Comparison of Corneal Nerve Regeneration and Sensitivity Between LASIK and Laser Epithelial Keratomileusis (LASEK)

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- PURPOSE: To compare changes in corneal nerve fibers and keratocyte density by confocal microscopy after laser-assisted in situ keratomileusis (LASIK) and laser epithelial keratomileusis (LASEK).
- DESIGN: Prospective, nonrandomized comparative clinical trial.
- METHODS: Fifty-six eyes of 28 patients who underwent LASIK and 52 eyes of 26 patients who underwent LASEK were included. Confocal microscopic data of the central cornea, corneal sensitivity, tear film breakup time, and Schirmer values were determined at three and six months after LASIK or LASEK treatment.
- RESULTS: In the LASIK group, corneal sensitivity was reduced from preoperative levels at six months after surgery. In the LASEK group, however, there was no difference between baseline and six-month postoperative values. The number of subbasal nerve fibers and the keratocyte density were also different in the LASIK and LASEK groups. The regeneration of corneal nerves correlated strongly with the recovery of corneal sensation and keratocyte density in both groups, whereas the tear film breakup time, Schirmer values, and epithelial thickness did not correlate with corneal nerve regeneration in either group.
- CONCLUSIONS: The greater decrease in the number of subbasal nerve fibers in the LASIK group compared with the LASEK group may relate to the greater decrease in corneal sensitivity. The pattern of corneal nerve regeneration and the recovery of corneal sensation after LASEK did not differ greatly from that after photorefractive keratectomy in previous studies. (Am J Ophthalmol 2006;141:1009–1015. © 2006 by Elsevier Inc. All rights reserved.)

Photorefractive keratectomy (PRK) has become popular for correcting refractive errors, and modifications such as laser epithelial keratomileusis (LASEK) and laser-assisted in situ keratomileusis (LASIK) have been introduced with the aim of improving postoperative outcomes. In LASIK, a flap is created with a microkeratome, the integrity of the anterior corneal layer is preserved, and laser ablation is performed at the stromal bed. The main advantages of LASIK are postoperative comfort, rapid recovery of vision, and absence of corneal haze. However, this procedure unavoidably destroys corneal nerve fibers and tissues. Many studies report decreases in the number of subbasal nerve fibers and keratocytes after LASIK, and recent studies suggest that epithelial remodeling can occur after LASIK despite preservation of the corneal epithelium and the Bowman layer.

LASEK, a relatively new laser surgical procedure for the correction of refractive errors, combines certain elements of LASIK and PRK. LASEK also disrupts corneal nerve fibers and tissues, but the degree and pattern of disruption may differ from that of LASIK. The wound-healing nature of LASEK distinguishes it from other techniques for excimer laser refractive surgery, and hence the regeneration of corneal nerves and the change of keratocyte density in the operated eye may differ between LASEK and PRK.

In this study, we used confocal microscopy to compare corneal nerve fiber regeneration and keratocyte density after LASIK and LASEK. In addition, we investigated whether there was any relationship between the regeneration of corneal nerve fibers, recovery of corneal sensation, keratocyte density, and ocular surface dryness.
METHODS

THIS SINGLE-SITE, PROSPECTIVE, NONRANDOMIZED, COMPARATIVE clinical trial was conducted at the Department of Ophthalmology, Yonsei University College of Medicine. All procedures conformed to the tenets of the Declaration of Helsinki, and informed consent was obtained from all patients after the study was approved by the institutional review board.

Before surgery, a study author (H.K.L) explained to patients the merits, demerits, and complications associated with the LASIK and LASEK procedures. Patients then selected their preferred method. After this process, two groups of patients were generated: the LASIK group, comprising 56 eyes of 28 patients; and the LASEK group, comprising 52 eyes of 26 patients. Preoperative examinations included visual acuity, manifest refraction, cycloplegic refraction, slit-lamp examination, pachymetry, applanation tonometry, keratometry and videokeratometry readings, fundus examination, and confocal microscopic examination. Tear function was assessed by the Schirmer test without corneal anesthesia, and the tear film breakup time (BUT) was determined. Exclusion criteria included anterior segment pathologies, any evidence of lid disease, progressive or unstable myopia or keratoconus, history of herpetic keratitis, and previous intraocular or corneal surgery. All surgical procedures were performed by the same surgeon (J.K.K.).

For the LASIK procedure, a microkeratome (MK 2000; NIDEK, Tokyo, Japan) was used to create a 130-μm flap, which was raised with a spatula to expose the stromal bed. An excimer laser (S4; VISX, Santa Clara, California, USA) with an eye tracker was directed at the dried corneal surface with the ablation centered over the entrance to the pupil. The flap was replace with a spatula guided by peripheral epithelial markings. The epithelial and stromal portions of the flap were then irrigated with a cannula.

For the LASEK procedure, an alcohol solution cone (J2905; Janach, Como, Italy) with a diameter of 8.5 mm was placed on the eye. A 20% alcohol solution was instilled inside the cone, left for approximately 30 seconds, and then carefully washed off with a balanced salt solution. The epithelial flap was gently lifted with an epithelial microhoe (J2915A; Janach) and peeled back as a single sheet toward the 12 o’clock position with a spatula (J2910A; Janach). Excimer laser treatment was performed in the usual manner by using the same nomogram and laser system as with LASIK. The flap was washed with a balanced salt solution and repositioned carefully. A therapeutic soft contact lens was applied to the ablated cornea until the complete epithelialization had occurred. The patients were instructed to apply one drop of diclofenac 0.1% and ofloxacin 0.3% every two hours, and artificial tears every hour until epithelial healing was complete.

The Snellen visual acuity, intraocular pressure, manifest refraction, and corneal sensation (with a Cochet-Bonnet esthesiometer) were measured, and topography and confocal microscopic corneal evaluations were performed at one, three, and six months after reepithelialization was complete.

Confocal microscopy was used to evaluate the thickness of the total cornea, corneal epithelium, the density of subbasal and stromal nerves, and keratocytes both before and after surgery. A confocal microscope (Confoscan 3; NIDEK) was used to examine all corneas in this study following the technique described by Patel and associates. In brief, one drop of hydroxypropyl methylcellulose 2.5% (Novartis Ophthalmics, Hettlingen, Switzerland) was placed on the tip of the objective lens as an optical coupling medium, and the lens was manually advanced until the medium contacted the central surface of the cornea.

During confocal microscopy examinations, a full-thickness scan comprising a series of confocal images was obtained as the focal plane was advanced at approximately 78 μm/s from anterior to the epithelium to posterior to the endothelium. Digital images were stored on a computer workstation at 30 frames/s. Each image represented a coronal section of approximately 475 × 350 μm (horizontal × vertical) and was separated from adjacent images by approximately 2.5 μm.

All confocal scans of sufficient quality for nerve visualization were evaluated by the method of Calvillo and associates. In brief, the nerves appeared as long, narrow structures, and only those longer than 50 μm were counted. The number of nerve fibers in the subbasal region (several frames anterior to the most anterior keratocyte) and the stromal region was recorded from each scan in all eyes before surgery. In all the eyes that underwent LASIK, the number of nerve fibers in the subbasal region, the stromal flap (the region between the most anterior keratocyte and the flap interface), and the stromal bed (the region between the flap interface and the most posterior keratocytes excluding the Descemet membrane) was re-
corded in each scan. In all eyes that underwent LASEK, the number of nerve fibers in the subbasal region and in the anterior (to a depth of ~130 μm) and posterior (from ~131 μm to the Descemet membrane) stromal beds was recorded.

We modified the method of Erie and associates\(^9\) to determine keratocyte density. The five scans with the least motion blur were selected from the anterior and posterior stromal bed at regular intervals. Images from the anterior stroma were selected at 15-μm intervals to a depth of 130 μm in the subbasal layer, and the posterior stroma was selected at 30-μm intervals from 131 μm to the Descemet membrane. This method was used to avoid selection bias. The images selected before LASIK or LASEK and at all posttreatment visits were presented in a random order to one masked observer (S.J.L.). Bright objects that resembled keratocyte nuclei were manually counted in each image. The number of cells in a stromal volume of 0.475 by 0.350 by 0.002 mm\(^3\) was counted, and then converted to the keratocyte density in cells per cubic millimeter. The cell density was compared between the procedures at each posttreatment visit. We also measured and analyzed changes in the epithelial thickness before and after surgery. The epithelial thickness was determined by either the subbasal peak or the visible subbasal nerves to demarcate the epithelium from the Bowman layer. All scans were evaluated and measured by one observer who was masked to both the patient and the time of the scan.

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### TABLE 1. Nerve Fiber Density in Each Confocal Microscopy Scan After LASEK and LASIK\(^*\)

<table>
<thead>
<tr>
<th>Site</th>
<th>LASIK</th>
<th>LASEK</th>
<th>P</th>
<th>LASIK</th>
<th>LASEK</th>
<th>P</th>
<th>LASIK</th>
<th>LASEK</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subbasal</td>
<td>4.39 ± 1.38</td>
<td>4.21 ± 1.23</td>
<td>.182</td>
<td>0.74 ± 1.06</td>
<td>1.28 ± 1.41</td>
<td>.034</td>
<td>1.01 ± 1.71</td>
<td>2.79 ± 0.61</td>
<td>.012</td>
</tr>
<tr>
<td>(2.1 to 5.8)</td>
<td>(1.7 to 5.9)</td>
<td>(1.3 to 2.2)</td>
<td>(0.4 to 6.5)</td>
<td>(0.2 to 2.1)</td>
<td>(0.4 to 3.2)</td>
<td>(0.6 to 2.2)</td>
<td>(0.3 to 3.0)</td>
<td>(1.8 to 3.9)</td>
<td>(0.8 to 4.1)</td>
</tr>
<tr>
<td>Anterior stroma (to 130 μm)</td>
<td>1.68 ± 1.79</td>
<td>1.71 ± 1.69</td>
<td>.128</td>
<td>0.56 ± 1.26</td>
<td>1.14 ± 1.32</td>
<td>.056</td>
<td>0.55 ± 1.12</td>
<td>1.53 ± 1.44</td>
<td>.019</td>
</tr>
<tr>
<td>(0.3 to 3.8)</td>
<td>(0.4 to 3.5)</td>
<td>(0.2 to 3.2)</td>
<td>(0.4 to 3.2)</td>
<td>(0.2 to 3.1)</td>
<td>(0.4 to 3.1)</td>
<td>(0.1 to 1.5)</td>
<td>(0.4 to 3.3)</td>
<td>(0.3 to 4.1)</td>
<td>(0.3 to 4.1)</td>
</tr>
<tr>
<td>Posterior stroma (from 131 μm)</td>
<td>0.51 ± 0.74</td>
<td>0.58 ± 0.77</td>
<td>.538</td>
<td>0.50 ± 0.61</td>
<td>0.61 ± 0.71</td>
<td>.288</td>
<td>0.47 ± 0.59</td>
<td>0.59 ± 0.70</td>
<td>.235</td>
</tr>
<tr>
<td>(0.0 to 1.3)</td>
<td>(0.0 to 1.1)</td>
<td>(0.0 to 1.0)</td>
<td>(0.1 to 1.0)</td>
<td>(0.1 to 1.0)</td>
<td>(0.1 to 1.0)</td>
<td>(0.1 to 1.0)</td>
<td>(0.1 to 1.0)</td>
<td>(0.1 to 1.0)</td>
<td>(0.1 to 1.0)</td>
</tr>
</tbody>
</table>

LASEK = laser epithelial keratomileusis.
\(^*\)Data are expressed as mean ± SD (range).

### TABLE 2. Comparison of Preoperative and Postoperative Tear Film Breakup Time (BUT) and Schirmer Values Between LASIK and LASEK\(^*\)

<table>
<thead>
<tr>
<th>Value</th>
<th>LASIK</th>
<th>LASEK</th>
<th>P</th>
<th>LASIK</th>
<th>LASEK</th>
<th>P</th>
<th>LASIK</th>
<th>LASEK</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUT (seconds)</td>
<td>9.9 ± 2.1</td>
<td>9.7 ± 1.9</td>
<td>.439</td>
<td>5.4 ± 4.0</td>
<td>7.0 ± 4.1</td>
<td>.012</td>
<td>7.5 ± 4.3</td>
<td>8.2 ± 4.3</td>
<td>.023</td>
</tr>
<tr>
<td>(8.1 to 11.8)</td>
<td>(8.3 to 12.3)</td>
<td>(4.0 to 8.0)</td>
<td>(5.1 to 8.5)</td>
<td>(5.0 to 8.0)</td>
<td>(4.0 to 8.0)</td>
<td>(5.1 to 8.5)</td>
<td>(5.0 to 8.0)</td>
<td>(4.0 to 8.0)</td>
<td>(5.1 to 8.5)</td>
</tr>
<tr>
<td>Schirmer value (mm/5 min)</td>
<td>11.4 ± 2.3</td>
<td>10.9 ± 1.9</td>
<td>.325</td>
<td>8.2 ± 6.9</td>
<td>11.1 ± 4.8 &lt;.01</td>
<td>10.1 ± 6.2</td>
<td>10.9 ± 5.5</td>
<td>.288</td>
<td></td>
</tr>
<tr>
<td>(8 to 13)</td>
<td>(9 to 14)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
<td>(6.0 to 10.5)</td>
</tr>
</tbody>
</table>

\(^*\)Data are expressed as mean ± SD (range).

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**FIGURE 2.** Change in corneal sensation after LASIK (solid bars) and LASEK (open bars) (*\(P < .05\), Student t test).
Statistical analysis was performed (SPSS for Windows, v12.0; SPSS Inc, Chicago, Illinois, USA). The BUT, Schirmer value, corneal sensitivity, number of corneal nerve fibers, and epithelial thickness at three time periods were compared by post hoc multiple comparisons by the Tukey method. An independent Student t test was used to compare the number of corneal nerve fibers and epithelial thickness between the two groups. The Pearson correlation coefficient was calculated to evaluate the relationship between regenerated corneal nerves, ocular surface dryness, and corneal sensitivity.

### RESULTS

The age of the LASIK patients was 28.3 ± 4.2 (mean ± SD) years (range 23 to 40 years), and that of the LASEK patients was 30.9 ± 4.5 years (range 21 to 45 years) (P = .249). The preoperative spherical equivalent refractive power was −4.69 ± 2.40 diopters (range −2.00 to −6.75 diopters) in LASIK patients and −4.93 ± 2.28 diopters (range −2.25 to −6.50 diopters) in LASEK patients (P = .142). The corneal thicknesses were 533.2 ± 49.7 μm (range 491 to 568 μm) and 529.5 ± 44.5 μm (range 489 to 571 μm) in LASIK and LASEK patients, respectively (P = .103). In the LASIK-operated group, the mean number and density of subbasal and anterior stromal (~130 μm) nerves were markedly reduced compared with the preoperative values, especially the subbasal nerve fibers, whose density reduced to almost zero at up to six months after surgery (Figure 1, Top left) (Table 1). Until six months after surgery, the anterior stromal region within the flap area and posterior stromal area showed sparse and narrow nerve fibers (Figure 1, Top, Middle, and Right). In LASEK-operated eyes, the nerve fiber density at three months after surgery did not differ from the preoperative value, except in the subbasal region (Table 1) where the density did not recover to the preoperative value until six months.

The density of nerve fiber bundles in the subbasal region was markedly decreased after LASIK and LASEK compared with that before surgery. At six months, fibrous membranes and regenerated nerve fibers were evident in the subbasal area, which recovered faster in LASEK- than in LASIK-operated eyes (Figure 1, Bottom left). The anterior stromal area showed more fibrous and fibrotic areas in LASEK-operated eyes (Figure 1, Bottom middle), and the nerve fibers in this area were more prominent and thicker than in LASIK-operated eyes. However, the density of nerve fibers in the posterior stromal bed did not decrease after either procedure and did not differ between the two techniques (Figure 1, Right column).

With the exception of the Schirmer value at six months after surgery, the mean postoperative BUT and Schirmer values were much lower in the LASIK group than in the LASEK group at all follow-up evaluations (Table 2). At six months, the BUT and Schirmer values did not differ significantly from the preoperative values in LASEK-operated eyes (P = .078 for BUT, P = .429 for the Schirmer value). In the LASIK group, the Schirmer value improved to the preoperative value from three months after operation (P = .099). The BUT value did not recover to the preoperative value until six months after surgery (P < .011).

Before surgery, the corneal sensation was 6.3 ± 0.5 cm in the LASIK group and 6.2 ± 0.5 cm in the LASEK group (P = .439). Up to six months after both procedures, the mean corneal sensation differed significantly between the groups (Figure 2) (P < .01 at three months, P = .017 at six months). LASIK-treated eyes had a lower corneal sensation compared with the preoperative value (6.3 ± 0.5 cm before surgery vs 2.56 ± 1.93 cm at three months after surgery and 3.75 ± 1.45 cm at six months after surgery, P < .01 at three and six months), and the value had not returned to baseline at six months. In the LASEK group, the mean corneal sensation recovered to the preoperative value by six months after surgery (5.01 ± 1.23 cm at three months after surgery and 5.45 ± 1.62 cm at six months after surgery vs 6.2 ± 0.5 cm before surgery).

At three months after surgery, the keratocyte density was decreased relative to the preoperative value in the LASIK group (Table 3). This reduction was more severe in the anterior than in the posterior stromal bed (20.0% vs 13.0% reduction, respectively). In LASEK-operated eyes, the keratocyte density increased significantly in the ante-
rior stromal bed (P < .001) and did not show a change in the posterior bed relative to the preoperative value (P = .482). At six months, the keratocyte density continued to differ in the anterior stromal bed but not in the posterior bed. The keratocyte density after LASEK was initially increased, then returned to the preoperative value at six months. However, in the LASIK group, the reduced keratocyte density had not recovered at six months after surgery. In the posterior segment, no difference was found in the anterior stromal bed but not in the posterior bed.

We then examined changes in epithelial thickness after surgery. The central corneal epithelial thickness increased more in the LASIK group than in the LASEK group (Figure 3). At six months after surgery, the LASIK-operated eyes continued to show an increased epithelial thickness (46.8 ± 8.9 µm before surgery vs 61.9 ± 13.0 µm at six months after surgery). However, in LASEK-operated eyes, the epithelial thickness did not differ from the preoperative value (47.3 ± 9.2 µm before surgery vs 50.9 ± 12.4 µm at six months after surgery).

The decrease in the density of subbasal corneal nerve fiber bundles was correlated with decreased corneal sensitivity in both LASIK- and LASEK-operated eyes (Table 4). The density of subbasal corneal nerves showed a strong positive correlation with corneal sensitivity in both groups at six months after surgery. In addition, the keratocyte density was strongly correlated with the regeneration of corneal nerves in the subbasal area (r = 0.892, P < .001 in LASIK; r = 0.811, P < .001 in LASEK) and the recovery of corneal sensitivity (r = 0.371, P < .001 in LASIK; r = 0.358, P = .022 in LASEK). However, the BUT and Schirmer values were not correlated with the density of subbasal and total corneal nerve fiber bundles in either the LASIK or the LASEK group.

**DISCUSSION**

**THE TIME COURSE AND PATTERN OF NERVE REGENERATION**

The time course and pattern of corneal nerve regeneration after refractive surgery are assumed to depend partly on where and at which depth the nerves are severed. Several in vivo studies have examined postoperative reductions in the number of subbasal nerve fibers in the human cornea after LASIK. However, no reported studies have used confocal microscopy in vivo to assess the effects of the LASEK procedure on corneal nerve fibers. To our knowledge, the present study is the first to demonstrate that the regeneration of corneal nerves is substantially superior after LASEK than after LASIK. Slowik and associates studied subbasal nerves in eight patients after LASEK, but they did not observe subbasal nerves in the central cornea during the first four months after surgery. Lee and associates demonstrated that subbasal nerves that were lost during LASIK slowly regenerated, but did not return to preoperative densities even after three years. Consistent with the above studies, we found few subbasal corneal nerves until six months after LASIK. Previous studies have shown that the corneal sensation in the central cornea recovers to the preoperative value between one and three months after PRK. Clinical studies have shown that corneal sensation recovers to the preoperative value by three to 16 months after LASIK.

In our study, the decreased corneal sensation immediately after LASEK had recovered to the preoperative value by three months after surgery. This result is comparable with those of previous PRK studies. Recently, Herrmann and associates reported that corneal sensation recovered more rapidly after LASEK—to the preoperative value by one month after surgery. However, they retrospectively investigated corneal sensation after LASEK and found a range of preoperative refractive errors that differed from that in our study. Some studies suggest that the extent and duration of corneal hypesthesia after PRK is dependent on the ablation depth. Therefore, different preoperative refractive errors can affect the recovery of postoperative central corneal sensation and corneal nerves.

Our confocal microscopy investigations revealed that corneal nerve regeneration was faster in LASEK-operated
eyes than in LASIK-operated eyes. However, the nerve regeneration pattern of LASEK did not differ from that previously reported for PRK-operated cases. Previous confocal microscopy studies found faint subbasal nerves in the central corneal at one to four months after PRK, which is similar to our findings for LASEK. In addition, considering that both LASEK and PRK involve epithelial healing, basement membrane reconstruction, and anterior stromal wound healing, subbasal corneal nerve regeneration may be similar with the two procedures. However, considering the discrepancy between in vivo confocal microscopy findings and histologic examinations of corneal nerve regeneration, and the fact that LASEK-operated eyes showed much less keratocyte apoptosis, leukocyte infiltration, and epithelial healing than PRK-operated eyes, future studies should prospectively compare the corneal nerve regeneration between the two procedures in a large number of cases.

We also could not determine why subbasal corneal nerve regeneration was delayed in LASIK compared with LASEK. However, we have previously reported differences between LASIK and PRK in tear nerve growth factor (NGF) in the early postoperative period, and the postoperative tear NGF value paralleled the decreased corneal sensation. Photoablation takes place in the same anterior stroma in both PRK and LASEK after the removal of the epithelium. It is possible that the higher NGF values in early post-LASEK eyes relative to post-LASIK eyes resulted in better corneal nerve regeneration during wound healing.

The increased keratocyte density in post–LASEK-operated eyes was correlated with corneal nerve regeneration in the present study. The keratocyte density of LASEK-treated eyes remained increased after six months and was similar to that in PRK-operated eyes. However, LASIK decreased the keratocyte density compared with the preoperative value or with LASEK-operated eyes. There are no data on the role of stromal keratocytes after excimer laser surgery in the regeneration of corneal nerves. However, the increased population of keratocytes in the anterior stromal area (which is the most vulnerable site for nerve fiber loss after excimer surgery) and the increased density of keratocytes noted after PRK or LASEK (which show more favorable corneal nerve and sensation restoration) suggest that keratocytes play an important role in corneal nerve regeneration and in the restoration of corneal sensation. Further studies are required to clarify the relationship between keratocytes and corneal nerve regeneration.

In the present study, BUT and Schirmer values did not correlate with subbasal corneal nerve regeneration. These findings are interesting given ocular surface dryness after refractive surgery is linked to corneal nerve blockade. BUT and Schirmer values are still widely used to measure the status of ocular surface dryness. However, clinicians with experience in treating subjects with symptoms but minimal surface damage and tear instability question the reliability of classical parameters for diagnosis and evaluation for dry eye such as Schirmer test and BUT. Meaningful diagnostic parameters are required for accurate evaluation of the inflammatory status of dry eyes. More reliable parameters (for example, tear osmolarity) would better correlate with corneal nerve regeneration, and would be more useful in planning appropriate treatment.

The major limiting factor of the present study is selection bias for the surgical method. Although the preoperative patient characteristics did not differ between LASIK and LASEK groups, the surgical method could not be randomly assigned to patients. More precise evaluation of corneal nerve regeneration, ocular surface dryness, and keratocyte density may require studies in which surgery is randomly assigned and the interpretation of data is performed in a masked fashion.

In conclusion, to our knowledge, this is the first study to compare corneal nerve regeneration and its correlation with corneal sensation and ocular surface dryness between LASIK and LASEK. This study has demonstrated that the disruption of corneal nerve fibers is greater for LASIK than for LASEK. The pattern of corneal nerve regeneration, recovery of corneal sensation, and recruitment of keratocytes after LASEK did not differ from that after PRK, a finding that is consistent with previous reports. Further studies are needed to determine the mechanisms underlying differences in corneal nerve regeneration after LASIK and LASEK.

**REFERENCES**

Biosketch

Seung Jae Lee, MD, is a resident in the Institute of Vision Research, Department of Ophthalmology, College of Medicine Yonsei University Yong, Dong Severance Hospital, Kangnam-gu, Seoul, Korea. Dr Lee’s primary research interests include corneal nerve generation and corneal epithelial wound healing.