

# Mitomycin-C assisted photorefractive keratectomy in the treatment of buttonholed laser in situ keratomileusis flaps associated with epithelial ingrowth

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The prophylactic intraoperative use of mitomycin-C (MMC) to prevent haze and scarring after excimer laser surface ablation (phototherapeutic/photorefractive keratectomy [PTK/PRK]) in an eye with a previous laser in situ keratomileusis (LASIK) flap buttonhole with epithelial ingrowth is described. A well-centered buttonhole measuring 2.0 mm in diameter was cut within a thin LASIK flap in an amblyopic eye. Over the next 8 weeks, corneal haze and progressive epithelial ingrowth formed centrally. An early transepithelial PTK/PRK approach was chosen to manage the buttonhole together with the epithelial ingrowth and to treat ametropia before the onset of scarring. The approach included epithelial removal with PTK, application of MMC 0.02% for 1 minute, irrigation, a short waiting period to allow for diffusion, PRK correction of  $-4.0$  diopters without nomogram adjustment, and bandage contact lens. A regimen of prednisolone acetate 1% and ofloxacin 0.03% 5 times a day for 1 week (steroid tapered) was prescribed. Epithelial ingrowth was removed successfully. Minimal haze formation was visible 2 weeks after the retreatment but did not reduce best spectacle-corrected visual acuity (BSCVA) and resolved within the next few weeks. After 6 weeks, uncorrected visual acuity was equal to BSCVA preoperatively (20/50). There was no evidence of recurrent epithelial ingrowth or central scarring after 24 months. Transepithelial PTK/PRK was effective in managing central epithelial ingrowth in a buttonholed LASIK flap. Prophylactic intraoperative use of MMC may reduce haze formation and corneal scarring in early treatments and may also prevent recurrent epithelial ingrowth. This approach may offer faster visual recovery and no risk for a repeated buttonhole creation compared with the widespread recutting a new flap after a couple of months. The optimal application time and concentration of MMC need to be established.

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Intraoperative flap complications are among the risks of laser in situ keratomileusis (LASIK) most feared by both patients and surgeons. A doughnut-shaped or buttonholed flap has been reported in 0.3% to 2.6% of cases.<sup>1–3</sup> Although most flap complications such as free caps and short flaps usually do not cause long-term loss of vision, buttonholed flaps are the flap complication most likely resulting in significant loss of visual acuity.<sup>1,2</sup> The conventional management is to carefully reapproximate the flap with the stromal bed and defer laser ablation for several months. A new flap is then created and the refractive error treated. Several disadvantages of this strategy led to the search for superior techniques. We report a case of a LASIK flap buttonhole leading to central epithelial ingrowth and discuss its management with transepithelial phototherapeutic/

photorefractive keratectomy (PTK/PRK) assisted by the intraoperative use of mitomycin-C (MMC) to prevent haze and scar formation and recurrent epithelial ingrowth.

## CASE REPORT

Contact lens intolerance developed in a 22-year-old healthy woman with no significant medical history and a stable refraction. The patient elected to have LASIK in the amblyopic left eye for the treatment of myopia and anisometropia. The best corrected visual acuity (BCVA) was 20/20 in the right eye and 20/50 in the left eye. The manifest refraction was plano in the right eye and  $-4.0$  sphere in the left eye. The cycloplegic refraction was plano  $-0.37 \times 96$  in the right eye and  $-4.0 - 0.62 \times 63$  in the left eye. Orbscan II analysis (Version 3.14, Bausch & Lomb) showed normal topography in both eyes. Keratometry was 46.3/46.0 in the right eye and

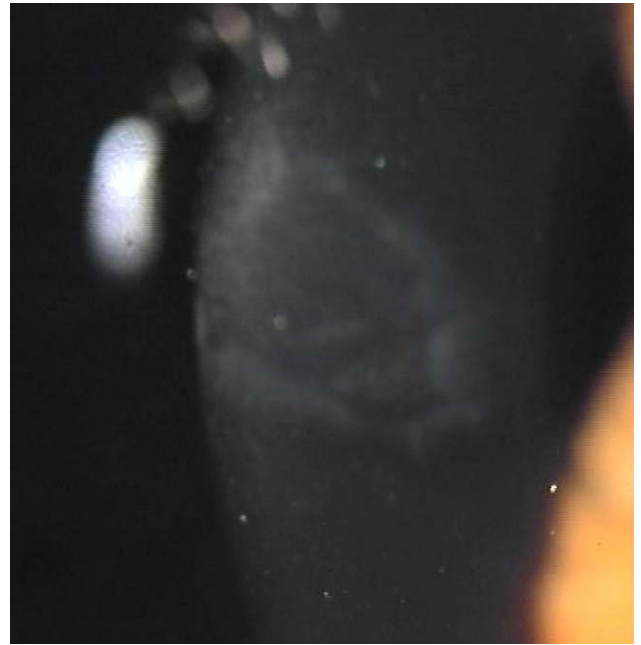
46.8 × 112/46.5 × 22 in the left eye. Central ultrasonic pachymetry (DGH Technology) was 548 μm and 560 μm, respectively.

A Hansatome (Bausch & Lomb) was used to create a corneal flap in the left eye. An 8.5 mm suction ring and a 180 μm zero-compression plate with a new flawless Accuglide blade were used to create a flap without loss of intended 25.6 mm Hg suction as measured at the pump during the microkeratome pass. However, suction had to be released twice before surgery to recenter the suction ring because of eye movement after suction was initiated.

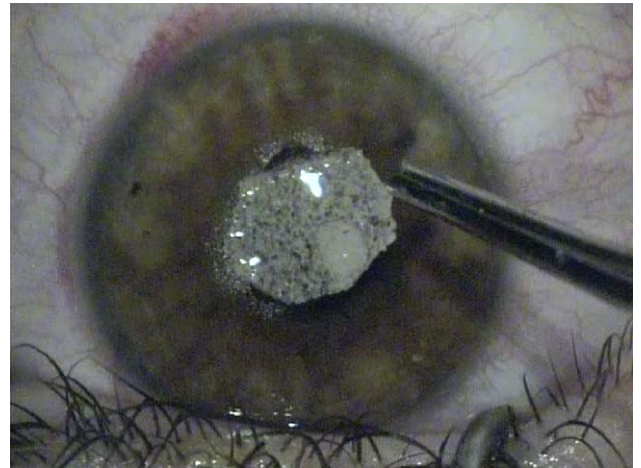
After the keratome was removed, a central flap irregularity was detected immediately. When the corneal flap was lifted, a well-centered buttonhole measuring 1.5 mm in diameter was identified within a thin flap. The interface was irrigated with Ringer's solution (B Braun). The flap was carefully repositioned over the buttonhole and allowed to adhere to the stromal bed for 5 minutes. Prednisolone acetate 1% (Inflanefran forte) and ofloxacin 0.03% (Floxal) were administered. A bandage contact lens (PureVision, Bausch & Lomb) was then placed. No laser was applied at this time. The patient was prescribed prednisolone acetate 1%, ofloxacin 0.03%, and hyaluronic acid 0.1% (Hyl-Comod) 5 times a day. The bandage contact lens was removed on the third postoperative day, and the patient was followed closely. The antibiotic drops were discontinued at 1 week, and the artificial tears and the steroid were tapered.

Over the next 8 weeks, corneal haze formed and progressive epithelial ingrowth from the buttonhole edges toward the periphery occurred (Figure 1). The left eye's manifest refraction stabilized at -4.0 sphere. The BSCVA was again 20/63 at this time. Keratometry in the left eye returned to baseline levels at 46.8 × 108/46.3 × 18. Orbscan axial and tangential topography were practically identical to preoperative values. However, difference maps of corneal pachymetry and posterior elevation suggested a central thinning of approximately 60 μm. This was in obvious contrast to central ultrasound pachymetry findings, which yielded baseline values at several follow-up examinations.

Because of progressive epithelial ingrowth and haze formation, an early retreatment was indicated. The Technolas 217z excimer laser system was used to remove the epithelium and widen the diameter of the buttonhole with a setting of 100 μm depth and 7.0 mm optical zone expanding to 10.0 mm. A round sponge cut from a conventional Merocel spear was soaked in MMC 0.02% and applied for 1 minute to the central corneal stroma (Figure 2). After irrigation, a short waiting period was provided for diffusion of the MMC. To correct the refractive error, a -4.0 PRK without nomogram adjustment was performed using a 7.0 mm optical zone expanding to 10.0 mm. Prednisolone acetate 1% and ofloxacin



**Figure 1.** Well-centered buttonhole with epithelial ingrowth after 8 weeks.



**Figure 2.** Intraoperative MMC application with a Merocel sponge.

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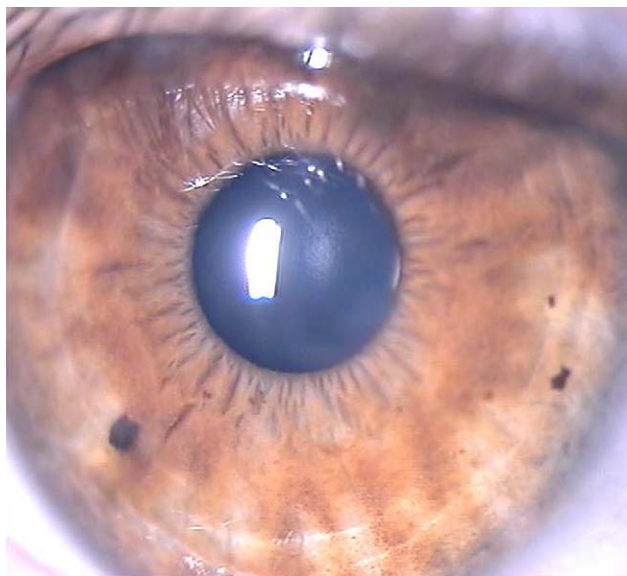
0.03% eyedrops were administered. A bandage contact lens was then placed, and oral analgesics were given.

Postoperatively, the patient was started on prednisolone acetate 1%, ofloxacin 0.03%, and hyaluronic acid 0.1% 5 times a day. The bandage contact lens was removed on the third postoperative day when the epithelial defect had healed completely, and the patient was followed closely. The antibiotic drops were discontinued at 1 week, and the artificial tears and the steroid were tapered. Two weeks after the procedure, the cornea was well healed without evidence of scarring and only minimal haze. The uncorrected visual acuity was equal to the preoperative BCVA (20/63) and remained at that level throughout the follow-up period. At 6 and 12 months,

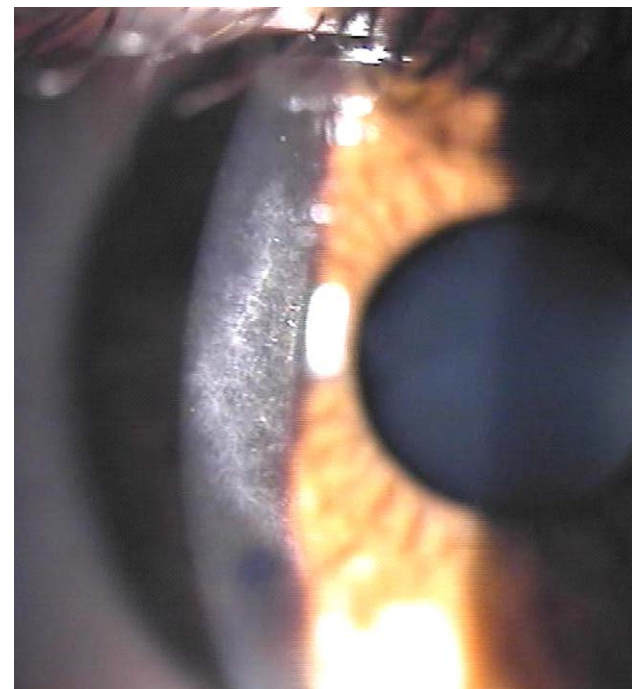
the corneal center remained clear (Figure 3); however, there was some fibrosis nasally at the central edge of the residual LASIK flap (Figure 4). Manifest refraction was plano. At 24 months, the cornea was perfectly clear (Figure 5). Visual acuity and refraction remained stable.

## DISCUSSION

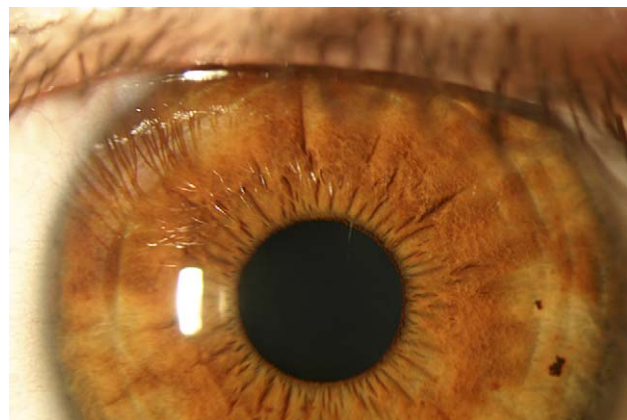
A doughnut-shaped or buttonholed flap is cut when the microkeratome blade exits through the epithelium during midincision and the reenters to complete the flap.<sup>4</sup> Different factors have been attributed to insufficient coupling of the microkeratome blade and the suctioned cornea.<sup>5</sup> Steep corneas are thought to offer higher resistance to the blade excursion when applanated, resulting in a more superficial pass. Another theory is that corneas with higher keratometric values may buckle in the center upon applanation so that a central dimple is spared by the blade. Other keratome-related factors include blunted blades, microflaws of blades, and poor oscillation. Inadequate coupling may also be the result of poor suction with sunken globes, small-diameter corneas or conjunctival incarceration in the suction port, and conjunctival scarring. The blade angle may also play a role in determining the pass depth. Because almost all these factors can be ruled out in this case, the reason for buttonhole formation in this patient remains unclear. However, I may speculate that because suction was released twice before a proper centration of the suction ring could be established, the already steep cornea may have been steepened more in the short term, leading to subsequent buckling during applanation.



**Figure 3.** Centrally clear cornea 6 months after MMC assisted transepithelial PTK/PRK treatment of a buttonholed LASIK flap.



**Figure 4.** Fibrosis at the nasal edge of the residual LASIK flap after 6 months.



**Figure 5.** Perfectly clear cornea 2 years after initial surgery.

laser ablation. Successful results have been obtained by cutting a new LASIK flap after 3 to 6 months. However, in cases in which the etiology of the buttonhole is not evident, a second microkeratome excursion through the cornea may interfere with the first pass and lead to the development of a second buttonhole or other flap abnormality.<sup>6</sup> Moreover, when fibrosis is present at the site of perforation through Bowman's membrane, this strategy is excluded because of the altered laser ablation rate through the scar. The different ablation patterns may result in irregular astigmatism and loss of BCVA. In these cases, a transepithelial PTK/PRK technique is effective before the onset of scarring.<sup>4,7-9</sup> Timing is crucial in this modality because immediate laser ablation after buttonhole creation has been associated with severe haze.<sup>10</sup> A waiting period of at least 2 weeks may allow activated stromal keratocytes to stabilize and the epithelial surface to remodel and smoothen.

We opted for an early treatment (ie, within 3 months after buttonhole formation) to stop the progressive epithelial ingrowth. But even in the absence of epithelial cells in the interface, it may be wise to treat a patient before the buttonhole's wound healing results in significant scarring, making ablation unpredictable. During the 8-week period until retreatment, the keratometric values did not change beyond testing variability. Central haze formation may explain the clear discrepancy between difference maps of Orbscan corneal pachymetry and posterior elevation findings and ultrasound pachymetry readings and may account for the invalid measurements obtained by the optic-based Orbscan device.<sup>11-14</sup> Real corneal thinning requires urgent treatment, which underscores the importance of verifying optical corneal thickness measurements by ultrasound pachymetry.

Although transepithelial PTK/PRK has been successful in removing epithelial ingrowth from the interface,<sup>7,8,10,15,16</sup> late scarring and haze formation may lead to significant visual loss.<sup>10</sup> Mitomycin-C was effective in preventing the recurrence of haze after radial keratotomy and PRK.<sup>17-19</sup> This finding is supported by experiments in animal models.<sup>20,21</sup> Recent reports<sup>9,22</sup> show that the intraoperative prophylactic use of MMC may reduce haze formation after PRK and LASIK and even after retreatment of buttonholed flaps.<sup>9,23-25</sup> In this case, MMC was well tolerated without apparent toxicity. The long-term safety profile of MMC in the management of buttonholed LASIK flaps is similar to that of MMC for the removal or prevention of haze after PRK.

The technique of MMC assisted transepithelial PTK/PRK described in this case report was successful in removing central haze formation and epithelial ingrowth originating from a buttonhole and in preventing its recurrence and any loss of visual acuity for a follow-up period of 12 months. The relatively quick visual rehabilitation after

buttonhole creation was advantageous. Furthermore, the risks associated with another attempt to create a flap are avoided. However, this approach could not prevent the development of fibrosis at the nasal portion of the margin of the residual original flap. This complication may have been prevented by ensuring the complete removal of the original flap. Nonetheless, we decided not to remove the entire flap because doing so would have resulted in greater central tissue ablation. Another feasible way to avoid fibrosis may be a greater concentration or application time of MMC or the period reserved for its diffusion. The optimal concentration and application of MMC in the treatment of buttonholed flaps or other flap abnormalities remains to be established.

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