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ORIGINAL RESEARCH

Short-Term Choroidal and Retinal Structural Changes in Myopic Children Treated with 0.05% Atropine

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Purpose: To evaluate daily 0.05% atropine's effects on structural changes in the choroid and retina in myopic children.

Methods: This prospective cohort study included 100 children aged 6–15 years, of whom 83 completed 6-month follow-up. Participants received either nightly 0.05% atropine eyedrops or no pharmacologic treatment (all wore single-vision spectacles). Spherical equivalent (SE) and axial length (AL) were measured, and swept-source OCT angiography was used to assess choroidal thickness (CT), retinal thickness (RT), outer retinal layer (ORL), ganglion cell layer plus inner plexiform layer (GCL+IPL), inner nuclear layer (INL), peripapillary retinal nerve fiber layer (RNFL), choroidal vascular volume (CVV), choroidal vascular index (CVI), superficial and deep vascular complexes (SVC/DVC), and nerve fiber layer vascular density (NFVD).

Results: Atropine reduced myopia progression compared to controls (ΔSE: 0.11 vs −0.30 D; ΔAL: 0.01 vs 0.17 mm; $P < 0.001$). In the atropine group, 55.56% showed SE improvement and 42.22% exhibited AL shortening. Significant increases were observed in macular CT, CVV, RT, ORL, GCL+IPL, INL, and peripapillary RT, ORL, and RNFL, whereas CVI, SVC, DVC, and NFVD remained unchanged. Changes in macular CT, CVV, RT, and GCL+IPL were positively correlated with ΔSE and negatively with ΔAL. Increases in ORL and peripapillary RNFL were negatively correlated with ΔAL.

Conclusion: Daily 0.05% atropine not only slowed myopia progression and axial elongation but also promoted thickening of choroidal and retinal layers. These structural changes suggest partial reversal of ocular growth, supporting the therapeutic role of atropine in myopia control.

Trial Registration: Chinese Clinical Trial Registry (ChiCTR2100043506, https://www.chictr.org.cn/showproj.html?proj=122214, registered 21 February 2021). This study represents a secondary analysis of the registered trial; the control group was drawn from an ethically approved observational cohort.

Keywords: 0.05% atropine eyedrops, myopia control, choroid, retina, OCTA

Introduction

Myopia has become a major global public health challenge, with prevalence increasing sharply over recent decades, particularly in East Asia.[1,2] Experimental studies suggest that choroidal thickness (CT) and blood perfusion may predict myopia development,[3] while clinical evidence indicates that choroidal vasculature plays a role in ocular elongation, such as during orthokeratology treatment.[4] The choroid is thus recognized as a key regulator of myopia progression, although its underlying mechanisms remain unclear.[3,4]

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Structural changes in the retina during myopia progression are also debated.[5–7] Most previous studies have focused on macular choroidal and retinal thickness, whereas the broader effects of myopia on fundus vasculature have received less attention. Understanding these changes is important, as effective myopia control can reduce the risk of long-term visual impairment with minimal treatment-related risk.[8]

Pharmacological interventions, particularly low-concentration atropine eyedrops, have demonstrated consistent efficacy in slowing myopia progression. Among them, 0.05% atropine has shown the greatest effect in reducing spherical equivalent (SE) progression and axial length (AL) elongation over one year.[9] Nightly use in young children significantly reduced both myopia incidence and rapid myopic shifts over two years.[10] Atropine treatment has also been associated with increased choroidal thickness, which correlates with slower SE progression and AL elongation.[11] However, evidence regarding its effects on fundus perfusion and broader retinal and choroidal morphology remains limited. For example, 0.01% atropine produced no significant effect on retinal vessel density, the foveal avascular zone, or choriocapillaris flow, though a modest increase in CT was observed after three months.[12] Given these gaps, further studies are needed to clarify how atropine affects fundus structure and blood flow in children.

This study uses swept-source optical coherence tomography angiography (SS-OCTA) to quantitatively evaluate morphological and vascular changes in the choroid and retina during 0.05% atropine treatment. The findings may help optimize myopia control strategies and provide insight into the roles of the choroid and retina in myopia progression.

Materials and Methods

Study Population

This prospective observational study was nested within a randomized controlled trial (RCT; ChiCTR2100043506) conducted from November 2021 to September 2023 to evaluate 0.05% atropine for myopia control. Participants were drawn from the nightly 0.05% atropine arm, which showed the greatest efficacy. The present secondary analysis focused on short-term (6-month) changes in choroidal and retinal structures.

The study was approved by the Changsha Aier Eye Hospital Ethics Committee (Approval ID: 2020KYPJ001) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants and their guardians. For comparison, an age- and sex-matched non-atropine control group wearing single-vision spectacles was enrolled from a separate, ethically approved observational cohort (IRB No. 2022KYPJ007).

Inclusion criteria were: age 6–15 years; SE −0.50D to −6.00D; astigmatism ≤2.00D; anisometropia ≤1.50D; BCVA ≥0.1 logMAR; and IOP ≤21 mmHg. Exclusion criteria included ocular pathology, prior ocular surgery, systemic illness, previous myopia interventions (eg, orthokeratology), or known hypersensitivity to atropine.

Based on previous studies reporting subfoveal choroidal thickness increases of 10–20 μm after low-dose atropine (0.01–0.05%) over 6 months,[13] a hypothesized difference of 15 μm between atropine and control groups was used for sample size calculation. Assuming a standard deviation of 20 μm, a two-sided alpha of 0.05, and 80% power, 28 children per group were required. To account for potential dropouts, a total of 100 children were recruited, of whom 83 completed the 6-month follow-up. Detailed attrition information is presented in Figure S1. Written informed consent was obtained from all participants and their guardians. All children wore single-vision spectacles throughout the study, and compliance was monitored via parent-reported medication logs and interviews by two trained research staff.

Ocular Measurements

Cycloplegic SE was measured using an auto-refractometer (ARK-510A, Nidek, Japan) after three instillations of 0.5% tropicamide at 5-minute intervals. Adequate cycloplegia was confirmed 30 minutes after the final instillation. Before cycloplegia, Axial length (AL) and corneal curvature were measured using optical low-coherence reflectometry (LENSTAR LS 900, Haag-Streit, Switzerland). IOP was measured with a non-contact tonometer (TX-20, Canon, Japan), with the mean of three consecutive readings recorded. All examinations were performed at baseline and 6 months.

SS-OCT/OCTA Imaging

After cycloplegia, macular and optic disc images were acquired between 9:00 AM and 4:00 PM using SS-OCT/OCTA (VG200S; SVision Imaging, Henan, China), operating at 1050 nm with 200,000 A-scans/s, axial/lateral resolutions of 5 μm and 13 μm, and a 3-mm scanning depth. Raster scans covered a 6×6 mm^2 area centered on the fovea. The system was equipped with an eye-tracking utility based on an integrated confocal scanning laser ophthalmoscope to minimize motion artifacts. All images were required to have a signal strength ≥8; scans below this threshold were excluded and repeated to ensure optimal quality. Two experienced examiners obtained all images, and segmentation was reviewed and manually corrected as needed.

Image Analysis

Macular analysis used the ETDRS grid: central 1 mm foveal, 1–3 mm parafoveal, and 3–6 mm perifoveal regions, each divided into superior(S), temporal(T), inferior(I), and nasal(N) quadrants (Figure 1A). Peripapillary measurements used the Optic Nerve Head (ONH) grid, analyzing the 2–4 mm ring to avoid central disc effects (Figure 1B).

Choroidal thickness (CT): distance from 10 μm above Bruch's membrane to choroid-scleral interface (Figure 1C and D). Choroidal vascular volume (CVV): volume of large/medium choroidal vessels; choroidal vascular index (CVI): CVV/total choroidal volume (Figure 1E). CT, CVV, and CVI measurements were quantified using a deep-learning algorithm over the entire 3D scan. Retinal thickness (RT): internal limiting membrane (ILM) to retinal pigment epithelium (RPE); Retinal nerve fiber layer thickness (RNFL): ILM to ganglion cell layer (GCL); Ganglion cell layer and inner plexiform layer complex (GCL+IPL): RNFL to IPL; Outer retinal layer (ORL): inner nuclear layer (INL) to RPE (Figure 1C and D). Inner retinal layers: superficial vascular complex (SVC) and deep vascular complex (DVC) defined from 5 μm above ILM to 25 μm below INL; Segmentation of the SVC and DVC was based on the boundary

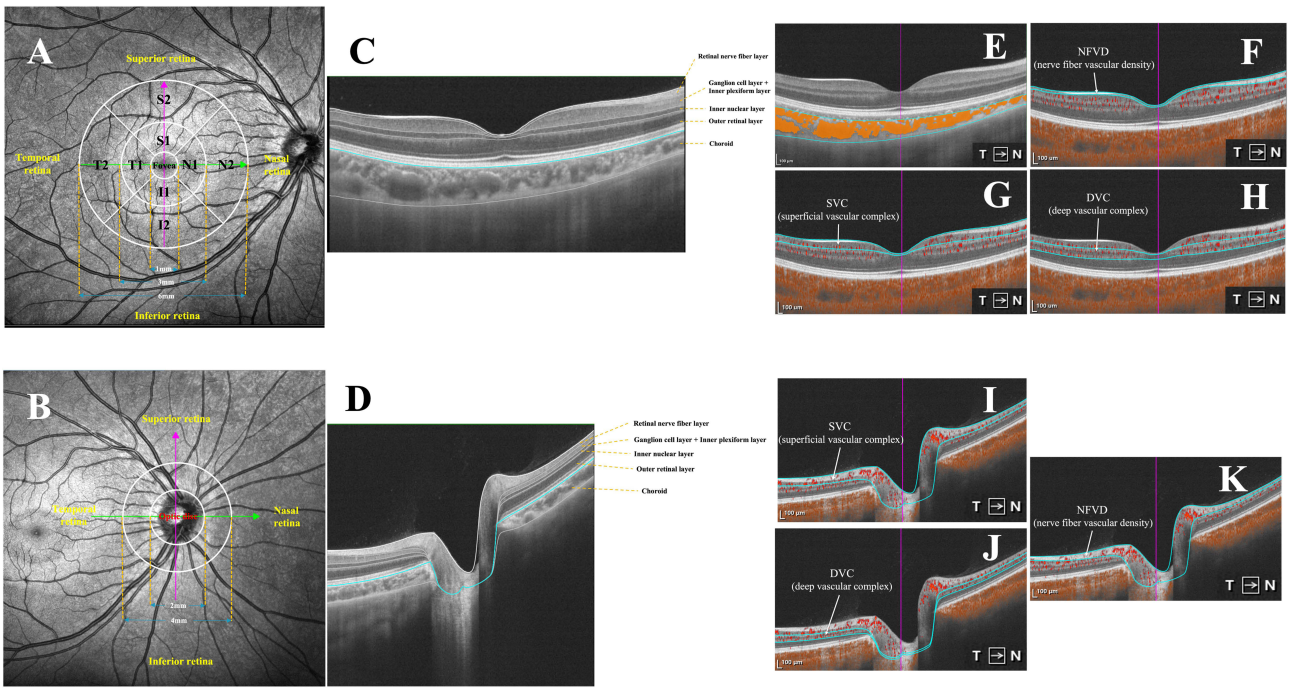

Figure 1 Schematic diagram of SS-OCTA zoning and quantitative parameters. (**A**) *Macular region (ETDRS grid)*: Orange dotted lines denote the central 1 mm, inner 1–3 mm, and outer 3–6 mm rings; yellow labels mark four quadrants (S, I, N, T); green labels indicate the nasal direction; purple arrow indicates the superior direction; (**B**) *Optic disc region*: Orange dotted lines delineate the 2–4 mm peripapillary ring; yellow labels mark four quadrants (S, I, N, T); green labels indicate nasal, and the purple arrow marks superior; (**C**–**D**) *Retinal/choroidal layers*: Orange dotted lines outline nerve fiber layer (RNFL), ganglion cell layer + inner plexiform layer (GCL+IPL), inner nuclear layer (INL), outer retinal layer (ORL), and choroid; blue curves show retinal/choroidal segmentation boundaries; (**E**–**H**) *Macular metrics*: Orange shading in (**E**) represents choroidal vascular volume (CVV) and choroidal vascular index (CVI); regions between blue segmentation curves (white arrowheads) in (**F**–**H**) represent nerve fiber layer vascular density (NFVD), superficial vascular complex (SVC) density, and deep vascular complex (DVC) density; (**I**–**K**) *Optic disc metrics*: Regions between blue segmentation curves (white arrowheads) denote SVC density, DVC density, and NFVD.

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between the inner two-thirds and the outer one-third of the GCL+IPL. Nerve fiber layer vascular density (NFVD): vessel density within RNFL (Figure 1F–K).

Statistical Analysis

Only the right eye of each participant was analyzed to minimize inter-eye correlation. Normally distributed data are presented as mean ± SD. Between-group comparisons used independent t-tests; within-group changes from baseline to 6 months were assessed using paired t-tests. Categorical variables (eg, sex) were compared using chi-square tests. Pearson correlation evaluated associations between changes in SE, AL, and fundus structural parameters. Two-tailed $P < 0.05$ was considered statistically significant. Analyses were performed using SPSS statistical software (version 26.0, IBM, USA).

Results

General Characteristics and Myopia Progression

A total of 83 myopic children were included in the final analysis. Baseline characteristics—including age, sex distribution, corneal curvature, and intraocular pressure—did not differ significantly between the atropine and control groups.

During the 6-month follow-up, the atropine group exhibited minimal refractive change (ΔSE: +0.11 ± 0.37 D), whereas the control group showed significant myopic progression (ΔSE: −0.30 ± 0.23 D; $P < 0.001$). Axial length increased by only 0.01 ± 0.13 mm in the atropine group compared with 0.17 ± 0.08 mm in the control group ($P < 0.001$). Detailed demographic data and refractive outcomes are presented in Table 1.

As illustrated in Figure 2, 55.56% of children receiving atropine demonstrated a hyperopic shift in SE, and 42.22% exhibited AL shortening. In contrast, all participants in the control group experienced continued myopic progression and axial elongation.

Choroidal Structural Changes

At 6 months, the atropine group exhibited significantly greater increases in choroidal thickness (CT) across all macular regions—except the peripapillary area—compared with controls ($P < 0.05$). Within-group comparisons confirmed CT thickening in all macular regions in the atropine group (excluding the peripapillary area), whereas no significant CT changes were detected in the control group (see Table S1).

Table 1 Characteristics of Participants and Myopia Progression (Mean ± SD)

Parameters	Atropine Group N = 45	Control Group N = 38	*P* (Atropine vs Control)
Age (years)	10.60 ± 2.02	11.42 ± 2.18	0.078
Male, n (%)	24 (53.3%)	19 (50%)	0.762
Baseline Flattest K (D)	42.74 ± 1.35	42.80 ± 1.35	0.833
Baseline Steepest K (D)	43.88 ± 1.63	43.94 ± 1.32	0.850
Baseline IOP (mmHg)	15.81 ± 2.31	15.14 ± 2.69	0.228
SE (D)			
Baseline	−2.71 ± 1.21	−2.28 ± 1.39	0.133
6 months	−2.61 ± 1.27	−2.58 ± 1.41	0.937
Changes	0.11 ± 0.37	−0.30 ± 0.23	< 0.001
P (6 mo vs baseline)	0.063	< 0.001	
AL (mm)			
Baseline	24.63 ± 0.96	24.57 ± 0.92	0.764
6 months	24.64 ± 0.95	24.74 ± 0.91	0.648
Changes	0.01 ± 0.13	0.17 ± 0.08	< 0.001
P (6 mo vs baseline)	0.632	< 0.001	

Abbreviations: IOP, intraocular pressure; SE, spherical equivalent; AL, axial length.

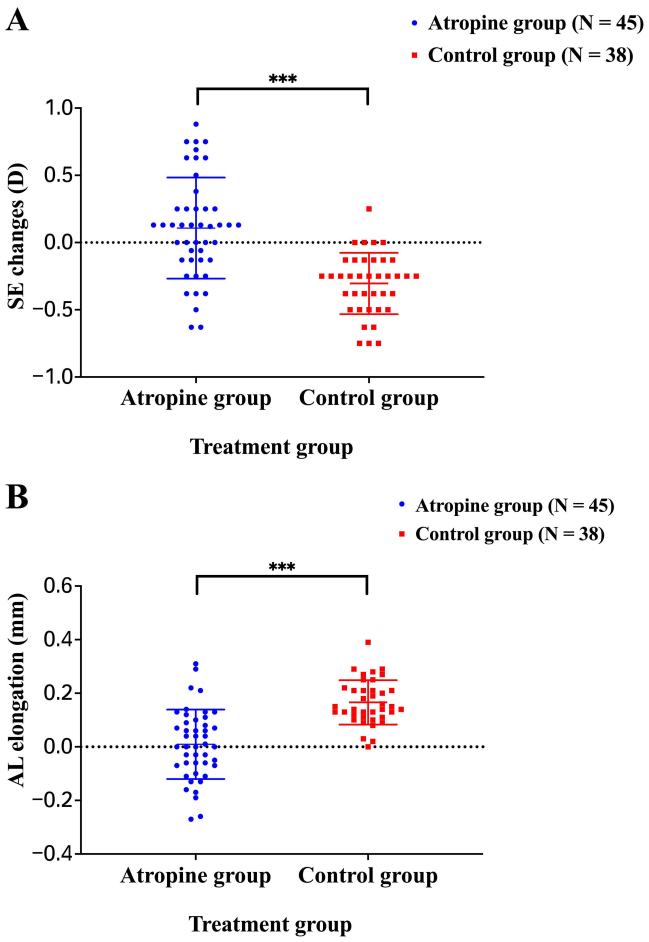

Figure 2 Changes in (**A**) spherical equivalent (SE) and (**B**) axial length (AL) after 6 months of intervention. ***$P < 0.001$ for data determined by SE and AL changes between the two groups (blue represents 0.05% atropine, and red represents control).

The pattern of CT thickening was consistent across inner and outer macular rings, with the greatest increase in the superior quadrant, followed by the temporal, inferior, and nasal quadrants. This regional trend was most pronounced in the outer ring (Figure 3).

Similarly, choroidal vascular volume (CVV) significantly increased in all macular regions in the atropine group compared with controls ($P < 0.05$), whereas no significant changes were observed in controls (Table 2).

No significant between-group differences were observed in choroidal vascularity index (CVI) changes ($P > 0.05$). However, within-group analysis showed a modest but significant increase in CVI in the control group over 6 months ($P < 0.05$, Table 3).

Retinal Structural Changes

After 6 months, children treated with atropine demonstrated significantly greater increases in retinal thickness (RT) and outer retinal layer (ORL) thickness across macular and peripapillary regions compared with controls ($P < 0.05$) (Figure 4A, B and Tables S2, S3).

Peripapillary RNFL thickness also increased significantly in the atropine group versus controls ($P < 0.05$) (Figure 4C and Table S4). Similarly, ganglion cell layer plus inner plexiform layer (GCL+IPL) thickness increased significantly in the macular region ($P < 0.05$) (Figure 4D and Table S5), and inner nuclear layer (INL) thickness significantly increased in the 6-mm macular region and superior/inferior outer quadrants ($P < 0.05$) (Figure 4E and Table S6).

No significant between-group differences were detected in superficial vascular complex (SVC) density, deep vascular complex (DVC) density, or nerve fiber vascular density (NFVD) ($P > 0.05$). However, within-group analysis revealed:

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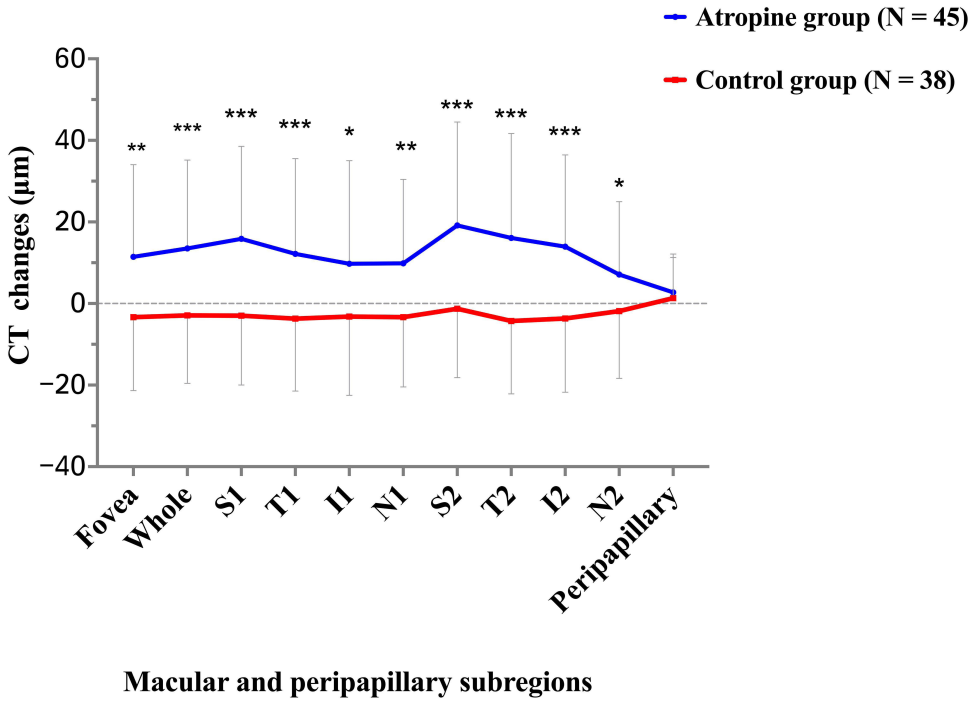

Figure 3 Changes in choroidal thickness (CT) after 6 months between the Atropine group (N=45) and the Control group (N=38). CT-Fovea: CT at the fovea; CT-Whole: CT within a 6mm radius around the fovea; CT-Peripapillary: CT in the peripapillary region, derived from the outer ring of the ONH grid to minimize optic disc influence. S1, T1, I1, N1: Superior, Temporal, Inferior, Nasal quadrants of the inner ETDRS ring (1–3 mm); S2, T2, I2, N2: Corresponding quadrants of the outer ring (3–6 mm). *P < 0.05, **P < 0.01, ***P < 0.001 (blue represents 0.05% atropine, and red represents control).

SVC density significantly increased in the atropine group at the 6-mm macular region, superior/inferior outer quadrants, and peripapillary area (P < 0.05); DVC density significantly decreased in the temporal outer macular ring and peripapillary region of the atropine group (P < 0.05); NFVD significantly increased in the 6-mm macular area, peripapillary region, and superior/nasal quadrants of the outer macular ring, but decreased in the temporal quadrant (P < 0.01) (Tables 4 and S7–S9).

Table 2 Comparison of Choroidal Vascular Volume (CVV) Between Groups (Mean ± SD)

	Atropine Group N = 45	**Control Group N = 38**	***P* (Atropine vs Control)**
CVV-Fovea (mm^3)			
Baseline	0.09±0.02	0.09±0.02	0.301
6 months	0.10±0.02	0.09±0.02	0.036
Changes	0.01±0.01	0.00±0.01	0.003
P (6 mo vs baseline)	< 0.001	0.844	
CVV-Whole (mm^3)			
Baseline	2.98±0.71	2.78±0.63	0.183
6 months	3.18±0.75	2.78±0.64	0.010
Change	0.21±0.28	0.00±0.23	0.001
P (6 mo vs baseline)	< 0.001	0.954	
CVV-S1 (mm^3)			
Baseline	0.18±0.05	0.17±0.04	0.207
6 months	0.19±0.05	0.17±0.04	0.018
Changes	0.01±0.02	0.00±0.01	0.001
P (6 mo vs baseline)	< 0.001	0.917	

(*Continued*)

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Table 2 (Continued).

	Atropine Group N = 45	Control Group N = 38	*P* (Atropine vs Control)
CVV-T1 (mm^3)			
Baseline	0.19±0.04	0.18±0.04	0.157
6 months	0.20±0.04	0.18±0.04	0.008
Changes	0.01±0.02	0.00±0.01	0.001
P (6 mo vs baseline)	< 0.001	0.994	
CVV-I1 (mm^3)			
Baseline	0.19±0.05	0.17±0.04	0.111
6 months	0.20±0.05	0.17±0.04	0.010
Changes	0.01±0.02	0.00±0.02	0.004
P (6 mo vs baseline)	< 0.001	0.791	
CVV-N1 (mm^3)			
Baseline	0.16±0.05	0.15±0.04	0.107
6 months	0.17±0.05	0.15±0.04	0.012
Changes	0.01±0.02	0.00±0.01	0.004
P (6 mo vs baseline)	< 0.001	0.636	
CVV-S2 (mm^3)			
Baseline	0.57±0.14	0.55±0.11	0.611
6 months	0.61±0.15	0.55±0.12	0.050
Changes	0.04±0.05	0.00±0.04	< 0.001
P (6 mo vs baseline)	< 0.001	0.933	
CVV-T2 (mm^3)			
Baseline	0.61±0.12	0.58±0.12	0.251
6 months	0.65±0.12	0.58±0.12	0.006
Changes	0.04±0.06	0.00±0.04	< 0.001
P (6 mo vs baseline)	< 0.001	0.795	
CVV-I2 (mm^3)			
Baseline	0.57±0.14	0.53±0.14	0.156
6 months	0.61±0.14	0.53±0.13	0.009
Changes	0.04±0.05	0.00±0.05	0.002
P (6 mo vs baseline)	< 0.001	0.865	
CVV-N2 (mm^3)			
Baseline	0.41±0.16	0.36±0.14	0.157
6 months	0.44±0.17	0.36±0.14	0.035
Changes	0.03±0.05	0.00±0.05	0.018
P (6 mo vs baseline)	0.001	0.859	

Notes: CVV-Fovea: choroidal vascular volume in the foveal region; CVV-Whole: choroidal vascular volume within a 6 mm radius around the fovea; S1, T1, I1, N1: Superior, Temporal, Inferior, Nasal quadrants of the inner ETDRS ring (1–3 mm); S2, T2, I2, N2: Corresponding quadrants of the outer ring (3–6 mm).

Table 3 Comparison of Choroidal Vascular Index (CVI) Between Groups (Mean ± SD)

	Atropine Group N = 45	Control Group N = 38	*P* (Atropine vs Control)
CVI-Fovea			
Baseline	0.49±0.06	0.49±0.07	0.892
6 months	0.49±0.06	0.50±0.08	0.620
Changes	0.00±0.03	0.01±0.03	0.347
P (6 mo vs baseline)	0.439	0.045	

(*Continued*)

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Table 3 (Continued).

	Atropine Group N = 45	Control Group N = 38	*P* (Atropine vs Control)
CVI-Whole			
Baseline	0.47±0.04	0.46±0.05	0.490
6 months	0.47±0.05	0.47±0.05	0.677
Changes	0.00±0.02	0.01±0.02	0.467
P (6 mo vs baseline)	0.057	0.022	
CVI-S1			
Baseline	0.48±0.06	0.47±0.07	0.321
6 months	0.48±0.06	0.48±0.07	0.651
Changes	0.00±0.02	0.01±0.02	0.117
P (6 mo vs baseline)	0.785	0.055	
CVI-T1			
Baseline	0.48±0.07	0.47±0.06	0.511
6 months	0.48±0.06	0.48±0.06	0.605
Changes	0.01±0.02	0.01±0.02	0.640
P (6 mo vs baseline)	0.122	0.038	
CVI-I1			
Baseline	0.49±0.06	0.49±0.06	0.577
6 months	0.50±0.06	0.50±0.06	0.597
Changes	0.01±0.03	0.01±0.03	0.984
P (6 mo vs baseline)	0.005	0.012	
CVI-N1			
Baseline	0.50±0.06	0.48±0.06	0.174
6 months	0.51±0.06	0.50±0.07	0.266
Changes	0.01±0.03	0.01±0.03	0.654
P (6 mo vs baseline)	0.006	0.004	
CVI-S2			
Baseline	0.45±0.05	0.45±0.05	0.920
6 months	0.45±0.05	0.46±0.05	0.639
Changes	0.00±0.02	0.00±0.02	0.336
P (6 mo vs baseline)	0.398	0.603	
CVI-T2			
Baseline	0.44±0.05	0.45±0.06	0.844
6 months	0.45±0.05	0.45±0.06	0.606
Changes	0.00±0.02	0.01±0.02	0.460
P (6 mo vs baseline)	0.472	0.059	
CVI-I2			
Baseline	0.47±0.05	0.46±0.06	0.585
6 months	0.48±0.05	0.47±0.05	0.920
Changes	0.00±0.02	0.01±0.02	0.290
P (6 mo vs baseline)	0.131	0.022	
CVI-N2			
Baseline	0.48±0.07	0.46±0.08	0.210
6 months	0.50±0.08	0.47±0.07	0.183
Changes	0.01±0.03	0.01±0.03	0.750
P (6 mo vs baseline)	0.033	0.097	

Notes: CVI-Fovea: Choroidal Vascular Index at the fovea center; CVI-Whole: Choroidal Vascular Index within a 6 mm radius around the fovea; S1, T1, I1, N1: Superior, Temporal, Inferior, Nasal quadrants of the inner ETDRS ring (1–3 mm); S2, T2, I2, N2: Corresponding quadrants of the outer ring (3–6 mm).

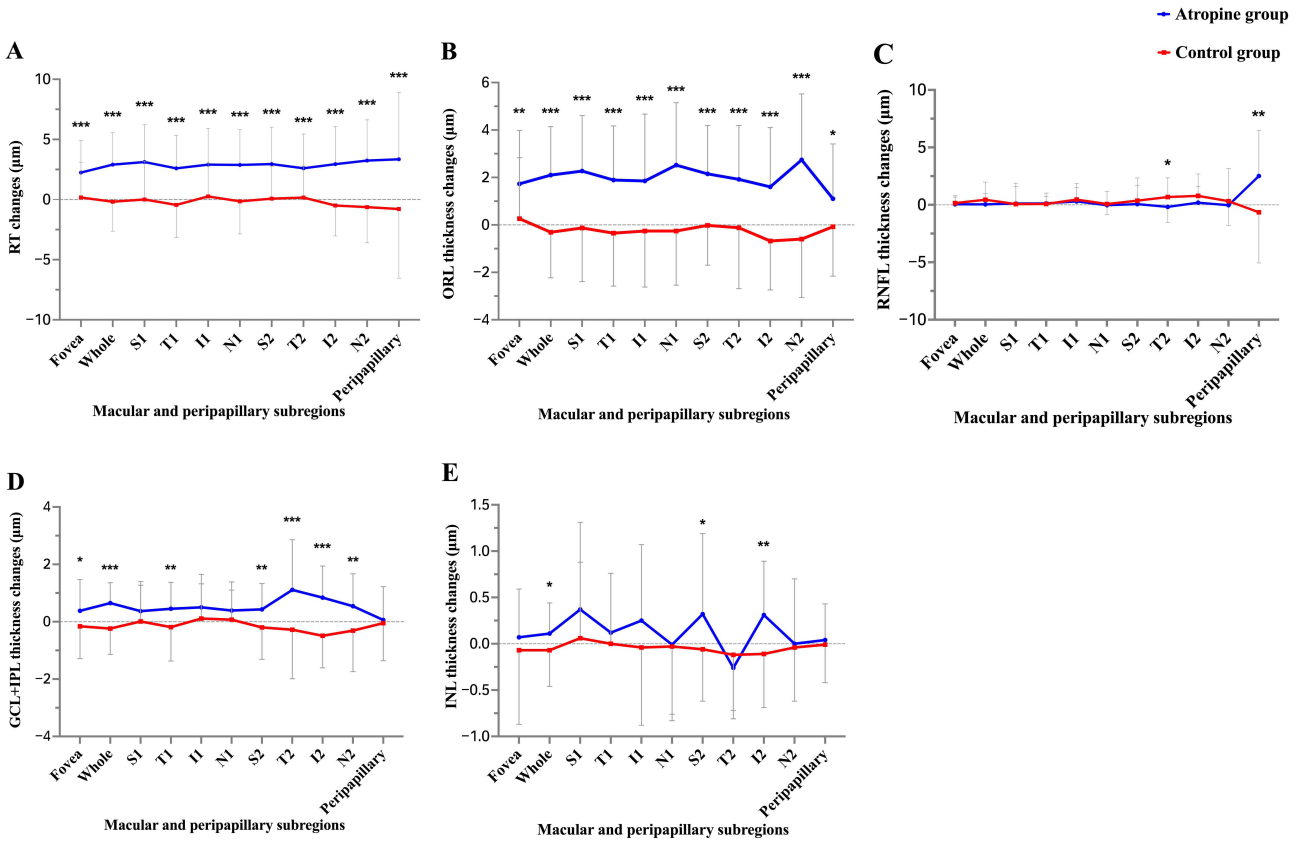

Figure 4 Changes in retinal layer thickness after 6 months between the Atropine group (N=45) and the Control group (N=38). (**A**) RT: Retinal thickness; (**B**) ORL: Outer retinal layer; (**C**) RNFL: Retinal nerve fiber layer; (**D**) GCL+IPL: Ganglion cell-inner plexiform layer; (**E**) INL: Inner nuclear layer. Whole: Retinal thickness within a 6 mm radius around the fovea; Peripapillary: Retinal thickness in the peripapillary area, using data from the outer ring of the ONH grid to minimize optic disc influence. S1, T1, I1, N1: Superior, Temporal, Inferior, Nasal quadrants of the inner ETDRS ring (1–3 mm); S2, T2, I2, N2: Corresponding quadrants of the outer ring (3–6 mm). Statistical significance: **P* < 0.05, ***P* < 0.01, ****P* < 0.001 (blue represents 0.05% atropine, and red represents control).

Correlation

In the atropine group, changes in macular CT, CVV, RT, and GCL+IPL thickness were significantly positively correlated with ΔSE and negatively correlated with ΔAL ($P < 0.05$). ORL thickness also showed a significant negative correlation with ΔAL ($P < 0.05$).

In the peripapillary region, changes in RNFL and ORL thickness were negatively correlated with ΔAL ($P < 0.05$) (Table 5).

Table 4 Comparison of Retinal Vascular Density Between Groups (Mean ± SD)

	Atropine Group N = 45	**Control Group N = 38**	***P*** **(Atropine vs Control)**
SVC-Fovea (%)			
Baseline	14.13±4.49	15.21±6.38	0.369
6 months	14.76±4.82	15.17±6.16	0.736
Changes	0.63±2.47	−0.04±2.60	0.231
P (6 mo vs baseline)	0.095	0.917	
SVC-Whole (%)			
Baseline	39.47±2.94	39.19±4.23	0.726
6 months	40.43±2.87	39.73±4.03	0.357
Changes	0.97±2.49	0.54±4.20	0.569
P (6 mo vs baseline)	0.013	0.432	

(*Continued*)

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Table 4 (Continued).

	Atropine Group N = 45	Control Group N = 38	*P* (Atropine vs Control)
SVC-Peripapillary (%)			
Baseline	64.34±3.14	63.89±5.21	0.630
6 months	65.82±3.41	64.68±4.54	0.195
Changes	1.49±2.25	0.80±3.62	0.291
P (6 mo vs baseline)	<0.001	0.183	
DVC-Fovea (%)			
Baseline	23.52±7.06	26.22±8.84	0.126
6 months	23.28±7.10	25.86±9.12	0.152
Changes	−0.24±4.55	−0.36±4.07	0.901
P (6 mo vs baseline)	0.721	0.586	
DVC-Whole (%)			
Baseline	49.80±2.36	49.88±5.70	0.938
6 months	49.71±3.09	49.26±3.10	0.512
Changes	−0.10±2.98	−0.62±5.52	0.586
P (6 mo vs baseline)	0.83	0.495	
DVC-Peripapillary (%)			
Baseline	23.49±4.33	21.52±5.35	0.068
6 months	21.31±4.87	20.80±4.29	0.617
Changes	−2.18±4.60	−0.72±4.06	0.134
P (6 mo vs baseline)	0.003	0.279	
NFVD-Fovea (%)			
Baseline	0.78±1.07	0.87±1.31	0.716
6 months	0.59±1.19	0.87±1.19	0.282
Changes	−0.19±1.18	0.00±0.82	0.409
P (6 mo vs baseline)	0.288	0.996	
NFVD-Whole (%)			
Baseline	18.49±1.50	19.31±2.38	0.062
6 months	18.91±1.66	19.72±2.65	0.096
Changes	0.42±0.95	0.41±1.45	0.971
P (6 mo vs baseline)	0.005	0.089	
NFVD-Peripapillary (%)			
Baseline	57.58±3.73	57.48±5.42	0.923
6 months	59.36±4.24	58.23±5.08	0.272
Changes	1.78±2.44	0.74±3.25	0.102
P (6 mo vs baseline)	<0.001	0.168	

Abbreviations: SVC, Superficial vascular complex density; DVC, Deep vascular complex density; NFVD, Retinal nerve fiber layer vascular density; Whole, within a 6 mm radius around the fovea; Peripapillary, the peripapillary region, using data from the outer ring of the ONH grid to minimize optic disc influence.

Table 5 Correlation Analysis Between Changes in Fundus Structure and Myopia Progression

Parameters	Atropine Group				Control Group			
	r-ΔSE	*p-ΔSE*	*r-ΔAL*	*p-ΔAL*	*r-ΔSE*	*p-ΔSE*	*r-ΔAL*	*p-ΔAL*
Fovea changes								
CT Fovea	0.460**	0.001	−0.644***	< 0.001	0.122	0.467	−0.590***	< 0.001
CT Whole	0.399**	0.007	−0.635***	< 0.001	0.134	0.423	−0.572***	< 0.001
CVV Fovea	0.355*	0.017	−0.451**	0.002	0.020	0.906	−0.513**	0.001
CVV Whole	0.431**	0.003	−0.590***	< 0.001	0.106	0.526	−0.482**	0.002

(*Continued*)

Table 5 (Continued).

Parameters	Atropine Group				Control Group			
	r-ΔSE	*p-ΔSE*	*r-ΔAL*	*p-ΔAL*	*r-ΔSE*	*p-ΔSE*	*r-ΔAL*	*p-ΔAL*
RT Whole	0.324*	0.030	−0.532***	< 0.001	−0.120	0.474	−0.297	0.070
GCL+IPL Whole	0.404**	0.006	−0.469**	0.001	−0.128	0.445	−0.048	0.775
ORL Whole	0.256	0.090	−0.486**	0.001	−0.145	0.386	−0.259	0.116
Peripapillary changes								
RNFL	0.152	0.320	−0.318*	0.033	0.074	0.660	−0.052	0.758
ORL	0.109	0.475	−0.302*	0.044	0.078	0.641	−0.113	0.499

Notes: Statistically significant intergroup differences: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
Abbreviations: ΔSE, Change in spherical equivalent; ΔAL, Change in axial length; Whole, within a 6 mm radius around the fovea; CT, Choroidal thickness; CVV, Choroidal vascular volume; RT, Retinal thickness; GCL+IPL, Ganglion cell layer and inner plexiform layer; ORL, Outer retinal layer; RNFL, Retinal nerve fiber layer.

Discussion

This prospective cohort study demonstrated that 0.05% atropine significantly reduced axial elongation (0.01 ± 0.13 mm) and myopic progression (+0.11 ± 0.37 D) compared with untreated controls (0.17 ± 0.08 mm and −0.30 ± 0.23 D, respectively) over 6 months. These findings support the short-term efficacy of 0.05% atropine in slowing myopia progression. To better understand its mechanisms, we evaluated regional choroidal and retinal structural and vascular changes using SS-OCTA.

CT is recognized as a regulator of ocular growth, with regional variations typically showing greater thickening on the temporal side compared to the nasal side.[14,15] Faster axial elongation was associated with less CT thickening or even thinning over time.[16] Previous reports suggest a dose-dependent effect of atropine, with higher concentrations (eg, 1%) inducing CT thickening, whereas lower concentrations (eg, 0.01%) may have minimal or even thinning effects.[11,17] In our cohort, 0.05% atropine produced a consistent increase in macular CT, most pronounced in the superior quadrant, followed by temporal, inferior, and nasal regions. This pattern may reflect the relatively thinner central choroid in myopic children, potentially due to mechanical constraints or fewer nonvascular smooth muscle cells in the fovea.[18–20]

Importantly, atropine also increased CVV while CVI remained largely unchanged. This contrasts with previous studies showing CVV reduction and CVI elevation with increasing myopia severity.[21] The discrepancy may be explained by atropine simultaneously expanding both vascular and stromal choroidal compartments, thereby stabilizing CVI values. In controls, CVI increased slightly, likely reflecting a reduction in total choroidal volume rather than enhanced vascularity. Unlike adult studies linking CVI decline to pathological myopia,[22,23] our pediatric cohort did not show such patterns, suggesting that atropine-related vascular remodeling may mask these associations. Overall, our data indicate that CVV expansion is closely related to reduced axial elongation, supporting the hypothesis that choroidal vascular modulation contributes to atropine's efficacy.

The association between retinal thickness (RT) and myopia remains debated. Some studies have reported regional RT thinning with increasing AL,[24] whereas others found preserved central RT in adults.[6,7] In this study, atropine significantly increased RT, and increased macular RT was positively correlated with SE and negatively with AL. Atropine also led to thickening of RNFL, GCL+IPL, and ORL layers, with peripapillary RNFL and ORL changes showing strong negative correlations with axial elongation. These findings contrast with previous reports of progressive RNFL and GCL+IPL thinning in high myopia,[25,26] particularly in males,[27] although some studies found no significant effect of axial elongation on RNFL thickness in children.[28] Importantly, RNFL alterations around the optic disc remain clinically relevant for glaucoma detection.[29,30] The observed ORL thickening in both macular and peripapillary regions is consistent with experimental data in non-myopic children and animal models, which suggest an effect of atropine on cone photoreceptors.[31,32] In high myopia, ORL thinning has been linked to photoreceptor dysfunction, reduced retinal sensitivity, and compensatory deep microvascular changes.[33] In pathological myopia, reductions in ORL thickness and

deep vascular density correlate with decreased BCVA,[34] highlighting the detrimental impact of axial elongation on retinal microvascular integrity.[5]

Unlike structural parameters, retinal vascular density showed no significant between-group differences, consistent with prior studies using 0.01% atropine.[12] Nevertheless, within the atropine group, modest increases in SVC and NFVD and localized reductions in DVC were observed. Retinal vascular responses are known to be dynamic, with DVC particularly sensitive to physiological fluctuations.[35] Generally, vascular density decreases with axial elongation in high myopia, whereas compensatory increases may occur around the optic disc.[36,37] These findings suggest that atropine's primary effects may lie in structural remodeling rather than retinal vascular modulation, although evaluation of outer retinal circulation is warranted in future studies.

A strength of this study is the combined evaluation of macular and peripapillary regions, which are rarely reported together, using SS-OCTA to capture subtle structural and vascular alterations. The correlations between atropine-induced changes and myopia control outcomes highlight the potential of these parameters as biomarkers. However, several limitations must be acknowledged. First, the follow-up was limited to six months, focusing on short-term responses; the long-term sustainability of these changes remains unknown. Second, causal relationships cannot be established due to the observational design. Finally, outer retinal vascular changes were not assessed, which may underestimate atropine's broader vascular effects. Future longitudinal studies with larger cohorts and extended follow-up are needed to clarify the durability of these effects and explore additional biomarkers, such as outer retinal vasculature, to further optimize clinical application of atropine therapy.

Conclusions

In conclusion, nightly 0.05% atropine effectively slowed myopia progression and axial elongation in children. The associated thickening of retinal and choroidal structures, especially in the macula and peripapillary regions, suggests structural remodeling that may underlie its therapeutic effect in myopia control.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author, Xiaoning Li, upon reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Changsha Aier Eye Hospital. Written informed consent was obtained from all participants and their legal guardians prior to enrollment.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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