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Research Article

Orthokeratology and Low-Intensity Laser Therapy for Slowing the Progression of Myopia in Children

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Orthokeratology (OK) is widely used to slow the progression of myopia. Low-level laser therapy (LLLT) provides sufficient low energy to change the cellular function. This research is aimed at verifying the hypothesis that LLLT treatment could control myopia progression and comparing the abilities of OK lenses and LLLT to control the refractive error of myopia. Eighty-one children (81 eyes) who wore OK lenses, 74 children (74 eyes) who underwent LLLT treatment, and 74 children (74 eyes) who wore single-vision distance spectacles for 6 months were included. Changes in axial length (AL) were 0.23 ± 0.06 mm for children wearing spectacles, 0.06 ± 0.15 mm for children wearing OK lens, and -0.06 ± 0.15 mm for children treated with LLLT for 6 months. Changes in subfoveal choroidal thickness (SFChT) observed at the 6-month examination were $-16.84 \pm 7.85\ \mu$m, $14.98 \pm 22.50\ \mu$m, and $35.30 \pm 31.75\ \mu$m for the control group, OK group, and LLLT group, respectively. Increases in AL at 1 month and 6 months were significantly associated with age at LLLT treatment. Changes in AL were significantly correlated with the baseline spherical equivalent refraction (SER) and baseline AL in the OK and LLLT groups. Increases in SFChT at 1 month and 6 months were positively associated with age at enrolment for children wearing OK lens. At 6 months, axial elongation had decelerated in OK lens-wearers and LLLT-treated children. Slightly better myopia control was observed with LLLT treatment than with overnight OK lens-wearing. Evaluations of age, SER, and AL can enhance screening for high-risk myopia, improve the myopia prognosis, and help determine suitable control methods yielding the most benefits.

1. Introduction

Myopia is a global epidemic, which is especially prevalent in East Asia [1]. Myopia, especially in higher levels, results in an increased risk of complications such as retinal detachment, myopic macular degeneration, glaucoma, cataracts, and permanent vision loss [2]. Therefore, a safe, reliable, and effective therapy to slow the progression of myopia would be advantageous for millions of individuals.

Oxidative stress, inflammation, and apoptosis may be key factors in the myopic regulatory pathways [3–6]. The low levels of 5-MTHF in myopia patients may lead to the increase of homocysteine, which closely correlated with oxidative stress, inflammation, and cellular apoptosis [5]. Furthermore, exogenous bFGF effectively ameliorates the excessive axial elongation in chronic form-deprivation myopia in chicks by suppressing retinal neuron apoptosis [3]. Finding a method to suppress the cell apoptosis may be an effective way to control the axial elongation. Thus, we first focused on low-level laser therapy (LLLT) as a new method that contributes to restricting the progression of myopia by preventing cell apoptosis, thereby minimizing inflammation and increasing cell turnover [7, 8].

Recent studies suggest that normal ocular growth and refractive development could be influenced by the spectral composition of ambient light in a variety of ways through chromatic cues [9, 10]. The laser is a device that is widely used for biomedical applications; it creates a pure, intense, monochromatic, and coherent collimated light beam [11, 12]. Laser therapy results in a broad range of molecular, cellular, and tissue effects [13]. LLLT differs from high-power laser therapy because it uses low levels of red and near-infrared light. Its wavelength ranges from 600 nm to 1100 nm, and its output can reach 500 mW [7]. Therefore, it is defined as a type of

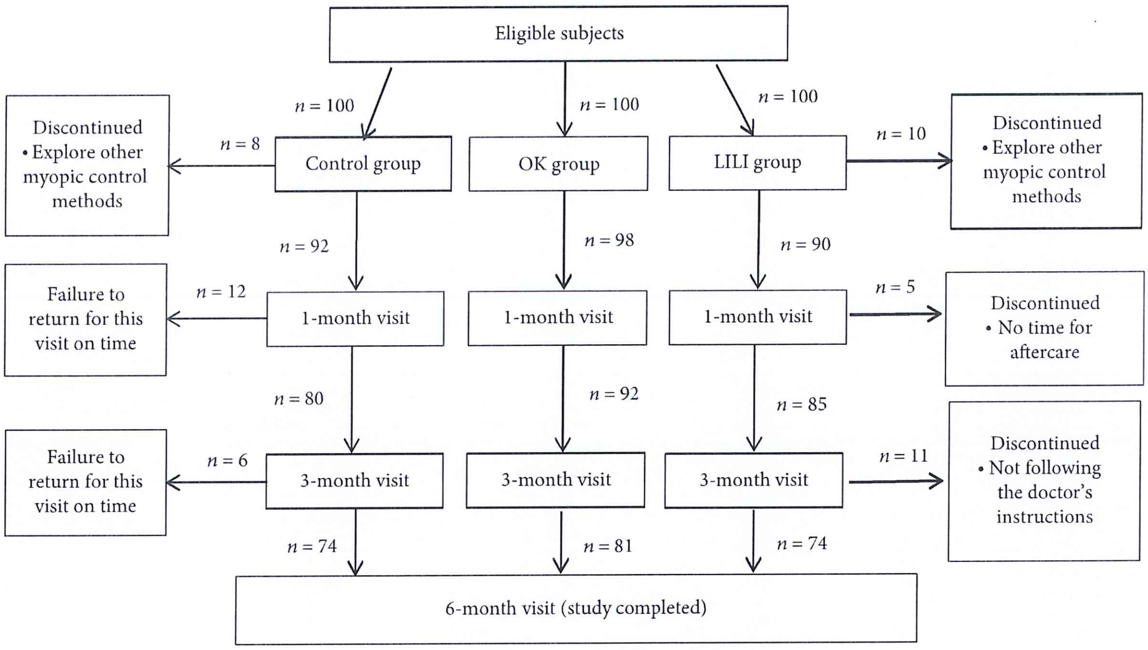


FIGURE 1: Flow chart of participant assignment.

phototherapy that produces sufficiently low energy to induce a stimulus response in tissues without changing the temperature of the surrounding tissues [7].

Various studies have demonstrated that modern orthokeratology (OK) is a key intervention for myopia control that has great effectiveness in children; however, the mechanism remains unclear [14–16]. The OK lens is characterized by its reverse-geometry design, which can form peripheral defocus in the central and peripheral retina by remodeling the cornea and changing the image quality [17, 18]. Recent studies in myopic chicks have demonstrated that the choroid tends to thin with myopia development before alterations in scleral growth [19, 20]. Therefore, the role of the choroid has been emphasized in the OK lens control mechanism [21, 22].

This study describes the research design and clinical 6-month follow-up examinations of children who wore OK lens, underwent LLLT treatment, or wore single-vision distance spectacles. This study is aimed at verifying the hypothesis that LLLT treatment could control myopia progression and comparing the abilities of OK lenses and LLLT to control the progression of myopia.

2. Participants and Methods

2.1. Participants. All participants had myopia; their data were collected from the Outpatient Clinic of the Nanchang University Affiliated Eye Hospital, Nanchang, China, from September 2018 to April 2019. The inclusion criteria were age 6 to 16 years, spherical power plus half cylinder power, spherical equivalent refractive error (SER) ≤ -0.50 D after cyclopentanone use, and 10 to 21 mmHg noncontact tonometer intraocular pressure. The exclusion criteria were presence of ocular or systemic diseases such as strabismus, amblyopia, and cardiac respiratory illness. Children already using OK and/or other myopia control modalities, except for wearing spectacles, were also excluded. We recruited a total of 300 children that were randomly assigned to control ($n = 100$), OK ($n = 100$), or LLLT ($n = 100$) groups. Consequently, 229 children completed the study (Figure 1). A total of 74 children 7 to 14 years of age (mean age, 10.33 ± 2.03 years; 54% male) were included in the control group. A total of 81 children 8 to 14 years of age (mean age, 10.88 ± 1.92 years; 54% male) were included in the OK group. A total of 74 children 7 to 15 years of age (mean age, 10.22 ± 2.38 years; 54% male) were included in the LLLT group. Differences in sex, age, SER, axial length (AL), and subfoveal choroidal thickness (SFChT) at baseline were not significant among the three groups. Table 1 lists the general characteristics of the enrolled children.

The present study was performed in compliance with the principles of the *Declaration of Helsinki* and was approved by the ethical committee of Nanchang University Clinical Research Centre (2018-KY-03). Parents understood the benefits and risks of this study before providing signed informed consent on behalf of their children.

2.2. Study Procedures. Researchers performed detailed ophthalmological examinations before treatment (baseline) and at every subsequent appointment; these examinations included uncorrected and corrected visual acuity tested at a distance of 4 m using a retro-illuminated Early Treatment of Diabetic Retinopathy Study chart, cycloplegic refraction testing (1% cyclopentolate hydrochloride), the spherical equivalent (SE) determined (obtained with the following formula: SE = spherical + astigmatism/2), slit-lamp examination (slit lamp; Haag-Streit, Köniz, Switzerland), ocular movement testing, tonometry (model NT-4000; Nidek Inc., Fremont, CA, USA), fundoscopy, AL measurements (Carl Zeiss Meditec Inc., Dublin, CA, USA), corneal endothelial

Table 1: Baseline characteristics of study groups.

Characteristics	Control ($n = 74$)	OK ($n = 81$)	LILI ($n = 74$)	p value
Sex (male : female)	40 : 34	44 : 37	40 : 34	0.412[a]
Age	10.33 ± 2.03	10.88 ± 1.92	10.22 ± 2.38	0.114[b]
SER (D)	−3.32 ± 1.36	−3.42 ± 1.28	−3.39 ± 2.17	0.937[b]
AL (mm)	25.07 ± 0.87	25.07 ± 0.92	25.07 ± 1.15	0.99[b]
SFCHT (μm)	286.81 ± 63.67	284.36 ± 72.58	288.61 ± 59.59	0.921[b]

SER: spherical equivalent refractive error; AL: axial length; SFCHT: subfoveal choroidal thickness. [a]Chi-square test. [b]One-way ANOVA.

cell density testing, and optical coherence tomography (OCT) (Carl Zeiss Meditec Inc., Dublin, CA, USA).

To avoid the effects of circadian rhythm on the results, OCT scanning was performed twice by the same investigator between 8:00 am and 2:00 pm at baseline, 1-month, 3-month, and 6-month follow-ups. Two independent skilled professionals measured the SFChT using a linear measurement program during the OCT scan. To increase the visibility of the choroid, the enhanced depth imaging mode was used. We defined the thinnest part of the macula in the image as the fovea. The SFChT was measured from the outermost part of the retinal pigment epithelium to the inner layer of the choroidoscleral interface.

Children in the control group wore single-vision distance spectacles the entire day and returned for detailed ophthalmological examinations after 1, 3, and 6 months. Children in the OK group were fitted with OK lenses by our fitting staff. The OK lenses (Euclid Systems Ortho-k; Euclid System Corp., Herndon, VA, USA) used in the present study were made of rigid gas-permeable material (Boston Equalens II; Bausch + Lomb, Laval, Quebec, Canada). The diameter of the lenses ranged from 10.2 to 11 mm. The lens consisted of a central base curve with a 6.2 mm optic zone diameter, 0.5 mm wide reverse curve, 1.2 mm wide alignment curve, and 0.5 mm wide peripheral curve. They wore them every night for at least 7 consecutive hours to guarantee myopia control. Children returned for ophthalmological examinations after 1, 3, and 6 months. In addition to the aforementioned examinations, we also used a corneal fluorescein stain to determine any complications and check the corneal topography to ensure the correct fit of the OK lens.

Children in the LLLT group wore single-vision distance spectacles the entire day and underwent LLLT (power, 2 ± 0.5 mW; wavelength, 650 nm; Ya Kun Optoelectronic Co., Ltd., Wuhan, China) twice per day for 3 minutes each session, with at least a 4-hour interval between sessions. There were no specific guidelines for room illumination. After the first measurement session, each child returned for follow-up examinations at 1, 3, and 6 months and completed all the aforementioned examinations.

2.3. Data Analysis. Statistical analyses were performed using IBM SPSS statistics version 23.0 (IBM Co., Armonk, NY, USA). Only the data of the left eyes were used. All values were first tested for normality and are presented as the mean ± the standard deviation unless otherwise stated.

One-way analysis of variance (ANOVA) followed by Tukey's *post hoc* tests were used to analyze the differences in basic variable data of the subgroups. A comparison of sexes among the three groups was performed using the chi-square test. Changes in SER, AL, and SFChT between baseline and each follow-up visit were analyzed by repeated-measures ANOVA. The Greenhouse-Geis test was used if the sphericity assumption was violated. The main effects of time, group, and the interaction of effect time and group were included in the model. Correlations between changes in parameters at 6 months and baseline factors were analyzed using the Pearson correlation analysis. To study the association of AL/SFChT changes at 6 months with baseline factors in all groups, we applied stepwise multiple linear regression models. p value < 0.05 was defined as statistically significant.

3. Results

The mean SER decreased slightly over time from baseline to the 6-month follow-up in the LLLT group, but it increased from baseline to the 6-month follow-up in the control group. This disparity between the control and LLLT groups was statistically significant. The mean AL increased in the control group and OK group, but decreased slightly in the LLLT group. These changes differed significantly from each other over time. During the same period, the mean AL was shorter in the LLLT group than that in the other two groups. The SFChT in the LLLT and OK groups compared to that in the control group was thicker at each examination, and the difference was statistically significant (Table 2, Figure 2).

Table 3 displays the different timetables of changes in parameters at each sampling point for the three groups. Changes in SER were significantly different in the control group and LLLT group at the time of the study ($p < 0.001$). At the 1-month follow-up, the mean changes in SER were −0.07 ± 0.11, −0.24 ± 0.16, and −0.50 ± 0.24 D in the control group and 0.11 ± 0.17, 0.22 ± 0.32, and 0.21 ± 0.34 D in the OK group at 1 month, 3 months, and 6 months, respectively. Increases in AL were significantly smaller in children wearing OK lens than in the control group at the 3-month follow-up and 6-month follow-up, but changes at the 1-month follow-up were not ($p = 0.184$). Decreases in AL in the LLLT group differed significantly from those in the control and LLLT groups at each sampling point. Increases in SFChT at 1 month, 3 months, and 6 months were significantly smaller in OK lens-wearers than in the LLLT group, whereas the SFChT in the control group significantly decreased.

To understand the relationship between parameter changes and baseline factors, Pearson's correlation coefficient

Table 2: Parameters at different sampling points (mean ± SD).

Parameters		Control ($n = 74$)	OK ($n = 81$)	LILI ($n = 74$)
SER (D)	Baseline	−3.32 ± 1.36	−3.42 ± 1.28	−3.39 ± 2.17
	One month	−3.39 ± 1.35		−3.28 ± 2.14
	Three months	−3.56 ± 1.37		−3.17 ± 2.13
	Six months	−3.82 ± 1.37		−3.17 ± 2.14
		F main effect/p value: 27.82/<0.001		
		F crossover effect/p value: 128.80/<0.001		
AL (mm)	Baseline	25.07 ± 0.87	25.07 ± 0.92	25.06 ± 1.14
	One month	25.09 ± 0.87	25.07 ± 0.91	25.01 ± 1.14
	Three months	25.16 ± 0.87	25.09 ± 0.88	24.99 ± 1.11
	Six months	25.30 ± 0.86	25.13 ± 0.89	25.00 ± 1.11
		F main effect/p value: 67.21/<0.001		
		F crossover effect/p value: 62.86/<0.001		
SFChT (μm)	Baseline	286.81 ± 63.67	284.36 ± 72.58	288.61 ± 59.59
	One month	286.45 ± 63.61	296.49 ± 72.61	311.84 ± 67.08
	Three months	278.59 ± 63.64	297.81 ± 73.62	320.18 ± 66.61
	Six months	269.97 ± 64.11	299.33 ± 73.65	323.91 ± 65.63
		F main effect/p value: 53.00/<0.001		
		F crossover effect/p value: 64.42/<0.001		

SER: spherical equivalent refractive error; AL: axial length; SFChT: subfoveal choroidal thickness.

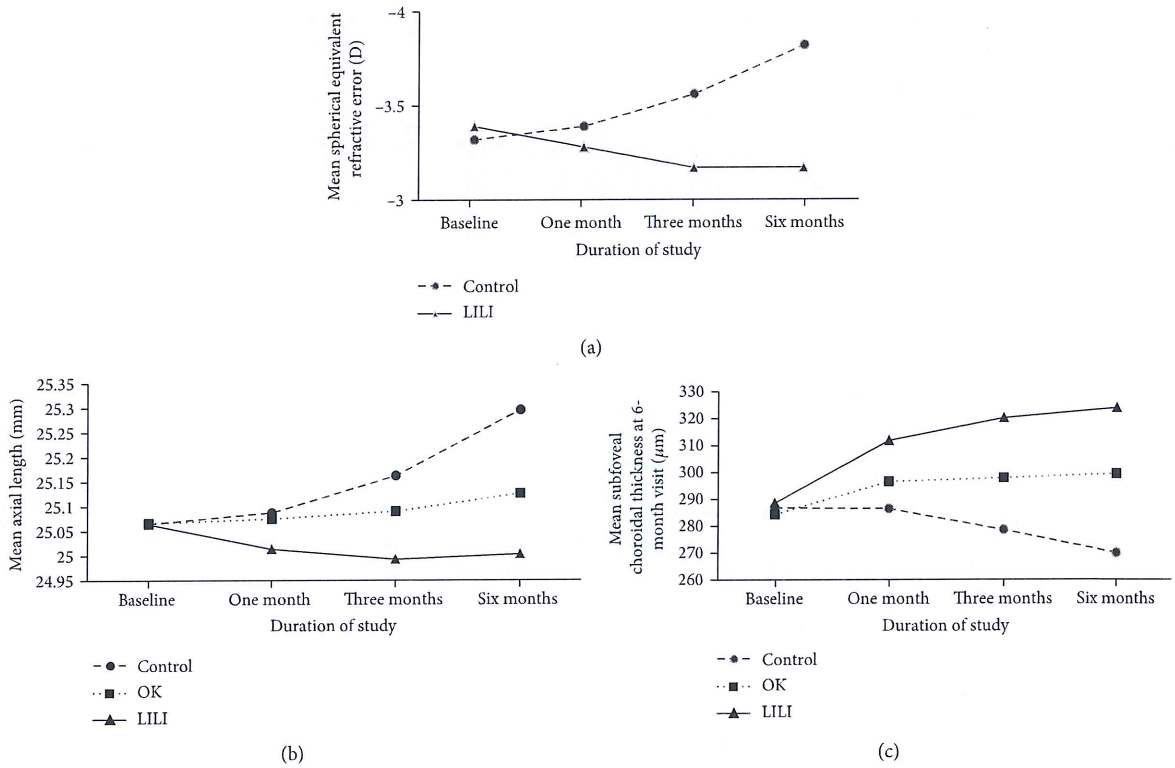


Figure 2: Time courses of mean spherical equivalent refractive error (SER), axial length (AL), and subfoveal choroidal thickness (SFChT). Error bars represent the standard deviation. (a) Time courses of mean SER in control group, and LLLT group. (b) Time courses of mean AL in control group, OK group, and LLLT group. (c) Time courses of mean SFChT in control group, OK group, and LLLT group.

Table 3: Change in parameters at each sampling point (mean ± SD).

Parameters		Control ($n = 74$)	OK (n = 81)	LILI ($n = 74$)	F value	p value
Change in SER (D)	1 month	-0.07 ± 0.11		0.11 ± 0.17	11.24	<0.001[a]
	3 months	-0.24 ± 0.16		0.22 ± 0.32	11.61	<0.001[a]
	6 months	-0.50 ± 0.24		0.21 ± 0.34	6.58	<0.001[a]
Change in AL (mm)	1 month	0.02 ± 0.02	0.01 ± 0.08	-0.05 ± 0.07	26.15	<0.001[b]
	3 months	0.10 ± 0.04	0.02 ± 0.17	-0.07 ± 0.12	35.92	<0.001[b]
	6 months	0.23 ± 0.06	0.06 ± 0.15	-0.06 ± 0.15	98.13	<0.001[b]
Change in SFChT (μm)	1 month	-0.36 ± 2.09	12.14 ± 15.30	23.23 ± 24.70	36.65	<0.001[b]
	3 months	-8.22 ± 3.24	13.46 ± 19.46	31.58 ± 31.72	63.50	<0.001[b]
	6 months	-16.84 ± 7.85	14.98 ± 22.50	35.30 ± 31.75	97.48	<0.001[b]

SER: spherical equivalent refractive error; AL: axial length; SFChT: subfoveal choroidal thickness. [a]Independent sample t-test. [b]One-way ANOVA.

was used. The scatter plot graph of the increase in AL at 6 months and age of the groups is shown in Figure 3(a). There were no statistically significant correlations in the control group ($r = -0.114$; $p = 0.335$) and the OK group ($r = -0.216$; $p = 0.053$) in terms of increased AL at 6 months and age at enrolment. However, in the LLLT group, there was a significant correlation between these two parameters at 1 month and 6 months (1 month: $r = -0.307$ and $p = 0.008$; 6 months: $r = -0.507$ and $p < 0.001$). We also found a significant correlation between the change in AL and baseline SER in the OK and LLLT groups (OK group: $r = 0.195$ and $p = 0.031$; LLLT group: $r = 0.281$ and $p = 0.015$, Figure 3(b)). A significant correlation was also found between the changes in AL and baseline AL in the OK lens group ($r = -0.296$ and $p = 0.007$) and the LLLT group ($r = -0.314$; $p = 0.006$, Figure 3(c)). Figure 3(d) presents the scatter plot graph of the increase in SFChT over 6 months and age in these groups. The increase in SFChT had a strong positive relationship with age of enrolment for OK lens-wearers not only at the 1-month follow-up but also at the 6-month follow-up (1 month: $r = 0.343$ and $p = 0.002$; 6 months: $r = 0.255$ and $p = 0.022$); the increase in SFChT was larger in individuals who were older.

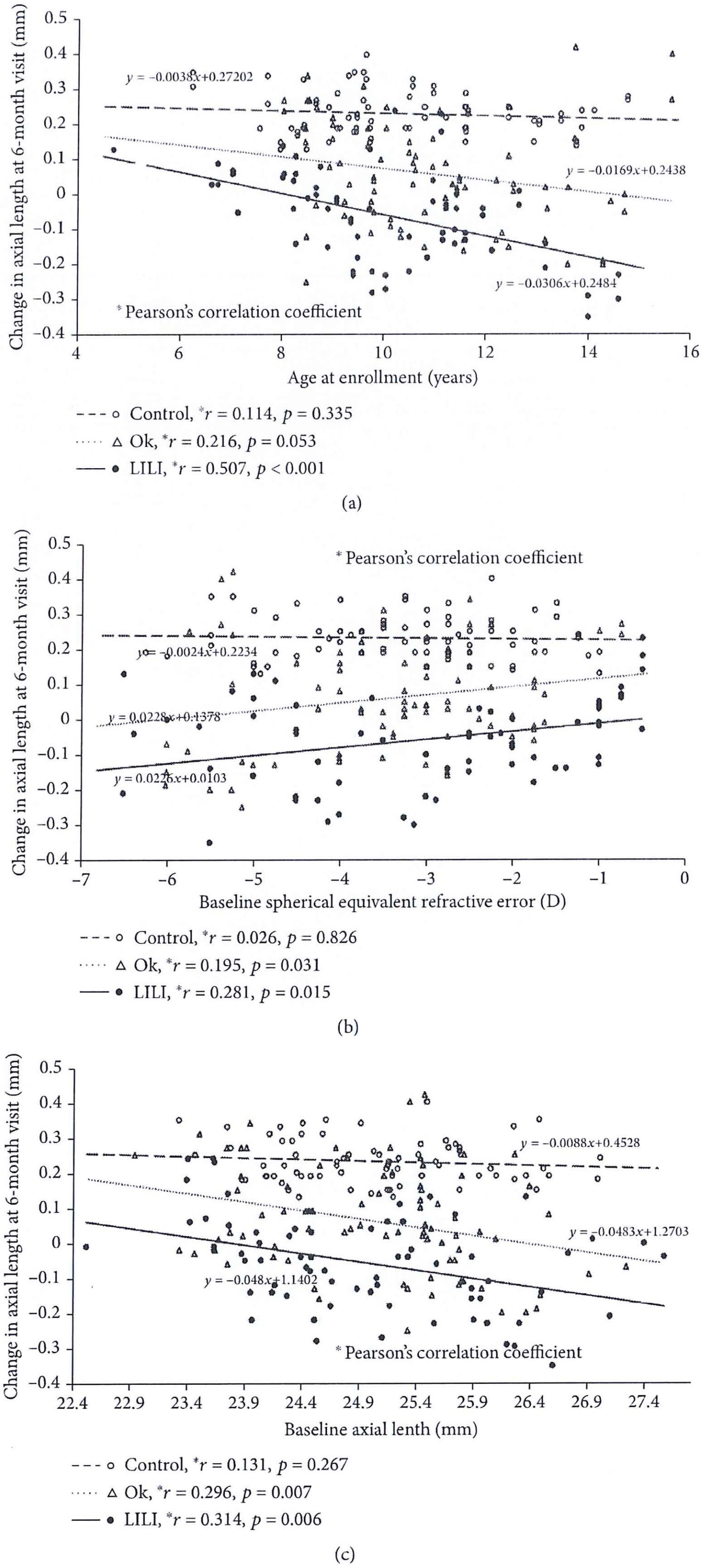
Changes in AL over 6 months had a strong positive connection with baseline AL according to the multiple linear regression analysis, and a significant association was modified by the sex effect in the multivariate model. The formula used to determine the changes in AL over 6 months was as follows: $0.007 *$ baseline AL mm $+ 0.034 *$ sex (male = 1, female = 2; $R^2 = 0.936$, $p < 0.01$). A negative correlation between baseline AL and changes in AL over 6 months according to the multiple linear regression was found in the OK group. In this model, baseline AL explained 15.4% of the variance ($\beta = -0.059$; $p < 0.01$). Among the children in the LLLT group, the baseline AL and age were independently related to changes in AL over 6 months ($R^2 = 0.387$). According to the model, shorter AL and older age were closely linked to fewer increases in AL (baseline AL: $\beta = 0.013$; age: $\beta = -0.03$; all $p < 0.01$).

Independent factors associated with changes in SFChT over 6 months were explored using a multiple regression analysis. In the model, there was a relationship between baseline AL and changes in SFChT over 6 months for the control group and LLLT group, but not for the OK group (control group: $\beta = -0.67$, $R^2 = 0.819$, $p < 0.01$; LLLT group: $\beta = 1.408$, $R^2 = 0.557$, $p < 0.01$). The significant correlation between age and changes in SFChT over 6 months in the OK group was confirmed by a multiple linear regression analysis ($\beta = 1.424$; $R^2 = 0.342$; $p < 0.01$). However, these two parameters were not relevant to the other two groups.

4. Discussion

To our knowledge, this is the first study specifically designed to test the hypothesis that LLLT can control the progression of myopia in children and to compare the effects of wearing OK lenses and undergoing LLLT to control myopia progression in children. Our results showed that LLLT can help control AL elongation and slow myopia progression better than OK lens-wearing (Table 2, Figure 2).

Most studies exploring OK lens-wearing have considered changes in AL as representative of myopia. The AL was defined as the distance from the corneal vertex to the retinal pigment epithelium. According to our results, wearing OK lenses is a more effective method of preventing axial elongation over the course of 6 months when compared to wearing single-vision glasses. As reported previously, AL in children after 1, 3, and 6 months of wearing OK lenses increases by 0.02 mm [23, 24], 0.02 mm [22], and 0.02-0.12 mm [23–25], respectively, which is consistent with our results (Table 3). At the time of our 6-month follow-up, the results of the single-vision spectacle lens group indicated an increase in AL of 0.23 ± 0.06 mm, which is consistent with previous studies (0.18-0.24 mm) [23–25], and the LLLT group exhibited a decrease in AL of -0.06 ± 0.15 mm. However, OK lens-wearing children had an AL increase of 0.06 ± 0.15 mm; therefore, LLLT treatment more effectively slowed the progression of myopia than OK lens treatment. Three principles formed the basis of the therapeutic LLLT treatments: (1) minimizing inflammation and edema and improving tissue microcirculation without puncturing the skin or entering a body cavity, (2) promoting neurological damage, and (3) treating neurological disorders [26]. Currently, vast quantities of empirical evidence have indicated



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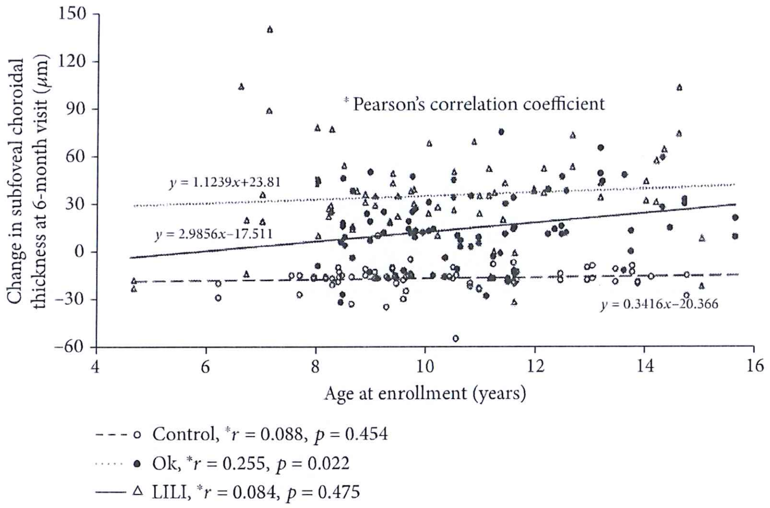

(d)

FIGURE 3: Scatter plots of the change in subfoveal choroidal thickness (SFChT) and axial length (AL) versus the baseline factors in the control group, OK group, and LILI group at the 6-month visit. (a) Scatter plots of the change in AL and age at enrolment at the 6-month visit. (b) Scatter plots of the change in AL and the baseline spherical equivalent refractive error at the 6-month visit. (c) Scatter plots of the change in AL and the baseline AL at the 6-month visit. (d) Scatter plots of the increase in the SFChT and the age at enrolment at the 6-month visit.

that oxidative stress and inflammation may account for the altered regulatory pathways in myopia and that oxidative damage associated with hypoxic myopia can alter the neuromodulation of nitric oxide and dopamine during eye growth [4, 5]. Analyzing the possible mechanisms of the inhibitory effects of LLLT treatment on myopia could help to protect patients from the effects of oxidative stress and decrease inflammation that accompanies myopia [27]. LLLT has maximal effects on the nitric oxide system and decreases the severity of oxidative stress in both animal studies [28] and clinical studies [29–31]. LLLT may reduce the levels of inflammatory cytokines such as interleukin-(IL-)1 and tumor necrosis factor-α by inhibiting them [32]. Furthermore, severe myopia could significantly increase the levels of IL-1 and IL-6 [33, 34], which could be associated with the myopic control mechanism.

The choroid has a variety of functions, including nourishing the retina [35] and changing the refractive state through the modulation of its thickness [18, 36]. Furthermore, the choroid has a crucial role in relaying signals derived from the retina to the sclera, further altering the synthesis of scleral extracellular matrix and changing the ocular size, resulting in refractive changes that have a vital function in the aetiology of myopia [19, 20]. Enhanced depth imaging OCT is a novel noninvasive imaging tool that produces high-resolution real-time images that allow visualization of the choroid *in vivo*, thereby allowing for a better understanding of changes in the choroid [37, 38]. Several studies have confirmed that visual signals not only change the process of emmetropization but also change the choroidal thickness in primates [39]. Furthermore, the most credible mechanism by which the OK lens could reduce myopia progression appears to be the increased myopic defocus in the central and peripheral retina [40, 41], but the exact mechanism remains unclear. Some researchers have speculated that choroidal thickening may contribute to the altered retinal defocus profile, but have reported conflicting results [22, 23, 42, 43]. Therefore, we chose to investigate SFChT using enhanced depth imaging OCT as another ocular biometric parameter to appraise the effects of control on slowing the progression of myopia.

In our study, OK and LLLT treatment increased the SFChT over time, and the rate was high at the 1-month examination ($12.14 \pm 15.30\,\mu m$ and $23.23 \pm 24.70\,\mu m$, respectively); then, it slowed compared with the increase resulting from spectacle wear ($-0.36 \pm 2.09\,\mu m$). Similar results were reported in individuals who wore OK lenses for 3 weeks [42] or 6 months [24], although no choroidal changes were found in another study [21]. These studies showed greater thickening of the choroid in patients wearing OK lenses than in spectacle wearers (approximately 16-21.8 μm) [23, 42]; however, this effect peaked after 1 month of treatment, and the amplitude of variation in choroidal thickening remained unchanged at the 6-month and 12-month examinations [23].

Changes in the SFChT at 1 month had a strong positive correlation with the age at which OK lens-wearing was started, which meant that older children showed thicker change in SFChT, and the positive effects persisted until the 6-month follow-up. Changes in AL were negatively correlated with baseline age only at the 6-month follow-up, with borderline significance ($p = 0.053$). Older children showed increased SFChT changes and slower axial elongation compared with younger children wearing OK lens, which was consistent with some randomized trials of OK treatment to reduce myopia progression [44, 45]. Changes in AL after 1 month of LLLT treatment were also significantly correlated with baseline age, and the negative effects persisted until 6 months. Although older children showed slower axial elongation than younger children after undergoing LLLT treatment, changes in the SFChT showed no significant correlation with age. Older children showed no advantage in SFChT changes when treated with LLLT. Thus, the mechanism for LLLT controlling axial elongation may not be by directly affecting the choroid, but through another pathway. The role of age in the effects on SFChT has been a divisive issue. Many authors have reported that increasing age is related to decreased SFChT in adults [46, 47]. However, in a population with emmetropia, from early childhood to adolescence, the SFChT increased significantly [48, 49]. Another study reported a positive relationship between SFChT and age for those with emmetropia and hyperopia [50].

Baseline SE and baseline AL might be predictive factors for AL changes in myopic individuals treated with OK lenses or LLLT. However, studies have shown conflicting results regarding the relationship between SER and changes in AL [44, 51, 52]. We found that more myopic diopter and longer AL were significantly related to decreased AL changes after wearing OK lenses and LLLT treatment. These results are in line with several studies that have confirmed that OK lenses provide more advantages for individuals with higher degrees of myopia and longer AL and that lower myopia at the start of OK lens-wearing makes the design less effective than it is for high myopia [52]. The authors hypothesized that this is due to the greater degree of corneal steepening in the midperiphery of eyes with higher myopia and greater peripheral retinal defocus, which slows myopia progression [51, 53]. Higher baseline myopia before LLLT treatment was associated with slower axial elongation compared to the control group. This may be due to the high levels of certain cytokines (IL-1, IL-6) in highly myopic eyes [33, 34], which absorb more energy and thus increase the effects of LLLT.

The most apparent limitation of our study was its short duration. Therefore, a long-term study of outcomes of all 3 groups is warranted to compare the effects and side effects of OK lens-wearing to those of LLLT treatment.

5. Conclusions

This study is the first to utilize LLLT to slow the progression of myopia and to compare OK lens-wearing and LLLT treatment with single-vision spectacle lens-wearing. Our study found that OK lens-wearing and treatment with LLLT more effectively slowed the progression of myopia than single-vision distance spectacles after a 6-month period of treatment. We also found some factors that were significantly correlated with changes in AL and SFChT. Therefore, an evaluation of basic characteristics, such as age, SE, and AL, can lead to advanced screening for high-risk myopia, predictions of myopia prognoses, and choosing suitable control methods for myopia that will provide the most benefit for children.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no competing interests.

Authors' Contributions

Fen Xiong and Tian Mao contributed equally to this article.

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研究文章

角膜塑形术和低强度激光治疗延缓儿童近视发展

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角膜塑形术(OK)被广泛用于减缓近视的进展。低强度激光治疗(LLLT)可以以充足的低能量来改变细胞功能。本研究旨在验证 LLLT 疗法能够控制近视进展的假设，并比较 OK 镜和 LLLT 控制近视性屈光不正的能力。81 例(81 只眼)配戴 OK 镜片的儿童，74 例(74 只眼)接受 LLLT 治疗的儿童，74 例(74 只眼)配戴 6 个月单光框架眼镜的儿童被纳入本次研究。配戴眼镜的儿童的眼轴长度(AL)变化为 0.23 ± 0.06 mm，配戴 OK 镜的儿童为 0.06 ± 0.15 mm，接受 LLLT 治疗 6 个月的儿童为-0.06 ± 0.15 mm。对照组、OK 镜组和 LLLT 组在 6 个月检查时观察到的黄斑中心凹下脉络膜厚度(SFChT)变化分别为-16.84 ± 7.85μm、14.98 ± 22.50μm 和 35.30 ± 31.75 μm。在 LLLT 治疗组，第 1 个月和第 6 个月的 AL 增加与年龄显著相关。在 OK 镜组和 LLLT 组，AL 变化与基线等效球镜值(SER)和基线 AL 值显著相关。配戴 OK 镜儿童组在第 1 个月和 6 个月时的 SFChT 增加与入组时的年龄呈正相关。在 6 个月时，OK 镜配戴者和接受 LLLT 治疗的儿童的眼轴增长减慢。在研究中，观察到 LLLT 治疗的近视控制效果好于通宵配戴 OK 镜。评估年龄、SER 和 AL 等方式可提高针对高危近视的筛查能力，改善近视预后，并有助于确定可产生最大效果的合适控制方法。

1、引言

近视是一种全球性流行病，在东亚尤为普遍[1]。近视，尤其是高度近视，更导致并发症风险增加，如视网膜脱离、近视性黄斑变性、青光眼、白内障和永久性视力丧失等[2]。因此，一种安全、可靠并能有效的减缓近视进展的疗法将造福数百万计的近视患者。

氧化应激、炎症和凋亡可能是近视调节途径的关键因素[3–6]。近视患者体内低水平的 5-MTHF 可能会导致同型半胱氨酸的增加，该过程与氧化应激、炎症和细胞凋亡密切相关[5]。此外，外源性 bFGF（碱性成纤维细胞生长因子）通过抑制视网膜神经元的凋亡，从而有效地减轻了慢性形觉剥夺性近视中过度的眼轴增长[3]。寻找抑制该细胞凋亡的方法可能是控制眼轴增长的有效途径。而低强度激光治疗（LLLT）通过防止细胞凋亡，可以最大限度地减少炎症并促进细胞更新，起到控制近视发展的作用[7，8]。因此我们首先关注到这一种新型治疗方法。

最近的研究表明，环境光的光谱组成可以通过颜色信号以多种方式影响正常的眼球生长和屈光发育[9，10]。激光设备广泛应用于生物医学领域；它可以产生纯净、强烈、单色和连续的平行光束[11，12]。激光治疗可产生广泛的分子、细胞和组织效应[13]。LLLT 不同于高功率激光疗法，因为它使用低强度的红光和近红外光，其波长范围从 600 nm 到 1100 nm，输出功率可达 500 mW [7]。因此，它被认为是一种可以在不改变周围组织温度的情况下，通过产生足够低的能量来诱导组织内的刺激反应的光疗方法[7]。

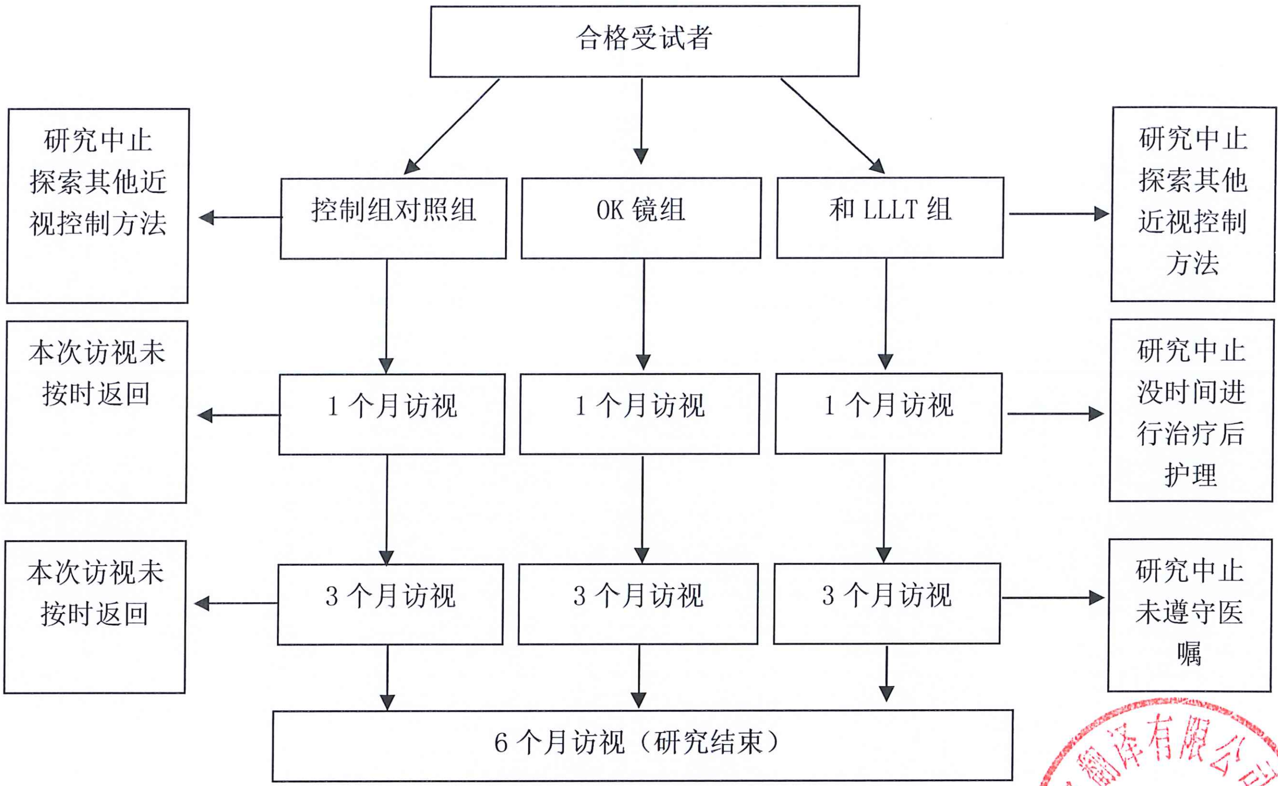


图 1. 参与者分配流程图

各种研究表明，现代角膜塑形术(OK 镜)是实现儿童近视控制的关键干预手段，对儿童近视控制效果显著；然而，其机制仍不清楚[14–16]。OK 镜的特征在于其逆向几何设计，通过重塑角膜和改变图像质量，可在中央和周边视网膜中形成周边离焦[17，18]。最近对近视小鸡的研究表明，随着近视的发展，在巩膜生长发生变化之前，脉络膜趋于变薄[19，20]。因此，在 OK 镜控制近视的机制研究中，脉络膜的作用受到了重视[21，22]。

本研究描述了配戴 OK 镜、接受 LLLT 治疗和配戴单光框架眼镜的儿童的研究设计和临床 6 个月随访检查，旨在验证 LLLT 疗法可以控制近视进展的假设，同时比较 OK 镜和 LLLT 控制近视进展的能力。

2、参与者和方法

2.1. 参与者。所有参与者都患有近视；数据来源于 2018 年 9 月至 2019 年 4 月中国南昌大学附属眼科医院门诊。纳入标准为年龄 6-16 岁，使用环戊酮后等效球镜 ≤ −0.50，非接触眼压计眼压为 10-21 mmHg。排除患有如斜视、弱视和心脏、呼吸系统等疾病的眼疾或全身性疾病的近视患者。除配戴眼镜之外，已配戴 OK 镜和/或使用其他近视控制方式的儿童也排除在外。我们共招募了 300 名儿童，他们被随机分配到对照组(n ＝ 100)、OK 镜组(n ＝ 100)和 LLLT 组(n ＝ 100)，共有 229 名儿童完成了研究(图 1)。共有 74 名 7 至 14 岁的儿童(平均年龄，10.33 ± 2.03 岁；54%为男孩)纳入对照组。共有 81 名 8 至 14 岁的儿童(平均年龄，10.88 ± 1.92 岁；54%男孩)被纳入 OK 镜组中，而 74 名 7 至 15 岁的儿童(平均年龄，10.22 ± 2.38 岁；54%男孩)被纳入 LLLT 组中。性别、年龄、SER、眼轴长度(AL)和黄斑中心凹下脉络膜厚度(SFChT)在基线值时的差异在三组之间没有显著性。表 1 列出了入组儿童的一般特征。

本研究遵照《赫尔辛基宣言》的原则进行，并经南昌大学临床研究中心伦理委员会批准(2018-KY-03)。儿童父母在代表孩子提供签字知情同意书之前，已了解该研究的利弊。

2.2. 研究程序。研究人员在治疗前(基线)和后续预约复查时对参试人员进行详细的眼科检查；检查包括使用 ETDRS 视力表在 4 米距离处检查参试人员的裸眼视力及矫正视力、睫状肌麻痹验光(1%盐酸环戊醇酯)、等效球镜测定(等效球镜=球镜+散光/2)、裂隙灯检查(裂隙灯；Haag-Streit，Köniz，瑞士)，眼球运动检查、眼压测量(型号 NT-4000；美国加利福尼亚州弗里蒙特 Nidek Inc.)、眼底检查、AL 测量(美国加利福尼亚州都伯林 Carl Zeiss Meditec Inc.)、角膜内皮细胞密度测定、和光学相干断层扫描(OCT)(美国加利福尼亚州都伯林 Carl Zeiss Meditec Inc.)。

表 1.研究组的基线值。

特征	控制组 (n = 74)	OK 镜组 (n = 81)	LLLT（n = 74）	P 值
性别（男:女）	40:34	44:37	40:34	0.412[a]
年龄	10.33 ± 2.03	10.88 ± 1.92	10.22 ± 2.38	0.114[b]
SER (D)	-3.32 ± 1.36	-3.42 ± 1.28	-3.39 ± 2.17	0.937[b]
AL (mm)	25.07 ± 0.87	25.07 ± 0.92	25.07 ± 1.15	0.99[b]
SFCHT (μm)	286.81 ± 63.67	284.36 ± 72.58	288.61 ± 59.59	0.921[b]

SER. 等效球镜；AL.眼轴长度；SFChT. 黄斑中心凹下脉络膜厚度。[a]卡方检验，[b]单因素方差分析。

为了避免生理节律对结果的影响，由同一名研究者在基线、1 个月、3 个月和 6 个月的随访时间的上午 8:00 至下午 2:00 进行了两次 OCT 扫描。OCT 扫描由两名独立的熟练专业人员操作，使用线性测量程序测量 SFChT。为增加脉络膜的可视性，使用了增强深度成像模式(EDI)。我们将图像中黄斑最薄的部分定义为中心凹。SFChT 从视网膜色素上皮的最外层测量到脉络膜巩膜界面的内层。

对照组的儿童全天配戴单光框架眼镜，并在 1 个月、3 个月和 6 个月后返院进行详细的眼科检查。我们的试镜人员为 OK 镜组儿童配戴 OK 镜。OK 镜（美国弗吉尼亚州埃尔顿 Euclid Systems Ortho-k; Euclid System Corp., Herndon）是由硬质透气材料(加拿大魁北克拉瓦尔波士顿 Boston Equalens II; Bausch + Lomb)制成。其直径范围为 10.2 至 11 mm。镜片由直径为 6.2 mm 的基弧区、0.5 mm 宽的反转弧区、1.2 mm 宽的定位弧区和 0.5 mm 宽的周弧组成。为防控近视，OK 镜组每天晚上至少连续配戴 7 个小时，在 1 个月、3 个月和 6 个月后返院进行眼科检查。除了上述检查外，我们还做角膜荧光素染色检查确认是否存在任何并发症，并做角膜地形图检查，以确保其所戴的 OK 镜适配。

LLLT 组的儿童全天配戴单焦眼镜，接受 LLLT 治疗(功率，2 ± 0.5 mW；波长，650 nm；中国武汉亚昆光电子有限责任公司)每天两次，每次 3 分钟，之间至少间隔 4 小时。房间照明没有具体的要求。第一次测量后，每位儿童在第 1、3 和 6 个月时返院进行随访检查，并完成所有上述检查。

2.3. 数据分析。本研究使用 IBM SPSS 统计 23.0 版进行统计分析(美国纽约州阿蒙克 IBM 公司)，只采用左眼数据。除非另有说明，所有值首先进行正态检验，并表示为均数±标准偏差。

使用图基(tukey's)事后检验法之单向方差分析(ANOVA)分析各亚组基本变量数据的差异。使用卡方检验对三组进行性别比较。通过重复测量单因素方差分析过程，分析基线和每次随访之间 SER、AL 和 SFChT 的变化。如果违反球形假设，则使用 Greenhouse-Geis 测试。模型中包括了时间、组的主要效应，以及效应时间与群体的相互作用。使用 Pearson 相关系数分析对 6 个月时参数变化和基线因素之间的相关性进行了分析。为了研究各组 6 个月时 AL/SFChT 变化与基线因素的相关性，我们采用了逐步多元线性回归模型。p 值 < 0.05 为具有统计学意义。

3.结果

在 LLLT 组中，从基线到 6 个月随访，平均 SER 值随着时间的推移有所下降，但在对照组中，从基线到 6 个月随访，平均 SER 值有所增加。这一对照组和 LLLT 组之间的差异具有统计学意义。对照组和 OK 镜组的平均 AL 值增加，而 LLLT 组略有下降。随着时间的推移，这些变化彼此之间差异显著。在同一时期内，LLLT 组的平均 AL 值小于其他两组。每次检查时 LLLT 组和 OK 镜组的 SFChT 均较对照组厚，差异有统计学意义（表 2，图 2）。

表 3 显示了三个小组在每个采样点参数变化的不同时间表。研究期间，对照组和 LLLT 组的 SER 变化存在显著差异($p < 0.001$)。在 1 个月开始随访时，对照组的 SER 值平均变化为−0.07 ± 0.11、−0.24 ± 0.16 和−0.50 ± 0.24 D，而 OK 镜组在 1 个月、3 个月和 6 个月随访时分别为 0.11 ± 0.17、0.22 ± 0.32 和 0.21 ± 0.34D。在 3 个月和 6 个月的随访时，配戴 OK 镜的儿童的 AL 增加值明显小于对照组，但在 1 个月随访时的变化没有统计学意义($p = 0.184$)。在每个采样点，LLLT 组 AL 的下降与对照组和 LLLT 组有显著差异。与 LLLT 组相比，OK 镜组 1 个月、3 个月和 6 个月时 SFChT 的增加明显减少，而对照组的 SFChT 则显著减少。

在处理数据过程中，皮尔逊相关系数被用以了解参数变化和基线因素之间的关系。图 3(a)显示了各组在 6 个月时 AL（Y 轴）和年龄（X 轴）关系的增加散点图。在该坐标系下，对照组($r = -0.114$；$p = 0.335$)和 OK 镜组($r = -0.216$；$p = 0.053$)之间在 AL 值增加方面无统计学显著相关性。然而，在 LLLT 组，这两个参数在 1 个月和 6 个月时存在显著相关性(1 个月.$r = 0.307$，$p = 0.008$；6 个月.$r = -0.507$，$p < 0.001$)。我们还发现，OK 镜组和 LLLT 组中 AL 和基线 SER 存在显著相关性(OK 镜组.$r = 0.195$，$p = 0.031$；LLLT 组.$r = 0.281$，

$p = 0.015$，图 3(b)）。同时，OK 镜组（$r = -0.296$ 和 $p = 0.007$）和 LLLT 组（$r = -0.314$；$p = 0.006$，图 3(c)）的 AL 变化和基线 AL 存在显著相关。图 3(d) 呈现了这些组中在 6 个月期间和年龄的 SFChT 增加散点图。OK 镜配戴者的 SFChT 增加与入组年龄存在强正相关性（1 个月.$r = 0.343$，$p = 0.002$；6 个月.$r = 0.255$，$p = 0.022$），即年龄越大，SFChT 的增加越大。

多元线性回归分析显示，在 6 个月以上的 AL 变化与基线 AL 呈现强正相关，且在多变量模型中，性别效应修正了显著相关性。确定 6 个月 AL 变化的公式为：0.007 *基线 AL mm + 0.034 *性别（男 = 1，女 = 2；$R2 = 0.936$，$p < 0.01$）。根据多元线性回归，在 OK 镜组中发现基线 AL 与 6 个月后 AL 的变化呈负相关。在该模型中，基线 AL 解释了 15.4%的方差（$\beta = -0.059$；$p < 0.01$）。在 LLLT 组儿童中，基线 AL 和年龄与 6 个月后 AL 的变化独立相关（$R2 = 0.387$）。根据该模型，根据该模型，AL 增长较少与较短 AL 和较大年龄密切相关（基线 AL.$\beta = 0.013$；年龄.$\beta = -0.03$；所有 $p < 0.01$）。

采用多元回归分析方法探讨 6 个月内 SFChT 变化的独立相关因素。在该模型中，对照组和 LLLT 组的基线 AL 与 6 个月后的 SFChT 变化之间存在关系，而 OK 镜组则不存在这种关系（对照组.$\beta = -0.67$，$R2 = 0.819$，$p < 0.01$；LLLT 组.$\beta = 1.408$，$R2 = 0.557$，$p < 0.01$）。多元线性回归分析（$\beta = 1.424$；$R2 = 0.342$；$p < 0.01$）确定了 OK 镜组在 6 个月期间年龄和 SFChT 变化之间的显著关系。这两个参数与其他两组无关。

表 2. 不同采样点的参数（平均值±标准差）

参数		对照组 ($n = 74$)	OK 镜 ($n = 81$)	LLLT($n = 74$)
SER (D)	基线	-3.32 ± 1.36	-3.42 ± 1.28	-3.39 ± 2.17
	1 个月	-3.39 ± 1.35		-3.28 ± 2.1
	3 个月	-3.56 ± 1.37		-3.17 ± 2.13
	6 个月	-3.82 ± 1.37		-3.17 ± 2.14
		F 主效应/p 值. 27.82/<0.001		
		F 交叉效应/p 值. 128.80/<0.001		
AL(mm)	基线	25.07 ± 0.87	25.07 ± 0.92	25.06 ± 1.1
	1 个月	25.09 ± 0.87	25.07 ± 0.91	25.01 ± 1.14
	3 个月	25.16 ± 0.87	25.09 ± 0.88	24.99 ± 1.11
	6 个月	25.30 ± 0.86	25.13 ± 0.89	25.00 ± 1.11
		F 主效应/p 值.. 67.21/<0.001		
		F 交叉效应/p 值. 62.86/<0.001		
SFChT (μm)	基线	286.81 ± 63.67	284.36 ± 72.58	288.61 ± 59.59
	1 个月	286.45 ± 63.61	296.49 ± 72.61	311.84 ± 67.08
	3 个月	278.59 ± 63.64	297.81 ± 73.62	320.18 ± 66.61
	6 个月	269.97 ± 64.11	299.33 ± 73.65	323.91 ± 65.63
		F 主效应/p 值. 53.00/<0.001		
		F 交叉效应/p 值. 64.42/<0.001		

SER. 等效球镜；AL.眼轴长度；SFChT. 黄斑中心凹下脉络膜厚度。

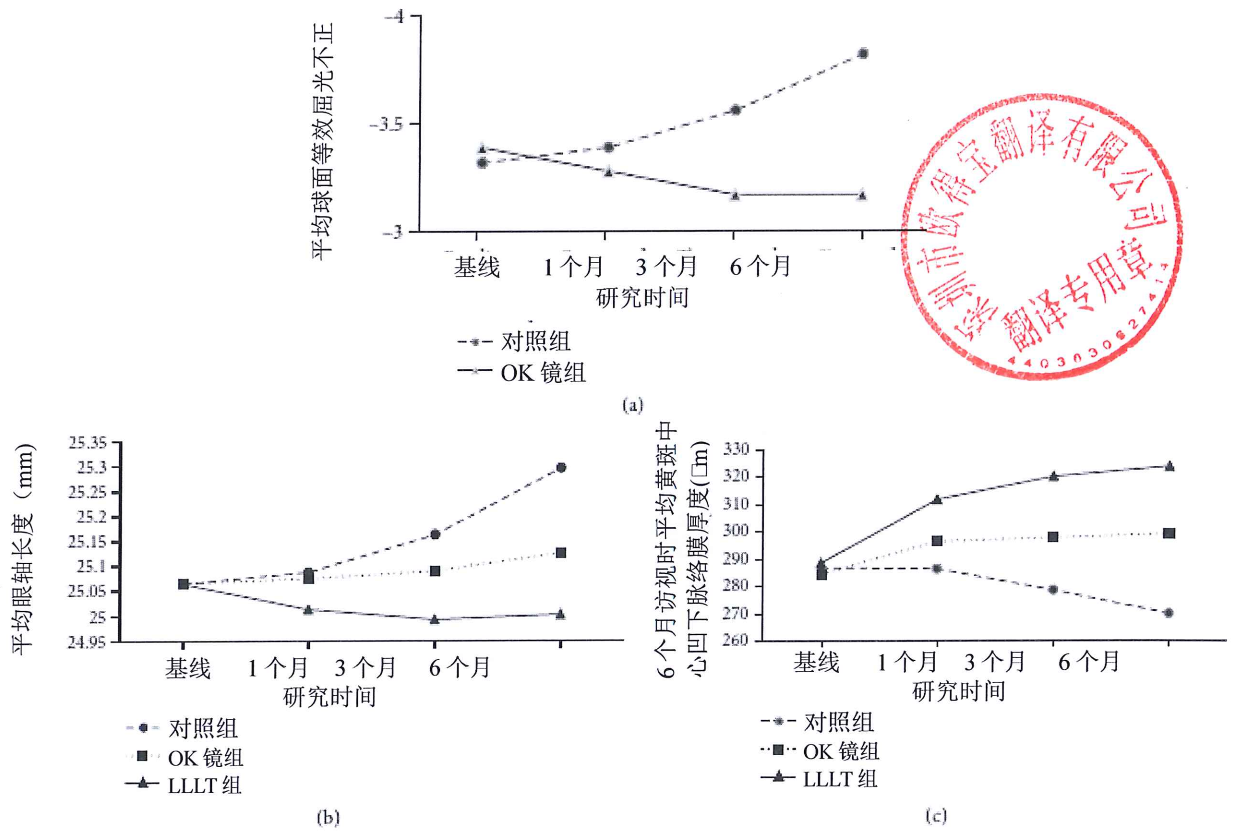


图 2：平均 SER.等效球镜；AL.眼轴长度；SFChT. 黄斑中心凹下脉络膜厚度的时间进程。误差条表示标准偏差。(a)对照组和 LLLT 组平均 SER 时间历程。(b)对照组、OK 镜组、LLLT 组平均 AL 时间历程。(c)对照组、OK 镜组、LLLT 组平均 SFChT 时间历程。

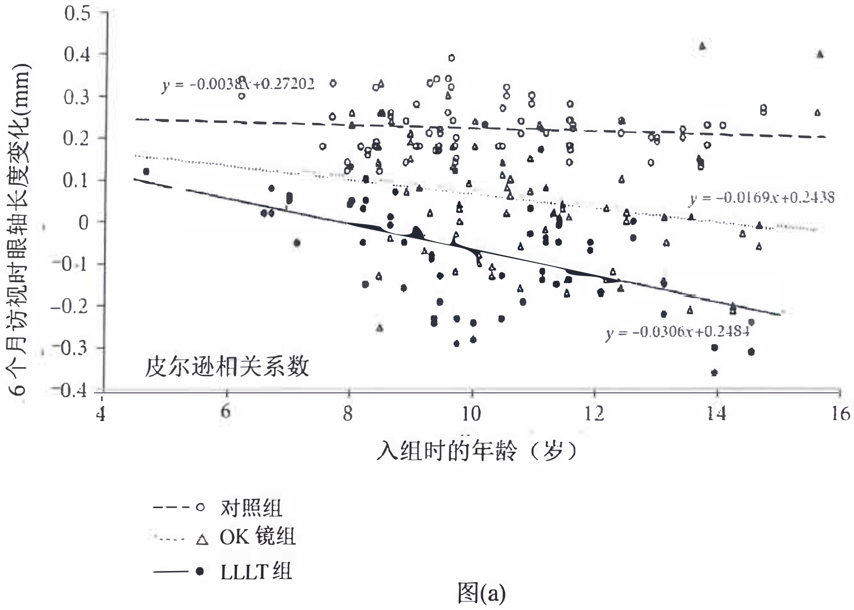
表 3. 各采样点的参数变化（平均值±标准差）

参数		对照组(n = 74)	OK 镜(n = 81)	LLLT (n = 74)	F 值	p 值
SER 变化 (D)	1 个月	−0.07 ± 0.11		0.11 ± 0.17	11.24	<0.001a
	3 个月	−0.24 ± 0.16		0.22 ± 0.32	11.61	<0.001a
	6 个月	−0.50 ± 0.24		0.21 ± 0.34	6.58	<0.001a
AL 变化 (mm)	1 个月	0.02 ± 0.02	0.01 ± 0.08	−0.05 ± 0.07	26.15	<0.001b
	3 个月	0.10 ± 0.04	0.02 ± 0.17	−0.07 ± 0.12	35.92	<0.001b
	6 个月	0.23 ± 0.06	0.06 ± 0.15	−0.06 ± 0.15	98.13	<0.001b
SFChT 变化 (μm)	1 个月	−0.36 ± 2.09	12.14 ± 15.30	23.23 ± 24.70	36.65	<0.001b
	3 个月	−8.22 ± 3.24	13.46 ± 19.46	31.58 ± 31.72	63.50	<0.001b
	6 个月	−16.84 ± 7.85	14.98 ± 22.50	35.30 ± 31.75	97.48	<0.001b

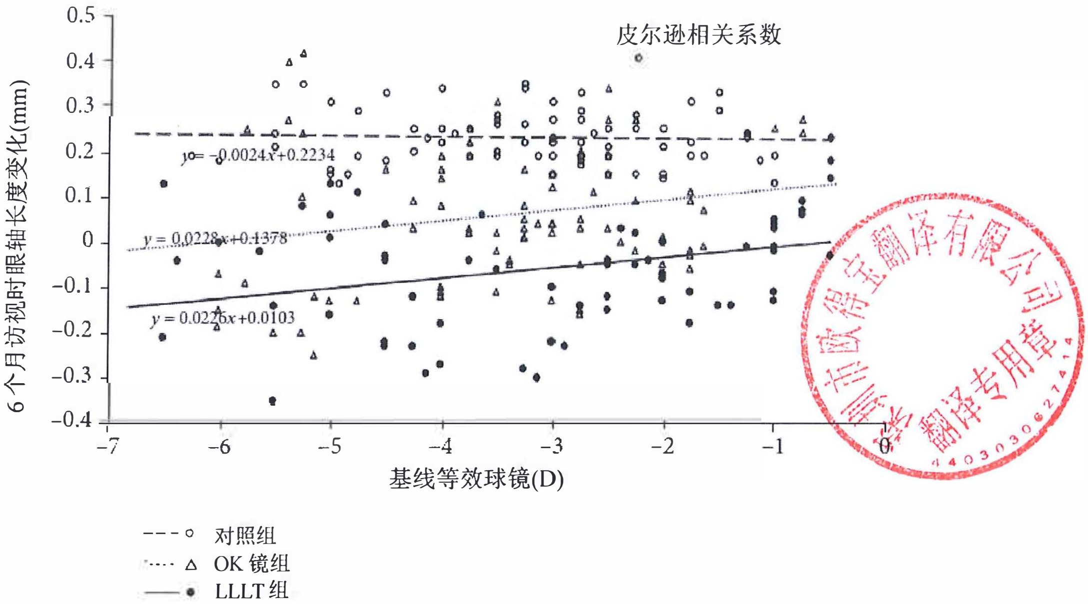
SER. 等效球镜；AL.眼轴长度；SFChT. 黄斑中心凹下脉络膜厚度。[a]独立样本 t 检验，[b]单因素方差分析。

4. 讨论

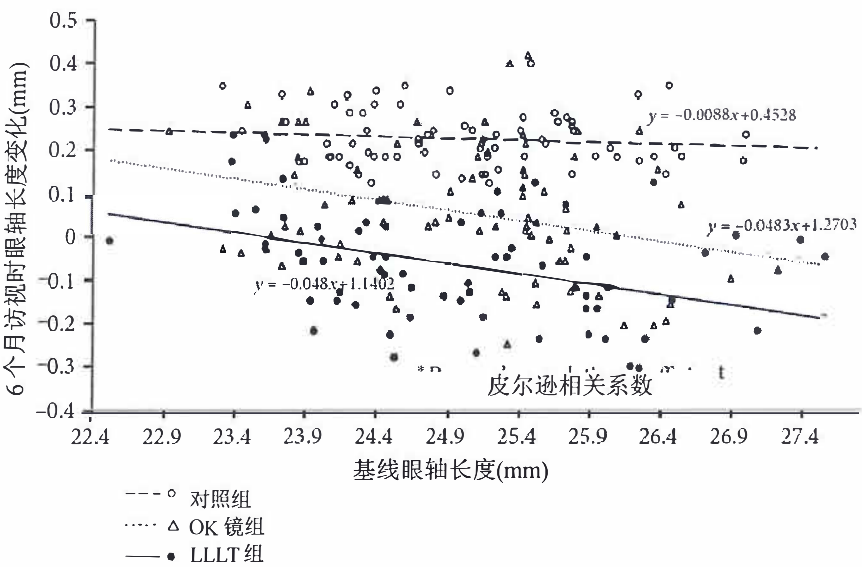
据我们了解，这是针对低强度激光治疗（LLLT）可以控制儿童近视发展以及比较 LLLT 与 OK 镜对控制儿童近视发展效果的首次专项研究。研究结果显示，在控制眼轴延长和减缓近视进展方面，低强度激光治疗（LLLT）优于 OK 镜 (表 2，图 2)。大多数探索佩戴 OK 镜的研究都把 AL 的变化做为观察近视进展的参考。眼轴（AL）是指从角膜顶点到视网膜色素上皮的距离。根据我们的研究结果，在 6 个月的疗程中，配戴 OK 镜比配戴单光眼镜更有效地防止眼轴增长。正如之前的报告，配戴 OK 镜 1 个月、3 个月和 6 个月后，儿童的 AL 分别增加了 0.02 mm [23、24]、0.02 mm [22]和 0.02 - 0.12 mm [23–25]，这与我们的结果一致(表 3)。在我们的 6 个月随访中，单光框架眼镜组的结果显示，AL 增加了 0.23 ± 0.06 mm，这与以前的研究(0.18-0.24 mm)[23–25]一致。LLLT 组的眼轴(AL)减少了−0.06 ± 0.15 mm。而配戴 OK 镜儿童的 AL 增加了 0.06 ± 0.15 mm；因此，LLLT 治疗比 OK 镜治疗更有效地减缓了近视的进展。LLLT 治疗的基础有三个原则：(1)以非侵入性的方法最大限度地减少炎症和水肿，改善组织微循环；(2)促进神经损伤恢复；(3)治疗神经系统疾病[26]。目前，大量实验证据表明，氧化应激和炎症可能是近视调节通路改变的原因，而与缺氧性近视相关的氧化损伤可以改变眼睛生长过程中一氧化氮和多巴胺的神经调节[4，5]。分析 LLLT 疗法对近视抑制作用的可能机制有助于保护患者免受氧化应激的影响，并减少伴随近视的炎症反应[27]。在动物研究[28]和临床研究[29–31]中，LLLT 对一氧化氮系统有最大的影响，并降低了氧化应激的严重程度。LLLT 可通过抑制炎症细胞因子如白细胞介素（IL）1 和肿瘤坏死因子-α等，大幅降低它们的水平[32]。此外，严重近视可显著增加 IL-1 和 IL-66 的水平[33，34]，这可能与近视控制机制有关。


6 个月访视时眼轴长度变化(mm)
入组时的年龄（岁）
y = -0.0038x+0.27202
y = -0.0169x+0.2438
y = -0.0306x+0.2484
皮尔逊相关系数
对照组
OK 镜组
LLLT 组

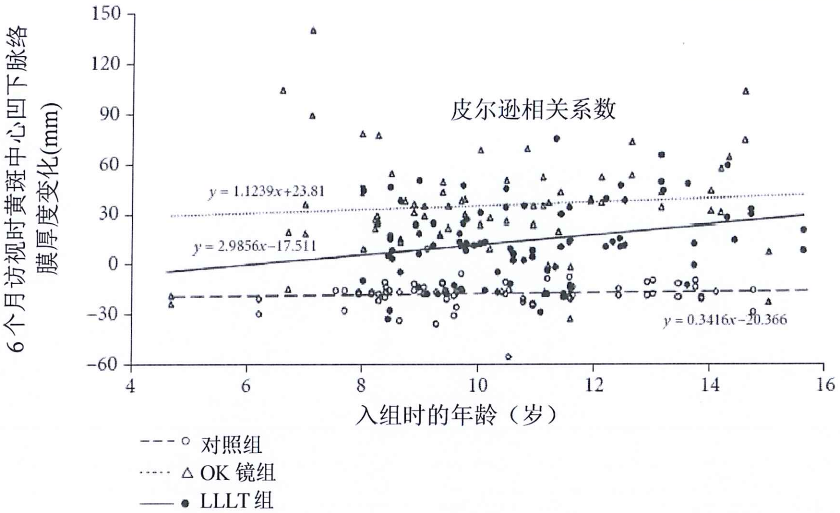
图(a)


6 个月访视时眼轴长度变化(mm)
基线等效球镜(D)
皮尔逊相关系数
y = -0.0024x+0.2234
y = 0.0228x+0.1378
y = 0.0226x+0.0103
对照组
OK 镜组
LLLT 组

图(b)


6 个月访视时眼轴长度变化(mm)
基线眼轴长度(mm)
y = -0.0088x+0.4528
y = -0.0483x+1.2703
y = -0.048x+1.1402
皮尔逊相关系数
对照组
OK 镜组
LLLT 组

图(c)



图(d)

图 3 在 6 个月随访时，对照组、OK 镜组和 LLLT 组的黄斑中心凹下脉络膜厚度（SFChT）和眼轴长度(AL)的变化与基线因素的散点图。(a)在 6 个月随访时，入组时 AL 和年龄变化的散点图。(b)6 个月随访时 AL 变化和等效球镜的散点图。(c) 6 个月随访时 AL 变化和基线 AL 的散点图。(d) 在 6 个月的访问时，SFChT 的增加和入组年龄关系的散点图。

脉络膜具有多种功能，包括滋养视网膜[35]和通过调节其厚度来改变屈光状态[18，36]。此外，脉络膜在将来自视网膜的信号传递到巩膜中起着至关重要的作用，进一步改变巩膜细胞外基质的合成并改变眼球的大小，从而导致在近视病因中具有重要作用的屈光变化 [19，20]。增强深度成像光学相干断层扫描是一种新型非侵入性成像工具，可产生高分辨率的实时图像，实现活体脉络膜的可视化从而更好地了解脉络膜的变化[37，38]。一些研究证实，视觉信号不仅会改变灵长类动物正视化过程，还会改变其脉络膜的厚度[39]。此外，OK 镜减少近视进展的最可信机制似乎是增加中央和周边视网膜中的近视性离焦 [40，41]，但其确切机制仍不清楚。一些研究人员推测脉络膜增厚可能导致视网膜离焦轮廓的改变，但已有的报告报告结果相互矛盾[22，23，42，43]。因此，我们选择使用增强深度成像 OCT 作为另一个眼部生物特征参数来研究 SFChT，以评估减缓近视进展的控制作用。

在我们的研究中，SFChT 在 OK 镜和 LLLT 治疗中，随时间增长而增加，并且在 1 个月的检查中该比率较高(分别为 12.14 ± 15.30 μm 和 23.23 ± 24.70 μm；而佩戴眼镜带来的是负增长（-0.36 ± 2.09 微米）。虽然在另一项研究[21]中没有发现脉络膜变化，但在配戴 OK 镜 3 周[42]或 6 个月[24]的个体中也报告了类似的结果。这些研究显示，配戴 OK 镜的患者的脉络膜增厚程度大于配戴眼镜的患者(约 16-21.8 μm) [23，42]；然而，这种效应在治疗 1 个月后达到高峰，在 6 个月和 12 个月的检查时，脉络膜增厚的变化幅度保持不变[23]。

1 个月时的 SFChT 变化与开始配戴 OK 镜的年龄呈强正相关，这意味着年龄较大的儿童 SFChT 增厚变化较大，这种积极影响持续到 6 个月随访。仅在 6 个月随访时，AL 变化与基线年龄呈负相关，具有临界意义(p = 0.053)。年龄较大的儿童与年龄较小的配戴 OK 镜的儿童相比，SFChT 变化增加，眼轴增长较慢，这与 OK 镜治疗减少近视进展的一些随机试验结果一致[44，45]。LLLT 治疗 1 个月后的 AL 变化也与基线年龄显著相关，并且这种影响持续到 6 个月。虽然在接受 LLLT 治疗后，年龄较大的儿童比年龄较小的儿童显示出较慢的增长，但 SFChT 的变化与年龄未呈现明显相关性。用 LLLT 治疗时，年龄较大的儿童在 SFChT 变化方面未表现出优势。因此，LLLT 可能不是通过直接影响脉络膜，而是通过另一种途径控制眼轴增长。年龄在 SFChT 效应中的作用一直是一个有争议的话题。众多作者报道，成年人年龄的增长与 SFChT 的降低有关[46，47]。然而，从幼儿期到青春期，正视眼人群的 SFChT 显著增加[48，49]。另一项研究报告了正视眼和远视患者的 SFChT 与年龄之间的正相关关系[50]。

基线 SE 和基线 AL 可能是接受 OK 镜或 LLLT 治疗的近视患者的 AL 变化的预测因素。然而，研究显示 SER 和 AL 变化之间的关系存在相互矛盾的结果[44，51，52]。我们发现，配戴合适 OK 镜和接受 LLLT 治疗后，较大近视屈光度和较长 AL 与越小的 AL 变化显著相关。这些结果与几项研究一致，这些研究已经证实，OK 镜对近视度数较高和 AL 较长的人更有优势，并且 OK 镜对于开始佩戴时度数较低的近视患者的有效性不如对患有更高度近视的患者有效[52]。作者推测，这是由于高度近视的眼睛中边缘的角膜变陡程度更大，周围视网膜离焦程度更大，从而减缓了近视的进展[51，53]。与对照组相比，LLLT 治疗前较高的基线近视与较慢的眼轴增长相关。这可能是由于高度近视

的眼睛中具有某些细胞因子(IL-1，IL-6)[33，34]，其能吸收更多的能量并因此增加了 LLLT 效应。

本研究的最明显的局限在于完整研究时长较短，因而未来需要对所有 3 组的结果进行长期研究，以比较佩戴 OK 镜治疗与 LLLT 治疗的效果和副作用。

5.结论

这项研究首次利用 LLLT 来减缓近视的发展，并比较了配戴 OK 镜和 LLLT 治疗与配戴单光框架眼镜的效果。我们的研究发现，经过 6 个月的治疗后，LLLT 治疗和配戴合适的 OK 镜比单光框架眼镜更有效地减缓了近视的发展。我们还发现了一些与 AL 和 SFChT 的变化显著相关的因素。因此，对基本特征(如年龄、SE 和 AL)的评估可提高对高风险近视水平的筛查以及近视预后预测，进而选择最有利于儿童的近视控制方法。

数据可用性

用于支持本研究结果的数据可应要求从通讯作者处获得。

利益冲突

作者声明没有利益冲突。

作者贡献

熊芬和毛甜对这篇文章的贡献相同。

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