically significant and was remedied by supplying new contact lenses or spectacles made to their new prescription.

Measurements

Cycloplegic auto-refraction. Three drops of chlorhydrate cyclopentolate 1% (Alcon Cusí, Masnou, Barcelona, Spain) were instilled 10 minutes apart in each of the subjects' eyes using a multidose bottle. Ten minutes after instillation of the third drop, three auto-refraction measurements were taken (Topcon RM 8000B, CA, USA) and their mean was calculated. Additionally, distance subjective refraction was also performed before and after cycloplegia.

Corneal Topography. Corneal topography measurements were performed with the Wavelight Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The first measurement taken in each eye, which provided an optimum index value according to the manufacturer's recommendations, was used for the study. Furthermore, the measurement generated a simulated central keratometry reading as well as the rate of peripheral corneal flattening/steepening with displacement from the corneal apex, the latter indicating the degree to which an aspheric surface differs from the spherical form (i.e. e-value).²⁴

Axial Length, Anterior Chamber Depth and Posterior Segment Depth Measurements.

Measurements of axial length and anterior chamber depth were performed with the Zeiss IOLMaster (Carl Zeiss Jena GmbH, Jena, Germany).¹⁸ Three separate measurements of axial length are recorded, whereas a single shot automatically recorded five measures of the anterior chamber depth. The posterior segment depth was calculated by subtracting the anterior chamber depth from the axial length obtained with the IOL Master. All biometric measurements were undertaken prior to cycloplegia.

Corneal Staining. The extent and depth of corneal staining were measured to the nearest 0.5 unit using the CCLRU grading scales.²² Additionally, the location (i.e. superior, inferior, nasal, temporal and central) of the staining was also recorded.

Subjective Questionnaires. The Pediatric Refractive Error Profile survey, employed by Walline et al., will be employed to assess and compare vision-specific quality of life of those children in the OK and the SV groups, both at the 12- and the 24-month follow-up visits.^{25,26} The survey was modified for both the OK and the SV groups and consists of 26 questions to which was added two additional questions:

27. The habitual handling of my contact lenses/glasses is normally done by my parents.

28. I usually perform the handling of my contact lenses/glasses.

All the questions have a stem of five possible responses: strongly disagree, disagree, neutral, agree and strongly agree. The surveys will be answered by the children, and parents will be asked not to participate.

The same format was used for two further questions to be answered only by the parents:

1. I think orthokeratology contact lenses/glasses are an excellent method of visual correction.

TABLE 3
Classification of adverse events. The table has been adapted from Morgan et al.²⁸

Classification Symptomatology	Serious Symptomatic	Significant Commonly symptomatic	Non-significant Asymptomatic
Description	An adverse event that produces or has the potential to produce significant visual impairment and might warrant permanent discontinuation from lens wear	An adverse event of sufficient clinical concern to warrant clinical intervention and perhaps temporary discontinuation from lens wear	An adverse event that is of no immediate clinical concern and that does not warrant discontinuation from lens wear
Condition	Central corneal opacity Corneal warpage Epithelial wrinkling Hypopyon Microbial keratitis Penetration of Bowman's membrane Persistent epithelial defect Corneal abrasion requiring medical intervention	3 and 9 o'clock staining Disorders of the eyelids and lashes (e.g. blepharitis, meibomitis, hordeolum) Conjunctival epithelial flaps Conjunctivitis Contact-lens-induced acute red eye (CLARE) Contact-lens-induced papillary conjunctivitis (CLPC) Contact-lens-induced peripheral ulcer (CLPU) Corneal scarring Epithelial microcysts Epithelial arcuate lesion Infiltrative keratitis (IK) Keratoconjunctivitis Ptosis Vascularized limbal keratitis Corneal abrasion requiring no medical intervention	Asymptomatic infiltrates (AI) Asymptomatic infiltrative keratitis (AIK) Blinking disorders Deep stromal opacities Epithelial vacuoles Localized allergic reaction Cornel white lines Corneal epithelial Iron lines

2. Once this study is finished, I intend to continue offering this method of visual correction to my child.

Number of Lenses Required. The number of contact lenses required to achieve an optimum fit during the initial contact lens fitting procedure was recorded, together with the reasons for the implemented changes (i.e. flat fit). At the follow-up visits, the number of lenses required throughout the study and the reasons for each change (i.e., lost and broken lenses, or change in refraction) are also recorded.

Adverse Events and Discontinuations. The classification of adverse events and discontinuations were adapted from Morgan et al.²⁷ Adverse events were classified as "serious," "significant," or "non-significant" according to *table 3*.^{27,28} Although *table 3* shows most of the ocular adverse events that could occur as a result of contact lens and spectacle wear, all adverse events, even those not shown in *table 3*, were recorded in this study. For obscure adverse reactions, the opinion of the ophthalmologist on duty at the clinic is sought and the condition treated in collaboration with the MCOS clinician. In all cases, an appropriate classification of the adverse reaction is obtained. Recurrences of the same adverse event(s) in the same or fellow eye at any of the subsequent follow-up visits were classified as separate events; bilateral events were counted as two separate events. The incidence

rate of each adverse event was recorded as a percentage of eyes per annum.²⁹

In this study, "discontinuation" is defined as the cessation of lens wear for the remainder of the study. Discontinuation may occur as a result of: adverse events, ocular discomfort, visual problems, lack of motivation, failure to follow up instructions, unacceptable visual acuity and other logistic or personal reasons that may or may not have been directly related to lens wear. Temporary suspension of lens wear of up to 2 weeks was allowed (at the investigator's discretion) should significant symptoms or slit-lamp findings occur. Although temporarily discontinued, subjects were examined at frequent intervals until the condition completely subsided, and attempts were made to limit the duration of the suspension period to as few days as possible. Some subjects were discontinued from the study as a result of "lost to follow up"; defined as a situation whereby a subject did not turn up at the next scheduled follow-up visit (despite active efforts to encourage attendance). The incidence rate of discontinuations was recorded as a percentage of subjects per annum.²⁹

Data Collection and Masking

Investigator CV-C was responsible for the data collection; investigator JS-R undertook all the data analysis without knowing the identity of the study groups.

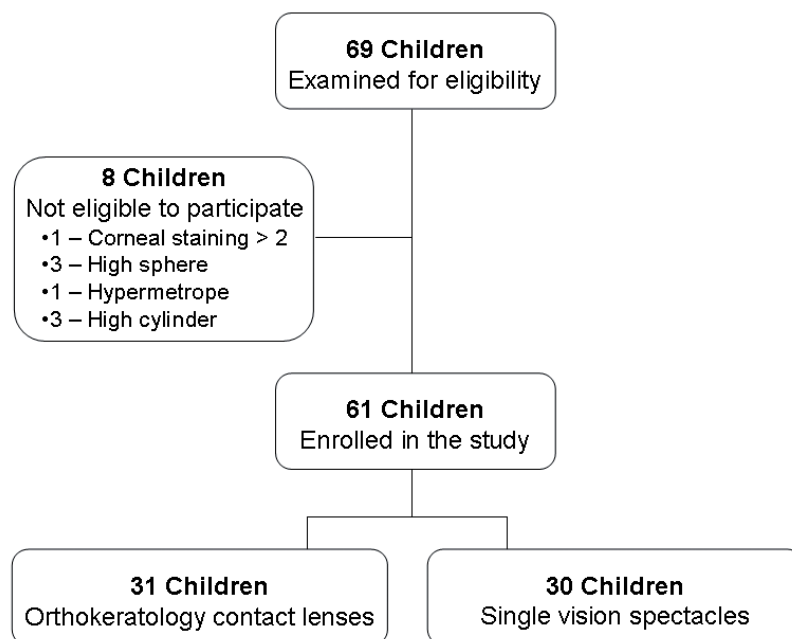


FIGURE 2
Subjects recruited for the study.

Statistical Analysis

The goodness-of-fit Kolomogorov-Smirnov test was employed to assess whether or not baseline demographics, refractive and biometric data from both groups were significantly different from one another, hypothesized on the basis of the assumption of a normal distribution. Normally and non-normally distributed data were expressed as mean \pm standard deviation (SD) and median [quartiles], respectively. The differences between the two study groups in terms of baseline demographics, refractive and biometric data were analyzed using unpaired t-tests and Mann-Whitney U tests, depending on whether the results of the Kolomogorov-Smirnov test demonstrated that the data were normally distributed or not normally distributed, respectively. Data for the right eye was only used to avoid the confounding effect of using non-independent data from both eyes.³⁰ The level of statistical significance was taken as 5%.

RESULTS

Sixty-nine subjects were recruited for the study between March 2007 and March 2008. Thirty-one children were prospectively allocated to OK and 30 to the SV correction modalities (Figure 2). Eight subjects could not be enrolled in the study because they failed to meet the inclusion criterion for refraction (Figure 2). A normal frequency distribution was found for all baseline demographics, refractive and biometric data in both groups ($P>0.05$), except for visual acuity and the cylindrical refractive component ($P<0.01$). Thus, parametric and non-parametric statistics were employed accordingly to assess differences between groups at baseline. Both study groups were well matched at baseline as no significant differences were found between the two groups neither in demographics, nor in refractive nor in biometric data (Table 4).

Of the 31 subjects that were assigned orthokeratology contact lens wear at baseline, an optimum lens fit was obtained in 21 subjects with the first contact lens fitted in accordance with the Menicon Professional Easy Fit software. Ten subjects required a total of 35 adjustments to attain an optimum lens fit. Of these, 5 subjects required more than 2 contact lens fit changes per eye; 5 subjects required just 1 change each; 2 subjects required 1 change per eye each; 2 subjects required 2 changes per eye each; and 3 subjects required 3 changes each. The reasons for the changes were: undercorrection (13), lens decentration (12) and central island (10). Across the whole group, an average of 1.6 lenses per eye were required to attain an optimum fit. Two subjects broke their lenses (2) and one subject lost one lens in the interim between initial contact lens fitting and final enrolment in the study (Figure 1).

None of the subjects showed corneal staining and no adverse events were found in any of the two groups at baseline.

DISCUSSION

To the authors' knowledge, the MCOS study is the first prospective clinical trial to assess the efficacy and safety of OK lens wear for myopia progression vs. a group of SV spectacle lens wearers. Subjects and parents engaged enthusiastically in the study and responded well to initial introduction of the study design and protocol. The number of contact lenses required to achieve an optimum fit were either lower than³¹ or similar to³² those reported in previous studies.

For the present study (MCOS), the subjects' baseline refractive and biometric data were markedly similar to those from other studies assessing the effects of orthokeratology contact lens wear on myopia progression in children.^{15,16} Also, similar age groups and male/female ratios were employed in MCOS compared to a previous study;¹⁵ another study

TABLE 4

Baseline subjects' demographics, and refractive and biometric data. Normally and non-normally distributed data were expressed as mean \pm standard deviation (SD) and median [quartiles], respectively. "P-value" refers to the statistical P-value; "p-value (units)" refers to the rate of peripheral corneal flattening or steepening

Subjects' demographics	OK	SV	P-value
Age (years)	9.6 \pm 1.6	9.9 \pm 1.9	0.76
Male/female ratio	15/16	15/15	-
Best corrected VA (decimal)	1.00 [1.00 – 1.20] (0.00 logMAR or 20/20 Snellen)	1.00 [1.0 – 1.15] (0.00 logMAR or 20/20 Snellen)	0.25
Refractive components			
Sphere (D)	-2.15 \pm 1.12	-2.08 \pm 1.23	0.79
Cylinder (mm)	-0.25 [-0.50 – 0.00]	0.00 [-0.50 – 0.00]	0.96
Biometric components			
Axial length (mm)	24.40 \pm 0.81	24.22 \pm 0.91	0.40
Anterior Chamber Depth (mm)	3.63 \pm 0.55	3.76 \pm 0.38	0.28
Posterior Segment Depth (mm)	20.76 \pm 0.90	20.46 \pm 0.90	0.17
Flat meridian (D)	42.97 \pm 1.65	43.41 \pm 1.56	0.36
Steep meridian (D)	43.69 \pm 1.46	44.01 \pm 1.77	0.50
Rate of peripheral corneal flattening or steepening (p-value)	0.69 \pm 0.10	0.72 \pm 0.08	0.16

OK: Orthokeratology; SV: single-vision spectacles; VA: visual acuity; D: diopters.

employed an older group and a higher percentage of female subjects.¹⁶

Although we are fully aware of the advantages of random allocation, to our knowledge no previous study on the effects of orthokeratology contact lens wear on myopia progression has used a randomized design. Subjects were not randomized into the two modalities of visual correction in MCOS, but both study groups were well matched, as shown by the similarity between the baseline demographics, refractive and biometric data collected in the two groups. Also, all subjects from both study groups in MCOS were monitored over the same time period. Previous studies have used historical prospective control groups that had not been monitored over the same time period; the latter feature might introduce a higher bias than that due to MCOS's design (e.g. it is possible that children from the historical control groups were monitored during times of different environmental exposure, such as greater levels of close work, compared to the experimental groups). Furthermore, the advantage of MCOS's approach is that it is apposite to actual clinical practice, where practitioners provide various options of visual correction and parents opt for a particular option with the child's approval.

A limitation of this study is that, in terms of statistical power, the sample size employed is theoretically too small to detect the absolute incidence rates of adverse events and discontinuations for each of the two modalities of visual correction under investigation. However, we envisage that it might be sufficiently powered to detect differences in incidence rate between the two groups, as previous studies with samples sizes similar to those used in the present study have effectively demonstrated differences in incidence rate for different contact lens types and wearing regimes.^{27,29}

The primary outcome measure of this study is, however, to compare in white European myopic children axial length growth following OK and SV lens wear over a 2-year period. In this respect, the comparison of axial growth between the two groups is optimized by the use of non-contact partial coherence interferometry, which has a resolution that is an order of magnitude better than that of the 10 Hz ultrasound technique.¹⁸

Since the start of the MCOS, the importance of peripheral imagery in the etiology of myopia has been acknowledged both in animal and in human studies.³³⁻³⁵ Consequently, as an adjunct to the present study, peripheral axial length measures in the horizontal plane (using partial coherence interferometry) will be recorded at the 24-month follow-up visit for both study groups, at successive eccentricities at successive eccentricities from from 10° to 30° temporally and nasally.³⁶

Another constraint of the MCOS study is that the investigator collecting clinical data (CV-C) was not masked with respect to the mode of visual correction. Full masking of data collection in clinical trials such as MCOS presents difficulties, in that the identity of the subject's group can be revealed by a variety of clinical observations such as, for example, limbal or conjunctival staining or corneal topography measurements. Nevertheless, the investigator collecting data was fully aware of the need to disregard where feasible the identity of the subject's group. Furthermore, data analysis was undertaken by an investigator (JS-R) who was masked with regard to the identity of the study groups.

Although some limitations in the MCOS study have been identified, the study offers a number of notable features: a prospective design; well-matched samples and high-resolution ocular biometry measures, which collectively should elucidate whether or not OK contact lens wear is a feasible and safe method for myopia progression control.

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RESEARCH PAPER

The effects of entrance pupil centration and coma aberrations on myopic progression following orthokeratology

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Background: The aim was 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 aged six to 12 years and with myopia of -0.75 to -4.00 DS and astigmatism up to 1.00 DC were fitted with OK contact lenses. Measurements of axial length and corneal topography were taken at six-month intervals over a two-year period. Additionally, baseline and three-month topographic outputs were taken as representative of the pre- and post-orthokeratology treatment status. Pupil centration relative to the CSCLR and magnitude of associated corneal coma were derived from corneal topographic data at baseline and after three months of lens wear.

Results: The centre of the entrance pupil was located superio-temporally to the CSCLR both pre- (0.09 ± 0.14 and -0.10 ± 0.15 mm, respectively) and post-orthokeratology (0.12 ± 0.18 and -0.09 ± 0.15 mm, respectively) ($p > 0.05$). Entrance pupil location pre- and post-orthokeratology lens wear was not significantly associated with the two-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-orthokeratology 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 root mean square (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 orthokeratological treatments at the CSCLR.

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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 to orthokeratology (OK) contact lens wear, where myopia is temporarily corrected through changes in corneal shape. Successful treatment with OK should produce a well-centred even treatment zone that encompasses the pupil.² In fact, a decentred treatment zone is 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 5.0 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 topographic measurements should be centred on the location of the cornea intersecting the entrance pupil of the eye; however, topographic measurements are centred on the coaxially sighted corneal light reflex (CSCLR), also known as the corneal vertex, which is the corneal position intersected by

the optical axis of the corneal topographer, also known as a vertex normal or video-keratographic 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 (usually nasally) due to the special characteristics of ocular alignment and the eccentric foveal position (Figure 1).⁹

Reports demonstrating control of myopic progression in children by 30 to 50 per cent with OK compared with conventional spectacle and soft contact lens wear have attracted much interest.¹⁰⁻¹⁵ The aetiological basis for the efficacy of OK in the control of myopic progression is unclear. Peripheral hyperopic defocus has significance in the development of myopia in animal models^{16,17} and in recent

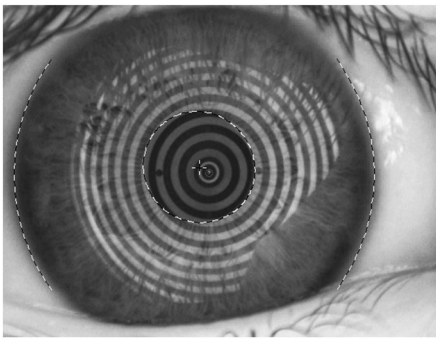


Figure 1. Corneal topographic image of a right eye showing pupil centration relative to the CSCLR. The central circle and the cross denote the CSCLR and the centration of the pupil, respectively. Right and left sides of the image represent nasal and temporal locations, respectively. CSCLR: coaxially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

work in humans, OK reduced peripheral hyperopic defocus¹⁸ compared with some designs of single vision spectacle lenses, which increase peripheral hyperopic defocus¹⁹ and over the naked eye of gas-permeable contact lens wearers, in whom no effect was found upon peripheral refraction.²⁰ Furthermore, in a recent study, corneal power changes induced by OK lens wear were predictive of myopic progression.²¹ More specifically, the latter study found that the larger the change in relative positive peripheral corneal power 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 two-year axial length growth. OK also significantly affects corneal and ocular aberrations^{22–26} and of interest is a recent report on myopic children treated with OK over a one-year period that found axial elongation was significantly correlated with orthokeratology-induced changes in spherical defocus, second-order, coma-like, spherical-like and total higher-order aberrations but not with changes in spherical aberration.²⁷ The change in coma-like aberration had the strongest correlation with the increase in axial elongation. How changes in ocular aberrations induced by OK lens wear may be associated with changes in axial length elongation is unknown; however, the authors of this last 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 myopic 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 centre of the entrance pupil relative to the CSCLR before and after OK lens wear has not been assessed previously, as well as whether such location is associated with the progression of myopia. Furthermore, it is well established that 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, is 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 myopic progression in children.^{14,29–33} The methods have been described in detail elsewhere.^{14,29} In brief, normal, healthy Caucasian European subjects six to 12 years of age with moderate levels of mean spherical myopia (−0.75 to −4.00 D) and astigmatism (up to 1.00 D) and free of systemic or ocular diseases, 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 Cornea and Contact Lens Research Unit (CCLRU) score regarding anterior eye segment signs up to one unit,³⁴ a ‘bull’s eye’ corneal topographic pattern and monocular and binocular visual acuities within one line of the spectacle visual acuity. All patients underwent ocular examinations, including slitlamp examination, manifest refraction, and corneal topography at baseline and after one day, two weeks and three months and at six-month intervals over a two-year period. Axial length was measured at the time of enrolment and six, 12,

18 and 24 months after the initiation of the treatment. Follow-up visits were scheduled to fall within two 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. Fully informed consent and child assent were 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 slitlamp findings occur. Subjects were instructed they could withdraw from the study at any time. The study was conducted in accordance with the Tenets of the Declaration of Helsinki and approved by the Institutional Ethics Committee Review Board of Novovision Ophthalmology Clinic.

Cycloplegic auto-refraction was performed following the instillation of three drops of cyclopentolate HCl one per cent separated by 10 minutes 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 (Topcon RM 8000B, San Diego, California, USA) were taken and a mean obtained.

Measurements of axial length were taken with the Zeiss IOLMaster (Carl Zeiss Jena GmbH, Jena, Germany).³⁶ Three separate measurements of axial length were recorded and a mean obtained. The two-year change in axial length relative to baseline was calculated as a percentage to normalise between-subjects differences in changes in axial length relative to the baseline axial length ($[\text{two-years change in axial length}/\text{baseline axial length}] \times 100$).

Corneal topographic 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 ± 0.10 D 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 three-monthly topographic outputs were taken as representative of the pre- and post-orthokeratology treatment status, as it is well established that OK treatment is

normally completed and stabilised following the first seven to 10 days of lens wear.² Corneal topographs were analysed using Oculus Keratograph software (Version 1.76, Oculus Optikgeräte GmbH, Wetzlar, Germany). The software provides an automatic measurement of the Cartesian co-ordinates of the centration of the entrance pupil relative to the CSCLR (Figure 1).

Individual corneal topographic images were visually inspected to ensure the software had correctly identified the entrance pupil for all subjects. Additionally, vertical and horizontal coma aberrations (that is, C_3^{-1} and C_3^1 , respectively) of the anterior cornea were derived from anterior corneal 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 an eight millimetre diameter. Subsequently, data were divided by the appropriate normalisation 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 the American National Standards Institute.³⁸ The normalisation factors were determined as follows:

$$\text{if } n - 2m \neq 0 \text{ then} \\ \text{Fnm} = \text{square root } (2[n + 1])$$

$$\text{if } n - 2m = 0 \text{ then} \\ \text{Fnm} = \text{square root } (n + 1)$$

Normalised height data were imported to an analytical software program (Zemax, Redmond, Washington, 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 five millimetre entrance pupil following previously described methodology by Gifford and colleagues.²⁵ To calculate coma aberrations for the entrance pupil centre, the cornea's location and tilt for the entrance pupil relative to the CSCLR were entered 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 (that is, C_3^{-1} and C_3^1) and the total root-mean-square (RMS) coma aberration was also assessed (that is, 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 and colleagues⁴⁰ as follows: if $C_3^1 \neq 0$

$$\text{axis} = \tan^{-1} \left(\frac{C_3^{-1}}{C_3^1} \right) (C_3^1 < 0)$$

$$\text{axis} = \tan^{-1} \left(\frac{C_3^{-1}}{C_3^1} \right) + 180 (C_3^1 > 0)$$

if $C_3^1 = 0$

$$\text{angle} = 90 (C_3^{-1} < 0)$$

$$\text{angle} = 270 (C_3^{-1} > 0)$$

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 three 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 analysis:⁴¹ a spherical lens of power M (mean spherical equivalent refraction = sphere + [cylinder/2]); Jackson cross cylinder at axis 0° with power J_0 (= -[cylinder/2] cos [2 × axis]) and Jackson cross cylinder at axis 45° with power J_{45} (= -[cylinder/2] sin [2 × axis]).

Differences between visits (that is, pre-versus post-orthokeratology) were tested using a paired t-test 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 two-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, San Jose,

California, USA). The level of statistical significance was set at five per cent.

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 the other for unknown reasons.³⁰ Subjects who discontinued the study were not included in the data analysis. A total of eight 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-orthokeratology and in one additional subject, the software was unable to identify the entrance pupil post-orthokeratology; in all the cases, entrance pupil centres were manually identified. The subjects' demographic and baseline data have been reported elsewhere.^{14,29} In brief, subjects had a mean age of 9.6 ± 1.6 years and 15 were male. Over two years of OK lens wear, axial length increased from 24.49 ± 0.78 mm to 24.96 ± 0.86 mm ($p < 0.001$).²⁹ Table 1 shows the mean (\pm SD) refractive components, entrance pupil centration and coma aberrations at baseline and after three 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 J_{45} refractive component ($p = 0.021$) compared to baseline. No significant changes were found in the J_0 refractive component following OK lens wear in comparison to baseline ($p = 0.225$) (Table 1).

On average, the centre of the entrance pupil was located superio-temporally with regards to the CSCLR both pre- and post-orthokeratology 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.

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-orthokeratology lens wear (Figure 3, all $p \leq 0.05$). OK lens wear induced a positive shift in vertical coma measured at both the CSCLR and entrance pupil centre in comparison to baseline (Figure 3, $p < 0.001$ and $p = 0.001$); however, no significant differences were found pre- versus post-orthokeratology

	Refractive components (D)			Entrance pupil centration relative to CSCLR (mm)		Coma aberrations (μm)					
	M	J ₀	J ₄₅	x-coordinate	y-coordinate	Vertical (C ₃ ⁻¹)		Horizontal (C ₃ ¹)		Total (RMS)	
						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

OK: orthokeratology, CSCLR: coaxially sighted corneal light reflex, M: mean spherical equivalent refraction, J₀: Jackson cross cylinder at axis 0°, J₄₅: Jackson cross cylinder at axis 45°, RMS: root-mean-square.
Data in bold denotes statistically significant changes in comparison to baseline.

Table 1. Mean (± SD) pre- and post-orthokeratology 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. The post-orthokeratology refractive components were those measured at the three-month follow-up visit.

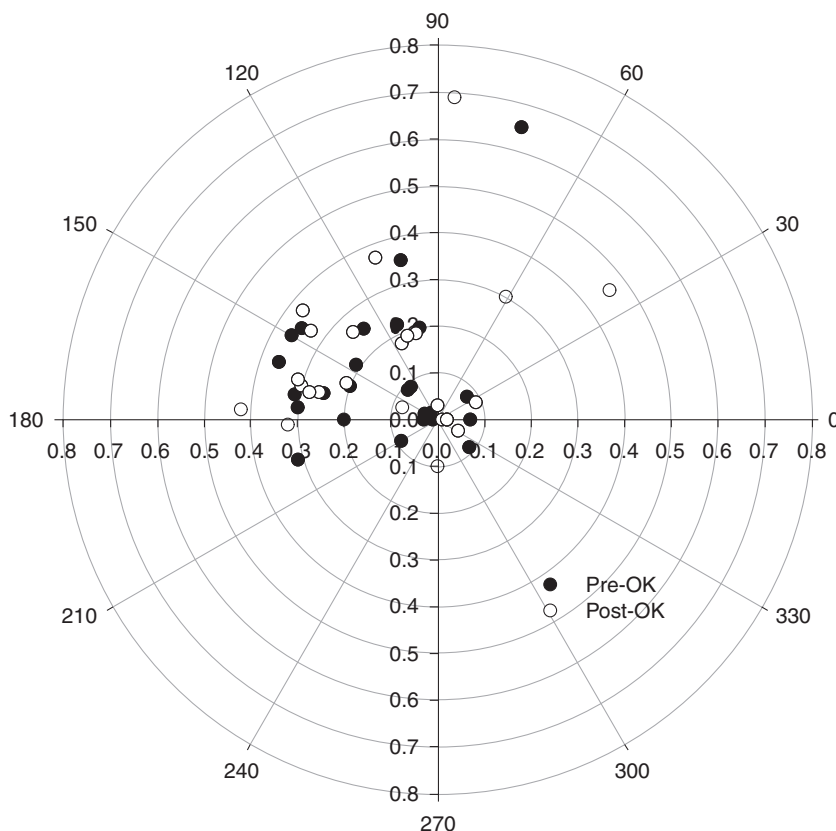


Figure 2. Pupil centration relative to the CSCLR before (black circles) and after (white circles) OK lens wear. Cartesian co-ordinates are expressed in millimetres. The designations 0°, 90°, 180° and 270° denote nasal, superior, temporal and inferior locations, respectively. CSCLR: coaxially sighted corneal light reflex, OK: orthokeratology.

in horizontal or total RMS coma at either the CSCLR or entrance pupil centre (Figure 3, $p < 0.05$ and $p = 0.05$).

Coma angle of orientation measured at the CSCLR changed significantly pre- (mean axis: 120°; range: five to 357°) in comparison to post-orthokeratology (mean axis: 271°; range: four to 358°) ($p < 0.001$); however, coma angle of orientation measured at the entrance pupil did not change significantly pre- (mean axis: 194°; range: four to 295°) in comparison to post-orthokeratology (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-orthokeratology 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-orthokeratology 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-orthokeratology lens wear ($r = 0.893$, $p < 0.001$) as well as with post-orthokeratology 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

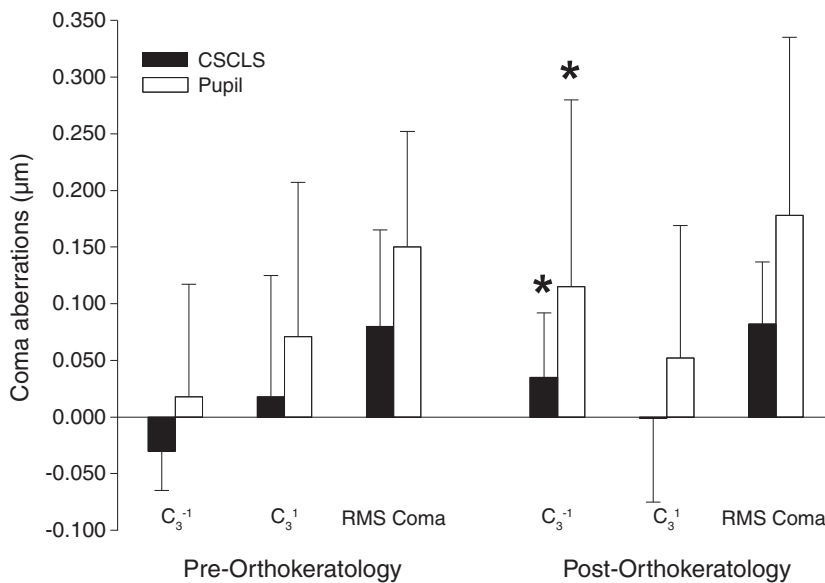


Figure 3. Coma aberrations before and after OK lens wear measured at both the CSCLR (black bars) and entrance pupil (white bars). Error bars represent one standard deviation of the mean. *Denotes statistically significant changes in comparison to baseline. CSCLR: coaxially sighted corneal light reflex,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

CSCLR at baseline were not significantly associated with the two-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 with the two-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 with the two-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 superio-temporal 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 limbal centre.^{7,42,43} Therefore, our results are in relatively good agreement with those previously reported.^{42,43} While previous studies have measured entrance pupil location relative to the limbus or

geometric 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 with significant changes in the refractive status of the eye, the pupil offset relative to the CSCLR was negligible and that probably explains its lack of association with the rate of myopic progression in this study. It should be noted that a significant correlation has been reported previously 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 ocular 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 OK treatments are centred on corneal topographic maps and thus on the CSCLR rather than on the entrance pupil centre. Therefore, OK treatments are likely to be slightly decentred 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 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 and colleagues²² reported statistically significant shifts from positive to negative and vice versa in vertical and horizontal corneal coma, respectively, measured at the CSCLR for a six millimetre pupil diameter. Anera and colleagues²⁴ found a significant negative shift in vertical coma, as well as a significant increase in third order RMS (that is, coma-like) corneal aberrations but no significant changes in horizontal corneal coma measured at the CSCLR for a five millimetre pupil diameter. Gifford and colleagues²⁵ 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 five millimetre pupil diameter. A very recent study by Lian and colleagues²⁶ 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 six millimetre pupil diameter. Comparison of coma aberrations found in OK studies should be carried out with special care, as differences in lens design, instruments and methods (that is, selection of the reference surface, pupil diameter, wavelength and normalisation 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-orthokeratology lens wear were different from those reported previously by Gifford and colleagues,²⁵ both studies found no statistically significant increase in coma angle of orientation post- in comparison to

pre-orthokeratology 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-orthokeratology, respectively.⁴³ 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.²⁸ Although one previous study reported that decentrations less than 0.10 mm in wavefront-guided refractive surgery treatments for myopia can induce significant amounts of aberrations,⁴⁵ another study did not find significant differences in coma aberrations between subjects with small (that is, up to 0.25 mm) versus large (that is, 0.55 mm or more) pupil offsets (defined as the distance in the corneal plane between the entrance pupil and the corneal vertex).⁴⁶

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 induces an increase in corneal spherical aberration,^{22–26} which is balanced to a 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 posterior surface of the crystalline lens.⁴⁸ Decreases in ocular spherical aberration have been associated with myopic 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 (that is, mechanical tension of the ciliary muscle and crystalline lens) and/or accommodative lag (that is, axial hyperopic blur) during near work and thus potentially slow myopic progression.²⁷ In our study, no significant associations were found between the change in coma aberrations following OK lens wear and the two-year change in axial elongation, results which are in agreement with a previous study that investigated the influence of

ocular wavefront aberrations on axial length elongation in myopic children treated with overnight OK over a one-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 (that is, 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 three-month follow-up visit as representative of the corneal shape following OK treatment stabilisation.² Although eight 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 three-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 for example, 0.50 D) in comparison to corneal shape changes induced at the three-month follow-up visit (to compensate for a mean baseline mean spherical equivalent refraction of -2.33 D). In fact, corneal shape (that is, corneal p-value) did not change significantly at follow-up visits after contact lens dispensing. More specifically, the mean corneal p-value changed by up to 0.02 units throughout the study in the eight subjects who 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 that the components of anterior corneal aberration 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 neutralised by the internal aberrations of the eye with seven days of OK lens wear,²⁵ a more recent study found almost identical anterior corneal and ocular aberrations at baseline and following one 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 two-year period. Similarly, coma aberrations measured at the entrance pupil centre were not significantly

correlated with the two-year 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.

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Myopia Control With Orthokeratology Contact Lenses in Spain: A Comparison of Vision-Related Quality-of-Life Measures Between Orthokeratology Contact Lenses and Single-Vision Spectacles

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Purpose: To compare vision-related quality-of-life measures between children wearing orthokeratology (OK) contact lenses and distance single-vision (SV) spectacles.

Methods: Subjects 6 to 12 years of age and with myopia of -0.75 to -4.00 diopters and astigmatism less than or equal to 1.00 diopters were prospectively assigned OK contact lens or SV spectacle correction. A pediatric refractive error profile questionnaire was administered at 12- and 24-month intervals to evaluate children's perceptions in terms of overall vision, near vision, far distance vision, symptoms, appearance, satisfaction, activities, academic performance, handling, and peer perceptions. The mean score of all items was calculated as the overall score. Additionally, parents/guardians were asked to rate their child's mode of visual correction and their intention to continue treatment after study completion.

Results: Thirty-one children were fitted with OK contact lenses and 30 with SV spectacles. Children wearing OK contact lenses rated overall vision, far distance vision, symptoms, appearance, satisfaction, activities, academic performance, handling, peer perceptions, and the overall score significantly better than children wearing SV spectacles (all $P < 0.05$). Near vision and handling were, respectively, rated better ($P < 0.001$) and similar ($P = 0.44$) for SV spectacles in comparison to OK contact lenses. No significant differences were found between 12 and 24 months for any of the subjective ratings assessed (all $P > 0.05$). Parents/guardians of children wearing OK contact lenses rated visual correction method and intention to continue treatment higher than parents of children wearing SV spectacles ($P \leq 0.01$).

Conclusion: The results indicate that the significant improvement in vision-related quality of life and acceptability with OK contact lenses is an incentive to engage in its use for the control of myopia in children.

Key Words: Orthokeratology—Myopia—Quality of life—Contact lenses—Spectacles—Children—Glasses—Pediatric.

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Eye care practitioners may perceive barriers to fitting children with contact lenses in comparison to adults, such as decreased capacity for children to care for contact lenses, more fitting and training time, and inferior risk-to-benefit ratio. Possibly as a result of the latter, children with refractive errors have traditionally been corrected with spectacles, despite many reports of successful contact lens wear in children and adolescents with gas-permeable, soft, and orthokeratology (OK) contact lenses.^{1–8} Studies have shown increasing numbers of contact lenses fitted to individuals younger than 18 years.^{9,10} Furthermore, in comparison to teenagers, it has been shown that children require the same fitting and aftercare time and only 15 additional minutes of training in lens insertion and removal.¹¹

Vision-specific quality of life questionnaires can be used to quantify the benefit of using contact lenses.¹ Generally, such surveys have been developed to undertake assessments in adults^{12–14} and therefore might be of limited value in children as often items refer to adult-related tasks such as, for example, driving. The pediatric refractive error profile questionnaire has been specifically designed to assess children's vision-specific quality of life.^{1,15} The questionnaire has shown significant improvements in vision-specific quality of life in children wearing contact lenses in comparison to children wearing spectacles, particularly in areas related to limitations in activity, appearance, and satisfaction with the correction.^{1,15–17} Although other studies have compared similar aspects of vision-related quality of life between adults wearing soft and OK contact lenses,^{18,19} none has compared children wearing OK contact lenses and spectacles, despite the growing evidence that OK contact lens wear can control myopia progression in children.^{20–23} As, worldwide, OK contact lenses now constitute a relatively large proportion of all contact lens fittings in patients younger than 18 years,¹⁰ it is important to understand how their performance and subjective acceptance compare with those for spectacles; the purpose of this study was to compare vision-related quality-of-life measures between children wearing OK contact lenses and distance single-vision (SV) spectacles.

MATERIALS AND METHODS

This study was part of the Myopia Control with Orthokeratology Contact Lenses Study designed to assess the safety, efficacy, and subjective acceptance of OK contact lenses versus distance

SV spectacles in white European myopic children for a 2-year period.^{23–25}

Methods have been described in detail elsewhere.²⁴ In brief, normal, healthy white European subjects 6 to 12 years of age with moderate levels of myopia (-0.75 to -4.00 diopters [D]) and astigmatism (≤ 1.00 D) and free of systemic or ocular disease were recruited for this study and prospectively assigned OK contact lens or SV spectacle correction. After an unbiased account of the advantages and disadvantages of OK contact lens and SV spectacle modes of vision correction, parents or guardians chose one of the two treatment modalities available.

Spectacles or contact lenses, contact lens care solutions (for the OK group only), and full ocular examinations were provided free of charge to all subjects throughout the study. Full informed parental consent and child assent was obtained before 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 slitlamp findings occur. Subjects were instructed that they could withdraw from the study at any time. 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.

At the recruitment session, all subjects underwent a full anterior eye biomicroscopy, indirect fundus microscopy, binocular vision, and refractive evaluation to elucidate whether they were eligible to participate in the study; baseline study measurements were then recorded in eligible subjects.

Subjects in the SV group were prescribed distance SV spectacles having the highest positive spherical power consistent with optimum visual acuity and asked to wear the spectacles at all times. Subjects in the OK group were fitted with Menicon Z Night contact lenses using Menicon Easy Fit Software (Menicon, Co, Ltd, Nagoya, Japan). After initial contact lens fitting, all contact lens subjects were instructed on procedures for insertion, removal, and cleaning/disinfection on the first day and instructions were reinforced at subsequent visits. Subjects were provided with MeniCare Plus multipurpose solution for the daily cleaning, rinsing, and disinfecting of their contact lenses and Menicon Progent intensive cleaner for use once a week (Menicon, Co, Ltd).

Subjects in the OK trial were informed that contact lenses should be inserted everyday just before going to sleep and removed immediately on waking the following morning. Subjects were requested to attend no later than 2 hours after lens removal on the morning after the first night of lens wear; the requirement also applied to all subsequent visits. A subsequent visit was scheduled 3 weeks later to ascertain whether the contact lens fitting was clinically acceptable; otherwise, new contact lens specifications were calculated and ordered. Subjective refraction was undertaken to ascertain whether changes in contact lens' back surface design were required to correct a change in refraction. A successful OK contact lens fit was considered to be that which after 3 weeks of lens wear showed CCLRU anterior eye signs less than or equal to 1 unit,²⁶ a "bull's eye" corneal topography pattern and monocular and binocular distance spectacle visual acuities within ± 1 line of the best-corrected decimal acuity.

It was made clear to all OK subjects that contact lenses should be removed if any problems were experienced. Subjects and their parents/guardians were instructed on steps to take in the event of an adverse reaction and instructed at length to assure adherence to the study protocol; compliance was monitored closely by one of the

authors (C.V.-C.). Subjects from both study groups were instructed to report to the clinic immediately should a reaction appear to be abnormal (e.g., red eye, pain, unusual discomfort or eye secretions).

After initial enrollment, subjects were followed at 1-, 6-, 12-, 18-, and 24-month intervals. 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 refraction²⁷ at any of the follow-up visits was considered clinically significant and was remedied by supplying contact lenses or spectacles made to the new prescription.

The pediatric refractive error profile survey was used to compare the vision-specific quality of life between children in the OK and SV groups at the 12- and 24-month visits.^{1,15} The survey consisted of 26 statements scored from 1 (poor quality of life) to 5 (good quality of life), then scaled from 0 to 100 by subtracting 1 from the raw score of each question and multiplying by 25. The mean score of all items was calculated as the overall score. The survey included 11 scales: overall vision, near vision, far distance vision, symptoms, appearance, satisfaction, activities, academics, handling, peer perception, and overall score. These surveys were identical for both study groups apart from the words "contact lenses" and "spectacles" being interchanged depending on the participating study group. Two additional questions (numbers 27 and 28) were added to the handling scale:

27. The habitual handling of my contact lenses/spectacles is normally done by my parents.

28. I usually perform the handling of my contact lenses/spectacles.

The surveys were requested to be answered by the children, and parents/guardians were asked not to participate.

The following two supplementary questions were also included in the survey to be answered by the parents/guardians:

1. I think orthokeratology contact lenses/spectacles are an excellent method of visual correction.
2. Once this study is finished, I intend to continue offering this method of visual correction to my child.

Statistical Analysis

Statistical analyses were conducted using SPSS 15.0 (SPSS, Inc, Chicago, IL). The level of statistical significance was taken as 5%. Differences between groups over time in vision-related quality-of-life measures in children and in parents/guardians' acceptance of the treatment options were assessed using repeated measures analysis of variance. Visual correction type (i.e., OK contact lenses vs. SV spectacles) was chosen as the factor of interest and time as the repeated measure. Equality of variances and sphericity were tested using the Levene and Mauchly tests, respectively. Data are expressed as mean \pm standard deviation.

RESULTS

Sixty-nine subjects were initially recruited for the study, but eight subjects could not be enrolled because they failed to meet the inclusion criterion for refraction. Thirty-one subjects were prospectively allocated to the OK trial and 30 to the SV trial. No statistically significant differences were found in any of the baseline demographics and refractive and biometric data between groups.²⁴ Furthermore, the distributions of spherical and cylindrical refractive errors were similar between the 2 groups (Figs. 1 and 2).

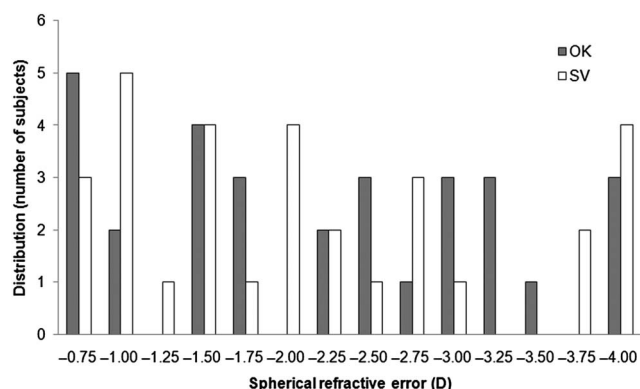


FIG. 1. Distribution of spherical refractive errors for the orthokeratology (OK) contact lens and single-vision (SV) spectacle groups.

Two and 6 children from the OK and SV groups, respectively, discontinued the study. In the OK group, one child discontinued the study at 6 months and another child at the 18-month follow-up visit. In the SV group, 3, 2, and 1 children discontinued the study at the 6-, 18-, and 24-month follow-up visits, respectively.

Children wearing OK rated overall vision, far distance vision, symptoms, appearance, satisfaction, effect on activities, academic performance, handling, peer perceptions, and the overall score significantly better than children wearing SV spectacles (Fig. 3, all $P < 0.05$). Near vision and handling were, respectively, rated better ($P < 0.001$) and similar ($P = 0.44$) for SV spectacles in comparison to OK contact lenses. No significant differences were found between 12 and 24 months for any of the subjective ratings assessed (all $P > 0.05$).

Parents/guardians of children wearing OK contact lenses rated visual correction method and intention to continue treatment higher than parents/guardians of children wearing SV spectacles (Fig. 4, both $P = 0.01$), but no significant differences were found over time.

DISCUSSION

The results of the study show significantly better vision-related quality of life in children wearing OK contact lenses in comparison

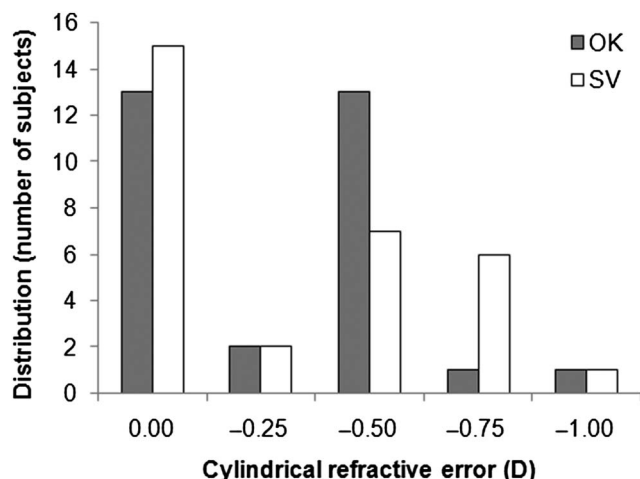


FIG. 2. Distribution of cylindrical refractive errors for the orthokeratology (OK) contact lens and single-vision (SV) spectacle groups.

to children wearing SV spectacles for all survey scales, with the exception of near vision and handling that were, respectively, rated better and similar for SV spectacles in comparison to OK contact lenses. The latter is in agreement with previous studies that found increased vision-related quality of life in children wearing soft contact lenses in comparison to spectacles.^{1,15} Orthokeratology contact lenses have also been reported to be preferred to soft contact lenses in an adult population with regard to limitations on activity, symptomatology, and dependence on correction, whereas soft contact lenses have been preferred over OK contact lenses in terms of glare.^{18,19} Furthermore, when subjects of the study of Lipson et al¹⁹ were questioned on completion whether they preferred OK or soft contact lenses, 67% of the respondents reported a preference for OK contact lenses. The preference for contact lens wear in comparison to spectacle lens wear might be the result of spectacle lens wear being associated to introversion,²⁸ anxiety,²⁹ and less attractiveness.³⁰

Better overall and far distance vision was found with OK contact lenses in comparison to spectacles in this study. Orthokeratology contact lenses have been shown to provide similar visual acuity levels than spectacle lens wear.³¹ However, it appears that OK contact lenses might provide better correction of peripheral vision³² than spectacle lens wear.³³

That near vision was worse for OK contact lenses versus SV spectacles might be related to how OK contact lenses correct refractive error. Typically, OK contact lenses are fitted to over-correct refractive error to account for the diurnal regression of corneal power and shape and thus myopia.³⁴ It is, therefore, possible that the greater amount of accommodation exerted for near tasks might alter the normal profile of oculomotor responses for sustained near vision.

Most survey scales were rated significantly better with OK contact lenses in comparison to SV spectacles, particularly those related to symptoms, appearance, and effect on activities,^{18,19} a finding that might be because of the freedom from lens wear and perceived enhancement of cosmetic appearance that overnight OK contact lens correction allows during the day.

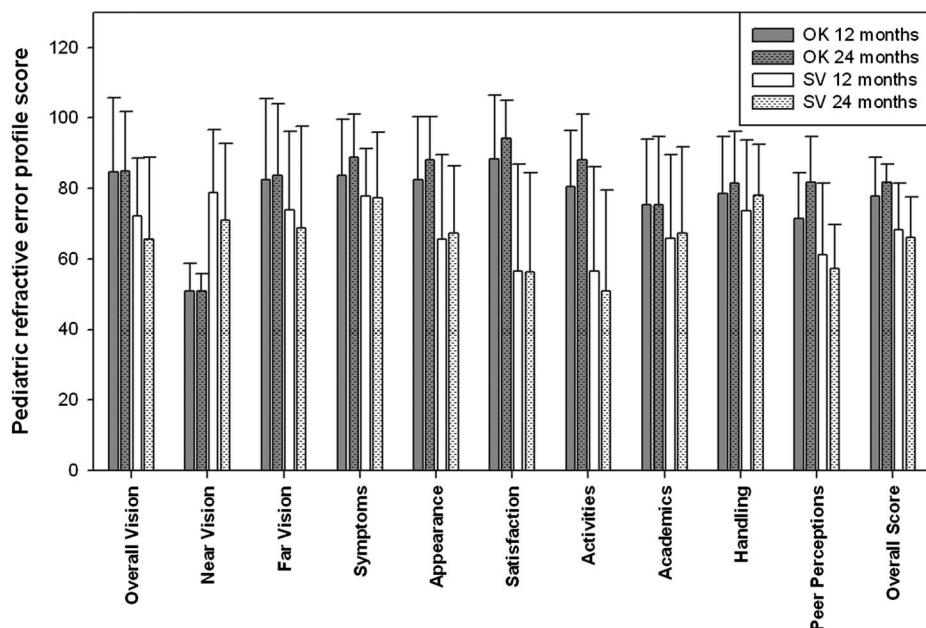
The fewer symptoms and less dependence on correction found with OK contact lenses in comparison to SV spectacles agree with previous reports^{18,19} and are likely to be related to the fact that OK contact lenses were worn overnight and removed in the morning.

The better rating of academic performance with OK contact lenses in comparison to SV spectacles could be attributed to a failure of children allocated to SV spectacles to actually wear their spectacles during school and homework time. On the contrary, subjects allocated to OK contact lens wear were provided with adequate visual acuity for the rest of the day on lens removal.

Similar ratings were found between both treatment groups with respect to handling. Numerous studies have shown children to be capable of successfully handling all types of contact lenses, including soft, gas-permeable, and OK contact lenses.¹⁻⁷ It is often assumed that spectacles are easier to handle in comparison to contact lenses. However, similar ratings of handling have been reported between children wearing soft contact lenses and spectacles.¹⁵ Furthermore, OK contact lenses are normally handled on fewer occasions (i.e., before going to sleep and on awaking) than spectacles, which can be handled at various times during the day.

Parents/guardians of children wearing OK contact lenses rated visual correction method and intention to continue treatment

FIG. 3. Vision-specific quality-of-life ratings for the orthokeratology (OK) contact lens (gray) and single-vision (SV) spectacle (white) groups. The plain and dashed bars represent the 12- and 24-month results, respectively.



higher than parents/guardians of children wearing SV spectacles. Although it might have been envisaged that parents/guardians would worry about their children being fitted with overnight OK contact lenses, such fears diminished as the study progressed and it became evident that the procedure was providing adequate levels of visual correction and limited complications.²⁵

The survey scales seem to change during the first 3 months of contact lens wear.^{1,15} That no change was found in any of the survey scales between 12- and 24-month follow-up suggests that both children's and parents/guardians' self-perceptions of OK contact lenses and SV spectacles develop relatively soon after treatment allocation and are maintained over time. Furthermore, self-concept esteem has been reported to change very little over time, even for children as they become teenagers.^{35,36}

A limitation of this study was that the pediatric refractive error profile survey used has not been previously validated. However, previous studies have demonstrated the survey to be sensitive in detecting differences in survey scales between children wearing soft contact lenses and spectacles.^{1,15} Another limitation of the study was that survey scales were not assessed at the beginning of the study, and thus, it was not possible to compare changes from baseline to the 12- and 24-month follow-up visit. However, the purpose of this study was to compare vision-related quality-of-life measures between children wearing OK contact lenses and SV spectacles and not changes from baseline.

In summary, this study demonstrates that, in comparison to SV spectacles, both children and parents/guardians respond preferentially to clinical management using OK contact lenses. The significant improvement in vision-related quality of life and acceptability with OK contact lenses is, when coupled with its well-established safety^{2,25} and efficacy in the temporary reduction of myopia,³¹ an incentive for practitioners to engage in its use for the control of myopia progression in children.²⁰⁻²³

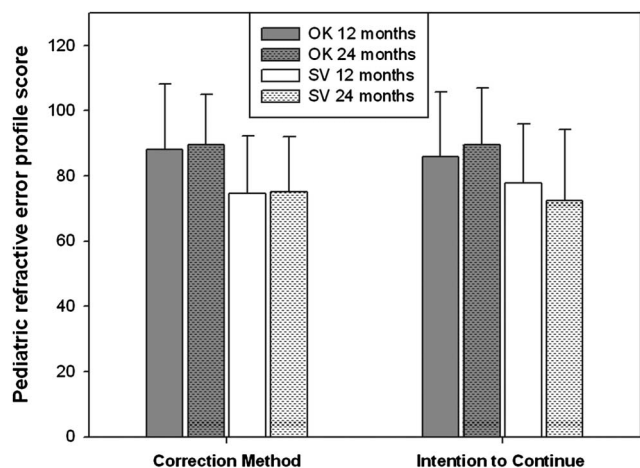


FIG. 4. Parents/guardians' ratings of their child's method of visual correction and their intention to continue treatment after study completion for the orthokeratology (OK) contact lens (gray) and single-vision (SV) spectacle (white) groups. The plain and dashed bars represent the 12- and 24-month results, respectively.

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