Original Article

Impact of corneal sub-basal nerve plexus on epithelial thickness after small incision lenticule extraction (SMILE): a quantitative assessment using in vivo confocal microscopy and optical coherence tomography

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Background: Quantitative assessment of corneal epithelial thickness (CET) has attracted a great attention for its wide application in refractive surgeries. The corneal nerves are crucial for epithelial homeostasis, and nerve injury due to corneal refractive surgery may affect the epithelia; however, few clinical studies have investigated this relationship. Our study aimed to observe changes in epithelial thickness and sub-basal nerve plexus (SNP) profile after small incision lenticule extraction (SMILE) for low-to-moderate myopia [spherical refraction of –6.0 to 0 diopters (D)], and investigate the relationship between them.

Methods: This prospective observational study included 52 eyes treated with SMILE from March to May 2023 at Tianjin Medical University Eye Hospital. The epithelial thickness was measured across the central and concentric (paracentral, mid-peripheral, and peripheral) regions using spectral-domain optical coherence tomography (SD-OCT). SNPs were observed in the central and peripheral (temporal, superior, nasal, and inferior) areas using in vivo confocal microscopy (IVCM), and seven nerve parameters were assessed. All eyes were examined preoperatively and 1 week, 1 month, and 6 months postoperatively. Pearson's correlation was employed to investigate the association between anterior Q-value (corneal asphericity) and epithelial thickness. Partial correlation was adopted to examine the relationship between epithelial thickness and corresponding nerve parameters.

Results: Both epithelial thickness and SNP exhibited changes after SMILE. Six months postoperatively, epithelial thickness in the central and paracentral regions increased (all $P<0.05$), with thickening particularly pronounced in the inferotemporal, temporal, and inferior sections of the paracentral region, and the anterior Q-value was positively correlated with epithelial thickness in the inferonasal, inferior, and inferotemporal sections (inferonasal section: $r=0.293$, $P=0.035$; inferior section: $r=0.396$, $P=0.004$; inferotemporal section: $r=0.374$, $P=0.006$). Furthermore, most central, superior, and nasal nerve parameters had still not reached preoperative levels, while most temporal and inferior nerve parameters had reached or exceeded preoperative levels, and epithelial thickness was positively correlated with corresponding nerve parameters [corneal nerve fiber density (CNFD): $r=0.171$, $P=0.006$; corneal nerve branch density (CNBD): $r=0.137$, $P=0.028$; corneal nerve fiber length (CNFL): $r=0.172$, $P=0.006$; corneal nerve fiber total branch density (CNTB): $r=0.141$,

P=0.024; corneal nerve fiber area (CNFA): r=0.164, P=0.008].

Conclusions: Uneven epithelial thickness changes were observed after SMILE, regional epithelial thickening increased corneal oblateness. Non-uniform SNP regeneration was also observed, positive correlation between epithelial thickness and nerve parameters indicated the impact of nerves on epithelia, which may enhance the clinical value of epithelial thickness measurement.

Keywords: Sub-basal nerve plexus (SNP); corneal epithelial thickness (CET); small incision lenticule extraction (SMILE); in vivo confocal microscopy (IVCM); optical coherence tomography (OCT)

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Introduction

The corneal epithelium is the outermost layer of the cornea and is crucial in maintaining corneal physiological integrity and refractive characteristics. Widespread application of refractive surgeries has garnered increased attention to quantitative assessment of corneal epithelial thickness (CET) for accurate preoperative examination, surgical design, and postoperative monitoring (1-3). Specifically, CET map is preoperatively used to diagnose keratoconus based on its unique epithelial features. A clear understanding of epithelial thickness is warranted during secondary corneal refractive surgery as the first surgery may have led to epithelial thickening (2). CET measurements are widely performed using spectral-domain optical coherence tomography (SD-OCT). CET changes after multiple refractive surgeries have been reported (3-6), and they correlate with corneal keratometry, preoperative refractions, and surgical parameters. However, few studies have investigated the relationship between CET and corneal nerve changes after surgery.

Corneal nerve fibers radially enter the corneal stroma and run forward towards the ocular surface to form the sub-epithelial nerve plexus and vertically pierce Bowman's membrane to form the sub-basal nerve plexus (SNP) (7). SNPs are commonly observed using in vivo confocal microscopy (IVCM) (8). Small incision lenticule extraction (SMILE) and femtosecond laser in situ keratomileusis (FS-LASIK) are two common laser refractive surgery techniques. SMILE removes the lenticule through a small side incision without creating a flap, protecting the corneal epithelium and nerves more effectively than FS-LASIK (9). Corneal denervation due to SMILE is not a major complication but may influence postoperative functional recovery (10). However, few studies have comprehensively investigated the actual condition of nerve regeneration after SMILE. Previous studies have focused on central corneal nerve recovery, and their results may be limited as they do not provide a full understanding of the complete nerve regeneration process (11-13). Furthermore, corneal nerves are crucial for epithelial homeostasis (14), and there are currently no clinical studies on the relationship between corneal nerves and epithelia after laser refractive surgeries. Therefore, our study aimed to investigate corneal denervation and reinnervation profiles throughout the entire cornea and explore the impact of corneal nerves on epithelia. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1887/rc).

Methods

Patients and ocular examinations

This prospective observational study recruited patients treated with SMILE for low-to-moderate myopia from March to May 2023 at Tianjin Medical University Eye Hospital. This study was approved by the ethics committee of Tianjin Medical University Eye Hospital (approval No. 2023KY-10) and was implemented according to the tenets of the Declaration of Helsinki (as revised in 2013). All patients signed the informed consent form before being enrolled.

The inclusion criteria were: age 18–50 years, spherical refraction of –6.0 to 0 diopters (D), cylindrical refraction of –2.0 to 0 D, and stable preoperative refractive power for at least 2 years. Eyes with thin corneas (central corneal thickness <480 μm) or eyes with ocular disorders, previous surgery, or trauma were excluded.

All patients received a comprehensive ocular examination,

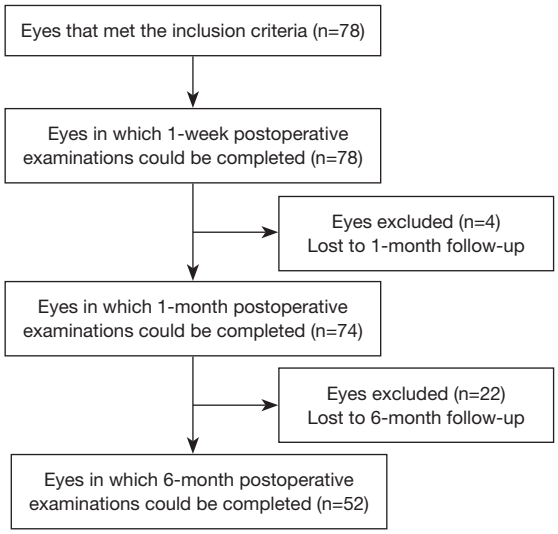

Figure 1 Eyes selection flowchart.

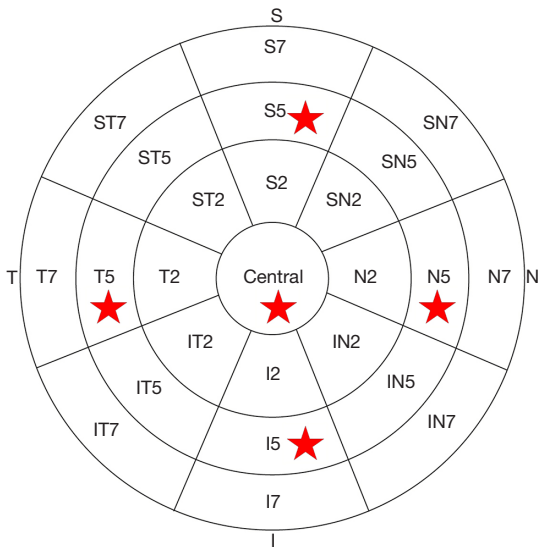

Figure 2 Schematic of epithelial thickness map sections generated by SD-OCT. The first concentric (paracentral) region possesses a 2–5 mm diameter range, the second concentric (mid-peripheral) region possesses a 5–7 mm diameter range, and the third concentric (peripheral) region possesses a 7–9 mm diameter range. The red star represents the scanning position of the confocal microscopy. The central, temporal, superior, nasal, and inferior area scanned using confocal microscopy were correspondingly included in the central, T5, S5, N5, and I5 section range of the map. T, temporal; ST, superotemporal; S, superior; SN, superonasal; N, nasal; IN, inferonasal; I, inferior; IT, inferotemporal; SD-OCT, spectral-domain optical coherence tomography.

including medical history, uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), slit-lamp biomicroscopy, corneal topography (Pentacam; Oculus GmbH, Wetzlar, Germany), SD-OCT, dry eye assessment, manifest and cycloplegic refraction, funduscopic examinations, and IVCM. The study time points were: before surgery and 1 week, 1 month, and 6 months after surgery; SD-OCT, and IVCM were repeated at every time point.

We initially recruited 40 patients; however, only 78 eyes were included, as two patients had myopia only in one eye. One week postoperatively, all patients came for follow-up as scheduled. One month postoperatively, two patients (four eyes) were lost to follow-up. Six months postoperatively, another 11 patients (22 eyes) were lost to follow-up. Patients who lost to any follow-up were excluded, and finally our study included 27 patients (52 eyes) (*Figure 1*).

CET measurement

CET was measured using SD-OCT with RTVue (Optovue Inc., Fremont, CA, USA). The corneal adapter module and the "PachymetryWide" mode were applied to acquire a 9-mm diameter epithelial thickness map. The maps were automatically generated and contained the central 2 mm and three concentric (paracentral, 2–5 mm; mid-peripheral, 5–7 mm; and peripheral, 7–9 mm) regions. Every region was divided by eight meridians into temporal, superotemporal, superior, superonasal, nasal, inferonasal, inferior, and inferotemporal sections, yielding a total of 25 sections (*Figure 2*).

SNP measurement

Corneas were observed using laser confocal microscopy (Heidelberg Retina Tomography III Rostock Cornea Module; Heidelberg Engineering GmbH, Heidelberg, Germany) to evaluate the SNPs. After topical anesthesia application, patients had to fix their gaze on a red light. SNPs in the central area were scanned first, followed by SNPs in the superior, inferior, temporal, and nasal areas, which were 3 mm apart from the central cornea. All the IVCM investigations were performed by an experienced examiner. Every confocal image was corresponded to a 400 μm × 400 μm area; the five areas scanned using IVCM were correspondingly included in the central, T5, S5, N5,

Table 1 Patient demographics and preoperative ocular parameters

Parameters	Data
Female/male	18/9
Eye	52
Age (years)	29.31±7.15 (19 to 41)
UDVA (logMAR)	1.10±0.25 (0.60 to 1.60)
CDVA (logMAR)	−0.06±0.06 (−0.20 to 0)
Spherical refraction (D)	−4.31±1.13 (−6.00 to −2.25)
Cylindrical refraction (D)	−0.56±0.50 (−2.00 to 0)
Corneal thickness (μm)	554.25±16.84 (523 to 588)
Anterior Km (D)	43.15±1.27 (40.30 to 46.60)
Anterior Q-value	−0.30±0.12 (−0.66 to −0.06)

Data are presented as number or mean ± standard deviation (range). UDVA, uncorrected distance visual acuity; logMAR, logarithm of the minimum angle of resolution; CDVA, corrected distance visual acuity; D, diopters; Km, keratometry mean.

and I5 section range of the CET map (*Figure 2*). All images were analyzed by a blinded examiner using ACCMetrics software (University of Manchester, Manchester, UK) (15). The seven corneal nerve parameters recorded were the following: corneal nerve fiber density (CNFD, number of fibers per mm^2), corneal nerve branch density (CNBD, number of branch points on the main fibers per mm^2), corneal nerve fiber length (CNFL, total length of nerves mm per mm^2), corneal nerve fiber total branch density (CTBD, total number of branch points per mm^2), corneal nerve fiber area (CNFA, total nerve fiber area mm^2 per mm^2), corneal nerve fiber width (CNFW, average nerve fiber width mm per mm^2), and corneal nerve fractal dimension (CNFrD, measure of corneal nerve complexity).

Surgical procedures and postoperative care

All SMILE procedures were uneventfully completed by the same practitioner (S.Z.) using VisuMax femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) and performed in accordance with those described previously (16). The principal surgical parameters were as follows: cap thickness 120 μm, optical zone 6.5–6.8 mm, lenticule edge thickness 15–30 μm, and side incision width 3 mm.

Patients were postoperatively prescribed with gatifloxacin (Otsuka, Tianjin, China) eye drops, to be administered four times per day for a week, with fluorometholone 0.1% (Santen, Shiga, Japan) eye drops to be administered four times per day while tapering the dose over 4 weeks, and with diquafosol sodium (Santen, Ishikawa, Japan) eye drops to be administered four times per day for at least 1 month.

Statistical analysis

Data were statistically analyzed using the SPSS software (version 29.0, IBM SPSS Statistics, Armonk, NY, USA). Data were presented as the mean ± standard deviation. The Snellen visual acuity was transformed to the logarithm of the minimum angle of resolution (logMAR). The Kolmogorov-Smirnov test was used to check data normality. A paired Student's *t*-test was employed to compare the normally distributed results, and the Wilcoxon's matched-pairs signed-rank test was employed for non-normally distributed results. The Kruskal-Wallis test was used to analyze nerve reduction in different areas. Pearson's correlation was employed to investigate the association between postoperative anterior Q-value and CET. Partial correlation was adopted to examine the relationship between CET and corresponding SNP with the position factor as the control factor. A two-tailed P value <0.05 was considered statistically significant.

Results

Patient demographics and preoperative and postoperative ocular parameters

In this study, 52 eyes treated with SMILE for low-to-moderate myopia were followed up for 6 months. The patient demographics and preoperative ocular parameters are shown in *Table 1*. Postoperatively, UDVA (logMAR) at 1 week, 1 month, and 6 months were −0.06±0.09, −0.10±0.07, and −0.11±0.07, respectively. The UDVA increased from 1 week to 1 month (P<0.001) and became stable from 1 to 6 months (P=0.593); all eyes achieved a UDVA of 20/25 or better without postoperative complications. The refractions of spherical equivalent were −0.13±0.53 D at 1 week, −0.07±0.47 D at 1 month, and −0.10±0.43 D at 6 months; no significant differences were observed. Six months postoperatively, the anterior keratometry mean (Km) was 39.47±1.41 D, and the anterior Q-value was 0.44±0.21.

CET profile changes

Compared with the preoperative CET, the CET of

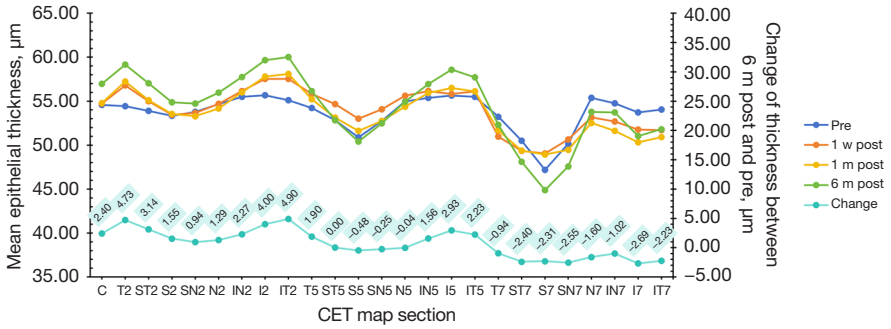

Figure 3 Mean preoperative and postoperative CET (μm) in 25 map sections and the change in thickness at 6 months postoperatively. Pre, preoperative; 1 w post, 1 week postoperatively; 1 m post, 1 month postoperatively; 6 m post, 6 months postoperatively. C, central; T, temporal; ST, superotemporal; S, superior; SN, superonasal; N, nasal; IN, inferonasal; I, inferior; IT, inferotemporal; CET, corneal epithelial thickness.

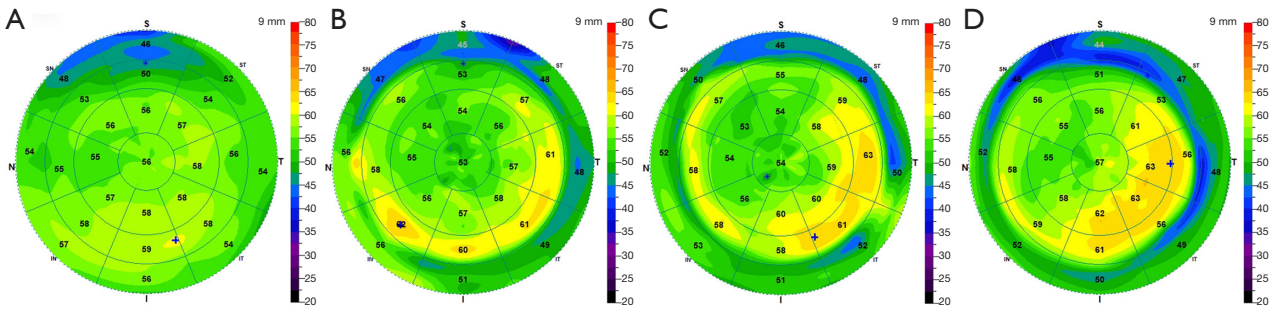

Figure 4 CET maps before and after SMILE in one eye. (A) Preoperative map. (B) One-week postoperative map. (C) One-month postoperative map. (D) Six-month postoperative map. Min/max thickness indicated as */+. T, temporal; ST, superotemporal; S, superior; SN, superonasal; N, nasal; IN, inferonasal; I, inferior; IT, inferotemporal; CET, corneal epithelial thickness; SMILE, small incision lenticule extraction.

the central region significantly increased 6 months postoperatively (P<0.001). In the paracentral region, the CET in all sections significantly increased 6 months postoperatively (P<0.05), whereas that in sections T2, ST2, I2, and IT2 significantly increased from 1 week postoperatively (all P<0.05). In the mid-peripheral region, CET in sections T5, IN5, I5, and IT5 significantly increased 6 months postoperatively (all P<0.05). In the peripheral region, except for sections T7 and IN7, CET significantly decreased 6 months postoperatively (all P<0.05; *Figure 3*). *Figure 3* also shows the change in CET before surgery and 6 months after surgery. In the paracentral region, the three sections exhibiting the highest thickening were IT2, T2, and I2 (4.90, 4.73, and 4.00 μm, respectively); in the mid-peripheral region, they were I5, IT5, and T5, (2.93, 2.23, and 1.90 μm, respectively). Uneven epithelial thickening was primarily observed in the paracentral and mid-peripheral regions, with thickened temporal, inferior, and inferotemporal sections. *Figure 4* shows the CET maps before and after SMILE in one eye.

SNP profile changes

Compared with preoperative levels, most SNP parameters (except for CNFW) in the five areas significantly decreased 1 week postoperatively (all P<0.05). One month postoperatively, most SNP parameters (except for CNFW) in the central, temporal, superior, and nasal areas remained significantly lower than that before surgery (all P<0.05). Meanwhile, SNP parameters in the inferior area had almost fully recovered, with no difference in CNFD, CNBD, CTBD, CNFW, and CNFrD (all P>0.05). Six months postoperatively, most central SNP parameters (CNFD, CNBD, CNFL, CTBD, CNFA, and CNFrD),

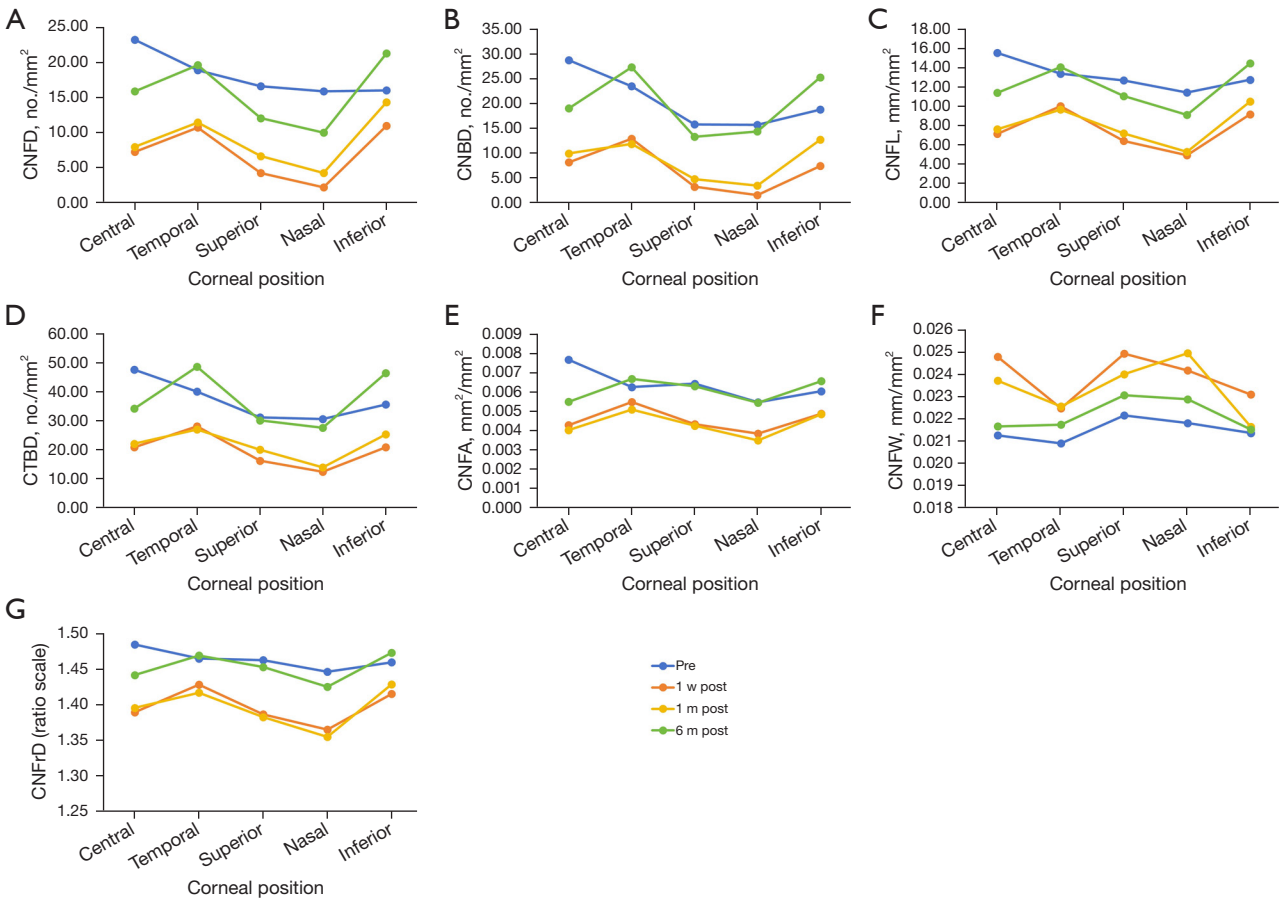

Figure 5 Mean preoperative and postoperative values of SNP parameters in five corneal areas. Pre, preoperative; 1 w post, 1 week postoperatively; 1 m post, 1 month postoperatively; 6 m post, 6 months postoperatively; CNFD, corneal nerve fiber density; CNBD, corneal nerve branch density; CNFL, corneal nerve fiber length; CTBD, corneal nerve fiber total branch density; CNFA, corneal nerve fiber area; CNFW, corneal nerve fiber width; CNFrD, corneal nerve fractal dimension; SNP, sub-basal nerve plexus.

superior SNP parameters (CNFD and CNFL), and nasal SNP parameters (CNFD and CNFL) had not reached preoperative levels (all P<0.05), whereas most temporal SNP parameters (CNFD, CNBD, CNFL, CTBD, CNFA, and CNFrD) and inferior SNP parameters (CTBD, CNFA, CNFW, and CNFrD) had reached preoperative levels (all P>0.05) and inferior SNP parameters (CNFD, CNBD, and CNFL) had exceeded preoperative levels (all P<0.05) (*Figure 5*). Because the CNFL has been reported to be the most reliable nerve parameter (17), we selected it for a more in-depth analysis. The nerve reduction from SMILE was the initial cause of the alteration in nerve distribution; we adhered to the same definition of nerve reduction as previously reported (9). After SMILE, CNFL in the central, nasal, and superior areas reduced 1 week postoperatively (54.5%±27.9%, 46.4%±41.6%, and 42.3%±38.9%, respectively), and the central and nasal CNFL reduction was still evident 6 months postoperatively (25.6%±31.3% and 7.1%±62.3%, respectively; *Table 2*). While CNFL reduction in the temporal and inferior areas was relatively low 1 week postoperatively (18.7%±38.3% and 22.7%±46.0%, respectively), as a result, CNFL had completely recovered 6 months postoperatively. *Figure 6* shows representative confocal images of SNP in the five areas before and after SMILE in one eye.

Correlation analysis

The anterior Q-value was positively correlated with CET in the inferonasal section of the paracentral region (IN2), in the inferior section of the paracentral region (I2), and in the inferotemporal section of the paracentral region (IT2)

Table 2 CNFL reduction in five areas and comparison of the values between postoperative follow-up timepoints

Area	1 week	1 month	P†	6 months	P‡
Central (%)	54.5±27.9	50.5±29.9	0.377	25.6±31.3	<0.001*
Temporal (%)	18.7±38.3	19.6±48.3	0.757	−12.5±43.3	<0.001*
Superior (%)	42.3±38.9	37.6±39.2	0.219	−5.4±87.5	<0.001*
Nasal (%)	46.4±41.6	46.7±40.8	0.870	7.1±62.3	<0.001*
Inferior (%)	22.7±46.0	13.4±39.2	0.140	−19.7±43.6	<0.001*
P§	<0.001*	<0.001*		<0.001*	

Data were presented as the mean ± standard deviation. †, P values comparing CNFL reductions at 1 month postoperatively and 1 week postoperatively; ‡, P values comparing CNFL reductions at 6 months postoperatively and 1 month postoperatively; §, P values comparing CNFL reductions in different corneal areas; *, P<0.05. CNFL, corneal nerve fiber length.

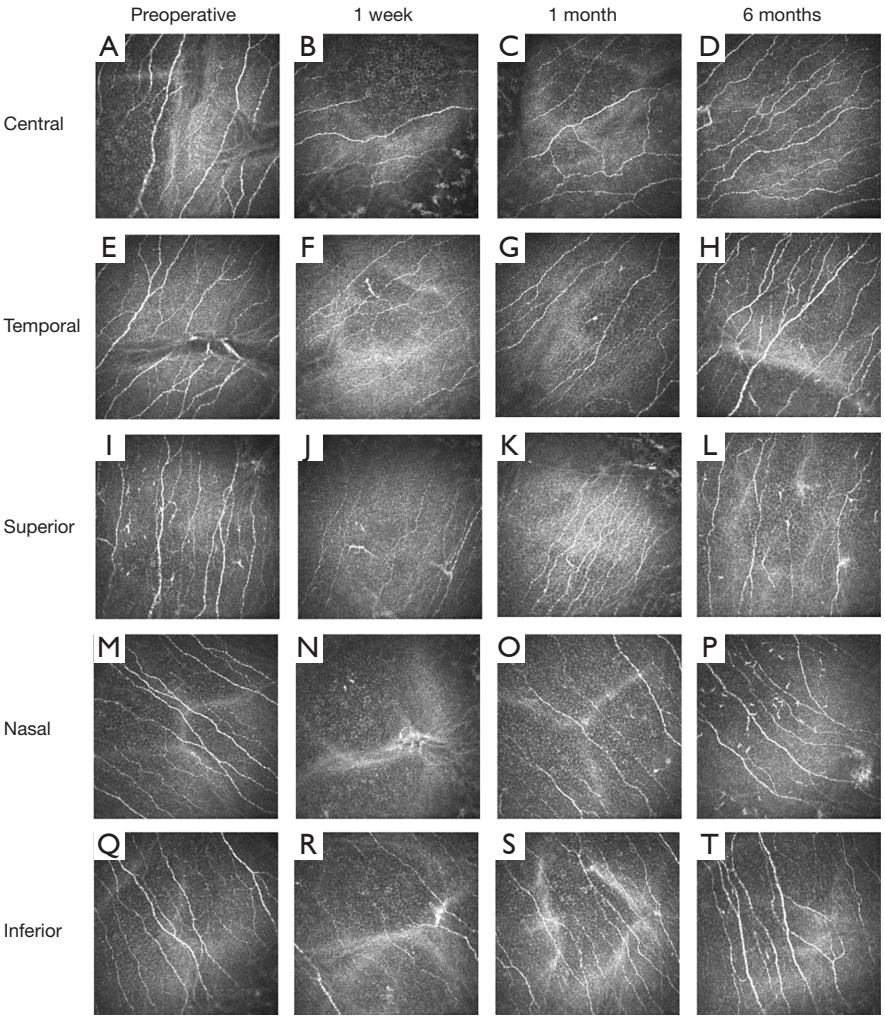

Figure 6 Representative confocal microscopy images of the SNP [(A-D) represented images in the central area; (E-H) represented images in the temporal area; (I-L) represented images in the superior area; (M-P) represented images in the nasal area; (Q-T) represented images in the inferior area] before and after SMILE in one eye. Every confocal image corresponded to a 400 μm × 400 μm area. SNP, sub-basal nerve plexus; SMILE, small incision lenticule extraction.

6 months postoperatively (IN2: r=0.293, P=0.035; I2: r=0.396, P=0.004; IT2: r=0.374, P=0.006). The anterior Q-value and CET were not correlated in other sections.

Partial correlation analysis showed that CET was positively correlated with SNP parameters 6 months postoperatively (CNFD: r=0.171, P=0.006; CNBD: r=0.137, P=0.028; CNFL: r=0.172, P=0.006; CTBD: r=0.141, P=0.024; CNFA: r=0.164, P=0.008); however, no correlations were observed 1 month postoperatively.

Discussion

SMILE has become the preferred procedure for refractive surgery because of its advantages. However, CET changes after SMILE have been reported, and they may induce refractive regression, irregular astigmatism, or increased high-order aberration (3,18). Here, CET in the central and paracentral regions significantly increased 6 months postoperatively, in agreement with previous reports (19). Furthermore, CET exhibited thickening in the inferotemporal, temporal, and inferior sections of the paracentral region, followed by the inferior and inferotemporal sections of the mid-peripheral region. Similar uneven CET changes were also reported by Zhu *et al.* (20), who identified the same trend in other surgeries. At the cellular level, one study (21) reported that epithelial thickening was due to increased cell layers and revealed that the cell density remained constant in every epithelial cell layer after SMILE. However, the underlying mechanisms have not yet been elucidated. Previous studies (3,6) suggested that the asymmetric epithelial thickness changes were related to changes in the corneal curvature gradient in different areas or to the Bell phenomenon.

Given the clinical application of CET measurement in our study, these uneven CET changes after SMILE for low-to-moderate myopia did not impact the postoperative visual acuity or refraction. Compared with low-to-moderate myopia correction, the degree of epithelial thickening after high myopia correction is more obvious (22). Under the similar degree of myopia, corneal refractive surgery like FS-LASIK can cause epithelial thickening more significantly than SMILE (20). Therefore, epithelial thickening induced by SMILE for low-to-moderate myopia is too subtle to affect the visual acuity. Additionally, the Q-value is the mathematical expression of corneal asphericity. Most original corneas are prolate, with negative Q-values, while corneas treated via myopic correction are modified to be more oblate, with positive Q-values. Here, anterior Q-values were altered from –0.30±0.12 to 0.44±0.21, consistent with other studies (23,24). Since postoperative oblateness may be the predominant factor in the decrease of functional vision (25), an appropriate knowledge of its influencing factors is necessary. A clinical study (26) has reported that corneal epithelial remodeling increased oblateness after transepithelial photorefractive keratectomy for myopia. Here, we explored the positive association between the anterior Q-value and CET in obviously thickened sections after SMILE, indicating that regional epithelial thickening aggravated the corneal oblateness and may compromise the visual quality. In brief, slight uneven CET changes after SMILE for low-to-moderate myopia may affect the visual quality but not visual acuity.

Corneal nerves are partly eliminated during ablation of the anterior corneal stroma in refractive surgeries. Postoperatively, patients may present with decreased corneal nerve density and length and increased nerve tortuosity, branching, and beading (27). Our study demonstrated that SNPs are non-uniformly distributed in different corneal areas before and after surgery, with the degree of non-uniformity being more pronounced in the postoperative state compared to the preoperative state. After SMILE, CNFL reduction is the most significant in the central area, which might have been due to the more pronounced loss of corneal volume in the center of the convex-shaped extracted lenticule. Central CNFL reductions of 54.5%±27.9% at 1 week postoperatively and 25.6%±31.3% at 6 months postoperatively indicated that recovery from serious nerve damage was not complete until 6 months postoperatively, in agreement with previous studies (13,21,28). Conversely, less evident nerve reduction in peripheral areas translated into faster recovery. Hou *et al.* (28) also reported that the SNP parameter values in peripheral areas recovered only to their preoperative level in high myopia. In our findings, for low-to-moderate myopia, SNP parameters in the inferior area had higher values than before surgery because of less procedure-associated injury. Moreover, uneven corneal denervation and reinnervation may be caused by SMILE-derived side incision, regional keratocyte repopulation (29), and uniformly distributed anatomy of corneal nerves (7). This study provides comprehensive information regarding the characteristics of SNP regeneration in different areas after SMILE.

Corneal nerve fibers terminate in the epithelia. Intra-epithelial nerve endings are intertwined with the epithelial cells, and are important for their health. When nerves are damaged, their supporting functions are altered, impairing

physiological activity of the epithelia (29). For example, neurotrophic epitheliopathy, characterized by punctate epithelial erosions after LASIK, may be due to surgical denervation (30). *In vitro*, the corneal epithelia are partly controlled by sensory nerves that secrete neuropeptides such as substance P and nerve growth factor, which are vital for cell proliferation and differentiation (29,31). Corneal nerves may support the epithelia *in vivo* by releasing various neuro-mediators that can be detected in tear samples (32). The interactions between corneal nerves and epithelia are profound and complex, and a few studies related to this topic were still restricted to animal experiments or disease researches. SMILE-treated corneas do not commonly display apparent epithelial lesions, which does not necessarily imply that surgical denervation and reinnervation do not affect the epithelia. Here, CET values were high in the inferior and temporal regions 6 months postoperatively. Correspondingly, SNP parameter values were high in the inferior and temporal areas, and the CET and SNP parameters were positively correlated. Sufficient corneal reinnervation in the inferior and temporal areas may have a more beneficial effect on epithelial thickening, while corneal reinnervation with incomplete recovery in other areas remains at a safe threshold to sustain normal epithelial homeostasis in low-to-moderate myopia correction. Additionally, there was no correlation between CET and SNP parameters at 1 month postoperatively, which might have been due to the interruption of postoperative reactions. To the best of our knowledge, our study is the first to investigate the correlation between CET and SNP profile changes after SMILE from a positional structural perspective, which may explain the uneven epithelial thickening.

There are some limitations in this study. First, only patients with low-to-moderate myopia were recruited; therefore, the results may not be applicable to patients with other myopia ranges. In our clinical practice, SMILE is the preferred choice for patients with low-to-moderate myopia, and other refractive surgeries such as FS-LASIK or implantable Collamer lens implantation are preferred for patients with high myopia, as a result, there are only a few high myopia cases treated by SMILE. Second, it was difficult to confirm whether the same corneal position was investigated at each follow-up, which may have caused measurement errors. Further studies on the causal relationship and not only the correlation between corneal nerves and epithelial thickening are needed in the future.

Conclusions

Our study provides new insights into the changes in CET and SNP profiles after SMILE for low-to-moderate myopia from a positional structural perspective. The postoperative CET and SNP profiles were uneven in different corneal areas and were positively correlated with each other, suggesting that non-uniform SNP regeneration may render the uneven CET changes.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-1887/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1887/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of Tianjin Medical University Eye Hospital (approval No. 2023KY-10). All patients signed the informed consent form before being enrolled.

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