

LASIK Flap-Related Complications

Common sense in the face of a complication will nearly always ensure an excellent outcome.

BY RICHARD FOULKES, MD

Even with the emergence of femtosecond laser flap creation, about half of all LASIK procedures are still performed using microkeratomes. Flap complications associated with the mechanical technique are due to how individual devices work. Therefore, it is appropriate to review first the process of creating a LASIK flap with a mechanical microkeratome.

CREATING A FLAP

The eye is fixated with a vacuum ring using a pressure of 60 to 160 mm Hg. The surgeon uses a Barraquer tonometer or his or her finger to check the pressure. Pupillary dilation confirms an IOP above 60 mm Hg. The microkeratome's oscillating blade protrudes below a plate that pushes the eye flat in front of the blade. The eye is lubricated with balanced salt solution, and the device is loaded onto a track with a screw mechanism that provides steady velocity as the device moves across the eye. The angle will be fairly flat, about 30° to 50°, as the cornea is tilted up from the inner edge of the ring to the flattening of the "ski" at the front of the microkeratome. Corneal curvature will dramatically affect the performance of the microkeratome-created flaps. The cord length between the ring edges will be longer in steep eyes and shorter in flat eyes. Because the epithelium is pushed ahead of the microkeratome, it can slide or dissect away even with proper lubrication. Patients at risk for epithelial slide include those with anterior basement membrane disease, rosacea, or meibomitis; pre- and postmenopausal women; and all patients with dry eye syndrome.

FLAP THICKNESS

The blade's sharpness, protrusion, angle, oscillation speed, and velocity determine flap thickness. Generally, the slower the pass, the thicker the flap. Dull blades cut more slowly and create a thinner flap. Although surgeons commonly use the same microkeratome blade on a patient's second eye, small defects in the blade's edge may lead to a thinner flap and a higher probability of a more advanced defect on the second eye.

The flap proceeds into the inner chamber of the microker-

atome behind the blade until the pass is complete. If a free cap results, the surgeon should orient the microkeratome back over the eye, slide the cap onto the bed using orientation marks, turn and fold the cap into a taco shape as usual, and proceed with ablation. Then, the surgeon reorients the cap onto the bed using a minimal amount of balanced salt solution. He or she dries the gutters well, places a bandage contact lens, allows the patient to rest for 30 minutes, and then checks the orientation of the flap.

A short flap is typically caused by the blade's not fully advancing across the eye. If a short flap is located near the visual axis, the case should be aborted. My preference is to then treat using surface ablation with mitomycin C. The use of ethyl alcohol 25% on a sponge will loosen epithelium, and it can be wiped away in the direction of the flap's base. A second cut flap may lead to slivers of tissue and significant loss of vision. In very steep eyes, as the ski moves over the central cornea, the amount of tissue in the ring will be greater. This can cause buckling as the blade passes through the central cornea, leaving a central zone uncut, called a *buttonhole*. The author's preferred strategy in such cases is to perform surface ablation with mitomycin C. It may be performed at the time of surgery; the author asks for patients' consent to this possibility.

DEFECTS IN THE BLADE

Defects in a microkeratome blade can occur out of the package, upon the blade's insertion, or after the blade begins to oscillate. A small defect causes a ridge of stroma visible in the bed, but this development is not significant if it is not located across the visual axis. This type of problem is common and typically modest in scope. A central strip can cause significant visual disturbance and should be aborted. Careful reorientation of the flap and surface ablation should follow.

Work done in the author's center using the Artemis arc-scanning ultra-high-frequency ultrasound device (Ultralink LLC, St. Petersburg, FL) demonstrated another common issue with microkeratome blades. Historically, the LASIK flap's thickness was determined by central subtraction pachymetry. The weaknesses of this technique are well

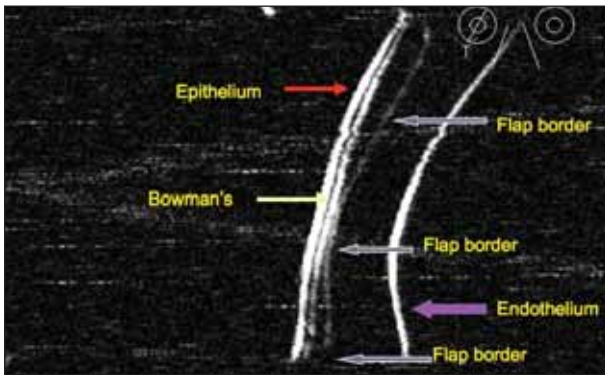


Figure 1. Flaps created with mechanical microkeratome show variability in central thickness as well as significant variability regionally within a flap.

known.¹ Aligning the pachymeter over the center of the pupil will often lead to alignment and angulation errors. More importantly, when lubricating a microkeratome, fluid spreads out on the bed while the flap is in the microkeratome, and water is immediately drawn up into the stroma, causing the surgeon to underestimate thickness. The Artemis provided 3D images of the flap's contour and revealed major variations in flaps from their center to their edge (Figures 1 and 2). Because the excimer laser's uptake is strongly influenced by hydration, deeper cuts into the mesodermic cornea are wetter, and shallow cuts through the cross-linked endodermic cornea are dryer. Water placed on deeper cornea is better absorbed than that administered to cross-linked cornea, further complicating the intended ablation.

POSITIONING ISSUES

An incorrectly positioned or slipped flap will add tension or slack to the hinge. Lines of tension in the flap will appear fan-like, are fairly straight, and orient from the hinge side where the flap is displaced. Bunching of a flap leads to curved lines that bow from the area of displacement. Undue tension or slack creates waveforms in the flap; if they cross the visual axis, they will create visual effects and often compromise best-corrected vision. Because the epithelium will then fill in this area and hold the striae in place, refloating the flap does not always remedy this complication. The author removes the epithelium from the flap in the central areas and then refloats the flap. Letting the eye dry slightly with the speculum in place will highlight striae and aid in assessment, especially with a side illumination with a muscle light or fiber optic. One must remember to clear away epithelium that has grown across the gutter when the flap is properly reoriented, as this will be epithelial ingrowth on day 1.

There are three types of epithelial ingrowth, and each should be treated differently. The rim epithelium finds a

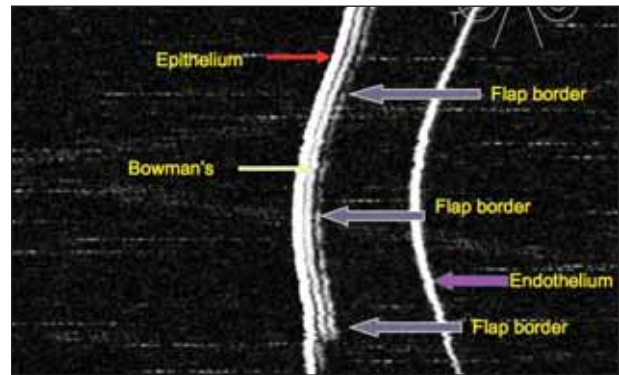


Figure 2. Flaps created with the IntraLase show minimal variability in central thickness across different flaps and minimal variability regionally within the flap.

tongue of access to the edge and typically grows 1 or 2 mm before running out of oxygen. It will die and then remodel the flap in this area, which can lead to late astigmatism, glare, and foreign-body sensation (this is also true for epithelial islands). This ingrowth can be addressed at the slit lamp with a forceps and debridement about 1 mm peripheral to the edge. A tight contact lens or patch may help. Persistent epithelium can be treated with tissue glue or a mattress suture. The "taco" form of ingrowth wraps around the flap and adheres to its underside. This form may require blade debridement, as it is harder to detach. A third form has occurred after the flap's creation with the IntraLase FS laser (Abbott Medical Optics Inc., Santa Ana, CA). Epithelial cells fill in a gap created by laser disruption.²

DIFFUSE LAMELLAR KERATITIS

Although not a specific issue related to the flap's creation, diffuse lamellar keratitis (DLK) is a common complication of LASIK.³ DLK is generally thought to be caused by inflammatory cells that find their way into the interface induced by chemoattractants like biofilm or blood. This inflammation can be suppressed by topical steroids. Polymorphonuclear neutrophil leukocyte (PMN) movement toward the central visual axis and "Indian" file organization will precede a corneal melt. Because the cytokines in the PMNs melt protein upward through the flap, typically on days 4 to 6, these patients should not be seen at 1 week. If the author observes central encroachment at 3 days, he will hold the patient's head at the slit lamp and use a cannula to rinse 1.5 mL of balanced salt solution from the side opening to as few as 3 to 4 clock hours of the flap. If rinsed at 24 hours before steroid suppression, a return of cells is sometimes seen. Melts will not occur in the first 3 days. In the case of a melt, the question of rinsing or not is confused by the fact that some stroma is rinsed away with the cells (K. D. Assil, personal communication, 2003).

Nevanac®

(nepafenac ophthalmic suspension) 0.1%

INDICATIONS AND USAGE

NEVANAC® ophthalmic suspension is indicated for the treatment of pain and inflammation associated with cataract surgery.

CONTRAINDICATIONS

NEVANAC® ophthalmic suspension is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formulation or to other NSAIDs.

WARNINGS

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory agents. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

With some nonsteroidal anti-inflammatory drugs including NEVANAC®, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied nonsteroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

PRECAUTIONS

General: Topical nonsteroidal anti-inflammatory drugs (NSAIDs) including NEVANAC®, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs including NEVANAC® and should be closely monitored for corneal health.

Postmarketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Postmarketing experience with topical NSAIDs also suggests that use more than 1 day prior to surgery or use beyond 14 days post surgery may increase patient risk for occurrence and severity of corneal adverse events.

It is recommended that NEVANAC® ophthalmic suspension be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Information for Patients: NEVANAC® ophthalmic suspension should not be administered while wearing contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Nepafenac has not been evaluated in long-term carcinogenicity studies. Increased chromosomal aberrations were observed in Chinese hamster ovary cells exposed *in vitro* to nepafenac suspension. Nepafenac was not mutagenic in the Ames assay or in the mouse lymphoma forward mutation assay. Oral doses up to 5,000 mg/kg did not result in an increase in the formation of micronucleated polychromatic erythrocytes *in vivo* in the mouse micronucleus assay in the bone marrow of mice.

Nepafenac did not impair fertility when administered orally to male and female rats at 3 mg/kg (approximately 90 and 380 times the plasma exposure to the parent drug, nepafenac, and the active metabolite, amfenac, respectively, at the recommended human topical ophthalmic dose).

Pregnancy: Teratogenic Effects.

Pregnancy Category C: Reproduction studies performed with nepafenac in rabbits and rats at oral doses up to 10 mg/kg/day have revealed no evidence of teratogenicity due to nepafenac, despite the induction of maternal toxicity. At this dose, the animal plasma exposure to nepafenac and amfenac was approximately 260 and 2400 times human plasma exposure at the recommended human topical ophthalmic dose for rats and 80 and 680 times human plasma exposure for rabbits, respectively. In rats, maternally toxic doses ≥ 10 mg/kg were associated with dystocia, increased postimplantation loss, reduced fetal weights and growth, and reduced fetal survival.

Nepafenac has been shown to cross the placental barrier in rats. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, NEVANAC® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic Effects: Because of the known effects of prostaglandin biosynthesis inhibiting drugs on the fetal cardiovascular system (closure of the ductus arteriosus), the use of NEVANAC® ophthalmic suspension during late pregnancy should be avoided.

Nursing Mothers: NEVANAC® ophthalmic suspension is excreted in the milk of pregnant rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when NEVANAC® ophthalmic suspension is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of NEVANAC® in pediatric patients below the age of 10 years have not been established.

Geriatric Use: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

In controlled clinical studies, the most frequently reported ocular adverse events following cataract surgery were capsular opacity, decreased visual acuity, foreign body sensation, increased intraocular pressure, and sticky sensation. These events occurred in approximately 5 to 10% of patients.

Other ocular adverse events occurring at an incidence of approximately 1 to 5% included conjunctival edema, corneal edema, dry eye, lid margin crusting, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, photophobia, tearing and vitreous detachment.

Some of these events may be the consequence of the cataract surgical procedure.

Nonocular adverse events reported at an incidence of 1 to 4% included headache, hypertension, nausea/vomiting, and sinusitis.

DOSAGE AND ADMINISTRATION

Shake well before use. One drop of NEVANAC® ophthalmic suspension should be applied to the affected eye(s) three-times-daily beginning 1 day prior to cataract surgery, continued on the day of surgery and through the first 2 weeks of the postoperative period.

NEVANAC® ophthalmic suspension may be administered in conjunction with other topical ophthalmic medications such as beta-blockers, carbonic anhydrase inhibitors, alpha-agonists, cycloplegics, and mydriatics.

Rx ONLY

Manufactured by:
Alcon Laboratories, Inc.
Fort Worth, TX 76134 USA
U.S. Patent No: 5,475,034

References:

1. Data on file. Alcon Laboratories, Inc. 2005. 2. Ke T-L, Graff G, Spellman JM, Yamni JM. Nepafenac, a unique nonsteroidal prodrug with potential utility in the treatment of trauma-induced ocular inflammation. *In vitro* bioactivation and permeation of external ocular barriers. *Inflammation*. 2000;24:371-384. 3. Lane SS, Modi SS, Holland EJ, et al. Nepafenac ophthalmic suspension 0.1% before and after surgery for postoperative anterior segment inflammation. Paper presented at American Society of Cataract and Refractive Surgery; April 19, 2005; Washington, DC. 4. NEVANAC® suspension prescribing information.

REFRACTIVE SURGERY

FOCUS ON THE LASIK FLAP'S CREATION

LASER-CREATED FLAPS

The creation of LASIK flaps with a femtosecond laser is not without problems. With the IntraLase and most other femtosecond systems (eg, Femtec [Technolas Perfect Vision GmbH, Heidelberg, Germany] and Wavelight [Alcon Laboratories, Inc., Fort Worth, TX]), large cavitation bubbles are part of the mechanism of dissection. Only the Ziemer LDV (Ziemer Group, Port, Switzerland) does not use cavitation inflation to separate the lamellae. If these bubbles move down into the stroma, the dissection will be poor, and it can be difficult to lift the flap; many techniques have evolved for overcoming these problems. Bubbles in the stroma may cause a reduction in the ablation rate.⁴ Transient light sensitivity syndrome remains a problem that relates to microjoule energy. Lowering energy reduces the incidence. Prompt topical steroid use will limit the length of sensitivity.⁵ Bubbles breaking through under the plate will push it away and create an undissected area. In this situation, retreatment with a deeper plate before lifting the flap is an option.⁶ If the affected area is located centrally, delaying the case seems prudent before either moving to surface ablation or retreatment. Centering the flap is important with the IntraLase, as the flap is small, and good centration will avoid missing part of the ablation in a decentered small flap. Parallax phenomena through the long-wavelength cone/patient interface will give the illusion of centration, and software centration merely shrinks the flap's size to give the appearance of centration.⁷ Marking the central cornea with water-based ink is suggested. Oil-based ink will slowly defeat the energy and create a poorly dissected area.

Surgeons strive to make LASIK a safe, highly accurate, and reproducible procedure. Using good judgment in the face of a complication will nearly always lead to an excellent outcome. Surgeons should always attempt to create a dry, smooth surface for the excimer laser ablation. ■

Richard Foulkes, MD, is medical director, Foulkes Vision Research Center, Lombard, Illinois. He is a medical monitor for Ziemer Group but he does not receive reimbursement. Dr. Foulkes may be reached at foulkes52@gmail.com.



1. Silverman RH. High-resolution ultrasound imaging of the eye—a review. *Clin Experiment Ophthalmol* 2009;37(1):54-67.
2. McCulley JP, Petroll WM. Quantitative assessment of corneal wound healing following IntraLASIK using *in vivo* confocal microscopy. *Trans Am Ophthalmol Soc*. 2008;106:84-92.
3. Haft P, Yoo SH, Kymionis GD, Ide T, O'Brien TP, Culbertson WW. Complications of LASIK flaps made by the IntraLase 15- and 30-kHz femtosecond lasers. *J Refract Surg* 2009;25(11):979-984.
4. Kaiserman I, Maresky HS, Bahar I, Rootman DS. Lasers with a speed of 60 Hz or faster allow the use of lower energy and create a less opaque bubble layer. *J Cat Refract Surg* 2008;34(3):417-423.
5. Stonecipher KG, Dishler JG, Ignacio TS, Binder PS. Transient light sensitivity after femtosecond laser flap creation: Clinical findings and management. *J Cat Refract Surg* 2006;32(1):91-94.
6. Chang JSM, Lau S. Intraoperative flap re-cut after vertical gas breakthrough during femtosecond laser keratotomy. *J Cat Refract Surg* 2010;36(1):173-177.
7. Ide T, Kymionis GD, Abbey AM, et al. Effect of marking pens on femtosecond laser-assisted flap creation. *J Cat Refract Surg* 2009;35(6):1087-1090.