Changes in Dimensions and Functions of Crystalline Lens in High Myopia Using CASIA2 Optical Coherence Tomography

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Keywords
High myopia · Lens shape · Lens power · Lens accommodation

Abstract
Introduction: Crystalline lens is the major dioptic component and varies with refractive status. In this study, we aim to evaluate the changes of dimensions and functions of crystalline lens in high myopia (HM) and its correlated variables using CASIA2 swept-source optical coherence tomography.

Methods: One hundred and thirty eligible eyes of myopic patients from 18 to 40 years old were enrolled and divided into low-to-moderate myopia (LMM) and HM groups according to spherical equivalent (SE). Anterior segment features, including lens thickness (LT), anterior radius of curvature (ARC), posterior radius of curvature (PRC), anterior chamber depth (ACD), and lens tilt were obtained by CASIA2. Lens power was calculated using Bennett’s formula. Sixty-seven participants were imaged at the static state and the accommodative state induced by −3 diopter (D) stimulus.

Results: Compared to the LMM group, the HM group exhibited a significantly reduction in LT, ARC, and lens tilt (all \( p < 0.01 \)). Each parameter correlated positively with SE (all \( p < 0.01 \)). Lens power increased with LT and tilt (\( r = 0.42, 0.45 \)) but decreased with ARC and axial length (AL) (\( r = −0.37, −0.62 \)) among highly myopic eyes. Multivariate regression analysis revealed that lower lens power appeared to be independently associated with axial elongation in both groups (LMM: \( \beta = −1.124, p = 0.002 \); HM: \( \beta = −1.603, p < 0.001 \), respectively). Decreases in ARC and ACD were accompanied by accommodative response in each group, while PRC reduced during accommodation (\( p = 0.009 \)) only in HM.

Conclusions: Young adults with HM presented a thinner thickness, smaller tilt, less lens power, and higher accommodative response. Lens shape was closely associated with SE; however, AL was a meaningful indicator of lens power.

Introduction

Myopia is the most common refractive error globally, affecting as much as 80–90% young adults in East and Southeast Asia [1]. The concomitant prevalence of high myopia (HM) has shown a rapid increase, and it is estimated that 10% of the world population will be related by 2050 [2, 3]. HM, characterized by excessive elongation...
of the globe, may result in a range of uncorrectable visual impairment such as myopic maculopathy, retinal detachment, glaucoma, and other significant complications [4, 5]. A considerable amount of studies have reported that precise balance between dioptric components including the cornea and crystalline lens and axial length (AL) should be in homeostasis during normal eye growth. The crystalline lens undergoes with continuous modulation by thinning, flattening, and decreasing power to compensate for ocular growth, thereby maintaining the emmetropia [6, 7]. When myopia occurs, the lens power loss will reach some limit at which it can no longer neutralize the effect of the increased rate of axial elongation [8–10]. Although the maximum adaption could not always project clear images onto the retina, the lens shape varies throughout refractive development from low-to-moderate myopia (LMM) to HM. Thus, the morphological changes of crystalline lens have been a pivotal issue in the emmetropization process and myopia progression.

Previous studies demonstrated that myopes exhibited thinner lens thickness (LT) and lower crystalline lens power compared to their emmetropic counterparts [11, 12]. Nevertheless, the correlation between lens shape and myopia has not been reached agreement in different degrees of myopia [13, 14]. A Singapore cohort study showed that the positive correlation of SE with lens power was only moderate, but the strongest correlation was seen for lens power and AL [15]. Another finding conducted by Cheng et al. [16] implied that the lens power was negatively associated with AL in highly myopic children and adolescents with AL <27 mm. These results indicated that lens change induced by HM may have a difference on anterior segment biometry statically compared to LMM. Most studies were carried out on populations with onset myopia and explored the patterns of alteration in lens power [9, 10]. However, lens shape and functions have scarcely been studied in HM population with stabilized refractive status. In addition, dynamic changes of crystalline lens during accommodation depend on the structural changes, and refractive status can be an interference factor for myopia patients in modulating the ocular dynamics [17].

To further elucidate these uncertain issues, we aimed to investigate the lens dimensions and lens power in highly myopic young adults and its associated factors using the CASIA2 system. This cross-sectional study was also conducted to analyze the different response of lens in ocular dynamics, which may reveal the underlying optical mechanisms of HM.

**Materials and Methods**

**Participants**

This observational cross-sectional study was conducted at Shanghai General Hospital between December 2018 and March 2019. One hundred and thirty eligible eyes of one hundred and thirty myopic patients from 18 to 40 years old were enrolled in this research. Only data from right eyes were included for analysis. Refractive error was presented in the form of spherical equivalent (SE), which was calculated as spherical dioptric power plus 1/2 cylindrical dioptric power, and SE lower than −5.0 diopters (D) was defined as HM. The inclusion criteria were as follows: refractive error ≤−0.5 D, best-corrected visual acuity ≥20/25, and between the ages of 18 and 40 years. Eyes were excluded if any previous history of ocular disease, ophthalmic surgery, laser treatment, or systemic disorders were true. Subjects were organized into 2 groups based purely on the refractive status: the LMM group consists of 54 cases with a refractive error >−5.0 D, and 76 cases with a refractive error ≤−5.0 D were assessed as the HM group. All procedures were performed in accordance with the tenets of the Declaration of Helsinki, and informed consent was obtained from all patients before enrollment. This study was registered at www.chictr.org.cn, number ChiCTR-OOC-15006620. (The flowchart and STROBE checklist were displayed in online suppl. materials; see www.karger.com/doi/10.1159/000526246 for all online suppl. material).

**Eye Examination and Lens Power Calculation**

All individuals underwent comprehensive ophthalmic examinations as follows: slit-lamp examination, best-corrected visual acuity, refractive status, and AL. All ophthalmic parameters were measured three times by two skilled doctors independently, and the mean value was used. Refractive error was measured with an autorefractor (KR-8900, Topcon, Tokyo, Japan) with 3 consecutive readings per eye. AL was obtained using Pentacam-AXL (Oculus, Wetzlar, Germany). If any two measurements varied by more than 0.5 D of SE and 0.02 mm of AL, another three consecutive measurements were obtained and repeated until the variation between each two measurements within a set which was less than the required value.

The right eye of each subject was scanned with CASIA2 (Tommy Corporation, Nagoya, Japan) by a trained operator blinded to the precedent diagnostic results. This latest swept-source optical coherence tomography (SS-OCT) device can image the lens and anterior part of the eye at 50,000 A-scans per second using a wavelength of 1,310 nm. Several studies have used CASIA2 to assess cataract, glaucoma, and other ocular surface diseases with high repeatability, especially in tilt measurements [18–20]. In a darkened room, each patient was requested to keep staring at 1 fixed internal point during the entire scanning process. Two consecutive scans were performed using Lens Biometry and Corneal Topography modes for CASIA2 image acquisition.

The Lens Biometry mode, which is comprised of 16 consecutive meridional scans (800 A-scans per line), produces 16 distinct 2-dimensional AS-OCT images from different angles of crystalline lens. Five parameters about lens geometry, including LT, anterior radius of curvature (ARC), posterior radius of curvature (PRC), decencentration, and tilt angle were defined and automatically measured in 3D analysis by CASIA2 build-in software (Version 3E.22). Afterward, the Corneal Topography mode facilitated the data col-

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The crystalline lens power \( (P_L) \) was calculated using Bennett’s formula that is as follows [21, 22]:

\[
P_L = \frac{-1000n (S_a + K)}{1000n - (ACD + cT)(S_a + K)} + \frac{1000n}{cT + V} \]

\[ V = AL - ACD - LT \]

The collection of central corneal thickness (CCT), anterior chamber depth (ACD), and anterior and posterior corneal radii of curvature. The scan was performed using the auto-alignment function, and the image quality was assessed during the acquisition by the operator. Figure 1 shows the representative image of crystalline lens and the diagram describing the definitions of anterior segment by CASIA2 SS-OCT.

**Fig. 1.** Representative image of the crystalline lens shape obtained from the CASIA2 device. Optic axis of lens (vertical orange dot lines), vertex normal (vertical blue solid line), and anterior and posterior lens boundary (orange dot lines) are automatically drawn. Crystalline LT (vertical orange solid line) and surface curvatures are calculated by the built-in software. **a** Lens shape of participants in the LMM group. **b** Lens shape of participants in the HM group. **c–d** Lens shape in each group before accommodation. **e–f** Lens shape in each group after 3-D accommodation.
in which \( T \) is the LT, \( V \) is the vitreous depth, \( n = 4/3 \) of the aqueous and vitreous indices, \( c_1 = 0.596 \), and \( c_2 = -0.358 \) as estimated using the Gullstrand-Emsley eye model. The SE refraction at the corneal vertex was defined as \( S_{cv} = SE/(1-0.014 \times SE) \). Additionally, the effective ACD in this formula contained the CCT, which was the same with that measured by CASIA2. The corneal power (\( K \), in D) was calculated from the CCT, anterior and posterior corneal radii curvature (\( R_{m,a} \) and \( R_{m,p} \)), and the corneal refractive index (\( n_c = 1.376 \)).

\[
K_{m,a} = \frac{n_c - 1}{R_{m,a}} \quad K_{m,p} = \frac{n_c - 1}{R_{m,p}}
\]

\[
K = K_{m,a} + K_{m,p} - K_{m,a} \times K_{m,p} \times \text{CCT} / n_c
\]

After correcting the refractive error using the CASIA2 built-in program, we obtained images in the static state (0 D of accommodation) and responses to different amplitudes of accommodative stimuli (using −3 D minus-lens accommodative stimuli) for partial subjects. Different accommodation states were achieved by a built-in program, and subjects were asked to clearly look forward at an internal fixation target symbol. The included biometric parameters of 29 eyes in the LMM group and 38 eyes in the HM group were measured in the same scanning mode as mentioned before (Fig. 1c–f).

### Statistical Analysis

Statistical analysis was performed using SPSS software (version 26.0; IBM, Chicago, IL, USA) and R programming language (version 3.6.1). All continuous variables were presented in the format of mean ± standard deviation (SD), while discrete variables are described as counts (proportions). The Student’s \( t \) test was used for comparing clinical and lens characteristics between the two groups. The distribution of gender was examined by the \( \chi^2 \) test. Linear regression between the ocular biometric parameters and refractive status was analyzed with Pearson correlation coefficients. Multiple regression analysis was performed to explore the association between lens power and SE and AL after adjusting for the other factors. Paired \( t \) tests were used to compare the two different accommodative states in each group. \( p < 0.05 \) was considered statistically significant (2-tailed).

### Results

**Decline of LT, ARC, and Tilt Angle in HM**

A total of 130 eyes of myopic patients were enrolled in this study and stratified into the LMM group and HM group according to SE. The demographic and basic biometric measurements are presented in Table 1. The mean age of 54 subjects (21 males and 33 females) in the LMM group and 76 subjects (28 males and 48 females) in the HM group were 24.87 ± 5.12 years and 25.72 ± 5.34 years, respectively. No statistical differences were observed in age and gender between two groups (\( p > 0.05 \)). The mean SE was −3.50 ± 0.94 D in the LMM group and −7.57 ± 2.25 D in the HM group, whereas the mean AL was 25.31 ± 0.81 mm in the LMM group and 26.49 ± 1.12 mm in the HM group. Compared to low-to-moderate myopic eyes, the results of \( t \) test showed that the mean LT (4.00 ± 0.73 vs. 3.68 ± 0.40, \( p < 0.01 \)), ARC (12.20 ± 1.36 vs. 11.35 ± 1.24, \( p < 0.01 \)), and tilt angle (3.86 ± 0.98 vs. 3.33 ± 1.21, \( p < 0.01 \)) in the HM group were significantly reduced. No significant differences were observed in PRC and decentration (\( p > 0.05 \)).

### Negative Correlations between Lens Characteristics and Refractive Diopter

To assess the performance of crystalline lens geometry, Pearson’s correlation coefficients between lens parameters and clinical features associated with myopic subjects were analyzed in Table 2. LT (\( r = 0.31, p < 0.01 \)), ARC (\( r = 0.25, p < 0.01 \)), and lens tilt (\( r = 0.23, p < 0.01 \)) all showed increasing trends with SE. By contrast, larger AL was positively associated with smaller lens tilt (\( r = -0.36, p < 0.01 \)). LT and ARC revealed no independent

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correlation with AL (all $p > 0.05$). As illustrated in Figure 2, smaller LT, ARC, and tilt angle were found in HM from scatter plots and corresponding linear regression lines.

**Associations between the Lens Power and AL and Lens Parameters in HM**

The mean lens power was $24.80 \pm 1.60$ in the LMM group and $24.61 \pm 1.54$ in the HM group ($p > 0.05$, Table 1). There was no correlation between lens power and SE in all participants when performing Pearson’s correlation analysis (all $p > 0.05$). However, lens power was negatively correlated with AL in subjects in both myopia groups (LMM: $r = -0.45$; HM: $r = -0.62$; all $p < 0.001$, Fig. 3a, b). We further analyzed the association between lens power and lens parameters in different refractive status. Figure 4 shows the lens power increased with LT (LMM: $r = 0.53$, HM: $r = 0.42$, all $p < 0.01$) and decreased with ARC (LMM: $r = -0.28$, $p = 0.04$; HM: $r = -0.37$, $p < 0.01$) in both groups. However, the negative association between lens power and lens tilt was only found in the HM group ($r = 0.45$, $p < 0.01$).

**Impact Factors of Lens Power in HM**

Multivariate regression analysis adjusted for age and sex was used to identify independent factors associated with lens power. As shown in Table 3, the analysis revealed that greater lens power was independently associ-
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**Fig. 3.** The correlation between lens power and other associated factors. The numbers in the figure represent correlation coefficient ($r$). Significant differences are masked by asterisks (*). **a** Regression coefficient matrix in the LMM group. **b** Regression coefficient matrix in the HM group.

|       | Age  | Gender | SE    | AL    | Lens power |
|-------|------|--------|-------|-------|------------|
| Age   | 1    |        |       |       |            |
| Gender| 0.15 | 1      |       |       |            |
| SE    | 0.26*| 0.07   | 1     |       |            |
| AL    | 0.06 | -0.39* | -0.53*| 1     |            |
| Lens power | -0.13 | 0.01 | 0.19 | -0.45* | 1 |

### Fig. 4.** Linear correlations between lens power and lens parameters. The numbers in the figure represent correlation coefficient ($r$). Significant differences are masked by asterisks (*). **a**–**c** LT, ARC, and lens tilt in the LMM group. **d**–**f** LT, ARC, and lens tilt in the HM group. Linear correlation coefficient ($r$) and $P$ value were presented in scatter graphs.

|       | Lens power, D | LT, mm | ARC, mm | Tilt, ° |
|-------|---------------|--------|---------|---------|
| **a** | 23.5          | 4      | 12      | 2       |
| **b** | 23.5          | 4      | 12      | 2       |
| **c** | 23.5          | 4      | 12      | 2       |
| **d** | 23.5          | 4      | 12      | 2       |
| **e** | 23.5          | 4      | 12      | 2       |
| **f** | 23.5          | 4      | 12      | 2       |
Discussion

Our study pointed out the changes in dimensions and functions of crystalline lens in HM observed by CASIA2. As one of the most important refractive components, various crystalline lens impacted by mechanical stretching of AL in myopia progression have been a consistent concern for ophthalmologists and patients [8–11]. With CASIA2 as the main tool, this cross-sectional study explored the obvious reduction of LT, ARC, and lens tilt in HM compared to LMM. We also determined that lens power increased with LT and tilt but decreased with ARC among highly myopic eyes. Lower lens power appeared to be independently associated with ocular elongation.

In the current study, the results revealed a significant difference in which LT, ARC, and lens tilt in LMM were markedly greater on average than those of the HM in young adults. We previously reported that myopia presented thinner lenses compared to emmetropia and hyperopia in school-aged children [23]. Meanwhile, the magnitude of natural crystalline lens tilt varied in differ-

Table 3. Multiple regression analysis of associations with lens power

| Variables | LMM (n = 54) | HM (n = 76) |
|-----------|--------------|-------------|
|           | β   | 95% CI  | standardized β | p value | β   | 95% CI  | standardized β | p value |
| Age, years | −0.016 | (−0.102, 0.070) | −0.051 | 0.71 | −0.014 | (−0.065, 0.037) | −0.049 | 0.584 |
| Gender    | −0.626 | (−1.554, 0.302) | −0.193 | 0.181 | 0.443 | (−0.219, 1.104) | 1.14 | 0.186 |
| SE, D     | −0.144 | (−0.690, 0.402) | −0.085 | 0.599 | −0.212 | (−0.389, −0.034) | −0.309 | 0.020* |
| AL, mm    | −1.124 | (−1.801, −0.446) | −0.567 | 0.002* | −1.603 | (−1.406, −0.721) | −0.776 | <0.001* |

* Significant correlations with lens power were tested by multivariate regression analysis after adjusting for age, gender, SE, and AL. Adjusted $R^2$ for subjects in LMM = 0.18, for subjects in HM = 0.47.

Table 4. Biometric parameters in static (0 D) and accommodative condition (3 D)

| Variables              | LMM                      | HM                      |
|------------------------|--------------------------|-------------------------|
|                        | 0 D | 3 D | p value | 0 D | 3 D | p value |
| LT, mm                 | 4.32±0.86 | 4.40±0.93 | 0.236 | 3.71±0.53 | 3.72±0.55 | 0.738 |
| ARC, mm                | 12.46±1.51 | 11.78±1.96 | <0.001* | 11.32±1.25 | 10.86±1.40 | 0.001* |
| PRC, mm                | 6.06±0.52 | 6.04±0.61 | 0.724 | 5.91±0.30 | 5.83±0.28 | 0.009* |
| Decentration, mm       | 0.19±0.06 | 0.19±0.07 | 0.691 | 0.18±0.07 | 0.18±0.07 | 1 |
| Tilt, degree           | 3.85±0.95 | 3.84±0.95 | 0.808 | 3.51±1.15 | 3.48±1.13 | 0.56 |
| Anterior chamber depth, mm | 3.85±0.23 | 3.81±0.25 | <0.001* | 3.80±0.23 | 3.78±0.23 | 0.007* |

* Statistical significance was tested by the paired t test.
ent studies and the similar trend found by Lu et al. [24, 25] in elderly patients with HM could be useful as reference points for our study. The relationship between a single parameter with SE and AL has already been analyzed in the published literature, while no studies have addressed the whole lens shape in HM with stable refraction [8, 12, 26]. Not completely consistent with the study of Muralidharan et al. [12], our findings indicated that LT, ARC, and lens tilt \((r = 0.31, 0.25, 0.23, \text{respectively}; \text{all } p < 0.01)\) were associated with an increase with SE ranging from \(-0.50 \text{ D} \) to \(-13.50 \text{ D} \), whereas the relationship with AL may become weaker. This phenomenon also observed in young adults with HM was speculated to arise from enlarged ciliary muscles in the developing eye that restricts equatorial expansion of the lens, resulting in an compensatory regulation of crystalline lens thinning and flattening [27, 28]. Additionally, high myopes exhibited a greater sagittal height in the nasal corneal periphery and anterior sclera, which may result in the smaller tilt in HM [29]. Consequently, the static shape of crystalline lens is one of the most important characteristics in HM and may affect the visual outcome in clinical interventions.

To our knowledge, Bennett’s formula was widely used to calculate lens power without the use of commercially unavailable devices [21]. Three-dimensional topography images captured by this novel SS-OCT allowed for the validity and accuracy in confirming the lens power. Our findings considered that lens power increased with LT and tilt \((r = 0.42, 0.45, \text{all } p < 0.01)\) but decreased with ARC and AL \((r = -0.37, -0.62, \text{all } p < 0.01)\) in HM. Given that corneal power stabilizes in a few years after birth, AL and lens power were the main determining factors of refractive status. AL, undergoing a combination of somatic and regulated growth, has experienced the rapid stage of ocular development before adulthood in myopia [6, 7]. As for crystalline lens, both the flattening of surface curvature and the decline of gradient index are responsible for lens power loss in the growing process. Based on several clinical observations of children, there is accelerated loss of lens power in emmetropia and early stage of myopia [10, 30]. However, the lens seems to reach a compensatory limit below which it is unable to lose power efficiently so that this loss is retarded when myopia persists in the later stage. We focused on the negative correlation between lens power and AL in HM, suggesting that ocular growth may still have an influence on lens power in further myopia progression, not just before myopia onset.

Numerous studies have investigated that the relationship between lens power and AL in children was different in different refractive groups, but the refractive index profile of human lens continued to change until the adult index plateau is developed [7, 15, 16]. According to the results, AL was the independent factor on lens power in each group but was more evident in HM \((\beta = -1.603, p < 0.001)\) than that in LMM \((\beta = -1.124, p = 0.002)\) after adjusted for age and sex. The specific effect of axial elongating on lower lens power remains unclear and may cause other lens functions change. Crystalline lens facilitated variable focusing of light onto the retina both statically and dynamically, confirming an important role for different degrees of myopia. Another interesting finding in our study was that the anterior lens curvature (all \(p < 0.01\)) became steeper in all subjects after 3-D accommodation stimuli, but posterior curvature only changed in HM significantly. An established report based OCT image found that ARC decreased with accommodation in non-HM [31]. Moreover, Shoji et al. [32] discussed the contribution of AL to the lens shape in accommodation, indicating the ARC became fatter as the AL increased. The reason why PRC showed different movement in HM was perhaps that the thinner LT needs more accommodative amplitude, in order to reach the same refractive power during stimuli. The disproportional pattern of accommodative response between the crystalline lens and the whole eye could be a distinction in highly myopic eyes, even for the effects on presbyopia and intraocular lens refilling approaches subsequently.

This study has several limitations. First, it is a cross-sectional research in young myopia adults, which thereby limits our ability to infer causality and determine the lens shape alterations during the progression of myopia. Therefore, our findings need further validation through follow-up studies. Second, our study included a relatively small sample size of young subjects. However, we performed sample size calculation with G*power (version 3.1.9) and found that our sample size was adequate to provide a detection power over 95% [33]. Third, the truly accommodative response of the whole eye was not quantified by pull-in method or open-field autorefractor so that the ratio of accommodation response between the crystalline lens and the whole eye cannot be confirmed. Even though the lag of accommodation was necessary to take into account, the morphological changes during accommodation may help clarify the existence of ocular dynamics.

**Conclusion**

In summary, using a novel, commercially available anterior segment SS-OCT system, our study demonstrated that young adults with HM presented the thinner thick-
ness, smaller tilt, less lens power, and higher accommoda-
tive response. Lens shape was closely associated with SE; however, AL was a meaningful indicator of lens power. The results contribute to explore the potential connection between ocular structure and visual function, which may provide a critical clue for understanding the pathophysiology of HM-associated diseases. Further longitudinal studies of different aged groups are warranted to identify the impact of HM on AS-OCT parameters.

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Statement of Ethics
The study protocol complied with the requirements of the Institutional Review Board of Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine (IRB No. 2015KY131), and adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from the subjects and at least one of the subject’s legal guardians before participation. This study was registered at www.chictr.org.cn, number ChiCTR-OOC-15006620.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

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Author Contributions
Study design: Xuetong Wang, Ying Yuan, and Bilian Ke; study performance: Xuetong Wang, Chengcheng Zhu, and Xiaojun Hu; data collection and management: Xuetong Wang and Chengcheng Zhu; data analysis and interpretation: Mingming Liu and Lu Liu; writing and review of the manuscript: Xuetong Wang and Bilian Ke. Xuetong Wang contributed to the manuscript as the first author, and Bilian Ke contributed to the manuscript as the corresponding author. All the authors have approved the manuscript.

Data Availability Statement
The datasets generated and/or analyzed during the present study are not publicly available because of patient privacy concerns (obtained from Shanghai General Hospital, of Shanghai Jiao Tong University, Shanghai repository) but are available from the corresponding author upon reasonable request.
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