Short-term impact of FS-LASIK and SMILE on dry eye metrics and corneal nerve morphology.

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Conflict of interest

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Keywords

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Abstract

Purpose

To analyse the short-term (up to one month) clinical outcomes in patients undergoing corneal laser refractive surgery and the impact on dry eye disease (DED) metrics and corneal nerves using in vivo confocal microscopy (IVCM).

Methods

Unaided distance visual acuity (UDVA), corrected distance visual acuity (CDVA) and spherical equivalent refraction (SEQ) were determined in 16 and 13 patients undergoing FS-LASIK and SMILE respectively. DED metrics assessed were Ocular Surface Disease Index (OSDI), Dry Eye Questionnaire 5-items (DEQ-5), tear film osmolarity, tear meniscus height (TMH), non-invasive Keratograph break-up time (NIKBUT), ocular staining and meibomian gland atrophy. Automated analysis of corneal nerve fibre density (CNFD), corneal nerve branch density (CNBD), corneal nerve fibre length (CNFL) and corneal nerve fibre fractal dimension (CNFrD) were obtained from IVCM scans using ACCMetrics software (University of Manchester).

Results

Both surgical techniques provided good refractive and visual outcomes. DED symptoms were found to be significantly higher after FS-LASIK compared to SMILE ($p<0.05$). A significant decrease in TMH (~31%) and NIKBUT (~40%) was reported after FS-LASIK ($p=0.005$ and $p=0.001$ respectively) but not after SMILE. Both procedures affected CNFD, CNBD, CNFL and CNFrD but the impact was significantly greater with FS-LASIK ($p= 0.001$). Only CNFL was correlated with reported symptoms (DEQ-5) after FS-LASIK ($r= -0.545$, $p= 0.029$).

Conclusion

FS-LASIK and SMILE provided good refractive and visual outcomes. There was an increased impact on DED symptoms following FS-LASIK compared to SMILE although there were no significant differences between the procedures for most of the other ocular surface metrics assessed. IVCM findings showed that SMILE had less impact on the corneal nerves compared to FS-LASIK.

Introduction

The corneal nerves have a key role in ocular surface homeostasis. Damage to the corneal nerves (stromal, subbasal nerve plexus and epithelial nerves) as a result of trauma, long-term topical drug exposure (glaucoma eyedrops), contact lens wear (orthokeratology) or corneal surgical procedures can adversely affect the homeostasis of the tear film.[1]

Many studies have demonstrated that transection of corneal nerves during laser vision correction procedures can temporarily lead to suppression of tear secretion from the lacrimal gland while the nerves regenerate[2], mucin expression on the corneal epithelium[3], blink rate changes and increasing signs and symptoms of dry eye disease (DED). Risk factors for post-LASIK dry eye include pre-existing dry eye disease[4], deeper laser ablations[5], flap size and location of the hinge[6]. Small incision lenticule extraction (SMILE) is a flap-less procedure whereby a stromal tissue lenticule is extracted through a small corneal incision in order to correct myopia or myopic astigmatism.[7] SMILE aimed to overcome some of the limitations of LASIK due to its minimal disruption of the anterior corneal nerve plexus. SMILE creates a side cut tunnel (less than 3-5 mm) rather than a flap and utilises removal of mid-posterior stromal tissue rather than more anterior stromal tissue; this has been demonstrated to impact less on the ocular surface and aids its recovery after surgery.[8] In LASIK, subbasal nerve bundles and superficial stromal nerve bundles in the flap interface are transected. Only nerves entering the flap through the hinge region are spared while the excimer laser ablation transects further stromal nerve fibre bundles. In SMILE the anterior cornea is largely preserved other than in the region of the small incision. Several studies suggest that SMILE patients often have less significant symptoms than patients undergoing LASIK procedures.[9,10]

To explore the possible benefits of newer ophthalmic procedures such as SMILE over more traditional approaches, different diagnostic techniques have been considered. One of the most advanced techniques in terms of examining corneal structure at the cellular level, is in-vivo confocal microscopy (IVCM). IVCM can potentially reveal changes in the corneal nerve structure through its high resolution scanning system. When applied to the ocular surface, IVCM can image the overall structure of the corneal nerves, including nerve fibre length and nerve fibre density. The quality of the IVCM acquisitions can be comparable with histological samples without the need for fixing and processing samples, as with conventional light and electron microscopy.[11] However, despite these advantages in the technique, limitations in the software to process the scans from IVCM has been an issue as most of the scans are subsequently processed using manual or semi-automated programs which can be time-consuming and subject to observer bias in terms of reproducibility and repeatability.[12]

The aim of the current study was to determine the impact of femtosecond laser assisted (FS)-LASIK and SMILE on the ocular surface using a protocol for DED assessment recommended by the Tear Film Ocular Society (TFOS) Dry Eye WorkShop II (DEWS II) report.[13] A secondary aim was to assess the changes in the subbasal corneal nerve fibre structure before and after both procedures using IVCM. A fully automated approach to quantifying corneal nerve fibre morphology was used and findings were correlated with the DED metrics.

Materials and Methods

Participants

This prospective, longitudinal and observational study was performed at a private eye hospital in the UK (Optegra Eye Hospital London, London, UK). The patients enrolled were divided into two groups according to the types of surgery they were undergoing (either FS-LASIK or SMILE). All the study procedures were performed before and 1 month after surgery. The FS-LASIK group was composed of 16 subjects (7 males; 9 females) with a mean ± SD age of 32.6 ± 9.1 years and mean pre-operative refraction of -3.48 ± 2.89 D while the SMILE group was composed of 13 subjects (5 males; 8 females) with a mean ± SD age of 32.2 ± 5.3 years and mean pre-operative refraction of -4.67 ± 2.12 D. Only the eye with better visual acuity (VA) or the dominant eye (assessed using motor and sensory dominance tests) was included for evaluation in the study. Exclusion criteria for both groups were: prior surgery on the selected eye, DED diagnosis, unstable refractive error, ocular abnormalities or disease, progressive myopia or astigmatism, systemic disease such as diabetes and unwillingness to adhere to the study instructions or to give written informed consent before any study procedure. The study was conducted in accordance with the tenets of the Declaration of Helsinki and received a favourable opinion from the Aston University Research Ethics Committee.

Surgery

All the surgeries were performed by two experienced consultant ophthalmic surgeons. In the FS-LASIK surgery group, all the flaps were created using the VisuMax femtosecond laser platform (Carl Zeiss Meditec AG, Jena, Germany) set to a 500-kHz frequency. The diameter of the flaps was 8.1 to 8.9 mm. The hinges were positioned at 90 degrees (superior) and the side-cut angle was 90 degrees. The flap thickness was between 90 to 110 µm. The stromal ablation was performed with the MEL 90 excimer laser platform (Carl Zeiss Meditec AG, Jena, Germany) using the Triple-A “Advanced Ablation Algorithm” with a 500-Hz pulse rate. In the SMILE group, the laser system used was the VisuMax femtosecond laser, and the frequency was set to 500 kHz with a spot energy of 140 nJ. The lenticule diameter was between 6.5 to 7.0 mm, with a cap thickness set to 120 to 135 µm. The tunnel size to extract the lenticule varied from 2 to 4 mm and the location was 90 and 120 degrees.

Refractive and ocular surface assessment

Monocular unaided distance visual acuity (UDVA), monocular corrected distance visual acuity (CDVA) were assessed with a logMAR chart and spherical equivalent refraction (SEQ) was determined using subjective refraction carried out by qualified optometrists experienced in examining corneal refractive surgery patients. The ocular surface assessment consisted of the following tests: Ocular Surface Disease Index (OSDI) and Dry Eye Questionnaire 5-items (DEQ-5) questionnaires; tear film osmolarity using the TearLab® Osmolarity System (TearLab® Corporation, Escondido, US); tear meniscus height (TMH), as the average of three objectively determined non-invasive Keratograph break-up times (NIKBUT); ocular staining using the Oxford Scheme grading scale with both fluorescein and Lissamine green and analysis of the meibomian glands (Meiboscore) was undertaken using an OCULUS Keratograph 5M® (K5M) (OCULUS, Wetzlar, Germany).

In vivo confocal microscopy

The laser scanning confocal microscope used in this study was the Heidelberg Retinal Tomograph with a Rostock Corneal Module (HRT-RCM) (Heidelberg Engineering GmbH, Dossenheim, Germany) which has demonstrated good repeatability and reproducibility in the assessment of corneal nerve fibres metrics.[14,15] Five to ten images of the corneal subbasal nerve plexus were acquired at a depth range between 50 to 80 µm (Fig. 1).The images were acquired at the optical centre of the cornea while the patient fixated a static light source, improving the chance that the images were from the same location. A real-time camera linked to the device was used by the examiner to manually optimize alignment between the central part of the cornea and the confocal probe. Five representative and complete images of the central corneal subbasal nerve plexus were selected for analysis. All the IVCM scans were performed by the same trained examiner (AR) after the application of a topical anaesthetic (Minims Oxybuprocaine Hydrochloride 0.4%, Bausch & Lomb, Florida, US) to reduce the blink reflex and increase patient comfort during the acquisitions.

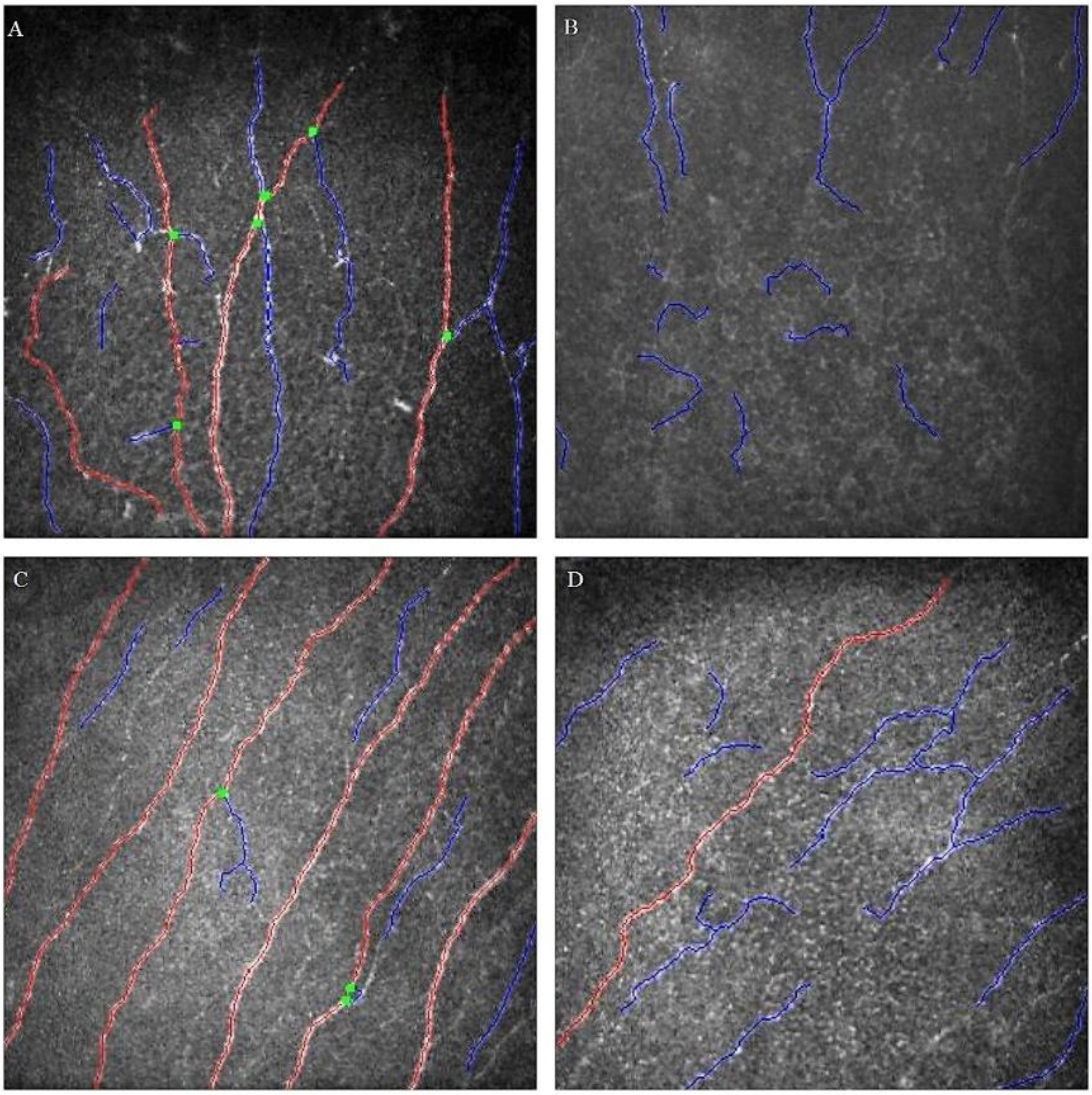

Figure 1 Sample of IVCM images of the subbasal corneal nerves fibre analysed with ACCMetrics: before LASIK surgery (A) and after (B), before SMILE surgery (C) and after (D). Main nerve fibres in red, nerve branches in blue and branch points in green.

Image analysis

The automatic quantification of the subbasal corneal nerves was performed using a software programme ACCMetrics designed by the University of Manchester Research Group (Manchester, UK). Specifically, the analysis included corneal nerve fibre density (CNFD, number of main fibres per mm^2), corneal nerve branch density (CNBD, number of branches per mm^2), corneal nerve fibre length (CNFL, total length of main fibres and branches per mm^2) and corneal nerve fibre fractal dimension (CNFrD). In brief, ACCMetrics analyses the images using two main processes: nerve-fibre detection and nerve-fibre quantification. The nerve-fibre detection works on methods based on machine learning able to report the detection of curvilinear features. The image is denoised and a threshold applied to generate a binary image of the nerves which is then filtered and thinned to obtain a one pixel wide skeleton. Branch and end points are identified to produce an optimised binary skeleton, as detailed by Chen et al.[16] The second process is the nerve-fibre quantification: the identification starts with the main nerve fibres (e.g. major length and width) considering length, orientation difference, intensity and width parameters. All these parameters are then compared with subscales of images previously loaded in the software to obtain a matrix match. In our study, the images were analyzed and those containing stromal or epithelium layers or artifacts (e.g. excessive compression of the layers/nerves) were discarded. Images with subbasal corneal nerves were analyzed with dimensions of 384 x 384 pixels with a pixel size of 1.0417 µm.

The CNFrD measure consisted of the nerve fibre detection step as described above. CNFrD considers the structural complexity of the image (in this case, scans from the subbasal corneal nerve plexus) by comparing the changes in details to the change in scale . For this study it was calculated using a box counting method based on the detected nerve fibres. As described by Liu et al.[34], the image considered is analysed using different sized boxes of 1x1, 2x2, 4x4, etc. where the pixel location in the image is checked. The number of boxes is increased by 1 when any part of the detected nerve fibre is within a box. A series of points are plotted based on the number of boxes against the corresponding box sizes. The slope of the line is the FD value where a higher value corresponds to a complex more evenly distributed nerve structure while fewer irregular nerves (e.g. increased tortuosity) will have a lower FD value. Chen et al.[17] used CNFrD measurement in diabetic patients and found that it is comparable with other subbasal corneal nerve metrics while Giannaccare et al.[18] have used it in patients with dry eye disease without showing a significant difference with a control group. However, more research is needed to confirm its utility.

Statistical analysis

All statistical analysis was performed using SPSS 23.0 (SPSS Inc., Chicago, US). Data normality was tested using the Shapiro-Wilk test. Group comparisons for normally distributed data were performed with Student's *t*-test comparing before and after the treatment while non-normally distributed variables were examined with the Wilcoxon signed rank test with 2 related samples while using Mann-Whitney U test with 2 independent samples. The bivariate correlation analysis for normally distributed data was performed using the Pearson's test whereas data not normally distributed were analysed using the Spearman's test. A guide to interpreting correlation strength was derived from the recommendations of Navarro et al.[19] A p-value < 0.05 was taken to be statistically significant.

Results

There was no significant difference between groups in post-operative UDVA (p= 0.721) and post-operative SEQ (p= 0.769). At one month, all eyes (100%) in the FS-LASIK group were able to achieve a post-operative UDVA of 0.0 logMAR compared to the SMILE group of which 92% achieved 0.0 UDVA at 1 month. 87% and 77% of eyes were found to be within ± 0.50 D of the intended target refraction in the FS-LASIK and SMILE groups respectively (Fig. 2).

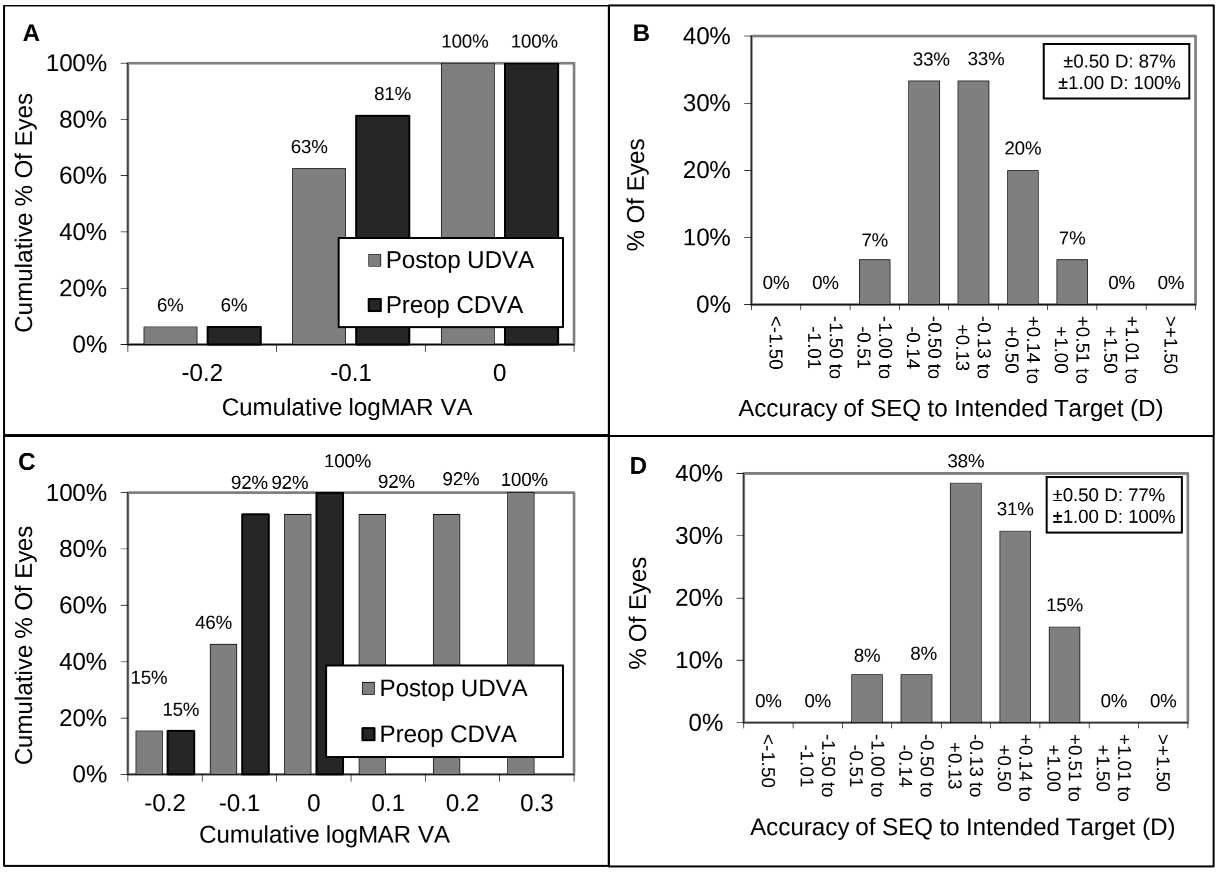

Figure 2 Standard graphs for reporting refractive surgery outcomes (Waring graphs): A) the visual acuity before and after FS-LASIK surgery (Preoperative (Preop) Corrected Distance Visual Acuity (CDVA) vs Postoperative (Postop) Uncorrected Distance Visual Acuity (UDVA)) and B) accuracy of the FS- LASIK surgical procedure in terms of residual refraction after surgery. C) the visual acuity before and after SMILE surgery (Preop CDVA vs Postop UDVA) and D) accuracy of the SMILE surgical procedure in terms of residual refraction after surgery.

The ocular surface metrics obtained in the two groups are reported in Table 1. Significantly higher symptomatology, assessed with both OSDI and DEQ-5 questionnaires, were found comparing pre- versus post- operative scores in FS-LASIK (OSDI and DEQ-5 both with p=0.001) but not when comparing pre and post-operative scores in SMILE (OSDI p= 0.374 and DEQ-5 p= 0.154). TMH and NIKBUT were significantly reduced after the LASIK procedure (p= 0.005 and 0.001 respectively), but not when compared with the SMILE technique at 1 month (p= 0.253 and 0.114 respectively). No significant changes were found for any of the remaining metrics such as tear film osmolarity, ocular staining and Meibography (Meiboscore).

Parameter	FS-LASIK group (mean ± SD)		*P*	SMILE group (mean ± SD)		*P*	
	Before	After	Within surgery	Before	After	Within surgery	Between surgeries
OSDI (score)	8 ± 10	34 ± 23	*0.001*	8 ± 12	11 ± 8	0.374	*0.039*
DEQ-5 (score)	5 ± 3	12 ± 5	*0.001*	6 ± 3	7 ± 3	0.154	*0.006*
Osmolarity (mOsm/L)	295 ± 12	300 ± 14	0.629	291 ± 10	289 ± 9	0.975	0.054
TMH (mm)	0.32 ± 0.13	0.22 ± 0.09	*0.005*	0.30 ± 0.07	0.33 ±0.08	0.248	0.253
NIKBUT (s)	11.3 ± 5.7	6.7 ± 3.6	*0.001*	10.2 ± 5.4	9.8 ± 4.6	0.121	0.114
Ocular staining (Oxford score)	0 ± 1	0 ± 1	0.609	0 ± 1	0 ± 1	0.742	0.938
MG (Meiboscore)	2 ± 2	2 ± 2	0.164	1 ± 1	1 ± 1	0.137	0.587

Table 1 Ocular surface parameters in FS-LASIK and SMILE group: statistically significant *p* value are noted in italics. ocular surface disease index (OSDI), dry eye questionnaire 5-items (DEQ-5), tear meniscus height (TMH), non-invasive keratography break-up time (NIKBUT), Meibomian gland (MG), standard deviation (SD)

The IVCM analysis using the ACCMetrics software before and after FS-LASIK (Table 2) showed significantly lower values for CNFD, CNBD, CNFL, and CNFrD post FS-LASIK (p= 0.001). Similarly, the SMILE procedure resulted in a significant reduction in CNBD, CNFL and CNFrD (p= 0.003, p=0.035 and p= 0.022 respectively) but no significant reduction in CNFD (p= 0.071). FS-LASIK had a greater impact on CNFD, CNBD and CNFL showing a significant reduction when compared with SMILE (p= 0.001).

Parameter	FS-LASIK group (mean ± SD)		*P*	SMILE group (mean ± SD)		*P*	
	Before	After	Pre- vs. post-op	Before	After	Pre- vs. post-op	FS-LASIK vs SMILE
CNFD (no. main fibres per mm²)	17.6 ± 4.3	4.9 ± 1.1	*0.001*	18.0 ± 7.1	15.6 ± 3.9	0.071	*0.001*
CNBD (no. branches per mm²)	12.8 ± 7.5	3.2 ± 0.7	*0.001*	15.5 ± 8.3	12.0 ± 5.4	*0.003*	*0.001*
CNFL (length fibres and branches per mm²)	12.4 ± 2.3	3.3 ± 1.3	*0.001*	11.3 ± 3.1	10.4 ± 2.4	*0.035*	*0.001*
CNFrD (changes in details (vague)	1.47 ± 0.04	1.38 ± 0.12	*0.001*	1.47 ± 0.04	1.40 ± 0.14	*0.022*	0.124

Table 2 Corneal nerve parameters analysed from IVCM scans in the FS-LASIK and SMILE groups: statistically significant differences are noted in italics. corneal nerve fibre density (CNFD), corneal nerve branch density (CNBD), corneal nerve fibre length (CNFL) and corneal nerve fibre fractal dimension (CNFrD).

A significant correlation was found between OSDI scores before *vs* after surgery (*r*= 0.652, p= 0.006) and between the pre-operative NIKBUT and post-operative TMH (*r*= -0.742, p= 0.001) in the FS-LASIK group. In the SMILE group, pre-operative symptoms (DEQ-5) were correlated with the stability of the tear film (NIKBUT) after the procedure (*r*= -0.566, p= 0.044). Considering the changes in parameters (delta values) in both procedures, the correlations between NIKBUT and TMH with the post-operative symptoms and signs (delta values) has confirmed that only the symptoms assessed using the DEQ-5 questionnaire were correlated with NIKBUT (*r*= -0.624, p= 0.023). In terms of subbasal corneal nerve parameter correlations with ocular surface metrics, only CNFL before surgery was correlated with the symptomatology scores (DEQ-5) after the FS-LASIK procedure (*r*= -0.545, p= 0.029).

Discussion

In light of the developments in corneal refractive surgery, a recommended protocol for DED assessment recommended by the TFOS DEWS II report together with a novel automated software programme (ACCMetrics) for nerve fibre analysis were used to determine the impact of two corneal refractive surgical techniques on the ocular surface. Both LASIK and SMILE have been shown to be safe and effective for correcting myopia and astigmatism.[20] In the current study, the refractive outcomes revealed a similar trend as reported by other authors [21], where no complications and good safety and efficacy were reported. There was no difference in mean VA although the small difference in the percentage of eyes achieving 0.0 logMAR in SMILE at four weeks post-op compared to FS-LASIK, might be attributed to the slightly delayed healing/recovery of the stromal tissue with SMILE as observed by Ağca et colleagues. [9] However, as previously reported by Shen et al.[22], all eyes in the study achieved a post-operative refraction within ± 1.00 D, showing no significant difference between the procedures for SEQ at only one month.

A significantly greater increase in DED symptomatology was observed in the FS-LASIK group compared to the SMILE group, which was reported with both the OSDI and DEQ-5 questionnaires. Previously, Denoyer et al.[8] and Li et al.[23] reported a similar finding and hypothesized that the cutting of the subbasal corneal nerve fibres during flap creation (FS-LASIK) has greater impact compared with creating and extracting a stromal lenticule (SMILE), inducing more symptoms up to 6 months after surgery by which time the nerves are expected to have largely regenerated.

Following the TFOS DEWS II Pathophysiology report, hyperosmolarity of the tear film was described as a core mechanism of DED. Despite the importance of quantifying the osmolarity of the tear film[24], it is not yet clear how robust its measurement is. Szczesna-Iskander reported the need for three consecutive measurements to achieve a reliable measurement, which naturally has resource implications in a busy clinical setting[25], while Bunya et colleagues described high variability when measuring osmolarity in patients with

DED.[26] In the present study, the results were obtained from a single measurement. The osmolarity data obtained showed no significant difference pre versus post-operatively for both procedure types as previously reported by Denoyer et al.[8]

The study protocol was aligned with the recommendations in the TFOS DEWS II report where tear film assessments should be performed non-invasively. As previously described by Jung et colleagues[27], TMH after LASIK was reduced. However, the difference in the cutting profile between SMILE (2 to 5 mm incision) and FS-LASIK (7 to 8 mm flap) led to no significant differences between the techniques for TMH. As most of the tear film volume is produced by the lacrimal gland that is innervated by parasympathetic and sympathetic nerves, any insult to the corneal trigeminal nerve branches or to the lacrimal gland reflex arc may reduce the secretion of tears, reducing TMH.

As with TMH, the stability of the tear film was also measured without the use of any vital dyes (e.g. fluorescein) which might have increased the variability of the measurement. The changes observed before versus after the surgery were greater with FS-LASIK (TMH reduced by 40%, p= 0.005), while there was only a small impact with SMILE (TMH reduced by 3%, p= 0.248) confirming the greater impact of the LASIK procedure on tear homeostasis.

Although other investigators[23] have demonstrated a greater impact on corneal and conjunctival staining with FS-LASIK compared to SMILE, attributing the cause as an interaction between the corneal nerves and the epithelial cells, this study supported the findings of Zhang et al.[28] that neither of the procedures increased ocular surface staining. Likewise the meibomian glands were not significantly affected by either type of surgery in this cohort.

This is the first study where the automated quantification of corneal nerve morphology with ACCMetrics was used to determine the impact of FS-LASIK and SMILE on the ocular surface. The advantages of using ACCMetrics are in reducing the bias from manual tracing of nerves and the time needed to analyse the IVCM scans (4 to 7x faster than non-automated methods) making it more feasible to apply in the clinical setting.[15] As expected, a significant reduction in the FS-LASIK group in terms of subbasal corneal nerves (up to 75% reduction considering CNFD, CNBD and CNFL before *vs*. after the procedure) was observed while in the SMILE group the impact was less (up to 23% reduction). The present results are in agreement with Denoyer et colleagues[8], confirming that the SMILE flap-less procedure is a safe and effective way to manage refractive error, with the benefit of being less impactful on corneal nerve structure. Additionally, the CNFrD values obtained by ACCMetrics, as previously described as a measure of structural complexity of the corneal nerves by Giannaccare et al.[18], were significantly reduced after both procedures. The reduction of this parameter might indicate its utility in describing the healing process of the subbasal nerve structure after surgery. However, further follow-up in a larger number of participants would be useful to confirm this.

As previously reported by Denoyer et colleagues[8], the increased DED symptomatology was associated with a decrease in corneal nerve fibres. However, as reported by Vestergaard et al.[29] comparing femtosecond laser procedures, none of the objective DED metrics (TBUT and TMH) were correlated with corneal nerve fibre morphology in the present study.

Patients undergoing both procedures were matched in terms of age, sex and refractive state, but were not randomised to a treatment which could have led to some bias in the results. Also, the patients and examiner (AR) were not masked as all the pre- and post-operative examinations were performed by the same clinician. ACCMetrics was not able to provide information on the tortuosity of the subbasal corneal nerves which has been demonstrated to have a possible role in early DED diagnosis.[18] In addition, the software might have included artefacts in the quantification leading to false-negative and false-positive results. Additionally, ACCMetrics was not able to assess the dendritic cells pre- and post surgery which have previously been found to increase in density close to the subbasal nerve plexus in patients with severe DED symptoms.[30] Finally, a larger sample size for the cohorts with longer follow-up schedules will provide further confirmation and insight into the possible benefits of SMILE versus LASIK in terms of ocular surface homeostasis and corneal nerve morphology.

In conclusion, FS-LASIK and SMILE provided favourable visual outcomes in both study groups. However, FS-LASIK surgery had more impact on DED symptomatology than SMILE, but this was not the case for the dry eye objective metrics when the surgeries were compared. Accordingly, TMH and NIKBUT might not be sensitive enough techniques to detect the post-surgical changes in this study, perhaps due to the modest sample size considered. SMILE surgery resulted in significantly less changes to the corneal nerve fibre metrics compared to FS-LASIK. This further confirms that SMILE surgery has less impact on the sensory neural loop of the cornea, which may account for less post-operative DED compared to LASIK, although the changes in the corneal nerve morphology were not correlated with DED metrics in this cohort.

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Conflict of interest

The authors have no conflicts of interest to disclose.

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Figure Legends

Figure 2 Sample of IVCM images of the subbasal corneal nerve fibres being analysed with ACCMetrics software: before (A) and after (B) FS-LASIK, before (C) and after (D) SMILE. Main nerve fibres shown in red, nerve branches shown in blue and branch points shown in green.

Figure 2 Visual and refractive outcomes for the two groups: A) visual acuity before and after FS-LASIK (Preoperative (Preop) Corrected Distance Visual Acuity (CDVA) vs. Postoperative (Postop) Uncorrected Distance Visual Acuity (UDVA)) and B) SEQ outcome after FS- LASIK compared to target (N=16) C) visual acuity before and after SMILE (Preop CDVA vs Postop UDVA) and D) SEQ outcome after SMILE compared to target (N=13).

Table 2 Ocular surface parameters in the FS-LASIK and SMILE groups: statistically significant differences are noted in italics. ocular surface disease index (OSDI), dry eye questionnaire 5-items (DEQ-5), tear meniscus height (TMH), non-invasive keratography break-up time (NIKBUT), Meibomian gland (MG), standard deviation (SD).

Table 2 Corneal nerve parameters analysed from IVCM scans in the FS-LASIK and SMILE groups: statistically significant differences are noted in italics. corneal nerve fibre density (CNFD), corneal nerve branch density (CNBD), corneal nerve fibre length (CNFL) and corneal nerve fibre fractal dimension (CNFrD).