

Modeling and Prediction of the Immediate and Short-Term Effect of Myopic Orthokeratology

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Purpose: To characterize the clinical changes occurring in the initial phase of the orthokeratology (OK) treatment for myopia correction, developing a model of prediction of the refractive changes in such phase.

Methods: Prospective study enrolling 64 eyes of 32 patients (range, 20–40 years) undergoing myopic OK treatment with the reverse geometry contact lens CRT (Paragon Vision Science). Changes in uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA), refraction, corneal topography, ocular aberrations, and corneal epithelial thickness were evaluated during the first hour of OK lens wear and after 1 week of OK treatment. Multiple linear regression analysis was used to obtain a model to predict the short-term refractive effect of OK.

Results: The UCVA improved at each visit, reaching normal visual acuity values after a week ($P < 0.001$) of OK treatment, which was consistent with the significant spherical equivalent (SE) reduction and central flattening ($P < 0.001$). Multiple linear regression analysis revealed that one night change in refraction ($\Delta R \times 1N$) could be predicted according to the following expression ($P < 0.001$, $R^2 = 0.686$): $\Delta R \times 1N = 1.042 + 0.028 \times \text{Age} + 1.014 \times \text{BCET}$ (baseline central epithelium thickness) $- 0.752 \times \text{BKm}$ (baseline mean keratometry) $- 1.405 \times \text{BSE}$ (baseline SE) $+ 1.032 \times \Delta R \times 1h$ (change in SE after 1 hr of OK lens use). Similarly, a statistically relevant linear relationship was obtained for predicting the refractive change after 1 week ($\Delta R \times 1W$) of OK use ($P < 0.001$, $R^2 = 0.928$): $\Delta R \times 1W = 3.470 - 1.046 \times \text{BSE} - 1.552 \times \text{BBCVA}$ (baseline BCVA) $- 0.391 \times \text{BKm} + 0.450 \times \Delta R \times 1h$.

Conclusions: The immediate and short-term refractive effects of myopic OK with the reverse geometry contact lens CRT can be predicted with enough accuracy from baseline and first trial visits data.

Key Words: Orthokeratology—Reverse geometry contact lens—Myopia—Corneal topography—Pachymetry.

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Orthokeratology (OK) is a corneal refractive treatment for the correction of myopia that has demonstrated to be safe and effective since many years ago.¹ This technique generates changes in corneal epithelial thickness profile, with a redistribution of the epithelial layer from the center to the midperiphery.^{2–4} Specifically, several studies have demonstrated that there is a thinning of the central epithelium, whereas the midperipheral area of this layer thickens due to the effect of the hydrodynamic forces associated with the OK treatment.⁴ These changes are reversible as the cornea returns to its original state when the lens is removed.

Unfortunately, the exact mechanism by which OK lenses change the shape and thickness of the cornea is not completely predictable in the initial phase of the treatment, with some eyes showing a faster response than others for the same level of refractive correction. It has been suggested that the mechanical properties of the cornea may play a fundamental role on this variability.^{5,6} However, the measurement systems that are currently available for characterizing the corneal biomechanical response did not seem to be adequate for evaluating the real impact on the mechanical properties of the cornea after OK.⁷

From the microstructural perspective, previously published studies have shown that OK treatment induces a series of morphological modifications associated with this procedure, such as changes in the basal cells of the epithelium (height and width) and anterior stroma, activation of keratocytes, or decreased nerve density of the sub-basal plexus leading to reduced corneal sensitivity.^{4,8,9} Still, it is not fully understood how the OK lenses change the thickness of the corneal epithelium during the first phase of the treatment or how these changes are correlated to topographic and refractive changes.

Considering this, the goal of this study was to characterize the visual, refractive, tomographic, and corneal epithelial changes occurring in the initial phase of the treatment, developing a model of prediction of the refractive changes occurring during this period. This is a critical aspect to give real expectancies to patients treated with OK because they are commonly worried about how long will the treatment take to provide an acceptable vision allowing spectacle independence during the day.

METHODS

Sample

A prospective study was conducted at the Optometric Clinic of the University of Alicante (Spain), recruiting a total of 32 patients between 20 and 40 years, with a gender-balanced distribution (17 women and 15 men). Before their inclusion in this study, all

patients were informed about the methodology of this study and the possible risks that may arise from the use of lenses. After this, a written informed consent was given to all of them to authorize the procedure if they agree to participate. This study (CEIm 2020-030, ISABIAL 190760) was approved by the ethics committee for medical research of the Health Department of Alicante (General Hospital, Alicante, Spain) and was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria were adults with less of 6 diopters (D) of myopia, less than 1.50 D of astigmatism including with-the-rule, against-the-rule and oblique axes, and a best-corrected visual acuity (BCVA) of 0.0 logMAR under monocular and binocular conditions at both near and distance vision. Exclusion criteria were eyes with active ocular pathology or previous refractive surgery and corneal diameters of 11 mm or below. Patients using contact lenses were asked to discontinue their use between two or 4 weeks before the first examination depending on whether they were using soft contact lenses (2 weeks) or rigid gas-permeable contact lenses (4 weeks).

Lens Characteristics and Cleaning Guidelines

The lens fitted in this study was the reverse geometry lens CRT (Paragon Vision Science, Gilbert, AZ) made of the Paragon HDS 100 material (paflucocon D), with an oxygen permeability (DK/t) of 140 barrier. All the CRT lenses had a diameter of 10.50 mm. The initial fit of all CRT lenses was performed following the empirical fitting guidelines provided by the laboratory. In particular, the trial lens was selected with the fitting rule of the manufacturer, introducing the average corneal curvature (Kmean) and the patient's spherical equivalent (SE), as requested by the fitting guidelines. To ensure a right fit of the lenses and to detect and solve any decentration problem, a slitlamp examination was performed for each trial lens, including a comprehensive analysis of the fluorogram. If the fit was not optimal, the parameters were recalculated again.

All patients were given a peroxide solution for cleaning and preserving the OK lenses. In addition, for the use and rinsing of the OK lenses, patients used saline solution without preservatives.

Clinical Protocol

The clinical protocol aimed at evaluating the effect of OK treatment at different stages. For this purpose, the protocol was divided into three main phases:

- (1) Phase 0: Prefitting visit.
- (2) Phase 1: Immediate effect of the OK treatment (Lens on the eye; 1 hr of use). This phase will help to understand the remodeling phase that occurs under the closed eye condition.
- (3) Phase 2: Short-term effect of the OK treatment without the lens (Lens OFF; 1 hr, 1 night and 1 week of use). This phase will help to understand how the cornea recovers during the day after removing the lens.

In phase 0, all patients came in for a prefitting visit in which the following parameters were measured: objective refraction by retinoscopy, subjective refraction, BCVA (logMAR BCVA), and uncorrected visual acuity (logMAR UCVA) at distance and near vision using a Snellen chart. Corneal topography, keratometry, and ocular aberrometry (5-mm pupil) were measured using a Visionix

VX120 multidagnostic device (Visionix Luneau, France). For each patient, the OK trial lenses were calculated using all these baseline parameters.

The corneal epithelial thickness was characterized using a spectral domain optical coherence tomography (OCT) device, the 3D OCT-1 Maestro System (Topcon Medical Laser Systems). The OCT was set to radial mode to measure the thickness along different meridians from the corneal center up to 3 mm in radius. Using the OCT's system caliper, the same experienced researcher (A.S.) performed five manual measurements along the horizontal and vertical meridians in three different corneal regions: the center (CET; R=0 mm), paracentral area (PCET; R=2 mm), and midperiphery (MPET; R=4 mm). Paracentral epithelial thickness (PCET) and MPET were measured at both the nasal and temporal areas, and the average of them was calculated. Average thickness values were determined for each five consecutive measurements, meridian, and region. Finally, thicknesses for each meridian were aggregated by the region (CET, PCET, and MPET) to get a single representative value of epithelial thickness per region.

After the prefitting visit, phase 1 evaluated the immediate effect (1 hr) of the OK treatment on corneal epithelium changes. First, participants were required to wear the OK lenses for 60 min with their eyelids closed to simulate the loading effect that occurs during sleep. Second, immediately after and with OK lenses in situ, the corneal epithelium thickness was evaluated with the OCT every 20 min using the previously described protocol during a period of 60 min. After these measurements, a fluorescein (NaFl) pattern evaluation of the lens was performed. Third, patients were required to remove OK lenses before evaluating their UCVA, residual refraction, topographic, aberrometric, and pachymetric changes (this time without the lenses). Ocular surface integrity was also verified with biomicroscopy and NaFl instillation.

In phase 2, the first measurement was made after finishing phase 1, when the lens was removed after 1 hr of use. Refractive, aberrometric, topographic, and epithelial thickness changes were measured again although without the lens in the eye. After this, patients were followed-up after one night and 1 week of treatment (short-term effect), performing at these visits the same clinical tests as in the prefitting evaluation. Whenever a fitting parameter change was needed, the examination protocol was restarted from phase 1 and measurements were re-taken.

Statistical Analysis

The statistical analysis was performed with the statistical software SPSS version 26.0 (IBM, Armonk, NY). Orthokeratology treatment was performed in both eyes of each subject, but data from right eyes were only considered for statistical analysis to avoid the potential bias associated with the correlation of the data of both eyes of each subject. The descriptive statistical data were presented as mean \pm SD and median \pm range. As a previous step, normality of data was assessed using a Kolmogorov-Smirnov test. Then, a repeated-measures analysis of variance with zero independent variables was used to study changes on the evaluated parameters across visits. A *P* value lower than 0.05 was considered as statistically significant.

As a first attempt to establish an empirical prediction of the orthokeratological effect for each visit, a multiple linear regression analysis with backward elimination was used to correlate the change in refraction with baseline clinical parameters. An analysis of the residuals and outliers (Cook's distance) was performed to

confirm the general assumptions of the multiple regression analysis. Finally, the Durbin–Watson test and the calculation of the variance inflation factor (VIF) were calculated to confirm the absence of correlation between the errors and to study whether there was multicollinearity.

The estimation of the required sample size was based on previous research on initial refractive changes related to ortho-k.³ The online GRANMO sample size calculator was used (<https://www.imim.es/ofertadeserveis/software-public/granmo/>). Considering an α -error of 0.05, a β -error of 0.20, and a patient drop-out rate of 30%, an initial sample size of 31 patients was required to detect 0.50 D changes in SE after 1 week of use (given a SD of ± 0.64 D).

RESULTS

This study finally included 32 patients (32 eyes), 15 men (46.9%) and 17 women (53.1%), with an mean age of 28.5 ± 5.4 years. No complications related to the use of OK lenses occurred during the follow-up period. Only three patients showed corneal staining in the central area after the first night of use, but they were resolved during the first week of use with the only use of preservative-free artificial tears. The Kolmogorov–Smirnov test confirmed the normality of data distributions for all the parameters, except for visual acuity and sex ($P < 0.001$).

Table 1 summarizes the mean \pm SD, median (\pm range) of refractive, visual, topographic, and aberrometric parameters at all visits. All parameters experienced statistically significant changes between visits, except coma aberration, which only showed a statistically significant change after 1 week of OK treatment ($P < 0.05$). The UCVA improved at each visit, reaching normal visual acuity values after a week of OK treatment ($P < 0.05$). The SE changed to less negative values, with the greater change in magnitude observed after 1 week of use ($P < 0.001$). The mean keratometry also decreased progressively at each visit ($P < 0.001$). Corneal asphericity changed significantly to positive values ($P < 0.001$), which implies a change of the corneal shape to an oblate profile. Regarding aberrometry, fourth order spherical aberration, coma, and high-order aberrations increased their values significantly ($P < 0.05$).

Table 2 presents the mean \pm SD and median (\pm range) for epithelial thickness changes measured during the first hour with the OK lens on the eye. There was a statistically significant change in CET at 40 and 60 min, with a thinning of the central area ($3.08 \pm 0.62 \mu\text{m}$, $3.08 \pm 0.60 \mu\text{m}$, respectively, $P < 0.001$). Paracentral epithelial thickness did not experience a significant change, although there was significant epithelial thickening after 20 min of use ($P < 0.05$). MPET showed a significant thickening at 40 and 60 min of use ($-1.99 \pm 0.62 \mu\text{m}$, $-1.81 \pm 0.60 \mu\text{m}$, respectively, $P < 0.05$). Changes in the epithelial thickness for each region and time are graphically displayed in Figure 1.

Table 3 presents epithelial changes for the rest of the visits in which patients were not wearing their OK lenses, that is, without wearing the lenses. CET was the parameter presenting the higher statistically significant intervisit difference ($P < 0.001$), with a thinning of the corneal epithelium of up to $8.17 \pm 0.59 \mu\text{m}$ after 1 week. Paracentral epithelial thickness only presented a statistically significant thinning after 1 week ($4.45 \pm 0.89 \mu\text{m}$, $P < 0.001$). Finally, although MPET showed a statically significant change after a 60-min use ($-2.09 \pm 0.56 \mu\text{m}$, $P < 0.05$), epithelium thickness returned to baseline values in just 1 hour after removing the OK lens (see Fig. 2).

Multiple linear regression analysis confirmed that an orthokeratological effect prediction equation could be obtained, defining the 1-night change in refraction ($\Delta R \times 1N$), which was as follows ($P < 0.001$, $R^2 = 0.771$, adjusted $R^2 = 0.716$, Durbin–Watson: 1.931):

$$\Delta R \times 1N = 1,042 + 0.028 \times \text{Age} + 1.014 \times \text{BCET} - 0.752 \times \text{BKm} - 1.405 \times \text{BSE} + 1.032 \times \Delta R \times 1 \text{ h}$$

where BCET is the baseline central epithelium thickness, BKm is the baseline mean keratometry, BSE is the baseline SE, and $\Delta R \times 1 \text{ h}$ is the change in SE after 1 hour of OK lens use.

The normality of the unstandardized residuals distribution ($P = 0.367$) and the absence of outliers (mean Cook distance = 0.023 ± 0.031) confirmed the homoscedasticity of this model. Similarly, no multicollinearity was detected in the model (VIF between 1.053 and 1.175).

Similarly, another statistically significant linear relationship was obtained for predicting the refractive change after 1 week ($\Delta R \times 1W$) of OK use ($P < 0.001$, $R^2 = 0.946$, adjusted $R^2 = 0.934$, Durbin–Watson: 1.795):

TABLE 1. Descriptive and Comparative Values for the Baseline (Pretreatment) Data and After Each Visit

Mean (\pm SD)								
Median (\pm Range)	Baseline	After 1 hr	P	After 1 Night	P	After 1 Week	P	
SE (D)	-2.10 (1.46) -1.75 (4.75)	-1.64 (1.51) -1.00 (5.25)	<0.001 ^a	-1.30 (1.34) -0.82 (4.00)	<0.001 ^a	-0.25 (0.67) -0.25 (2.50)	<0.001 ^a	
UCVA (logMAR)	0.54 (0.40) 0.42 (1.20)	0.47 (0.42) 0.30 (1.30)	<0.05 ^a	0.37 (0.38) 0.18 (1.30)	<0.001 ^a	0.09 (0.20) 0.05 (1.10)	<0.001 ^a	
Km (D)	43.53 (1.61) 43.70 (6.75)	42.90 (1.57) 43.18 (7.63)	<0.001 ^a	42.69 (1.65) 42.81 (6.00)	<0.001 ^a	42.14 (1.34) 42.00 (5.63)	<0.001 ^a	
Q	-0.22 (0.16) -0.19 (0.56)	0.16 (0.28) 0.14 (1.64)	<0.001 ^a	0.28 (0.38) 0.26 (1.58)	<0.001 ^a	0.63 (0.47) 0.51 (2.00)	<0.001 ^a	
SA (μm)	0.02 (0.05) 0.01 (0.18)	0.05 (0.07) 0.05 (0.23)	<0.05 ^a	0.09 (0.09) 0.07 (0.36)	<0.001 ^a	0.16 (0.13) 0.14 (0.47)	<0.001 ^a	
Coma (μm)	0.13 (0.08) 0.10 (0.39)	0.13 (0.08) 0.12 (0.38)	1.00	0.14 (0.09) 0.14 (0.37)	0.393	0.18 (0.14) 0.15 (0.57)	<0.05 ^a	
HOAs (μm)	0.19 (0.08) 0.10 (0.33)	0.22 (0.11) 0.18 (0.48)	<0.05 ^a	0.27 (0.13) 0.22 (0.50)	<0.05 ^a	0.31 (0.17) 0.29 (0.41)	<0.001 ^a	

^aStatistical significance with $P < 0.05$.

D, diopters; HOAs, high-order aberrations; logMAR, logarithm of the minimum angle of resolution; Km, mean keratometry; Q, asphericity; SA, spherical aberrations; SE, spherical equivalent; UCVA, uncorrected visual acuity

TABLE 2. Phase 1 One-Hour Molding Changes on Epithelial Thickness (Lens ON)

Mean (±SD)								
Median (± Range)	Baseline	20 min	P	40 min	P	60 min	P	
CET (μm)	47.98 (4.10)	46.13 (4.21)	0.09	45.14 (3.71)	<0.001 ^a	45.13 (3.64)	<0.001 ^a	
PCET (μm)	47.00 (18.20)	47.00 (18.00)	<0.05 ^a	44.00 (15.00)	1.00	44.00 (12.00)	1.00	
	52.29 (4.34)	55.25 (4.78)		51.68 (4.66)		50.16 (3.47)		
MPET (μm)	51.00 (14.00)	53.20 (14.00)	1.000	51.00 (19.00)	<0.05 ^a	51.00 (11.00)	<0.05 ^a	
	60.53 (4.79)	61.24 (3.64)		62.56 (3.83)		62.62 (2.87)		
	60.25 (16.00)	62.00 (15.00)		62.00 (14.00)		62.00 (13.00)		

^aStatistical significance with $P < 0.05$ or $P < 0.001$.

CET, central epithelial thickness; MPET, midperiphery epithelial thickness (4 mm from the center); PCET, paracentral epithelial thickness (2 mm from de center).

$$\Delta R \times 1 W = 3.470 - 1.046 \times BSE - 1.552 \times BBCVA - 0.391 \times BKm + 0.450 \times \Delta R \times 1 h$$

where BSE is the baseline SE, BBCVA is the baseline best-corrected visual acuity, BKm is the baseline mean keratometry, and $\Delta R \times 1 h$ is the change in SE after 1 hour of OK lens use.

The homoscedasticity of this model was confirmed by the normality of the unstandardized residuals distribution ($P = 0.285$) and the absence of outliers (mean Cook distance = 0.021 ± 0.155). Similarly, no multicollinearity was detected in the model (VIF between 1.069 and 1.870).

DISCUSSION

Orthokeratology, as previously reported in the scientific literature,^{1,10,11} has been shown to be an effective and safe procedure for the correction of myopia. In this short-term prospective experimental study, changes in refraction, corneal topography, ocular aberrations, and epithelial thickness were analyzed and characterized for the first hour post-treatment, first night, and first week. The results are comparable with those published in previous studies for CRT lenses and

for other OK lens designs.^{1,12,13} During the first hour of OK use, a total of 24% of the refractive error was corrected, increasing up to 42.6% after the first night and nearly 100% after 1 week. These outcomes are in good agreement with those obtained by Singh et al.,¹³ who reported significant changes after 1 and 6 hr of treatment, with a correction of 60% of the refractive error after the first night of OK use and almost 100% after a week.

Regarding the change in epithelial thickness, the results of the current series suggest that the area experiencing the greatest pachymetric change is the corneal center (CET) after, at least, 40 min of lens use. The largest thinning was achieved 1 week after starting the treatment ($8.17 \pm 0.59 \mu m$), being this outcome in agreement with those reported by other authors.¹⁴⁻¹⁶ In particular, Quian et al.¹⁴ published an OCT-based pachymetry map of the corneal epithelium that showed a thinning of the central and paracentral area of the cornea after using OK for 2 weeks. Zhang et al.¹⁵ reported changes in central epithelium thickness (CET) from the first night, showing a fast change from 5 to 13 μm .

Paracentral epithelial thickness presented a reduction of $4.45 \pm 0.89 \mu m$ after 1 week of OK use, as in previous studies.¹⁴ In the current series, midperipheral regions yielded constant

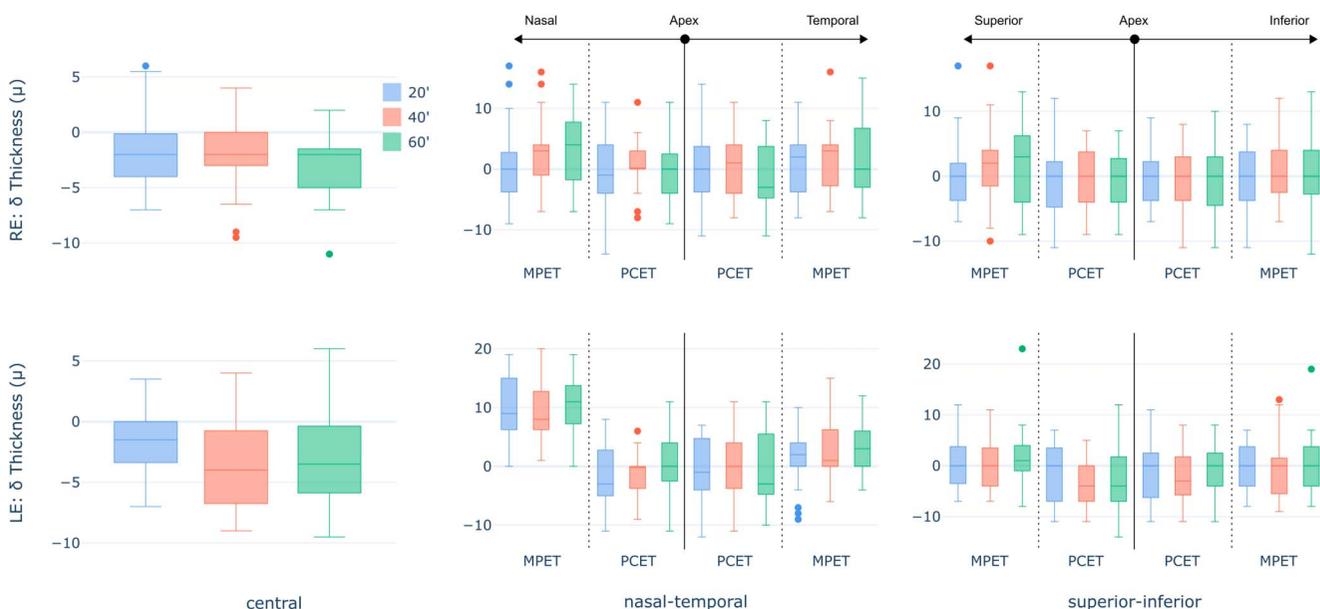


FIG. 1. Changes in epithelial thickness during the use of orthokeratology lenses for 1 hour. (20 min: blue; 40 min: red; 60 min: green; top panel: right eye; bottom panel: left eye).

TABLE 3. Phase 2 One-Hour, One-Night, and One-Week Recovering Changes on Epithelial Thickness (Lens OFF)

Mean (±SD)								
Median (± Range)	Baseline	60 min	P	1 Night	P	1 week	P	
CET (μm)	47.98 (4.10)	45.13 (3.64)	<0.001 ^a	44.59 (5.68)	<0.001 ^a	39.81 (4.69)	<0.001 ^a	
PCET (μm)	47.00 (18.20)	44.00 (12.00)	1.00	44.00 (26.00)	0.197	40.00 (22.00)	<0.001 ^a	
MPET (μm)	52.29 (4.34)	50.16 (3.47)	<0.05 ^a	49.94 (5.43)	0.168	47.84 (5.23)	1.00	
	51.00 (14.00)	51.00 (11.00)		51.00 (30.00)		47.00 (15.00)		
	60.53 (4.79)	62.62 (2.87)		61.78 (5.56)		60.71 (5.40)		
	60.25 (16.00)	62.00 (13.00)		61.00 (29.00)		62.00 (27.00)		

^aStatistical significance with $P < 0.05$ or $P < 0.001$.

CET, central epithelial thickness; MPET, midperiphery epithelial thickness (4 mm from the center); PCET, paracentral epithelial thickness (2 mm from de center).

intervisit values despite the initial thickening after 1 hour of use. The results regarding MPET are controversial. There are several studies not detecting short-term significant changes in MPET or reporting a temporal initial thickening with a posterior regression to baseline values,^{15,16} while other studies have reported a significant thickening in MPET.^{2,3,14,17,18} These contradictory results could be explained due to the difference in lens design, given that the curvature radii are different for each geometry. The CRT design, which was fitted in this study, was also used by Kim et al.,³ who found a MPET thickening after 2 weeks of OK use and, therefore, their follow-up period was longer than ours. Another possible explanation could be related to the degree of refractive error studied. According to the state of the art, a larger refractive correction was associated with a larger change in epithelial thickness (always thinner at CET, regardless midperipheral data), and a smaller treatment diameter in the corneal topography.^{3,19,20} Related to this, lens design can influence changes in epithelial thickness because of different sizes of treatment zones and number of lens curves. Zhang et al.²¹ showed that lenses with a smaller back optic zone diameter yielded a faster myopic reduction and a smaller aspheric treatment zone.

Finally, the axial resolution of the OCT also plays a role when measuring the corneal/epithelial thickness.²² The uncertainty of the

measurement procedure was analyzed using a Monte Carlo strategy.^{23,24} For each patient, 1,000 OCT measurements were simulated by introducing a random Gaussian error equivalent to an axial resolution error of 6 μm (μ : 0, σ : 2.55) on the baseline measurements taken by the clinical expert. The sensitivity of the measurements to the axial resolution was assessed to be 9% (6%, 15%). The authors acknowledge and quantify this limitation which, nonetheless, is present in most of the OK studies using standard clinical devices.

A new contribution of this study is the multivariable prediction model for the orthokeratological changes after one night of use, which provides insights ($R^2=0.718$) into how OK will act using prefitting knowledge such as the baseline refraction, the baseline keratometry, age, and the refractive change after 1 hour of lens use. To the best of our knowledge, no similar models have been published yet. Nevertheless, Xu et al.²⁵ published a multivariable prediction model that incorporated corneal topography data, axial length, and demographic information to predict OK changes and improve the fitting of the lenses. Santodomingo-Rubido et al., Zhong et al., and Lee et al. published effective models to predict the change in axial elongation of myopic eyes for myopia control.^{26–28} All these authors agreed that refraction and topographic values were predictive parameters of OK efficacy. However, these

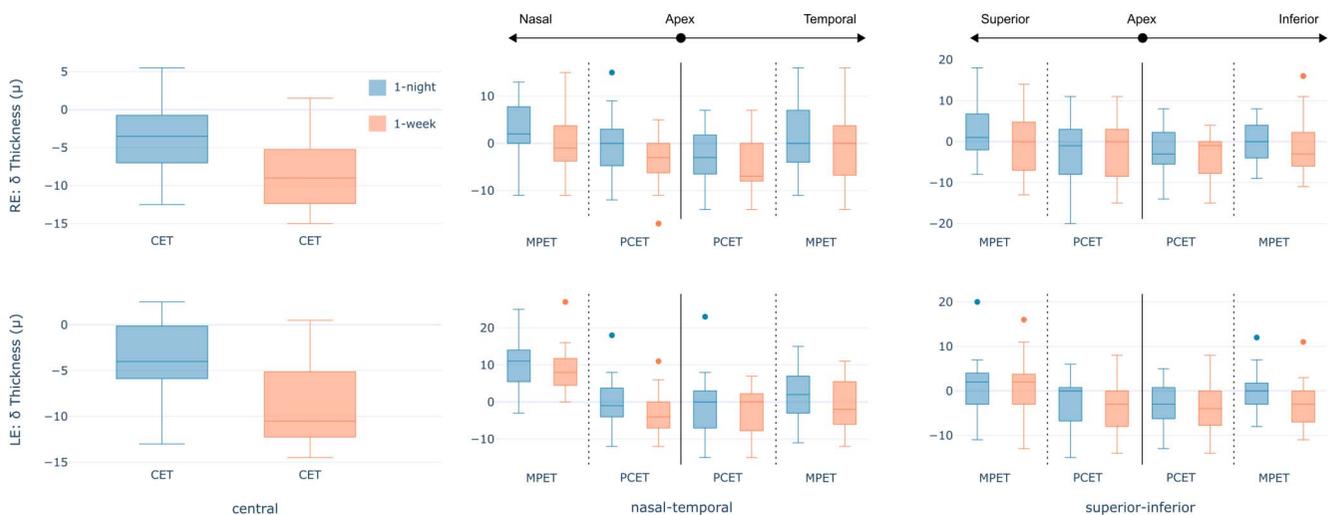


FIG. 2. Changes in epithelial thickness during the use of orthokeratology lenses for 1 week. (One night: blue; 1 week: orange; top panel: right eye; bottom panel: left eye).

models do not consider changes in epithelial thickness, especially during the first phase of corneal shaping with OK, despite having been suggested that corneal biomechanics and morphological changes may play a fundamental role in the efficacy of OK.^{4,6,7}

Another factor that might be influencing the results is the age of the population group. Many studies focused on changes in epithelial thickness have been performed in children, whereas this study only included adults, being the youngest patient 20 years. Although the orthokeratological effect develops effectively regardless of the patient's age, there is an increase in higher-order aberrations that can compromise visual quality. The impact of the visual quality compromise due to aberrations with OK is not the same in adults and in children, being a potential cause of discontinuation of the OK treatment in adults as the visual quality demands and requirements are higher for this type of patients. In a study published by Santolaria et al.,²⁹ the degree of satisfaction with OK in adults after 1 year of treatment was found to be conditioned by the increase in light distortion, especially in low-light conditions, after OK. More studies are needed to understand other potential influences of age on the OK effect, including potential age-related differences in the corneal mechanical response to OK pressures.

This study is not exempt of limitations, being the size of the sample the most important. Another limitation is the protocol for measuring epithelial thickness. Manual measurement was chosen because the integrated software of the OCT system did not provide the user with reliable results. Despite the high quality of the image obtained, the image segmentation of the epithelial layers was not successful because it was performed on a screenshot (no access to raw image files). This limitation was circumvented by taking several measurements in the same area to later average them.

In conclusion, the refractive changes induced during the initial period of OK treatment for myopia correction can be predicted with enough accuracy considering some baseline parameters and the refractive change occurred after 1 hr of use of the OK lens. These models can be considered as a tool for providing real expectancies to patients about the initial refractive changes that the patient is going to experience during the first days of OK treatment. These models must be validated and refined in future studies including larger sample sizes fitted with different designs of OK lenses. All these refractive changes are associated to corneal epithelial changes, with a significant thinning of the central cornea (CET) after the first 40 min of treatment.

REFERENCES

- Hiraoka T, Sekine Y, Okamoto F, et al. Safety and efficacy following 10-years of overnight orthokeratology for myopia control. *Ophthalmic Physiol Opt* 2018;38:281–289.
- Zhou J, Xue F, Zhou X, et al. Thickness profiles of the corneal epithelium along the steep and flat meridians of astigmatic corneas after orthokeratology. *BMC Ophthalmol* 2020;20:240.
- Kim WK, Kim BJ, Ryu IH, et al. Corneal epithelial and stromal thickness changes in myopic orthokeratology and their relationship with refractive change. *PLoS One* 2018;13:e0203652.
- Sánchez-García A, Ariza MA, Büchler P, et al. Structural changes associated to orthokeratology: A systematic review. *Cont Lens Anterior Eye* 2021;44:101371.
- Wu J, Fang W, Xu H, et al. The biomechanical response of the cornea in orthokeratology. *Front Bioeng Biotechnol* 2021;9:743745.
- Nieto-Bona A, González-Mesa A, Villa-Collar C, Lorente-Velázquez A. Biomechanical properties in corneal refractive therapy during adaptation period and after treatment interruption: A pilot study. *J Optom* 2012;5:164–170.
- Piñero DP, Alcón N. Corneal biomechanics: A review. *Clin Exp Optom* 2015;98:107–116.
- Nombela-Palomo M, Felipe-Marquez G, Teus MA, et al. Long-term impacts of orthokeratology treatment on sub-basal nerve plexus and corneal sensitivity responses and their reversibility. *Eye Contact Lens: Sci Clin Pract* 2018;44:91–96.
- Nieto-Bona A, Gonzalez-Mesa A, Nieto-Bona MP, et al. Long-term changes in corneal morphology induced by overnight orthokeratology. *Curr Eye Res* 2011;36:895–904.
- Gispets J, Yébana P, Lupón N, et al. Efficacy, predictability and safety of long-term orthokeratology: An 18-year follow-up study. *Contact Lens and Anterior Eye* 2022;45:101530.
- Bullimore MA, Johnson LA. Overnight orthokeratology. *Contact Lens and Anterior Eye* 2020;43:322–332.
- Wen D, Huang J, Chen H, et al. Efficacy and acceptability of orthokeratology for slowing myopic progression in children: A systematic review and meta-analysis. *J Ophthalmol* 2015;2015:1–12.
- Singh K, Bhattacharyya M, Goel A, et al. Orthokeratology in moderate myopia: A study of predictability and safety. *J Ophthalmic Vis Res* 2020;15:210–217.
- Qian Y, Xue F, Huang J, et al. Pachymetry map of corneal epithelium in children wearing orthokeratology contact lenses. *Curr Eye Res* 2014;39:263–270.
- Zhang J, Li J, Li X, et al. Redistribution of the corneal epithelium after overnight wear of orthokeratology contact lenses for myopia reduction. *Contact Lens and Anterior Eye* 2020;43:232–237.
- Wan K, Yau HT, Cheung SW, Cho P. Corneal thickness changes in myopic children during and after short-term orthokeratology lens wear. *Ophthalmic Physiol Opt* 2021;41:757–767.
- Reinstein DZ, Gobbe M, Archer TJ, et al. Epithelial, stromal, and corneal pachymetry changes during orthokeratology. *Optom Vis Sci* 2009;86:E1006–E1014.
- Lian Y, Shen M, Jiang J, et al. Vertical and horizontal thickness profiles of the corneal epithelium and Bowman's layer after orthokeratology. *Invest Ophthalmol Vis Sci* 2013;54:691–696.
- Swarbrick HA, Wong G, O'Leary DJ. Corneal response to orthokeratology. *Optom Vis Sci* 1998;75:791–799.
- Alharbi A, Swarbrick HA. The effects of overnight orthokeratology lens wear on corneal thickness. *Invest Ophthalmol Vis Sci* 2003;44:2518–2523.
- Zhang Z, Chen Z, Zhou J, et al. The effect of lens design on corneal power distribution in orthokeratology. *Optom Vis Sci* 2022;99:363–371.
- Drexler W, Fujimoto JG. *Optical Coherence Tomography: Technology and Applications*. 2nd ed. Switzerland: Springer International Publishing, 2015.
- Motra HB, Hildebrand J, Wuttke F. The Monte Carlo Method for evaluating measurement uncertainty: Application for determining the properties of materials. *Probabilistic Eng Mech* 2016;45:220–228.
- Malektaji S, Lima IT, Sherif SS. Monte Carlo simulation of optical coherence tomography for turbid media with arbitrary spatial distributions. *J Biomed Opt* 2014;19:046001.
- Xu S, Li Z, Hu Y, et al. Development and validation of a prediction model for axial length elongation in myopic children treated with overnight orthokeratology. *Acta Ophthalmol* 2021;99:e686–e693.
- Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Factors preventing myopia progression with orthokeratology correction. *Optom Vis Sci* 2013;90:1225–1236.
- Zhong Y, Chen Z, Xue F, et al. Corneal power change is predictive of myopia progression in orthokeratology. *Optom Vis Sci* 2014;91:404–411.
- Lee EJ, Lim DH, Chung TY, et al. Association of axial length growth and topographic change in orthokeratology. *Eye Contact Lens* 2018;44:292–298.
- Santolaria E, Cerviño A, Queirós A, et al. Subjective satisfaction in long-term orthokeratology patients. *Eye Contact Lens* 2013;39:388–393.