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Laser Subepithelial Keratomileusis for Low to Moderate Myopia: 6-Month Follow-up

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Purpose: To examine the effectiveness, safety, and stability of laser subepithelial keratomileusis (LASEK), a modified photorefractive keratectomy for low to moderate myopia.

Methods: This study evaluated the results of LASEK in 48 myopic patients (84 eyes) with a consecutive 6-month follow-up period. Preoperative myopia ranged from 3.25 to 7.00 diopters (D). Uncorrected and corrected visual acuity, manifest refraction, epithelial healing time, postoperative pain, subepithelial corneal haze, and complications were examined.

Results: Uncorrected visual acuity of 20/30 or better was achieved in 78.6% of eyes at 1 week and in 96.4% at 6 months after surgery. A mean refraction of within ±0.50 D was measured in 42 eyes (50.0%) and ±1.0 D in 79 eyes (94.0%) at 6 months. The epithelial healing time was 3.68 ± 0.69 days (range, 3–6 days) and postoperative pain scores were 1.49 ± 0.65. The subepithelial corneal haze scores were 0.56 ± 0.34 and 0.16 ± 0.25 at 1 and 6 months, respectively. As for complications, alcohol leakage during surgery occurred in 3 eyes, incomplete epithelial detachment in 3 eyes, contact lens intolerance in 5 eyes and steroid-induced elevated intraocular pressure (>21 mm Hg) in 1 eye.

Conclusions: LASEK is an effective and safe procedure for low to moderate myopia. It can be considered an alternate type of refractive surgery for correction of low to moderate myopia. **Jpn J Ophthalmol 2002;46:299–304**

Key Words: Laser subepithelial keratomileusis, low to moderate myopia, photorefractive keratectomy, refractive surgery.

Introduction

After the successful experiments of Trokel et al[1] the first human eye was treated successfully with photorefractive keratectomy (PRK) in 1988.[2] PRK has been accepted as a reasonably predictable, effective, and safe method for the correction of low to moderate myopia.[3–7] However, postoperative pain, relatively slow recovery, subepithelial corneal haze, and myopic regression are shortcomings of PRK.[8]

Laser subepithelial keratomileusis (LASEK), is a modified PRK technique that is based on the detachment of an epithelial flap after the application of an alcohol solution, and then the repositioning of this flap following laser application. We were able to observe that the LASEK-treated eye had less postoperative pain and early postoperative corneal haze than the PRK-treated eye in the same patient.[9] Therefore, in this study, we examined the effectiveness and safety of LASEK for treatment of low to moderate myopia during a 6-month follow-up.

Materials and Methods

This prospective study comprised 48 consecutive myopic patients (84 eyes) between November 1999 and August 2000. All subjects had received full ex-

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planations of the procedures, and informed consent was obtained before surgery. The corrected visual acuity of all patients was 20/20 or better. All eyes had comprehensive preoperative ophthalmic examinations, including slit-lamp microscopy, fundus examination, cycloplegic and manifest refraction, corneal keratometry, corneal topography, central corneal thickness measurement, and Goldmann tonometry. Exclusion criteria included amblyopia, cataract, glaucoma, keratoconus or keratoconus suspected by videokeratography, active ocular disease, and systemic diseases such as diabetes mellitus and connective tissue disease. Emmetropia was the refractive goal in all eyes.

LASEK Procedure

After instillation of topical anesthesia with proparacaine hydrochloride 0.5%, pre-incision of the corneal epithelium was performed to circumscribe the flap area with a special microtrephine with an 8.0-mm diameter, 70-μm depth calibrated blade (J 2900S; Janach, Como, Italy). The trephine was designed to leave a hinge of about 90° at the 12-o'clock position. An alcohol solution cone (J 2905, Janach,) with an 8.5-mm diameter, which could cover the pre-trephinized area, was placed on the cornea. A 20% alcohol solution was made with 100% alcohol diluted with distilled water, and contained in a 5-cc glass syringe. Then, 0.2 cc of the solution was instilled inside the cone and left for 30 seconds. After 30 seconds, the ethanol in the cone was absorbed using a dry cellulose sponge followed by thorough irrigation on the surface of the eye with balanced salt solution. The precut margin was then lifted and epithelial detachment was carried out with an epithelial micro-hoe (J 2915 A). The epithelial flap was gently detached, gathered, and folded up to 12-o'clock position. From this point, the treatment proceeded like that of traditional PRK, using an excimer laser (Keratome II®; Coherent-Schwind, Neuostheim, Germany) with the following operative parameters: energy fluence 240 mJ/cm^2, repetition rate 13 Hz. After laser ablation, the stromal surface was irrigated with balanced salt solution and the epithelial flap was repositioned using a spatula (J 2920 A). After repositioning the epithelial flap, we let the flap adhere to the underlying stromal bed for 1 minute. At the end of the surgery, a drop of ofloxacine 0.3% (Ofloxacine®; Samil Pharmaceutical, Korea) and a drop of diclofenac 0.1% (Optanac®; Samil) were administered, and a therapeutic contact lens (Hypa day®; diameter 14.2 mm, BC 8.7 mm, Chonan, Korea) was applied to the eye.

Subsequent to surgery, patients were instructed to apply one drop of the Ofloxacine and Optanac four times a day and artificial tear drops (Tears Naturale Free®; Alcon Lab, Fort Worth, TX, USA) every 2 hours until the epithelium healed. After complete re-epithelialization, Ofloxacine and fluorometholon 0.1% (Fluorometholon®; Samil) were administered four times daily for the first postoperative month, three times daily for the second month, twice daily for the third month, and then once a day for the fourth month.

Following surgery, all patients were given mefenamic acid 250 mg (Pontal®; Yuhan, Korea) to be used every 8 hours for 3 days for pain relief. All patients were examined daily at the same time of the day until the epithelial defect closed, and the time to complete epithelialization was recorded. We checked uncorrected visual acuity daily until the epithelial wound healed and also checked the corrected visual acuity and refractive errors at 1 week, and at 1, 3, and 6 months. Seven days following surgery, every patient was asked: "How much pain did you experience after the surgery?" They were asked to grade their pain on the following four-point scale: 0 = no pain or discomfort, 1 = mild burning pain, 2 = moderate and more prolonged burning pain, 3 = severe constant or sharp pain that required more medication to relieve the pain.

Subepithelial corneal haze levels were detected using slit-lamp microscopy examination and subjectively graded according to Hanna's method,[10] at 1, 3, and 6 months after surgery. Subepithelial haze was graded from 0 to 4 as follows: 0, totally clear; 0.5, a faint corneal opacity seen only by oblique indirect illumination; 1, opacity of minimal density seen with difficulty with direct and diffuse illumination; 2, easily visible opacity; 3, denser opacity that significantly decreased the visualization of intraocular structures such as the iris and retina; and 4, an opaque cornea.

Data was entered into an Excel spreadsheet (Microsoft, Redmond, WA, USA), which was also used for analysis.

Results

Patients ranged in age from 19 to 45 years (mean ± SD = 26.4 ± 4.7 years). Of the 48 patients (84 eyes), there were 20 male patients (34 eyes) and 28 female patients (50 eyes). The mean preoperative spherical equivalent refraction was −4.72 ± 1.08 D (range, −3.25 to −7.00 D) (Table 1). The mean epithelial healing time was 3.68 ± 0.69 days and the epithelium completely healed without infection in 3 to 5 days

Table 1. Preoperative Characteristics of Patients*

Characteristics	Mean ± SD	Range
Mean age of patients (years)	26.4 ± 4.7	19–45
Mean spherical equivalent (diopter)	−4.72 ± 1.08	−3.25–7.00
Mean keratometry (diopter)	43.6 ± 1.3	41.50–46.25
Mean central corneal thickness (μm)	531.3 ± 40.2	495–612

*20 men and 28 women.

with the exception of 2 eyes, which were healed by 6 days after surgery. As for creation of the epithelial flap, at first, we succeeded in making the epithelial flap without any tear or buttonhole in 7 out of 10 cases during the LASEK procedure, but later, the percentage of such cases increased to approximately 96% following the initial 10 cases in this study. The change of uncorrected visual acuity is shown in Table 2. At 1 week after surgery, 66 eyes (78.6%) had a visual acuity of 20/30 or better without correction. At 6 months, the uncorrected visual acuity was 20/30 or better in 81 eyes (96.4%). Two eyes (2.4%) lost one Snellen line of spectacle-corrected visual acuity, and no eyes lost more than one Snellen line of spectacle-corrected visual acuity. Table 3 summarizes the refractive results during follow-up. A mean refraction of within ±0.50 D was measured in 42 eyes (50.0%) and ±1.0 D in 79 eyes (94.0%) at 6 months. The postoperative pain scores were 1.49 ± 0.65, 4 eyes (4.8%) had a +3 grade pain, and 3 eyes (3.6%) did not report any pain after surgery (Figure 1). The subepithelial corneal haze scores were 0.56 ± 0.34 and 0.16 ± 0.25 at 1 and 6 months, respectively. As shown in Figure 2, 20 eyes (23.8%) showed corneal haze of not less than +1 grade at 1 month. One eye (1.2%) had +1 grade corneal haze, the manifest refraction was sph −0.75 = cyl −0.50 Axis 170°, and the uncorrected visual acuity was 20/30 at 6 months.

As for complications, alcohol leakage occurred in 3 eyes and incomplete epithelial detachment, in 3 eyes during surgery. Contact lens intolerance was seen in 5 eyes. Corticosteroid-induced elevated intraocular pressure (≥21 mm Hg) was seen in 1 eye, which was controlled with β-blocker (Table 4). There were no early postoperative complications, such as infection or recurrent erosion.

Discussion

Photorefractive keratectomy has been widely used due to its precise predictability and safety as a corrective procedure for low to moderate myopia.[3–7] However, its predictability decreases in cases of high myopia, and its effects are limited by postoperative pain, corneal haze and myopic regression.[4,11,12]

LASEK is an alternative to refractive surgery.[9,13,14] Theoretically, it offers the advantage of avoiding the flap-related complications of laser in situ keratomileusis (LASIK). We also learned that LASEK-treated eyes had less significant postoperative pain and corneal haze than PRK-treated eyes in the early postoperative period.[9]

The beneficial effects of using various concentrations of alcohol to mechanically debride the corneal epithelium in PRK have been reported.[15–19] Shah et al[16] reported that the 18% ethanol-treated group had improved uncorrected and mean spherical equivalent refraction over the mechanical debridement group at 12 weeks. This may be because mechanical epithelial debridement can lead to microcuts and roughness of the stroma, which, in turn, lead to an irregular ablation in PRK.[17] Although a histological evaluation was not made, a smoother and more regular surface can be seen through the operating microscope following the epithelial debridement with 20% ethanol than after the mechanical debridement in PRK.[17]

As shown in Table 2, at 1 week, 66 eyes (78.6%) had 20/30 or better visual acuity without correction. We believe that the remaining epithelial flap acts as a smooth refractive surface and this results in relatively good initial visual acuity. Relatively good postoperative visual acuity and early visual recovery may enable the LASEK procedure to be performed simultaneously as LASIK.

Table 2. Changes in Uncorrected Visual Acuity after Laser Subepithelial Keratomileusis*

	1 Day	2 Days	3 Days	4 Days	1 Week	1 Month	3 Months	6 Months
Visual Acuity	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
≥20/20	1 (1.2)	1 (1.2)	0 (0)	1 (1.2)	20 (23.8)	48 (57.1)	39 (46.4)	33 (39.3)
20/25 to 20/30	9 (10.7)	7 (8.3)	6 (7.1)	11 (13.1)	46 (54.8)	34 (40.5)	43 (51.2)	48 (57.1)
20/50 to 20/70	54 (64.3)	48 (57.2)	47 (56.0)	46 (54.7)	18 (21.4)	2 (2.4)	2 (2.4)	3 (3.6)
≤20/100	20 (23.8)	28 (33.3)	31 (36.9)	26 (31.0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	84 (100)	84 (100)	84 (100)	84 (100)	84 (100)	84 (100)	84 (100)	84 (100)

*n: Number of eyes.

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Table 3. Distribution of Refractive Errors Over Time in All Patients*

Spherical Equivalent Refraction (D)	1 week n (%)	1 month n (%)	3 months n (%)	6 months n (%)
+1.5 to 1.1	3 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)
+1.0 to 0.6	18 (21.4)	8 (9.5)	5 (6.0)	3 (3.6)
+0.5 to 0.1	26 (31.0)	14 (16.7)	19 (22.6)	13 (15.5)
0 to −0.5	30 (35.7)	34 (40.4)	27 (32.1)	29 (34.5)
−0.6 to −1.0	7 (8.3)	25 (29.8)	29 (34.5)	34 (40.4)
−1.1 to −1.5	0 (0.0)	3 (3.6)	4 (4.8)	5 (6.0)
−1.6 to −2.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mean	+0.06	−0.30	−0.38	−0.43
SD	0.48	0.50	0.51	0.53

*N = 84. n: number of eyes; D: diopter; SD: standard deviation.

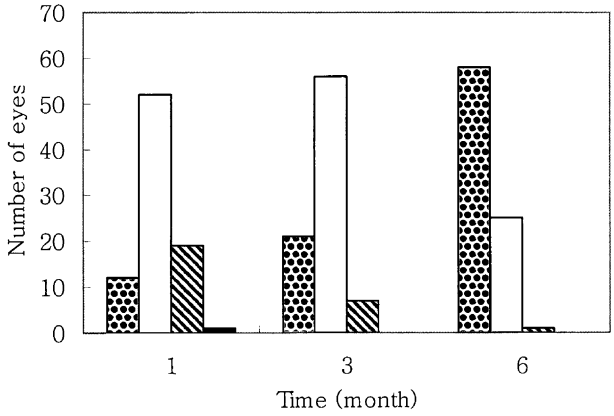

Figure 2. Change of corneal haze scores after laser subepithelial keratomileusis. Haze scores: ▩ 0, □ 0.5, ▨ 1, ■ 2.

Although the degree of subepithelial corneal haze may depend on the type of laser, use of topical steroid and ethnic group, the corneal haze scores of our patients at 6 months were 0.16 ± 0.25, and 1 eye (1.2%) had +1 grade haze. From the viewpoint of the decreased corneal haze after LASEK, although the details of underlying cellular events remain unclear, we speculate that if an epithelial flap is made, it becomes loose and lengthens enough to cover the cut epithelial border. It seals up the bare stroma. That prevents the release of cytokines and growth factors from the stroma and damaged epithelium, which decreases the initial inflammatory damage to the stroma. This may reduce the apoptosis of anterior stromal keratocytes and subsequent replenishment with activated keratocytes, later decreasing the synthesis of collagens.[20] Also, an epithelial flap becomes a mechanical barrier that protects the bare surface of stroma from the tears. Zhao et al demonstrated that tears may be a major factor in the induction of keratocyte loss after de-epithelialization in the mouse cornea.[21]

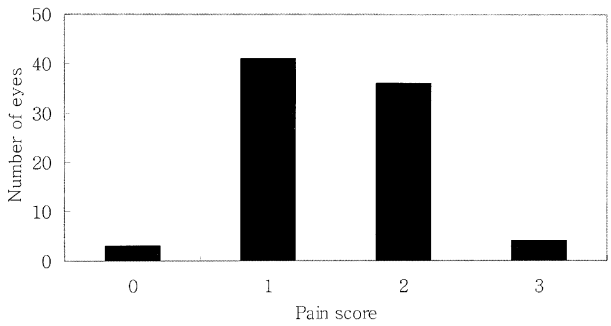

Figure 1. Distribution of pain scores after laser subepithelial keratomileusis.

As for complications, alcohol leakage occurred in 3 eyes during surgery. Two of these eyes had +3 grade and 1 eye had +2 grade pain following surgery. None of the 3 eyes, however, showed complications such as conjunctival and corneal erosion or limbal cell deficiency later. Incomplete epithelial detachment occurred in 3 eyes. Two of these eyes had more than one tear in the epithelial flap during epithelial detachment. One of the three eyes had fragmented epithelial flaps that were placed on the stroma after laser ablation, and the epithelium healed by 6 days following surgery. Contact lens intolerance following surgery occurred in 5 eyes and all of these had folds of Descemet's membrane (Figure 3) and all were switched to pressure patch. Four of these eyes were in patients over 40 years old, and 1 eye was in a 35-year-old patient. Although the reason for the contact lens intolerance is not certain, we do not

Table 4. Complications After Laser Subepithelial Keratomileusis

Complications	Frequency (No. of Eyes)	
Alcohol leakage during surgery		3
Incomplete epithelial detachment		3
Tear in the flap	2	
Fragmented epithelial flap	1	
Contact lens intolerance		5
Contact lens intolerance only	3	
Contact lens intolerance and filamentary keratitis	2	
Steroid-induced elevated intraocular pressure		1
Total		12

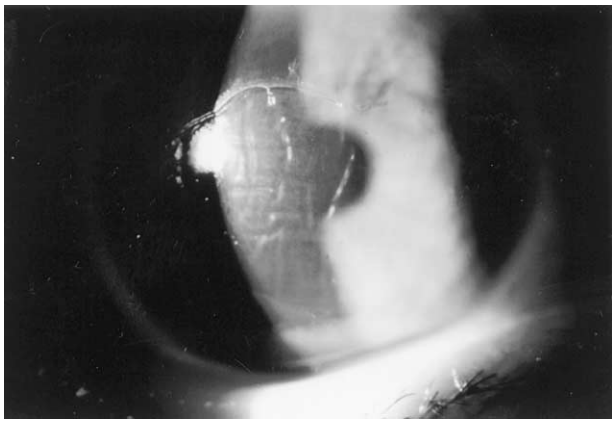

Figure 3. Epithelial defect and clinically significant stromal edema with folds in Descemet's membrane on the second postoperative day of laser subepithelial keratomileusis.

recommend the LASEK procedure in patients over 40 years of age. Two eyes with contact lens intolerance developed filamentary keratitis after application of the pressure patch (Figure 4) following the cessation of eyedrops including lubricant solution. Frequent lubrication such as with artificial tears would be recommended when LASEK is used.

The limitations of LASEK are that it requires more complex surgical procedures, additional expenses for surgical instruments, and more training in surgery.

In summary, LASEK is an effective and safe procedure for use in mild to moderate myopia. However, patient-selection criteria, such as age, and the additional frequent lubrication required should be considered. Further investigation of LASEK, with a comprehensive surgical normogram, long-term evaluation, and histological and molecular biological studies, should be carried out in the near future.

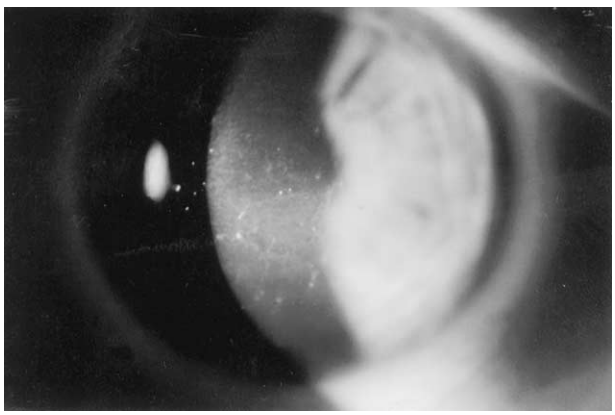

Figure 4. Filamentary keratitis with infiltration is visible on the third postoperative day of laser subepithelial keratomileusis. This is 2 days after application of the pressure patch.

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