Flap Complications from Femtosecond Laser-assisted in Situ Keratomileusis

Steven H Tucker1 and Priyanka Sood2
1. Emory Eye Center, Atlanta, GA, USA; 2. Emory University Hospital Midtown, Atlanta, GA, USA

Purpose: To review common flap complications of femtosecond laser-assisted in situ keratomileusis (LASIK) and discuss management options. Methods: The PubMed database was used to identify relevant published literature. The search was conducted using LASIK flap complications as a search term, as well as LASIK and all the associated complications that have been noted in the results section. Results: Flap creation is a pivotal step in LASIK surgery. Femtosecond laser-assisted flap creation allows a more reliable and reproducible flap and has led to more predictable and safe lamellar dissections. However, intraoperative complications can still occur and include issues with suction, epithelial defects, opaque bubble layer, vertical gas breakthrough, anterior chamber gas bubble, flap tears, bleeding, and interface debris. Postoperative complications can include striae, diffuse lamellar keratitis, rainbow glare, dry eye, dislocated flaps, keratitis, epithelial ingrowth, transient light-sensitivity syndrome, interface haze, and corneal ectasia. Conclusions: While femtosecond laser use has decreased several complications that are prominent with microkeratome use (e.g. buttonholes, incomplete flaps, epithelial erosions), it has introduced others (e.g. rainbow glare, opaque bubble layer, vertical gas breakthrough). Predictability has however, continued to improve over time, creating a safer LASIK procedure. Surgeons who understand all possible LASIK complications and have good knowledge of the laser mechanisms specific to the unit they are using, can help safely deliver reliable outcomes for their patients.

Keywords
Femtosecond laser-assisted flap creation, laser-assisted in situ keratomileusis, LASIK, LASIK complications

Disclosures: Steve Tucker and Priyanka Sood have no relevant conflicts of interest to declare.
Compliance with Ethics: This study involves a review of the literature and did not involve any studies with human or animal subjects performed by any of the authors.
Authorship: The named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.
Received: January 15, 2019
Accepted: April 1, 2019
Citation: US Ophthalmic Review. 2019;12(1):21–7
Corresponding Author: Priyanka Sood, Emory University Hospital Midtown, The Emory Clinic Building B, 1365B Clifton Road, NE Atlanta, Georgia 30322, USA. E: psood2@emory.edu

Support: No funding was received in the publication of this article.

Advantages of femtosecond laser flap creation include reduced variation in flap thickness and increased repeatability. Some studies have suggested better final visual acuity, lower intraocular pressure (IOP) during the flap creation, and lower incidence of dry eye. Additionally, some prominent microkeratome complications including free/incomplete flaps, buttonholes, and epithelial erosions are less common due to the femtosecond’s precision. However, disadvantages of the femtosecond include transient light sensitivity, diffuse lamellar keratitis, rainbow glare, opaque bubble layer, and cost. Both device classes are still used, but femtosecond has grown in popularity over time. Several femtosecond laser systems are approved by The Food and Drug Administration (FDA) for LASIK use. However, discussion on each individual system is beyond the scope of this review.

Understanding, avoiding and managing potential femtosecond flap complications is essential for anyone performing femtosecond-assisted LASIK. This review will discuss intraoperative and postoperative flap complications associated with femtosecond-assisted LASIK using PubMed-identified relevant published literature. The PubMed search was conducted using “LASIK flap...”
Intraoperative complications

Suction loss

While not unique to femtosecond flap creation, issues with suction are one of the most commonly encountered problems. Reported rates of suction loss range from 0.06–0.8%. Given the unique lamellar cutting ability of femtosecond lasers, suction issues can often be overcome without compromising patient outcomes. Unlike keratome flaps, procedures are not automatically aborted when suction loss occurs.

Opaque bubble layer

Opaque bubble layer (OBL) occurs when cavitation gas bubbles formed by the femtosecond laser expand in the cleavage plane and become trapped in the anterior stroma. Visualizing this layer is a well-known finding intraoperatively with all femtosecond platforms. The incidence of OBL when using the laser for flap creation ranges from 5–48%.

Epithelial defects

Epithelial defects are defined in most studies as an area 2.0 mm x 2.0 mm with a break in the epithelium or loose epithelial cells. Defect frequencies have ranged from 0–0.6% in femtosecond studies. While less common with femtosecond technology, the pocket and shock waves can predispose to epithelial defects. Additionally, inserting the dissecting spatula at the flap edge has the potential to cause a defect. Risk factors include anterior basement membrane dystrophy, older age, large flap diameter, recurrent erosion syndrome, or excessive use of topical anesthetic.
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Flap tears
Flap tears during femtosecond LASIK typically occur during flap dissection. Femtosecond laser-created flaps can be more difficult to dissect and lift compared to microkeratome-created flaps. Thin flaps are at the highest risk of flap tears. One study showed flap tear incidence of 0.5% while a similar study showed a 0.4% rate of tears at the hinge.

For small peripheral flap tears, complete dissection of the flap followed by stromal ablation is acceptable. When a larger flap tear involving the pupillary axis occurs, most surgeons recommend repositioning the flap and aborting the procedure, and considering future surface ablation as a safe way to proceed. For those that proceed with surface ablation and a free flap, a loose anchoring suture to secure the flap after stromal ablation can be used.

Bleeding
There are two main bleeding complications that can occur with femtosecond LASIK. The first results in a subconjunctival hemorrhage (SCH) and is due to suction. This occurs more frequently (up to 69% in one study) with systems that dock on the conjunctiva/sclera such as the IntraLase® (Abbott Medical Optics, CA, USA) rather than platforms that dock on the cornea such as the VisuMax® (Carl Zeiss Meditec, Germany). Subconjunctival hemorrhage is not visually significant and clears over 1–2 weeks. SCH can be decreased by using slow, controlled use of suction and ensuring centration. The second type of bleeding occurs due to limbal vessel rupture at the edge of the flap. Risk factors include Meibomian gland secretions, eyelash hairs, fibers from sponges, or talc from gloves. Methods to prevent interface debris include powder-free gloves, moistened gauze, clothes covers for the patient, and scrubs for the surgeon. During the procedure, adequate irrigation is essential. Prior to repositioning the flap, the surface should be irrigated to remove debris. If noted in the postoperative period and determined not to be infectious or inflammatory, it can be observed. If large amounts of debris are present and visually significant, flap lifting and copious irrigation may be necessary. In our experience, a slit lamp exam shortly after the treatment to look for significant debris with gentle irrigation and flap repositioning at the slit lamp can successfully manage this complication. Larger amounts may require flap lift with a lid speculum in the supine position under the microscope. Mimouni et al. reported rates of flap lift for interface debris to be 0.06%.

Interface debris
Debris is frequently present in the flap interface following LASIK and is typically due to Meibomian gland secretions, eyelash hairs, fibers from sponges, or talc from gloves. Methods to prevent interface debris include powder-free gloves, moistened gauze, clothes covers for the patient, and scrubs for the surgeon. During the procedure, adequate irrigation is essential. Prior to repositioning the flap, the surface should be irrigated to remove debris. If noted in the postoperative period and determined not to be infectious or inflammatory, it can be observed. If large amounts of debris are present and visually significant, flap lifting and copious irrigation may be necessary. In our experience, a slit lamp exam shortly after the treatment to look for significant debris with gentle irrigation and flap repositioning at the slit lamp can successfully manage this complication. Larger amounts may require flap lift with a lid speculum in the supine position under the microscope. Mimouni et al. reported rates of flap lift for interface debris to be 0.06%.

Postoperative complications
Striae and folds
After LASIK, striae and folds are a relatively common flap complication and can be characterized as macro or microstriae. Macrostriae are due to misaligned flaps and are often visually significant, whereas microstriae are not typically visually significant. Several causes have been theorized, including dryness that leads to shrinkage, misalignment, and changes in the corneal contour. Microstriae are typically observed if best corrected visual acuity is not affected. Management of visually significant macrostriae can range from use of a moist microspatula to gently stroke the flap, to lifting and repositioning the flap. In two very large retrospective studies, macrostriae requiring surgical intervention occurred at rates of 0.79–1.17%. Further techniques include the use of hypotonic solutions to swell the flap, removal of central epithelium, or suturing the flap. To prevent striae, marking the flap to ensure correct final positioning is useful. Early intervention leads to best outcomes and we recommend evaluation at the slit lamp immediately following the procedure to ensure appropriate approximation.

US OPHTHALMIC REVIEW
Keratitis

There are several types of keratitis that can affect patients after LASIK including infectious, diffuse lamellar keratitis, pressure-induced stromal keratitis (PISK), and central toxic keratopathy.

Diffuse lamellar keratitis

DLK, also known as diffuse interstitial keratitis or “sands of the Sahara,” is an uncommon, nonspecific sterile inflammatory response that occurs within one week of LASIK. It presents as inflammatory sterile infiltrate at the interface of the flap and stroma without an anterior chamber reaction. Its incidence in one large study was 0.3%. There are four stages of DLK that are based on a system developed by Linebarger et al. Stage 1 usually presents on day 1 as white granular cells in the periphery with no involvement of the visual axis. Stage 2 often presents during days 1–3 with white granular cells in the visual axis. Stage 3 includes clumping of granular cells, haze, and reduced vision. Stage 4 results in stromal necrosis and melt leading to irregular astigmatism and induced hyperopia (see Figure 2).

Some studies have indicated a higher frequency of DLK in femtosecond LASIK cases compared to microkeratome with an incidence of Stage 1 or 2 DLK as high as 10.6% of patients, though all responded to steroids without visual consequence. New studies using updated femtosecond laser models suggest that the incidence is similar to LASIK performed with the microkeratome. Patients are often asymptomatic but can present with pain or decreased vision. Factors that increase the risk of DLK are blood in the interface and flap epithelial defects. If either of these two findings are found, topical corticosteroid use should be increased. Early treatment is paramount with a focus on topical corticosteroids and occasionally oral steroids. In early stages, many surgeons increase topical prednisolone 1% to every hour and consider oral prednisone. If Stage 3 DLK is present, the flap is lifted, scraped, irrigated, and cultured, with possible application of steroids to the stromal bed. When this condition is recognized, it is important to follow closely to avoid stromal melt. Late-onset DLK can also happen and has been reported to occur as late as 17 years after LASIK.

Infectious keratitis

Infectious keratitis is a rare complication following LASIK but one of the most dreaded (see Figure 3). It is not specific to femtosecond laser. Studies have reported an incidence of 0–1.5% in LASIK patients and one retrospective case-control study looking at over 500,000 post LASIK patients found an incidence of 0.0046%. Presenting symptoms can occur acutely or over days to weeks and include decreased vision, erythema, photophobia, and pain. Bacterial keratitis occurs earlier, typically within 3–5 days, while atypical infections such as mycobacteria or fungal present after a few weeks. Treatment is typically with flap lift and irrigation, culture, broad-spectrum antibiotics, and possible flap amputation if necessary. Prevention includes aseptic technique, good lid hygiene, broad spectrum antibiotics in the early postoperative period, and continuous evaluation of sterile technique and instruments.

Pressure-induced stromal keratitis

PISK occurs as a result of increased intraocular pressure, typically with prolonged steroid use. In this condition, fluid can accumulate in the interface, leading to falsely low readings which can delay the diagnosis. Since the fluid amount is often small, it results in diffuse haziness in
the interface and stroma, with no obvious fluid layer, though it can occasionally result in a visible fluid cleft separating the stromal cleavage plane.\[\textsuperscript{11,12}\] It has been reported to occur acutely in the postoperative setting and as a delayed complication, with some cases occurring after the original LASIK surgery.\[\textsuperscript{13,14}\] As PISK is frequently misdiagnosed as DLK, further use of steroids can exacerbate the clinical condition. Routine IOP checks for patients on prolonged postoperative steroids is essential to diagnose this condition. However, interface fluid can lead to falsely low IOP, necessitating peripheral corneal pressure measurements and maintaining suspicion for the presence this condition. Treatment is typically to remove the steroid and consider a pressure-lowering drop as the IOP will follow suit, resolving the underlying problem.\[\textsuperscript{20}\]

**Central toxic keratopathy**

Central toxic keratopathy is a rare non-inflammatory central corneal opacification that is acute and non-inflammatory in nature (see Figure 4). It occurs within days of stromal ablation procedures. The etiology is unknown but it presents acutely and does not worsen, unlike many of the other interface processes. It presents without pain, which can help distinguish it from DLK. Some surgeons attempt aggressive topical steroid use or flap irrigation, though interventions have not been shown to improve the final outcomes.\[\textsuperscript{12,13,24,26}\] The central opacity often spontaneously resolves in 2–18 months without intervention.

**Rainbow glare**

Rainbow glare is an optical aberration first noted in 2008 that appears to be more common with specific brands of femtosecond lasers due to diffractive light scattering and irregularities in the lamellar surface created by the laser.\[\textsuperscript{57}\] Rainbow glare typically presents within three months of the procedure, with patients describing bands of 4–12 colors.\[\textsuperscript{57,58}\] It has been reported to be most common when the femtosecond flap is created but the excimer laser ablation is aborted. Treatment can be difficult, though symptoms typically do improve over time as well as with ocular surface treatment. Some experts have suggested surface ablation over an aborted flap to reduce symptoms if the patient considers them to be bothersome.\[\textsuperscript{4}\]

**Dry eye**

Dry eye is the most common complication after LASIK surgery. Etiologies include damage to the sensory nerves during flap creation, decreased tear production, decreased blink rate, and injured goblets cells at the limbus.\[\textsuperscript{14}\] Nerves typically regenerate with a reduction in dry eye symptoms. Some studies have indicated that dry eye is less common after femtosecond LASIK,\[\textsuperscript{16}\] though others have found little difference.\[\textsuperscript{19}\] In most cases, extensive lubrication with preservative-free artificial tears is used until the corneal nerves regenerate, which usually takes 6–8 months after surgery. Traditional dry eye treatment strategies including topical cyclosporine A, lifitegrast, punctal plugs, and short-term use of corticosteroids have been used effectively.\[\textsuperscript{2}\] Some surgeons recommend using punctal plugs prior to LASIK to mitigate dry eye symptoms while others treat the patient based on the symptoms that are present afterwards.

**Dislocated flaps**

Dislocated flaps are a concerning complication of LASIK as the risk is present both early on and throughout life following surgery. Mechanical trauma is the most common cause of a dislocated flap, with minor trauma such as eyelid squeezing and eye rubbing being the most common in the immediate postoperative period. More significant trauma is generally the cause in the later postoperative period. Thankfully, rates are low, with early flap dislocation ranging from 0.08–0.012% in two large retrospective reviews.\[\textsuperscript{40,49}\] The frequency of a dislocated flap has decreased with the use of femtosecond flap creation.\[\textsuperscript{61,62}\] This is thought to be due to improved flap stability and adhesion strength.\[\textsuperscript{5}\]

When encountered, a dislocated flap should immediately be repositioned. Overall, the more quickly the flap is repositioned, the better the outcome. The exposed stromal surfaces, both on the flap and on the stromal bed, may need to be scraped to remove any epithelial ingrowth and undergo extensive irrigation. Folds in the flap can be stretched out. Prevention includes use of a shield, contact lens use, and eyelid closure immediately following the procedure. Most surgeons recommend that patients take a nap for a few hours after returning home from the procedure.\[\textsuperscript{4}\]

**Transient light-sensitivity syndrome**

Transient light-sensitivity syndrome is a rare, femtosecond flap-associated complication that results in patients experiencing bothersome photophobia typically 2–6 weeks after LASIK. The visual acuity is unaffected and a slit lamp examination is normal. Several theories exist on its etiology but the most common revolves around insult to the ciliary body and resultant inflammation.\[\textsuperscript{17}\] In line with that theory, studies have indicated that using lower energy settings reduces its incidence. Treatment is with aggressive topical corticosteroid use, with initial application up to every hour, followed by a taper. If recalcitrant, oral steroids can be used with good results.

**Interface haze**

Since the central corneal epithelial basement membrane remains intact during LASIK, the incidence of interface haze is much less than surface ablation. When it does present in LASIK patients, it typically is due to damage to the epithelial basement membrane such as a buttonhole flap. It also can be seen with PISK. The mainstay of treatment is corticosteroids with fairly rapid resolution.\[\textsuperscript{7}\] Interface haze can also be caused by various types of keratitis as described in an earlier section.
Review Refractive Surgery

Figure 6: Corneal ectasia

Image courtesy of William Trattler, MD.

Epithelial ingrowth

Epithelial ingrowth occurs when clusters of epithelial cells insert into the stromal interface resulting in fluorescein staining at the flap edge, a fibrotic demarcation line and, in severe cases, a blockage of nutrient diffusion and keratolysis at the flap edge (see Figure 5). It can advance circumferentially from the edge and induce irregular astigmatism. While far less common in femtosecond cases compared with microkeratome, this growth can still occur and typically occurs within two months of the procedure. Most researchers theorize that the epithelial cells are captured in the interface during flap positioning or by back flow of fluid into the flap. There is a higher incidence in epithelial basement membrane dystrophy or after an enhancement. Treatment typically includes lifting the flap, copious irrigation, and debriding epithelial cells with a blade on the stromal and flap surface. Most surgeons then apply a bandage contact lens for 24 hours and consider suturing the flap or using fibrin glue to seal the wound. The addition of suturing may decrease rates of recurrence of epithelial ingrowth. Ethanol can be used during debridement in recurrent cases. Prevention centers around avoiding epithelial defects and using extreme caution in patients with epithelial basement membrane dystrophy. Steeper side cut angle when creating the flap may decrease the incidence.

Corneal ectasia

Postoperative corneal ectasia is a rare, but potentially devastating LASIK complication typically associated with a predisposing factor such as former fruste keratoconus (see Figure 6). During stromal ablation, removal of tissue leads to a weakening of the corneal biomechanics which can lead to ectasia. Other risk factors associated with iatrogenic ectasia include eye rubbing, young age and pregnancy. Many hypothesize that the thinner, more predictable flaps of femtosecond leads to decreased postoperative corneal ectasia but the research has shown mixed results. Prevention is the most effective approach. Using topographic analysis, various scoring systems, and calculations to identify at-risk patients has been shown to effectively decrease the risk of post-LASIK ectasia. In a large retrospective review of over 30,000 cases between 2007 and 2015, incidence of ectasia was 0.033% in patients with at least 2 years of follow up. Management options include collagen crosslinking using ultraviolet light and riboflavin or allogeneic corneal lenticules.

Discussion

The introduction of femtosecond laser technology has created a more reproducible and safe LASIK procedure and its use has increased over time. Microkeratomes have also improved with the rates of various complications, decreasing in both femtosecond and microkeratome-assisted LASIK cases. Over time, techniques, treatments and technologies have continued to improve, resulting in fewer complications.

Conclusions

Femtosecond laser-assisted flap creation has improved the predictability and thickness of LASIK flaps making LASIK safer. Compared to microkeratome-created flaps, there are fewer complications overall, though femtosecond laser has resulted in a few new complications. It is important for any surgeon performing femtosecond laser-assisted LASIK to be aware of all possible intraoperative and postoperative complications. While the complications are applicable to all femtosecond lasers, it is essential that the surgeon also review the mechanism of suction and flap creation for the specific unit being used to carry out the procedure, as each model has different features that may help reduce certain complications but could predispose the patient to others. In addition to gaining a clear understanding of the mechanisms specific to the laser being used, by reviewing all potential procedural complications and ensuring they have the knowledge to manage any complications that may arise, surgeons can utilize femtosecond laser technology in a way that enables them to perform safe, reliable LASIK.

References
