**Original article**

**PRK vs LASEK vs Epi-LASIK: A comparison of corneal haze, post-operative pain and visual recovery in moderate to high myopia**

Reilly CD¹, Panday V¹, Lazos V², Mittelstaedt BR³
¹Wilford Hall, Warfighter Refractive Surgery Center, San Antonio, Texas, USA
²Brooke Army Medical Center, San Antonio, Texas, USA
³Aerospace Medicine Department, Joint Base McGuire-Dix-Lakehurst Wrightstown New Jersey USA

**Abstract**

**Introduction:** The field of refractive surgery continues to evolve amid continued concerns as to which surgical technique minimizes the risk of inducing ectasia.

**Purpose:** To compare clinical outcomes between PRK, LASEK and Epi-LASIK in moderately to highly myopic eyes (-4.00 D to -8.00 D).

**Materials and methods:** A retrospective chart review of 100 PRK eyes, 100 LASEK eyes (with alcohol) and 97 Epi-LASIK eyes was performed. Post-operative pain, uncorrected visual acuity, and corneal haze data was recorded and analyzed at post-op days 1, 4 and 7 and at post-op months 1, 3, 6 and 12.

**Results:** In all groups surgical corrections ranged from -4.00 D to -8.00 D. There was less pain associated with the epi-LASIK procedure especially early (post-op days 1 and 4). Visual recovery was superior within the PRK group during the first post-operative week but by post-op week 4 all three were equal. Haze scores were similar but a trend for less haze was demonstrated with epi-LASIK at 6 and 12 months.

**Conclusion:** Epi-LASIK has a slight advantage over PRK and LASEK early on in the post-op course with regards to pain. Visual recovery is similar by 4 weeks and is better with PRK early. In addition, epi-LASIK trends toward less significant haze.

**Keywords:** LASIK, epi-LASIK, LASEK, PRK, haze

**Introduction**

Refractive surgery techniques have evolved circumferentially over the past several years. After the abandonment of RK due to the advent of the excimer laser (Scerrati E, 2001), photorefractive keratectomy (PRK) burst onto the scene and has been a steady performer ever since its approval for use by the FDA in the mid-90s (COPARSP, 1999). Laser in situ keratomileusis (LASIK) has largely supplanted PRK and has become the mainstay of refractive surgery because of its effectiveness and ability to offer fast, less painful recovery (Danasoury MAE et al 1999). Recently there has been a re-emergence of surface ablation with the advent of wavefront technology and continued concerns to minimize the risk of inducing ectasia.

LASIK has not shared the same acceptance in the military as it has in the civilian sector in large part
because of the increased risk for trauma related flap complications during military duties. At the Warfighter Refractive Surgery Center, (Lackland Air Force Base, San Antonio, Texas), and at many other US military facilities, PRK has remained the procedure of choice. Recently, in an effort to minimize discomfort, speed visual recovery time and reduce the incidence of corneal haze with PRK, other surface ablation techniques such as LASEK and epi-LASIK are being utilized, especially with higher myopes.

The advantages LASIK has over PRK are related to preservation of the central corneal epithelium and Bowman’s membrane which allow for increased patient comfort in the early post-operative period, quicker visual recovery, and a reduced wound healing response. Reduced wound healing correlates with less regression in high corrections and a lower rate of sub-epithelial haze (Netto MV, 2005) which has historically been a concern of refractive surgeons (Caubet E, 1993).

Camellin & Cimberle (2000) first described the laser-assisted sub-epithelial keratectomy (LASEK) in 1999. In this procedure, the epithelium is lifted as a sheet generally by alcohol application and instead of being discarded as in PRK, the sheet is replaced after the laser ablation. Advocates of LASEK suggest that similar to LASIK, there is less discomfort in the early post-operative period, faster visual recovery and less haze compared to standard PRK for correction of similar levels of refractive error. Thus far, the body of research comparing PRK and LASEK with regards to visual recovery times, pain and haze post operatively have shown the two procedures to be comparable with some studies citing some mild benefit with LASEK while others have them equal (Lee JB et al 2001; Hashemi H et al 2004; Bowman CB et al 1997; Kaya V et al 2004; Litwak S et al 2002; Cimberle M, 1999; Ghirlando A et al 2007). Yet LASEK is a more complicated and labor intensive procedure than PRK. Furthermore with LASEK, alcohol is used to break the basement membrane bonds to facilitate the mechanical separation of the epithelium. Concerns over the likely toxic effect of alcohol on the epithelium and underlying Bowman’s layer (Braunstein RE et al 1996) has spurred the development of alternative ways to create the epithelial separation.

LASEK has also been compared to LASIK (Danasoury MAE et al 1999; Kaya V et al 2004; Scerrati E, 2001; Teus MA et al 2007; Tobaigy FM et al 2006). Conclusions have shown that safety and efficacy are similar for the correction of moderate myopia. This has lead researchers to believe there is little difference in outcome between the two techniques. Yet concerns over the depth of corneal cut remain.

Epi-LASIK, first described by Palikaris I et al (2003), provides a mechanical method of epithelial separation using a microkeratome-like instrument with a customized blade design. This technique offers the advantage of being quicker and less damaging to the epithelial integrity than LASEK. With a more viable epithelial sheet to replace following the laser treatment, it has been hypothesized that this will lead to less postoperative pain and haze along with faster visual recovery times. It is also felt to be a safer technique as complications due to modification of stromal architecture are avoided and has been successful in early, large-scale studies (Katsanevakis VJ et al 2007, Dai J et al 2006, Juhás TM et al 2007). Case reports of complications are published as well (Kim JH et al 2006).

Due to their only recent widespread use, the body of research comparing epi-LASIK, LASEK and PRK with regards to visual recovery times, pain, and haze post operatively is minimal. In addition to the comparison papers mentioned above, several papers have compared LASEK with Epi-LASIK (Zdenek G, 2005; Teus MA et al 2008), LASIK vs. Epi-LASIK (Kalyvianaki MI et al 2006), PRK vs. epi-LASIK (Gamaly TO et al 2007), epi-LASIK vs PRK (Torres LF et al 2008), epi-LASIK vs LASEK vs. LASIK O’Doherty M et al 2007), LASIK vs. LASEK vs. PRK (Ghadhafan F et al 2007) and even epi-LASIK vs. epi-LASEK (Camellin & Wyler, 2008). No study has been published involving the breath of objective outcomes (corneal haze, postoperative pain and visual recovery) important to the civilian and military sector comparing epi-LASIK, LASEK and PRK.

Although our study is a retrospective chart review, consistent detailed follow-up data has been obtained by our refractive surgery clinic for 12 months post-
operatively. This facilitates the comparison of UCVA, visual recovery times, post-operative pain and corneal haze between LASEK, PRK, and epi-LASIK over a twelve month post-operative period. The potential for a strong study lies in the meticulous recording of our clinical results along with consistent follow-up with very few patients lost over the period studied.

Materials and methods
Charts were reviewed from the Warfighter’s Refractive Surgery Center at Wilford Hall Medical Center. 297 eyes ranging from –4.00 D to –8.00 D were reviewed and surgery was performed from 2002 to 2005. All eyes included in this study were from patients undergoing bilateral eye surgery except one epi-LASIK case performed unilaterally. 100 eyes underwent PRK (Average SE = -5.38), 100 eyes LASEK (Average SE = -5.00) and 97 eyes epi-LASIK (Average SE = -5.34). All refractive surgeries were performed at Wilford Hall Medical Center by one of three surgeons.

Data for post-operative pain was collected at post-op day 1, post-op day 4 and post-op day 7. Pain was reported on the Visual Analog Pain (VAS) scale of 0 to 10 with zero being no pain and 10 being very severe pain. This scale was divided into three pain groups: mild (1-3), moderate (4-6) and severe (7-10). Only patients who reported having no pain in either eye on any of the follow-up days were recorded as negative for pain. Non-parametric analysis using Fisher’s exact test was used to determine statistical significance for post-operative pain comparisons between patients.

Data for corneal haze was collected at 3 months, 6 months and 12 months. Any degree of haze recorded in the chart on any of these days for any eye individually was designated as positive for haze. The scale used was 0, +1, +2, >+2. Previous research was our guide as to our cutoff for significant haze (+2) and haze study design (Pallikaris I et al 2003). Only those eyes that did not have any haze at any of the data collection points were designated as negative for haze. Fisher’s exact test was used to determine statistical significance of differences in corneal haze between the three groups.

Finally, uncorrected visual acuity (UCVA) was collected from post-op days 1, 4, 7, and at 1 month. Visual recovery for the purpose of this study will be designated as 20/40 UCVA (Snellen). UCVA of 20/40 or better was used as the cutoff for visual recovery while any recording worse than 20/40 will be considered negative for recovery. Fisher’s exact test was used to analyze differences in visual recovery between the groups.

Surgical technique
All surgeries were performed at the Wilford Hall Warfighter Refractive Surgery Center. The VISX Star S4 (VISX technology, Santa Clara, CA) was used for all procedures. Laser parameters and ablation nomograms were the same for all three procedures, and ablations of 6.5 mm with a blend were used. The same preparatory procedures were used for all three procedures including topical anesthesia (tetracaine) without systemic sedation and use of an angulated Barraquer lid speculum. A bandage contact lens (Acuvue) was kept in place from 4 to 7 days. Topical fluromethalone 1% starting QID and tapered on drop a month for a total of four months was used for all patients postoperatively. Topical moxifloxacin (Vigamox) QID was used for 7 days. Dilute non-preserved Tetracaine was used as a rescue drop for the first 24 hours and oral Percocet was given as oral pain control as needed.

PRK
The epithelium was removed using an automatic epithelial brusher (Amoils; Innovative Excimer Solutions, Inc, Toronto, Ontario). The laser treatment was performed and the cornea was irrigated using chilled balanced salt solution (BSS). The bandage contact lens was then placed.

LASEK
After adequate exposure was obtained, the cornea was marked inferiorly. An 8.5 mm alcohol well containing 20% ethanol was applied to the center of the cornea for 30 seconds, the alcohol was removed, then the cornea thoroughly rinsed using BSS. An epithelial micro-hoe (Katena, Denville, NJ) was used to create an 8.5 mm epithelial defect using a superior epithelial hinge. The epithelial flap was reflected back
from the cornea with a Shahinian epithelial peeler (Katena). The exposed Bowman’s layer was dried using a merocel sponge. The excimer laser treatment was performed and the cornea was rinsed with chilled BSS before the epithelium was repositioned with the edges overlapping the original intact epithelium. One minute was allowed for the re-adherence of the epithelium to the underlying stromal tissue before a bandage contact lens was placed in the eye.

Epi-LASIK
The automatically rotational epi-LASEK microkeratome (Amadeus II Intelligent Microkeratome, SJS, Switzerland) was used to create the epithelial sheet with its central circular opening centration around the limbus. For all patients the 9.0 mm ring was used. A Barraquer tonometer ensured adequate suction before separation and several drops of Refresh artificial tear drops were used as a lubricant to the operative cornea. Suction was released and the sheet was hinged in the nasal position. After ablation, the cornea was rinsed with chilled BSS or a Weck-cell sponge soaked in BSS and frozen was applied to the cornea before the epithelial sheet was replaced with the aid of a Merocel sponge and an anterior chamber irrigation cannula. A bandage contact lens was then applied.

Results
Post-op pain
The 1, 4, 7 day post-op any pain results are displayed in Table 1. Epi-LASIK held a slight advantage over PRK and LASEK early (33 % to 48 %), but all became minimal at post-op day 7 (0 %-5 %). The trend continued when the results were subdivided into mild pain as epi-LASIK was less painful on POD 1 (Table 3) and PRK was the only procedure with pain on POD 7. POD 1 and 4 showed similar results between all three procedures when subdivided into severe pain, yet interestingly only epi-LASIK resulted in severe pain on POD 7 (Table 3).

Visual acuity
The 1, 4, 7 day post-op UCVA (20/40 or better) results are displayed in Table 4. Visual recovery was similar by four weeks in all groups. PRK showed the highest percentage of visual recovery to 20/40 vision on POD 1. By POD 7 there was no statistically significant difference between PRK and LASEK; however, the epi-LASIK group did demonstrate a statistically significant difference compared to PRK but not LASEK. By one month there was no difference between the groups.
Table 4

<table>
<thead>
<tr>
<th>POD</th>
<th>PRK</th>
<th>LASEK</th>
<th>epi-LASIK</th>
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<tr>
<td>1</td>
<td>74%</td>
<td>39%</td>
<td>52%</td>
<td>0.0023</td>
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<tr>
<td></td>
<td>(73/96)</td>
<td>(38/98)</td>
<td>(47/90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>71%</td>
<td>37%</td>
<td>47%</td>
<td>0.0006</td>
</tr>
<tr>
<td></td>
<td>(70/98)</td>
<td>(36/96)</td>
<td>(41/88)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>7</td>
<td>87%</td>
<td>82%</td>
<td>72%</td>
<td>0.0165</td>
</tr>
<tr>
<td></td>
<td>(80/92)</td>
<td>(79/96)</td>
<td>(65/90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1 month</td>
<td>98%</td>
<td>100%</td>
<td>98%</td>
<td>NS</td>
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<tr>
<td></td>
<td>(96/98)</td>
<td>(100/100)</td>
<td>(83/85)</td>
<td>&lt;0.0001</td>
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Haze
The 3, 6, 9 month post-op haze results are displayed in Table 5. Epi-LASIK trended towards less haze and LASEK had the highest percentage of haze at each follow-up. When subdivided into severe haze, LASEK actually had no reported significant haze until the 12 month mark but all procedures had minimal percentages of significant haze.

Table 5

<table>
<thead>
<tr>
<th>Any haze</th>
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<tbody>
<tr>
<td>Post-op period</td>
</tr>
<tr>
<td>PRK</td>
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<tr>
<td>3 months</td>
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<tr>
<td></td>
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<td>6 months</td>
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<tr>
<td>12 months</td>
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Table 6

| Significant haze ( >2+ ) |
| Post-op period |
| PRK | LASEK | epi-LASIK | Significance |
| 3 months | 1.0% | 0% | 0% | not |
|           | (1/96) | (0/92) | (0/77) | significant |
| 6 months | 3.1% | 0% | 1.5% | not |
|           | (3/97) | (0/92) | (1/65) | significant |
| 12 months | 3.6% | 2.8% | 0% | not |
|           | (2/56) | (2/72) | (0/21) | significant |

Discussion
Clinical results between LASEK and PRK have shown to be comparable with some studies citing some mild benefit with LASEK (Claringbold TV, 2002; Lee JB et al 2001; Shah S et al 2001; Kaya V et al 2004; Litwak S et al 2002; Cimberle M, 1999). Other studies have demonstrated the two procedures equal in regards to pain, quicker visual recovery and haze (Hashemi H et al 2004; Leccisotti A, 2003). Yet another study demonstrated increased pain in LASEK patients post-operatively yet less intense wound healing (Ghirlando A et al 2007).

Since LASEK and epi-LASIK are more complicated and labor-intensive procedures than PRK, there is still controversy as to whether these procedures offer true advantages over PRK. Post-operative pain has been compared between the three techniques demonstrating epi-LASIK patients to have less pain immediately after surgery but all being equal at 4 hours post-operatively (O’Doherty M et al 2007). Other work has shown faster rehabilitation of corneal sensitivity and tear function of Epi-LASIK treated eyes over LASIK treated eyes (Kalyvianaki MI et al 2006). Post-operative pain has been documented comparing epi-LASIK to PRK which demonstrated similar pain on post-operative day 1 but with epi-LASIK having more pain on day 3 and 6 (Torres LF et al 2007).

In our study, epi-LASIK showed a slight advantage in post-operative pain over PRK and LASEK in the early post-operative period. This is consistent with outcomes described by Litwack et al (2002) as they showed no difference between LASEK and PRK post-operative pain (Cimberle M, 1999). They noted the epithelial flap may not lie smoothly on the stromal bed and sometimes sloughs which could induce pain and discomfort. It may be that with blunt separation of the epithelium with the micro-keratome separator, a smoother epithelial sheet is created that allows for a quicker, smoother and more adherent reattachment once repositioned.

This finding is corroborated by the histological evaluation performed by Palikaris et al who showed the epithelial flap created by mechanical separation to have a basement membrane with normal cellular morphology compared to alcohol-assisted which
showed many irregularities and blebbing of the basement epithelial cells.

At 1 month visual recovery was similar between all techniques studied. This finding has previously been reported for LASEK and PRK comparisons (Lee JB et al 2001, Shah S et al 2001, Hashimi H et al 2004, Gamaly TO et al 2007, O’Doherty M et al 2007). We found a difference in the early post-operative days where we noted PRK had a higher percentage of eyes with at least 20/40 UCVA. This difference has also been reported by patients in Liwack’s study (Cimberle M, 1999). Epi-LASIK did have a slight edge over LASEK at POD 1 and 4 (by 13% and 10% respectively) for percentage of eyes with UCVA of 20/40 or better. We hypothesize that the epithelial sheet created with epi-LASIK needs less manipulation than LASEK and hence maintains more viable epithelial cells that are able to reattach to the underlying stroma quicker and provide a smoother, clearer epithelial sheet with less edema since they have not been exposed to the toxic effects of alcohol.

It is well documented that subepithelial haze may develop in the cornea after PRK (COPARSP, 1999). In a study by Lee and colleagues, haze was seen in LASEK but was less than that of PRK (Lee JB et al 2001). Gamaly and colleagues found that epi-LASIK had less haze than LASIK and PRK (Gamaly TO et al 2007). It has also been hypothesized by Kaya V et al (2004) that higher myopes (higher than -6.00 diopters) who require more excimer laser energy have higher haze rates as result of the increased laser energy and increased healing response (Litwak S et al 2002). Our study included up to -8.00 D and an average SE of -5.0 D in all three groups. Overall the incidence of haze was low in all three groups. No statistical difference was seen between the three groups at 3 months, 6 months or 12 months. However, early results show a trend towards less significant haze (>2+) with the epi-LASIK group at 6 and 12 months. We do not utilize prophylactic mitomycin C in any of our surface ablation procedures and all the patients underwent a full four-month topical steroid taper and some who demonstrated haze were treated for additional time using topical steroids and none went on to require surgical intervention to treat the haze seen. Also of note, the study is not masked which introduces bias in relation to interpretation of corneal haze. In assessing the relative merits of the procedures, it is difficult to draw a useful conclusion about haze in particular because of the potential bias in assessments. We feel this bias by the clinician observer during post-operative examinations would be slight yet it did warrant note in the discussion.

**Conclusion**

Epi-LASIK has a slight advantage over PRK and LASEK early on in the post-op course with regards to pain. Visual recovery is similar by 4 weeks and is better with PRK early. In addition, epi-LASIK trends toward less significant haze. These results are very encouraging and epi-LASIK should be seen as an attractive alternative to LASEK and PRK in treating moderate to high myopes.

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