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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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
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 (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., Fremont, 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.](image-url)
(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
**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 greater 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 retinal 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 (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).

**Comparison of visual acuity and refractive error before and after LASIK**

| 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.

**DISCUSSION**

Currently, LASIK is the most popular surgery to treat refractive error. It is safe and effective to use LASIK to treat refractive amblyopia. However, the peroperative 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. 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. OCT can provide repeatable measurements of the retinal and RNFL thickness. 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. 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. However, how LASIK affects the retina and RNFL in children is still unclear.

Lin et al. 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. 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...
| 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.

| 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.

| 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 central 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 Lester 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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