

Comparison of LASIK flap created by
two different types of femtosecond laser and
a microkeratome with Fourier-domain optical
coherent tomography analysis

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a microkeratome with Fourier-domain optical
coherent tomography analysis

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We will always be together.

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<ABSTRACT>

Comparison of the LASIK flap created by two different types of femtosecond laser and a microkeratome with Fourier-domain optical coherent tomography analysis

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Purpose : To evaluate thickness and side cut angle of LASIK flap made by two different types of femtosecond laser system and a microkeratome using Fourier-domain optical coherent tomography (FD-OCT).

Methods : One hundred and sixty six eyes (83 patients) which had underwent LASIK surgery were allocated to 3 groups according to the method for flap creation. Fifty eyes (25 patients) were subject to the IntraLase group, 64 eyes (32 patients) to the Femto-LDV group, and 52 eyes (26 patients) to the microkeratome group. Fourteen measuring points of the flap thickness and four directions of incision angle at the margin were measured with the RTVue FD-OCT system (Optovue Inc., Fremont, CA, USA) at 2 months postoperatively. Morphologic analysis was performed in four aspects. Flap configuration was evaluated with mean flap thickness at each measuring point. Predictability was defined as the disparity between measured and intended thickness. And regularity of flap thickness was analyzed by identifying statistical interactions between measuring points in each flap. Differences between peripheral and central flap thickness also were evaluated as regularity index. Side cut angles at the flap margin were compared.

Results : Two femtosecond laser groups presented with relatively even configuration of flap in comparison to microkeratome group. Femto-LDV group showed better predictability comparing to other groups ($p < 0.001$). Statistical interactions between measuring points and differences between

peripheral and central flap thickness were the least in the IntraLase group ($p < 0.001$). Side cut angles at the flap margin were more acute and close to a right angle in IntraLase group at four directions ($p < 0.001$). But there was no significant difference between Femto-LDV and microkeratome group.

Conclusion : Flap made with femtosecond laser systems showed even configuration and better regularity in thickness. Microkeratome made predictable flap thickness in central area, but there is disparity between central and peripheral areas. Between two different femtosecond laser systems, there also are morphological differences. Because each method has different character depending on its own mechanism, it is important to consider these differences in flap creation.

Key words : LASIK flap, femtosecond laser, microkeratome, Fourier-domain optical coherent tomography, flap configuration

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I. INTRODUCTION

Since femtosecond laser was applied to LASIK surgery for flap creation, differences between using femtosecond laser and conventional microkeratome have received increasing attention. Many comparative studies have focused on the visual outcome and aberrations. Durrie and colleagues¹ reported that femtosecond laser provided a better visual acuity and manifest refractive outcome than microkeratome. And other studies have presented better contrast sensitivity and astigmatic neutrality, but less induction of postoperative higher order aberrations in patients who had undergone femtosecond laser-assisted LASIK in comparison to patients with microkeratome.²⁻⁶ However, this issue is still controversial. Patel and associates⁷ claimed that the method of flap creation did not affect visual outcomes during the first 6 months after surgery and another report showed comparable clinical outcomes between femtosecond laser and microkeratome groups.⁸

Morphological evaluation of LASIK flap quality is a crucial pre-requisite step to clarify the difference between methods for flap creation and correlate it to previous results. One important aspect of flap quality is thickness. Mean value, as well as predictability and regularity in terms of thickness should be carefully considered. Some studies evaluated the thickness of flap made by femtosecond laser and microkeratome.^{3, 9-14} Most of these reports applied ultrasound pachymetry to measure flap thickness at corneal center. But it is difficult to evaluate various or intended locations of corneal flap using ultrasound pachymetry in identifying flap configuration. Recently, alternative methods such as very high-frequency digital ultrasound or optical coherent tomography (OCT) have been adopted,^{13, 15}

but these have limitations for measuring various and intended location with high resolution. Another aspect of flap quality is side cut angle of flap margin. Side cut angle of flap margin is related to development of epithelial ingrowth and stability of the flap location.¹⁶ Only few studies with animal cornea reported marginal configuration of LASIK flap so far.¹⁶⁻¹⁸ And none of them evaluated flaps made by femtosecond laser.

In this study, we evaluated and compared quality of LASIK flap created by two different types of femtosecond laser system and a conventional microkeratome in aspect of thickness and side cut angle with Fourier-domain OCT (FD-OCT) analysis.

II. MATERIALS AND METHODS

1. Subjects

One hundred and sixty six eyes (83 patients) which had underwent LASIK surgery were included in our institution and two private clinics. Mean age of patients was 28.2 years old (range 20 to 47 years old). Twenty three were male and 40 were female patients. All patients were well indicated to receive LASIK for myopia or myopic astigmatism. Subjects who have any kind of corneal abnormality, estimated residual stromal bed thickness less than 250 μm , or history of systemic disease contraindicated for LASIK such as collagen vascular disease were excluded. Patients with intraoperative and postoperative complications were excluded at the end of follow-up. All eligible subjects were allocated to 3 groups according to the method for flap creation.

A. IntraLase group : 50 eyes (25 patients) underwent LASIK with aid of IntraLase femtosecond laser (Abott Medical Optics Inc., Santa Ana, CA, USA) were included.

B. Femto-LDV group : 64 eyes (32 patients) underwent LASIK using Femto-LDV femtosecond laser (Ziemer Ophthalmic AG, Port, Switzerland) were included.

C. Microkeratome group : 52 eyes (26 patients) were subject to conventional microkeratome

group. Moria M2 microkeratome with 110 head (Moria S.A., Antony, France) was applied for flap creation.

2. Flap creation

IntraLase femtosecond laser which has 1.8 μJ of laser energy and 60 kHz of repetition frequency was intended to create flap thickness of 110 μm with 70-degree of side cut angle and superior hinge. Femto-LDV femtosecond laser delivers nanojoule of pulse energy with frequency more than 1 MHz. Programmed flap thickness was 110 μm and temporal hinge was made in this group. Moria M2 microkeratome with 110 μm of compression head is designed for 130 μm of flap thickness. In microkeratome group, superior hinge was created.

3. Flap evaluation

All the patients were examined at preoperatively and 2 months postoperatively as below.

- A. Preoperative central corneal thickness (CCT), corneal curvature (K-value), and spherical equivalents (SE) were examined. Postoperative visual acuity, corneal curvature, and SE were evaluated at 2 months after surgery.
- B. Morphological flap quality was evaluated using RTVue (Optovue Inc., Fremont, CA, USA) FD-OCT system. RTVue can acquire 26,000 A-scan images per second with 5.0 μm of resolution. Flap thicknesses at 14 measuring points were used for analysis. At first, 6 mm sized of 2 cross sectional axial scans were performed horizontally and vertically. Each axial scan has 5 measuring points: center, 2 points 1 mm apart from the center (center -1, center +1), and 2 points 2 mm apart from the center (center -2, center +2). And 3mm sized of 4 linear scans were performed at 0, 90, 180, and 270 degree clockwise positions of flap margin. At each marginal scan, we obtained flap thickness at 1 mm apart from flap margin (margin +1 or margin -1) and

side cut angle (Figure 1).

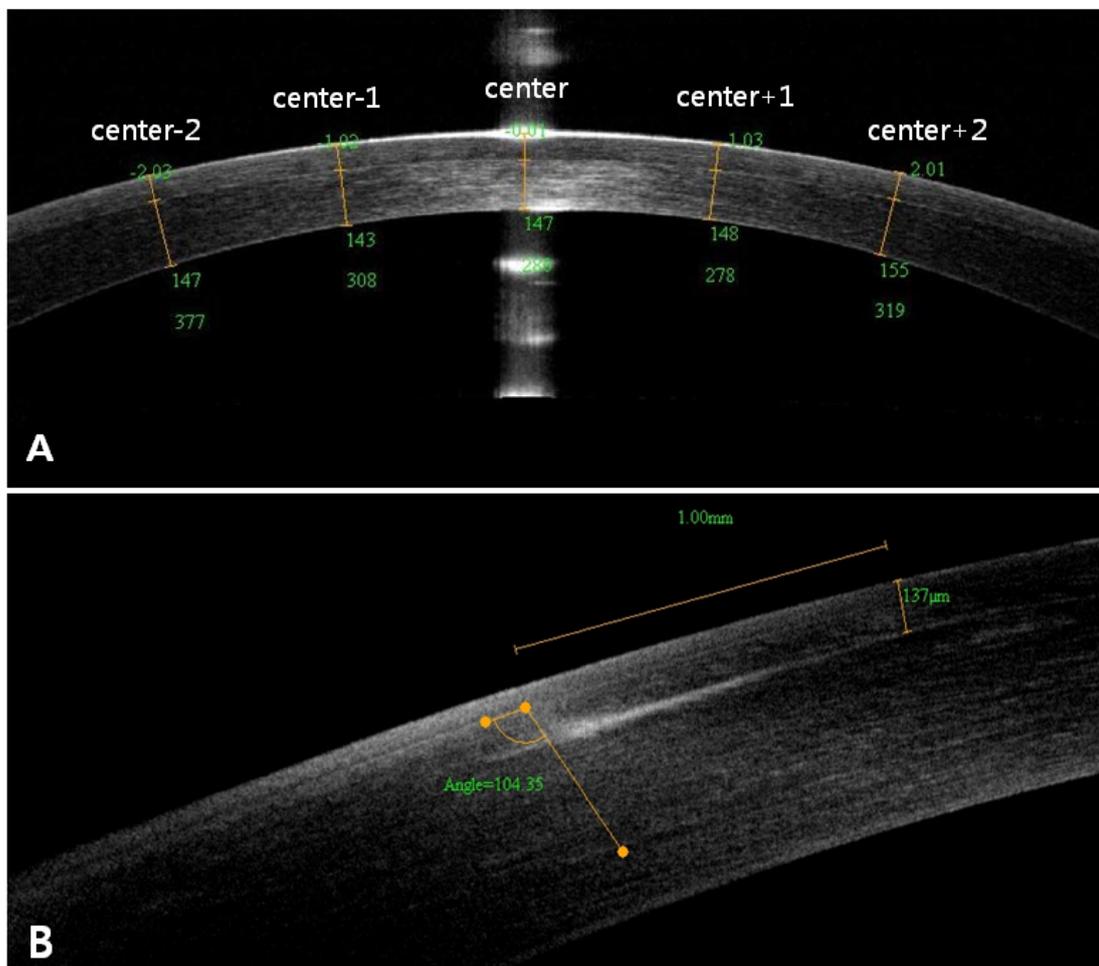


Figure 1. A. An example of axial scan and 5 measuring points: center, 1 mm apart from center (center -1, center +1), 2 mm apart from center (center -2, center +2). At each measuring point, thickness of flap and residual stromal bed were displayed using integrated software in RTVue system. B. An example of linear scan at flap margin. Side cut angle and flap thickness of 1 mm apart from the margin (margin +1) were displayed using integrated software in RTVue system.

4. Data analysis

- A. Baseline characteristics and postoperative visual outcomes were compared.
- B. Mean thicknesses at each measuring point were evaluated to identify flap configuration.

C. Predictability in flap creation

We compared the mean of differences between measured and intended thickness for evaluation of the predictability at each measuring point.

D. Regularity in flap creation

The regularity was evaluated in two ways. Firstly, relations of all the differences between measured and intended thickness at 14 measuring points in each cornea were analyzed. Secondly, we defined and compared 'Regularity index' as the difference between peripheral thickness (mean of margin +1 and margin -1) and central thickness (mean of center -1, center and center +1) at each cornea.

E. Side cut angle

Mean side cut angle at each marginal location and mean of all the angle measurements in each group were compared.

5. Statistical methods

To compare the difference in baseline characteristics, postoperative visual outcomes, and side cut angle, we used one-way ANOVA with post hoc analysis. And generalized linear mixed model (GLMM) for repeated measure was employed to clarify statistical interactions among 14 measuring points in the difference between measured and intended thickness in each group. All of the statistical analysis were performed with SAS Ver. 9.1 (SAS Institute Inc., Cary, NC, USA).

III. RESULTS

1. Baseline characteristics and postoperative visual outcomes

Baseline characteristics and postoperative visual outcomes of three groups are summarized in Table 1. Mean age of microkeratome group (32 ± 6.5 years, range 22 to 47 years) was older than that of IntraLase group (25.9 ± 6.6 years, range 20 to 42 years) and Femto-LDV group (27 ± 4.2 years, range 20 to 37 years). Mean CCT and preoperative SE of IntraLase group were higher than other groups, whereas there was no statistical difference among three groups in visual outcomes such as postoperative visual acuity and SE.

Table 1. Baseline characteristics and postoperative visual outcomes of three groups

	IntraLase	Femto-LDV	Microkeratome
Age (year)	25.9 ± 6.6	27 ± 4.2	$32 \pm 6.5^*$
CCT (μm)	565 ± 19.6	541.1 ± 21.8	$548.9 \pm 24.6^*$
Postoperative VA	1.0 ± 0.17	1.1 ± 0.11	1.0 ± 0.07
Preoperative SE	-5.63 ± 2.37	-3.78 ± 1.36	$-3.53 \pm 1.2^*$
Postoperative SE	-0.2 ± 0.35	0.21 ± 0.37	0.18 ± 0.46
Preoperative K value	42.37 ± 2.0	43.31 ± 1.48	43.57 ± 1.13
Postoperative K value	38.39 ± 2.34	40.36 ± 2.15	40.45 ± 1.4

All data represented as mean \pm standard deviation; CCT = central corneal thickness; VA = visual acuity; SE = spherical equivalents. * $p < 0.05$ in one-way ANOVA analysis among three groups.

2. Mean thickness and flap configuration

All the results of mean thickness at each measuring point are listed in Table 2. Microkeratome group showed typical meniscus shape (peripheral flap is much thicker than central flap). Femto-LDV group also demonstrated similar shape, but the asymmetry was less. Flap configuration of IntraLase

group did not present this pattern.

Table 2. Thickness at each measuring point.

Location	margin +1	center -2	center -1	center	center +1	center +2	margin -1
IntraLase							
H	127.3 ± 11.0	136.1 ± 12.4	132.3 ± 11.5	130.3 ± 13.2	131.6 ± 13.2	137.8 ± 13.3	131.8 ± 12.7
V	124.4 ± 10.2	136.4 ± 12.8	132.9 ± 13.0	129.9 ± 12.6	132.6 ± 12.4	137.8 ± 12.5	129.7 ± 10.6
Femto LDV							
H	120.1 ± 6.7	117.9 ± 6.4	109.2 ± 7.3	105.8 ± 8.2	109.1 ± 6.1	119.7 ± 6.5	120.4 ± 7.0
V	120.6 ± 6.6	118.9 ± 7.2	109.1 ± 6.7	103.8 ± 6.3	108 ± 5.4	118.3 ± 7.2	121.4 ± 5.5
Microkeratome							
H	190.1 ± 16.6	160.5 ± 21.2	136.6 ± 22.5	126 ± 19.9	129.9 ± 21.3	155 ± 23.4	182.9 ± 16.0
V	179.6 ± 21.5	163.2 ± 20.6	140.8 ± 22.0	124.8 ± 19.2	128.8 ± 19.6	151.3 ± 18.2	166.3 ± 24.1

All data represented as mean ± standard deviation; H = horizontal scan; V = vertical scan

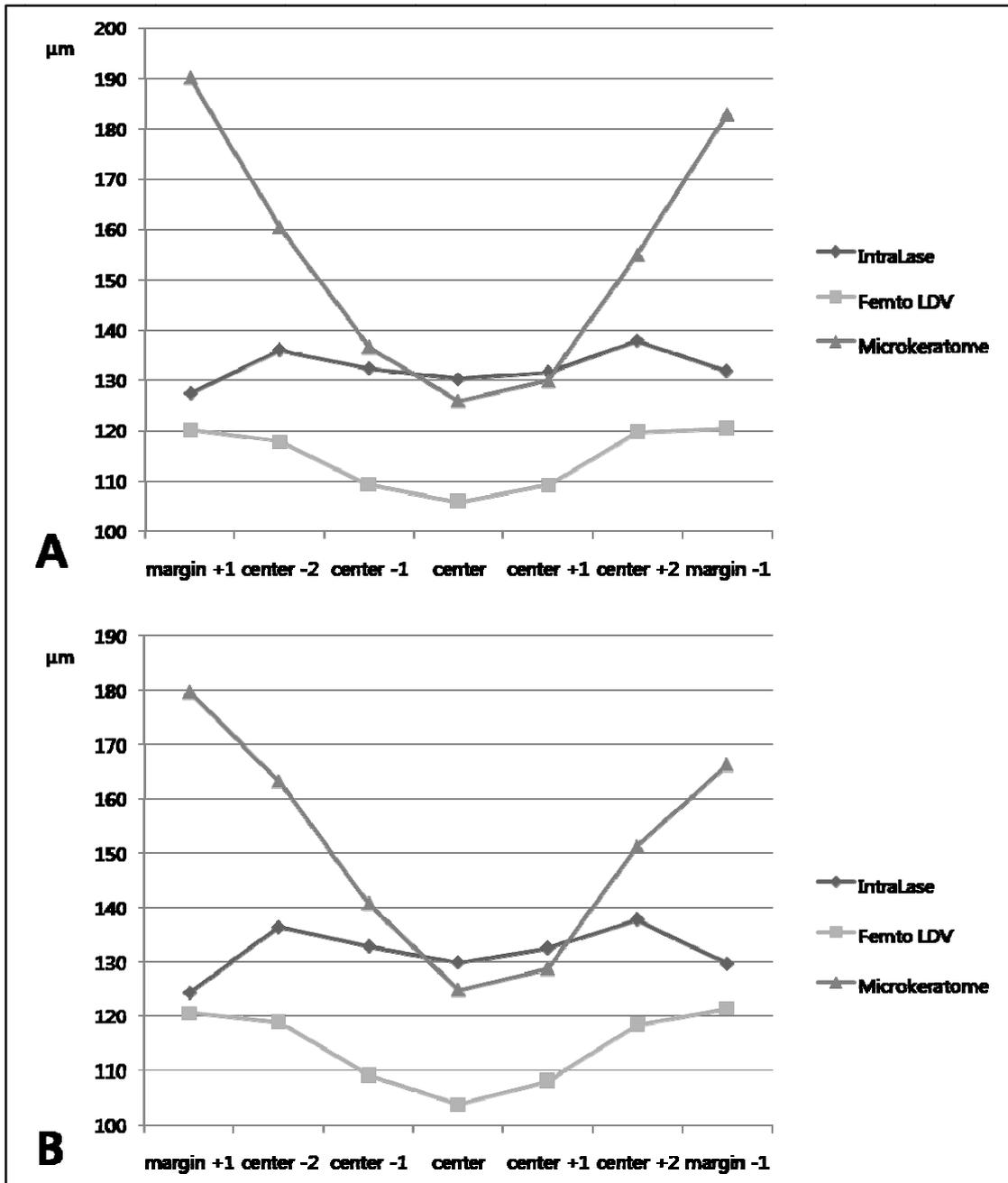


Figure 2. Flap configuration. Mean flap thickness at each measuring point. A. Horizontal scan, B. Vertical scan.

3. Predictability in flap creation

Mean differences between measured thickness and intended thickness in each measuring point are listed in Table 3. and Figure 3. At each measuring point, flap thicknesses of Femto-LDV group were

the closest to the intended thickness. Microkeratome group showed nearer value to the intended thickness than IntraLase group in central area, but vice versa in peripheral measuring points.

Table 3. Predictability which is differences between measured thickness and intended thickness in each measuring point.

Location	margin +1	center -2	center -1	center	center +1	center +2	margin -1
IntraLase							
H	16.4 ± 12.4	25.2 ± 13.9	21.3 ± 12.9	19.3 ± 14.7	20.6 ± 14.6	26.9 ± 14.5	20.9 ± 13.8
V	13.6 ± 11.8	25.5 ± 14.4	22 ± 14.5	19.1 ± 14.1	21.7 ± 13.7	26.9 ± 13.6	18.8 ± 12.0
T	15.0 ± 10.9	25.3 ± 13.7	21.6 ± 13.4	20.7 ± 13.2	21.4 ± 13.5	26.9 ± 13.0	20.2 ± 12.1
Femto-LDV							
H	10.1 ± 6.7	7.9 ± 6.4	-0.8 ± 7.3	-4.2 ± 8.2	-0.9 ± 6.1	9.7 ± 6.5	10.4 ± 6.9
V	10.6 ± 6.6	8.9 ± 7.2	-0.9 ± 6.7	-6.2 ± 6.3	-1.9 ± 5.4	8.4 ± 7.2	11.3 ± 5.5
T	10.2 ± 5.2	8.4 ± 5.9	-0.7 ± 6.0	-1.9 ± 5.5	-1.2 ± 5.2	9.2 ± 6.3	10.9 ± 5.4
Microkeratome							
H	63.3 ± 17.1	33.6 ± 19.9	10.7 ± 22.6	-0.8 ± 21.1	1.9 ± 22.7	24.1 ± 30.4	56.2 ± 17.3
V	53.1 ± 20.9	33.2 ± 20.6	13.1 ± 21.5	-1.9 ± 20.2	2 ± 19.1	23.3 ± 17.8	38.4 ± 22.6
T	58.4 ± 17.9	32.4 ± 19.9	12.4 ± 20.1	5.6 ± 18.5	2.4 ± 19.6	24.8 ± 21.9	48.9 ± 17.8

All data represented as mean ± standard deviation; H = horizontal scan; V = vertical scan;

T = total of scans

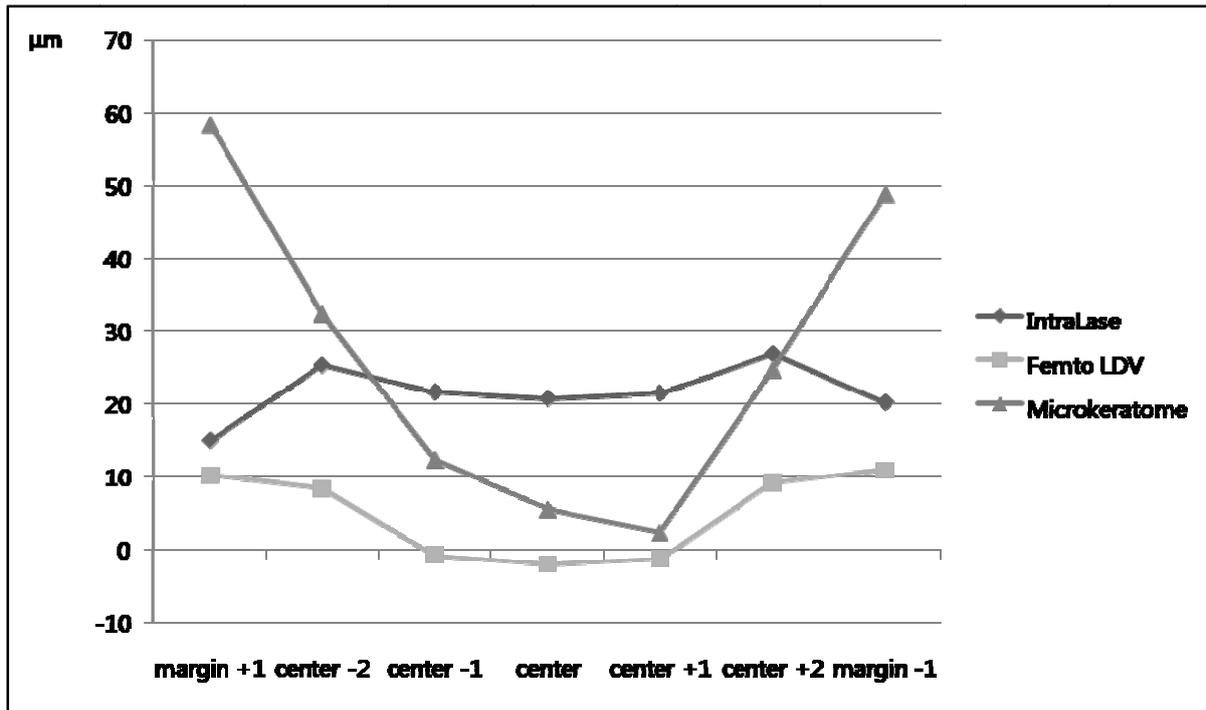


Figure 3. Predictability in flap creation. Mean difference between measured and intended thickness in total measurements of each measuring point.

4. Regularity in flap creation

A. Generalized linear mixed model analysis

IntraLase group showed the least statistical interactions among 14 measuring points in analysis of the differences between measured and intended thickness (2 of 21 pairs of location variables). This implies that values of IntraLase group are even in each others. On the other hand, Femto-LDV group (12 of 21 pairs of location variables) and microkeratome group (20 of 21 pairs of location variables) had much more statistical interactions between measuring points (Table 4.).

Table 4. Statistical interactions between measuring points.

group	Measuring points						
		margin -1	center -2	center -1	center	center +1	center +2
IntraLase	center -2	0.0381*					
	center -1	0.2696	0.3552				
	center	0.5086	0.153	0.6415			
	center +1	0.3461	0.2764	0.8733	0.7627		
	center +2	0.0159*	0.7292	0.2078	0.0764	0.1547	
	margin -1	0.2785	0.3154	0.9593	0.6696	0.9101	0.1775
Femto-LDV	center -2	0.5049					
	center -1	0.0015*	0.0121*				
	center	< 0.0001*	0.0003*	0.2623			
	center +1	0.0008*	0.0079*	0.9005	0.3151		
	center +2	0.8957	0.5951	0.0024*	< 0.0001*	0.0015*	
	margin -1	0.8874	0.4242	0.001*	< 0.0001*	0.0006*	0.7873
micro-keratome	center -2	< 0.0001*					
	center -1	< 0.0001*	< 0.0001*				
	center	< 0.0001*	< 0.0001*	0.0063*			
	center +1	< 0.0001*	< 0.0001*	0.0117*	0.8091		
	center +2	< 0.0001*	0.0288*	0.0002*	< 0.0001*	< 0.0001*	
	margin -1	0.0388*	< 0.0001*	< 0.0001*	< 0.0001*	< 0.0001*	< 0.0001*

Each number in a cell represents the p-value of the statistical interaction between variables in the corresponding column and row. * p<0.05, in generalized linear mixed model analysis. Statistically significant interaction (p<0.05) between those two variables represented with dark gray color.

B. Regularity index

Differences between peripheral flap thickness and central flap thickness at each cornea was smaller in IntraLase group than other groups ($p < 0.001$). In horizontal plane, regularity index were $7.1 \pm 5.6 \mu\text{m}$ in IntraLase group, $11.9 \pm 6.8 \mu\text{m}$ in Femto-LDV group, and $55.4 \pm 13.1 \mu\text{m}$ in microkeratome group. It showed similar pattern in vertical plane ($7.2 \pm 6.0 \mu\text{m}$ in IntraLase group, $13.6 \pm 5.8 \mu\text{m}$ in Femto-LDV group, and $37.2 \pm 11.4 \mu\text{m}$ in microkeratome group) (Figure 4.). All the differences were statistically significant among all groups.

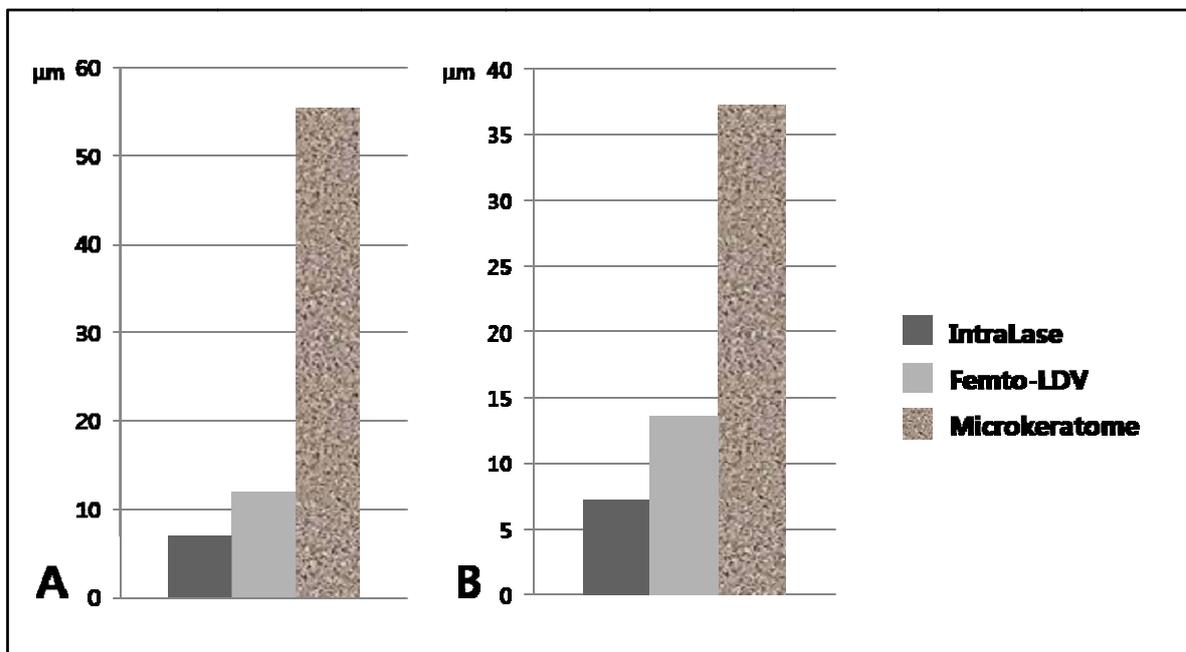


Figure 4. Regularity index (difference between central and peripheral thickness) of three groups in horizontal scan (A) and vertical scan (B). All the differences were statistically significant among all groups.

5. Side cut angle at the flap margin

IntraLase group presented significantly different incision angle comparing to other two groups ($p < 0.001$). Considering total measurements of four directions in each group, mean incision angle was

105.5 ± 10.9 degrees in IntraLase group, 151.9 ± 7.3 degrees in Femto-LDV group, and 150.2 ± 7.1 degrees in microkeratome group. Mean incision angle of Femto-LDV group and microkeratome group were not different statistically. Mean incision angles at each measuring location are listed in Table 5.

Table 5. Side cut angle

	0°	90°	180°	270°	Total
IntraLase	105 ± 10.6		104.8 ± 11.2	106.7 ± 11.2	105.5 ± 10.9
Femto-LDV	156.4 ± 6.9	150.9 ± 7.8	149.8 ± 5.6	151.5 ± 7.1	151.9 ± 7.3
Microkeratome	149.7 ± 7.3		150.1 ± 6.4	150.7 ± 7.9	150.2 ± 7.1

All data represented as mean ± standard deviation

IV. DISCUSSION

Although ultrasound pachymetry has been the gold standard for measurement of central corneal thickness (CCT), it has obvious limitation when evaluating various locations or specific part of cornea. Furthermore, when measuring flap thickness in LASIK patients, there is no choice but to estimate it indirectly by subtracting intraoperative stromal bed thickness from preoperative corneal thickness.¹⁹ Optical coherent tomography (OCT) is one of the prominent alternatives for measurement of corneal flap thickness.²⁰⁻²² Currently used OCTs are divided into time-domain OCT (TD-OCT) and Fourier-domain OCT (FD-OCT) with respect to the way of data acquisition and processing.^{23, 24} Comparative studies between two OCT types in measurement of flap thickness showed that FD-OCT was better in accuracy though both OCTs had good repeatability and reproducibility.²⁵ And CCT values measured by Visante (Carl Zeiss Meditec Inc., Dublin, CA, USA), the TD-OCT, were appeared to be lower than that of ultrasound pachymetry consistently in a series of reports and have a possibility of underestimating due to its own algorithm.²⁶⁻²⁸ Moreover, FD-OCT has much faster scanning speed and higher resolution to obtain more anatomic details.²⁹ Thus FD-OCT could be better for evaluating fine morphology of LASIK Flap than TD-OCT.³⁰ In current study, we used RTVue FD-OCT system which has 5 μm of depth resolution and a speed of 26,000 axial-scan/second with a frame rate of 256 to 4,096 axial-scans/frame. The high magnification lens in the CAM (Cornea-Anterior module) set provided corneal scan with a lateral resolution of 10 μm .

On the RTVue analysis of flap thickness, microkeratome group showed meniscus shape of configuration which has thick periphery with thinner central area, whereas IntraLase group did not have a significant difference between central and peripheral thickness. This finding is consistent with previous reports.¹⁴ Femto-LDV group also showed this tendency of microkeratome group, but the difference were much smaller. We clarified these differences in regularity in each cornea with GLMM analysis and regularity index. There are two possible reasons regarding to the different flap configuration between IntraLase and microkeratome group. First, IntraLase makes corneal curvature to flat surface with zero K value by applanation before the delivery of laser, and thus minimizes the

effect on unique thickness and curvature of each cornea.³¹ So it is possible for laser beam to focus on the intended depth of uniform distance. Second, the amount of vacuum pressure for suction is only about 35 mmHg in IntraLase femtosecond laser while in microkeratome system, about 650 mmHg of vacuum is employed. This difference in suction pressure may cause the regularity of flap. Femto-LDV group showed mixed pattern in flap configuration of former two groups. Because Femto-LDV system has similar cutting geometry with microkeratome in absence of vertical side cut, it is thought to make less even flap than IntraLase, which employs separated laser beam delivery for lamellar and side cut.

Femto-LDV group appeared to make flap that is the closest to the intended thickness. Recently published reports suggested that femtosecond laser could create more precise flap than microkeratome.^{3,14} Various factors can influence the thickness made by microkeratome, which include preoperative corneal thickness, corneal diameter, consistency across the cornea, quality and the entry angle of the blade, cutting mechanism, translation and oscillation rate, suction ring pressure setting, suction duration, room humidity, first-second eye difference, and repeated use of blade.^{18, 19, 32-35} Femtosecond laser system is relatively free from these variables. And this independence from environmental and mechanical factors can contribute to better predictability. We could not find a literature that compared predictability in flap creation between different femtosecond laser systems in PubMed search. In current study, Femto-LDV group was better than IntraLase group in terms of creating flap with intended thickness. We speculated that beam delivery mechanism is related to the difference, which are 'high pulse, low frequency (1 μ J of pulse energy, 60 KHz of repetition frequency)' of IntraLase and 'low pulse, high frequency (nJ level of pulse energy with MHz of repetition frequency)' of Femto-LDV.³⁶ The former is expected to cut tissue more effectively, and the latter is considered to induce less tissue damage and opaque bubble layer. But stromal flap beds of porcine eyes made by both femtosecond laser systems were equally smooth and excellent in quality.³⁷ And their influence on accuracy is unclear and needs further study.

Another concern of this study was incision angle of flap margin, which is considered to be related to epithelial ingrowth. Wang and Maloney³⁸ suggested two possible hypothesis about pathogenesis of epithelial ingrowth. One is direct seeding of isolated cell from epithelium intraoperatively, and the

other is epithelial invasion from the flap margin. From their observation, they believed that the second hypothesis might be true in more cases of epithelial ingrowth. Naoko and colleagues¹⁶ reported that the incidence of epithelial ingrowth was different with respect to the type of microkeratome. And they showed in porcine eyes that the microkeratome with a higher incidence of epithelial ingrowth made the flap edge with smaller incision angle and longer epithelium-traveling distance of incision, comparing to the other one that made nearly a vertical cut at the flap margin. Thus it is desirable for LASIK flap to have vertical incision angle for reducing epithelial ingrowth. In current study, we observed side cut angle of flap margin with RTVue in vivo. IntraLase group showed more acute angle than other two groups. Femto-LDV and microkeratome commonly showed flat and tapered side cut angle. And it fairly corresponded to the similar cutting mechanisms of Femto-LDV and microkeratome, which did not make vertical side cut. There is no report to compare the incidence of epithelial ingrowth between microkeratome and femtosecond laser group yet. Incidence of epithelial ingrowth in conventional LASIK have reported variously from 1 to 20%³⁸⁻⁴², but it was 1.3~1.7% for significant cases that require surgical management.^{16, 43} On the other hand, large cohort study with IntraLase femtosecond laser reported incidence from 0 to 0.3%.^{11, 44, 45} These results suggest that acute side cut angle at flap margin might account for low incidence of epithelial ingrowth.

V. CONCLUSION

In this study, we found that morphological characters of LASIK flap show typical patterns depending on the methods of flap creation. Flap made with femtosecond laser systems showed relatively even configuration and better regularity in thickness. Microkeratome showed excellent predictability in central area of flap, but the disparity between central and peripheral thickness was observed. Morphological differences were also demonstrated between two different femtosecond laser systems. Considering the importance of flap in terms of visual outcome and postoperative complication, it is important to consider these differences in flap creation.

REFERENCES

1. Durrie DS, Kezirian GM. Femtosecond laser versus mechanical keratome flaps in wavefront-guided laser in situ keratomileusis: prospective contralateral eye study. *J Cataract Refract Surg* 2005;31(1):120-6.
2. Buzzonetti L, Petrocelli G, Valente P, Tamburrelli C, Mosca L, Laborante A, et al. Comparison of corneal aberration changes after laser in situ keratomileusis performed with mechanical microkeratome and IntraLase femtosecond laser: 1-year follow-up. *Cornea* 2008;27(2):174-9.
3. Kezirian GM, Stonecipher KG. Comparison of the IntraLase femtosecond laser and mechanical keratomes for laser in situ keratomileusis. *J Cataract Refract Surg* 2004;30(4):804-11.
4. Krueger RR, Dupps WJ, Jr. Biomechanical effects of femtosecond and microkeratome-based flap creation: prospective contralateral examination of two patients. *J Refract Surg* 2007;23(8):800-7.
5. Medeiros FW, Stapleton WM, Hammel J, Krueger RR, Netto MV, Wilson SE. Wavefront analysis comparison of LASIK outcomes with the femtosecond laser and mechanical microkeratomes. *J Refract Surg* 2007;23(9):880-7.
6. Montes-Mico R, Rodriguez-Galietero A, Alio JL, Cervino A. Contrast sensitivity after LASIK flap creation with a femtosecond laser and a mechanical microkeratome. *J Refract Surg* 2007;23(2):188-92.
7. Patel SV, Maguire LJ, McLaren JW, Hodge DO, Bourne WM. Femtosecond laser versus mechanical microkeratome for LASIK: a randomized controlled study. *Ophthalmology* 2007;114(8):1482-90.
8. Chan A, Ou J, Manche EE. Comparison of the femtosecond laser and mechanical keratome for laser in situ keratomileusis. *Arch Ophthalmol* 2008;126(11):1484-90.
9. Binder PS. Flap dimensions created with the IntraLase FS laser. *J Cataract Refract Surg* 2004;30(1):26-32.
10. Stahl JE, Durrie DS, Schwendeman FJ, Boghossian AJ. Anterior segment OCT analysis of thin

- IntraLase femtosecond flaps. *J Refract Surg* 2007;23(6):555-8.
11. Sutton G, Hodge C. Accuracy and precision of LASIK flap thickness using the IntraLase femtosecond laser in 1000 consecutive cases. *J Refract Surg* 2008;24(8):802-6.
 12. Cheng AC, Ho T, Lau S, Wong AL, Leung C, Lam DS. Measurement of LASIK flap thickness with anterior segment optical coherence tomography. *J Refract Surg* 2008;24(9):879-84.
 13. Kim JH, Lee D, Rhee KI. Flap thickness reproducibility in laser in situ keratomileusis with a femtosecond laser: optical coherence tomography measurement. *J Cataract Refract Surg* 2008;34(1):132-6.
 14. von Jagow B, Kohnen T. Corneal architecture of femtosecond laser and microkeratome flaps imaged by anterior segment optical coherence tomography. *J Cataract Refract Surg* 2009;35(1):35-41.
 15. Alio JL, Pinero DP. Very high-frequency digital ultrasound measurement of the LASIK flap thickness profile using the IntraLase femtosecond laser and M2 and Carriazo-Pendular microkeratomes. *J Refract Surg* 2008;24(1):12-23.
 16. Asano-Kato N, Toda I, Hori-Komai Y, Takano Y, Tsubota K. Epithelial ingrowth after laser in situ keratomileusis: clinical features and possible mechanisms. *Am J Ophthalmol* 2002;134(6):801-7.
 17. Ivarsen A, Laurberg T, Moller-Pedersen T. Characterisation of corneal fibrotic wound repair at the LASIK flap margin. *Br J Ophthalmol* 2003;87(10):1272-8.
 18. Seo KY, Wan XH, Jang JW, Lee JB, Kim MJ, Kim EK. Effect of microkeratome suction duration on corneal flap thickness and incision angle. *J Refract Surg* 2002;18(6):715-9.
 19. Flanagan GW, Binder PS. Precision of flap measurements for laser in situ keratomileusis in 4428 eyes. *J Refract Surg* 2003;19(2):113-23.
 20. Maldonado MJ, Ruiz-Oblitas L, Munuera JM, Aliseda D, Garcia-Layana A, Moreno-Montanes J. Optical coherence tomography evaluation of the corneal cap and stromal bed features after laser in situ keratomileusis for high myopia and astigmatism. *Ophthalmology* 2000;107(1):81-7; discussion 8.

21. Ustundag C, Bahcecioglu H, Ozdamar A, Aras C, Yildirim R, Ozkan S. Optical coherence tomography for evaluation of anatomical changes in the cornea after laser in situ keratomileusis. *J Cataract Refract Surg* 2000;26(10):1458-62.
22. Thompson RW, Jr., Choi DM, Price MO, Potrzebowski L, Price FW, Jr. Noncontact optical coherence tomography for measurement of corneal flap and residual stromal bed thickness after laser in situ keratomileusis. *J Refract Surg* 2003;19(5):507-15.
23. Chen TC, Cense B, Pierce MC, Nassif N, Park BH, Yun SH, et al. Spectral domain optical coherence tomography: ultra-high speed, ultra-high resolution ophthalmic imaging. *Arch Ophthalmol* 2005;123(12):1715-20.
24. de Boer JF, Cense B, Park BH, Pierce MC, Tearney GJ, Bouma BE. Improved signal-to-noise ratio in spectral-domain compared with time-domain optical coherence tomography. *Opt Lett* 2003;28(21):2067-9.
25. Prakash G, Agarwal A, Jacob S, Kumar DA, Banerjee R. Comparison of fourier-domain and time-domain optical coherence tomography for assessment of corneal thickness and intersession repeatability. *Am J Ophthalmol* 2009;148(2):282-90 e2.
26. Li H, Leung CK, Wong L, Cheung CY, Pang CP, Weinreb RN, et al. Comparative study of central corneal thickness measurement with slit-lamp optical coherence tomography and visante optical coherence tomography. *Ophthalmology* 2008;115(5):796-801 e2.
27. Li EY, Mohamed S, Leung CK, Rao SK, Cheng AC, Cheung CY, et al. Agreement among 3 methods to measure corneal thickness: ultrasound pachymetry, Orbscan II, and Visante anterior segment optical coherence tomography. *Ophthalmology* 2007;114(10):1842-7.
28. Zhao PS, Wong TY, Wong WL, Saw SM, Aung T. Comparison of central corneal thickness measurements by visante anterior segment optical coherence tomography with ultrasound pachymetry. *Am J Ophthalmol* 2007;143(6):1047-9.
29. Wylegala E, Teper S, Nowinska AK, Milka M, Dobrowolski D. Anterior segment imaging: Fourier-domain optical coherence tomography versus time-domain optical coherence tomography. *J Cataract Refract Surg* 2009;35(8):1410-4.

30. Rosas Salaroli CH, Li Y, Huang D. High-resolution optical coherence tomography visualization of LASIK flap displacement. *J Cataract Refract Surg* 2009;35(9):1640-2.
31. Pfaeffl WA, Kunze M, Zenk U, Pfaeffl MB, Schuster T, Lohmann C. Predictive factors of femtosecond laser flap thickness measured by online optical coherence pachymetry subtraction in sub-Bowman keratomileusis. *J Cataract Refract Surg* 2008;34(11):1872-80.
32. Hsu SY, Chen HY, Chung CP. Analysis of actual corneal flap thickness and confounding factors between first and second operated eyes. *Ophthalmic Surg Lasers Imaging* 2009;40(5):448-52.
33. Kasetuwan N, Pangilinan RT, Moreira LL, DiMartino DS, Shah SS, Schallhorn SC, et al. Real time intraocular pressure and lamellar corneal flap thickness in keratomileusis. *Cornea* 2001;20(1):41-4.
34. Miranda D, Smith SD, Krueger RR. Comparison of flap thickness reproducibility using microkeratomes with a second motor for advancement. *Ophthalmology* 2003;110(10):1931-4.
35. Solomon KD, Donnenfeld E, Sandoval HP, Al Sarraf O, Kasper TJ, Holzer MP, et al. Flap thickness accuracy: comparison of 6 microkeratome models. *J Cataract Refract Surg* 2004;30(5):964-77.
36. Lubatschowski H. Overview of commercially available femtosecond lasers in refractive surgery. *J Refract Surg* 2008;24(1):S102-7.
37. Kermani O, Oberheide U. Comparative micromorphologic in vitro porcine study of IntraLase and Femto-LDV femtosecond lasers. *J Cataract Refract Surg* 2008;34(8):1393-9.
38. Wang MY, Maloney RK. Epithelial ingrowth after laser in situ keratomileusis. *Am J Ophthalmol* 2000;129(6):746-51.
39. Walker MB, Wilson SE. Incidence and prevention of epithelial growth within the interface after laser in situ keratomileusis. *Cornea* 2000;19(2):170-3.
40. Ambrosio R, Jr., Wilson SE. Complications of laser in situ keratomileusis: etiology, prevention, and treatment. *J Refract Surg* 2001;17(3):350-79.
41. Farah SG, Azar DT, Gurdal C, Wong J. Laser in situ keratomileusis: literature review of a developing technique. *J Cataract Refract Surg* 1998;24(7):989-1006.

42. Helena MC, Meisler D, Wilson SE. Epithelial growth within the lamellar interface after laser in situ keratomileusis (LASIK). *Cornea* 1997;16(3):300-5.
43. Stulting RD, Carr JD, Thompson KP, Waring GO, 3rd, Wiley WM, Walker JG. Complications of laser in situ keratomileusis for the correction of myopia. *Ophthalmology* 1999;106(1):13-20.
44. Binder PS. One thousand consecutive IntraLase laser in situ keratomileusis flaps. *J Cataract Refract Surg* 2006;32(6):962-9.
45. Kamburoglu G, Ertan A. Epithelial ingrowth after femtosecond laser-assisted in situ keratomileusis. *Cornea* 2008;27(10):1122-5.

<ABSTRACT(IN KOREAN)>

푸리에 도메인 (Fourier-domain) 방식 빛간섭 단층촬영을 이용한 두 종류의 펨토초레이저와 미세각막절개도에 의해 만들어진 라식(LASIK) 절편의 형태학적 비교

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목적 : 푸리에도메인 방식 전안부 빛간섭단층촬영을 통해, 두 종류의 서로 다른 펨토초레이저를 이용하여 제작된 라식 절편과 미세각막절개도를 사용한 경우의 각막 절편의 두께와 변연부 절단각을 비교하고자 하였다.

방법 : 펨토초레이저 및 미세각막절개도를 이용하여 라식 수술을 시행받은 환자를 대상으로, 각막 절편 제작에 사용한 도구에 따라 IntraLase (AMO Inc., Santa Ana, CA, USA) 군 30명 (60안), Femto-LDV (Ziemer, Port, Switzerland) 군 32명 (64안), 미세각막절개도군 26명 (52안)으로 구분하여 술 후 2개월째에 나안시력, 굴절검사를 시행하였고, RTVue (Optovue Inc., Fremont, CA, USA) 를 이용하여 총 14 지점에서 절편의 두께를 측정하였으며 4 방향에서 절편의 변연부 절단각을 측정하였다. 형태학적 분석은 네 가지 측면에서 이루어졌다. 각막 절편의 평균 두께를 통해 절편의 형태를 비교하였고, 의도한 절편 두께와 측정값과의 차이를 절편 제작의 예측도로 정의하여 평가하였다. 각막 절편의 균일성을 평가하기 위해 모든 측정 위치 사이에서의 통계학적 연관성을 분석하는 동시에 각각의 각막 절편에서 중심부와 주변부의 두께 차이를 비교하였다. 마지막으로 절편 변연부의 절단각을 비교하였다.

결과 : 두 종류의 펄초레이저를 이용하여 만든 각막 절편이 미세각막절개도로 제작한 절편에 비해 비교적 고른 형태를 나타내었다. 절편 두께의 예측도는 Femto-LDV 군에서 다른 두 군에 비해 적었다 ($p < 0.001$). 각 측정 지점 사이의 통계적 연관성 및 각막 중심부와 주변부 두께의 차이는 IntraLase 군에서 가장 적었다 ($p < 0.001$). 절편 변연부 절단각은 IntraLase 군이 다른 두 군에 비해 유의하게 적었던 반면 ($p < 0.001$), Femto-LDV 군과 미세각막절개도군 사이에서는 차이를 보이지 않았다.

결론 : 펄초레이저를 이용하여 제작한 라식 절편은 비교적 균일한 두께와 형태를 가지며, 미세각막절개도는 중심부에서 훌륭한 예측도를 보인 반면 주변부와는 차이를 보였다. 또한 두 종류의 펄초레이저 사이에도 형태학적 차이가 존재하였으므로, 라식 절편의 제작 시에는 이러한 제작 도구의 특징을 세심하게 고려해야 할 것이다.

핵심되는 말 : 라식 절편, 펄초레이저, 미세각막절개도, 푸리에 도메인 방식 빛 간섭 단층촬영, 절편 형태