Original Article

Analysis of Macular and Retinal Nerve Fiber Layer Thickness in Children with Refractory Amblyopia after Femtosecond Laser-assisted Laser *In situ* Keratomileusis: A Retrospective Study

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Abstract

Background: Localized macular edema and retinal nerve fiber layer (RNFL) thinning have been reported shortly after laser *in situ* keratomileusis (LASIK) in adults. However, it is still unclear how LASIK affects the retina of children. This study aimed to investigate the macular retina and RNFL thickness in children with refractive amblyopia who underwent femtosecond laser-assisted LASIK (FS-LASIK).

Methods: In this study, we included 56 eyes of 32 patients with refractive amblyopia who underwent FS-LASIK in our hospital from January 2012 to December 2016. Foveal (foveal center retinal, parafoveal retinal, and perifoveal), macular inner retinal (superior and inferior), and peripapillary RNFL thicknesses (superior, inferior, temporal, and nasal) were measured using Fourier-domain optical coherence tomography before surgery and 1 day, 3 days, and 1 week after surgery. We divided these patients into three groups based on their refractive error: High myopic group with 22 eyes (equivalent sphere, >6.00 D), mild myopic group with 19 eyes (equivalent sphere, 0–6.00 D), and hyperopic group with 15 eyes (equivalent sphere, >+0.50 D). We compared the macular retina and RNFL thickness before and after LASIK. A paired simple *t*-test was used for data analysis.

Results: One week after surgery, the visual acuity for all 56 eyes of the 32 patients reached their preoperative best-corrected vision. Visual acuity improved two lines or better for 31% of the patients. The residual refractive errors in 89% of the patients were within ±0.5 D. In the high myopic group, the foveal center retinal and parafoveal retinal thicknesses were thicker 1 day and 3 days after surgery than before surgery ($t = 2.689$, $P = 0.012$; $t = 2.383$, $P = 0.018$, respectively); no significant difference was found 1 week after surgery ($P > 0.05$). The foveal center retinal and parafoveal retinal thicknesses were greater 1 day after surgery than they were before surgery ($P = 0.000$ and $P = 0.005$, respectively) in the mild myopic and hyperopic groups. No significant difference was found 3 days or 1 week after surgery ($P > 0.05$). In all three groups, no significant difference was found in the macular inner retinal or peripapillary RNFL thickness 1 day, 3 days, or 1 week after surgery ($P > 0.05$).

Conclusions: The foveal center retinal edema after FS-LASIK is mild and reversible in children, that mostly occurred in the high myopic group with no effect on the visual acuity, and is always relieved within 1 week.

Key words: Child; Laser *In situ* Keratomileusis; Optical Coherence Tomography; Retinal

Introduction

Laser *in situ* keratomileusis (LASIK) has been widely used to treat refractive error in adults since 1990.[1-4] It is safe and effective for the treatment of amblyopia because of severe anisometropia in children.[5-9] Previous studies have shown mild, reversible, and localized macular edema and thinning of the retinal nerve fiber layer (RNFL) soon after LASIK in adults.[10-13] However, it is still unclear how LASIK affects the retina and optic nerve in children. To assess the safety of

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femtosecond laser LASIK (FS-LASIK) in children, we used Fourier-domain optical coherence tomography (FD-OCT) to evaluate the thickness of the fovea, macular inner retina, and peripapillary (RNFL) before surgery and 1 day, 3 days, and 1 week after surgery in 56 eyes of 32 patients.

Methods

Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the local ethics committee of Beijing Tongren Hospital. Informed written consent was obtained from all patients before their enrollment in this study.

Subjects

In this study, we included 56 eyes of 32 patients with refractive amblyopia in our refractive surgical center. From 2012 to 2016, 56 eyes of 32 patients aged 6–12 years (9.68 ± 2.56) were included in this study, with 18 males (30 eyes) and 14 females (26 eyes). Criteria for recruiting patients included: Age between 6 and 12 years; best-corrected vision was stable between 20/30 and 25/30 for more than 1 year with no response to treatment[14] (including reduced visual acuity, no change in visual acuity, or visual acuity improved less than one line); stopped wearing soft contact lens for more than 2 weeks or rigid contact lens for more than 4 weeks; cooperative with OCT examination (RTVue OCT, Optovue Inc., Gremont, CA, USA); and able to obtain follow-up. We divided these patients into three groups based on their refractive error: high myopic group with 22 eyes (equivalent sphere more than 6.00 D), mild myopic group with 19 eyes (equivalent sphere between 0 and 6.00 D), and hyperopic group with 15 eyes (equivalent sphere more than +0.50 D). Consent forms were obtained from all patients' parents after the surgical procedure; benefits and limitations of the surgery and possible complications were explained.

Complete eye examinations were performed before surgery, including naked eye visual acuity, best-corrected vision, noncontact intraocular pressure (IOP), slit-lamp examination, binocular ophthalmoscope retinal examination, refractive error check before and after cycloplegia, curvature of the cornea, and corneal thickness measurement using an ultrasound and corneal tomography.

Optical coherence tomography examination

OCT examination was performed by the same experienced technician using RTVue FD-OCT. The thickness of the fovea, inner macular retina, and peripapillary RNFL were measured before surgery and 1 day, 3 days, and 1 week after surgery. Scanning patterns included:

a. Foveal retina thickness: An MM6 scanning program was used. Each scan was 6 mm, and the scanning interval was 15°. Three circles around the foveal center were generated by the OCT program: the inner circle within 1 mm was defined as the foveal center; the circular area between 1 and 3 mm was the parafoveal region; and the area between 3 and 6 mm was the perifoveal region. Parafoveal and perifoveal regions were divided into superior, inferior, temporal, and nasal, and the thickness of these nine regions was calculated [Figure 1].
b. Macular inner retinal thickness: The ganglion cell complex (GCC) scanning mode was used to measure the macular inner retinal thickness. A 7-mm line scan was performed, and the thickness of the superior region

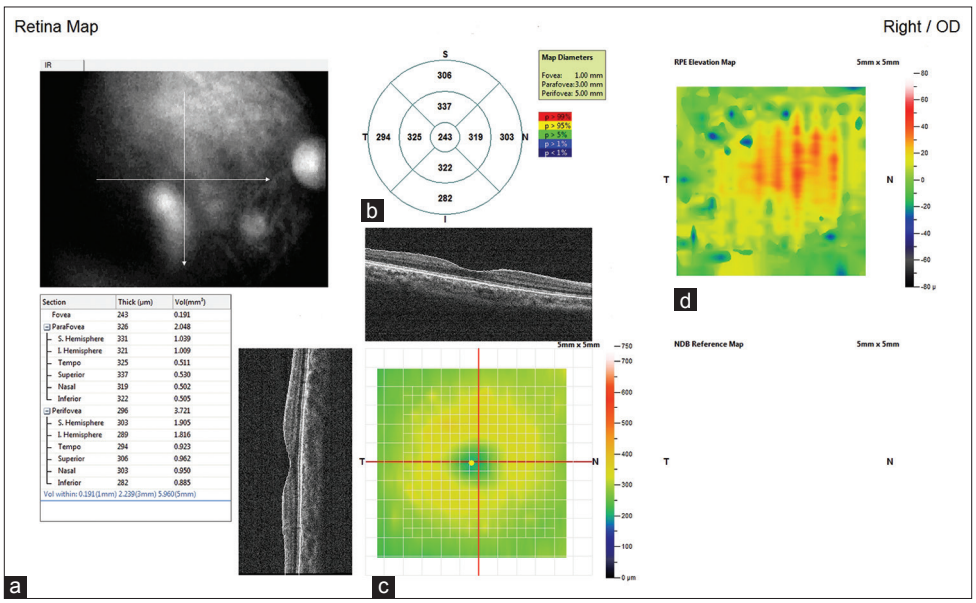

Figure 1: Optical coherence tomography scan of foveal center retinal thickness (MM6 program scan). (a) The thickness and volume at different sites of macula lutea. (b) The mean thickness of macula lutea at the sites of 1 mm, 3 mm, and 5 mm. (c) The thickness of macula lutea. (d) The height of retinal pigment epithelial layer.

(from 315° to 45°) and inferior region (135° to 225°) and mean of the superior and inferior regions were calculated, as shown in Figure 2.

c. Peripapillary RNFL thickness: 12-line scans centered at the optic disk were performed with a 30° scanning interval. The thickness of the RNFL layer around the optic disk within a 4.93 diameter was measured. The results were used to generate an RNFL thickness topography [Figure 3]. We divided the circle around the optic disk into four regions: superior (315°–45°), inferior (135°–225°), nasal, and temporal (225°–315° or 45°–135°) depending on if the right or left eye. The RNFL thickness for these four meridians and mean RNFL thickness were calculated and compared.

Surgery

All surgeries were performed by one experienced surgeon under topical anesthesia using Femto LDV

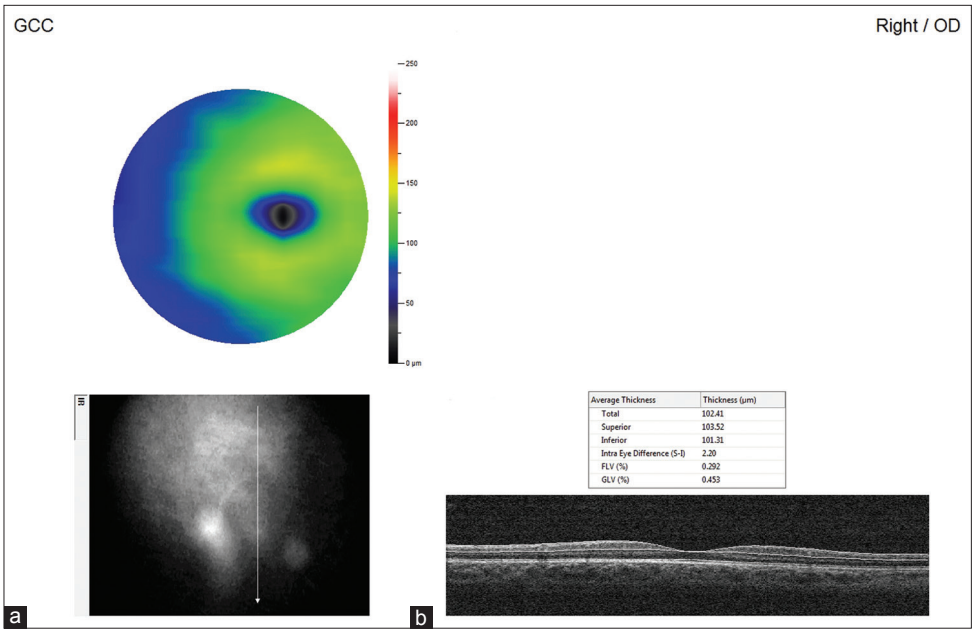

Figure 2: Optical coherence tomography scan of the macular inner retinal thickness (ganglion cell; ganglion cell complex thickness). (a) The thickness of retinal ganglion cell complex. (b) The thickness of retinal ganglion cell complex, and variances of local loss and overall loss.

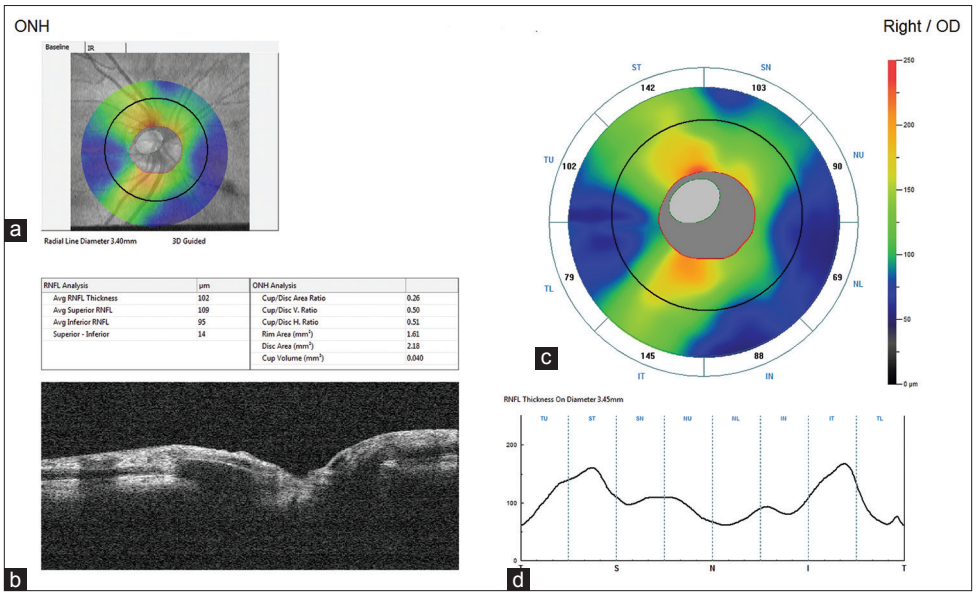

Figure 3: Optical coherence tomography scan measurements of the retinal nerve fiber layer thickness around the optic disk (optic nerve head) with a diameter of 4.39 mm, shown in 16 regions. (a) Thickness of retinal nerve fiber layer besides optic disk. (b) Thickness of retinal nerve fiber layer, cup-disc ratio, optic cup area, optic disk area, and horizontal to steep diameter ratio. (c) Optical coherence tomography section of optic disk. (d) Thickness of retinal nerve fiber layer in a patient.

(Ziemer Ophthalmic Systems AG, Port, Switzerland). A flap with a 110-micron thickness and diameter of 8.5–9.0 mm was generated with a hinge placed superiorly. The suction time was between 19 and 26 s. After the flap had been lifted, ablations were performed using a Visx S4 excimer laser (VISX Inc., Santa Clara, CA, USA). The corneal flap and stroma surface were irrigated with a balanced normal saline solution after ablation, and the flap was repositioned.

Statistical analysis

Data are expressed as mean ± standard deviation (SD) and were analyzed using SPSS 16.0 software (SPSS Inc., Chicago, IL, USA). A paired simple *t*-test was used to analyze the measured data conforming to a normal distribution. $P < 0.05$ was considered statistically significant.

Results

Comparison of visual acuity and refractive error before and after surgery

One week after surgery, the visual acuity of all 56 eyes of the 32 patients improved to their preoperative best-corrected vision (100%); 17 eyes (31%) experienced improved visual acuity of two lines or better; and 50 eyes (89%) had a residual refractive error within ±0.50 D [Table 1].

Comparison of macular retinal thickness before and after surgery

The average foveal and parafoveal retinal thicknesses for all 56 eyes of the 32 patients were significantly thicker than those before surgery ($P = 0.003$ and $P = 0.004$, respectively) 1 day after surgery, but not 3 days or 1 week after surgery ($P > 0.05$). Further, 1 day, 3 days, and 1 week after surgery, no significant difference was found in the average perifoveal retinal thickness ($P > 0.05$).

In the high myopic group, the average foveal and parafoveal thicknesses were significantly thicker 1 day ($t = 2.689$, $P = 0.012$) and 3 days ($t = 2.383$, $P = 0.038$) after surgery, but not 1 week after surgery. No significant difference was found in the perifoveal retinal thickness (all $P > 0.05$) 1 day, 3 days, or 1 week after surgery. In the mild myopic and hyperopic groups, we found the foveal retinal and parafoveal thicknesses were significantly greater 1 day after surgery ($t = 4.301$, $P = 0.000$; $t = 2.736$; $P = 0.005$, respectively), but not 3 days or 1 week after surgery ($P > 0.05$). No significant difference was found in the perifoveal thickness 1 day, 3 days, or 1 week after surgery (all $P > 0.05$) [Table 2].

Table 1: VA and refractive error before and after LASIK surgery

VA and refractive error	Before surgery	1 week after surgery	*t*	*P*
VA	0.04 ± 0.03	0.69 ± 0.33	−2.261	0.040
Best-corrected VA	0.63 ± 0.21	0.73 ± 0.33	−0.617	0.540
Equivalent sphere (D)	−3.56 ± 4.34	0.33 ± 0.47	−4.942	0.000

Data were shown as mean ± SD. LASIK: Laser *in situ* keratomileusis; VA: Visual acuity; SD: Standard deviation.

Comparison of macular inner retinal thickness (ganglion cell complex) before and after surgery

In the high myopic, mild myopic, and hyperopic groups, no significant difference was found in the macular inner retinal thickness ($P > 0.05$), including average GCC thickness and superior and inferior GCC thicknesses [Table 3].

Comparison of peripapillary retinal nerve fiber layer thickness before and after laser *in situ* keratomileusis surgery

In the high myopic, mild myopic, and hyperopic groups, no significant difference in the peripapillary RNFL thickness was found ($P > 0.05$), including the average RNFL thickness; and superior, temporal, inferior, and nasal RNFL thicknesses [Table 4].

Discussion

Currently, LASIK is the most popular surgery to treat refractive error.[1-4] It is safe and effective to use LASIK to treat refractive amblyopia.[5-9] However, the perioperative suction can cause elevation of the IOP to a level greater than 65 mmHg. Recently, the application of FS-LASIK can create a more precise, uniform corneal flap.[15-17] The elevation of the IOP (about 30 mmHg) is less than that demonstrated with the use of microkeratome; however, the amount of time the suction is applied is longer than that of microkeratome (25 s vs. 10 s, respectively). The IOP can drop to normal or 5 mmHg less than normal immediately after the suction is stopped. This massive change in IOP might cause damage to the optic nerve and RNFL.

From the OCT images, the retinal thickness usually increases with diffuse decreased reflectivity in patients with macular edema.[10] OCT can provide repeatable measurements of the retinal and RNFL thickness.[18] In patients with macular edema because of retinal blood vessel disease, we can usually find localized retinal thickening with a normal retinal pigment epithelium layer and choroidal capillary layer.[19] Some researchers have found that the foveal edema and RNFL decreased after LASIK in adults. The foveal edema and RNFL thickness changes were mild and reversible. Patients usually recover within 1 month without long-lasting pathological damage.[10,12,13,20] However, how LASIK affects the retina and RNFL in children is still unclear.

Lin *et al*.[6] used LASIK to treat children with refractive amblyopia, and they evaluated the visual acuity, refractive error, and binocular vision after surgery. They reported that LASIK was a safe and effective treatment with predictable results, but they did not study the foveal or RNFL layer.[6] In our study, OCT images indicated an increase in foveal retina thickness and a decrease in diffuse reflectivity without any signs of foveal retinal detachment. One day after surgery, we noticed thickening of the foveal and parafoveal retina in all 56 eyes, but not the perifoveal retina. Further, 3 days

Table 2: Foveal retinal thickness presurgery and 1 day, 3 days, and 1 week after LASIK surgery (μm)

Groups	Before surgery	1 day after surgery	3 days after surgery	1 week after surgery
High myopic group				
Foveal center	229.87 ± 25.34	233.94 ± 25.57*	235.53 ± 27.69*	229.54 ± 23.58
Parafovea	294.42 ± 16.35	299.79 ± 15.57*	299.34 ± 15.78*	293.91 ± 13.48
Perifovea	263.39 ± 12.97	263.03 ± 12.56	263.51 ± 15.32	264.03 ± 12.09
Mild myopic group				
Foveal center	230.54 ± 22.67	236.36 ± 22.41*	231.11 ± 18.61	230.21 ± 21.36
Parafovea	302.75 ± 14.95	308.25 ± 15.02*	304.55 ± 13.73	303.27 ± 14.43
Perifovea	280.56 ± 10.86	281.14 ± 10.57	281.98 ± 13.62	279.79 ± 11.86
Hyperopic group				
Foveal center	228.37 ± 21.56	232.94 ± 22.53*	230.04 ± 23.76	228.08 ± 18.26
Parafovea	311.69 ± 12.97	316.43 ± 13.92*	312.61 ± 15.17	311.39 ± 10.67
Perifovea	297.75 ± 11.05	298.32 ± 12.05	298.83 ± 13.17	297.96 ± 10.29

Data were shown as mean ± SD. Compared with preoperative thickness, *P<0.05. Foveal center: Foveal center thickness; Parafovea: Parafoveal retinal thickness; Perifovea: Perifoveal retinal thickness; SD: Standard deviation; LASIK: Laser *in situ* keratomileusis.

Table 3: Comparison of the macular inner retinal thickness at different time (μm)

Groups	Before surgery	1 day after surgery	3 days after surgery	1 week after surgery
High myopia group				
Mean	102.56 ± 7.13	102.58 ± 8.52	103.23 ± 7.38	102.77 ± 6.55
Superior	103.52 ± 7.09	104.21 ± 8.96	104.19 ± 7.27	104.09 ± 7.16
Inferior	101.31 ± 7.46	101.38 ± 10.08	101.44 ± 8.54	101.49 ± 7.90
Mild myopia group				
Mean	102.29 ± 6.35	103.09 ± 8.22	102.67 ± 6.76	103.19 ± 6.82
Superior	102.67 ± 6.71	103.34 ± 8.28	102.32 ± 6.89	102.57 ± 6.74
Inferior	102.06 ± 6.06	102.10 ± 8.68	102.19 ± 7.15	102.23 ± 6.51
Hyperopic group				
Mean	101.97 ± 6.63	102.91 ± 9.23	102.06 ± 7.71	102.13 ± 7.08
Superior	102.14 ± 6.84	102.81 ± 8.41	102.45 ± 7.25	102.03 ± 6.87
Inferior	101.02 ± 6.27	101.82 ± 8.15	101.42 ± 6.68	101.92 ± 6.69

Data were shown as mean ± SD. Mean: GCC thickness; Superior: Superior GCC thickness; Inferior: Inferior GCC thickness.SD: Standard deviation; GCC: Ganglion cell complex.

Table 4: Comparison of the peripapillary RNFL thickness (μm)

Groups	Before surgery	1 day after surgery	3 days after surgery	1 week after surgery
High myopic group				
Mean	102.54 ± 11.43	102.46 ± 11.04	103.95 ± 11.67	102.81 ± 11.02
Temporal	112.01 ± 15.26	110.90 ± 14.36	111.61 ± 16.04	111.93 ± 14.38
Superior	101.76 ± 17.02	101.08 ± 18.71	101.09 ± 18.42	101.71 ± 18.45
Nasal	86.55 ± 14.37	86.95 ± 14.57	86.95 ± 14.73	86.81 ± 13.65
Inferior	109.83 ± 14.53	109.13 ± 15.57	120.23 ± 15.77	109.87 ± 16.23
Mild myopic group				
Mean	103.09 ± 11.03	102.21 ± 10.64	103.18 ± 11.28	103.13 ± 10.62
Temporal	99.11 ± 14.06	98.44 ± 15.11	100.04 ± 15.29	99.13 ± 15.76
Superior	109.01 ± 16.97	108.92 ± 16.97	108.33 ± 18.62	87.76 ± 15.85
Nasal	87.50 ± 16.57	87.02 ± 16.76	87.89 ± 16.93	87.76 ± 15.85
Inferior	116.75 ± 14.94	116.46 ± 15.73	116.76 ± 14.04	116.68 ± 14.05
Hyperopic group				
Mean	103.85 ± 10.95	103.53 ± 9.51	104.51 ± 10.11	104.32 ± 9.47
Temporal	101.21 ± 14.82	100.93 ± 13.93	101.11 ± 15.06	101.09 ± 13.94
Superior	109.71 ± 16.44	108.52 ± 16.44	109.02 ± 18.09	109.65 ± 17.87
Nasal	87.04 ± 13.97	87.48 ± 14.16	87.44 ± 14.34	87.66 ± 13.25
Inferior	117.46 ± 14.20	116.79 ± 15.24	118.37 ± 15.45	118.41 ± 15.89

Data were shown as mean ± SD. Mean: Mean RNFL thickness of the whole circle; Temporal: Temporal RNFL thickness; Superior: Superior RNFL thickness; Nasal: Nasal RNFL thickness; Inferior: Inferior RNFL thickness. RNFL: Retinal nerve fiber layer; SD: Standard deviation.

and 1 week after surgery, we did not find a significant difference in the foveal center, parafoveal, or perifoveal retinal thickness, as compared with the preoperative retinal thickness. This suggests that after LASIK, retinal edema occurs mainly at the foveal center and parafoveal retina, with little effect on the perifoveal retina. Retinal edema is reversible, and patients usually recover within 1 week after surgery. Possible reasons for retinal edema are as follows: (1) suction has an effect on the microcirculation of the retina. It has been reported that blood flow velocity around the optic disk decreases by 7.4–8.4% with every 10-mmHg elevation in IOP.[21] The sudden change in IOP might cause ischemic reperfusion injury of the retina. (2) Suction might have a mechanical traction effect on the retina. The sudden change in IOP might cause disruption of the vitreous and have a mechanical traction effect on the vitreous, causing posterior detachment of the vitreous; this traction might sometimes even cause retinal tears or a retinal detachment.[22] (3) Light damage to the cone photoreceptors during surgery might cause foveal center retinal edema. (4) The fovea is the most sensitive area perhaps susceptible to damage because of its anatomical structure and blood supply.

In our study, in the high myopic group, we found that the retinal thickness at the foveal center and parafovea was significantly thicker 1 day and 3 days after surgery than before surgery. In the mild myopic group and hyperopic group, the foveal center retinal and parafoveal retinal thicknesses were greater 1 day after surgery than they were before surgery, and relieved in three days to one week. These results suggest that the post-LASIK foveal edema occurred mainly in the high myopic group. Two possible reasons for this difference are: (1) the blood viscosity was higher in the high myopic group, causing blood flow changes. Age-related microvascular changes have been found in children with high myopia: the retinal arteries and the muscular layer of small arteries becoming significantly thinner, the mid- and small-sized arteries being locally damaged in the choroidal layer.[23] (2) In the high myopic group, the longer duration of laser ablation might cause more damage to the retina.[24] In the high myopic group in our study, most patients have a myopia of more than 8.00 D; the duration of laser ablation was much longer in the mild myopic group and hyperopic group.

Changes in the thickness of the peripapillary RNFL after LASIK in adults is still controversial. Some researchers have reported no changes in the peripapillary RNFL thickness.[25,26] and other researchers reported that the peripapillary RNFL thickness is thinner soon after LASIK.[22,27] However, a few, rare studies reported changes in the peripapillary RNFL thickness in children. It has been proven that the retina is well developed at birth, except for the macula, and at the age of 4 years, the macular development is close to that of an adult.[28] In our study, we did not find a significant difference in the RNFL thickness at different retinal meridians 1 day, 3 days, and 1 week after LASIK. Guan *et al*. and Iester *et al*. reported that during LASIK, the temporarily high IOP (100 mm Hg, lasting 45 s) would not cause ischemic damage, nerve fiber loss, or decreased retinal RNFL thickness.[29,30] In our study, the duration of vacuum suction was less than 45 s, and the shorter duration might be the reason why the RNFL thickening stabilized after surgery.

In summary, the postoperative foveal edema was ameliorated within a week. The visual acuity of all patients reached their best-corrected vision, suggesting that the temporary foveal edema causes no visual damage. Our results suggest that LASIK is safe in children with amblyopia. To evaluate FS-LASIK more accurately and thoroughly in the retina of children with refractive amblyopia; our future investigation will be a multicenter study with a larger sample size.

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Conflicts of interest

There are no conflicts of interest.

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