

# Effectiveness of an Eyelid Thermal Pulsation Procedure to Treat Recalcitrant Dry Eye Symptoms After Laser Vision Correction

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## ABSTRACT

**PURPOSE:** To provide an initial retrospective evaluation of the effectiveness of a thermal pulsation system to treat intractable patient-reported dry eye symptoms following laser vision correction.

**METHODS:** A total of 109 eyes of 57 patients underwent thermal pulsation therapy (LipiFlow; TearScience, Morrisville, NC) for the treatment of dry eye symptoms following laser vision correction. A standardized dry eye questionnaire, the Standard Patient Evaluation of Eye Dryness (SPEED II), was administered to all patients before and after thermal pulsation therapy. The primary outcome was patient-reported dry eye symptoms as measured by this questionnaire.

**RESULTS:** The mean patient age was 49 years (interquartile range [IQR]: 38 to 60), 70% were female, and the primary refractive procedure was LASIK ( $n = 91$ , 83%) or photorefractive keratectomy (PRK) ( $n = 18$ , 17%). Patients underwent thermal pulsation therapy at a mean of 40.5 months (IQR: 27.6 to 55.0) after the primary procedure. The mean pre-therapy SPEED II questionnaire score was 17.5 (IQR: 14 to 21), with a reduced mean post-therapy score of 10.2 (IQR: 6 to 14; 95% confidence interval [CI]: 8.8 to 11.5,  $P < .001$ ). Patients with PRK tended to report more improvement. At the follow-up clinical evaluation, objective improvements were noted in tear break-up time (+1.9 sec; 95% CI: 1.3 to 2.5), reduction in grade of meibomian gland dysfunction (-0.69; 95% CI: -0.54 to -0.84), and corneal staining (-0.74; 95% CI: -0.57 to -0.91).

**CONCLUSIONS:** In this initial retrospective evaluation, a significant improvement in patient-reported dry eye symptoms was observed following thermal pulsation therapy. This treatment modality may have utility in the management of dry eye symptoms following laser vision correction, but further study is needed to define its role.

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**D**ry eye symptoms following laser vision correction surgery are well documented. Patients with postoperative dry eye may transiently experience symptoms such as pain, foreign body sensation, photophobia, visual fatigue, epiphora, and fluctuating or blurry vision. Incidence has been reported to be as high as 50% following laser vision correction.<sup>1,2</sup> Several studies have demonstrated a decrease in corneal sensation, tear secretion, and tear film stability early in the postoperative period following refractive surgery, possibly as a result of loss of neurotrophic influence from severed nerve bundles after corneal incision or flap creation.<sup>3-7</sup> Independent of these factors, it is possible that meibomian gland function may be altered following surgery.<sup>8</sup>

Effective management of dry eye after laser vision correction remains an area of interest, with the emergence of novel in-office diagnostic and therapeutic devices. Recent studies have documented the potential benefit of eyelid thermal pulsation therapy (TearScience, Morrisville, NC) as primary treatment for meibomian gland dysfunction and dry eye symptoms.<sup>9-12</sup> A single treatment may be at least as effective as a 3-month regimen of eyelid margin hygiene for dry eye symptoms secondary to blepharitis, although the effects are transient.<sup>13</sup> It is of particular interest to evaluate the role this therapeutic measure may have in the treatment of dry eye symptoms after refractive surgery, which has not previously been described. The current study was an initial retrospective evaluation for the role of eyelid thermal pulsation therapy in a population of patients after laser vision correction with persistent, intractable dry eye symptoms recalcitrant to conventional management.

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## PATIENTS AND METHODS

This study was deemed exempt from review by the Committee on Human Research at the University of California–San Francisco because it used only de-identified patient data.

The study was a retrospective review of patients from a large refractive surgery practice (Optical Express, Glasgow, United Kingdom) who underwent thermal pulsation therapy using the LipiFlow device (TearScience) for the treatment of postoperative patient-reported dry eye symptoms. The Optical Express database was searched for all patients who had undergone thermal pulsation treatment between November 2012 and March 2013 for the treatment of dry eye symptoms following LASIK or photorefractive keratectomy (PRK). Patients who completed both pre-treatment and post-treatment dry eye symptoms questionnaires were included for analysis. All refractive surgery procedures were performed at Optical Express centers located in the United Kingdom.

The patients included in this study had been observed clinically for persistent dry eye symptoms that began in the early postoperative period. They were invariably noted to suffer from severe to disabling dry eye symptoms, as defined by the grading scheme proposed by the International Task Force of dry eye disease experts.<sup>14</sup> After failing to adequately respond to treatment of dry eye symptoms with available measures, the patients in this study were selected for a trial of thermal pulsation therapy.

Prior to consideration for thermal pulsation therapy, these patients had received treatment with tear supplementation, tear retention, and anti-inflammatory therapies as previously described.<sup>15</sup> Treatment regimens included the use of preservative-free artificial tears, viscosity agents, blepharitis treatment (warm compresses, eyelid scrubs), and pharmacotherapy with topical cyclosporine, topical steroids, and oral tetracycline therapy. Many patients also had received non-standard therapies for dry eye, including essential fatty acid supplementation, sodium chloride ointment, or hydroxypropyl cellulose ophthalmic insert (Lacrisert; Bausch & Lomb, Rochester NY). Only patients with chronic symptoms despite the above therapies were referred for thermal pulsation as auxiliary therapy. Thermal pulsation therapy was not routinely offered to patients with postoperative dry eye symptoms.

Study patients received clinical ocular surface evaluation before laser vision correction, after surgery but prior to thermal pulsation therapy, and after treatment. This evaluation consisted of a slit-lamp assessment of the tear film quality, corneal staining with fluorescein, and tear break-up time (TBUT). Corneal staining patterns were

graded on a scale of 0 (none) to 4 (severe) in accordance with dry eye grading schemes previously defined.<sup>14</sup> Meibomian gland dysfunction or posterior blepharitis, if documented, was similarly graded on a scale of 0 (none) to 4 (severe). Prior to thermal pulsation therapy, measurements were conducted on the tear film lipid layer thickness using a lipid layer interferometer (LipiView; TearScience), and meibomian gland evaluation using the Korb Meibomian Gland Evaluator (TearScience).<sup>16</sup> The meibomian gland evaluator standardizes the force applied to the glands during examination to reproduce the physiological pressure on the glands during an intentional blink.<sup>17</sup> All study eyes received a single thermal pulsation treatment using the LipiFlow device and methods described previously.<sup>10,13</sup> Patients continued with their home dry eye regimens after thermal pulsation therapy, and no new treatments were initiated after therapy. No eyes included in this study received further surgical procedures in the follow-up period. Follow-up clinical evaluation occurred at a mean 89 days after therapy (interquartile range [IQR]: 43 to 121).

A standard dry eye questionnaire was administered to all patients before thermal pulsation therapy using the Standard Patient Evaluation of Eye Dryness questionnaire (SPEED II). The SPEED II questionnaire has been previously shown to have good correlation between subjective symptoms and clinical findings, with reproducible results.<sup>18</sup> The SPEED II scores range from 0 (no symptoms) to 28 (severe symptoms).

All patients included in this study completed an index questionnaire for affected eyes prior to treatment and a follow-up questionnaire via telephone or office visit. Patients were again contacted at a later date via telephone or office visit for completion of a secondary follow-up questionnaire. The primary questionnaire was completed 25 days (IQR: 9 to 31) following treatment, and the secondary questionnaire was completed 208 days (IQR: 190 to 219) after treatment.

The primary outcome was degree of SPEED II response following therapy at primary follow-up questionnaire. Mixed-effects linear regression analysis was used to account for inpatient covariance of SPEED II score reporting. Secondary outcomes included degree of SPEED II response at second questionnaire, clinical examination findings at follow-up visit, and survival analysis to identify clinical features that may influence duration of response to treatment. Mixed-effect regression analysis was conducted to identify variables associated with primary and secondary outcomes independent of inpatient covariance. For survival analysis, risk factors for symptomatic relapse after therapy were identified using Cox proportional hazards and Nelson–Aalen cumulative hazard estimates. Symptomatic relapse was defined by a

TABLE 1  
Patient Demographics

Characteristic	Value
Age (y)	48.9 (IQR: 38 to 60)
Sex (female)	70%
Procedure	
LASIK	91 (83%)
PRK	18 (17%)
Pupil (mm) <sup>a</sup>	5.8 (IQR: 5 to 6.5)
Pachymetry ( $\mu\text{m}$ ) <sup>a</sup>	538 (IQR: 512 to 558)
Average keratometry (D) <sup>a</sup>	44.06 (IQR: 43.00 to 44.75)
Manifest sphere (D) <sup>a</sup>	-1.42 (IQR: -4.25 to +1.75)
Manifest cylinder (D) <sup>a</sup>	-0.86 (IQR: -1.00 to -0.25)
Preoperative CDVA (logMAR) <sup>b</sup>	-0.09 (IQR: -0.1 to -0.1)
Postoperative UDVA (logMAR) <sup>b</sup>	-0.03 (IQR: -0.1 to 0)
Enhancement (%)	19%
Interval LVC to thermal pulsation therapy (months)	40.5 (IQR: 27.6 to 55)
Primary questionnaire interval (days)	25 (IQR: 9 to 31)
Secondary questionnaire interval (days)	208 (IQR: 190 to 219)

IQR = interquartile range; PRK = photorefractive keratectomy; D = diopters; CDVA = corrected distance visual acuity; UDVA = uncorrected distance visual acuity; LVC = laser vision correction

<sup>a</sup>Reported from before LVC.

<sup>b</sup>In this study, preoperative CDVA is superior to postoperative UDVA (difference -0.6,  $P < .0001$ ).

follow-up SPEED II report of worsened symptoms at the secondary questionnaire. Time for analysis was the duration from treatment to secondary questionnaire.

All visual acuities are reported in logMAR format. Statistical analysis was done using Stata 12 (Stata-Corp., College Station, TX) and Microsoft Excel 2013 (Microsoft Corporation, Redmond, WA) software. A  $P$  value of less than .05 was considered the threshold for statistical significance.

## RESULTS

A total of 109 eyes of 57 patients who underwent thermal pulsation therapy were identified for retrospective analysis. The mean patient age was 49 years (IQR: 38 to 60), 70% were female, and the primary refractive procedure was LASIK ( $n = 91$ , 83%) or PRK ( $n = 18$ , 17%). The mean time from laser vision correction to treatment with thermal pulsation therapy was 40.5 months (IQR: 27.6 to 55). Patient demographics and examination on initial refractive consultation can be found in **Table 1**. Distribution of treated eyes by age and sex can be found in **Figure A** (available in the

online version of this article). After primary laser vision correction procedure, 21 eyes (19%) underwent subsequent enhancement or touch-up prior to thermal pulsation therapy.

Clinical evaluation before and after refractive surgery and after thermal pulsation therapy is summarized in **Table 2**. After surgery, all study patients were noted to report visual symptoms including foreign body sensation, irritation, pain, visual fatigue, poor visual quality, and excessive tearing or discharge. These visual symptoms, documented prior to thermal pulsation therapy, were often described as debilitating and disruptive to daily activities, and included specific complaints of glare (38% of study eyes) and halo (17%). In this study group, pre-therapy lipid layer thickness was 66 nm (IQR: 49 to 88.5), and meibomian gland evaluation values were 4.4 (IQR: 3 to 6).

Notable events after laser vision correction that occurred prior to thermal pulsation treatment included corneal erosions in 8 eyes with PRK (44%) and 11 eyes with LASIK (11%). These cases occurred after initial surgical intervention and were unrelated to dry eye treatment. Additionally, one eye of a patient who had LASIK developed presumed microbial keratitis 24 days after surgery, as did one eye of a patient with PRK 3 days after surgery. These patients were aggressively treated with fortified antibiotics. Both eyes did well with uncorrected distance visual acuity of 0 (Snellen 20/20) and -0.1 (Snellen 20/16), respectively, at 6 months after surgery.

SPEED II questionnaire scores before and after treatment can be found in **Table 3**. The cumulative pre-treatment SPEED II score was 17.5 (IQR: 14 to 21). Treatment with thermal pulsation therapy occurred at a mean of 40.5 months (IQR: 27.6 to 55) after primary refractive procedure. The primary follow-up questionnaire was completed at a mean of 25 days (IQR: 9 to 31) following treatment. The primary outcome of post-treatment SPEED II score was significantly decreased to 10.2 (IQR: 6 to 14; 95% confidence interval [CI]: 8.8 to 11.5), for an average improvement of 7.3 (95% CI: 5.6 to 8.8) after thermal pulsation therapy ( $P < .001$ ). Distribution of SPEED II scores before and after surgery can be found in **Figure 1**.

Within the study group, 72% of patients ( $n = 79$ ) were noted to complete the secondary follow-up questionnaire at a mean 208 days (IQR: 190 to 219). Fewer patients with LASIK completed the secondary questionnaire (69%), as compared to PRK (89%), but this difference was not significant ( $P = .09$ ). The secondary follow-up questionnaire SPEED II score was also improved compared to baseline (mean: 9.9; IQR: 6 to 13; 95% CI: 8.4 to 11.4), but not significantly changed from the primary follow-up questionnaire score (mean difference: -0.35;  $P = .68$ ).

TABLE 2  
**Clinical Findings Before and After LVC and  
 After Treatment With Thermal Pulsation Therapy<sup>a</sup>**

Clinical Findings	Before LVC	After LVC	After Therapy
TBUT (sec)	11.6 (IQR: 12 to 12)	3.7 (IQR: 2 to 5)	5.75 (IQR: 4 to 7.50)
	–	0 (27)	–
Meibomian gland dysfunction/blepharitis grade	0 (94%)	1 (48%)	0 (77%)
	1 (6%)	2 (24%)	1 (15%)
	–	3 (2%)	2 (8%)
	–	0 (20%)	–
	0 (91%)	1 (41%)	1 (15%)
Corneal staining grade <sup>b</sup>	1 (7%)	2 (30%)	2 (10%)
	2 (2%)	3 (7%)	3 (6%)
	–	4 (2%)	3 (6%)
Meibomian gland evaluator score	–	4.4 (IQR: 3 to 6)	–
Lipid layer thickness (μm)	–	66 (IQR: 49 to 88.5)	–

LVC = laser vision correction; TBUT = tear break-up time; IQR = interquartile range

<sup>a</sup>Clinical evaluation following thermal pulsation therapy occurred at a mean 89 days after therapy (IQR: 43 to 121). In comparison to clinical findings documented following surgery in this study group, thermal pulsation therapy was associated with improvement in TBUT (difference +1.9 sec; 95% confidence interval: 1.3 to 1.5), reduction in grade of meibomian gland dysfunction (difference -0.69; 95% confidence interval: -0.54 to -0.84), and grade of corneal staining (difference -0.74; 95% confidence interval: -0.57 to -0.91).  $P < .001$  for all clinical findings.

<sup>b</sup>Corneal staining grading used previously described methods for defining severity from 0 (none) to 4 (severe).<sup>14</sup>

After thermal pulsation therapy, follow-up clinical evaluation occurred at a mean 89 days after therapy (IQR: 43 to 121). In comparison to clinical findings documented before therapy in this study group, there was a statistically significant increase in TBUT (difference: +1.9 sec; 95% CI: 1.3 to 2.5) and reduction in grade of meibomian gland dysfunction (difference: -0.69; 95% CI: -0.54 to -0.84) and grade of corneal staining (difference: -0.74; 95% CI: -0.57 to -0.91) ( $P < .001$  for all clinical findings).

Mixed effect regression analysis identified several variables associated with degree of SPEED II response. Eyes with PRK tended to report a higher degree of improvement by an average of 4.5 points (95% CI: 0.2 to 8.8;  $P = .04$ ) on the primary follow-up questionnaire. A small percentage of eyes with LASIK (11%) saw no benefit or reported worse symptoms after therapy. Variance in SPEED II score following treatment stratified by primary surgery can be seen in **Figure 2**, which illustrates this trend. This trend vanished on analysis of SPEED II responses at secondary questionnaire, such that there was no significant difference in degree of response between eyes with LASIK and PRK at this longer follow-up time. Additionally, increasing grade of pre-treatment corneal staining was negatively associated with response to therapy. Eyes with more severe staining patterns before treatment reported -1.62 less benefit per degree of severity (95% CI: -0.32 to -2.92;  $P = .015$ ).

TABLE 3  
**SPEED II Questionnaire Results  
 Before and After Thermal Pulsation  
 Therapy and Time to Completion<sup>a</sup>**

SPEED II Questionnaire	Results	Follow-up Interval (days)
Pre-treatment	17.5 (IQR: 14 to 21)	–
Primary follow-up	10.2 (IQR: 6 to 14)	25 (IQR: 9 to 31)
Secondary follow-up	9.9 (IQR: 6 to 13)	208 (IQR: 190 to 219)

SPEED II = Standard Patient Evaluation of Eye Dryness II; IQR = interquartile range

<sup>a</sup>The mean time from laser vision correction to treatment with thermal pulsation therapy was 40.5 months (IQR: 27.6 to 55). Patients tended to report an average improvement of 7.3 (95% confidence interval: 5.6 to 8.8) on primary follow-up questionnaire ( $P < .001$ ), which was completed 25 days (IQR: 9 to 31) following treatment. Improvement over baseline pre-treatment SPEED II score persisted at secondary questionnaire, but was not significantly changed from primary follow-up questionnaire (mean difference -0.35;  $P = .68$ ). The secondary questionnaire was completed by 72% of patients ( $n = 79$ ) at a mean 208 days (IQR: 190 to 219) after treatment.

**Figure B** (available in the online version of this article) illustrates this trend.

Survival analysis with Cox proportional hazard was performed using data at the secondary questionnaire to identify risks for symptomatic relapse that may influence duration of response to treatment. The pattern and degree of corneal staining was found to be associated with recurrent symptoms. For every graded in-



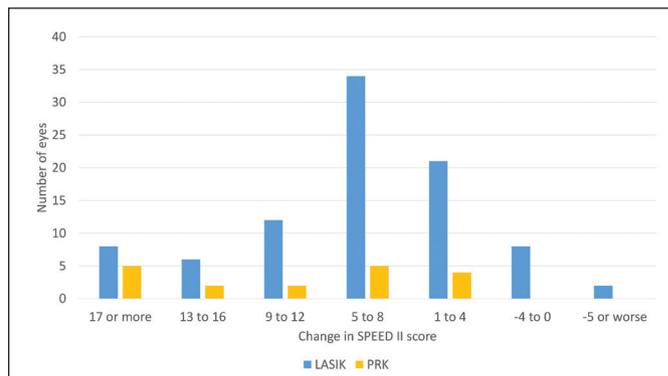
**Figure 1.** Graphic distribution of Standard Patient Evaluation of Eye Dryness (SPEED II) scores before and after treatment ( $P < .001$  for difference). The mean pre-therapy SPEED II questionnaire score was 17.5 (interquartile range [IQR]: 14 to 21), with a reduced mean post-therapy score of 10.2 (IQR: 6 to 14; 95% CI: 8.8 to 11.5,  $P < .001$ ). In this graphical representation, the appreciable shift in scores to the left of the figure corresponds to patient reported improvement in symptoms. The mean time from laser vision correction to treatment with thermal pulsation therapy was 40.5 months (IQR: 27.6 to 55). Primary SPEED II questionnaire reports after treatment were acquired a mean 25 days (IQR: 9 to 31) following treatment with thermal pulsation therapy.

crease in severity of corneal staining, a reduced risk of symptomatic relapse was observed (hazard ratio: 0.48; 95% CI: 0.30 to 0.75;  $P = .001$ ). **Figure C** (available in the online version of this article) offers graphical representation of the cumulative hazard functions defined by the Nelson–Aalen estimator stratified by corneal staining pattern.

Notable clinical findings that were not significantly associated with degree of SPEED II reported response or risk for symptomatic relapse included the presence or grade of meibomian gland dysfunction (0.94 points per degree; 95% CI: -1.2 to 3.0;  $P = .38$ ), pre-treatment TBUT (0.37 points per second; 95% CI: -0.43 to 1.18;  $P = .36$ ), patient age (0.01 points per year; 95% CI: -0.12 to 0.13,  $P = .93$ ), and patient sex (-0.5 points if female; 95% CI: -4.1 to 3.1;  $P = .78$ ). Meibomian gland evaluator and lipid layer thickness were also not significantly associated with degree of SPEED II response or risk for symptomatic relapse.

**DISCUSSION**

Effective management of dry eye symptoms after laser vision correction remains an area of interest, and this study offers an initial retrospective evaluation on the role of thermal pulsation therapy for the treatment of persistent dry eye symptoms following refractive procedures. The patients selected for inclusion in this study were those with the most intractably symptomatic dry eye in a large refractive surgery practice and were only offered thermal pulsation therapy as auxiliary treatment after failing all conventional methods. They represented the minority in a practice consist-



**Figure 2.** Histogram of change in Standard Patient Evaluation of Eye Dryness II (SPEED II) scores at primary follow-up questionnaire after one treatment with thermal pulsation therapy. Positive values to the left of this figure denote improvement in symptoms. Photorefractive keratectomy (PRK) eyes tended to report more improvement compared to LASIK eyes by an average of 4.5 points (95% confidence interval: 0.2 to 8.8;  $P = .04$ ). A small percentage of LASIK eyes (11%) saw no benefit or reported worse symptoms after therapy. Primary SPEED II questionnaire results were acquired at a mean 25 days (interquartile range: 9 to 31) following treatment with thermal pulsation therapy.

ing of more than 100,000 annual treatments. Many of them had received refractive procedures several years prior to being offered thermal pulsation therapy. These patients invariably developed ocular surface dysfunction in the period following laser vision correction, but they did not necessarily have the most severe objective findings often associated with dry eye, and they were not exclusively experiencing sequela related to laser vision correction, such as aqueous deficiency.

In essence, the patients were effectively self-selecting for thermal pulsation therapy. Of more than 100,000 annual cases performed during the study period, the current patient population may be indicative of the 0.1% of total cases who developed forms of evaporative dry eye or aqueous deficiency by virtue of the natural history and incidences of these conditions. This consideration is supported by the increased prevalence of meibomian gland dysfunction in the study group after refractive surgery: after surgery 73% of patients were noted to have some degree of meibomian dysfunction, an increase from 9% before surgery. The increased prevalence may be attributable to the natural history and incidence of meibomian gland dysfunction. The patients were also characterized by reduced TBUT in the period after surgery, supporting the development of at least some component of evaporative dry eye.

The primary outcome of this study suggests that thermal pulsation therapy may be beneficial for symptoms related to dry eye in patients after laser vision correction. Treated eyes showed significant improvement over baseline on follow-up questionnaire at 1 month, with benefits of a single treatment persisting on

secondary follow-up questionnaire approximately 6 to 8 months after treatment. A small portion of eyes with predominantly LASIK were noted to report worsened subjective outcomes, but the significance of this finding is unclear because there were no adverse sequela related to treatment in these cases.

With regard to secondary outcomes in this study, several findings were encountered that may provide insight into patient characteristics suggestive of positive response to treatment. Patients with PRK may experience increased benefit early after thermal pulsation therapy compared to LASIK. However, this benefit may be transient and does not appear to persist at 6 months, and thus may not be of clinical relevance. Increasing severity of corneal staining was found to be associated with a decreased response on initial questionnaire. Patients with more profound staining patterns thus may be 'low responders' to treatment. However, these patients were noted to have a reduced risk of symptomatic relapse on survival analysis, and thus patients with documented staining patterns may experience longer duration of effect. The forces behind these findings are unclear and have to be placed in the context of our understanding of the mechanism of thermal pulsation therapy. It is plausible to suspect that more overt clinical findings of dry eye (as evidenced by corneal staining) will contribute to less dramatic response to an isolated treatment, but measures that improve the function and health of the ocular surface may provide stable relief over time. Further study is needed to understand the role, if any, that corneal staining patterns may have on outcomes following thermal pulsation therapy.

Objectively, treated eyes were noted to have statistically significant increases in TBUT, improved meibomian gland patency, and reduced grade of corneal staining at follow-up clinical evaluation when compared to values obtained before therapy was administered. These data correlate well with the improved subjective outcomes reported on the SPEED II questionnaire, providing limited objective support for the validity of thermal pulsation therapy in patients after laser vision correction. However, clinical documentation of meibomian gland dysfunction, as well as the parameters TBUT, meibomian gland evaluator, and lipid layer thickness, did not reveal significant associations with SPEED II response or duration, as would have been anticipated.

The results of the primary outcome must be placed within the context of the limitations of this study. Due to its retrospective design, patient selection for thermal pulsation therapy was not randomized and thus subject to many potential areas of bias. There was no standardized treatment regimen prior to offering ther-

mal pulsation therapy. The patients who were initially offered treatment were patients with the most severe or persistent symptoms of dry eye, not necessarily those with the most profound objective clinical findings. The patients were not exclusively suffering sequela related to laser vision correction, and the etiology of dry eye disease was not thoroughly evaluated in this study. Patients did not routinely receive evaluation with tear osmolarity, Schirmer's test, or matrix metalloproteinase 9, which would have provided additional insight. Furthermore, the secondary outcomes of this study should be carefully weighed because the retrospective nature of this study did not incorporate observer masking and rigorous and impartial clinical evaluation and documentation was not enforced at each follow-up visit. As such, the secondary outcomes may be skewed by observer or reporting bias.

Given the lack of a control group, it is difficult to attribute the presence or degree of patient-reported improvement in dry eye symptoms encountered in the current study solely to thermal pulsation therapy. However, the close temporal relationship of treatment with improvement on the primary follow-up questionnaire when compared with the chronic nature of many of the patients' symptoms suggests that the effects observed may be the result of thermal pulsation therapy and not the natural history of dry eye disease. In a recent controlled trial evaluating thermal pulsation therapy using the SPEED questionnaire, the unadjusted patient-reported benefit of therapy appeared to be in excess of 6 points when compared to baseline, for an increased response of more than 3 points when compared to controls.<sup>10</sup> In the current study, the mean reported benefit of more than 7 points supports the conclusion that thermal pulsation therapy contributed significantly to relief of symptoms.

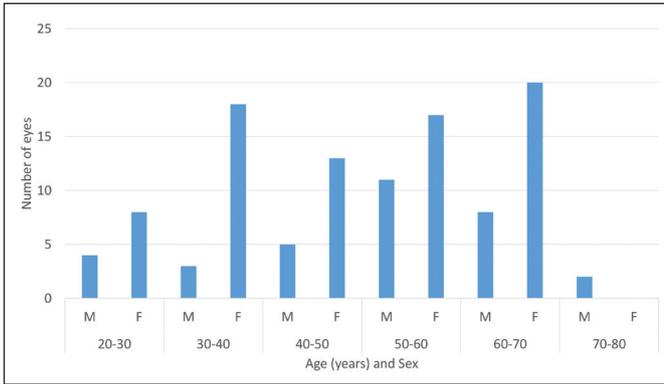
The current study was designed to offer an initial retrospective evaluation on the subjective response to thermal pulsation therapy in a population of patients with dry eye after laser vision correction. The evidence suggests that thermal pulsation therapy may offer significant improvement in dry eye symptoms for these patients following a single treatment. Response to therapy appears to persist for at least 6 months after treatment. Patients with adverse corneal staining patterns indicative of dry eye may experience longer lasting subjective benefit. There may be a positive impact of thermal pulsation therapy on the objective clinical parameters of TBUT, meibomian gland dysfunction, and corneal staining. Further evaluation with prospective, randomized, masked studies is needed to better define the role of thermal pulsation therapy in patients after laser vision correction.

**AUTHOR CONTRIBUTIONS**

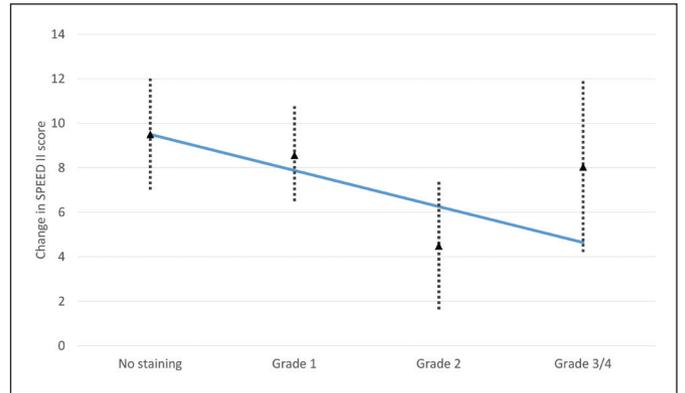
Study concept and design (CSS, JMS, SCS); analysis and interpretation of data (CSS, JMS, SH, SCS); writing the manuscript (CSS, SCS); critical revision of the manuscript (CSS, JMS, SH, SCS); supervision (SCS)

**REFERENCES**

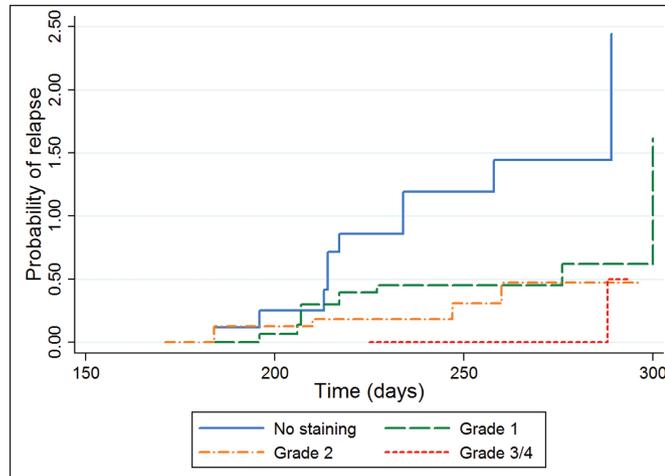
1. De Paiva CS, Chen Z, Koch DD, et al. The incidence and risk factors for developing dry eye after myopic LASIK. *Am J Ophthalmol.* 2006;141:438-445.
2. Kasetsuwan N, Satitpitakul V, Changul T, Jariyakosol S, Incidence and pattern of dry eye after cataract surgery. *PLoS One.* 2013;8:e78657.
3. Hassan Z, Szalai E, Berta A, Modi L Jr, Nemeth G. Assessment of tear osmolarity and other dry eye parameters in post-LASIK eyes. *Cornea.* 2013;32:e142-e145.
4. Yu EY, Leung A, Rao S, Lam DS, Effect of laser in situ keratomileusis on tear stability. *Ophthalmology.* 2000;107:2131-2135.
5. Wilson SE, Laser in situ keratomileusis-induced (presumed) neurotrophic epitheliopathy. *Ophthalmology.* 2001;108:1082-1087.
6. Nejima R, Miyata K, Tanabe T, et al. Corneal barrier function, tear film stability, and corneal sensation after photorefractive keratectomy and laser in situ keratomileusis. *Am J Ophthalmol.* 2005;139:64-71.
7. Chuck RS, Quiros PA, Perez AC, McDonnell PJ. Corneal sensation after laser in situ keratomileusis. *J Cataract Refract Surg.* 2000;26:337-339.
8. Han KE, Yoon SC, Ahn JM, et al. Evaluation of dry eye and meibomian gland dysfunction after cataract surgery. *Am J Ophthalmol.* 2014;157:1144-1150.
9. Greiner JV. A single LipiFlow(R) Thermal Pulsation System treatment improves meibomian gland function and reduces dry eye symptoms for 9 months. *Curr Eye Res.* 2012;37:272-278.
10. Lane SS, DuBiner HB, Epstein RJ, et al. A new system, the Lipi-Flow, for the treatment of meibomian gland dysfunction. *Cornea.* 2012;31:396-404.
11. Greiner JV. Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. *Clin Experiment Ophthalmol.* 2013;41:524-530.
12. Finis D, Konig C, Hayajneh J, Borelli M, Schrader S, Geerling G. Six-month effects of a thermodynamic treatment for MGD and implications of meibomian gland atrophy. *Cornea.* 2014;33:1265-1270.
13. Finis D, Hayajneh J, Konig C, Borelli M, Schrader S, Geerling G. Evaluation of an automated thermodynamic treatment (LipiFlow(R)) system for meibomian gland dysfunction: a prospective, randomized, observer-masked trial. *Ocul Surf.* 2014;12:146-154.
14. Definition and Classification Subcommittee of the International Dry Eye WorkShop. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf.* 2007;5:75-92.
15. Management and Therapy Subcommittee of the International Dry Eye WorkShop. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf.* 2007;5:163-178.
16. Finis D, Pischel N, Schrader S, Geerling G, Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for Meibomian gland dysfunction. *Cornea.* 2013;32:1549-1553.
17. Korb DR, Blackie CA. Meibomian gland diagnostic expressibility: correlation with dry eye symptoms and gland location. *Cornea.* 2008;27:1142-1147.
18. Ngo W, Situ P, Keir N, Korb DR, Blackie C, Simpson T. Psychometric properties and validation of the Standard Patient Evaluation of Eye Dryness questionnaire. *Cornea.* 2013;32:1204-1210.



**Figure A.** Distribution of treated eyes by age and sex. A total of 109 eyes of 57 patients underwent thermal pulsation therapy. The mean patient age was 49 years (interquartile range: 38 to 60), 70% were female, and the primary refractive procedure was LASIK ( $n = 91$ , 83%) or photorefractive keratectomy ( $n = 18$ , 17%).



**Figure B.** Relationship of corneal staining severity and degree of response following thermal pulsation therapy. Grading scale used previously described methods for defining severity from 0 (none) to 4 (severe).<sup>14</sup> Primary Standard Patient Evaluation of Eye Dryness II (SPEED II) questionnaire results were acquired at a mean 25 days (interquartile range: 9 to 31) following treatment with thermal pulsation therapy. Positive values in the figure correspond to reported improvement on SPEED II questionnaire. The points represent the estimated average change in SPEED II score for each degree of corneal staining, with vertical bars denoting the 95% confidence interval. In this study, eyes with more severe staining patterns tended to report less benefit, with reported scores of 1.62 less per degree of severity (95% confidence interval: -0.32 to -2.92;  $P = .015$ ).



**Figure C.** Nelson-Aalen cumulative hazard estimates for treated eyes stratified by severity of corneal staining patterns graded with previously described methods for defining severity from 0 (none) to 4 (severe).<sup>14</sup> Corneal staining was obtained at clinical evaluation prior to thermal pulsation therapy. Increasing severity was associated with reduced likelihood of symptomatic relapse, defined as recurrent symptoms on secondary Standard Patient Evaluation of Eye Dryness II (SPEED II) (hazard ratio: 0.48; 95% confidence interval: 0.30 to 0.75;  $P = .001$ ). In this study, more profound corneal staining patterns were associated with a lesser degree of improvement on primary SPEED II questionnaire (see Figure B). However, these eyes may experience longer lasting effect. The primary questionnaire was completed 25 days (interquartile range [IQR]: 9 to 31) following treatment, and the secondary questionnaire was completed 208 days (IQR: 190 to 219) after treatment.