Thickness Measurements of Corneal Flaps Created with the IntraLase™ FS Laser

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Abstract

Purpose: To evaluate thickness accuracy and predictability of corneal flaps created with the IntraLaser™ FS Laser.

Materials and Methods: Subtraction pachymetry was performed at the time of flap creation, as well as 1 month post-operatively in a series of 30 eyes (17 patients), where intended flap thickness was 130 μm.

Results: Mean flap thickness in humans measured 132 ± 15 μm at both 45 minutes and at 1 month following flap creation.

Conclusion: The IntraLase™ FS Laser creates corneal flaps with highly accurate and reproducible thickness. By reducing the range of potential achieved flap thickness, the safety profile of the overall procedure is significantly improved.

Introduction

Due to its rapid visual rehabilitation, minimal post-operative discomfort and high predictability, laser in situ keratomileusis (LASIK) has become the dominant surgical procedure for the correction of refractive error.[1-3] These LASIK attributes result largely due to creation of a corneal flap, which allows the surgeon to avoid significant disruption of the epithelial surface. While advantageous from these perspectives, creation of a LASIK flap raises a separate set of concerns, many arising from the accuracy and reproducibility of flap thickness with traditional mechanical microkeratomes. Flaps that are too thick increase the potential for a residual bed thickness less than 250 μm, risking compromise of corneal biomechanical strength and the development of corneal ectasia.[4-6] Attempts to create thin flaps pose an increased risk of complications such as buttonholes, due to the relatively large standard deviations in flap thickness associated with mechanical microkeratomes. In addition, thin flaps created with mechanical microkeratomes may be more prone to striae or folds that can affect the visual quality.[7]

The accuracy and predictability of corneal flap thickness has been evaluated extensively for various mechanical keratomes. Significant deviations from both indicated and (more importantly) average flap parameters have been identified, making accurate flap thickness predictions problematic.[8-13] For the traditional microkeratomes, achieved flap thickness is affected by the particular head, plate or blade used, the turbine velocity and translation speed, as well as patients factors such as preoperative corneal pachymetry.[14-16] Flap thickness predictability as reported in the literature range from standard deviations of +/- 26-45 μm. Assuming a normal distribution, these values suggest a range of actual flap thickness +/- 75-130 μm from the average for a particular microkeratome.[17] While the clinical success of LASIK has demonstrated the utility of traditional microkeratome devices, additional safety and precision in this initial step of the procedure has been sought via a number of technical innovations.

The IntraLase ™ FS Laser is the first alternative to standard mechanical keratome technology to be commercially introduced in the United States for flap creation in LASIK. In contrast to excimer lasers, femtosecond lasers do not rely on the inherent wavelength absorption characteristics of corneal tissue to produce their surgical effect. Instead, the near-infrared laser pulses pass through the superficial corneal tissue unabsorbed, until focused to a small spot at a depth determined by the relative position of the focusing lens and the corneal surface. Each pulse initiates a process called laser induced optical breakdown (LIOB) as it reaches this focal point. Multiple pulses placed at the same focal depth produce a resection plane via formation of a layer of small diameter bubbles.[18] Unlike LIOB with nanosecond Nd:YAG or picosecond Nd:YLF lasers, femtosecond LIOB requires very low energy and produces no thermal damage or shock wave transmission to surrounding tissue.[19-24]

To attain micron level depth accuracy, corneal procedures utilize an applanation system consisting of a suction ring and a flat contact lens located at the tip of the laser delivery system. The suction ring fixates the eye, allowing the contact lens to temporarily flatten the front surface of the cornea. The flat contact lens is securely attached to the suction ring by an internal cylindrical clamp, mechanically coupling the eye to the beam delivery system. Corneal flap procedures performed in human eyes with a prototype femtosecond laser systems have demonstrated excellent safety and performance profiles, without alterations in excimer laser refractive nomograms [25,26] Although not evaluated in these studies, a potential reduction in surgical complications has been hypothesized for this technology based on its presumed higher degree of accuracy and predictability of key corneal flap parameters. The goal of the current study was to evaluate thickness accuracy and predictability of corneal flaps created with the femtosecond laser keratome, using standard intra-operative ultrasound techniques.

Materials and Methods

IntraLase™ FS Laser

All procedures utilized the IntraLase FS Laser (IntraLase, Irvine CA) to create the corneal flap or pattern in human, porcine or glass substrates. Laser settings varied according to the particular study performed.

Subtraction Pachymetry

All subtraction pachymetry measurements utilized a single DGH 500 ultrasonic pachymeter (DGH Technology Inc., Exton, PA). Five measurements were collected for each study point.

Surgical and Subtraction Pachymetry Procedures

All (17) patients provided informed consent prior to inclusion in the study. Four patients were male and 13 were female. The mean age was 29 ± 5.0 years. Four patients underwent unilateral procedures, while 13 underwent bilateral procedures. Patients were placed in the supine position and a lid speculum was placed after application of topical anesthesia. Central corneal thickness (CCT) was initially measured prior to placement of the suction ring. The suction ring was then centered on the cornea, the syringe depressed to the 0 ml mark and released to achieved vacuum. CCT was again measured after applying the suction ring (post-suction, PS CCT). The cornea was applanated and the IntraLase flap procedure performed. In preliminary studies, it was found that measurement of the bed was more difficult to perform if the flap was lifted soon after it was created, often requiring moistening to obtain a reading. For consistency, initial flap elevation was delayed for 45 minutes, allowing bubbles in the interface to resolve and obviating the need for such moistening. The CCT was then re-measured, the flaps lifted and bed pachymetry performed. To determine if this delayed post-operative measurement was accurate, excimer treatments were delayed until 4 weeks later. One month after the original IntraLase procedure, total CCT (1 month CCT) and stromal bed (1 month stromal bed) were repeated and the excimer treatment performed. Following the original flap creation, and then again following excimer laser treatment, eyes were treated with tobradex (Tobramycin 0.3% / Dexamthasone 0.1%) four times per day for 7 days. While flap depth, diameter, hinge position and size, can all be customized for a particular eye by the surgeon, these parameters were restricted in this study. All flaps utilized an intended depth of 130 μ, diameter of 8.8 mm, superior hinge placement and 45-degree hinge size. Excimer ablations were performed with a NIDEK EC-5000 (Freemont, CA), using the standard nomogram and operative technique of the primary surgeon. Post-operative examinations were performed at 1 day, 1 week, 1, 3 and 6 months and included uncorrected visual acuity (UCVA), manifest refraction (MR), best corrected visual acuity (BCVA), central pachymetry, corneal topography and slit lamp examination.

Statistical Analysis

All statistical analyses were performed using SAS v 8.02. One sample T-test was used to compare means achieved flap thickness to the intended thickness. Pearson Correlation coefficients were used to determine relationship between achieved flap thickness and preoperative central corneal thickness and average keratometry. A p value of ≤ 0.05 was considered statistically significant.

Results

Clinical Outcomes

No intra-operative or post-operative flap complications were noted in any eye, either during the initial flap creation or the subsequent re-lift and excimer treatment. All eyes retained their pre-operative manifest refraction following the initial flap creation procedure, with no loss of BCVA. Following excimer treatment, all eyes attained UCVA of 20/20 or better by 1 month post-operatively.

Central Corneal Thickness Measurements

CCT was measured at four different time points; after placement of lid speculum, following placement of lid speculum and suction ring, 45 minutes following flap creation (after resolution of gas bubbles), and prior to re-lift procedure 4 weeks after flap creation. As seen in Table 1, statistically significant differences were noted at each of these time points.

Table 1

Central Corneal Thickness Measured at Different Time Points

CCT Measurement Time Point	After placement of lid speculum	Following placement of lid speculum and suction ring	45 minutes following flap creation (after resolution of gas bubbles)	Prior to re-lift procedure 4 weeks after flap creation
Average (+/- SD)	549 ± 25	531± 26	567± 25	559 ± 28
Average Change from Preoperative	N/A	-18 ± 10	18 ± 8	11 ± 12

On average, corneal thinning of 18 μm was noted following suction ring placement, while an average of 18 μm thickening was noted 45 minutes following flap creation. The majority of this thickening was also noted 4 weeks later (11 μm, prior to the re-lift procedure, suggesting a predominately biomechanical etiology, rather than transient corneal edema.

Flap Thickness Calculations

Corneal bed thickness (CBT) measurements could be attained reliably when gas bubbles were no longer present, approximately 30-45 minutes after the flap creation procedure. Mean corneal flap thickness (CFT) was calculated by subtracting CBT from the corresponding CCT at 45 minutes and 1 month (Table 2)

Table 2

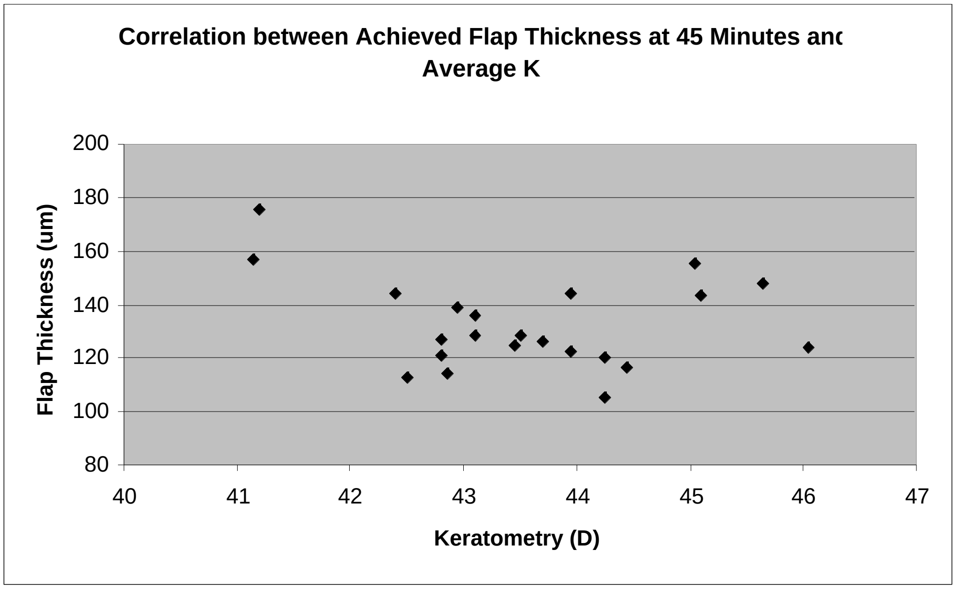
Calculated Flap Thickness at 45 minutes and 4 weeks

		45 Minutes After Flap Creation		4 Weeks After Flap Creation	
Number of Eyes	Intended Flap Thickness (um)	Achieved Flap Thickness (Mean ± SD um)	Range (um)	Mean ± SD Flap Thickness (um)	Range (um)
30	130	132 ± 15	106–175	132 ± 15	103–180

At both the 45 minutes and 4-week time points, no significant difference was noted between the intended 130 μm flap thickness and the achieved 132 μm flap thickness (p = 0.40 and p = 0.46, respectively).

Correlation of Flap Thickness with Preoperative Keratometry

No statistically significant correlation was identified between the preoperative keratometry and achieved flap thickness at 45 minutes ($r = -0.24$, $p = 0.27$) or at 1 month ($r = -0.36$, $p = 0.10$) however a trend toward thicker flaps with flatter keratometry was observed. (Figure 1).



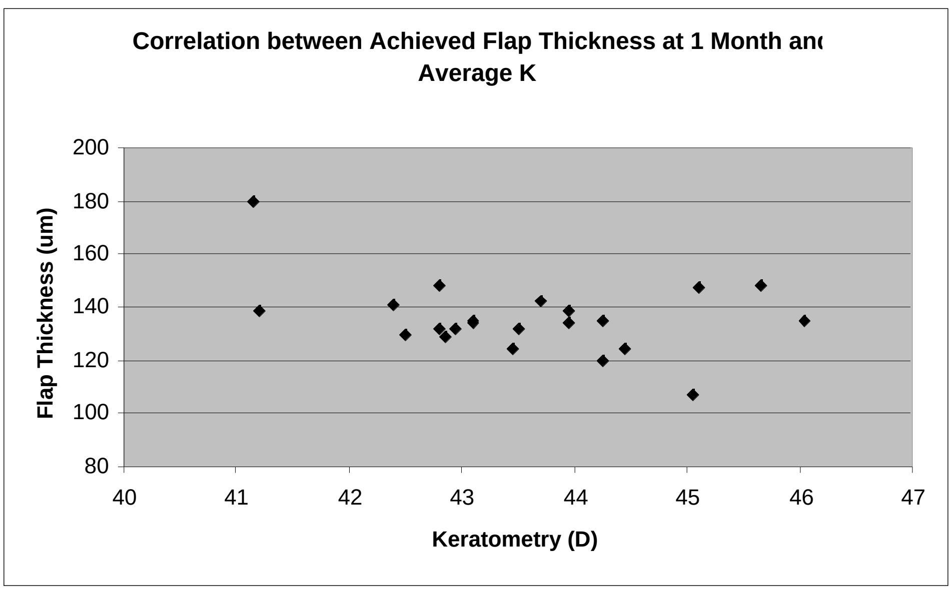
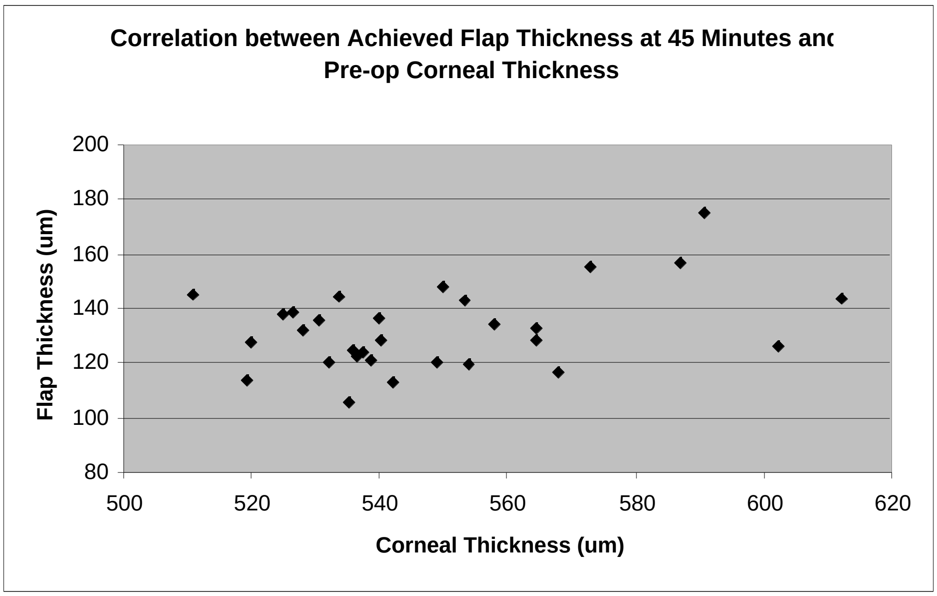


Figure 1: Correlation between achieved flap thickness and average corneal keratometry at 45 minute (A) and 4 week (B) measurement points.

Correlation of Flap Thickness with Preoperative Central Corneal Thickness

There was a weak, but statistically significant positive correlation between preoperative central corneal thickness and achieved flap thickness at 45 minutes ($r = 0.38$, $p = 0.03$) but not at 1 month ($r = 0.25$, $p = 0.17$) (Figure 2).



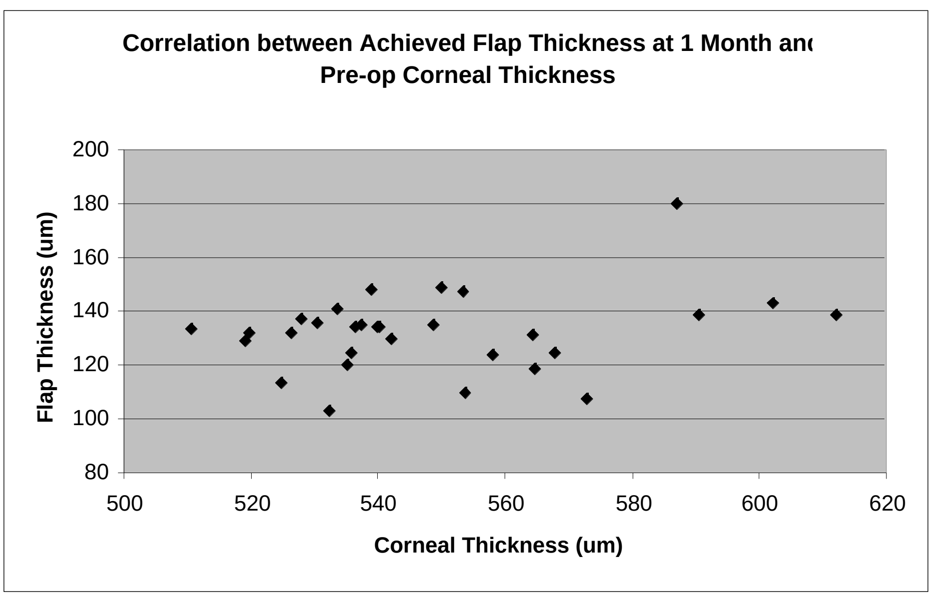
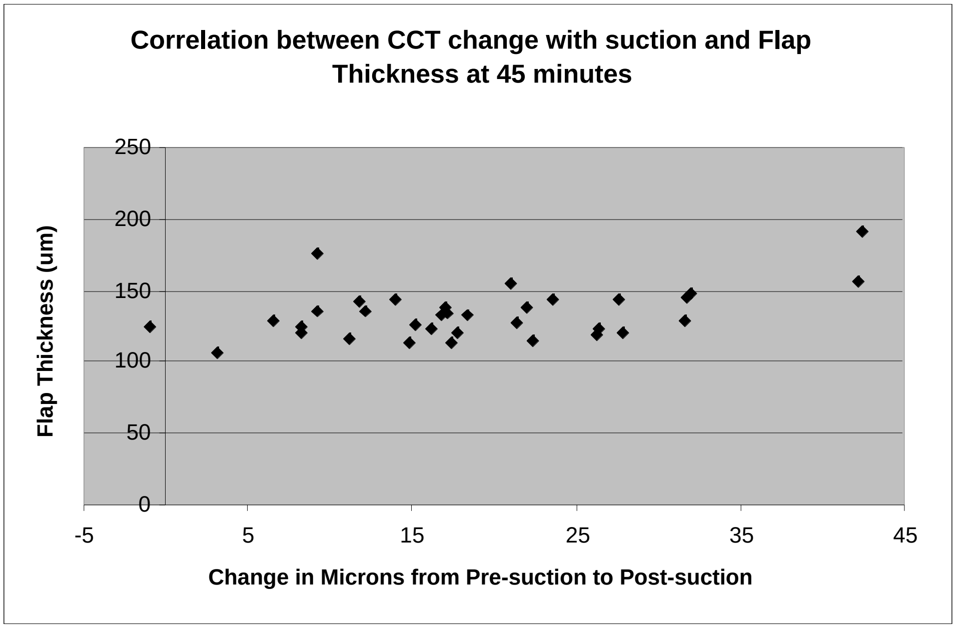


Figure 2: Correlation between pre-operative full corneal thickness and achieved flap thicknesses at 45 minutes (A) and at 4 weeks (B).

Correlation of Flap Thickness with Degree of Corneal Thinning after Suction Ring Placement

There was a small positive correlation between the change in CCT after suction ring placement and flap thickness at 45 minutes (*r* = 0.45) and 4 weeks (*r* = 0.32) (Figure 3).



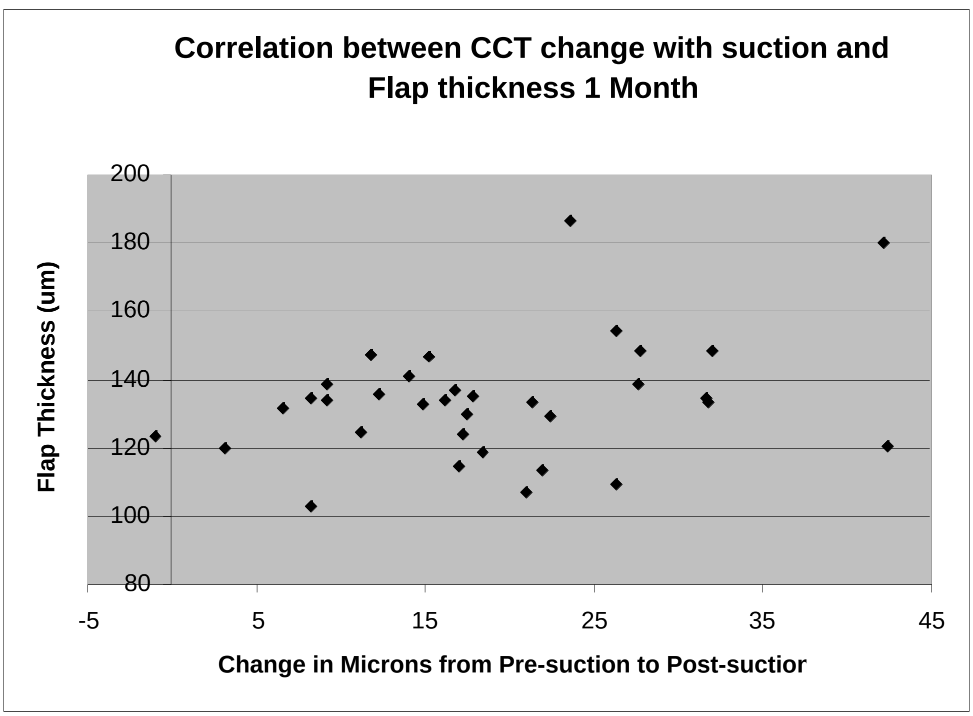


Figure 3: Correlation between corneal thickness change after suction ring and flap thickness at 45 minutes (A) and 4 weeks (B).

Discussion

The accuracy and predictability of corneal flap creation has a significant impact on the safety of the LASIK procedure, with both thinner and thicker than anticipated flaps having the potential for clinical impact. While marked microkeratome head values have been shown to be consistently inaccurate, even the use of the average achieved values does not correct for the fact that these devices have large standard deviations and therefore can produce, in any single cut, a wide range of flap thickness.

Assuming a normal distribution, approximately 15% of flaps will be more than one standard deviation thinner or thicker than the average achieved value for a given keratome, while 2.5% will be more than 2 standard deviations thinner or thicker. Put another way, about 1 in a 100 cases will have flaps more than 2 standard deviations thinner and 1 in a 100 will have flap more than 2 standard deviations thicker.

In our series of 30 cases where intended thickness was 130 μm and standard deviation was 15 μm, no flap measured below 2 standard deviations from the mean (<100 μm) and one flap measured above 2 standard deviations from the mean (>160 μm). If we assume a 30 μm standard deviation for standard microkeratomes (published values range from 25-40 μm) and approximately the same average achieved flap thickness, we would expect approximately 7 times the number of cases with flaps less than 100 μm or greater than 160 μm. Using these same numbers, approximately 1 in 100 flaps would be less than 70 μm and another 1 in 100 would measure greater than 190 μm (see Figure 4). By reducing the standard deviation and range of achieved flap thickness to approximately half that achievable with traditional microkeratomes, the IntraLase FS Laser significantly reduces the risk of an overly thin or thick flaps.

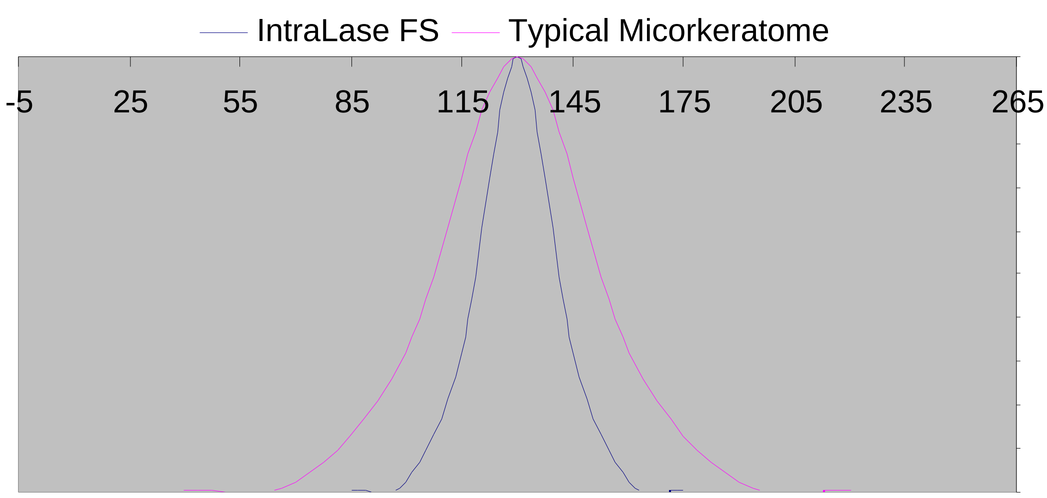


Figure 4: Distribution of flap thickness around mean for 15 μm (blue) and 30 μm (pink) standard deviations.

The flexibility to select flap depth adds another degree of safety to the IntraLase™ FS Laser, providing the surgeon the ability to tailor the risk of a flap thickness error to a particular patient's needs. By selecting a particular desired flap thickness, the surgeon can utilize the smaller standard deviation to more closely approximate a desired flap thickness range, something not possible with mechanical keratomes (that typically have only a few surgical heads). For example, a thicker cornea undergoing a small refractive correction would pose a smaller risk for a residual bed thickness below the 250-300 μm recommended minimum. Assuming a standard deviation of 15 μm, changing to a thicker flap selection (from 130 μm to160 μm) would shift the 2 standard deviation range of achieved thickness from 100-160 μm to 130-190 μm, and the 3 standard deviation range of achieved thickness from 115-205 μm reducing the risk of an overly thin flap. In contrast, in a thinner cornea undergoing a higher correction, selection of thinner corneal flap setting of 120 microns would shift the 2 standard deviation range of achieved thickness to 90-150 μm, and the 3 standard deviation range of achieved thickness to 75-165 μm reducing the risk of an overly thick flap. Based on a particular surgeon's results, the risk profile for a clinically significant flap depth error can be tailored continuously for a given patient's circumstances. Such tailoring is not practical with typical keratomes with more limited average flap depths and standard deviations.

Flap the thickness achieved with the microkeratome has been shown to be affected by several factors including: pre-operative corneal thickness.[15,16] In contrast, weak correlation with corneal thickness was identified for the IntraLase™ FS Laser. The weakly positive correlation between and achieved flap thickness would tend to add to the safety potential of the procedure, as thinner corneas would be less likely to have thicker flaps, thus preserving more corneal tissue in the bed.

The trend toward thicker achieved flaps when there is a larger change in corneal thickness after suction ring placement can be understood from the mechanism of depth registration for the IntraLase™ FS Laser. Since depth is calibrated from the bottom contact glass that applanates the cornea, any change in total corneal thickness will directly affect the achieved flap thickness. On average, thinning of approximately 20 microns is seen after suction ring placement, a number that is accounted for in the system's depth nomogram. Changes in central corneal thickness that are larger or smaller than this average thinning will add to the deviation from the average flap thickness. Measurement and correction during the procedure of large deviations from the average might further reduce the range of achieved flap thickness.

These studies give guidance on the performance of subtraction pachymetry after creation of the flap with the IntraLase™ FS Laser. We determined flap thickness at two time points to identify any potential short-term effects, such as corneal edema, that might affect the accuracy of our measurements. This possibility was investigated due to the longer time interval between flap creation and subtraction pachymetry (necessitated by the presence of intrastromal cavitation bubbles that distort the ultrasound signal). In fact, flap thickness measurements at the two time points were similar, reinforcing the accuracy of the measurement made on the first surgical day. Interestingly, total corneal thickness increased at both time points, suggesting a biomechanical change that others have also noted.[27]

Although other in vivo measurement techniques (such as high frequency ultrasound or confocal microscopy)[17,28] may provide greater absolute accuracy, the use of relative measurements in subtraction pachymentry (pre-lift CCT versus post-lift CBT) already provides for a high degree of reproducibility. In our study, the standard deviation of individual measurements was less than 3 μm, suggesting that more sophisticated measurement techniques are not required to demonstrate a high degree of central flap thickness reproducibility. Regional flap thickness, as demonstrated by Reinstein et al,[17] may provide important information regarding flap thickness uniformity, something not addressed in this study.

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