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The effect of back optic zone diameter on relative corneal refractive power distribution and corneal higher-order aberrations in orthokeratology

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ABSTRACT

Purpose: To compare axial elongation, relative corneal refractive power (RCRP) distribution within the pupillary diameter, and corneal higher-order aberrations (HOAs) in myopic children wearing orthokeratology (ortho-k) lenses with different back optic zone diameters (BOZD).

Methods: Children aged 8–11 years were fitted with 5.0 or 6.2 mm-BOZD ortho-k lenses (groups A and B, respectively). Axial length (AL) and corneal topography were measured at baseline and during the annual visit. RCRP and corneal HOAs were compared between the two groups after one-year treatment. Multivariate linear regression analysis was performed to determine the association between AL elongation and RCRP parameters, corneal HOAs, and other variables between the groups.

Results: After one-year treatment, axial elongation was slower in group A than in group B, with a difference of 0.15 mm. Children in group A showed smaller treatment zone size, smaller 3/4X value (describing the distance from the apex RCRP profile rising to its three-quarter-peak level), greater RCRP sum value within the pupillary area, and higher increases in corneal total HOAs and horizontal coma (Z_3^1). AL elongation was significantly correlated with baseline age, baseline spherical equivalent refraction (SER), treatment zone size, and 3/4X value.

Conclusions: Ortho-k lenses designed with smaller BOZD increased myopia control efficacy, induced a steeper distribution of the RCRP profile within the pupillary diameter, and induced greater increases in corneal total HOAs and horizontal coma (Z_3^1). Lens-induced RCRP profile within pupillary diameter, rising to its three-quarter-peak level at a smaller distance, may show a better myopia control effect.

1. Introduction

The growing prevalence of myopia worldwide and its associated pathologic complications have raised public concern for identifying effective solutions to control myopia [1]. Orthokeratology (ortho-k), which can temporarily correct refractive errors by wearing specially designed reverse-geometry rigid gas permeable lenses overnight to reshape the cornea, has been considered an effective optical intervention for retarding myopia progression in children [2]. The inhibitory effect on axial elongation in myopic children for 2-year ortho-k treatment has been reported to vary from 32 % to 63 % [3–9]. This variation in results may be explained, in part, by the usage of different lens designs and their application in different populations.

Although the underlying mechanism by which ortho-k retards myopia progression is not completely known, altered relative peripheral defocus [10,11] and higher-order aberrations (HOAs) [12,13] have been thought to be major factors influencing the myopic control effect of ortho-k. The relative corneal refractive power (RCRP) to the apex induced by central corneal flattening and mid-peripheral corneal steepening can be used to indicate the extent of myopic defocus induced on the peripheral retina [14,15]. Recent studies have proposed that the amount or distribution of RCRP is closely correlated with axial length (AL) elongation in children undergoing ortho-k [16–18]. Furthermore, following corneal reshaping, notable changes in the HOA profile occur post-ortho-k, including total HOAs, spherical aberration (SA), and comatic aberration (coma) [19,20]. An increase in HOAs has been confirmed to correlate with slower AL elongation in myopic children after ortho-k treatment [12,13,21]. However, measurements of peripheral defocus and HOAs vary with pupil size [2]. A larger pupil size, allowing more of the corneal annular steepened zone to fall within the

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pupil margin, yields more relative peripheral myopic defocus and positive HOAs following ortho-k treatment [22], thereby driving greater myopia control efficacy [23]. Hence, modification of the ortho-k lens parameter should aim to change the RCRP or HOAs in the direction helpful for myopia management in younger children or fast progressors.

Recent studies call for changing the designs of ortho-k lenses to improve myopia control [17,24,25]; however, the effects of back optic zone diameter (BOZD) change on RCRP and corneal HOAs have rarely been studied. The current study aimed to investigate the myopia control effect of ortho-k lenses with different BOZD, evaluate the RCRP distribution within the pupillary diameter, and compare the changes in the corneal HOA profile of the eye. The results will improve our understanding of the effects of ortho-k lens parameter manipulation on the corneal power profile and corneal aberrations.

2. Materials and methods

2.1. Participants

This prospective study was conducted at the Tianjin Medical University Eye Hospital (Tianjin, China) between October 2019 and May 2021. A total of 102 participants were enrolled in this study. The inclusion criteria for ortho-k lens-fitting were: age between 8 and 11 years, cycloplegic spherical power from –1.00 to –4.00 diopters (D), with-the-rule astigmatism less than –0.75 D, and best-corrected visual acuity better than 20/20. The exclusion criteria were strabismus or ocular surface disease, history of ocular surgery, and history of contact lens wear in the past 30 days. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Tianjin Medical University Eye Hospital. Written assent was obtained from the participants and their guardians after they were informed of the study details.

2.2. Ortho-k lens fitting

Two types of ortho-k lenses, Double Reservoir Lens (DRL) (Precilens, Creteil, France) and Euclid (Euclid Systems Corporation, Herndon, VA), were used in this study, and their detailed information is listed in Table 1. Participants were randomly assigned to either group A or group B. In detail, random numbers were generated in three blocks using a spreadsheet generator (Excel; Microsoft, Redmond, WA) throughout the study and packed in envelopes. Even numbers indicated assignment to the group A and odd numbers, to the group B. In order to ensure allocation concealment, the envelope was handed directly to the subjects at randomization. Group A was fitted with DRL lenses of 5.0 mm BOZD, and group B was fitted with Euclid lenses of 6.2 mm BOZD. All lenses used in this study had a spherical design. The lens fitting procedures strictly followed the manufacturer's guidelines. Lenses were ordered with over-refraction targeted at + 0.75D. After lens dispensing, the participants were advised to wear the lenses for more than 8 h per night for at least 6 days per week. Follow-up visits were scheduled at one day, one week, one month, six months, and one year after initial lens wear. All participants underwent a comprehensive ocular examination assessment, including visual acuity testing, slit lamp examination, and corneal topography at each visit. All the measurements were performed between 8 a.m. to 10 a.m. and within 2 h of ortho-k lens removal. Examiners were masked to the treatment group assignment.

Table 1
Detailed information about two types of lenses studied.

	Double Reservoir Lens (DRL)	Euclid
Design	Base curve, reverse curve, alignment curve and peripheral curve	Base curve, reverse curve, alignment curve and peripheral curve
TD	8.0–12.6 mm	9.6–11.6 mm
BOZD	5.0 mm	6.2 mm
Central thickness	0.20 mm	0.20 mm–0.32 mm
DK	100(ISO)10^{-11}(cm^2/seg)/(ml*mm Hg)	87(ISO)10^{-11}(cm^2/seg)/(ml*mm Hg)
Material	Boston XO	Boston Equalens II

TD, total lens diameter; BOZD, back optic zone diameter; DK, oxygen permeability.

2.3. Corneal topography

Corneal topography was measured using TMS-4 (Tomey, Nagoya, Japan) at least three times at baseline and at each scheduled follow-up visit, the map which provided an optimum index value according to the manufacturer's recommendations, was used for data analysis. Each exported map had 31 rings with 256 data points for each ring. The pupil sizes were extracted from the topographic data obtained under ambient mesopic room illumination referring to Kang et al. [26]. The treatment zone size and decentration were determined as previously described [27]. Briefly, to calculate the treatment zone size, a difference map was obtained by subtracting the tangential curvature map at the 12-month visit (Fig. 1B) from the baseline map (Fig. 1A). The area containing locations reduced by >0.00 D was defined as the treatment zone, and its boundary was fitted to a circle using a custom MATLAB function (MathWorks, Natick, WA, USA) (Fig. 1C). The distance between the center of the circle (red across) and the geometric center of the cornea (white across) was defined as the treatment zone decentration.

Axial topographic maps were used to analyze the RCRP [28]. The RCRP map (Fig. 1F) was derived by subtracting the center value from each point on the 12-month axial map (Fig. 1E). Since the average pupil diameter of participants in this study was 4.8 mm (±0.73 mm), the sum of the points on the first 14 rings (from the center of the cornea to the outside) reflected the power shift within the pupillary area (referred to as Sum 4.8). The points were averaged along each ring to derive the mean RCRP profile, and a quadratic curve was fitted using the 14 mean values. The mean RCRP profiles of participants who wore ortho-k lenses of 5.0 mm (group A) or 6.2 mm (group B) BOZD are shown in Fig. 2. Different Y values indicate different amounts of RCRP, and the corresponding X value indicates the distance from the corneal apex. The X values corresponding to 1/4Y, 1/2Y, and 3/4Y were defined as 1/4X, 1/2X, and 3/4X, respectively, and were calculated.

2.4. Calculation of wavefront aberrations of the anterior cornea

Anterior corneal elevation data files obtained from the TMS-4 were used for the following analysis. Corneal wavefront aberrations of the anterior cornea were calculated by expanding anterior corneal height data into a set of orthogonal Zernike polynomials [29]. The details of the calculations were based on the methods previously described by Howland [30] and Oshika [31,32]. The RMS values of total HOAs, SA and coma of cornea were computed as the square root of the sum of squares of corresponding Zernike terms: total HOAs, from third- to sixth-order terms; SA, Z_4^0 and Z_6^0 combined; coma, Z_3^{-1}, Z_3^1, Z_5^{-1}, and Z_5^1 combined, as applied in the analyses of previous studies [13]. These calculations were performed on each subjects' pupil diameter obtained from the topographic data.

2.5. Axial length measurement

AL was measured at baseline and at the 6-month and 12-month visits using a non-contact optical biometry (Lenstar 900; Haag-Streit AG, Switzerland). At each visit, three measurements above the minimal signal-to-noise ratio recommended by the manufacturer were obtained by the same operator, and the median value was used. AL elongation was defined as the difference between the measurements obtained at the baseline and at each visit.

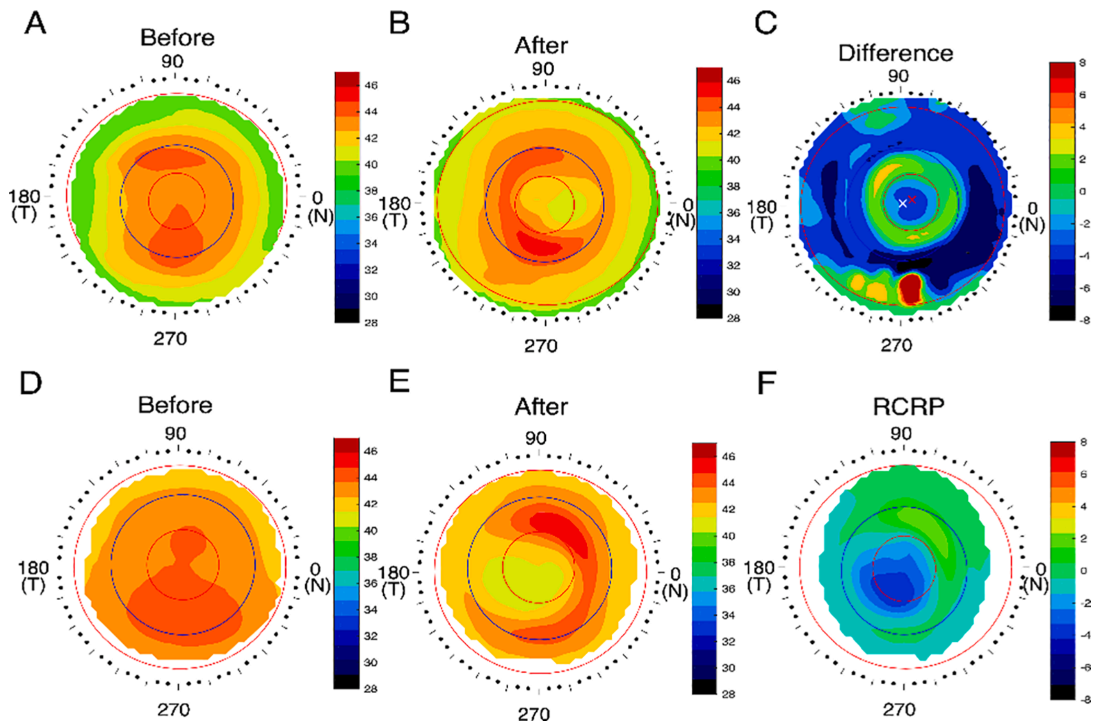

Fig. 1. Methods to determine the treatment zone size and the RCRP. (A) A representative topographic map at baseline, (B) Tangential curvature map at the 12-month visit, (C) The difference map, (D) A representative axial map at baseline, (E) Axial map at the 12-month visit, (F) The RCRP map.

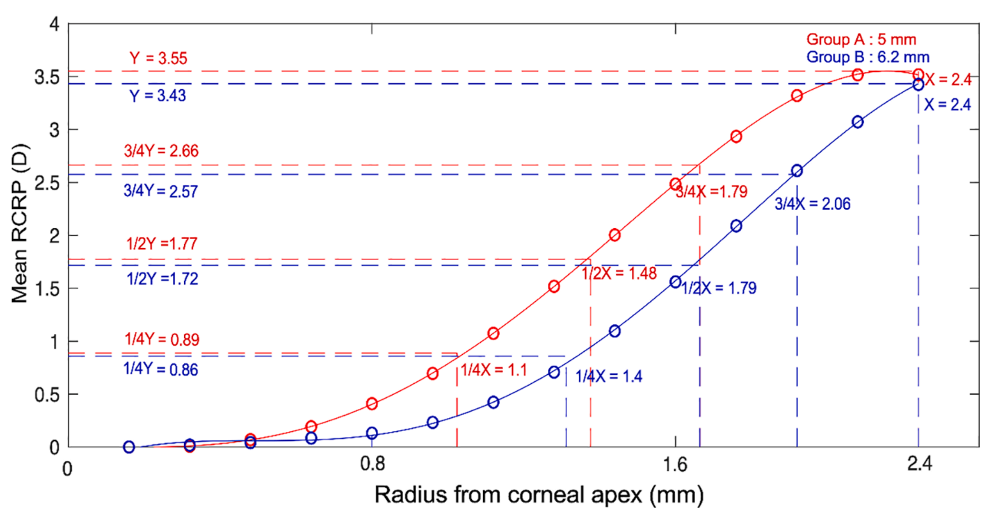

Fig. 2. Mean RCRP profiles within pupillary diameter shown with quadratic curves (Group A wearing lenses with 5.0 mm-BOZD and group B wearing lenses with 6.2 mm-BOZD).

2.6. Statistical analysis

All statistical analyses were performed using R software (version 3.2.2, http://www.R-project.org/), and only the data from the right eyes were used for analysis. The normality of the data was tested using the Shapiro-Wilk test. Differences between the two groups were tested using the unpaired *t*-test for quantitative data and Chi-square test for proportional data. Changes of AL over time between groups were analyzed using repeated-measures analysis of variance (ANOVA). For significant outcomes, post hoc comparisons using Bonferroni corrections were performed. Multiple linear regressions were used to analyze the relationships between AL elongation and baseline age, baseline SER, treatment zone size, treatment zone decentration, aberration RMS, and RCRP parameters. Statistical significance was set at $p < 0.05$.

3. Results

A total of 90 (88.2 %) patients completed all follow-up measurements. Twelve participants were considered dropouts due to failure to adapt to lens wear (two), broken lens (three), poor vision (two), and loss to follow-up (five), and their data were excluded from the final analysis. Baseline biometrics and comparisons among the groups are shown in Table 2. No significant differences were observed in age, sex, SER, or pupil diameter between the two groups (both $P > 0.05$, unpaired *t*-test and Chi-square test).

3.1. Axial length growth

There were significant differences in axial growth between two

Table 2
Baseline data of participants in two groups.

	Group A (n = 46)	Group B (n = 44)	P value
Age (year)	10.65 ± 1.80	10.40 ± 1.64	0.51
Sex (M/F)	18/28	22/22	0.30
SER (D)	−2.63 ± 0.85	−2.67 ± 0.91	0.82
Pupil diameter (mm)	4.84 ± 0.71	4.78 ± 0.76	0.69

SER, spherical equivalent refraction.

groups over one-year period (P < 0.01, repeated-measures ANOVA). The following Bonferroni-adjusted post hoc comparisons indicated that, axial elongation for children in group A wearing lenses with 5.0 mm-BOZD was 0.04 ± 0.11 mm and 0.13 ± 0.13 mm at the 6-month and 12-month visits, respectively, which were significantly smaller than those in group B wearing lenses with 6.2 mm-BOZD: 0.14 ± 0.17 mm at the 6-month visit (p < 0.01) and 0.28 ± 0.22 mm at the 12-month visit (p < 0.01, Fig. 3).

3.2. Treatment zone size and treatment zone decentration

Compared with group B wearing lenses with 6.2 mm-BOZD, the treatment zone radius in group A was significantly smaller at the 12-month visit (2.12 ± 0.70 mm for group A vs 2.62 ± 0.41 mm for group B, p < 0.01, unpaired *t*-test, Fig. 4A). However, the treatment zone decentration was not significantly different between the groups (0.20 ± 0.21 mm for group A vs 0.24 ± 0.17 mm for group B, p = 0.27, unpaired *t*-test, Fig. 4B).

3.3. Distribution of RCRP

The RCRP profiles in groups A and B are illustrated by representative examples in Fig. 1. The sum of RCRP within the pupillary diameter (4.8 mm) zone (Sum 4.8) in group A (15.71 ± 8.72 D*mm^2) was significantly larger than that in group B (10.68 ± 9.10 D*mm^2, p < 0.01, unpaired *t*-test, Fig. 5A). However, there was no significant difference in maximum RCRP (called Y), 3/4Y, 1/2Y, or 1/4Y between two groups (Y = 2.24 ± 1.09 D, 3/4Y = 1.68 ± 0.82 D, 1/2Y = 1.12 ± 0.54 D and 1/4Y = 0.56 ± 0.27 D for group A vs Y = 2.10 ± 1.20 D, 3/4Y = 1.57 ± 0.90 D, 1/2Y = 1.05 ± 0.60 D and 1/4Y = 0.52 ± 0.30 D for group B, all p > 0.05, unpaired *t*-test, Fig. 5B-E). When the RCRP value changed, the corresponding distance from the corneal apex differed. Although no significant difference in X value which corresponds to Y was observed between two groups (2.30 ± 0.39 mm for group A vs 2.33 ± 0.37 mm for group B, P = 0.66, unpaired *t*-test, Fig. 5F), at 3/4Y, 1/2Y, and 1/4Y, the corresponding 3/4X, 1/2X, and 1/4X for group A

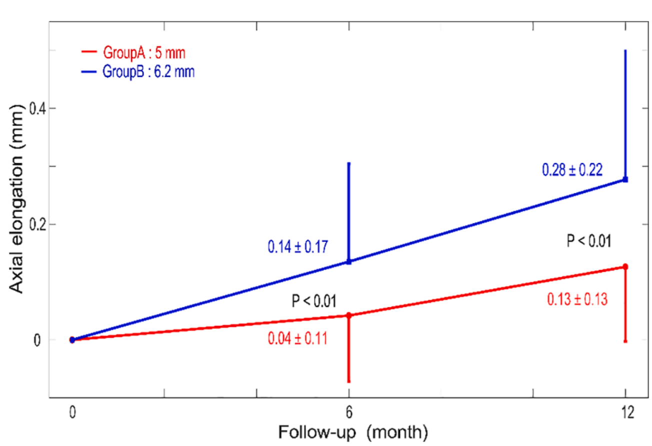

Fig. 3. Axial elongation over one year in Group A (wearing lenses with 5.0 mm-BOZD) and group B (wearing lenses with 6.2 mm-BOZD). Data are expressed as the mean ± SD.

(1.46 ± 0.38 mm; 1.15 ± 0.31 mm and 0.91 ± 0.38 mm, respectively) were significantly smaller than those for group B (1.82 ± 0.44 mm; 1.55 ± 0.40 mm and 1.31 ± 0.37 mm, respectively; all p < 0.01, unpaired *t*-test, Fig. 5G-I), meaning that the RCRP profile of group A wearing lenses with 5.0 mm-BOZD rose more rapidly.

3.4. Corneal total HOAs, comatic and spherical aberrations

Table 3 showed the changes in Zernike coefficients and RMS values of corneal HOAs in two groups post-treatment. Compared with those in group B, eyes fitted with 5.0 mm-BOZD lenses showed a significantly greater increase in corneal primary horizontal coma (Z_3^1), the RMS of corneal total HOAs and coma after one-year treatment (both p < 0.01, unpaired *t*-test). There were no significant differences in the changes in other Zernike terms and the RMS of corneal SA between the two groups (both p > 0.05).

3.5. Multiple regression for axial elongation and ocular biometrics

A multiple regression was conducted between one-year AL elongation and ocular biometrics including baseline age, baseline SER, treatment zone size, treatment zone decentration, sum 4.8, 3/4X, 1/2X, 1/4X, X, changes in the RMS values of corneal total HOAs and coma, and change in horizontal coma (Z_3^1). The analysis showed that the change in AL was significantly correlated with baseline age (t = -3.87, p < 0.001), baseline SER (t = 2.88, p < 0.01), treatment zone size (t = 2.27, p = 0.03), and 3/4X (t = 2.78, p < 0.01) (R^2 = 0.26), but not with the other factors being analyzed.

4. Discussion

The current study shows that ortho-k lenses with smaller BOZD can significantly retard AL elongation and induce smaller treatment zone size, greater RCRP sum, steeper distribution of the RCRP profile within pupillary diameter, higher increase in RMS of corneal total HOAs and coma, and more positive corneal primary horizontal coma (Z_3^1), compared with larger BOZD ortho-k lenses. We first proposed that ortho-k lens designs that result in an RCRP profile rising to its three-quarter-peak level at a smaller distance from the apex may achieve better control of AL elongation.

The ortho-k-induced treatment zone is surrounded by a mid-peripheral steepened corneal annulus. Recent studies have developed newer ortho-k lens designs with smaller BOZD in attempts to decrease the treatment zone size and move more of the annular steepened zone into the pupil margin, aiming to improve the myopic control effect of ortho-k lenses [24,25]. To verify these results, the present study recruited children with a mean age of 10, fitting lenses with different BOZDs, and as expected, found that 5.0 mm-BOZD lenses produced a significantly smaller treatment zone size without influencing lens centration compared with 6.2 mm-BOZD lenses. Putting aside the variety of measurement method, the average 1.0 mm difference in treatment zone diameter in our study was greater than the 0.72 mm difference reported by Guo et al. using 5.0 mm or 6.0 mm-BOZD ortho-k lenses (KATT BE Free, Precision Technology Services) for one year [25], and greater than the 0.3 mm difference showed in Carracedo et al.'s study utilizing Paragon CRT lenses (Paragon Vision Sciences) with either 5.0 or 6.0 mm BOZD for 2 weeks [33]. In addition, it should be noted that ortho-k lenses with different designs but the same BOZD of 6.0 mm can also obtain different treatment zone sizes. The comparison of the 4-zone Dreamlite lenses (Procornea BV) and Paragon CRT lenses conducted by both Marcotte-Collard et al. [34] and Yang et al. [17] revealed that the former created a smaller treatment zone size with a difference of 0.38–0.70 mm. In this sense, future lenses may be designed with a smaller BOZD or other specific changes in lens parameters to achieve an ideal and reduced treatment zone size.

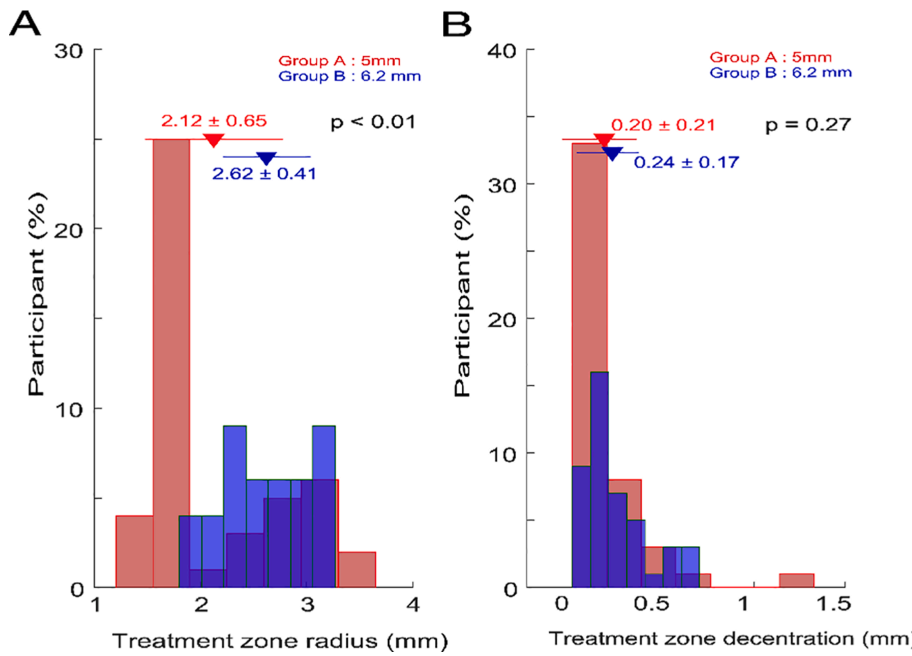

Fig. 4. Treatment zone size (A) and treatment zone decentration (B) in Group A (wearing lenses with 5.0 mm-BOZD) and group B (wearing lenses with 6.2 mm-BOZD). Data are expressed as the mean ± SD.

Limited data is available regarding the one-year myopia control effect of reduced BOZD design in ortho-k treatment. Our results showed that the AL increased significantly less in the 5.0 mm-BOZD group than the 6.2 mm-BOZD group, with a mean difference of 0.15 mm at the 12-month visit. This indicates 53.6 % less AL growth in the smaller BOZD group. Similarly, Guo et al. reported a 0.13 mm/year lesser AL growth in those with 5.0 mm-BOZD KATT lenses compared with those wearing 6.0 mm-BOZD lenses, but showed an efficacy of 76.5 % in reduction [25]. The use of different types of ortho-K lenses may partly explain the discrepancy between these two studies. In a recent study using DRL lenses similar to those in our study, Pauné et al. found that AL changes in children with smaller BOZDs decreased by 0.06 mm/year compared with those with larger BOZDs, representing a reduction of 40 % [24]. Aside from the influence of ethnicity, one possible reason for the decrease in the relative reduction of AL elongation is that children in Pauné's study had a mean age of 13 years, much older than those in our study and Guo's study [25]. This might indicate that older children benefit relatively less from smaller BOZD designs because their myopic progression has naturally slowed. The synthesis of the available findings suggests that fitting with 5.0 mm-BOZD ortho-k lenses increases the efficacy in reducing AL growth.

The annulus of mid-peripheral steepening induced by ortho-k imposes myopic defocus on the peripheral retina, which is commonly considered a potential mechanism by which ortho-k slows myopia progression [14,35,36]. RCRP relative to the corneal apex presumably represents the degree of peripheral retinal defocus after ortho-k treatment [14,15]. Several studies have reported that maximum RCRP post-treatment is negatively correlated with axial elongation in children undergoing ortho-k [12,18,37,38]. In addition, Zhong et al. proposed that the greater the summed RCRP shift from the baseline value after ortho-k treatment, the slower the myopia progression [11]. Thereafter, Hu et al. reported that areal summed corneal power shift within the central 4 mm-diameter zone is an important determinant of AL elongation in myopic children treated with ortho-k [16], implying a regional role for RCRP in myopia control. Considering that pupil size was a potential contributor to the myopia control effect of ortho-k [23,24], we calculated the mean RCRP profiles within the pupillary diameter (4.8 mm) zone, and the results showed that the maximum RCRP value was similar in both groups, while the summed RCRP in the 5.0 mm-BOZD group was significantly larger than that in the 6.2 mm-BOZD group. Similarly, Yang et al. showed that subjects with smaller treatment zone size post-ortho-k treatment had a significantly larger RCRP sum within the central 4-mm diameter zone [17]. These indicate that RCRP within the central region especially the pupillary diameter zone may be a potential influencing factor on axial elongation after ortho-k treatment.

Nevertheless, regardless of using either a maximum or a sum value, the shape or distribution of the RCRP profile is ignored. Yang et al. developed the index X50 to describe how quickly an RCRP shift profile within 8 mm-diameter zone can rise to its half-peak value and found that X50 was significantly associated with AL elongation in ortho-k-wearing children [17]. Zhang et al. established a polynomial function in modeling RCRP change within a 6.2 mm-diameter zone and proposed that a lower power exponent, representing a higher asphericity of the treatment zone, was correlated with a lower AL elongation after one year of ortho-k treatment [39]. These findings indicate a significant impact of RCRP distribution after corneal reshaping on AL growth in children wearing ortho-k. In the present study, we developed the indices 3/4X, 1/2X, and 1/4X to describe how quickly an RCRP profile can rise and found that only the index 3/4X was significantly associated with one year of AL growth after ortho-k treatment. The RCRP profile in the 5.0 mm-BOZD group with a smaller 3/4X value reached its three-quarter-peak level at a smaller distance from the apex, holding a steeper rising edge than that in 6.2 mm-BOZD group. Thus, it is reasonable to speculate that reduction of the treatment zone size causes the corneal annulus to steepen faster within the pupil margin, which in turn contributes to reduced axial elongation. The findings of Zhang et al. [40] and Yang et al. [17] appear to support this view. However, Zhang et al. only focused on the corneal power distribution in children undergoing ortho-k with different BOZD after one month of treatment, and did not show the myopia control effect. Yang et al. utilized different designs of ortho-k (Dreamlite and Paragon CRT) lenses to obtain different treatment zone size. Therefore, more long-term studies using ortho-k lenses with different BOZD are required to illustrate the impact of the distribution of RCRP on axial elongation.

Ortho-k treatment reshaped cornea, and significantly alters the profile of corneal and total ocular HOAs [41]. Elevated HOAs have been reported to be an important factor influencing myopia progression

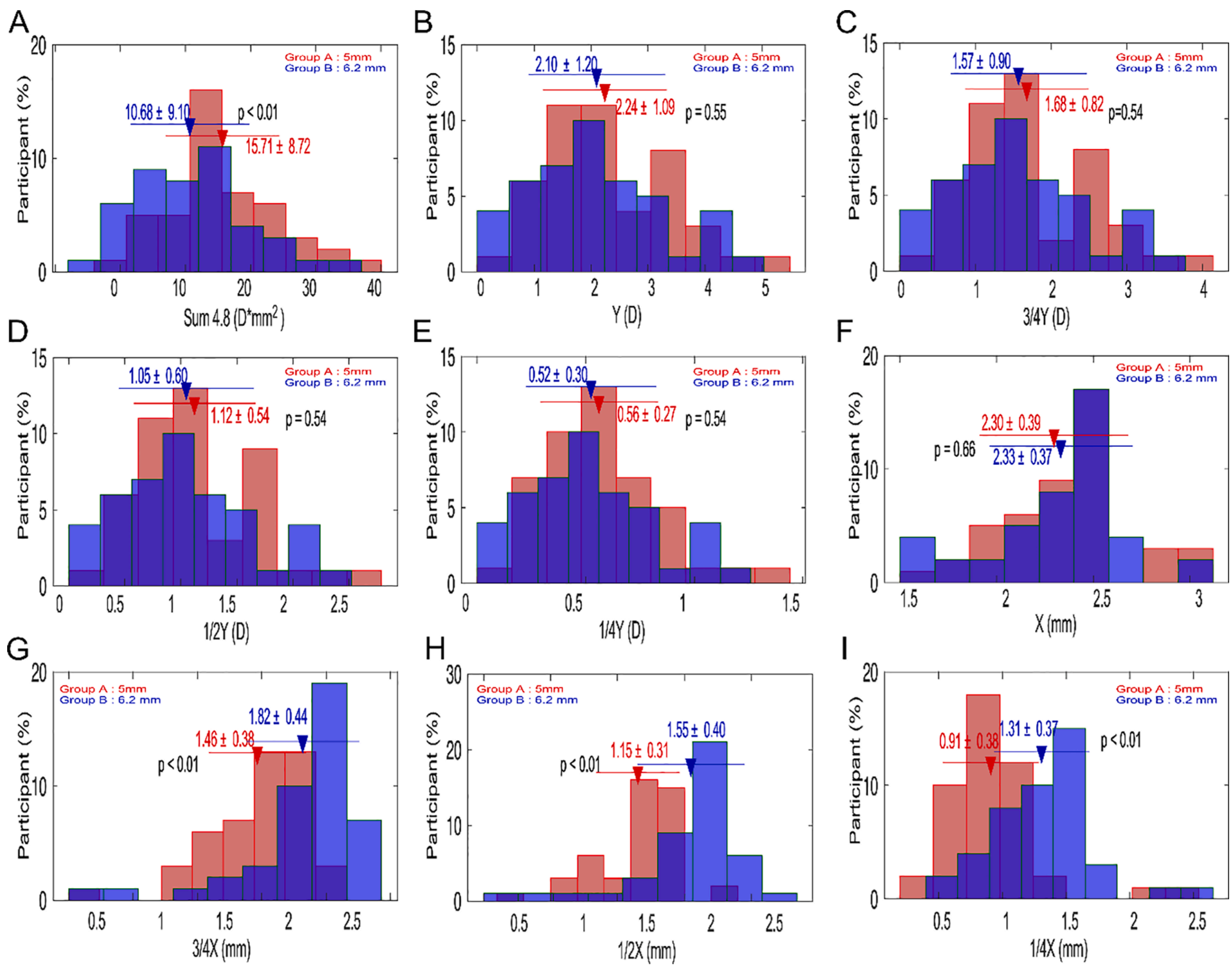

Fig. 5. Comparison of different RCRP value and the corresponding corneal radial distance between two groups. (A) RCRP sum within a 4.8 mm diameter called Sum 4.8, (B) maximum RCRP called Y value, (C) 3/4Y value, (D)1/2Y value, (E)1/4Y value, (F) X value, (G) 3/4X value, (H)1/2X value, (I)1/4X value. Data are expressed as the mean ± SD.

Table 3
Corneal HOAs before and after treatment in group A (wearing lenses with 5.0 mm-BOZD) and group B (wearing lenses with 6.2 mm-BOZD) and a comparison of changes between two groups. Data are expressed as the mean ± SD.

Corneal HOAs (μm)	Baseline		One year		Change		
	Group A	Group B	Group A	Group B	Group A	Group B	P
Total HOAs RMS	0.6416 ± 0.2726	0.7061 ± 0.2289	0.6945 ± 0.3281	0.5439 ± 0.2374	0.0529 ± 0.1998	−0.1622 ± 0.2559	< 0.001
SA RMS	0.1855 ± 0.1178	0.2216 ± 0.1598	0.2419 ± 0.1579	0.2806 ± 0.1997	0.0529 ± 0.1998	−0.1621 ± 0.2559	0.9432
Primary spherical aberration (Z_4^0)	−0.0036 ± 0.0510	−0.0143 ± 0.0452	−0.0110 ± 0.0470	−0.0047 ± 0.0645	−0.0074 ± 0.0585	0.0096 ± 0.0683	0.2197
Secondary spherical aberration (Z_6^0)	−0.0023 ± 0.0170	−0.0015 ± 0.0170	−0.0009 ± 0.0204	0.0022 ± 0.0276	0.0014 ± 0.0226	0.0038 ± 0.0313	0.6843
Coma RMS	0.5211 ± 0.3411	0.5513 ± 0.3113	0.5320 ± 0.3875	0.3642 ± 0.2321	0.0109 ± 0.2212	−0.1871 ± 0.3018	< 0.001
Primary vertical coma (Z_3^{-1})	−0.0529 ± 0.1081	−0.0638 ± 0.1065	−0.0394 ± 0.1476	−0.0414 ± 0.1326	0.0136 ± 0.1183	0.0224 ± 0.1339	0.7478
Primary horizontal coma (Z_3^1)	0.2390 ± 0.3886	0.3116 ± 0.4086	0.2603 ± 0.3943	0.1359 ± 0.3319	0.0212 ± 0.3119	−0.1757 ± 0.3158	0.0052
Secondary vertical coma (Z_5^{-1})	0.0185 ± 0.0291	0.0245 ± 0.0227	0.0238 ± 0.0309	0.0177 ± 0.0471	0.0053 ± 0.0410	−0.0069 ± 0.0503	0.2237
Secondary horizontal coma (Z_5^1)	−0.0003 ± 0.0358	0.0018 ± 0.0260	0.0009 ± 0.048	−0.0006 ± 0.0542	0.0012 ± 0.0343	−0.0024 ± 0.0579	0.7274

HOA, higher-order aberrations; Coma: comatic aberration; SA: spherical aberration; RMS: root mean square.

[12,13]. Here, we compared the changes in corneal total HOAs, coma, and SA between 5.0 and 6.2 mm-BOZD groups after one year of treatment and found a remarkable increase in RMS values of corneal total HOAs and coma, and a higher level of corneal primary horizontal coma (Z_3^1) in eyes wearing 5.0 mm-BOZD lenses, suggesting smaller BOZD-induced steeper corneal annulus within the pupillary area contributes to the increase in corneal total HOAs and horizontal coma (Z_3^1), but not corneal SA. In line with the findings of Chen et al. [42], corneal horizontal coma (Z_3^1) was one of the most affected individual Zernike coefficients during ortho-k treatment. Significant change in coma implies that asymmetric optical changes after ortho-k may contribute to the slowing of AL growth [12]. Inconsistently, Carracedo et al. proposed

that the 5.0 mm-BOZD design showed a greater positive corneal SA than the 6.0 mm-BOZD design after 15 days of lens wearing [33]. The difference in results could partially be attributed to the different methods used to evaluate corneal HOAs and different follow-up time. Despite this difference, in our multiple regression analysis, the change in horizontal coma (Z_3^1), or the increase in the RMS of corneal total HOAs and coma did not display the strongest correlation with AL elongation, but other confounding factors, including baseline age, baseline SER, treatment zone size, and 3/4X affected AL elongation. These results suggest that the improved myopia control effect of 5.0 mm-BOZD ortho-k lenses is mainly influenced by the peripheral myopic defocus signal within a certain threshold, but more studies are needed to test this hypothesis.

One limitation of the present study was that corneal HOAs were calculated based on the corneal elevation data files obtained from TMS-4 and not measured using wavefront aberrometers. Despite the reliability of the calculation method [29–31], errors may exist between the calculated and measured values. In addition, considering the compensatory effect of internal aberrations from the posterior cornea or the crystalline lens [41,42], analyzing corneal anterior HOAs only may not provide a comprehensive understanding of the influence of HOAs on myopic control effect. Third, the follow-up duration was only one year. Long-term studies would provide answers on whether smaller-BOZD design-induced effects on axial elongation can be sustained over time.

In this study, we showed that a smaller BOZD design of ortho-k lenses improved efficacy in slowing the progression of myopia, mainly by inducing a faster corneal annulus steepening within the pupillary area and subsequently changing the distribution of myopic defocus. More complex lens design changes, such as decreasing BOZD or changing back optic zone asphericity, which lead to an RCRP profile within the pupillary area rising to its three-quarter-peak level at a smaller distance from the apex, may be considered to enhance myopia control efficacy in younger children or fast progressors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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