

# 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  $\leq 1.00$  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.<sup>1,2</sup> Furthermore, high levels of myopia (i.e.,  $\leq -6.00$  diopters [D]) are associated with a range of ocular pathologies, such as vitreous and retinal detachment, macular degeneration, and glaucoma.<sup>3-6</sup> Therefore, myopia can incur significant ocular-related morbidity and substantial healthcare costs.<sup>7,8</sup>

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Several treatment therapies have been used in the past with limited success to eliminate or, at least, reduce myopia progression.<sup>9-11</sup> Spectacle intervention does not appear to significantly affect the progression of human myopia.<sup>12</sup> Bifocal and progressive addition spectacle lens wear have shown very modest treatment effects in controlling myopia progression,<sup>13-17</sup> although the effect is enhanced in children with larger accommodative lags in conjunction with near esophoria, short reading distances, and low baseline myopia.<sup>18</sup> 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.<sup>19</sup> Whereas progressive addition lenses produced a slowing of progression that reached statistical significance, the effect was not considered to be clinically significant.<sup>19</sup>

Although it has been reported that soft single-vision spherical contact lenses do not affect the progression of myopia in children and young adolescents,<sup>20,21</sup> 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.<sup>22</sup> 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.<sup>23</sup>; 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.<sup>24-28</sup> However, most of these studies have limitations in study design.<sup>29</sup> 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.<sup>30</sup> At beginning of this decade, a retrospective study<sup>31</sup> and a case report<sup>32</sup> suggested that modern orthokeratology<sup>33</sup> 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.<sup>34-36</sup>

Over a 2-year period, Cho et al.<sup>34</sup> 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 coworkers<sup>35</sup> 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.<sup>36</sup> 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).<sup>34,35</sup> Childhood myopia has been shown to progress faster between 6 to 13 years of age and to stabilize thereafter.<sup>37–39</sup> 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.<sup>36</sup>

The above three studies differ in methodology and design. Cho et al.<sup>34</sup> and Walline et al.<sup>35</sup> 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).<sup>40</sup>

Cho et al.<sup>34</sup> and Kakita et al.<sup>36</sup> 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.<sup>35</sup> Since the baseline level and progression of myopia in East Asian children are generally significantly greater than those for children from Western countries,<sup>1,2</sup> 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.<sup>41</sup>

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.<sup>42</sup> 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 ( $\leq 1.00$  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.<sup>36</sup> 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 refraction<sup>43</sup> 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).<sup>40</sup> 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).<sup>44</sup> 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	P 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 (P 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  $\chi^2$  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).<sup>42</sup>

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 (P 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. <sup>39</sup>	OK vs. SV	0.21	0.18	0.28	0.25
Walline et al. <sup>40</sup>	OK vs. SCL	...	0.15	...	0.32
Kakita et al. <sup>41</sup>	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.<sup>33</sup> 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.<sup>31,32</sup> 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.<sup>34-36</sup>

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.<sup>33,45,46</sup> In agreement with results of previous studies,<sup>37-39</sup> 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.<sup>34-36</sup> 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.<sup>47</sup> 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.<sup>47,48</sup>

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.<sup>49-53</sup> 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.<sup>54,55</sup> 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.<sup>47,48,56</sup> Two recent investigations have specifically assessed the effect of peripheral refraction on development of central refractive error. Measuring peripheral refraction at a single point  $30^\circ$  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.<sup>57</sup> 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.<sup>58</sup>

Recent work also shows that OK contact lens wear reduces peripheral hyperopic defocus<sup>59</sup> compared with SV, which increases peripheral hyperopic defocus,<sup>60</sup> and gas-permeable contact lens wear, which has no effect in peripheral refraction.<sup>61</sup> 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.<sup>36,62</sup> Future studies should consider randomization to allocate subjects to treatment groups.

In summary, the present study (and that of Kakita et al.<sup>36</sup>) 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

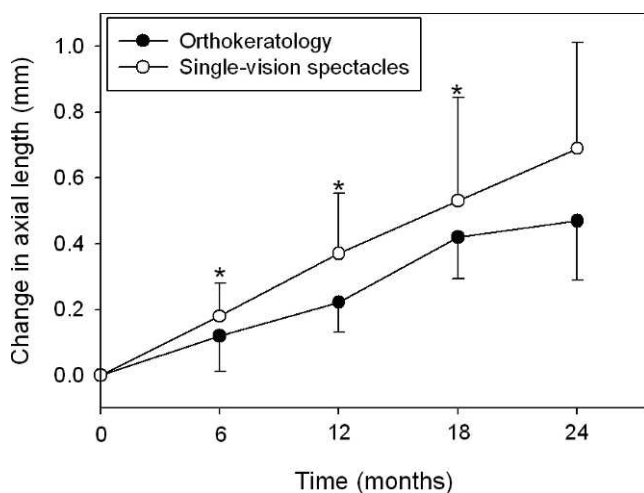


FIGURE 1. Changes (mean  $\pm$  SD) in axial length (mm) from baseline over time. Asterisk indicates statistically significant interactions between refractive correction and time at 6-, 12-, and 18- vs. 24-months (all  $P < 0.05$ ).

discontinuation of long-term lens wear on subsequent progression of myopia.

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