Femtosecond Laser-Assisted LASIK Flap Complications

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ABSTRACT

PURPOSE: To discuss intraoperative and postoperative femtosecond laser-assisted LASIK flap complications and their management.

METHODS: Review of published literature.

RESULTS: Flap creation is a critical step in LASIK. The femtosecond laser has improved the overall predictability and safety of the lamellar incision, but complications can still occur during or after flap creation. Although many complications (eg, epithelial ingrowth and flap striae) were reduced with the femtosecond laser application, other specific complications have emerged, such as vertical gas breakthrough, opaque bubble layer, and transient light-sensitivity syndrome.

CONCLUSIONS: The application of femtosecond laser technology to LASIK flap creation has increased greatly since its introduction. These lasers have improved the safety and predictability of the lamellar incision step. The majority of the femtosecond laser-assisted flap complications can be well managed without significant effects on refractive outcomes.

peripheral asymmetric meniscus. Once detected, it is important to discontinue the laser treatment immediately. Typically, the femtosecond laser cut can be repeated at the same depth and, importantly, the same applanation cone should be used unless a manufacturing defect is noted. The vertical limbal pocket is typically created to absorb the cavitation bubbles and this portion of the procedure can be deactivated if it was already created during the first pass. If the loss of suction occurs during the side cut, the surgeon must ensure that the subsequent side cut is created within the lamellar cut used to fashion the flap. The laser manufacturer recommends decreasing the subsequent side cut by 0.5 mm in diameter.

Shah and Melki\textsuperscript{1} reported that multiple raster passes do not result in an irregular stromal bed or intersecting flaps. Surface ablation can be considered over the incomplete flap if repeated suction attempts prove unsuccessful,\textsuperscript{11} but we recommend doing this at least 2 months later so that an excessive healing response resulting from the simultaneous lamellar cut and surface ablation does not lead to stromal haze. A published study found a 4.4\% rate of suction loss with the VisuMax laser, whereas other studies found rates of 0.8\% and 0.2\% with the IntraLase laser.\textsuperscript{12}

**Bleeding**

 Conjunctival hemorrhages can occur during suction or when multiple suction applications are needed due to suction loss or decentration.\textsuperscript{5} When they occur, these conjunctival hemorrhages clear over 1 to 2 weeks and do not affect the outcome of the surgery. One study found subconjunctival hemorrhage in 68.9\% of eyes that had LASIK with the IntraLase platform but no eyes that had LASIK with the VisuMax platform.\textsuperscript{12} This difference could be attributed to differences in the docking mechanisms between the two lasers. Thus, suction is applied to the conjunctiva/sclera with the IntraLase laser but is applied to the cornea with the VisuMax laser.

Concomitant neovascularization associated with rosacea, atopy, prominent limbal vascularization or prior contact lens use, along with decentered or large diameter flaps, may contribute to bleeding at the edge of the flap.\textsuperscript{12} This bleeding is easily controlled with sponges during the ablation and tamponade is achieved when the flap is replaced.\textsuperscript{1} If the bleeding is not controlled and enters the ablated zone during excimer laser treatment, it can create irregular astigmatism. Also, blood must be irrigated from the interface during flap reposioning or there will be a high risk of diffuse lamellar keratitis (DLK). Avoiding superior flap decentration and the use of a smaller flap diameter can prevent bleeding at the flap edge in patients with peripheral corneal neovascularization.

**Epithelial Defects**

 Trauma to the epithelium can occur with femtosecond laser-assisted LASIK when the laser makes the pocket and shock waves traumatize the overlying epithelium or when surgeons have difficulty in inserting the dissecting spatula under the flap edge. It is important to identify preoperatively risk factors for large epithelial defects such as surgery in elderly patients, patients having anterior basement membrane dystrophy, a history of recurrent erosion syndrome, use of larger flap diameters, and application of excessive topical anesthetic. Studies have shown that epithelial defects are much less likely to occur during femtosecond laser-assisted LASIK flap formation compared to the mechanical microkeratome LASIK flap formation.\textsuperscript{13,14} The main advantage of the femtosecond laser is the absence of the microkeratome rotational movement, which can lead to tearing or shearing of the epithelium.\textsuperscript{1}

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**TABLE 1**

| Intraoperative and Postoperative Complications Related to Femtosecond Laser-Assisted LASIK Flap Creation |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Intraoperative | | | | | | | | | | | |
| Loss of suction | | | | | | | | | | | |
| Bleeding | | | | | | | | | | | |
| Epithelial defects | | | | | | | | | | | |
| Vertical gas breakthrough\textsuperscript{a} | | | | | | | | | | | |
| Anterior chamber gas bubble\textsuperscript{a} | | | | | | | | | | | |
| Opaque bubble layer\textsuperscript{a} | | | | | | | | | | | |
| Flap tears | | | | | | | | | | | |
| Interface debris | | | | | | | | | | | |
| Postoperative | | | | | | | | | | | |
| Dislocated flaps | | | | | | | | | | | |
| Striae and folds | | | | | | | | | | | |
| Dry eye | | | | | | | | | | | |
| Epithelial ingrowth | | | | | | | | | | | |
| Diffuse lamellar keratitis | | | | | | | | | | | |
| Infectious keratitis | | | | | | | | | | | |
| Transient light-sensitivity syndrome\textsuperscript{a} | | | | | | | | | | | |
| Rainbow glare\textsuperscript{a} | | | | | | | | | | | |
| Corneal ectasia | | | | | | | | | | | |
| Interface haze | | | | | | | | | | | |

\textsuperscript{a}Complication specific to femtosecond laser.
Patients with a small epithelial defect can proceed with LASIK as planned and are treated with a bandage contact lens and antibiotics. Importantly, topical corticosteroids should be given every 2 hours while awake for the first 24 to 48 hours as prophylaxis against the development of DLK.15-17 The epithelium produces large quantities of cytokines such as interleukin-1 alpha that are released by epithelial injury and, in turn, stimulate keratocytes to produce chemokines that attract inflammatory cells.15

**Vertical Gas Breakthrough**

A thin flap, previous radial keratotomy surgery, corneal scars, and microscopic breaks in the Bowman’s membrane may contribute to buttonhole flaps with vertical gas breakthrough.18 Cavitation bubbles from the femtosecond laser can dissect upward toward the epithelium and may either stay below Bowman’s membrane or break through the epithelium (buttonhole). A true buttonholed flap should not be lifted because it can lead to scarring or epithelial ingrowth.19 When a full buttonhole occurs, the eye can typically be treated with photorefractive keratectomy and mitomycin C several months later so that the area of the buttonhole is removed completely.20 If the eye with a buttonhole has hyperopia, it may be necessary to use a combination of phototherapeutic keratectomy and photorefractive keratectomy for hyperopia to remove the buttonhole while providing refractive correction.

**Anterior Chamber Gas Bubbles and Opaque Bubble Layer**

Cavitation gas bubbles are formed during femtosecond flap creation and can expand into a cleavage plane at the stromal interlamellar space, which connects to the surface via the side cut. Thus, the presence of an opaque bubble layer is a well-known intraoperative finding on all femtosecond laser platforms (Figure 1).21 It is hypothesized that when the laser energy is too high (causing excessive bubbles) or too low (resulting in an inadequate pocket to vent the bubbles), microplasma bubbles can travel in errant directions and push apart collagen fibrils around them and expand into space between the bubbles.11

Opaque bubble layer may lead to a tighter flap adhesion, which can result in flap tears if the flap dissection is not performed carefully.1,21 In the majority of cases, cavitation bubbles and opaque bubble layer clear spontaneously and the authors prefer to wait 30 minutes prior to excimer laser ablation so that the features applied by custom ablation that are measured in a few microns are not confounded by these transient space-occupying bubbles.

Some femtosecond laser platforms produce a venting canal incision at the hinge of the flap to facilitate the release of the cavitation bubbles.21,22 A smaller diameter flap should be selected by the surgeon when excessive scleral show is noted after application of the suction ring.11

Anterior chamber gas bubbles are occasionally noted during femtosecond laser flap formation and these bubbles can interfere with pupil tracking by the excimer laser.15 Gas bubbles in the anterior chamber appear to correlate with femtosecond laser dissections that are too close to the limbus. Most surgeons test the excimer laser tracking prior to lifting the LASIK flap and then wait for the bubbles to reabsorb if interference is noted.21

**Flap Tears**

Femtosecond laser-created flaps are often more difficult to lift compared to microkeratome-created flaps,9 and the risk of a tear is even higher because the flaps tend to be thinner. Thus, unless adequate care is taken during the passage of an instrument to release the femtosecond laser flap from the underlying bed, the flap can inadvertently be torn. If the tear occurs at the hinge, then a free cap can be produced. If a torn flap compromises the pupillary axis, then it is better to reposition the flap and abort the procedure. Surface ablation photorefractive keratectomy/phototherapeutic keratectomy can be done at another time to complete the treatment and remove the resulting scar. Stromal ablation can be performed in some cases with a small peripheral flap tear.23

This complication should be exceedingly rare if the surgeon ensures that adequate suction is obtained, uses optimized energy settings, and uses careful technique. In most cases, it is better to wait and perform surface ablation treatment several months later.1

**Figure 1.** Opaque bubble layer (arrow) noted immediately after femtosecond laser-assisted LASIK flap creation.
**INTERFACE DEBRIS**

Debris in the interface is common after all LASIK procedures and is generally attributable to meibomian gland secretions, eyelashes, fibers from sponges, or talc from gloves. Adequate irrigation is the most effective approach to remove debris in the flap interface.\(^1\) When debris is noted after surgery, usually it is inert and can simply be observed if there is no inflammatory reaction or visual symptoms associated with the debris. However, debris overlying the pupil should be removed if visual symptoms or a loss of corrected distance visual acuity is noted. Debris is best removed by complete lifting of the flap with copious irrigation.

**POSTOPERATIVE FLAP COMPLICATIONS**

**Dislocated Flaps**

The incidence of postoperative flap dislocation is low after femtosecond laser-assisted LASIK, but it can occur any time after surgery and most commonly presents with acute pain and decreased vision after mechanical trauma to the flap. In the first 24 hours following the procedure, it can be secondary to minor insults such as rubbing the eye or eyelid squeezing.\(^2\)

The highest incidence of flap displacements was found after surgery for hyperopia and the lowest rates after surgery for mixed astigmatism and myopia with femtosecond lasers.\(^2,24\) Other studies also showed a low incidence of flap displacements in LASIK flaps created with femtosecond lasers, which is most likely related to better flap stability associated with better angulation of the side cut and resulting increased flap adhesion strength.\(^1,2,25\)

A dislocated flap should be repositioned immediately. The underside of the flap and the stromal bed may need to be scraped to remove epithelial ingrowth. Any folds should be treated with flap elevation, hydration, and repeated massage with an iris spatula, and epithelial debridement may be needed to flatten recalcitrant flap folds. Use of contact lenses, placing a shield over the eyes while sleeping, and encouraging eyelid closure in the immediate postoperative period are some protective measures used to avoid this complication.

**STRIAE AND FOLDS**

Striae and folds are common postoperative flap complications that can lead to symptoms such as halos, diplopia, glare, and starbursts. If they involve the visual axis, folds can induce irregular astigmatism and decrease the corrected distance visual acuity (Figure A, available in the online version of this article). Femtosecond laser flaps have stronger adhesion than microkeratome flaps, which may lead to a lower incidence of striae or folds. Proposed etiologies include trauma, dryness of the flap leading to shrinkage, misalignment, flap desiccation and contraction, and changes in the corneal contour in corrections for both myopia and hyperopia (the flap and bed do not retain the same contour after application of the excimer laser treatment).\(^2,27\)

Management can range from light stroking with a moist surgical sponge to lift the flap, to hydrating and stretching the flap radially, followed by repositioning, and swelling the flap with hypotonic solutions. Suturing the flap can also be considered if the striae do not resolve with less invasive treatment.\(^1,9\) In cases of flap striae that are resistant to multiple treatments, surface ablation\(^26\) and phototherapeutic keratectomy with masking smoothing can be considered as helpful alternatives.

**DRY EYE AND LASIK-INDUCED NEUROTROPIC EPITHELIOPATHY**

Dry eye or LASIK-induced neurotrophic epitheliopathy is the most common complication after LASIK (Figure B, available in the online version of this article). Proposed mechanisms to explain its etiology include destruction of the corneal nerve endings, decreased blinking rate, decreased normal and reflex stimulation of tear production, decreased tear film stability and distribution, increased evaporation of the tears, and loss of limbal goblet cells.\(^7,27,28\) Furthermore, injury to the corneal sensory nerves after refractive surgery could produce aberrant impulse discharges that might evoke sensations of dryness.\(^7\) Reduction in symptoms with nerve regeneration into the flap suggests that neurotropic loss is likely the leading factor.\(^27\)

Femtosecond lasers seem to induce less nerve damage due to thinner and more planar flaps with less damage to corneal nerves, as well as limbal and goblet architecture.\(^28\) Other studies failed to show a correlation between flap thickness or ablation depth and the incidence of dry eye.\(^29\)

Lubrication with preservative-free artificial tears is all that is required in many patients until the corneal nerves regenerate at 6 to 8 months after surgery. In more severe cases, topical cyclosporine A should be considered to treat the underlying inflammatory dry eye condition because in most cases there is a combination of both inflammatory dry eye and LASIK-induced neurotrophic epitheliopathy.\(^28,30\) Temporary collagen plugs or longer-lasting silicone punctal plugs, along with the short-term use of corticosteroids, have been used to control dry eye symptoms.\(^30,31\)

**EPITHELIAL INGROWTH**

The incidence of epithelium ingrowth is lower in LASIK flaps created with femtosecond lasers compared
Epithelial ingrowth typically presents as islands of cells in the lamellar stromal interface associated with a fibrotic demarcation line (Figure C, available in the online version of this article). When severe, this epithelium can mechanically block nutrient diffusion to the overlying flap and cause flap necrosis. The majority of the growth is seen within the first 2 months after LASIK.

Some of the proposed mechanisms include epithelial cell implantation by a microkeratome blade or capture of epithelial cells in the interface when the flap is repositioned. It has also been proposed to occur by backflow of fluid carrying epithelial cells beneath the flap and epithelial cell invasion under the flap through a fistula or buttonhole. It appears to be more common in patients with epithelial basement membrane dystrophy.

The incidences of DLK, epithelial defects, and thinner flaps were correlated with a higher incidence of epithelial ingrowth.

Epithelial ingrowth is categorized in Table 2. Usually, treatment of epithelial ingrowth involves lifting the flap and debriding epithelial cells from the stromal bed and the posterior aspect of the flap with a scalpel blade. Some have proposed the use of ethanol or phototherapeutic keratectomy, but those measures are rarely needed. Copious irrigation of the interface, pushing any tongues of epithelium back from the flap edge, and use of a bandage contact lens for the first 24 hours after removal of epithelial ingrowth are helpful in preventing recurrence. Suturing the flap or the use of fibrin glue to seal the interface can be considered in recurrent cases, but are only rarely necessary. Ayala et al. suggested Nd:YAG laser as a treatment option for epithelial ingrowth, but we do not recommend this procedure due to the difficulty of removing all epithelial cells and the risk of progression and further vision loss if the treatment fails. A steeper side cut angle when creating the femtosecond flap can also help decrease the incidence of epithelial ingrowth.

**Diffuse Lamellar Keratitis**

DLK is a rare, nonspecific sterile inflammatory response typically seen within the first week after LASIK that occurs in the interface of the flap and underlying stroma (Figure D, available in the online version of this article). Patients can be asymptomatic or present with decreased vision and pain. The design of the 60-, 150-, or 200-kHz femtosecond laser models allowed for much lower energy delivery to cut the flap and, therefore, a substantial reduction in keratocyte necrosis to the point that the overall inflammatory response is not significantly different from that noted with mechanical microkeratomes. Two factors commonly associated with DLK are flap epithelial defects and blood retained in the interface, and increased frequency of topical corticosteroids is needed to prevent DLK in the first 48 hours after surgery when either of these occur after LASIK. Bacterial endotoxin or exotoxin from sterilizers, meibomian secretions, and infectious keratitis can also cause DLK.

Linebarger et al. classified DLK according to Table 3. Central toxic keratopathy mimics stage 4, but it occurs early in the postoperative period and is noninflammatory. It is important to exclude infection and it is wise to do so by culture if the condition is sufficiently severe that the flap should be lifted.
DLK can occur even years after LASIK when there is trauma to the corneal epithelium. DLK is acutely responsive to aggressive topical corticosteroid use as frequently as every hour in the early stages for stage 1 and 2 disease. Higher potency steroids, such as dexamethasone, and oral prednisone 60 mg per day can be considered for more severe stage 3 and 4 cases. For stage 3 and 4 DLK, lifting the flap and profuse irrigation, along with frequent potent corticosteroids, are crucial to arrest the progression of the inflammatory response to stromal necrosis.

MICROBIAL KERATITIS

Microbial keratitis after LASIK is rare, but it is one of the most dreaded postoperative complications and is not specific to the femtosecond laser. Erythema (redness), decreased vision, photophobia, and pain can occur acutely or gradually, and begin within days or weeks of surgery. Bacterial keratitis tends to present earlier, within 3 to 5 days, whereas atypical mycobacteria or fungus presents a few weeks later. It is treated with broad-spectrum antibiotics, flap lift and irrigation, culture, and possible flap amputation for recalcitrant cases.

One prophylactic measure that can be taken is to use broader spectrum antibiotics in the early postoperative period following LASIK. If the surgeon experiences multiple cases, then a switch to a broader spectrum antibiotic should be considered, in addition to investigation into a possible breakdown in sterilization methods or a new tool, such as marker pens, that can be contaminated.

PRESSURE-INDUCED STROMAL KERATITIS

Pressure-induced stromal keratitis is caused by acute corticosteroid response and resolves only with cessation of corticosteroid use and intraocular pressure lowering. It is often diagnosed incorrectly as DLK, with failure to recognize or measure the increased intraocular pressure, which is often elevated from prolonged corticosteroid use. Because fluid can accumulate in the interface, it may cause a false low intraocular pressure, which can delay the diagnosis and treatment and result in severe optic nerve damage.

TRANSIENT LIGHT-SENSITIVITY SYNDROME

Transient light-sensitivity syndrome is a rare and unique side effect of femtosecond laser-assisted LASIK that was primarily associated with the 6- and 15-kHz IntraLase models, but has been noticed rarely with 30- and 60-kHz or even later models. It has been described as an intense light sensitivity with normal visual acuity and unremarkable slit-lamp examination. It is observed within 2 to 6 weeks after femtosecond laser-assisted LASIK, although it can rarely occur several months after surgery. Although the etiology is unknown, it is most likely that the expelled gases traumatize the ciliary body and trigger localized inflammation.

Symptoms usually regress with intensive topical corticosteroids every hour while awake for 48 hours followed by a taper over 2 weeks. Oral steroids are useful in recalcitrant cases.

RAINBOW GLARE

Rainbow glare is another side effect that is unique to the femtosecond laser, and appears to be much more common with specific brands of femtosecond lasers. This phenomenon is believed to be secondary to diffractive light scattering and we believe it results from irregularities in the lamellar interface produced by the laser, especially when there is slight misalignment between the flap and bed so that these irregularities are not masked but are transmitted to the corneal surface. Symptoms occur within 3 months and patients describe seeing 4 to 12 bands of color.

It is difficult to treat rainbow glare and other visual dysphotopsias. The symptoms tend to improve after some time and treating the ocular surface can also help. If residual refractive error is present, one can do a wavefront measurement and treat the residual correction. In some cases, masking smoothing phototherapeutic keratectomy performed on the bed and posterior surface of the flap can eliminate the condition.

POSTOPERATIVE CORNEAL ECTASIA

Iatrogenic corneal ectasia is a rare complication of LASIK that usually occurs in eyes with predisposing factors such as forme fruste keratoconus. It is hypothesized that thinner and more predictable flaps obtained using the femtosecond laser lead to better biomechanical stability of the cornea and a lower risk of ectasia.

It is important to carefully screen patients with a detailed history and examination, including corneal topography, to ascertain whether they present risk factors or characteristics suggestive of keratoconus or pellucid marginal degeneration. In addition, maintaining the posterior residual stromal bed thickness greater than 300 µm can also decrease the incidence of corneal ectasia.

A new metric to evaluate ectasia risk factor after LASIK was recently introduced. Percentage of tissue altered (PTA) determines the integrated relationship between central corneal thickness (CCT), flap thickness (FT), ablation depth (AD), and the residual stromal bed. It is calculated by the formula PTA = (FT + AD)/CCT and recent studies have shown that a PTA of 40% or
more is associated with increased ectasia risk, even in eyes with normal preoperative corneal topography.\textsuperscript{48,49}

**INTERFACE HAZE**

The incidence of haze is significantly less after LASIK compared to surface ablation. This is due to maintenance of the central corneal epithelial basement membrane and a consequential decrease in myofibroblast generation, which in turn decreases the incidence of fibrosis and haze.\textsuperscript{41,50,51} Any damage to the epithelial basement membrane, such as with a buttonhole flap, is usually associated with the development of localized haze. The mainstay of treatment for these eyes remains corticosteroids.\textsuperscript{1}

**CONCLUSION**

Femtosecond laser-assisted LASIK has made flap creation more predictable compared to microkeratome-assisted flap creation. Although there are fewer complications as a consequence, they can still occur and it is important to be able to identify and manage them as soon as possible. Most of the specific femtosecond laser-assisted LASIK flap complications can be managed without significant effects on refractive outcomes.

**AUTHOR CONTRIBUTIONS**

Study concept and design (AMS, AAMT, GKM, RG, MVN, SJB, SEW); data collection (AMS, AAMT); analysis and interpretation of data (AMS, AAMT); writing the manuscript (AMS, AAMT); critical revision of the manuscript (AMS, AAMT, GKM, RG, MVN, SJB, SEW); statistical expertise (AMS, AAMT); supervision (RG, MVN, SJB, SEW)

**REFERENCES**


Figure A. (A) Large flap striae visible with green lissamine (arrows indicate flap edge) after LASIK with a mechanical microkeratome. (B) One day after flap hydration, stroking with an iris spatula and repositioning.

Figure B. Slit-lamp photograph of cornea with LASIK-induced neurotrophic epitheliopathy. Note the diffuse punctate epithelial erosions with lissamine green staining (x indicates flap edge).
Figure C. (A) Slit-lamp photograph of epithelial ingrowth (arrows) after LASIK with a mechanical microkeratome. (B) Corneal topography shows induced changes on corneal curvature and elevation that simulate ectasia. These changes disappeared after removal of the epithelial ingrowth (not shown). (C) Optical coherence tomography provided the location (arrows) of the cells between the flap and the posterior corneal stromal bed.

Figure D. Slit-lamp photograph of cornea with diffuse lamellar keratitis. Arrows indicate the diffuse white, granular infiltrate occurring 2 days after LASIK.