EFFECTS OF LASER IN SITU KERATOMILEUSIS ON THE CORNEAL ENDOTHELIUM

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The purpose of this study was to assess the effects of laser in situ keratomileusis (LASIK) on the corneal endothelium. In a prospective study, the corneal endothelium of 87 eyes (45 patients) was examined before and 1 month after LASIK. Patients were divided into two groups: people who wear contact lenses (48 eyes) and people who had never worn contact lenses (39 eyes). The corneal endothelium was analyzed for cell density, percentage of hexagonal cells, and coefficient of variation (CV) of cell size. The mean cell density and percentage of hexagonal cells was significantly higher 1 month after LASIK for all 87 eyes. However, the mean CV of cell size was not significantly different. In contact lens wearers, there was a significant increase in mean cell density and percentage of hexagonal cells, but there was no significant change in mean CV of cell size after LASIK. Among patients who had never worn contact lenses, no significant changes were noted in mean cell density, percentage of hexagonal cells, or mean CV of cell size. In this study, LASIK caused no damage to the corneal endothelium. Postoperative improvements in the mean cell density and percentage of hexagonal cells in patients who were contact lens wearers may be related to the discontinuance of contact lens use after LASIK.

Key Words: LASIK, corneal endothelium, contact lens (Kaohsiung J Med Sci 2005;21:272–6)

First described by Pallikaris et al [1], laser in situ keratomileusis (LASIK) has become a widely used procedure to correct myopia. It combines the creation of a corneal flap with a microkeratome and excimer laser ablation of the underlying corneal stroma. Several studies have reported that LASIK has good efficacy and predictability for treating myopia [2–4]. However, its safety has not been well established.

One major concern about LASIK is its effect on the corneal endothelium. Previous studies have reported contradictory results on corneal endothelial cell density after LASIK [4–10].

In this study, we evaluated the effects of LASIK on corneal endothelium density, percentage of hexagonal cells, and coefficient of variation (CV) of cell size.

PATIENTS AND METHODS

Consecutive patients undergoing LASIK between April and October 2000 were enrolled in this prospective study. All patients who underwent LASIK were aged 18 years or older, had visual acuity correctable to 20/40 or better, normal topography, normal anterior segment by slit-lamp microscopy, normal posterior pole by dilated funduscopy, did not have glaucoma, ocular hypertension, or systemic collagen vascular disease, and were not pregnant or using systemic corticosteroids. Patients were eligible for inclusion...
Effects of LASIK on the corneal endothelium

in this study when they had a best corrected visual acuity of 20/20 or more and not more than 1.50 D of astigmatism. All operations were performed by the same surgeon (SHT) using the VISX Star S2 (VISX Inc, Santa Clara, CA, USA) and an automated microkeratome (Automated Corneal Shaper, Chiron Vision Irvine, CA, USA). After LASIK, topical fluorometholone 0.1% (FML, Allergan, Irvine, CA, USA) and ciprofloxacin 0.3% (Ciloxan, Alcon Laboratories, Fort Worth, TX, USA) were instilled four times daily during the first postoperative week.

Endothelial specular microscopy was performed preoperatively and 1 month postoperatively using a noncontact specular microscope (Konan NONCON-ROBO SP8000, Konan Medical Corp, Fairlawn, NJ, USA).

Patients were assessed as a whole group and in subgroups of contact lens wearers and patients who had never worn contact lenses.

**Results**

This prospective study comprised 87 eyes from 45 patients (15 men, 30 women). Mean age was 29.9 ± 6.1 years (range, 18–47 years). Mean preoperative spherical equivalent refractive error was –8.59 ± 3.61 D (range, –1.25 to –20.5 D). The mean cell density and percentage of hexagonal cells were significantly increased 1 month after LASIK (p = 0.02 and 0.049), but the mean CV of cell size was not significantly changed (p = 0.95) (Table 1).

**Contact lens wearers**

There were 24 patients (4 men, 20 women; 48 eyes) who were contact lens wearers. Mean patient age was 30.2 ± 5.5 years (range, 19–47 years). Mean preoperative spherical equivalent refractive error was –9.08 ± 4.04 D (range, –1.25 to –20.5 D). One month postoperatively, the mean cell density and percentage of hexagonal cells was significantly increased (p = 0.04 and 0.02) (Table 2). The mean CV of cell size decreased, but the change was not significant (p = 0.79).

**Non-contact lens wearers**

There were 21 patients (11 men, 10 women; 39 eyes) who did not wear contact lenses. Mean patient age was 29.5 ± 6.8 years (range, 18–47 years). Mean preoperative spherical equivalent refractive error was –7.98 ± 2.95 D (range, –2.25 to –13 D). There was no significant difference in mean cell density, percentage of hexagonal cells, and mean CV of cell size before and after LASIK (all p > 0.05) (Table 3).

**Comparison between contact lens and non-contact lens wearers**

There were no significant differences between the two groups in age (p = 0.73) and spherical equivalent refractive error (p = 0.16).

Preoperatively, patients who were contact lens wearers had significantly lower mean cell density and percentage of hexagonal cells than patients who had never worn contact lenses (p = 0.02 and 0.001) (Table 4). The contact lens wearers also had a higher CV of cell size, but the difference was not significant (p = 0.35). Postoperatively, there were no significant differences in mean cell density and CV of cell size between the two groups (Table 4). Although the percentage of hexagonal cells increased in patients who were contact lens wearers after LASIK,

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**Table 1.** Mean cell density, percentage of hexagonal cells, and coefficient of variation of cell size in 87 eyes preoperatively and 1 month postoperatively

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<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>Cell density (cells/mm²)</td>
<td>2,617 ± 218</td>
<td>2,666 ± 228</td>
<td>0.02</td>
</tr>
<tr>
<td>Hexagonality (%)</td>
<td>50.8 ± 5.9</td>
<td>52.3 ± 6.1</td>
<td>0.049</td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>0.490 ± 0.06</td>
<td>0.489 ± 0.07</td>
<td>0.95</td>
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**Table 2.** Mean cell density, percentage of hexagonal cells, and coefficient of variation of cell size in 48 contact lens-wearing eyes preoperatively and 1 month postoperatively

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<th>Preoperative</th>
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<tbody>
<tr>
<td>Cell density (cells/mm²)</td>
<td>2,569 ± 232</td>
<td>2,628 ± 237</td>
<td>0.04</td>
</tr>
<tr>
<td>Hexagonality (%)</td>
<td>48.8 ± 5.8</td>
<td>51.1 ± 5.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>0.499 ± 0.07</td>
<td>0.496 ± 0.07</td>
<td>0.79</td>
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**Table 3.** Mean cell density, percentage of hexagonal cells, and coefficient of variation of cell size in 39 non-contact lens-wearing eyes preoperatively and 1 month postoperatively

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<tr>
<td>Cell density (cells/mm²)</td>
<td>2,676 ± 184</td>
<td>2,713 ± 208</td>
<td>0.22</td>
</tr>
<tr>
<td>Hexagonality (%)</td>
<td>53.3 ± 5.1</td>
<td>53.8 ± 6.1</td>
<td>0.68</td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>0.479 ± 0.06</td>
<td>0.482 ± 0.06</td>
<td>0.80</td>
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</table>
it was still lower than in patients who had never worn contact lenses \( (p = 0.04) \).

**Discussion**

LASIK corrects myopia using a predictable corneal wound healing response [5,11,12]. To be clinically feasible, LASIK must not only have good efficacy and predictability, but be safe as well. Because the corneal endothelium cannot regenerate after birth, any endothelial cell loss or damage after LASIK would lower its acceptance and application. To better understand the impact of LASIK on the corneal endothelium, we compared the preoperative and postoperative endothelial cell density, hexagonality, and CV of cell size. In all 87 eyes, the mean cell density and percentage of hexagonal cells were significantly higher 1 month after LASIK than before. However, the mean CV of cell size was not significantly changed. When we divided patients into two groups, contact lens wearers and those who had never worn contact lenses, we found similar results in patients who were contact lens wearers; there was a significant increase in mean cell density and percentage of hexagonal cells and no significant change in mean CV after LASIK. However, among patients who had never worn contact lenses, there were no significant changes in any of the parameters. Our results suggest that LASIK has no adverse effect on the corneal endothelium.

The possible mechanisms for endothelial loss or damage by excimer laser photoablation include thermal damage, mechanical damage from shock waves, and actinic damage from ultraviolet light [13,14]. Because the depth of ablation is closer to the endothelium in LASIK than in photorefractive keratectomy, there is greater concern about the state of the endothelium after LASIK. Experimental studies show endothelial cell loss after deep incisions performed with a 193-nm excimer laser [15,16]. Significant changes in morphology and function have also been reported, with a residual posterior corneal stroma of less than 190 µm after ablation [17]. However, Seiler et al and Krueger et al show that the 193-nm beam penetrates less than the diameter of a cell, so direct irradiation is unlikely to lead to endothelial cell loss [18,19].

Kim et al reported that LASIK induces an acute effect on the corneal endothelium that may represent transient and reversible endothelial cell edema [20]. They suggest that the combination of excimer laser ablation and increased intraocular pressure associated with the LASIK procedure exerts a cumulative force on the corneal endothelium, but the exact etiology remains unclear. However, they did not investigate the long-term result.

A MEDLINE search revealed only two reports of corneal endothelial cell loss after LASIK. Pallikaris and Siganos reported that LASIK does not appear to induce serious endothelial cell loss, but the higher the attempted correction, the greater the endothelial cell loss [4,5]. They concluded that endothelial cell loss is unavoidable because of the shock waves produced by the excimer laser ablation and the corneal manipulation during keratomileusis. However, the endothelial cell loss stabilizes at 12 months postoperatively and regresses thereafter. This stabilization may result from a form of central endothelial cell rearrangement.

In contrast, most studies have shown that corneal endothelial cell density remains unchanged or even increases. Jones et al demonstrated the short-term effect of LASIK on corneal endothelium in 98 eyes in 65 myopic patients (range, −2.75 to −14.50 D) and concluded that LASIK had no significant effect on central corneal endothelial cell density and morphology at 2 and 12 weeks postoperatively [6]. Collins et al found no significant changes in central endothelial cell density and the percentage of hexagonal cells 3 years after LASIK, although there was a significant improvement in the CV of cell size [9]. They proposed that, after LASIK, patients would have a thinner cornea, which could allow oxygen to diffuse across the corneal endothelium more easily, thereby improving its

| Table 4. Comparison between contact lens wearers (CL) and patients who had never worn contact lenses (No CL) |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| | Preoperative | Postoperative | Preoperative | Postoperative | Preoperative | Postoperative |
| CL \((n = 48)\) | 2,569 | 2,628 | 48.8 | 51.1 | 0.499 | 0.496 |
| No CL \((n = 39)\) | 2,676 | 2,713 | 53.3 | 53.8 | 0.479 | 0.482 |
| \(p\) | 0.02 | 0.09 | 0.0001 | 0.04 | 0.15 | 0.35 |
health [9]. Perez-Santonja et al also found that LASIK did not cause significant damage to the corneal endothelium [7]. In addition, they showed that patients who previously wore contact lenses had improvement in endothelial cell density and CV of cell size postoperatively. Our study had consistent results, which we speculate might be attributed to discontinuation of contact lens use before LASIK and reestablishment of a normal endothelial pattern by cell migration from the peripheral to central cornea.

There is one limitation to our study. Because most patients did not return to the clinic for regular follow-up due to a satisfactory visual outcome, postoperative data beyond 1 month in our study were incomplete. Further evaluation is necessary. However, Collins et al showed that there is no difference in corneal endothelial cell condition between 1 month and 3 years postoperatively [9]. We suggest that the corneal endothelium remains unchanged even after long-term follow-up.

In conclusion, LASIK appears to be a feasible surgical procedure to correct refractive error and, most importantly, has no apparent adverse effect on the corneal endothelium.

**References**

雷射角膜內層重塑術 (LASIK) 對角膜內皮細胞之影響

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評估雷射角膜內層重塑術 (LASIK) 術後對角膜內皮細胞之影響。前瞻性研究角膜內皮細胞在 LASIK 術前和術後一個月的狀況。病人分為術前使用隱形眼鏡和從未使用過隱形眼鏡兩組。角膜內皮細胞分析指標為細胞密度、六角形細胞比例及細胞大小變異係數。在 87 隻眼睛中，平均細胞密度及六角形細胞比例在 LASIK 術後一個月明顯上升。平均細胞大小變異係數則無顯著差異。在術前使用隱形眼鏡的病人中 (48 隻眼睛) 平均細胞密度及六角形細胞比例在 LASIK 術後一個月明顯增加，但平均細胞大小變異係數則無顯著差異。在從未使用過隱形眼鏡的病人中 (39 隻眼睛) 細胞密度、六角形細胞比例平均及細胞大小變異係數皆沒有顯著差異。LASIK 並不會造成角膜內皮細胞的傷害。術前使用隱形眼鏡的病人，在平均細胞密度及六角形細胞比例上的改善可能與術後不再配戴隱形眼鏡有關。

關鍵詞：雷射角膜內層重塑術，角膜內皮細胞，隱形眼鏡
（高雄醫誌 2005;21:272－6）

收文日期：94 年 3 月 25 日
接受刊載：94 年 4 月 25 日
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