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# Myopia Control Effect of Repeated Low-Level Red-Light Therapy in Chinese Children

## *A Randomized, Double-Blind, Controlled Clinical Trial*

*Jing Dong, MD,[1,*] Zhuoting Zhu, MD, PhD,[2,3,*] Haifeng Xu, MD,[4,*] Mingguang He, MD, PhD[2,3,5]*

***Purpose:*** Repeated low-level red-light (RLRL) therapy is an emerging treatment for myopia control. Nevertheless, previous studies are limited by open-label design. Our study aimed to assess the efficacy and safety of RLRL therapy in controlling myopia progression compared to a sham device with only 10% of the original power.

***Design:*** Randomized, double-blind, controlled clinical trial.

***Participants:*** A total of 112 Chinese children aged 7 to 12 years with myopia of at least −0.50 diopter (D), astigmatism of 1.50 D or less, and anisometropia of 1.50 D or less.

***Methods:*** Participants were assigned randomly in a 1:1 ratio to the RLRL group or the sham device control group, following a schedule of 3 minutes per session, twice daily, with an interval between sessions of at least 4 hours. The RLRL therapy was provided by a desktop red-light therapy device and administered at home. The sham device was the same device but with only 10% of the original device's power. Cycloplegic refraction and axial length (AL) were measured at baseline and 6 months.

***Main Outcome Measures:*** Changes in cycloplegic spherical equivalence refraction (SER) and AL between 2 groups were compared using a generalized estimating equation (GEE).

***Results:*** A total of 111 children were included in the analysis (n = 56 in the RLRL group and n = 55 in the sham device control group). The mean SER change over 6 months was 0.06 ± 0.30 D in the RLRL group and −0.11 ± 0.33 D in the sham device control group ($P = 0.003$), with respective mean increases in AL of 0.02 ± 0.11 mm and 0.13 ± 0.10 mm ($P < 0.001$). In the multivariate GEE models, children in the RLRL group showed less myopia progression and axial elongation than those in the sham device control group (SER: coefficient, 0.167 D; 95% confidence interval [CI], 0.050–0.283 D; $P = 0.005$; AL: coefficient, −0.101 mm; 95% CI, −0.139 to −0.062 mm; $P < 0.001$). No treatment-related adverse events were reported.

***Conclusions:*** In myopic children, RLRL therapy with 100% power significantly reduced myopia progression over 6 months compared with those treated with a sham device of 10% original power. The RLRL treatment was well tolerated without treatment-related adverse effects. *Ophthalmology 2023;130:198-204 © 2022 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

*Supplemental material available at www.aaojournal.org.*

Myopia is the most common ocular condition globally, with the prevalence of myopia and high myopia projected to increase from 23% to 54% and 3% to 20% between 2000 and 2050, respectively.[1–4] Notably, high myopia is associated with substantial risk of irreversible sight-threatening complications, including myopic maculopathy, glaucoma, and retinal detachment.[5–8] Thus, myopia is an important public health concern, and an effective and safe method to control myopia progression is needed urgently.

Repeated low-level red-light (RLRL) therapy is an emerging effective treatment for myopia control with no documented functional or structural damage.[9,10] A clinical study demonstrated that RLRL significantly reduced the rate of myopia progression and axial elongation over 6 months compared with orthokeratology and single-vision spectacles (SVS).[9] Another 12-month, multicenter, randomized clinical trial involving 264 children 8 to 13 years of age showed that RLRL therapy was an effective treatment for myopia control compared with SVS, and no documented functional and structural damages were observed.[10] However, these studies were limited by the lack of an appropriate control group; thus, patients masked to treatment could not be applied. The open-label design may bias the effectiveness, may affect participants' behavior, may lead to imbalanced dropout rates, and may bias the observation of outcome measures, especially in trials with subjective end points.[11] Therefore, we conducted, to our knowledge, the first prospective, randomized, double-masked, controlled clinical trial to evaluate the efficacy of RLRL therapy in myopia control compared with a sham device with only 10% of the original power.

https://doi.org/10.1016/j.ophtha.2022.08.024
ISSN 0161-6420/22

## Methods

### Study Design and Setting

This prospective, randomized, double-masked, controlled clinical trial of children with myopia was conducted from November 2019 to April 2021 at 2 hospitals in Baotou, China. All investigators and personnel were trained and certified on the study's procedures before its initiation. All eligible children in this study were randomized at an allocation ratio of 1:1 to the RLRL group or the sham device control group, following a treatment schedule of 3 minutes per session, twice daily, with an interval between sessions of at least 4 hours.

Ethical approval was obtained from the institutional review boards at The First Affiliated Hospital of Baotou Medical College of Inner Mongolia University (identifier, 2020(08)) and Baotou Central Hospital (identifier, 2020-QX-01). Written informed and verbal consent were provided by a parent or legal guardian and the child. The trial was conducted according to the tenets of the Declaration of Helsinki. This trial is registered with chictr.org.cn (no. ChiCTR2100052322).

### Eligibility Criteria

A total of 114 children were recruited between November 2019 and August 2020. Children aged 7 to 12 years with myopia of cycloplegic spherical equivalent refraction (SER) of at least −0.50 diopter (D), astigmatism of 1.50 D or less, and anisometropia of 1.50 D or less who were willing to participate in the study and accept random allocation in grouping were enrolled in this clinical trial. Excluded were those with secondary myopia, ocular diseases (e.g., amblyopia, strabismus, congenital ocular diseases), previous use of methods for myopia control (e.g., orthokeratology, atropine, and pirenzepine), history of ocular surgeries (e.g., cataract surgery and LASIK), or systemic diseases (e.g., cardiac and respiratory diseases). Children were excluded further if investigators thought they had contraindications that made them unsuitable for participation.

### Randomization and Masking

After verifying eligibility and obtaining consent, eligible participants were allocated randomly in a 1:1 ratio to either the intervention group (RLRL treatment plus SVS) or the sham device control group (sham device with 10% of original power plus SVS). Treatment allocation was completed by 2 investigators (J.D. and H.X.) 1 at each site, unmasked) using closed sealed envelopes that had randomized numbers printed on them by the investigators. The random allocation sequence was generated using randomized block methods in SAS software, version 9.1.3 (SAS Institute) by a statistician who was not involved in participant recruitment or data collection. Only 2 investigators (J.D. and H.X.) were responsible for group allocation and device dispensing and were aware of the study allocation. Other investigators, participants, and the statistician were masked to study allocation.

### Intervention

In addition to SVS, children in the intervention group received RLRL therapy, and those in the sham device control group received sham light therapy, both at a treatment schedule of 3 minutes per session, twice daily, with an interval between sessions of at least 4 hours. The RLRL group received a desktop red-light therapy device (Eyerising; Suzhou Xuanjia Optoelectronics Technology) that has been widely used for amblyopia treatment in China over the past few decades. The sham device control group received the same device but with only 10% of the original device's power. The light power entering a 4-mm pupil (the maximum pupil size under the condition of bright light exposure over 10 seconds) was 0.29 mW for the RLRL device and 0.03 mW for the sham device. These power levels are classified as class 1 under the International Electrotechnical Commission 60825-1:2014 standard,[12] which is at a level considered safe for direct ocular exposure. Children brought their corresponding RLRL or sham device home, where they used the device under the supervision of their parents or guardians.

### Intervention Compliance Monitoring

Intervention compliance was monitored by a treatment log recorded by the child's parents or guardians. If a child's treatment compliance was $<$ 12 sessions per week, study personnel contacted the parent or legal guardian to facilitate improvements in compliance. Participants who completed treatment of at least 12 sessions per week were considered to have good compliance.

### Outcomes

The primary outcome was myopia progression, which was the difference between the cycloplegic SER at baseline and the 6-month visit. The secondary outcomes were changes in axial length (AL) and uncorrected visual acuity (UCVA), which were the differences between AL and UCVA, at baseline and the 6-month visit.

Refraction was performed 3 times using an autorefractor (KR-8900; Topcon) after cycloplegia, which was achieved using 1 drop of proparacaine 0.5% (Alcon), followed by 3 drops of tropicamide 1% (Santen) to each eye at 0, 5, and 20 minutes. Refraction measurements were obtained 15 minutes after the third drop of tropicamide 1% if full cycloplegia was achieved. Further drops of tropicamide 1% would be administered if the pupil size was $<$ 6 mm or the pupillary light reflex was still present. The SER was calculated as spherical power plus half of the cylindrical power.

Axial length was measured using the partial coherence interferometry device IOLMaster (Carl Zeiss 500, Meditec). Five readings with a desired precision (i.e., $\leq$ 0.05 mm) were obtained and averaged. Distance UCVA in logarithm of the minimum angle of resolution (logMAR) was assessed by trained optometrists using the Early Treatment Diabetic Retinopathy Study visual acuity chart (Xingkang Medical Tech).

### Adverse Events

Participants who underwent at least 1 session of treatment were analyzed for safety. At each follow-up visit and any unplanned visits if needed, participants and their parents were asked about any side effects. They also were asked specifically about dazzling, short-term glare, flash blindness, and afterimages after treatment and whether participants had been ill or hospitalized since the last visit. Any adverse events were documented, and a final determination of the adverse event related to treatment was conducted by the data safety monitoring committee.

### Sample Size

Sample size calculations assumed an $\alpha$ level of 0.025 (1-tailed), 80% power, and a 1.20-D difference (2.0 D of standard deviation) in myopia progression between the RLRL and sham device control groups. The minimum sample size required was 45 participants per group, or a total sample size of 90 participants. Adjusting for 20% loss to follow-up and block randomization yielded at least 56 participants in each group, or a total sample size of 112 participants.

### Statistical Analyses

All data were analyzed based on intention-to-treat principles. Data from children who participated in at least 1 follow-up visit were

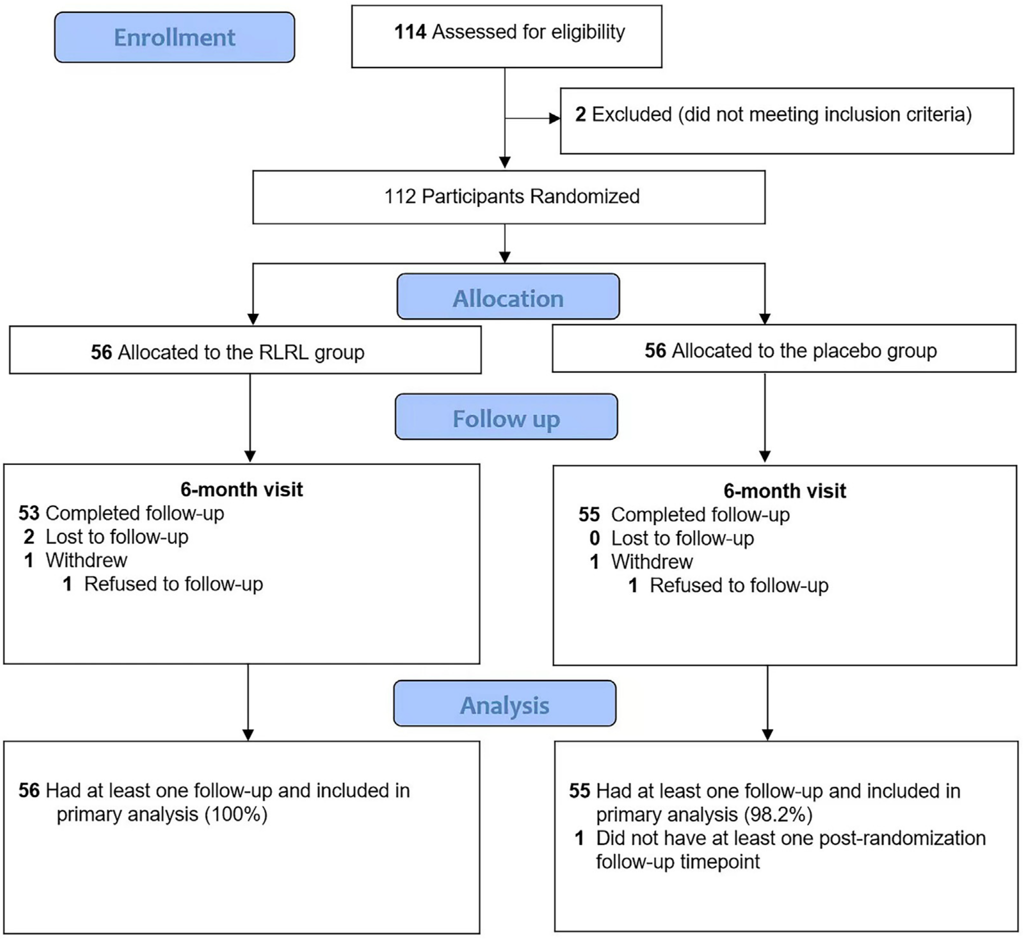


**Figure 1.** Study design and flow diagram of the randomized, double-masked, controlled clinical trial. RLRL = repeated low-level red-light.

included in the present analysis. Missing data on the primary outcome (change of SER) were imputed based on the last observation carried forward. Mean ocular parameter values were calculated from both eyes. The unpaired *t* test or Mann−Whitney *U* test were used to test group differences in continuous data, and the chi-square test was used to test group differences in categorical data. A generalized estimating equation (GEE) with robust standard errors for longitudinal data analysis was used to adjust the correlation between eyes. To evaluate the potential for confounding, analyses were adjusted for age, gender, ethnicities (Han and others), and baseline values.

Sensitivity analyses based on the protocol strategy were performed to verify the robustness of findings. The protocol strategy analysis included only children who achieve good compliance with the treatment originally allocated (at least 12 treatment sessions per week according to the treatment log). We used STATA software, version 14 (StataCorp LP), for statistical analyses. All statistical tests were 2-sided and were performed at the 5% significance level except where otherwise indicated.

## Results

Between November 2019 and August 2020, a total of 114 children were recruited and assessed for eligibility at 2 study sites. A total of 112 children (98.2%) were included in the study, with 56 children with myopia randomly assigned to the RLRL group and 56 children with myopia randomized to the sham device control group by block random sampling. Figure 1 illustrates the number of participants who completed enrollment, baseline examination, intervention, and the 6-month follow-up visit. Of 112 eligible children, 108 children (96.4%) completed the 6-month study, consisting of 53 children (94.6%) in the RLRL group and 55 children (98.2%) in the sham device control group. One hundred eleven of 112 eligible children (99.1%) were included in the analysis (56 children in the RLRL group and 55 children in the sham device control group). This cohort for analysis was determined after excluding 1 child in the sham device control group who did not attend any of the follow-up visits.

### Baseline Characteristics

The mean ± standard deviation age and proportion (%) of children of male sex were similar between the RLRL and sham device control groups (10.3 ± 2.07 years vs. 9.86 ± 1.41 years; male sex, 46.4% [n = 26] vs. 53.6% [n = 30]). No significant difference was found between groups in demographics, baseline SER, AL, and UCVA (Table 1). The proportion of participants who achieved good compliance, defined as at least 12 treatment sessions per week, was 87.5% (n = 49) and 94.5% (n = 52) in the RLRL and sham device control groups, respectively (*P* = 0.195).

Table 1. Baseline Characteristics of Study Participants

| Characteristics | All Patients Randomly Assigned<br>*Intervention Group (n = 56)* | <br>*Sham Device Control Group (n = 55)* | **P Value** |
|---|---|---|---|
| Age, yrs | | | |
| Mean ± SD | 10.3 ± 2.07 | 9.86 ± 1.41 | 0.244 |
| Median (IQR) | 10.4 (8.96−11.4) | 9.91 (8.65−11.0) | |
| Sex, no. (%) | | | |
| Male | 26 (46.4) | 30 (53.6) | 0.450 |
| Female | 30 (53.6) | 26 (46.4) | |
| Ethnicity, no. (%) | | | |
| Han | 52 (92.9) | 50 (89.3) | 0.508 |
| Others | 4 (7.14) | 6 (10.7) | |
| SER, D | | | |
| Mean ± SD | −3.13 ± 1.91) | −2.82 ± 1.86 | 0.389 |
| Median (IQR) | −2.69 (−4.72 to −1.44) | −2.63 (−3.50 to −1.50) | |
| AL, mm | | | |
| Mean ± SD | 24.7 ± 1.04 | 24.6 ± 0.96 | 0.480 |
| Median (IQR) | 24.6 (24.0−25.3) | 24.7 (23.8−25.2) | |
| UCVA, logMAR | | | |
| Mean ± SD | 0.43 ± 0.29 | 0.44 ± 0.25 | 0.907 |
| Median (IQR) | 0.40 (0.20−0.68) | 0.45 (0.20−0.65) | |

AL = axial length; D = diopter; IQR = interquartile range; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; SER = spherical equivalent refraction; UCVA = uncorrected visual acuity.

## Primary Outcome

At the end of 6 months, SER change was 0.06 ± 0.30 D and −0.11 ± 0.33 D in the RLRL and sham device control groups, respectively, with significant differences between the groups ($P = 0.003$; Table 2). In the multivariate GEE model, children in the RLRL group showed less SER progression than those in the sham device control group (coefficient, 0.167 D; 95% confidence interval [CI], 0.050−0.283 D; $P = 0.005$; Table 3). The percentages of myopic children showing SER regression (change in SER of > 0.25 D, and to account for measurement errors in refraction data) in the RLRL group and the sham device control group were 16.1% (n = 9) and 9.09% (n = 5), respectively ($P = 0.268$).

## Secondary Outcomes

Mean AL change at 6 months was greater in the sham device control group (0.13 ± 0.10 mm) than in the RLRL group (0.02 ± 0.11 mm; $P < 0.001$; Table 2). Changes in AL progressed more slowly for children in the RLRL group than for those in the sham device control group in the multivariate GEE model (coefficient: −0.101 mm; 95% CI, −0.139 to −0.062 mm; $P < 0.001$; Table 3). Adjusted mean AL change was slightly slower in older children (coefficient: −0.019 mm; 95% CI, −0.030 to −0.008 mm; $P = 0.001$; Table 3). A total of 23.2% (n = 13) and 5.45% (n = 3) of myopic children in the RLRL and sham device control groups, respectively, achieved AL shortening of > 0.05 mm at the 6-month follow-up, exceeding AL measurement error using the IOLMaster ($P = 0.008$).

At the final visit, distance visual loss was significantly greater for children with myopia in the sham device control group than for those in the RLRL group (0.076 ± 0.189 logMAR vs. −0.002 ± 0.172 logMAR; $P = 0.013$). Similar findings were observed in the GEE model when comparing the RLRL and sham device control groups (coefficient: −0.075 logMAR: 95% CI, −0.143 to −0.007 logMAR; $P = 0.030$).

## Adverse Events

A total of 18 adverse events were reported in 13 participants, but none were deemed by the data safety monitoring committee to be related to the light therapy. In the RLRL group, 1 case each of influenza, an eyelid injury requiring surgical repair, and acute mesenteric lymphadenitis occurred; 2 cases each of earwax blockage and allergic rhinitis occurred; and 3 cases of dental caries occurred. In the sham device control group, 2 cases each of pharyngitis, respiratory tract infection, gastroenteritis, and skin disease were observed.

Table 2. Change in Cycloplegic Spherical Equivalent Refraction and Axial Length from Baseline to 6 Months

| Outcome | Intervention Group (n = 56) | Sham Device Control Group (n = 55) | Mean Difference (95% Confidence Interval) | P Value* |
|---|---|---|---|---|
| Primary | | | | |
| Change of SER, D | 0.06 ± 0.30 | −0.11 ± 0.33 | 0.17 (0.05−0.29) | **0.003** |
| Secondary | | | | |
| Change of AL, mm | 0.02 ± 0.11 | 0.13 ± 0.10 | −0.11 (−0.15 to −0.07) | **< 0.001** |

AL = axial length; D = diopter; SER = spherical equivalent refraction.
Data are presented as mean ± standard deviation, unless otherwise indicated. Bold indicates statistically significant.
*One sided.

Table 3. Generalized Estimating Equation Model Analysis of Factors and Effects on Changes of Cycloplegic Spherical Equivalent Refraction and Axial Length

| Factors | Coefficient (95% Confidence Interval) | *P* Value |
|---|---|---|
| Primary outcome | | |
| Change of SER, D | | |
| Age, yrs | 0.015 (−0.018 to 0.049) | 0.377 |
| Sex (female/male) | −0.053 (−0.168 to 0.063) | 0.372 |
| Ethnicity (Han/other) | −0.039 (−0.241 to 0.163) | 0.703 |
| Baseline SER, D | −0.001 (−0.031 to 0.030) | 0.959 |
| Group (RLRL/sham) | 0.167 (0.050–0.283) | **0.005** |
| Laterality (right/left) | −0.021 (−0.072 to 0.030) | 0.421 |
| Secondary outcome | | |
| Change of AL, mm | | |
| Age, yrs | −0.019 (−0.030 to −0.008) | **0.001** |
| Sex (female/male) | 0.015 (−0.025 to 0.055) | 0.469 |
| Ethnicity (Han/other) | −0.038 (−0.103 to 0.027) | 0.257 |
| Baseline AL, mm | −0.009 (−0.030 to 0.011) | 0.376 |
| Group (RLRL/sham) | −0.101 (−0.139 to −0.062) | **< 0.001** |
| Lateral (right/left) | 0.009 (−0.007 to 0.025) | 0.255 |

AL = axial length; D = diopter; RLRL = repeated low-level red light; SER = spherical equivalent refraction.
Bold indicates statistically significant.

## Sensitivity Analyses

Sensitivity analyses using a per-protocol analysis strategy were performed to verify the robustness of the main findings. Similar results were observed (Tables S1 and S2, available at www.aaojournal.org).

## Discussion

In this randomized, double-blind, controlled clinical trial, RLRL treatment slowed myopia progression by 0.167 D and reduced axial elongation by 0.101 mm over 6 months when compared with sham device treatment. No reported treatment-related adverse events occurred. Our results provide new evidence for RLRL treatment as an effective intervention against myopia progression with no documented functional or structural damage.

### Sham Device–Controlled Study

The use of RLRL therapy for myopia control has surged in popularity.[9,10] In a clinical study of 81 Chinese children (6–16 years of age) in Nanchang, China, the RLRL group showed a mean AL progression rate of −0.06 ± 0.15 mm over 6 months, less than that of the orthokeratology group at 0.06 ± 0.15 mm and the SVS control group at 0.23 ± 0.06 mm.[9] In another 12-month, multicenter randomized clinical trial of 264 Chinese children in Guangzhou, China, RLRL treatment slowed axial elongation by 0.26 mm/year and SER progression by 0.59 D/year compared with SVS in children between 8 and 13 years of age, representing a 69.4% and 76.6% reduction in axial elongation and myopic refraction progression, respectively, compared with SVS.[10] Nevertheless, the open-label designs from previous studies may overestimate the efficacy. To the best of our knowledge, our study is the first sham device–controlled study to account for open-label design and to provide more robust evidence of the myopia control effect of RLRL therapy.

Interestingly, we found potential efficacy in reducing myopic progression and axial elongation with the sham device that used 10% of the original device's power compared with the historic SVS control group. In the present study, mean SER change at 6 months was −0.11 ± 0.33 D in the sham device control group. This compared with mean SER changes at 6 months of −0.50 ± 0.24 D and −0.38 ± 0.05 D in the SVS control groups within the Nanchang[9] and Guangzhou[10] studies, respectively. Similarly, efficacy in reducing axial elongation within the sham device control group of our study (0.13 ± 0.10 mm) seemed to be more than that of the SVS group in the Nanchang (0.23 ± 0.06 mm)[9] and Guangzhou (0.23 ± 0.02 mm)[10] trials. Potential efficacy observed within this study's sham device control group may be the result of placebo effects. However, placebo effects are likely to have a minimal impact on outcomes monitored in this study, especially the outcome of AL, because they are objective measures recorded with high precision.[13] Efficacy instead may be attributable to the true myopia control effect of the sham device with 10% of original power. Of note, direct comparison between our study's findings and those from historic SVS control groups should be approached cautiously, given the different inclusion criteria and populations of the studies and the possible differences in exposure to myopigenic factors such as near work and time outdoors in the different sites.[9] An ideal design could have been a randomized trial including 100% power treatment, 10% power treatment, and no treatment.

### Reversal of SER Myopia Progression and Axial Shortening

In the current study, we demonstrated that RLRL treatment was able to achieve SER regression of > 0.25 D and AL shortening of > 0.05 mm at the 6-month follow-up in 16.1% and 23.2% of children with myopia, respectively. Reversal of SER progression and axial shortening also were observed in the Guangzhou trial (15.8% and 32.9%, respectively).[10] Furthermore, findings from the Guangzhou trial suggested that the observed axial shortening could not be explained fully by choroidal thickening.[10] The myopia control, and potentially even reversal mechanisms, of the RLRL treatment are not understood fully. Most forms of experimental myopia seem to involve a pathway that involves choroidal thinning and decreased blood flow, with subsequent hypoxia. Interventions that slow axial elongation seem to promote reversal of these changes. Thus, we believe it is likely that this may form part of the pathway involved in RLRL therapy.

Although the results in this study, and in others, demonstrate the efficacy of RLRL therapy in controlling the progression of myopia, at present, the molecular and cellular mechanisms involved in the relevant interactions of red light with ocular tissues are not clear. Similarly, the changes in presumably retinal and choroidal pathways that lead from these initial interactions to alterations in the sclera are not clear. These issues are being investigated actively by our research group.

## Strengths and Limitations

Strengths of this study include its randomized, double-blinded, controlled design, the low dropout rate, and the comprehensive evaluation of myopia progression (both SER and AL). This study had several limitations to note. First, the duration of the trial was 6 months, which was insufficient to observe the full myopia control effects. Second, the rebound or carry-on effect of the RLRL treatment is yet to be elucidated. Third, this randomized clinical trial overlapped with the COVID-19 lockdown, and thus, online screen-based learning may have accelerated myopia, although this is likely to affect both arms equally. Fourth, in the sham device control group, we used 10% of RLRL energy, assuming this very low level of energy would not have a treatment effect. However, when completing the trial, we noted that a potential treatment effect was present even among this arm of participants when compared with the SVS control group in the original 12-month study in Guangzhou, despite these 2 groups being not comparable directly because the 2 randomized controlled trials had different study populations and myopigenic environments. A randomized controlled trial comprising 100% power and 10% sham and no treatment would be ideal to address this problem. Finally, masking of participants might have been compromised if the participants had any contact with each other. However, the study participants were recruited individually at hospital clinics, instead of at schools; therefore, they were unlikely to know each other and contact each other during the study.

## Conclusions

In summary, this randomized controlled trial has provided new evidence supporting the efficacy of RLRL therapy in reducing myopia progression compared with the sham device with 10% of original power. The RLRL treatment was well tolerated without apparent adverse effects. Further studies with long-term follow-up are needed to confirm our findings and to evaluate the potential dose-response relationship and the optimal power intensity of the RLRL treatment for myopia control.

## Footnotes and Disclosures

Originally received: March 14, 2022.
Final revision: August 20, 2022.
Accepted: August 23, 2022.
Available online: August 29, 2022. Manuscript no. OPHTHA-D-22-00457

[1] Department of Ophthalmology, The First Affiliated Hospital of Baotou Medical College, Baotou, China.

[2] Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, Melbourne, Australia.

[3] Ophthalmology, Department of Surgery, University of Melbourne, Melbourne, Australia.

[4] Department of Ophthalmology, Baotou City Central Hospital, Baotou, China.

[5] State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China.

*These authors contributed equally as first authors.

Disclosure(s):
All authors have completed and submitted the ICMJE disclosures form.

The author(s) have made the following disclosure(s): Z.Z.: Patent – CN201910490186.6 (“A Method to Increase Retinal Blood Flow and Metabolism” – related to the study)

M.H.: Board member and Equity owner - Eyerising Ltd., Eyerising International Pty Ltd.; Patent – CN201910490186.6 (“A Method to Increase Retinal Blood Flow and Metabolism” – related to the study)

Supported in part by the Fundamental Research Funds of the State Key Laboratory of Ophthalmology (grant no.: 303060202400362); and Eyerising Ltd. The sponsor or funding organization had no role in the design or conduct of this research.

HUMAN SUBJECTS: Human subjects were included in this study. Ethical approval was obtained from the institutional review boards at The First Affiliated Hospital of Baotou Medical College of Inner Mongolia University [2020(08)] and Baotou Central Hospital (2020-QX-01). Written informed and verbal consent were provided by a parent/legal guardian and the child. The trial was conducted according to the tenets of the Declaration of Helsinki.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Dong, He

Analysis and interpretation: Dong, Zhu, Xu

Data collection: Dong, Zhu, Xu

Obtained funding: N/A

Overall responsibility: Dong, Zhu, Xu, He

Abbreviations and Acronyms:
**AL** = axial length; **CI** = confidence interval; **D** = diopter; **GEE** = generalized estimating equation; **logMAR** = logarithm of the minimum angle of resolution; **RLRL** = repeated low-level red-light; **SER** = spherical equivalent refraction; **SVS** = single-vision spectacles; **UCVA** = uncorrected visual acuity.

Key words:
Repeated low-level red-light (RLRL) therapy, Myopia, Randomized clinical trial.

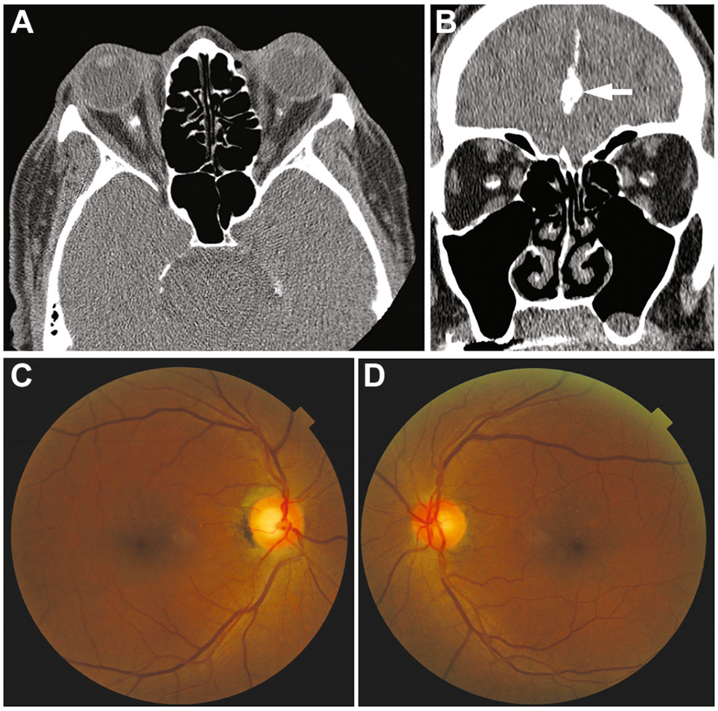
Correspondence:
Mingguang He, MD, PhD, Centre for Eye Research Australia, University of Melbourne, Level 6, 75 Commercial Road, Melbourne, Victoria 3004, Australia. E-mail: mingguang_he@yahoo.com.

## References

1. Baird PN, Saw SM, Lanca C, et al. Myopia. *Nat Rev Dis Primers*. 2020;6(1):99.
2. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123(5):1036–1042.
3. Dolgin E. The myopia boom. *Nature*. 2015;519(7543):276–278.

4. Morgan IG, Ohno-Matsui K, Saw S-M. *Myopia*. Lancet. 2012;379(9827):1739–1748.
5. Holden BAWD, Jong M, Sankaridurg P, et al. Myopia: a growing global problem with sight-threatening complications. *Community Eye Health*. 2015;28(90):35.
6. Saw SM, Gazzard G, Shih-Yen EC, et al. Myopia and associated pathological complications. *Ophthalmic Physiol Opt*. 2005;25(5):381–391.
7. Wakazono T, Yamashiro K, Miyake M, et al. Association between eye shape and myopic traction maculopathy in high myopia. *Ophthalmology*. 2016;123(4):919–921.
8. Mitchell P, Hourihan F, Sandbach J, Jin Wang J. The relationship between glaucoma and myopia. *Ophthalmology*. 1999;106(10):2010–2015.
9. Xiong F, Mao T, Liao H, et al. Orthokeratology and low-intensity laser therapy for slowing the progression of myopia in children. *Biomed Res Int*. 2021;2021:8915867.
10. Jiang Y, Zhu Z, Tan X, et al. Effect of repeated low-level red-light therapy in myopia control in children: a multicenter randomized controlled trial. *Ophthalmology*. 2022;129(5):509–519.
11. Finniss DG, Kaptchuk TJ, Miller F, Benedetti F. Biological, clinical, and ethical advances of placebo effects. *Lancet*. 2010;375(9715):686–695.
12. International Electrotechnical Commission. *IEC 60825-1 Ed. 3.0. Safety of Laser Products—Part 1: Equipment Classification and Requirements*. Geneva: International Electrotechnical Commission; 2014.
13. Santodomingo-Rubido JME, Gilmartin B, Wolffsohn JS. A new non-contact optical device for ocular biometry. *Br J Ophthalmol*. 2002;86(4):458–462.

## Pictures & Perspectives



### Optic Nerve Sheath Calcification

A 72-year-old man underwent computed tomography to evaluate upper airway congestion. Imaging revealed the incidental findings of calcification in each optic nerve sheath (Fig **A**, **B**) and the falx cerebri (Fig **B**, arrow). The patient had undergone a parathyroidectomy 5 years prior for primary hyperparathyroidism. His serum calcium levels subsequently remained within normal limits. Examination showed no evidence of optic nerve dysfunction, although there was asymmetric optic disc cupping (Fig **C**, **D**). Optic nerve sheath calcification may lead to optic atrophy with reduced visual acuity or remain asymptomatic, as in our patient (Magnified version of Fig **A**-**D** is available online at www.aaojournal.org).

Danielle R. Isen, DO[1]
Siddhartha Gaddamanugu, MD[2]
Lanning B. Kline, MD[1]

[1] *Department of Ophthalmology, University of Alabama School of Medicine, Birmingham, Alabama;* [2] *Department of Radiology, University of Alabama School of Medicine, Birmingham, Alabama*