Effect of hinge width on corneal sensation and dry eye after laser in situ keratomileusis

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Purpose: To investigate the effect of hinge width on corneal sensation and dry-eye syndrome after laser in situ keratomileusis (LASIK).

Setting: TLC Laser Eye Center, Garden City, New York, USA.

Methods: Fifty-four patients at least 18 years of age had bilateral LASIK with a narrow nasal hinge microkeratome flap in 1 eye and a wider nasal hinge microkeratome flap in the other eye. In all eyes, the flaps were 160 μm in thickness with a diameter of 9.5 mm. Masked Cochet-Bonnet esthesiometry was performed in the central cornea preoperatively and at 1 week and 1, 3, and 6 months. Dry eye was evaluated at the same intervals by lissamine green corneal and conjunctival staining, Schirmer test with anesthesia, and tear-film breakup time.

Results: Corneal sensation was significantly reduced from preoperative levels through 6 months in the narrow-hinge group and through 3 months in the wider-hinge group ($P \leq .002$). The mean corneal sensation was greater in corneas with a wider hinge flap than in those with a narrow hinge flap at all postoperative examinations; the difference was significant at 1 and 3 months ($P \leq .002$). The loss of sensation was greatest at 1 week and improved at all subsequent examinations. Overall, dry-eye signs and symptoms were greatest immediately postoperatively and improved at subsequent intervals.

Conclusions: Corneal sensation and dry-eye signs and symptoms improved at all intervals between 1 week and 6 months. The loss of corneal sensation and presence of dry-eye syndrome were greater in eyes with a narrow hinge flap than in eyes with a wider hinge flap.

J Cataract Refract Surg 2004; 30:790–797 © *2004 ASCRS and ESCRS*

The human cornea is one of the most densely innervated and highly sensitive tissues in the body. The corneal sensory nerves are vital for maintaining corneal epithelial integrity, stimulating lacrimal gland tear production, and initiating the blink reflex. Corneal sensation is provided by the long ciliary nerves of the ophthalmic division of the fifth (trigeminal) cranial nerve. The long ciliary nerve trunk travels in the suprachoroidal space, where it branches several times before entering the cornea at the limbus. After entering the cornea, the nerves run in the middle third of the stroma, branch anteriorly, and form a dense subepithelial plexus.[1] The sensory nerves enter the limbus predominantly at the 9 o'clock and 3 o'clock positions with little innervation entering the eye superiorly and inferiorly. The nerves bifurcate several times before forming a dense plexus in the sub-Bowman's layer, which densely innervates the central cornea.[2,3] The nerves then penetrate Bowman's membrane and terminate in the epithelium at the wing cell layer.

The long ciliary nerves entering the eye at the 9 o'clock and 3 o'clock positions explain why corneal sensation is significantly greater at the temporal and nasal limbus than inferiorly.[4] The neural architecture of the cornea also explains the finding that loss of corneal sensation and dry-eye signs and symptoms are greater

Accepted for publication September 17, 2003.

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Published by Elsevier Inc.

0886-3350/04/$–see front matter
doi:10.1016/j.jcrs.2003.09.043

with a superior hinge and milder with a nasal hinge flap for at least 6 months after laser in situ keratomileusis (LASIK).[5] Corneal sensation is greatest in the central cornea and decreases toward the limbus.[5] Sensitivity declines with age and is not affected by iris color.[6]

Corneal sensation is decreased after LASIK and photorefractive keratectomy; the return of function generally occurs over 6 months.[7,8] Additionally, tear secretion decreases after LASIK and normalizes by 6 months.[9] In vivo confocal microscopy has shown that LASIK-induced alterations in the subbasal nerve plexus are directly related to decreased corneal sensation[10–12] and corneal sensation after LASIK is greatest near the hinge and decreases toward the central cornea and the peripheral cornea away from the hinge.[10] The depth of corneal ablation also affects the extent of corneal sensitivity loss and recovery.[11] In the corneal flap, the number of subbasal and stromal nerve fiber bundles decreases by 90% immediately after LASIK. During the first postoperative year, subbasal nerve fiber bundles gradually return, although by 1 year their number remains less than half that before LASIK.[12]

Early stages of neurotrophic keratopathy are associated with an interpalpebral punctate keratitis and visual fluctuation.[10] The physiological role of corneal innervation is unclear, but active involvement of neuroregulation may be responsible for maintaining the integrity and repair of the corneal epithelium.[13] Additionally, intact corneal sensation is partially responsible for tear secretion. With decreased corneal sensation, there is a decrease in tear production.[13–15] Topical proparacaine, which causes complete loss of sensation, results in a 60% to 75% decrease in tear secretion and an increase in tear osmolarity.[16] An increase in tear-film osmolarity is also associated with the ocular surface changes of keratoconjunctivitis sicca.[17] Patients with dry eye have a significant decrease in corneal sensation.[17] The combination of a neurotrophic cornea with dry eye can result in epithelial breakdown, poor wound healing, and visual diminution.

Dry-eye syndrome has emerged as a common complication of LASIK surgery.[18–21] While estimates of its incidence vary widely,[18–21] almost all patients will have transient dry eye during the immediate postoperative period. Dry-eye symptoms are often associated with a loss of corneal sensation and range from mild irritation and foreign-body sensation to pain, photophobia, and decreased visual acuity with visual fluctuation. This study investigated the effect of the width of the corneal flap hinge on corneal sensation and dry-eye signs and symptoms after LASIK.

Patients and Methods

This prospective masked clinical trial comprised 108 consecutive eyes of 54 consecutive patients who had LASIK and were willing to participate in the study and return for all follow-up examinations. All patients had bilateral simultaneous LASIK performed by the same surgeon (E.D.D.) in 1 center. A horizontal flap was created in both eyes with the nasal hinge Amadeus microkeratome (AMO) that allows the hinge width to be varied. The hinge width was set at 0.6 mm in 1 eye and 1.2 mm in the other eye. The width was randomly assigned to the first eye, and the alternate width was created in the other eye.

Preoperatively, baseline visual acuity and fluorescein tear-film breakup time (TBUT) were determined and Cochet-Bonnet esthesiometry, Schirmer test with anesthesia, and lissamine green corneal and conjunctival staining were performed. Corneal sensation was measured at the central cornea, and the mean of 3 sensation measurements was recorded. The standard for measuring corneal sensation is the Cochet-Bonnet esthesiometer (Luneau Ophthalmologia). This esthesiometer has a 6.0 cm long nylon monofilament that can be adjusted in length. To measure corneal sensation, the nylon monofilament is applanated against the corneal surface and the patient responds when corneal sensation is appreciated. By adjusting the length of the nylon monofilament, pressure gradients can be created ranging from 11 to 200 mg/mm^2. Individuals with normal corneal sensation will sense the touch of the monofilament at 6.0 cm. If a patient does not note touch at 6.0 cm, the monofilament is reduced at intervals of 0.5 cm until sensation is perceived. A response was considered positive if the nylon filament was felt at a given length at least 2 of 3 times.

Fluorescein TBUT is considered a test of tear-film stability and is decreased in patients with aqueous tear deficiency; it can also be decreased in patients with meibomian gland disease and corneal irregularity. Tear-film breakup time was performed with a fluorescein strip moistened with balanced salt solution (BSS®) applied to the inferior cul-de-sac without anesthesia. The patient was asked not to blink, and a stopwatch was used to measure the time from lid opening to tear breakup. The Schirmer test with anesthesia is a measure of basal tear production.

Lissamine green is a supravital stain with minimal toxicity that stains damaged corneal and conjunctival epithelium as well as areas of mucin loss within the tear film.[22] Lissamine green is more accurate than fluorescein in diagnosing dry-eye syndrome and less toxic than rose bengal.

Surgery was performed under topical anesthesia consisting of proparacaine 1% with the Visx Star 3 excimer laser. The flap created by the Amadeus microkeratome was 9.5 mm in diameter, and the depth plate was 160 μm. In all cases, the horizontal corneal diameter, flap diameter, and hinge-chord length were measured with calipers at the time of surgery. The photorefractive ablation was performed using a 6.0 mm or 6.5 mm ablation zone. All patients received a topical antibiotic agent (ofloxacin 0.3%), an antiinflammatory drug (preservative-free ketorolac tromethamine 0.5%), and corticosteroids (prednisolone acetate 1%) at the time of surgery. Postoperatively, patients received topical ofloxacin 0.3% and prednisolone acetate 1% 4 times daily for 5 days, as well as topical carboxymethylcellulose 1% at the conclusion of surgery[23] and 4 times on the first postoperative day. Patients were instructed to use preservative-free carboxymethylcellulose (Refresh Tears®) 4 times daily as needed for the first week.

Patients were seen at 1 day, 1 week, and 1, 3, and 6 months. The examinations were done by a masked ophthalmologist, who was not involved in the preoperative evaluation or surgery. Corneal sensation was measured at 1 week and 1, 3, and 6 months using the Cochet-Bonnet esthesiometer. Additionally, patients had corneal and conjunctival staining with lissamine green (graded on a scale of 0 to 3 with 0 = no staining, 1 = mild staining, 2 = moderate staining, and 3 = severe staining), fluorescein TBUT, and a Schirmer test with anesthesia at these times. The corneal and conjunctival staining patterns were compared to those on a standardized reference chart.

Paired *t* tests were used to compare the pachymetry and ablation depth. For all other clinical measures, the Wilcoxon signed rank test was used to compare scores between eyes with wide or narrow hinges. The McNemar test for correlated proportions was used to compare the proportion of eyes with and without corneal or conjunctival staining. Because of the large number of statistical comparisons performed, the significance level of 0.05 was adjusted so a *P* value of .002 or less was considered statistically significant. A *P* value greater than 0.002 but less than 0.05 indicated a trend toward significance.

Results

Fifty-four patients had bilateral LASIK (108 eyes) with 1 eye randomly having a narrow hinge flap and the other a wider hinge flap. The mean hinge width was 4.22 mm (range 3.00 to 5.50 mm) in the narrow-hinge group and 6.48 mm (range 6.00 to 7.50 mm) in the wide-hinge group. The mean age of the 26 men (48%) and 28 women (52%) was 39.8 years ± 10.8 (SD) (range 22 to 59 years). All patients were myopic with a mean preoperative spherical equivalent of −4.50 D in the narrow-hinge group and −4.37 D in the wide-hinge group; the between-group difference was not statistically significant ($P = .3754$). There was no significant difference between the mean preoperative ultrasonic pachymetry in the narrow-hinge corneas (553.54 μm) and in the wide-hinge corneas (554.98 μm) ($P = .3232$). The mean ablation depth in the narrow-hinge corneas, 57.24 μm, was not statistically significantly different than that in the wide-hinge corneas, 55.33 μm ($P = .120$).

Preoperatively, the mean corneal sensation was 5.88 out of 6.00 in the narrow-hinge group and 5.90 in the wide-hinge group ($P = .7500$) (Table 1). At 1 week, it was significantly decreased in both groups ($P < .0001$) but the between-group difference was not significant ($P = .1968$). At 1 and 3 months, the mean corneal sensation improved but was significantly reduced from the preoperative levels in both groups ($P < .0001$). The mean score was significantly lower in the narrow-hinge group than in the wide-hinge group at 1 month ($P = .0005$) and 3 months ($P = .0013$). At 6 months, the mean corneal sensation remained significantly lower than preoperatively in the narrow-hinge group ($P = .0006$) with a trend toward significance in the wide-hinge group ($P = 0.0093$) and there was no significant between-group difference ($P = .0811$).

Preoperatively, 54 corneas in both groups showed no lissamine green corneal staining ($P = 1.000$) (Figure 1). At 1 week, 42 of 51 corneas with a narrow hinge and 43 of 51 corneas with a wide hinge showed no staining ($P = 1.000$); 9 corneas and 8 corneas, respectively, had grade 2 or 3 staining (Figure 2).

Table 1. Mean corneal sensation in the 2 nasal-hinge groups.

	Cochet-Bonnet Esthesiometry (cm)				
Group	Preop n = 54	1 Week n = 51	1 Month n = 54	3 Months n = 51	6 Months n = 51
Narrow hinge	5.88	2.25	2.86	4.09	5.65
Wide hinge	5.90	2.39	3.15	4.28	5.74
P value	.7500	.1968	.0005	.0013	.0811

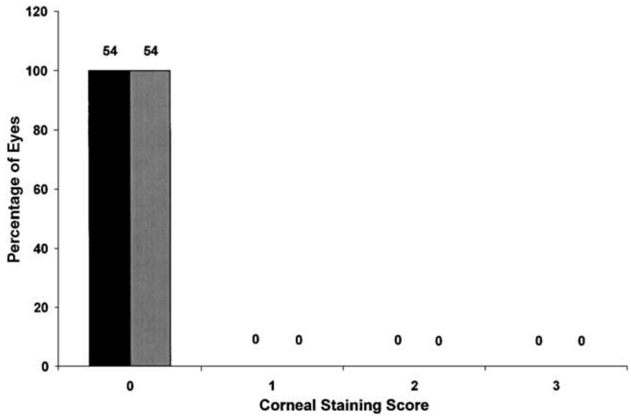

Figure 1. (Donnenfeld) Preoperative distribution of corneal staining scores (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

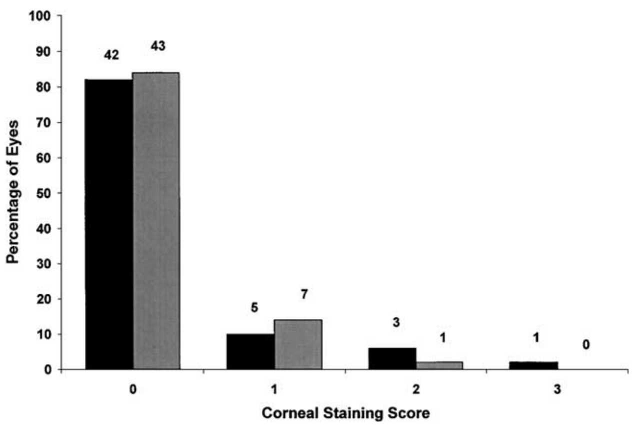

Figure 2. (Donnenfeld) Distribution of corneal staining scores at 1 week (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

At 1 month, the between-group difference approached significance; 44 of 54 narrow-hinge corneas and 50 of 54 wide-hinge corneas showed no lissamine green staining (P = .0313) (Figure 3). At 3 months, 48 of 52 narrow-hinge corneas and 52 of 52 wide-hinge corneas showed no staining (P = .1250) (Figure 4). By 6 months, 49 of 51 and 49 of 51, respectively, showed no staining (P = 1.000) (Figure 5).

Preoperatively, 32 eyes in the narrow-hinge group and 33 eyes in the wide-hinge group showed no lissamine green conjunctival staining (P = 1.000) (Figure 6). At 1 week, the between-group difference approached significance. Nineteen of 51 eyes with a narrow-hinge flap and 29 of 51 eyes with a wide-hinge flap showed no staining (P = .0063); 32 eyes and 22 eyes, respectively, showed grade 2 or 3 staining (Figure 7).

At 1 month, 28 of 54 eyes with a narrow hinge and 33 of 54 eyes with a wide hinge showed no lissamine

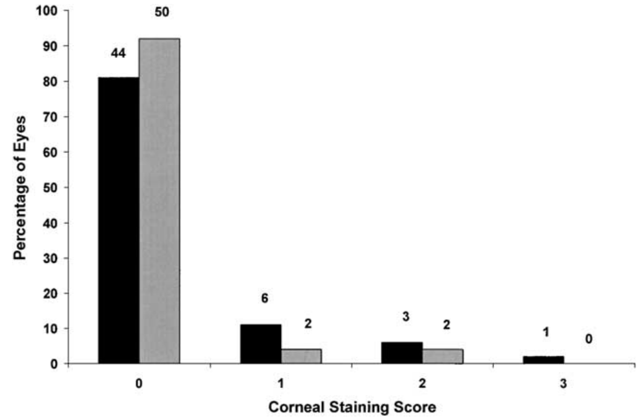

Figure 3. (Donnenfeld) Distribution of corneal staining scores at 1 month (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

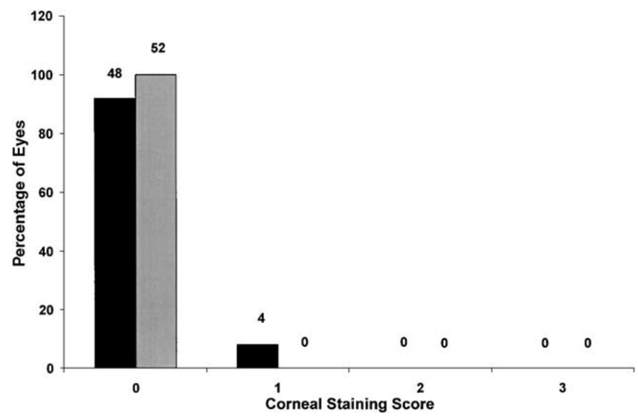

Figure 4. (Donnenfeld) Distribution of corneal staining scores at 3 months (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

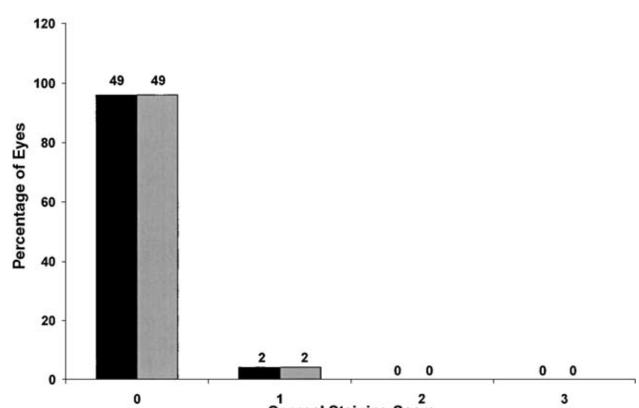

Figure 5. (Donnenfeld) Distribution of corneal staining scores at 6 months (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

green conjunctival staining (P = .2266) (Figure 8). At 3 months, 32 of 52 narrow-hinge eyes and 36 of 52 wide-hinge eyes showed no staining (P = .2891) (Figure

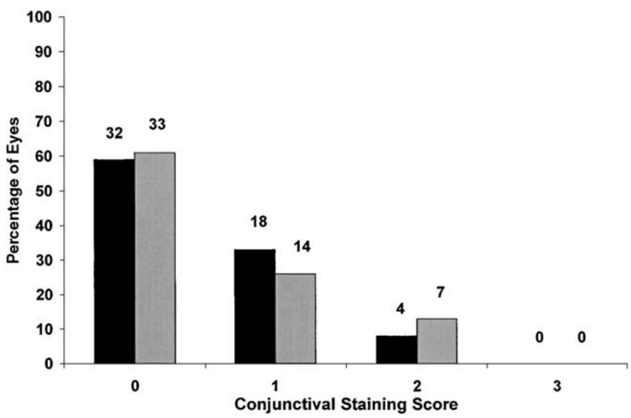

Figure 6. (Donnenfeld) Preoperative distribution of conjunctival staining scores (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

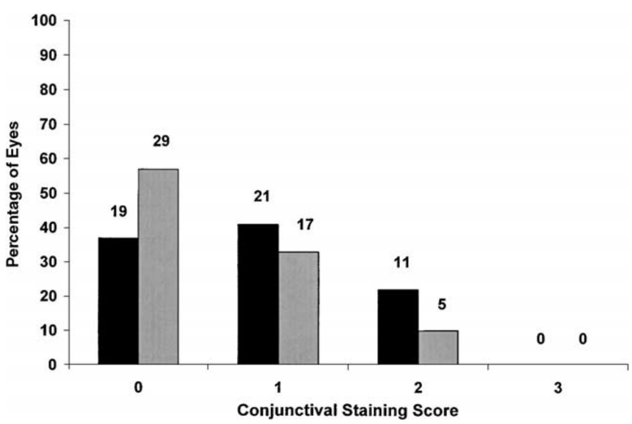

Figure 7. (Donnenfeld) Distribution of conjunctival staining scores at 1 week (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

9). By 6 months, 30 of 51 eyes and 30 of 51 eyes, respectively, showed no staining ($P = 1.000$) (Figure 10).

Preoperatively, there was no significant between-group difference in mean Schirmer values or TBUT. The mean Schirmer scores were greater in the wide-hinge group than in the narrow-hinge group at all postoperative visits. The between-group difference approached statistical significance at 1 month ($P = .0367$) (Table 2). The TBUT was not significantly different between the 2 groups at any time (Table 3).

Discussion

Dry eye has become an increasingly prominent and well-documented complication after LASIK. Most patients experience dry eye during the immediate post-LASIK period. Yu and coauthors[19] report that 60% of patients experienced dry eye 1 month after LASIK. Hovanesian and coauthors[24] report that 6 months after

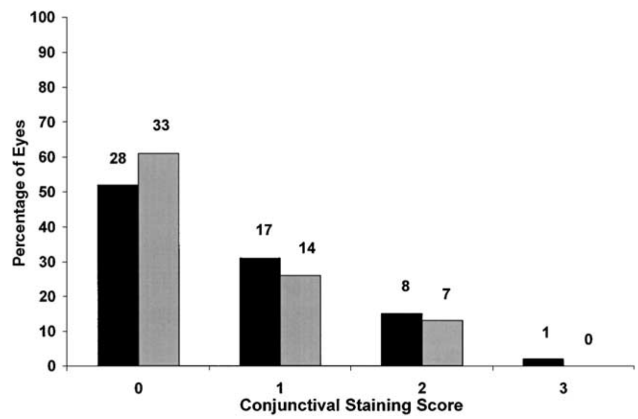

Figure 8. (Donnenfeld) Distribution of conjunctival staining scores at 1 month (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

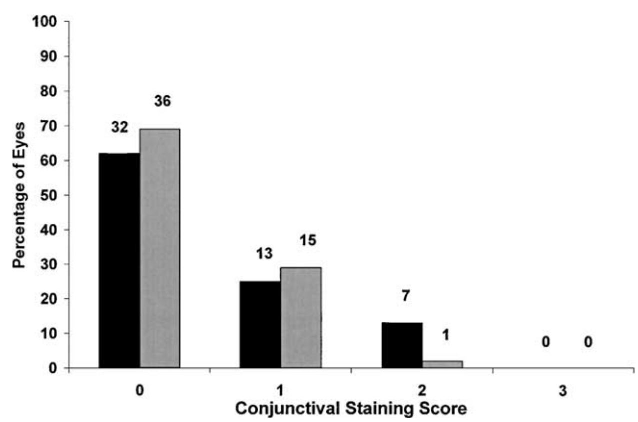

Figure 9. (Donnenfeld) Distribution of conjunctival staining scores at 3 months (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

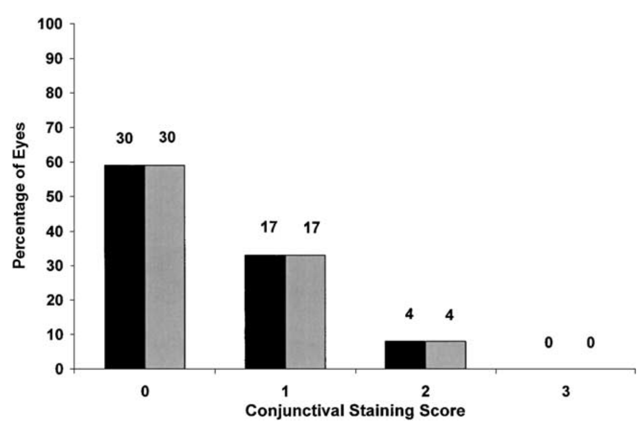

Figure 10. (Donnenfeld) Distribution of conjunctival staining scores at 6 months (black bar = 0.6 mm hinge; gray bar = 1.2 mm hinge).

LASIK, 50% of patients experienced symptoms related to dry eye. Dry eye after LASIK is at least partly caused by the corneal denervation associated with LASIK. In

Table 2. Mean Schirmer scores in the 2 nasal-hinge groups.

	Schirmer Score (mm)				
Group	**Preop n = 54**	**1 Week n = 51**	**1 Month n = 54**	**3 Months n = 52**	**6 Months n = 51**
Narrow hinge	14.44	10.78	11.61	12.17	13.59
Wide hinge	13.83	10.84	12.17	12.60	14.10
P value	.6585	.3059	.0367	.2170	.1795

the normal eye, a neuronal feedback loop links the lacrimal glands with the ocular surface, including the cornea, in a single functional unit that is responsible for maintaining ocular surface homeostasis.[25] It is suggested that basal tear production does not occur but ocular drying between blinks induces subclinical corneal irritation that creates the blink reflex and stimulates the lacrimal gland to produce tears.[25] Only when ocular surface drying becomes severe does the patient experience discomfort. Laser in situ keratomileusis-associated corneal denervation disrupts this reflex arc causing dry-eye syndrome. Many patients may not have the traditional symptoms of post-LASIK dry eye because of the lack of corneal sensation; visual fluctuation due to damage to the ocular surface may be their only symptom.

A common symptom in all patients with dry-eye syndrome is reduced ocular surface sensation.[26,27] The mild anesthesia found in dry-eye patients results in decreased sensory stimulation of tear production by the lacrimal gland. Decreased tear production and the accompanying damage to the ocular surface cause further anesthesia, creating a cycle of decreased tears, ocular damage, and anesthesia.

The feedback loop between the lacrimal gland and the ocular surface begins at the corneal surface and travels via neuronal pathways that are mediated by the brain stem. In LASIK, the corneal nerves are severed by the microkeratome and the deep corneal nerves are photoablated at the time of laser surgery. Both processes damage corneal innervation. The reduction in corneal neuronal feedback to the brain stem reduces brain stem innervation of the lacrimal glands, diminishing tear production. This may account for the transient dry eye seen after LASIK.

In a subset of patients with corneal staining after LASIK, it is hypothesized that the corneal breakdown is secondary to neurotrophic epitheliopathy[28] in addition to dry eye. Patients with neurotrophic keratitis with corneal staining after LASIK have been shown to have Schirmer tests that are not significantly different from those of post-LASIK patients without staining. Most cases of neurotrophic epitheliopathy resolve by 6 months.

Laser in situ keratomileusis significantly decreases TBUT, Schirmer test values, and basal tear secretion.[19,20,29,30] In our study, the Schirmer scores were higher in the wide-hinge group than in the narrow-hinge group at all times, although the difference was only statistically significant at 1 month. There were no significant between-group differences in TBUT.

An advantage of the hinge on the LASIK flap is that it provides a conduit for corneal innervation. The corneal nerves that enter through the hinge are preserved, maintaining corneal sensation in this area. Since the corneal nerves predominantly enter the cornea at 9 o'clock and 3 o'clock,[1,2] a vertical flap (superior hinge) will transect both major areas of corneal innervation,

Table 3. Mean tear breakup time in the 2 nasal-hinge groups.

	TBUT (s)				
Group	**Preop n = 54**	**1 Week n = 48**	**1 Month n = 54**	**3 Months n = 52**	**6 Months n = 51**
Narrow hinge	11.28	9.38	9.96	9.48	10.18
Wide hinge	11.19	9.35	10.13	9.40	10.57
P value	.6714	.7968	.9389	.7853	.1554

TBUT = tear breakup time

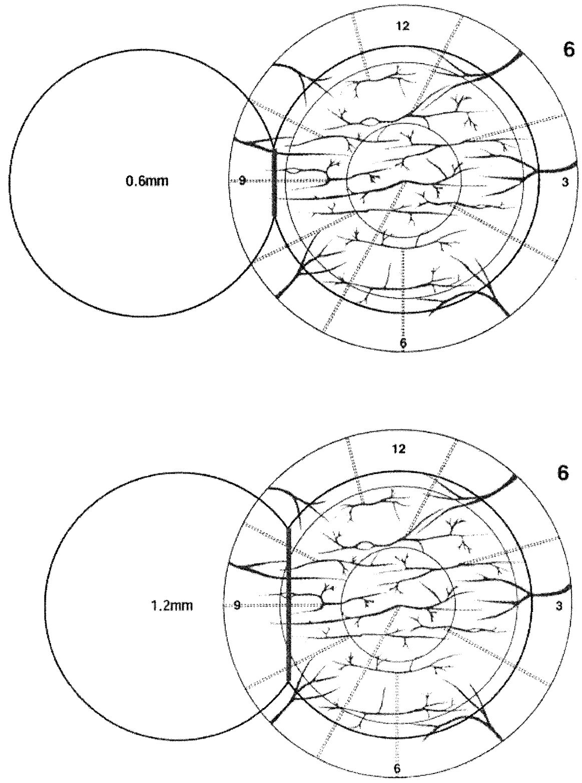

Figure 11. (Donnenfeld) Wide nasal hinge corneal flap preserves greater innervation of the cornea than narrow nasal-hinge corneal flap.

whereas a horizontal corneal flap (nasal hinge) will transect only 1 area. Hypothetically, the greater the loss of corneal sensation, the greater the risk for post-LASIK dry-eye syndrome. A wide hinge will preserve a greater percentage of the corneal neural architecture than a narrow hinge (Figure 11). The current data support this hypothesis. Eyes with a narrow nasal hinge flap showed a significantly greater loss of corneal sensation, a greater incidence of corneal and conjunctival lissamine staining, and lower Schirmer scores than eyes with a wide nasal hinge flap at 1 or more time intervals. Different microkeratomes cut flaps with different thicknesses and standard deviations. The Amadeus microkeratome with a 160 μm spacer and 9.5 mm ring cuts corneal flaps with a mean thickness of 175 ± 37 μm.[31] Hinge width has not been shown to affect flap thickness. To our knowledge, the effect of flap thickness on corneal sensation and dry eye has not been studied.

Over the past few years, there has been increased documentation of dry eye after LASIK. There are many possible contributing factors to this, including increased physician and patient awareness. Other factors include an increased prevalence of superior hinge flaps, the need for larger flaps with smaller hinges to accommodate the larger ablation zones required for hyperopic treatments, and the larger optical and blend zones common to newer software delivery systems. These larger ablation zones may decrease the risk for glare and halos associated with scotopic conditions but may also be responsible for the increased incidence of post-LASIK dry eye. We recommend using the smallest flap necessary with the largest hinge possible to complete the photoablation in the stromal bed without ablating the corneal hinge. Myopic patients with mild dry eyes who have small pupils and against-the-rule astigmatism (ablation profile is vertical) are good candidates for flaps with as large a nasal flap as possible.

In conclusion, there is a significant reduction in corneal sensation immediately after LASIK. In our patients, sensation improved at all time intervals but did not return to preoperative levels even 6 months postoperatively. Associated with the corneal denervation is an immediate postoperative increase in dry-eye syndrome signs and symptoms that improves at subsequent visits. Furthermore, loss of corneal sensation and dry-eye syndrome were less pronounced in corneas with a wide nasal-hinge flap. We postulate that this can be explained anatomically by the finding that the wider hinge flap severs a smaller percentage of the corneal innervation than a narrow hinge flap. We suggest that surgeons operating on patients with preexisting neurotrophic corneas or dry-eye syndrome consider performing LASIK with as wide a nasal hinge flap as possible.

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Supported in part by an unrestricted grant from AMO and the Lions Eye Bank for Long Island.

Dr. Donnenfeld is a consultant to AMO. None of the other authors has a financial or proprietary interest in any material or method mentioned.