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Retinal measurements using time domain optical coherence tomography imaging before and after myopic Lasik

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Abstract

Purpose—To compare retinal measurements obtained by time domain optical coherence tomography (OCT) devices before and after myopic laser in situ keratomileusis (Lasik) and to assess the interaction of Lasik and retinal structures as measured by time domain OCT.

Methods—53 patients randomly selected participated in the study. Only the right eye of each subject was included in the study. Comprehensive ophthalmic examinations including refraction examination, slitlamp examination, dilated fundus examination, corneal topography, corneal thickness, intraocular pressure, and retinal Stratus OCT scans were acquired for each patient before myopic Lasik and 3 months after surgery.

Results—Total macular volume (TMV) changed significantly between preoperative and postoperative measurements ($p=0.003$). No statistical differences were found between preoperative and postoperative disc area, rim area, cup/disk vert. ratio, or average foveal thickness ($p>0.05$). The variation in TMV correlated significantly with the change in spherical refraction equivalent, maximal corneal curvature, minimal corneal curvature, and corneal ablation depth.

Conclusion—Most retinal OCT measurements undergo no obvious changes after myopic Lasik. The increased TMV measurements we measured after Lasik seem to be correlated with the alteration in corneal shape. The exact mechanism for this change is not clear, while we examined several possibilities including subclinical macular edema, magnification changes, errors in OCT analysis and IOP, none of these seem to be a likely cause.

Keywords

Optical coherence tomography; laser in situ keratomileusis; macular volume; retina

Introduction

Laser in situ keratomileusis (Lasik) has become a common surgical procedure for patients with myopia. It is a surgical technique combining the creation of a lamellar corneal flap and an excimer laser ablation in the stromal tissue to reshape the cornea and correct myopia.^{1,2} During the creation of the corneal flap, the suction ring is applied to fixate the globe, which causes an increase of intraocular pressure to approximately 60 mmHg³. While posterior segment complications of Lasik have received attention, they are rare.⁴

An increasingly common approach to detecting retinal diseases and for understanding retinal anatomic variation is to use optical coherence tomography (OCT). Among the prevalent technologies, OCT is a useful imaging device for high-resolution, noninvasive imaging of the human retina.⁵ It is based on the backscattering of low-coherence laser light as it passes through layers of differing index of refraction and is recorded by an interferometer and amplified to construct a high-resolution cross-sectional image of tissue.⁶ With the application of OCT, Rodriguez-Agirretxe et al reported retinal nerve fiber layer remained unchanged 2 weeks after LASIK and Sharma et al also found no change in retinal nerve fiber layer 1 day and 1 month postoperatively.^{7, 8}

The present paper investigated the change in OCT measures of retinal thickness, area, and volume from the optic disc and macular regions. We compare measurements before surgery to measurements made 3 months after Lasik using a Stratus OCT.

Methods

Patients

Fifty three patients participated in the experiment. There were 29 female (54.7%) and 24 male (45.3%) subjects whose ages ranged from 18 to 42 years old (mean 26.7 years, standard deviation 5.7 years). While both eyes were measured, results from right and left eyes were highly correlated and therefore for this study we report results of only the right eye. All subjects had no history of ocular or systemic abnormalities. Preoperative routine examinations for LASIK were performed for each patient. Subjects with clinical evidence of retinal diseases, glaucoma, neurologic diseases, corneal diseases or diabetes were excluded. Appropriate informed consent was obtained from all participants in accordance with the Declaration of Helsinki and following procedures approved by the Zhejiang Institutional Review Board.

Procedure

Comprehensive ophthalmic examinations were performed on all subjects including slitlamp examination, dilated fundus examination, manifest and cycloplegic refraction with best corrected visual acuity (BCVA). BCVA was tested using a Snellen chart in a controlled testing environment under calibrated and room lighting. In order to measure BCVA accurately, automatic refractometry (ARK-700, Nidek Co., Ltd., Tokyo, Japan, <http://www.nidekintl.com/ophthalmology/index.html>) was performed first, and then the values from automatic refractometry were further refined by subjective refraction with a phoropter (Rodenstock, Germany, <http://rodenstockinstruments.com/en.html>) providing and estimate of both spherical and toroidal refractive error. The spherical equivalent (SE) of refractive error was calculated as the spherical value of refractive error plus half of the cylindrical value. An experienced technician measured Corneal power and shape information was collected using an Orbscan II corneal topographer (Orbtek Inc., Bausch & Lomb, Rochester, NY, USA, <http://www.urmc.rochester.edu/eye-institute/lasik/technology/orbscan-corneal-topographer.cfm>), Central corneal thickness was measured using pachymetry Tomey SP-3000 (Tomey corporation, Nagoya, Japan, http://www.tomeyusa.com/products_SP3000.html, <http://www.emtron.com/oftalmoloji/tomey/tomey-e.htm>). Intraocular

pressure was measured by Goldmann applanation tonometry (Haag-streit, Bern, Switzerland, <http://www.haag-streit.com/products/tonometry.html>), and time domain OCT imaging was performed using a Stratus OCT (Carl Zeiss Meditec Inc., Dublin, CA, <http://www.meditec.zeiss.com/>). Finally, Lacrimal secretion, and wavefront analysis were performed as preoperative routine examinations for LASIK on each patient, but the data were not used for the current study.

Optical Coherence Tomography

Time domain OCT imaging was performed with Stratus OCT-3, version 4. Data were collected from the fast optical disc scan, and fast macular thickness scan. Disc area, rim Area, cup/disk vert. ratio, average fovea thickness, and TMV were calculated from the values of the two scans. The images are generated by the third-generation OCT system which provides ~10- μ m axial and 20- μ m transverse resolution in the eyes. In the fast macular thickness scan, six linear scans were used. Scans are centered at the fovea and equally spaced 30° apart in a continuous automated sequence, each of the six linear scans is composed of 128 equally spaced axial scans. In the fast optical disc scan, data was similarly obtained from six linear scans centered on the optic nerve head, and the disc margin was determined as the end of the retinal pigment epithelium layer. The length of linear scans was 6 mm for the macula and 4 mm for the optic disk. Therefore 768 locations were measured for each scan, but over a different area. In order to maintain quality control, only sharp images with a signal strength (Max10) >6 were considered for this study.

LASIK Surgery Procedure

All patients underwent Lasik surgery to correct myopia at the second hospital affiliated to Zhejiang University, Hangzhou, China. During surgery, a Moria-2 microkeratome (Moria, Antony, France, <http://www.moria-surgical.com/>) was used to create a superiorly hinged corneal flap. Then the laser ablation was performed using the MEL80 laser system (Carl Zeiss, Jena, Germany, <http://www.meditec.zeiss.com/>). All Lasik operations were performed by the same surgeon (Y.Y.). Postoperative medications included artificial tears and 0.1% fluorometholone eye-drops (Flumetholon, Japan) instilled in all patients four times a day for 14 days. A routine eye examination was carried out again at 1 day, 7 day, and 1 month postoperatively.

Statistical Analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 17.0. The one-sample Kolmogorov-Smirnov test was used to test for a normal distribution. A paired t test was used to compare the two sets of measured data before and after LASIK. Statistical correlations between parameters were assessed using the bivariate Pearson's correlation coefficient and stepwise regression. Quantitative variables were expressed as the mean $\pm$ standard deviation. All tests were two-tailed, statistical significance was considered for p values of less than 0.05.

Results

The data of disc area, rim area, cup/disk vert. ratio, average fovea thickness, and TMV were normally distributed (Kolmogorov-Smirnov test). Preoperative spherical refraction equivalent (SRE) preoperatively was -5.72 ± 2.80 diopters (D) (range: -1.375 to -14.125 D). Postoperative SRE was -0.24 ± 0.76 D (range: $+1.00$ to -3.75 D). The decrease in SRE was 5.46 ± 2.34 D after Lasik at 3 months postoperatively. Mean corneal stromal ablation depth was $93.30 \pm 21.79 \mu\text{m}$ (range: 40.000 to $132.000 \mu\text{m}$). The decrease in maximal corneal curvature and minimal corneal curvature measured by corneal topography were -3.87 ± 1.35 D and -3.71 ± 1.30 D, respectively. The decrease in intraocular pressure was -3.87 ± 1.71 mmHg.

In all eyes, no posterior segment complications of Lasik such as retinal detachment, macular-hole and choroidal neovascularization, were found at 3 months postoperatively. Intraocular pressure was normal at all postoperative examinations. The postoperative uncorrected visual acuity was improved in all eyes, and ranged from 20/40 to 20/20.

Table 1 shows the preoperative and 3-month postoperative measurements from 53 right myopic eyes. The data of TMV measurements, maximal corneal curvature, minimal corneal curvature, and intraocular pressure were significantly different at 3 months after Lasik, compared to the data measured preoperatively ($p < 0.005$).

We also examined the relation between TMV, and the change in SRE, maximal corneal curvature, minimal corneal curvature, and corneal ablation depth. Table 2 presents the bivariate Pearson's correlation coefficient and the TMV change is significantly related to all three parameters of the surgery ($p < 0.05$ in all cases) as well as to the intraocular pressure and SRE outcome of the surgery. Similarly, the change in intraocular pressure and change in SRE, maximal corneal curvature, minimal corneal curvature, and corneal ablation depth were also significant ($p < 0.05$ in all cases). To determine the major correlate with the changed TMV we used a stepwise regression to produce the model:

total macular volume changes = $-0.104 + 0.031 \times \text{SRE changes}$. ($p = 0.001$)

Figure 1 present the relation between the TMV changes and the SRE changes.

Discussion

OCT provides a means for performing high axial resolution, noninvasive cross-sectional imaging and offers the potential for objective morphological evaluation and quantitative analysis of retinal structural changes.⁹⁻¹⁰ Using this technology, previous investigations reported that postoperative retinal nerve fiber layer thickness measurements were not significantly changed with Lasik surgery.^{7,8,11,12} However, these previous studies concentrated primarily on retinal nerve fiber layer thickness. Increasingly, macular thickness is being used in studies of both diabetic complications and cystoid macular edema after cataract surgery^{13, 14}, but few studies have addressed its use in assessing retinal structural changes after Lasik and with the increasing numbers of post-Lasik patients in the population it is critical to understand whether LASIK surgery influences the outcome of these measures of retinal health. In our study, we compared measurements from optic disc and macular

before surgery to measurements made 3 months after Lasik using a Stratus OCT. While ideally corneal refractive surgery should not alter retinal structure, surprisingly we did find a change in the total macular volume. To perform an informal check on this result we examined the result for the fellow eyes of this patient cohort. While this is not a truly independent result, since surgical response can be similar across eyes, we did find the same result. If the change with surgery were simply arising from noise and poor measurement accuracy, we might expect the other eye to have a different result, it did not. TMV is intended to be a direct measurement of macular swelling and has been reported to have a low interobserver variability.¹⁵ All of the eyes in our study had improved postoperative visual acuity and no posterior segment abnormalities including macular edema were detected on retina exam postoperatively, suggesting that the result is not related to post-surgical retinal complications.

However, we did find that the variation in TMV correlated significantly with changes of SRE, maximal corneal curvature, minimal corneal curvature, and corneal ablation depth. This suggests that the slight volume changes we measure are somehow related to either artifact, the surgery due to an optical change in the eye, or the surgery due to a biological mechanism or response of the eye.

There are two potential artifactual reasons that might cause the change with surgery. The first is that variation in TMV could be resulting because the total macular border was mistakenly placed during the scanning and this error differed between pre- and post- surgical eyes. Measurement of TMV by the Stratus OCT instrument software depends on accurate identification of its boundary. However, in this study care was taken to place the border and we do not believe that there was a systematic change in placement depending on the ablation depth of the eye. The second potential artifact we considered was a systematic change in signal strength. Previous studies have documented that OCT measurements can be affected by segmentation error which presents a challenge to automated algorithms.¹⁶ Segmentation errors can be worse with weaker signals. However, we did not notice any consistent change in signal strength of OCT measurements pre- and post- surgery. Thus, we do not believe these artifact produced our results, although in retrospect these are potential weaknesses of the current study and they might be better controlled with spectral domain systems where there is more data to control placement of the volume estimate and better segmentation.

Along with the change in refraction, the changes to the optical surfaces of the eye could also be causing a systematic change in the apparent volume of retina scanned by changing the magnification. As we know, the Stratus OCT (time domain OCT) must scan the sample in two lateral dimensions, the axial depth (along the incident light beam) and transversal area (perpendicular to the incident light beam). The real diameter of an object on the retina is determined by the vergence of the light along the internal axis of the eye.¹⁷ According to the Gullstrand-Emsley schematic eye¹⁸, the refractive power of each spherical surface is calculated as $F = (n_2 - n_1)/r$, where n_1 and n_2 are the indices of refraction to the left and right of the surface, respectively, and r is the radius of the surface's curvature. After Lasik, n_1 and n_2 were not changed, whereas the radius of the cornea increased. Therefore, the refractive power of the cornea and its optical power decreased accordingly as expected for a myopic surgery. To better evaluate the potential impact of this change in curvature we

implemented a model of the Gullstrand model eye in ZEMAXtm (radiant ZEMAX, www.zemax.com). To model the effect we varied the anterior corneal curvature from a K of 39 to 47, and measured the change in field positions for beams entering the eye at different angles. The linear magnification change was between 1 and 2 percent and this represents an overestimate because the posterior surface also flattens with surgery and this change is opposite in sign to the anterior surface. However the role of the posterior surface is quite small, both because the index of refraction difference between the cornea and the aqueous is much smaller than between air and the cornea, and also because the posterior surface is closer to the nodal point of the eye. While including axial length would have allowed us to individually tune the eye model for each subject we did not have pre- and post- surgical axial length data for our subjects. While a better model would require computing not only the difference in volumetric magnification, but also the distribution of macular volume across the retina, since the slight changes in field size would interact with the retinal topographical changes. SDOCT devices may allow this level of analysis, however our conclusion for the current study is that while the magnification effect is in the right direction it seems too small to account for the volume change measured.

Lasik has also been reported to alter other aspects of the eye most notably the measurement of IOP.¹⁹⁻²³ Montes-Mico and Charman have documented that IOP was reduced after LASIK because of the reduced corneal thickness and curvature.¹⁹ Our measurement of a reduced intraocular pressure after surgery confirmed this affect with IOP decreasing from 14.65 ± 2.42 before Lasik to 10.88 ± 2.45 after Lasik. The close relationship between IOP and the data changes of SRE, maximal corneal curvature, minimal corneal curvature, and corneal ablation depth were also found in agreement with a mechanical model for the change in IOP that links the change to changes in the stiffness of the cornea decreases. Most studies²⁴ consider the biomechanical changes arising to LASIK to be the main cause of changes in IOP measured with applanation tonometry. If some of the decrease in IOP is real, perhaps also due to a change in stiffness, then it is conceivable that a slight decrease in IOP would produce a change in the perfusion pressure of the retina and a slight increase in volume. However, testing this possibility is beyond the scope of the current study and would require highly reliable measures of IOP independent of corneal stiffness

Prior studies have shown that Lasik has high efficacy, predictability, stability and safety,²⁵⁻²⁷ Although a low incidence of retinal disease was reported after Lasik,²⁸ there is no evidence of a relationship between myopic Lasik and retinal disease and the incidence rate of retinal disease after Lasik is similar to the risks of myopic retinal abnormalities itself. In our studies, posterior segment complications were absent and most of the retinal OCT measurement parameters were unchanged except for TMV. It is important to note that the changes we measured are relatively small and the postoperative TMV (6.77 ± 0.30) was still normal in terms of the normative database of the stratus OCT. The normal values of total macular volume ranged from 6.18 to 7.42 mm³. The findings of the current study confirm that Lasik does no harm to retina but does argue that when looking at other properties of the retina it might be useful to control for prior LASIK surgery.

In summary, this study shows that small but statistically significant increases in OCT measurements of TMV occur after Lasik. These increases are related to alterations in corneal curvature and should not be considered as macular edema.

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Figure 1. Correlations between TMV measurements changes and the spherical equivalent of refractive error. TMV= Total macular volume.

Table 1

Preoperative and 3 Months Postoperative Measurements from 53 Right Myopic Eyes

Parameter	Preoperative	Postoperative	t-values	df	P value *
SRE	-5.72±2.80	-0.24±0.76	-16.61	52	<0.0001
K1	44.40±1.46	40.53±1.65	20.90	52	<0.0001
K2	43.40±1.28	39.67±1.57	20.79	52	<0.0001
IOP	14.65±2.42	10.88±2.45	14.32	52	<0.0001
Disc Area(mm ²)	2.39±0.41	2.38±0.46	0.09	52	0.932
Rim Area(mm ²)	1.74±0.42	1.68±0.35	1.45	52	0.153
Cup/Disk Vert. Ratio	0.46±0.16	0.47±0.15	-1.26	52	0.214
Fovea Thickness(μm)	224.47±20.21	222.45±17.41	0.85	52	0.401
TMV (mm ³)	6.70±0.34	6.77±0.30	-3.13	52	0.003

Data are mean ± SD

SRE=spherical refraction equivalent; K1= Maximal corneal curvature; K2= Minimal corneal curvature; IOP=intraocular pressure; TMV= Total macular volume; df=degree of freedom. If the Bonferroni correction is applied for statistical significance the p-value required would be $p < 0.0055$.

* Paired t test

Table 2

Correlations between increased TMV measurements changes, decreased intraocular pressure changes and the alterations in refractive error, corneal curvature, and corneal ablation depth in 53 right myopic eyes.

Parameter	TMV changes			Intraocular pressure		
	Pearson correlation	sig.(2-tailed)	N	Pearson correlation	sig.(2-tailed)	N
SRE changes	0.439	0.001	53	−0.350	0.01	53
K1 changes	−0.368	0.007	53	0.303	0.027	53
K2 changes	−0.394	0.004	53	0.373	0.006	53
Corneal ablation depth	0.339	0.013	53	−0.353	0.009	53
Intraocular pressure	−0.376	0.006	53	----	----	

SRE=spherical refraction equivalent; K1 changes= Maximal corneal curvature changes; K2 changes= Minimal corneal curvature changes; TMV= Total macular volume; Degree of freedom=52 in all groups.