

# Comparison of choroidal thickness in high myopic eyes after FS-LASIK versus implantable collamer lens implantation with swept-source optical coherence tomography

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## Abstract

• **AIM:** To investigate the changes in choroidal thickness (CT) in high myopic eyes after femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) surgery or central hole implantable collamer lens (ICL V4c) implantation using swept-source optical coherence tomography (SS-OCT).

• **METHODS:** We examined the right eyes of 116 patients with high myopia who were candidates for FS-LASIK surgery and ICL implantation. Sixty eyes underwent ICL V4c implantation and 56 eyes were subjected to FS-LASIK surgery. The CT was measured with SS-OCT. All data were recorded preoperatively and 2h, 1wk, 1 and 3mo postoperatively. Other demographic information was collected, including age, sex, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), spherical equivalent (SE), intraocular pressure (IOP) and axial length (AL).

• **RESULTS:** The UCVA improved in both groups and showed no significant differences between groups. There also were no significant differences between the two groups in postoperative BCVA and SE ( $P=0.581$  and  $0.203$ , respectively). The foveal CTs, inner nasal and outer nasal CTs were significantly thicker at 2h postoperatively in both groups ( $P<0.05$ ) but returned to baseline levels in 1wk; after 1mo, no significant differences were found relative to the preoperative values. At 3mo in each group, nine

regions showed variations in the CT as compared with preoperative thickening, but only the foveal and nasal area CTs preoperative differences were statistically significant ( $P<0.05$ ). In addition, there was no significant difference in 9 regions of CT between the two groups at all follow-up times ( $P>0.05$ ).

• **CONCLUSION:** The CTs after ICL implantation and FS-LASIK surgery are significantly thicker than those before operation, especially in the foveal and nasal areas, but there is no significant difference between the two methods.

• **KEYWORDS:** choroidal thickness; high myopia; laser *in situ* keratomileusis; implantable collamer lens implantation; swept-source optical coherence tomography

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## INTRODUCTION

Currently, corneal refractive surgery and intraocular lens implantation are the main surgical methods to correct refractive errors. Femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) is one of the most commonly used corneal refractive surgeries for correction of myopia, hyperopia and astigmatism<sup>[1-2]</sup>. However, when patients with thin corneal thickness or corneal ectasia have limited ablation in laser refractive surgeries, implantable collamer lens (ICL) implantation, a precise, reproducible, reversible technique for correcting high myopia, is another option<sup>[3-5]</sup>. Regardless of the type of operation, possible complications must be considered, including increased intraocular pressure (IOP) and inflammation<sup>[6-7]</sup>, which may influence the chorioretinal regions.

In previous studies, the safety, efficacy and predictability of these refractive surgeries have been assessed on the basis of changes in visual function<sup>[6-7]</sup> and ocular anterior segment

structure<sup>[8-9]</sup>. However, the changes in the ocular posterior segment, particularly the choroid, have not been evaluated after refractive surgery, especially to determine the influence of different operations. The focus of myopia-related research has gradually shifted from the dioptric media of the anterior segment to the tissues of the posterior segment, such as the choroid.

The choroid is located between the retina and sclera, and it plays a critical role of providing nutrients and oxygen to the retina<sup>[10]</sup>. With the lengthening of the ocular axis in patients with high myopia, the choroid expands or thins, and eventually causes myopia-related retinopathy<sup>[11-13]</sup>. As shown in previous studies, the choroid plays an important role in the growth of the ocular axis in animal models<sup>[14]</sup>. During the process of myopic recovery in chicks, the choroid compensates by becoming thicker<sup>[15]</sup>.

During the FS-LASIK procedure, with the creation of a corneal flap, a suction ring is applied to fixate the globe, thus increasing the IOP to  $\geq 60$  mm Hg<sup>[16]</sup>. This sudden spike in IOP (which can damage the eye) is often observed during LASIK<sup>[17-18]</sup>. The same increase in IOP has been observed during or after ICL implantation<sup>[19]</sup>. Previous studies have explored the effects of refractive surgery on the retina<sup>[17]</sup>. Because the retina and the choroid are closely associated, we sought to examine whether the choroidal thickness (CT) might also be affected.

The aim of this study was to evaluate the potential changes in the CT after FS-LASIK and ICL implantation, by using the swept-source optical coherence tomography scan technique (SS-OCT), and to determine whether the variations in CT might correlate with the different types of refractive surgeries. The recently developed SS-OCT was used to obtain 256 raster scan images covering the entire macula to generate a CT map in a single session, and each choroidal layer was detected automatically. In addition, the "follow-up" function ensured that the same choroidal areas were scanned after surgery.

### SUBJECTS AND METHODS

**Ethical Approval** The study was approved by the Ethics Committee of the Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, and all procedures adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from all subjects after the nature and possible consequences of the study were explained.

**Subjects** This cross-sectional observational pilot study included the right eyes from 116 patients with myopia (57 females and 59 males) recruited from October 2017 to September 2018 at the Department of Ophthalmology, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

The mean age of the patients was  $29.4 \pm 8.27$  (21-45)y. The patients were divided into two groups receiving different

operations: 56 patients underwent FS-LASIK and 60 patients underwent ICL V4c implantation, depending on the patients' corneal conditions and willingness to incur the different costs. All patients underwent preoperative comprehensive ophthalmic examinations at the Refractive Surgery Center and met the surgical requirements. The inclusion criteria for ICL implantation included an anterior chamber depth of 2.80 mm or more, and an endothelial cell density  $>2000$  cells/mm<sup>2</sup>. Patients with pregnancy, keratoconus, cataracts, glaucoma and systemic disease were excluded.

**Surgical Procedures** All surgeries were performed by the same experienced surgeon (Zhang J). Antibiotic medications (levofloxacin, Santen, Japan) and a non-steroidal anti-inflammatory drug (pranoprofen, Senju, Japan) were administered four times daily for 3d. Routine eye examinations were performed 2h, 1d, 1wk, 1 and 3mo postoperatively.

**Implantable Collamer Lens implantation** The ICL model used in this study was ICL V4c with a 0.36-mm central artificial hole (Hole ICL™, STAAR Surgical, Switzerland). Mydriasis agents (Tropicamide Eye Drops, Santen) were instilled four times at 10-min intervals before surgery. After topical anesthesia, a model ICL V4c was inserted through a 3-mm temporal transparent cornea incision after placement of a viscosurgical device (Opegan; Santen, Japan) into the anterior chamber. The ICL V4c was placed in the posterior chamber and adjusted to the center position, the viscosurgical device was completely washed out of the anterior chamber with balanced salt solution.

**FS-LASIK** A femtosecond laser (Wavelight FS200; Alcon Laboratories Inc., Fort Worth, TX, USA) was used to create a superiorly hinged corneal flap of depth 100-110  $\mu$ m depending on the preoperative corneal thickness. The femtosecond laser had a bed energy of 0.65  $\mu$ J, with a side-cut energy of 0.8  $\mu$ J and a repetition frequency of 200 kHz. After creation of the flap, stromal ablation was performed using the WaveLight Allegretto Wave Eye-Q excimer laser (WaveLight Laser Technologie AG, Erlangen, Germany) in the conventional manner.

**Swept-source Optical Coherence Tomography** In this study, all enrolled eyes were examined with SS-OCT (DRI-1; Topcon) using a longer wavelength of approximately 1050 nm as the light source with a 1000-Hz repetition rate. This new technique enables the cross-sectional structure and thickness of the choroid to be evaluated. It can cover a  $6 \times 6$  mm<sup>2</sup> macular area centered on the fovea, was selected. This protocol can acquire a 3D imaging set consisting of 512 A-scans and 256 B-scans.

We classified captured OCT images into four categories. The CT was measured between the retinal pigment epithelium-Bruch's membrane complex and choroid-scleral junction. An ETDRS-style topographic map of CT was generated

**Table 1 Demographic and clinical information**

Variable	FS-LASIK group	ICL group	mean±SD <i>P</i>
No. of patients	56	60	0.291
Female/male	30/26	27/33	0.356
Age, y	27.62±7.42	28.14±6.37	0.686
Preoperative logMAR UCVA	1.37±0.34	1.41±0.39	0.558
Preoperative logMAR BCVA	0.03±0.10	0.04±0.09	0.572
Preoperative SE, D	-8.74±2.35	-9.86±3.17	0.032
Preoperative AL, mm	28.19± 0.85	28.46±1.04	0.130
Preoperative IOP, mm Hg	13.49±2.56	14.73±2.82	0.015
Endothelial cell count/mm <sup>2</sup>	2672.45±93.12	2657.94±85.73	0.384
Postoperative logMAR UCVA	0.06±0.11	0.05±0.08	0.579
Postoperative logMAR BCVA	0.03±0.07	0.03±0.06	1.000
Postoperative SE, D	-0.36±0.22	-0.27±0.20	0.223
Postoperative IOP, mmHg	13.17±2.68	15.12±2.91	0.316

UCVA: Uncorrected visual acuity; BCVA: Best corrected visual acuity; SE: Spherical equivalent; AL: Axial length; IOP: Intraocular pressure. Statistically significant difference using *t*-test.

automatically by built-in segmentation software. After surgery, OCT images were obtained using the “follow-up” function to ensure the same choroidal areas were being scanned. The program divides the area into three concentric rings as follows: an inner 1.0 mm ring, an intermediate 3.0 mm ring, and an outer 6.0 mm ring. The parafoveally 3.0 mm or 6.0 mm ring was also subdivided into four quadrants; each data in all sections represented the mean of the relative area. Mydriasis agents were instilled four times at 10-min intervals prior to measure. All measurements were performed between 9:00 and 10:00 a.m. to avoid the potential influence of diurnal variations of CT. Scans were repeated until a good-quality image was obtained, which was defined as those with a signal strength  $\geq 40$  (maximum=100), and without motion artefact, overt misalignment or decentration. To obtain accurate data, two good-quality images were measured and the data were averaged for analysis. All examinations were conducted by the same experienced doctor (He FL).

**Statistical Analysis** All statistical analyses were performed with the software package GraphPad Prism (version 7.00 for Windows). All data are expressed as means±SD. Analysis of variance *t*-test and Pearson’s  $\chi^2$  test were used to compare the demographic and clinical characteristics in different groups. Changes in CT before and after the two types of refractive surgeries were analyzed with repeated-measures ANOVA. Bonferroni post-hoc analysis, and independent sample *t*-tests (two groups) were used to analyze the significant differences between the two groups. A *P* value<0.05 was considered statistically significant.

## RESULTS

All participants completed the follow-up visits. At baseline,

no significant differences were found in terms of sex, age, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), spherical equivalent (SE), axial length (AL) and IOP ( $P>0.05$ ) between the FS-LASIK and ICL groups. Table 1 summarizes the demographic and clinical characteristics of the participants. The postoperative UCVA improved in both groups without significant differences ( $P=0.637$ ). There were no significant difference between the two groups in BCVA, SE and IOP postoperatively ( $P=0.581$ , 0.203 and 0.192, respectively).

Because the outcomes of the CT in the right and left eyes were highly correlated, we report only data on the right eyes. The nine sections of the CT at the fovea and inner and outer nasal, temporal, superior and inferior area were measured before surgery and 2h, 1wk, and 1 and 3mo after surgery, as shown in Tables 2 and 3 and Figures 1 and 2.

Repeated-measures ANOVA revealed that, compared with the baseline, the choroid became thicker 2h postoperatively, but this was a temporary phenomenon; the CT returned to the preoperative level by 1wk postoperatively. Between the preoperative and 1-month postoperative periods, the mean CTs in the nine regions were slightly thicker than the corresponding preoperative values, but no significant difference was observed between the two groups (Table 4). Similarly, the mean CTs were also no statistical difference between the two groups in the 3mo after surgery (Table 4). Figure 3 shows the changes of the foveal CTs in comparisons between the two groups at different time points. Figures 4 and 5 show the changes of the inner nasal and outer nasal CTs in comparisons between the two groups at different time points, respectively.

**Table 2 Detailed data and statistical analysis of mean regional choroidal thicknesses for the 9 sectors in FS-LASIK group**

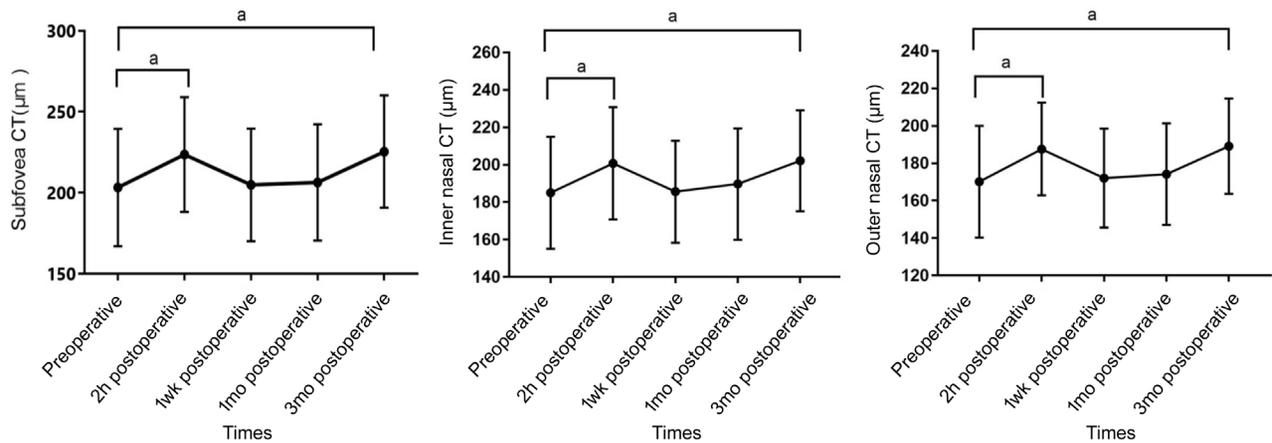
Parameters	Pre-operation	Post-operation						mean±SD, μm					
		Variations											
		2h	1wk	1mo	3mo	2h	1wk		1mo	3mo			
Fovea	209.12±31.15	226.31±32.71	213.82±30.27	214.43±33.43	228.32±28.21	17.19±4.36	4.71±3.17	5.31±4.24	19.22±5.46	0.034 <sup>a</sup>	0.596	0.478	0.027 <sup>a</sup>
TIM	211.78±34.21	218.12±36.12	212.43±33.78	216.38±32.28	217.26±28.21	6.74±4.36	1.30±3.16	4.61±2.08	5.48±3.22	0.413	0.898	0.688	0.450
SIM	206.37±31.71	213.39±34.14	207.49±33.03	210.22±37.01	215.24±29.53	7.02±4.13	1.19±0.91	3.85±2.13	8.87±3.34	0.350	0.774	0.691	0.147
NIM	185.44±27.30	201.69±24.31	185.65±30.09	189.51±26.15	202.44±27.32	16.25±4.64	0.21±1.21	4.07±2.17	17.00±7.02	0.042 <sup>a</sup>	0.997	0.375	0.013 <sup>a</sup>
IIM	204.30±32.32	209.29±34.12	206.32±34.25	206.44±32.58	213.25±35.40	4.99±2.39	2.32±4.20	2.14±2.39	8.95±4.56	0.406	0.706	0.897	0.104
IOM	220.48±35.01	227.05±41.13	219.18±34.62	226.64±31.22	224.29±25.73	6.53±3.41	-1.3±2.25	6.16±2.96	3.81±1.67	0.206	0.915	0.776	0.106
SOM	216.64±35.32	227.14±31.27	220.49±28.52	220.32±36.39	228.24±36.53	10.5±5.36	3.85±4.12	3.68±2.05	11.60±5.03	0.116	0.642	0.555	0.376
NOM	170.07±32.04	187.36±33.61	172.05±29.83	174.32±24.75	189.72±31.09	17.29±8.64	2.02±3.09	4.25±2.35	19.65±4.21	0.017 <sup>a</sup>	0.928	0.582	0.006 <sup>a</sup>
IOM	207.12±33.83	214.32±34.65	207.45±34.50	209.74±33.22	218.36±40.15	7.20±4.83	0.33±2.47	2.62±4.92	11.24±5.83	0.106	0.982	0.486	0.086

TIM: Temporal inner macula; SIM: Superior inner macula; NIM: Nasal inner macula; IIM: Inferior inner macula; TOM: Temporal outer macula; SOM: Superior outer macula; NOM: Nasal outer macula; IOM: Inferior outer macula. Statistically significant difference using the repeated-measures ANOVA, <sup>a</sup>P<0.05.

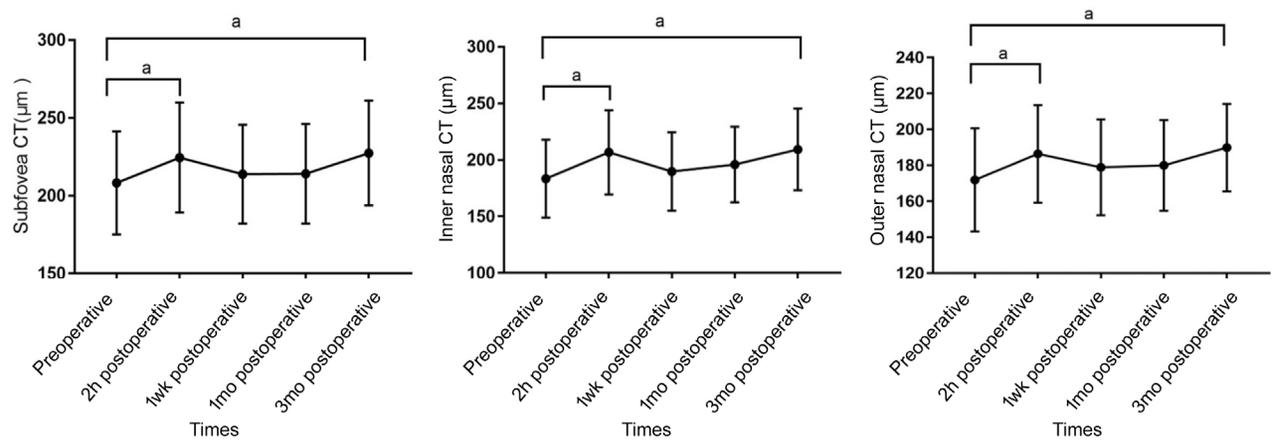
**Table 3 Detailed data and statistical analysis of mean regional choroidal thicknesses for the 9 sectors in ICL group**

Parameters	Pre-operation	Post-operation						mean±SD, μm					
		Variations											
		2h	1wk	1mo	3mo	2h	1wk		1mo	3mo			
Fovea	202.38±34.23	220.31±30.12	203.51±34.04	204.83±31.72	221.28±35.24	17.93±5.21	1.13±1.70	2.45±1.52	18.90±3.05	0.021 <sup>a</sup>	0.917	0.849	0.015 <sup>a</sup>
TIM	201.43±32.34	210.38±33.14	204.29±36.29	207.18±32.43	211.15±34.41	8.95±4.13	2.86±4.26	5.75±4.27	9.72±3.46	0.206	0.758	0.543	0.136
SIM	196.46±38.25	208.43±42.59	201.71±33.21	203.12±35.27	209.64±34.16	11.97±4.34	5.25±3.43	6.66±3.12	13.18±4.72	0.242	0.715	0.416	0.120
NIM	186.59±31.25	208.60±33.54	190.37±25.24	196.35±30.35	210.78±33.27	22.01±4.37	3.78±4.03	9.76±4.35	24.19±6.28	0.029 <sup>a</sup>	0.669	0.378	0.013 <sup>a</sup>
IIM	191.74±32.16	199.27±25.24	199.34±27.14	199.28±26.34	201.52±25.12	7.53±3.11	7.60±2.23	7.54±3.55	9.78±4.19	0.306	0.346	0.846	0.087
TOM	203.21±33.42	207.62±36.55	204.52±37.22	205.79±34.27	211.16±30.25	4.41±1.26	1.31±2.21	2.58±1.23	7.95±3.18	0.664	0.416	0.876	0.294
SOM	196.36±31.35	205.42±34.37	201.41±26.27	201.35±24.51	206.60±26.14	9.06±4.23	5.05±2.68	4.99±2.43	10.24±5.53	0.215	0.761	0.684	0.086
NOM	171.32±24.18	187.23±27.76	178.38±24.35	180.35±30.29	191.25±21.12	15.91±4.15	7.06±3.24	9.03±3.15	19.93±5.27	0.043 <sup>a</sup>	0.421	0.095	0.035 <sup>a</sup>
IOM	201.44±29.29	209.30±34.16	205.21±29.31	204.07±30.94	206.47±31.21	7.96±2.37	3.77±3.31	2.63±2.57	5.03±2.17	0.208	0.753	0.735	0.315

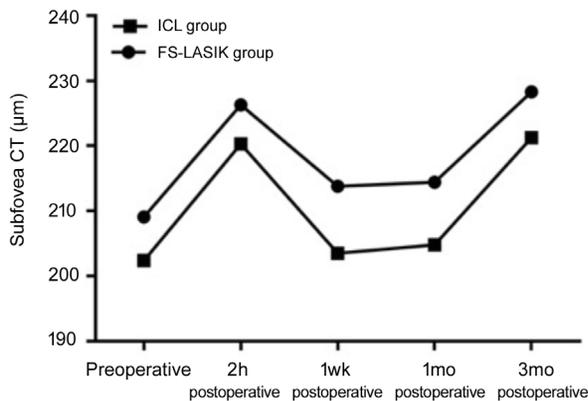
TIM: Temporal inner macula; SIM: Superior inner macula; NIM: Nasal inner macula; IIM: Inferior inner macula; TOM: Temporal outer macula; SOM: Superior outer macula; NOM: Nasal outer macula; IOM: Inferior outer macula. Statistically significant difference using the repeated-measures ANOVA, <sup>a</sup>P<0.05.



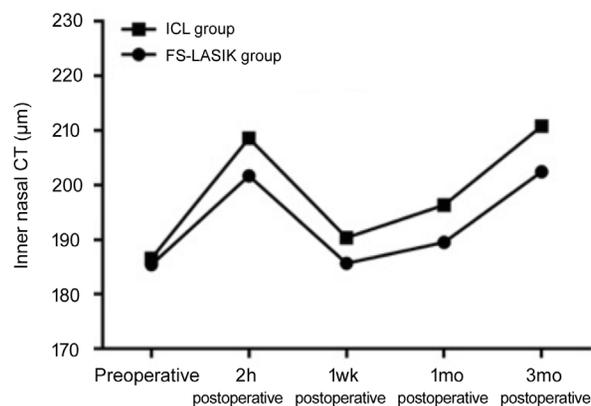
**Figure 1 Changes in CTs in the FS-LASIK group** Results are presented as medians and ranges (min to max) at different time points. <sup>a</sup> $P < 0.05$ .



**Figure 2 Changes in CTs in the ICL group** Results are presented as medians and ranges (min to max) at different time points. <sup>a</sup> $P < 0.05$ .



**Figure 3 Changes in Fovea CTs in comparisons between the two groups at different time points.**



**Figure 4 Changes in inner nasal CTs in comparisons between the two groups at different time points.**

**DISCUSSION**

With the wide application of refractive surgery worldwide, there is substantial concern about complications of the operation, especially regarding the posterior segment in high myopia. Some studies have explored the effects of refractive surgery on the retina<sup>[17-19]</sup>. However, no data exist regarding the possible effects of different refractive surgeries on the choroid. To determine the potential influence of refractive surgery on the choroid, we evaluated the morphological changes in the choroid status. Previous studies have indicated

that a decreased CT is critical to the onset and progression of choroidal diseases, such as polypoidal choroidal vasculopathy and central serous chorioretinopathy<sup>[13,20]</sup>. An obvious thinning in CT in myopia patients has been observed, and the CT is negatively correlated with AL, refractive power and age<sup>[11,21]</sup>. Our study aimed to evaluate CT changes in myopia patients who underwent different types of refractive surgeries. This research provides the first report of the changes in CT after FS-LASIK and ICL implantation in high myopic patients.

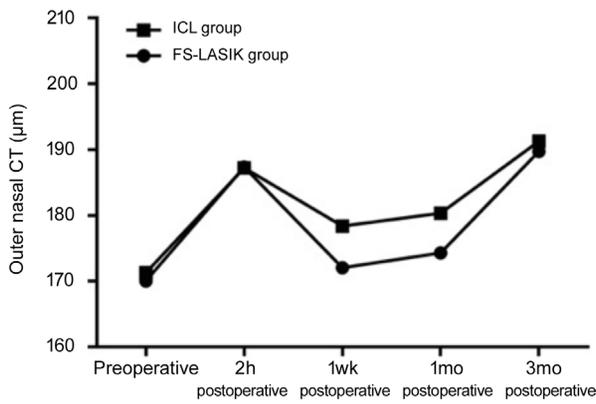


Figure 5 Changes in outer nasal CTs in comparisons between the two groups at different time points.

We found that the CT in the foveal and nasal areas, as observed in SS-OCT, significantly increased 2h after surgery in both groups, especially in the fovea. We postulated that there might be two major reasons for these results. The first reason is that the transient increase in IOP during refractive operation stimulates the choroid, which is a highly vascularized tissue<sup>[10]</sup>. In the ICL group, the IOP measured 2h after surgery was 3-5 mm Hg higher than that at baseline before operation. We speculated that the intraoperative anterior chamber irrigation and postoperatively retained viscoelasticity might contribute to the high IOP<sup>[22]</sup> after surgery. As the IOP increased, ocular perfusion pressure (OPP) decreased, and partial oxygen reduced and nitric oxide synthesis released increasingly via vascular endothelium. Thus, nitric oxide may influence choroidal thickening, possibly through changes in blood flow or relaxation of the non-vascular smooth muscle<sup>[23]</sup>, which may also play a role in choroidal blood flow auto-regulation<sup>[24]</sup>. Previous studies have confirmed the evidence in humans that the choroidal blood flow is autoregulated during changes in the OPP induced by artificial IOP increases<sup>[25-26]</sup>. Similarly, in the FS-LASIK group, intraoperative vacuum aspiration with a pneumatic suction ring might have caused slight local macular edema shortly after surgery, mainly in the foveal region, owing to mechanical stretching of the choroid. With the aim of avoiding damage to the corneal flaps, we did not measure IOP 2h after FS-LASIK surgery. The transient rise in IOP during suction might have slightly increased the CT 2h after surgery, but the CT returned to normal values by 1wk after surgery. Second, the increase in CT may also be due to the inflammatory response and vascular permeability after surgery. Surgical trauma induces release of prostaglandins in the aqueous humor, thus damaging the blood/aqueous barrier in ICL implantation and resulting in the accumulation of inflammatory mediators<sup>[27]</sup>. These mediators can spread to the vitreous cavity and reach the retina, causing the internal blood/retinal barrier to be broken, leading to the secretion of inflammatory

Table 4 Between-group comparison of preoperative and postoperative choroidal thickness variation for the 9 sectors

Subfield	Variation			
	2h	1wk	1mo	3mo
mean±SD, µm				
Fovea				
FS-LASIK	17.19±4.36	4.71±3.17	5.31±4.24	19.22±5.46
ICL	17.93±5.21	1.13±1.70	2.45±1.52	18.90±3.05
<i>P</i>	0.981	0.204	0.205	0.517
TIM				
FS-LASIK	6.74±4.36	1.30±3.16	4.61±2.08	5.48±3.22
ICL	8.95±4.13	2.86±4.26	5.75±4.27	9.72±3.46
<i>P</i>	0.642	0.778	0.646	0.235
TOM				
FS-LASIK	6.53±3.41	-1.3±2.25	6.16±2.96	3.81±1.67
ICL	4.41±1.26	1.31±2.21	2.58±1.23	7.95±3.18
<i>P</i>	0.565	0.211	0.224	0.061
NIM				
FS-LASIK	16.25±4.64	0.21±1.21	4.07±2.17	17.00±7.02
ICL	22.01±4.37	3.78±4.03	9.76±4.35	24.19±6.28
<i>P</i>	0.154	0.558	0.098	0.236
NOM				
FS-LASIK	17.29±8.64	2.02±3.09	4.25±2.35	19.65±4.21
ICL	15.91±4.15	7.06±3.24	9.03±3.15	19.93±5.27
<i>P</i>	0.481	0.062	0.148	0.992
SIM				
FS-LASIK	7.02±4.13	1.19±0.91	3.85±2.13	8.87±3.34
ICL	11.97±4.34	5.25±3.43	6.66±3.12	13.18±4.72
<i>P</i>	0.154	0.806	0.712	0.112
SOM				
FS-LASIK	10.5±5.36	3.85±4.12	3.68±2.05	11.60±5.03
ICL	9.06±4.23	5.05±2.68	4.99±2.43	10.24±5.53
<i>P</i>	0.738	0.567	0.714	0.893
IIM				
FS-LASIK	4.99±2.39	2.32±4.20	2.14±2.39	8.95±4.56
ICL	7.53±3.11	7.60±2.23	7.54±3.55	9.78±4.19
<i>P</i>	0.343	0.133	0.157	0.832
IOM				
FS-LASIK	7.20±4.83	0.33±2.47	2.62±4.92	11.24±5.83
ICL	7.96±2.37	3.77±3.31	2.63±2.57	5.03±2.17
<i>P</i>	0.953	0.229	0.992	0.065

TIM: Temporal inner macula; TOM: Temporal outer macula; NIM: Nasal inner macula; NOM: Nasal outer macula; SIM: Superior inner macula; SOM: Superior outer macula; IIM: Inferior inner macula; IOM: Inferior outer macula. Statistically significant difference using the repeated-measures ANOVA.

mediators in another cascade, and increasing the permeability of perifoveal capillaries<sup>[28-29]</sup>, which may result in choroidal thickening. We observed no differences in CT between the two types of surgeries at 2h postoperatively.

Over time, the CT in the ICL group was still greater than that before the operation, whereas that in the FS-LASIK group was restored to the baseline at 1wk. These results indicate that the choroidal thickening caused by an increase in temporary IOP and an inflammatory response during the operation is transient and reversible. The foveal CTs in the ICL group changed from  $202.38 \pm 34.23 \mu\text{m}$  preoperatively to  $220.31 \pm 30.12 \mu\text{m}$  2h postoperatively to  $203.51 \pm 34.04 \mu\text{m}$  1wk postoperatively, and the results showed no significant differences.

After 1mo, the two groups' CT values compared with the preoperative values were not statistically significant, results in contrast to those from previous research. Previous studies have found that increases in CT were statistically significant 1mo after cataract surgeries<sup>[30-32]</sup>. Cataract surgeries in cataract patients were the focus of the previous instrument, whereas we examined patients with high myopia through different operation methods by using different OCT inspection equipment. In the past, most studies used SD-OCT (Zeiss-Humphrey, Jena, Germany) to evaluate the CT<sup>[21,30]</sup>. SD-OCT with enhanced depth imaging was used to measure the CT. However, the values of the CT must be measured manually, because there is no automated software commercially available to quantify CT through SD-OCT. In the present study, we used SS-OCT to detect the CT and generated the data automatically through built-in segmentation software. After surgery, OCT images were obtained with the "follow-up" function to ensure that the same choroidal areas were scanned. In addition to the scanning speed, SS-OCT has the advantages of detecting depth deepening<sup>[33]</sup>. The SS-OCT imaging system is superior to SD-OCT because it can detect other traditional clinical fundus undetectable on the basis of chronic pathological changes and identify the retinal vascular microaneurysms and the polypoidal choroidal vasculopathy<sup>[34-35]</sup>. Similarly, Li *et al*<sup>[36]</sup> have found that the CT increases 1mo postoperatively after LASIK or laser-assisted subepithelial keratomileusis (LASEK) surgery to correct myopia. They used the SD-OCT to evaluate the CT, in contrast to our research. Moreover, Li *et al*'s assessment focused on low and moderate degrees of myopia, whereas we focused on high myopia.

On the basis of the findings of our study, the CT tended to become thicker and peaked 3mo after surgery in both groups. Our results were consistent with those in Gudauskiene *et al*'s<sup>[37]</sup> reports. Although our study population and operation methods were different from that, our SS-OCT inspection instrument was the same. An insignificant subclinical increase in foveal CT was observed 1mo after the operations in the two groups. A significant increase in foveal CT was detected 3mo postoperatively and was correlated with surgery-induced IOP increment and the use of antibiotics and steroids after surgery. Interestingly, only the changes in the fovea and nasal CT were

statistically significant, thus suggesting that the minimum values measured around the central fovea were inadequate to evaluate the entire macula.

In addition to the above, the accommodation was also involved in the change in the CT. High myopia has a lag in accommodation, poor accommodation flexibility and a slow accommodation response<sup>[38-39]</sup>, thus resulting in a low accommodation reserve. Previous studies have speculated that in the absence of a clear retinal image, ocular accommodation may be induced<sup>[39]</sup>. We postulated that 3mo after the operation, the corrected refractive errors in retinal imaging quality can achieve the most clear and stable level, thereby decreasing the need for accommodation. Therefore, a loss of ciliary muscle tension and attached to the eyeball stretching and choroid thickening occur. Alternatively, to our knowledge, compared with spectacles, the visual field was widened and the retinal imaging was magnified after refractive surgery. According to the previous study, the increased artificial light stimulation can cause choroidal thickening in humans and chickens<sup>[40]</sup>, so we speculated that the choroidal thickening might be related to the increased visual stimulation, which was increased in the retina, postoperatively. Ultimately, with the improvement of visual acuity, the relative peripheral myopia defocus induced by FS-LASIK surgery might cause choroidal thickening, which was similar to the mechanism of orthokeratology in treating myopia<sup>[41-42]</sup>. Previous clinical and animal experiments demonstrated that choroidal thickening was induced by the peripheral myopia defocusing, and choroidal thinning was induced by the peripheral hyperopia defocusing<sup>[43-44]</sup>. However, whether choroidal thickening is related to the peripheral myopia defocusing after ICL implantation in high myopia needs further research.

As with most studies, our findings must be considered in light of our study limitations. First, our follow-up time was only 3mo after surgery, and further studies with a long follow-up period should be performed. Secondly, all patients were examined before and after operation under dilated pupil conditions, but only the FS-LASIK group 2h after operation was examined under small pupil conditions, thereby influencing the data. Finally, further studies are needed to confirm our observation, this research reported CT changes following ICL and FS-LASIK surgery and compared the variations between patients underwent different surgeries.

In summary, our study indicated that the CTs after ICL implantation and FS-LASIK surgery were significantly thicker than those before operation, especially in the foveal and nasal areas, but the increased CTs showed no significant difference between the two surgical procedures. Early postoperative choroidal thickening was associated with the inflammatory response and increased choroidal vascular permeability. With

the improvement of visual acuity, the decrease of the need for accommodation might be the important reason for choroidal thickening. Further large sample size and long-term studies are needed to observe the effect of two different surgical methods on choroid.

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**REFERENCES**

1 Sugar A, Rapuano CJ, Culbertson WW, Huang D, Varley GA, Agapitos PJ, de Luise VP, Koch DD. Laser *in situ* keratomileusis for myopia and astigmatism: safety and efficacy: a report by the American Academy of Ophthalmology. *Ophthalmology* 2002;109(1):175-187.

2 Varley GA, Huang D, Rapuano CJ, Schallhorn S, Boxer Wachler BS, Sugar A, Ophthalmic Technology Assessment Committee Refractive Surgery Panel, American Academy of Ophthalmology. LASIK for hyperopia, hyperopic astigmatism, and mixed astigmatism: a report by the American Academy of Ophthalmology. *Ophthalmology* 2004;111(8):1604-1617.

3 Sanders DR, Doney K, POCO M; ICL in Treatment of Myopia Study Group. United States Food and Drug Administration clinical trial of the Implantable Collamer Lens (ICL) for moderate to high myopia: three-year follow-up. *Ophthalmology* 2004;111(9):1683-1692.

4 Alfonso JF, Baamonde B, Fernández-Vega L, Fernandes P, González-Méijome JM, Montés-Micó R. Posterior chamber collagen copolymer phakic intraocular lenses to correct myopia: five-year follow-up. *J Cataract Refract Surg* 2011;37(5):873-880.

5 Moya T, Javaloy J, Montés-Micó R, Beltrán J, Muñoz G, Montalbán R. Implantable collamer lens for myopia: assessment 12 years after implantation. *J Refract Surg* 2015;31(8):548-556.

6 Igarashi A, Shimizu K, Kamiya K. Eight-year follow-up of posterior chamber phakic intraocular lens implantation for moderate to high myopia. *Am J Ophthalmol* 2014;157(3):532-539.

7 Sari ES, Pinero DP, Kubaloglu A, Evcili PS, Koytak A, Kutlutürk I, Ozerturk Y. Toric implantable collamer lens for moderate to high myopic astigmatism: 3-year follow-up. *Graefes Arch Clin Exp Ophthalmol* 2013;251(5):1413-1422.

8 Gyldenkerne A, Ivarsen A, Hjortdal JØ. Comparison of corneal shape changes and aberrations induced By FS-LASIK and SMILE for myopia. *J Refract Surg* 2015;31(4):223-229.

9 Gao SH, Li SQ, Liu LP, Wang Y, Ding H, Li LL, Zhong XW. Early changes in ocular surface and tear inflammatory mediators after small-incision lenticule extraction and femtosecond laser-assisted laser *in situ* keratomileusis. *PLoS One* 2014;9(9):e107370.

10 Nickla DL, Wallman J. The multifunctional choroid. *Prog Retin Eye Res* 2010;29(2):144-168.

11 Flores-Moreno I, Lugo F, Duker JS, Ruiz-Moreno JM. The relationship between axial length and choroidal thickness in eyes with high myopia.

*Am J Ophthalmol* 2013;155(2):314-319.

12 Gupta P, Cheung CY, Saw SM, Bhargava M, Tan CS, Tan M, Yang A, Tey F, Nah G, Zhao P, Wong TY, Cheng CY. Peripapillary choroidal thickness in young Asians with high myopia. *Invest Ophthalmol Vis Sci* 2015;56(3):1475-1481.

13 Grossniklaus HE, Green W. Choroidal neovascularization. *Am J Ophthalmol* 2004;137(3):496-503.

14 Lan WZ, Feldkaemper M, Schaeffel F. Bright light induces choroidal thickening in chickens. *Optom Vis Sci* 2013;90(11):1199-1206.

15 Fitzgerald ME, Wildsoet CF, Reiner A. Temporal relationship of choroidal blood flow and thickness changes during recovery from form deprivation myopia in chicks. *Exp Eye Res* 2002;74(5):561-570.

16 Mirshahi A, Kohlen T. Effect of microkeratome suction during LASIK on ocular structures. *Ophthalmology* 2005;112(4):645-649.

17 Tsai YY, Lin JM. Effect of laser-assisted *in situ* keratomileusis on the retinal nerve fiber layer. *Retina* 2000;20(4):342-345.

18 Hosny M, Sobhi Zaki RM, Ahmed R, Khalil N, Mostafa H. Changes in retinal nerve fiber layer thickness following mechanical microkeratome-assisted versus femtosecond laser-assisted LASIK. *Clin Ophthalmol* 2013;7:1919-1922.

19 Zhang J, Zhou YH. Effect of suction on macular thickness and retinal nerve fiber layer thickness during LASIK used femtosecond laser and Moria M2 microkeratome. *Int J Ophthalmol* 2015;8(4):777-783.

20 Saw SM, Gazzard G, Shih-Yen EC, Chua WH. Myopia and associated pathological complications. *Ophthalmic Physiol Opt* 2005;25(5):381-391.

21 Ho M, Liu DT, Chan VC, Lam DS. Choroidal thickness measurement in myopic eyes by enhanced depth optical coherence tomography. *Ophthalmology* 2013;120(9):1909-1914.

22 Almalki S, Abubaker A, Alsabaani NA, Edward DP. Causes of elevated intraocular pressure following implantation of phakic intraocular lenses for myopia. *Int Ophthalmol* 2016;36(2):259-265.

23 Poukens V, Glasgow BJ, Demer JL. Nonvascular contractile cells in sclera and choroid of humans and monkeys. *Invest Ophthalmol Vis Sci* 1998;39(10):1765-1774.

24 Haddad A, Laicine EM, Tripathi BJ, Tripathi RC. An extensive system of extravascular smooth muscle cells exists in the choroid of the rabbit eye. *Exp Eye Res* 2001;73(3):345-353.

25 Polska E, Simader C, Weigert G, Doelemeyer A, Kolodjaschna J, Scharmann O, Schmetterer L. Regulation of choroidal blood flow during combined changes in intraocular pressure and arterial blood pressure. *Invest Ophthalmol Vis Sci* 2007;48(8):3768-3774.

26 Akahori T, Iwase T, Yamamoto K, Ra E, Terasaki H. Changes in choroidal blood flow and morphology in response to increase in intraocular pressure. *Invest Ophthalmol Vis Sci* 2017;58(12):5076-5085.

27 Miyake K, Ibaraki N. Prostaglandins and cystoid macular edema. *Surv Ophthalmol* 2002;47(Suppl 1):S203-S218.

28 Flach AJ. The incidence, pathogenesis and treatment of cystoid macular edema following cataract surgery. *Trans Am Ophthalmol Soc* 1998;96:557-634.

- 29 Pendrak K, Papastergiou GI, Lin T, Laties AM, Stone RA. Choroidal vascular permeability in visually regulated eye growth. *Exp Eye Res* 2000;70(5):629-637.
- 30 Falcão M, Goncalves N, Freitas-Costa P, Beato J, Rocha-Sousa A, Carneiro A, Brandão E, Falcao-Reis F. Choroidal and macular thickness changes induced by cataract surgery. *Clin Ophthalmol* 2014;8:55-60.
- 31 Biró Z, Balla Z. OCT measurements on the foveal and perifoveal retinal thickness on diabetic patients after phacoemulsification and IOL implantation. *Eye (Lond)* 2010;24(4):639-647.
- 32 Abdellatif MK, Ebeid WM. Variations in choroidal and macular thickness maps after uneventful phacoemulsification. *Semin Ophthalmol* 2018;33(5):719-725.
- 33 Novais EA, Adhi M, Moulton EM, Louzada RN, Cole ED, Husvagt L, Lee B, Dang SB, Regatieri CV, Witkin AJ, Bauman CR, Hornegger J, Jayaraman V, Fujimoto JG, Duker JS, Waheed NK. Choroidal neovascularization analyzed on ultrahigh-speed swept-source optical coherence tomography angiography compared to spectral-domain optical coherence tomography angiography. *Am J Ophthalmol* 2016;164:80-88.
- 34 Cheng S, Leng T. Noninvasive detection of microaneurysms in diabetic retinopathy by swept-source optical coherence tomography. *Clin Ophthalmol* 2016;10:1791-1795.
- 35 de Castro-Abeger AH, de Carlo TE, Duker JS, Bauman CR. Optical coherence tomography angiography compared to fluorescein angiography in branch retinal artery occlusion. *Ophthalmic Surg Lasers Imaging Retina* 2015;46(10):1052-1054.
- 36 Li M, Cheng H, Yuan Y, Wang J, Chen Q, Me R, Ke B. Change in choroidal thickness and the relationship with accommodation following myopic excimer laser surgery. *Eye (Lond)* 2016;30(7):972-978.
- 37 Gudauskienė G, Matulevičiūtė I, Mockutė R, Maciulaitė E, Zaliūnienė D. Changes in subfoveal choroidal thickness after uncomplicated cataract surgery. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2019;163(2):179-183.
- 38 Pandian A, Sankaridurg PR, Naduvilath T, O'Leary D, Sweeney DF, Rose K, Mitchell P. Accommodative facility in eyes with and without myopia. *Invest Ophthalmol Vis Sci* 2006;47(11):4725-4731.
- 39 Sreenivasan V, Aslakson E, Kornaus A, Thibos LN. Retinal image quality during accommodation in adult myopic eyes. *Optom Vis Sci* 2013;90(11):1292-1303.
- 40 Wang M, Aleman AC, Schaeffel F. Probing the potency of artificial dynamic ON or OFF stimuli to inhibit myopia development. *Invest Ophthalmol Vis Sci* 2019;60(7):2599-2611.
- 41 Queirós A, Amorim-de-Sousa A, Lopes-Ferreira D, Villa-Collar C, Gutiérrez ÁR, González-Méjome JM. Relative peripheral refraction across 4 meridians after orthokeratology and LASIK surgery. *Eye Vis (Lond)* 2018;5:12.
- 42 Li ZY, Hu Y, Cui DM, Long W, He MG, Yang X. Change in subfoveal choroidal thickness secondary to orthokeratology and its cessation: a predictor for the change in axial length. *Acta Ophthalmol* 2019;97(3):e454-e459.
- 43 Troilo D, Nickla DL, Wildsoet CF. Choroidal thickness changes during altered eye growth and refractive state in a primate. *Invest Ophthalmol Vis Sci* 2000;41(6):1249-1258.
- 44 Gardner DJ, Walline JJ, Mutti DO. Choroidal thickness and peripheral myopic defocus during orthokeratology. *Optom Vis Sci* 2015;92(5):579-588.