

# Early changes to dry eye and ocular surface after small-incision lenticule extraction for myopia

Pei-Jin Qiu, Ya-Bo Yang

Eye Center, the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310009, Zhejiang Province, China

**Correspondence to:** Pei-Jin Qiu. Eye Center, the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310009, Zhejiang Province, China. qpeijin@zju.edu.cn

Received: 2015-04-21 Accepted: 2015-06-26

## Abstract

• **AIM:** To investigate the early changes in dry eye symptoms, tear function and ocular surface following small-incision lenticule extraction (SMILE) for myopia.

• **METHODS:** Ninety-seven consecutive patients (193 eyes) who underwent SMILE for myopia were observed in this longitudinal and retrospective study. Parameters evaluated included: subjective dry eye symptoms (dryness, foreign body sensation and photophobia), tear film breakup time (TBUT), Schirmer I test without anesthesia (S | T), tear meniscus height (TMH) and corneal fluorescein staining. Each parameter was evaluated before, and subsequently at 1d, 1wk, 1 and 3mo after surgery.

• **RESULTS:** Compared with preoperative data, dryness was noted to be significantly increased at 1wk and 1mo postoperatively ( $P < 0.01$ ). Symptoms of photophobia and foreign body sensation demonstrated significant differences at 1d and 1wk as compared with preoperative scores respectively ( $P < 0.01$ ). These values were decreased at 1 and 3mo post-surgery ( $P > 0.05$ ). Conversely the corneal staining scores were higher than the preoperative data at 1d, 1wk and 1mo ( $P < 0.01$ ), but were close to the preoperative level at 3mo postoperatively. There was a significant decrease in TMH at 1wk and 1mo ( $P < 0.01$ ), but the value was close to the preoperative level at 3mo postoperatively ( $P = 0.16$ ). The examination outcomes of S | T were significantly increased at 1d then reduced at 1wk after surgery ( $P < 0.01$ ). Each value subsequently returned to the baseline value at 1 and 3mo ( $P > 0.05$ ). TBUT was significantly decreased at all postoperative time points ( $P < 0.01$ ).

• **CONCLUSION:** SMILE resulted in mild dry eye symptoms, tear film instability and ocular surface damages; however, these complications can recover in a short period of time.

• **KEYWORDS:** dry eye; myopia; ocular surface; small-incision lenticule extraction

**DOI:10.18240/ijo.2016.04.17**

Qiu PJ, Yang YB. Early changes to dry eye and ocular surface after small-incision lenticule extraction for myopia. *Int J Ophthalmol* 2016;9(4):575-579

## INTRODUCTION

Femtosecond laser works similarly to infrared laser pulse, which was approved by the Food and Drug Administration (FDA) of the United States in 2001 for use in laser *in situ* keratomileusis (LASIK) [1]. With the development of corneal refractive surgery, small-incision lenticule extraction (SMILE) was invented. SMILE is considered to be a brand new procedure and is a major advancement in the field of ophthalmic refractive surgery. SMILE is most useful in the surgical correction of myopia without the creation of a corneal flap, which, theoretically, can maximally maintain corneal anatomical structure and bio-mechanical properties [2]. However, some patients who underwent SMILE surgery have complained of postoperative symptoms such as dryness, foreign body sensation and photophobia. These side effects indicate that SMILE may, to some extent, affect the tear film stability and ocular surface. To further investigate, we conducted a comprehensive study to evaluate the changes in pre- and post-surgical dry eye symptoms, tear function and ocular surface damages following SMILE in the treatment of myopia.

## SUBJECTS AND METHODS

**Subjects** Ninety-seven consecutive patients (193 eyes) who underwent SMILE procedures for the treatment of myopia and myopic astigmatism at Eye Center, the Second Affiliated Hospital of Zhejiang University School of Medicine (Hangzhou, Zhejiang Province, China) were recruited between June and December of 2013. This research was approved by the Institutional Review Board at Zhejiang University College of Medicine and followed the tenets of the Declaration of Helsinki regarding research involving human subjects. Each of the patients provided written informed consent to participate after the purpose of the study had been explained. The inclusion criteria [3]: 18 to 40 years old, standard qualifications for conventional laser refractive surgery for myopia (including: a normal ophthalmic

examination except for refractive error, stable refraction, and minimum calculated residual corneal stromal bed thickness >250  $\mu\text{m}$ ). Patients were excluded based on: 1) those who had severe dry eye with Schirmer test values of <5 mm without anesthesia; 2) those with a history of arthritis or connective tissue disease; 3) those who were pregnant; or 4) those who were part of another dry eye study.

## **Methods**

**Surgical technique**<sup>[4]</sup> The same surgeon (Qiu PJ) performed all procedures. VisuMax femtosecond laser system (VisuMax; Carl Zeiss Meditec, Inc., Jena, Germany) was used in SMILE procedures with repetition rate of 500 kHz and pulse energy of 115 nJ. The intended thickness of the upper tissue arcade was 100-130  $\mu\text{m}$ , and its intended diameter was 7.0-7.5 mm, which was 1 mm larger than the diameter of the refractive lenticule (6.0-6.5 mm). The side-cut angle was 90° and a small incision (2.0 mm) was created at a 120° angle. The refractive lenticule was manually removed through the incision using forceps.

**Dry eye symptoms** We evaluated the subjective symptoms related to 3 ocular symptoms (dryness, foreign body sensation, and photophobia) by use of a questionnaire, which is the popular method for evaluating the subjective dry eye symptoms in Japan<sup>[5-7]</sup>. Each of the subjective dry eye symptoms was scored on a 4-point scale from 0 to 3. Scoring criteria: 0=never, 1=occasional, 2=often, and 3=always. The temperature and humidity of the examination room were controlled at 20°C-24°C and 30%-50%, respectively.

**Schirmer secretion test** The Schirmer test without anesthesia (S I T) for tear secretion function was performed by inserting a 30 mm Schirmer tear test strip (HESSEN Biotechnology, Inc., Beijing, China) into the inferior fornix at the junction of the middle and lateral thirds of the lower eyelid margin. Schirmer tear test strip remained in place for 5min with eyes closed. The extent of wetting was subsequently measured according to the scale provided by the manufacturer.

**Tear meniscus height** A fluorescein-impregnated strip (Jingmin, Jingmin New Technological Development Co. Ltd., Tianjin, China) saturated with a non-preservative saline solution was placed in the lower conjunctival sac for 1s, then the patient was asked to blink several times. The lower tear meniscus height (TMH) of eyelid center was measured by slit lamp marker lens (magnification 10 ×) (McIntyre; Haag-Streit, Inc., Zurich, Swiss). Each eye was measured three times and the average value was recorded.

**Tear break-up time and fluorescein staining** Tear break-up time (TBUT) was measured at 5min after the above procedure, the tear film was observed under cobalt blue filtered light. The interval between the last complete blink and the first appearance of randomly distributed dry spots was measured. An average of the three measurements was

obtained. Fluorescein staining was evaluated according to the Shimmura method<sup>[7]</sup>. Three sections, the superior, inferior and mid-cornea were scored on a 0-3 point scale, 0 (without any damage) to 3 (damage in the entire area).

**Follow-up** All patients had preoperative and postoperative examinations (within 2wk before laser refractive surgery, at 1d, 1wk, 1 and 3mo after surgery) in the following sequence by the same research observer: S I T, lower TMH, TBUT, corneal fluorescein staining, and the subjective dry eye symptom survey. After surgery, 0.3% ofloxacin eye drops (Tarivid; Santen, Inc., Tokyo, Japan) and 0.1% fluorometholone (Flumetholon; Santen, Inc.) were topically administered 4 times daily for 2wk, and then the frequency was reduced.

**Statistical Analysis** Data were analyzed using SPSS 18.0 statistical software (SPSS Inc, Chicago, Illinois, USA). Preoperative and post-operative score comparisons for subjective dry eye symptoms and corneal fluorescein staining were respectively analyzed by the Wilcoxon rank sum test. The *t*-tests were used to compare TMH, TBUT, and S I T postoperatively at different time points using preoperative parameters.  $P < 0.01$  was considered to be significant for all analyses.

## **RESULTS**

Patients' ages ranged from 18 to 40y (mean: 22.58±5.05y). Preoperative spherical equivalents ranged from -2.50 to -10.00 diopters (D) (mean: -5.51±2.03 D). No visually threatening complications were observed. Comparison of subjective dry eye symptoms before and after surgery (Table 1).

**Dryness** At 1wk and 1mo postoperatively, a statistically significant difference was observed compared with preoperative values ( $Z=4.14, 4.53, P < 0.01$ ); No significant difference was recorded at 1d and 3mo ( $Z=1.52, 1.47, P=0.13, 0.14$ ).

**Photophobia** At 1d and 1wk after surgery, there was a statistically significant increase compared to preoperative values ( $Z=6.48, 3.07, P < 0.01$ ). At 1 and 3mo, there was an obvious decrease, but the difference was not statistically significant ( $Z=0.64, 0.77, P=0.52, 0.44$ ).

**Foreign Body Sensation** At 1d and 1wk after operation, there was a statistically significant increase compared to preoperative values ( $Z=10.26, 5.26, P < 0.01$ ). At 1 and 3mo, there was an apparent decrease, but the difference was not statistically significant ( $Z=0.99, 0.07, P=0.32, 0.94$ ).

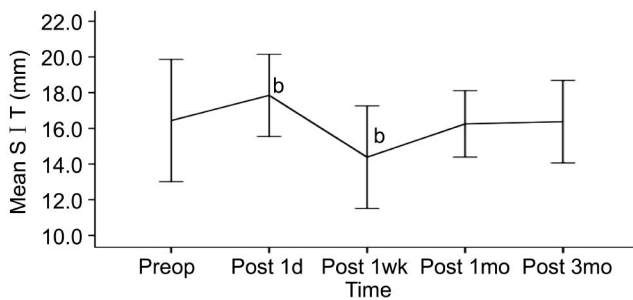
**Ocular Surface and Tear Function** Corneal fluorescein scores were higher than the preoperative data at 1d, 1wk and 1mo ( $Z=16.66, 13.83, 4.74, P < 0.01$ ), but they were close to the levels observed at 3mo postoperatively (Table 1).

**Schirmer I Test** S I T was significantly increased at 1d and decreased at 1wk after surgery (all  $P < 0.01$ , by *t*-test). These values returned to the baseline values at 1 and 3mo ( $P=0.62, 0.89$ , respectively, by *t*-test) (Table 2, Figure 1).

**Table 1 Preoperative and postoperative distribution of dry eye symptom scores and corneal staining scores**

Timepoint	n	Dryness (score)					Photophobia (score)					Foreign body sensation (score)					Corneal staining (score)			
		0	1	2	3	P	0	1	2	3	P	0	1	2	3	P	0-3	4-6	7-9	P
Preop.	193	118	22	53	0		186	7	0	0		183	8	2	0		191	2	0	
Postop.																				
1d	160	112	10	38	0	0.13	117	0	42	1	<0.01	77	5	76	2	<0.01	141	17	2	<0.01
1wk	132	58	2	67	5	<0.01	116	1	15	0	<0.01	100	2	30	0	<0.01	113	15	4	<0.01
1mo	98	39	1	54	4	<0.01	93	2	3	0	0.52	90	7	1	0	0.32	96	2	0	<0.01
3mo	62	35	10	0	17	0.14	61	1	0	0	0.44	59	1	2	0	0.94	61	1	0	0.47

P<0.01 was significant according to the Wilcoxon rank sum test.



**Figure 1 S I T was increased at 1d and reduced at 1wk postoperatively (<sup>b</sup>P<0.01, by t-test)** These values returned to the baseline values at 1 and 3mo (P=0.62, 0.89, by t-test).

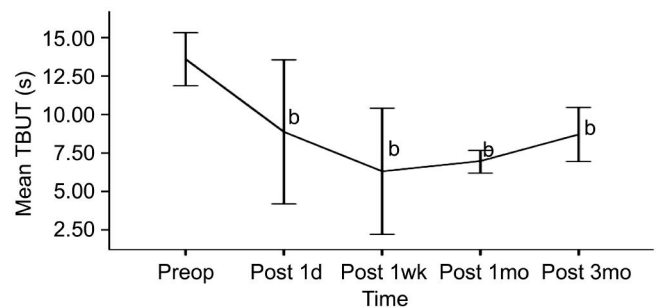
**Tear Break-up Time** TBUT was significantly decreased at all postoperative time points compared with preoperative values (P<0.01, for the four comparisons, by t-test) (Table 2, Figure 2).

**Tear Meniscus Height** TMH was significantly increased at 1d and decreased at 1wk and 1mo after surgery (all P<0.01, by t-test). These values were close to the preoperative level at 3mo postoperatively (P=0.16, by t-test) (Table 2, Figure 3).

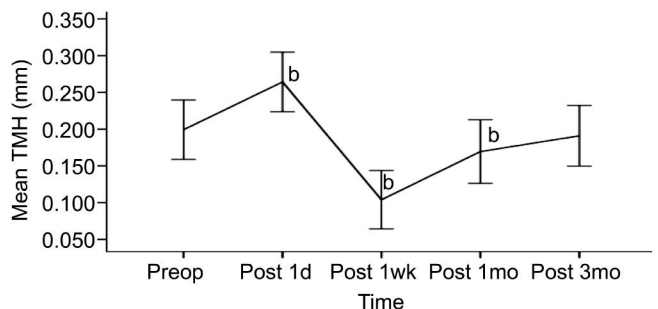
**DISCUSSION**

Dry eye is often caused by abnormalities in tear quality or quantity, defective circulation leading to tear film instability and/or ocular surface damage, as well as inducing ocular discomfort and visual impairment. There is currently no uniform standard for the diagnosis of dry eye [8]. This study aims to explore the early variations in subjective dry symptoms, tear function, and ocular surface after SMILE surgery, by observing and documenting changes in subjective dry symptoms including dryness, photophobia, foreign body sensation, tear secretion indexes, and corneal staining both before and after surgery.

Dry eye is considered to be the most common early complication after conventional LASIK surgery[9]. It has been reported [10-11] that 95% of post-LASIK patients suffer certain degrees of dry eye immediately following surgery and 60% still suffer after 1mo, but the majority of patients showed diminished symptoms from 6-12mo. In the current study, 56% of patients showed dry eye symptoms at 1wk after SMILE surgery. In the majority of cases, the symptoms



**Figure 2 TBUT was significantly decreased at all postoperative time points compared with preoperative values (<sup>b</sup>P<0.01, for the four comparisons, by t-test).**



**Figure 3 TMH was increased at 1d and decreased at 1wk and 1mo (all <sup>b</sup>P<0.01, by t-test)** These values were close to the preoperative level at 3mo postoperatively (P=0.16, by t-test).

**Table 2 Preoperative and postoperative BUT, TMH and S I T**  $\bar{x} \pm s$

Timepoint	n	BUT (s)	S I T (mm)	TMH (mm)
Preop.	193	13.60±1.72	16.44±3.43	0.20±0.04
Postop.				
1d	160	8.87±4.68 <sup>b</sup>	17.85±2.31 <sup>b</sup>	0.26±0.05 <sup>b</sup>
1wk	132	6.31±4.10 <sup>b</sup>	14.38±2.87 <sup>b</sup>	0.10±0.04 <sup>b</sup>
1mo	98	6.98±0.69 <sup>b</sup>	16.25±1.86	0.17±0.05 <sup>b</sup>
3mo	62	8.70±1.76 <sup>b</sup>	16.37±2.31	0.19±0.06

BUT: Break-up time; S I T: Schirmer I test; TMH: Tear meniscus height; <sup>b</sup>P<0.01 according to the t-test.

returned to near preoperative levels after 3mo. Our results indicated a lower incidence of dry eye early after SMILE surgery, and faster recovery from symptoms, possibly due to reduced variations in tear quality and quantity from the SMILE surgery.

The Schirmer secretion test and TMH indicators reflect the

quantity of tear secretion. In the current study, we observed that at 1d after surgery, the examination outcomes of the Schirmer secretion test and TMH all increased compared to preoperative values, possibly due to direct stimulation of the eye from surgery. At 1wk and 1mo, there was a statistically significant reduction in TMH. At 3mo, the TMH returned to near preoperative levels. At 1wk after surgery, there was a statistically significant reduction in tear secretion volume compared to pre-surgery. Even after 1 and 3mo, the S I T values did not return to pre-operative level but they were close to normal. Compared to traditional LASIK [12], SMILE surgery resulted in smaller changes to tear secretion, possibly due to a smaller incision (2.0 mm) and the incision position (being located at superior cornea), maintained the maximum integrity of the shallow corneal nerve, reduced damage to the nerve plexus of the corneal basement membrane, and subsequently lessened the impact on corneal sensation [13]. These results are to be confirmed *via* subsequent corneal nerve studies.

Tear quality changes and ocular surface damage often leads to a reduction in TBUT and increased corneal staining. The possible pathogenesis includes: 1) negative suction during laser cutting of the corneal flap inducing damage to the conjunctival goblet cells leading to a corresponding reduction in mucin secretion, thus affecting the formation and sustenance of the tear film [3,14-15]; 2) the postoperative ocular surface inflammatory response could lead to intensified symptoms of eye dryness, resulting in reduced stability of the tear film [16-17]; 3) if the surgery has caused the corneal surface regularity to drop and mucin cannot be absorbed, this could result in the tear film breakage or simply failure to form [18]. In addition, postoperative use of corticosteroids and preservatives in eye drops further hinder and delay the repair of corneal and conjunctival epithelium, resulting in a shorter TBUT [19]. Our study found that postoperative TBUT values were lower than the preoperative during the 3-month follow-up period. At 1d, 1wk and 1mo postoperatively, the corneal fluorescein staining score was much higher than before surgery and the difference was statistically significant, suggesting that the integrity of the corneal epithelium was compromised. At 3mo after the surgery, the score returned to near preoperative values. Possible reasons for those results include [16,20]: 1) compared with traditional flap surgery, SMILE surgery using size "S" control suction with a small diameter (per manufacturer's recommendation) resulted in reduced contact area with the perilimbal conjunctiva, and less impact on the goblet cell density and function; 2) the control suction lens was applied close to the cornea, with a stable suction to avoid relative movement between the two. During SMILE surgery, a small amount of negative pressure was applied compared to microkeratome flap surgery, to allow for less damage to the

corneal epithelial cells and to maintain corneal regularity; 3) SMILE surgery allowed for a smaller and more precise incision, promoting faster healing after surgery, reducing inflammatory reactions and accelerating corneal surface repair. In summary, SMILE procedure temporarily altered dry eye symptoms, tear secretion, tear film stability and corneal staining in a reversible manner.

Dry eye is the leading factor in determining patient satisfaction after surgery. We should pay attention to the prevention and treatment of dry eye, both to improve the patient's satisfaction and overall visual quality. In clinical practice, it is recommended to: 1) be vigilant with the consultation and screening of preoperative patients to reduce cases of severe eye dryness, and provide treatment for mild symptoms, which can effectively reduce the occurrence of postoperative dry eye [21]; 2) shorten surgery duration to reduce negative suction time and minimize the possibility of damage to the bulbar conjunctiva. The surgical procedure should be gentle, paying attention to the protection of the ocular surface; 3) postoperative use of preservative-free eye drops. Patients with severe symptoms may consider using tear plugs [5,22], or oral tetracyclines and a low concentration of cyclosporine eye drops to alleviate the symptoms of dry eye, and promote the repair of the ocular surface.

In summary, SMILE significantly altered dry eye symptoms, tear secretion, the tear film stability and corneal staining; however, these complications can recover in a short period of time.

### ACKNOWLEDGEMENTS

**Foundations:** Supported by Project of National Clinical Key Discipline of Chinese Ministry of Health; Zhejiang Key Laboratory Fund of China (No.2011E10006).

**Conflicts of Interest:** Qiu PJ, None; Yang YB, None.

### REFERENCES

- 1 Shtein RM. Post-LASIK dry eye. *Expert Rev Ophthalmol* 2011;6(5): 575-582.
- 2 Wu D, Wang Y, Zhang L, Wei S, Tang X. Corneal biomechanical effects: small-incision lenticule extraction versus femtosecond laser-assisted laser in situ keratomileusis. *J Cataract Refract Surg* 2014;40(6):954-962.
- 3 Xu Y, Yang Y. Dry eye after small incision lenticule extraction and LASIK for myopia. *J Refract Surg* 2014;30(3):186-190.
- 4 Sekundo W, Kunert KS, Blum M. Small incision corneal refractive surgery using the small incision lenticule extraction (SMILE) procedure for the correction of myopia and myopic astigmatism: results of a 6 month prospective study. *Br J Ophthalmol* 2011;95(3):335-339.
- 5 Yung YH, Toda I, Sakai C, Yoshida A, Tsubota K. Punctal plugs for treatment of post-LASIK dry eye. *Jpn J Ophthalmol* 2012;56(3):208-213.
- 6 Koh S, Ikeda C, Takai Y, Watanabe H, Maeda N, Nishida K. Long-term results of treatment with diquafosol ophthalmic solution for aqueous-deficient dry eye. *Jpn J Ophthalmol* 2013;57(5):440-446.
- 7 Takamura E, Tsubota K, Watanabe H, Ohashi Y; Diquafosol Ophthalmic Solution Phase 3 Study Group. A randomized, double-masked comparison study of diquafosol versus sodium hyaluronate ophthalmic solutions in dry eye patients. *Br J Ophthalmol* 2012;96(10):1310-1315.

- 8 The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop. *Ocul.Surf* 2007;5(2):75-92.
- 9 Solomon KD, Holzer MP, Sandoval HP, Vargas LG, Werner L, Vroman DT, Kasper TJ, Apple DJ. Refractive surgery survey 2001. *J Cataract Refract Surg* 2002;28(2):346-355.
- 10 Yu EY, Leung A, Rao S, Lam DS. Effect of laser in situ keratomileusis on tear stability. *Ophthalmology* 2000;107(12):2131-2135.
- 11 Hovanesian JA, Shah SS, Maloney RK. Symptoms of dry eye and recurrent erosion syndrome after refractive surgery. *J Cataract Refract Surg* 2001;27(4):577-584.
- 12 Huang JC, Sun CC, Chang CK, Ma DH, Lin YF. Effect of hinge position on corneal sensation and dry eye parameters after femtosecond laser-assisted LASIK. *J Refract Surg* 2012;28(9):625-631.
- 13 Li M, Zhao J, Shen Y, Li T, He L, Xu H, Yu Y, Zhou X. Comparison of dry eye and corneal sensitivity between small incision lenticule extraction and femtosecond LASIK for myopia. *PLoS One* 2013;8(10):e777797.
- 14 Rodriguez AE, Rodriguez-Prats JL, Hamdi IM, Galal A, Awadalla M, Alio JL. Comparison of goblet cell density after femtosecond laser and mechanical microkeratome in LASIK. *Invest Ophthalmol Vis Sci* 2007;48(6):2570-2575.
- 15 Shin SY, Lee YJ. Conjunctival changes induced by LASIK suction ring in a rabbit model. *Ophthalmic Res* 2006;38(6):343-349.
- 16 Battat L, Maeri A, Dursun D, Pflugfelder SC. Effects of laser in situ keratomileusis on tear production, clearance, and the ocular surface. *Ophthalmology* 2001;108(7):1230-1235.
- 17 Solomon R, Donnenfeld ED, Perry HD. The effects of LASIK on the ocular surface. *Ocul.Surf* 2004;2(1):34-44.
- 18 Lee JB, Ryu CH, Kim J, Kim EK, Kim HB. Comparison of tear secretion and tear film instability after photorefractive keratectomy and laser in situ keratomileusis. *J Cataract Refract Surg* 2000;26(9):1326-1331.
- 19 Toda I, Asano-Kato N, Hori-Komai Y, Tsubota K. Laser-assisted in situ keratomileusis for patients with dry eye. *Arch Ophthalmol* 2002;120(8):1024-1028.
- 20 Mian SI, Shtein RM, Nelson A, Musch DC. Effect of hinge position on corneal sensation and dry eye after laser in situ keratomileusis using a femtosecond laser. *J Cataract Refract Surg* 2007;33(7):1190-1194.
- 21 Albietz JM, McLennan SG, Lenton LM. Ocular surface management of photorefractive keratectomy and laser in situ keratomileusis. *J Refract Surg* 2003;19(6):636-644.
- 22 Raouf D, Pineda R. Dry eye after laser in-situ keratomileusis. *Semin Ophthalmol* 2014;29(5-6):385-362.