Ocular biological characteristics of children with myopia and rapid axial length changes treated with spectacles with highly aspherical lenslets

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Abstract

• **AIM**: To investigate the ocular biological characteristics of children with myopia and rapid axial length (AL) changes prescribed spectacles with highly aspherical lenslets (HAL).

• **METHODS:** Data were collected from 156 children (252 eyes) with myopia and HAL treatment who were aged 7-13 and had rapid AL changes. The participants were divided into groups with AL reduction and elongation according to the changes in AL within 6mo. Paired *t*-tests were used to compare the ocular biological parameters at baseline and after rapid changes post-HAL treatment. Pearson's correlation analysis was used to determine the association between the ocular parameters and AL changes.

• **RESULTS:** The ocular biological parameters significantly changed in the children with myopia and rapid AL changes after HAL treatment. In the group with AL reduction, the anterior chamber depth (ACD) and vitreous chamber depth (VCD) decreased. The crystalline lens thickness (CLT) increased, corneal flat keratometry (FK) decreased, and steep keratometry (SK) increased (all *P*<0.001). The eyes in the group with AL elongation had increased ACD and VCD and steepened SK, but the CLT or FK findings were not different. AL change was negatively associated with baseline astigmatism (*r*=-0.171; *P*=0.007).

• CONCLUSION: In the eyes with HAL treatment,

decreased ACD and VCD, thickened CLT, flattened FK, and steepened SK are observed during AL reduction. Lower baseline astigmatism is associated with AL reduction. The AL reduction may suggest the potential efficacy of HAL intervention in myopia control, while providing evidence for optimizing personalized myopia management strategies. Further longitudinal studies are warranted to validate whether rapid AL changes predict sustained treatment efficacy.

• **KEYWORDS:** myopia; axial length; astigmatism; highly aspherical lenslets

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INTRODUCTION

M yopia is a global public health problem with an increasing prevalence and marked social and economic burden^[1-3]. Axial elongation is characteristic of myopia progression^[4-7] and critical risk factor for vision-threatening complications, such as glaucoma, myopic maculopathy, chorioretinal atrophy, and retinal detachment^[8-10]. Therefore, the goal of myopia control is mainly to reduce axial elongation and delay myopia progression.

Several available myopia control interventions have been implemented to slow myopic axial length (AL) elongation, based on myopic defocus, such as orthokeratology and spectacle lenses with specific optical designs^[11]. Orthokeratology lenses delay myopic axial elongation by steepening the midperipheral cornea to increase relative peripheral myopic defocus. This biomechanical response aligns with animal models demonstrating axial shortening in response to myopic defocus *via* positive lenses^[12]. While AL shortening is uncommon in humans, emerging evidence suggests certain optical interventions could induce AL reduction, potentially through similar pathways. Chen *et al*^[13] revealed that 49% of orthokeratology lens wearers experienced AL reduction for three weeks. Zhao *et al*^[14] reported a mean AL change of 0.04 ± 0.12 mm in 33% of eyes treated with orthokeratology lenses during the six-month follow-up, comparable to the 0.03±0.13 mm reported by Cho et $al^{[15]}$. Tang et $al^{[16]}$ investigated that a one-year follow-up of changes in AL reduction of -0.18±0.06 mm, and 16.22% of participants had a reduction of more than 0.25 mm in AL. Hu et al^[17] reported a 16.5% incident probability and a maximum magnitude of 0.19 mm for long-term AL shortening after myopic orthokeratology based on a large database. Spectacle lenses with highly aspherical lenslets (HAL), designed to impose myopic defocus across the retina, demonstrate comparable efficacy^[18-20]. A randomized trial by Bao *et al*^[19-20] showed that HAL reduced AL elongation by 60% compared to single-vision lenses, with annual growth rates of 0.13 mm vs 0.36 mm. Despite its promising myopia control efficacy, individual variability in AL responses with HAL intervention remains understudied. The characteristics of AL reduction and corresponding changes in the AL components have not yet been reported.

This study aimed to investigate the characteristics of AL component changes in children with myopia exhibiting rapid AL reduction and progressive elongation during HAL treatment. By quantifying ocular biometric changes, our findings address knowledge gap in defocus-based myopia control: despite lots of research on slowing AL elongation, the structural correlates and temporal patterns of clinically significant AL shortening remain poorly characterized. The findings may be helpful in guiding the optimization of myopic defocus-inducing optical signals, ultimately enabling personalized myopia management strategies.

PARTICIPANTS AND METHODS

Ethics Approval The study was approved by the Ethics Committee of the Affiliated Eye Hospital of Wenzhou Medical University (Approval: 2021-231-K-201-01). It was performed following the tenets of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from the parents of all participants.

Participants In this retrospective study, all pertinent data were extracted from the clinical records and device readouts of children who visited the Eye Hospital of Wenzhou Medical University for vision correction with HAL between January 2021 and July 2023.

The participants were selected according to the following inclusion criteria: 1) 7-13y; 2) cycloplegic spherical equivalent refraction (SER) between 0 and -4.75 D; 3) astigmatism not exceeding 1.50 D; 4) anisometropia of no more than 1.50 D; 5) monocular best-corrected distance visual acuity of no worse than 20/20. Children with a history of myopia control treatment

(such as multifocal contact lenses or atropine use), strabismus or nystagmus, ocular or systemic pathology that may affect vision, and abnormal intraocular pressure were excluded. By combining subjective refraction, eyes with myopia were fully corrected using spectacle lenses with HAL. All participants wore lenses continuously daily, and there have been no reports of discomfort or decreased visual performance.

Based on the changes in AL, the parameters of both eyes or only one eye were collected as individual data for analysis. Rapid AL changes were defined as the difference between the baseline value and the value after wearing HAL within 6mo. The group with AL reduction included children wearing HAL lenses, which resulted in AL shortening by 0.1 mm within 6mo. The children with axial elongation of more than 0.2 mm within 6mo constituted the group with AL elongation.

All patients underwent cycloplegic refraction examination with an autorefractor (KR800; Topcon, Japan). Ocular biometric parameters were measured using an OA-2000 (Tomey, Nagoya, Japan), which is based on swept-source optical coherence tomography technology with a laser wavelength of 1060 nm to measure AL, central corneal thickness (CCT), anterior chamber depth (ACD), and crystalline lens thickness (CLT). The vitreous chamber depth (VCD) was calculated by subtracting CCT, ACD, and CLT from AL. Placidodisk corneal topography was used to determine the flatness or steepness of the cornea. The dioptric difference between the corneal curvatures of the two principal power meridians represented the corneal astigmatism and was recorded as ΔK . Participants were asked to blink completely before the measurement and keep their eyes open during imaging. Measurements were captured within the shortest time. The device obtained the images automatically when a blink was detected. Ten individual measurements with a difference of no more than 0.02 mm were obtained and averaged for the analysis. All examinations were completed on the same day between the times 8:00 and 17:00.

Statistical Analysis All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Normally distributed variables were presented as the mean±standard deviation (SD), and categorical data were presented as the frequency (proportion). Categorical variables, including the differences in the male/female and right/left ratios of the groups, were analyzed using the Chi-squared test. Paired *t*-tests were used to compare the SER, corneal flat keratometry (FK), corneal steep keratometry (SK), Δ K, AL, ACD, CLT, and VCD at baseline and after rapid changes post HAL treatment. The values of the two groups were compared using Student's *t*-test. Pearson's correlation analysis was used to determine the factors associated with AL changes. Univariate and multivariate linear regression models were used



Figure 1 Flow chart of the study AL: Axial length; SER: Spherical equivalent refraction; BCVA: Best corrected visual acuity.

to evaluate the association between each factor and the changes in AL. Standardized regression coefficients from the regression models were presented with 95% confidence intervals (CIs). The threshold for statistical significance was set at P < 0.05.

RESULTS

Baseline Characteristics One hundred and fifty-six participants with 252 eyes and a mean \pm SD age of 9.07 \pm 1.72y (range: 7-13y) met the inclusion criteria and were allocated to the groups with AL reduction and elongation. A total of 115 eyes of 68 participants showed AL shortening, and 137 eyes of 88 participants showed AL elongation (Figure 1). No significant differences in age or gender were observed between the groups. The baseline ocular parameters, including SER, AL, ACD, CLT, VCD, and corneal keratometry, were not significantly different for the groups (all *P*>0.05; Table 1).

Changes in Ocular Parameters with Axial Length Changes The eyes in the group with AL reduction showed a mean AL shortening of 0.17 ± 0.06 mm (range: 0.10-0.33 mm) over a mean duration of 3.99mo. Of these eyes, 26.1% (30/115) showed a reduction of >0.2 mm. Significant differences were observed among the baseline and follow-up values of SER, FK, SK, Δ K, ACD, CLT, and VCD (all *P*<0.05; Table 2).

The mean elongation of the AL was 0.26 ± 0.06 mm. There was a steeper SK and increased ACD and VCD with AL elongation (all *P*<0.05). The measured FK and CLT values showed no significant changes over time (all *P*>0.05).

Contribution Analysis of Ocular Biometric Factors to Axial Length Changes Pearson's correlation analysis and multivariate linear regression models revealed a significant association between changes in AL and alterations in various ocular biometric parameters (Figure 2). Specifically, changes in anterior chamber depth (Δ ACD) and crystalline lens thickness (ΔCLT) showed minimal variability and weak correlations with AL changes (\triangle ACD: R^2 =0.089, P<0.001; \triangle CLT: $R^2=0.041$, P=0.001). In contrast, changes in vitreous chamber depth (Δ VCD) demonstrated a strong positive correlation with AL changes (R^2 =0.883, P<0.001), indicating a significant contribution to AL variations. The equation y=0.951x+0.002 suggests that for every unit change in ΔVCD , AL changes by approximately 0.951 units. This highlights the predictive capability of Δ VCD changes for AL variations, emphasizing its significant contribution.

Factors Associated with Axial Length Reduction Pearson's correlation analysis showed that the initial degree of astigmatism was significantly associated with AL changes (r=-0.171; P=0.007). In the univariate and multivariate linear regression models, none of the other ocular biometric factors had a significant impact on rapid AL change (all P>0.05; Table 3). **DISCUSSION**

The current study demonstrated the baseline and variable characteristics of the ocular parameters in children with rapid AL changes after HAL treatment. In children with myopia and

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Table 1 Baseline characteristics and demographic data of participantsmean±SD or median (interquartile range					
Characteristics AL reduction (<i>n</i> =115)		Range	AL elongation (n=137)	Range	Р
Male, n (%)	52 (45.2)		69 (50.3)		0.415
Right eye, n (%)	57 (49.5)		69 (50.3)		0.899
Age, y	9.17±1.74	8 to 11	8.96±1.66	7 to 10	0.348
SER, D	-1.79±0.93	-2.25 to -1.00	-1.86±1.10	-2.63 to -1.00	0.919
Sphere, D	-1.63±0.87	-2.00 to -1.00	-1.62±1.07	-2.25 to -0.75	0.600
Cylinder, D	-0.30±0.39	-0.50 to 0	-0.47±0.56	-0.75 to 0	0.056
AL, mm	24.16±0.70	23.72 to 24.75	24.30±0.96	23.67 to 24.89	0.396
FK, D	42.72±1.23	41.82 to 43.60	42.55±1.32	41.70 to 43.49	0.290
SK, D	43.91±1.38	42.88 to 45.00	43.81±1.50	42.96 to 44.70	0.581
ΔΚ, D	1.19±0.54	0.79 to 1.57	1.26±0.56	0.81 to 1.56	0.412
ACD, mm	3.69±0.23	3.53 to 3.87	3.73±0.23	3.59 to 3.88	0.204
CLT, mm	3.42±0.16	3.33 to 3.51	3.41±0.15	3.31 to 3.49	0.520
VCD, mm	16.51±0.71	16.09 to 16.99	16.63±0.94	15.94 to 17.21	0.543

SER: Spherical equivalent refraction; AL: Axial length; FK: Flat keratometry; SK: Steep keratometry; ACD: Anterior chamber depth; CLT: Crystalline lens thickness; VCD: Vitreous chamber depth; D: Dioptres; K: Keratometry; SD: Standard deviation.

Table 2 Changes in the ocular	parameters of the AL reduction a	nd elongation groups

Table 2 Changes in the ocular parameters of the AL reduction and elongation groups mean±SD								
Variables —		AL reduction			AL elongation			
	Baseline	Follow-up	Р	Changes	Baseline	Follow-up	Р	Changes
AL, mm	24.16±0.70	23.99±0.71	<0.001	-0.17±0.06	24.30±0.96	24.57±0.97	<0.001	0.26±0.06
Sphere, D	-1.63±0.87	-1.39±0.88	<0.001	0.25±0.21	-1.62±1.07	-2.20±1.10	<0.001	-0.58±0.25
Cylinder, D	-0.30±0.39	-0.36±0.41	0.003	-0.06±0.19	-0.47±0.56	-0.62±0.66	<0.001	-0.15±0.49
FK, D	42.72±1.23	42.64±1.22	<0.001	-0.08±0.16	42.55±1.32	42.56±1.31	0.326	0.01±0.16
SK, D	43.91±1.38	43.97±1.37	0.003	0.06±0.22	43.81±1.50	43.95±1.50	<0.001	0.14±0.23
ΔK, D	1.19±0.54	1.33±0.54	<0.001	0.14±0.28	1.26±0.56	1.38±0.57	<0.001	0.12±0.26
ACD, mm	3.69±0.23	3.65±0.24	<0.001	-0.04±0.10	3.73±0.23	3.74±0.23	<0.001	0.01±0.07
CLT, mm	3.42±0.16	3.46±0.17	<0.001	0.03±0.08	3.41±0.15	3.42±0.15	0.981	0±0.09
VCD, mm	16.51±0.71	16.35±0.71	<0.001	-0.16±0.12	16.63±0.94	16.88±0.94	<0.001	0.25±0.08

AL: Axial length; FK: Flat keratometry; SK: Steep keratometry; ACD: Anterior chamber depth; CLT: Crystalline lens thickness; VCD: Vitreous chamber depth; D: Dioptres; K: Keratometry; SD: Standard deviation.

Table 3 Pearson	's correlation	analysis of tl	he associations	between
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the related factors and AL changes				
Variables	r	Р		
Age, y	-0.092	0.144		
SER, D	-0.046	0.471		
Sphere, D	-0.004	0.946		
Cylinder, D	-0.171	0.007		
AL, mm	0.091	0.152		
FK, D	-0.082	0.193		
SK, D	-0.043	0.497		
ΔΚ, D	0.079	0.211		
ACD, mm	0.106	0.093		
CLT, mm	-0.044	0.490		
VCD, mm	0.079	0.212		

SER: Spherical equivalent refraction; AL: Axial length; FK: Flat keratometry; SK: Steep keratometry; ACD: Anterior chamber depth; CLT: Crystalline lens thickness; VCD: Vitreous chamber depth.

AL reduction after HAL treatment, thickened CLT, decreased ACD and VCD, flattened FK, and steepened SK were found

within a mean of 3.99mo. The study also investigated the association between lower astigmatism and AL reduction.

AL reduction is not fully understood because it is rare, and data on it are limited. In this study, the AL in the group with AL reduction was shortened by 0.17 mm; it was shortened by more than 0.3 mm for four participants. AL is a crucial parameter for evaluating myopia progression. OA-2000 has been widely used for AL measurement and biometric component imaging of the whole eye for refractive errors, with the advantages of rapid scanning speed and low failure rate^[21-23]. In the study by Huang et al^[24], the instrument showed intraobserver repeatability with a low intra-subject standard deviation (0.02 mm), testretest repeatability (0.06 mm), and intra-subject coefficient of variation (0.10%). Because AL was measured from the anterior surface of the retina, the possible cause of axial shortening was choroidal thickening. Huang et al^[25] found that the macular choroidal thickness in children with myopia wearing HAL increased by 11-16 µm in the first year. The extent of choroidal thickening did not equally explain the extent of eye shortening.



Figure 2 Scatter plot illustrating the relationship between changes in AL and ocular biometric factors AL: Axial length; Δ ACD: Change in anterior chamber depth; Δ CLT: Change in crystalline lens thickness; Δ VCD: Change in vitreous chamber depth.

AL is partially affected by physiological factors, such as diurnal variations and accommodation. Ranjay revealed that AL underwent significant diurnal variation with a mean amplitude of AL change of $32\pm18 \ \mu m^{[26]}$. Several studies have reported transient changes in the AL with accommodation, and the magnitude of AL elongation correlates with that of the accommodation stimulus^[27]. Zhong *et al*^[28] revealed an AL elongation of 26.1±13.4 μm between the rest and accommodative states using ultralong scan depth OCT. These changes were transient and minimal. Combining the above factors, AL remains shortened relative to the initial status.

However, the exact cause for this phenomenon remains unclear. Previous animal studies have revealed that the eyes of various species shorten axially during active compensation for superimposed myopic defocusing^[12]. The eyes of shrews exhibited active scleral remodeling by boosting glycosaminoglycan synthesis in the sclera, which contrasted with the axial elongation. The control of myopia progression by HAL may be attributed to periretinal myopic retinal defocus. Whether AL reduction compensates for myopic defocus imposed by a positive lens during HAL treatment should be further studied.

Ocular parameters, particularly corneal curvature, and crystalline lens morphology, are generally associated with refractive errors. While Park *et al*^[29] demonstrated an inverse correlation between AL and corneal curvature in emmetropization, the relationship between corneal remodeling and axial elongation remains debated. The AL reduction group

demonstrated significant flattening of FK and steepening of SK, resulting in increasing ΔK , whereas minimal changes occurred in AL elongation cases. This contrasts with Singapore longitudinal study showing stable corneal curvature despite myopia progression^[30]. Zadnik *et al*^[31] revealed that the crystalline lens exhibits adaptive thinning during ocular growth, potentially counterbalancing axial elongation through two mechanisms: 1) compensating thinning and reducing optical properties, 2) passive stretching from equatorial globe expansion. Although CLT thinning typically correlates with ACD increases^[32], our cohort displayed significant ACD changes with only subtle changes in CLT alterations in AL elongation subjects. The result may be due to the methodological limitations of potentially confounding accommodation effects of crystalline lens. Notably, VCD reduction paralleled AL changes ($R^2=0.883$, P<0.001), with the AL reduction group demonstrating 0.16±0.12mm VCD decreases. The AL-VCD association indicates their coupled contribution to refractive error development. In our study measurements of VCD was calculated rather than direct measured. More reliable and accurate measurement methods are needed in future studies.

The current cohort found no significant associations between demographic factors and AL changes. However, baseline refractive astigmatism (0.30±0.39 D vs 0.47±0.56 D in AL reduction vs elongation group) showed tiny but significantly association with rapid AL changes in children with HAL treatment, despite no corneal astigmatism correlation. Totally 16.3% of the 252 eligible cases exhibited cylindrical refractive error of ≥1.00 D. The current study included children with myopia with equal baseline SER. Both spherical and spherocylindrical lenses achieved equal mean magnitude of SER, yet astigmatic blur clearly altered the refractive and ocular endpoints in the current study, suggesting separate regulatory pathways from spherical defocus mechanism. Animal experiments and clinical research have revealed a positive association between refractive astigmatism and myopia development^[33-36]. Previous studies have revealed that induced refractive astigmatism is more strongly correlated with internal astigmatism than with corneal astigmatism, which may be correlated with posterior eye shape parameters, such as equatorial diameters and ocular expansions^[33,37]. The absence of off-axis astigmatism and the outstanding visual performance in the far peripheral visual field of chickens stems from an internal refractive element, like the crystalline lens, rather than from the cornea^[38]. That may explain the weak cornea-AL relationship. Observation of human choroidal thickness after short-term exposure to astigmatic defocus have shown that with-the-rule astigmatic defocus induces transient choroidal thickening distinct from spherical defocus patterns^[39]. This research provides evidence that the processing of astigmatic defocus may involve a different signaling pathway from that of spherical defocus. Given the results of the current and previous studies, further investigation is needed to determine the longterm effects of HAL induced astigmatic profile modifications The current study has several limitations. First, although ocular parameter measurements were consistently conducted between 8:00 and 17:00, subtle diurnal fluctuations in AL may persist. Second, the retrospective design inherently introduces selection bias and unmeasured confounders. Factors such as near-work duration and outdoor activity time were not systematically recorded, which might have influenced the observed outcomes. Third, this study did not establish whether AL reduction could serve as a predictor for the sustained efficacy of HAL treatment in myopia control. A longitudinal follow-up study is currently ongoing to evaluate the durability of HAL interventions in participants with AL reduction and explore associated biomechanical mechanisms. Fourth, choroidal thickness measurements were not included in the analysis. Previous studies have found that choroidal thickening may contribute to the compensatory effect of AL reduction. Further studies are required to determine the definitive attributes of the choroidal changes.

Children with myopia undergoing HAL treatment may have thickened CLT and decreased ACD and VCD, as well as increased corneal astigmatism with AL reduction. Lower baseline astigmatism is associated with AL reduction. These findings are helpful for analyzing the biological characteristics of AL reduction and provide insights for further studies of the mechanisms underlying myopia progression to achieve better myopia control.

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