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Within-cohort associations between corneal epithelial remodeling and anterior corneal higher-order aberrations after FS-LASIK and KLEx (SMILE): a two-cohort descriptive study

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Abstract

Objective: To describe corneal epithelial remodeling patterns after femtosecond LASIK (FS-LASIK) and keratorefractive lenticule extraction (KLEx; SMILE in this study), and to evaluate within-cohort associations between epithelial thickness changes and anterior corneal higher-order aberrations (HOAs).

Methods: This study included 245 patients (138 eyes in the SMILE cohort and 107 eyes in the FS-LASIK cohort; right eyes only). Corneal epithelial thickness in the central, paracentral, and mid-peripheral zones was measured preoperatively, 1 month, and 3 months postoperatively using optical coherence tomography (OCT). Corneal HOAs were assessed using the Pentacam system with a 6 mm pupil diameter. Repeated-measures analysis of variance and Spearman correlation analyses were used to characterize postoperative changes and examine within-cohort associations between epithelial remodeling and HOAs.

Results:

In both cohorts, postoperative epithelial thickening was observed in the central and paracentral zones; in the SMILE cohort, thickening was also observed in the mid-peripheral zone. The spatial distribution of epithelial thickening differed between cohorts, and the magnitude of thickening varied by zone across time points. Both cohorts demonstrated postoperative changes in HOAs. In the SMILE cohort, changes in spherical aberrations (Z_4^0, Z_6^0) and coma-related terms (Z_3^{-1}, Z_3^{-3}) were observed over follow-up. In the FS-LASIK cohort, HOA changes showed greater regional variability across time points. Within-cohort correlation analyses indicated that epithelial thickening in the SMILE cohort was positively associated with spherical aberrations and negatively associated with coma-related terms, whereas correlations in the FS-LASIK cohort were generally weaker and region-dependent.

Conclusion: Across two clinical cohorts undergoing SMILE or FS-LASIK, postoperative epithelial thickening and changes in anterior corneal HOAs were observed, with measurable within-cohort associations between epithelial remodeling and HOA metrics. Because preoperative refractive status (spherical equivalent) differed markedly between cohorts, these findings should be interpreted as descriptive patterns and within-cohort associations rather than evidence of isolated procedure effects or between-procedure superiority.

Keywords: Corneal epithelial remodeling; Higher-order aberrations; Visual quality; Optical coherence tomography; Postoperative visual outcomes

Introduction

Femtosecond Laser-Assisted in Situ Keratomileusis (FS-LASIK) is one of the most popular methods for correcting myopic refractive errors and is also a primary surgical option for patients with thin corneas. In FS-LASIK, a corneal flap is created using a femtosecond laser, followed by stromal ablation with an excimer laser. Small Incision Lenticule Extraction (SMILE), on the other hand, uses a femtosecond laser to create a lenticule within the corneal stroma, which is then extracted through a small incision approximately 2 mm in size [1]. Despite not directly involving the corneal epithelium, both SMILE and FS-LASIK have been consistently associated with varying degrees of postoperative epithelial remodeling [2-4]. Numerous studies have investigated the primary factors contributing to corneal epithelial remodeling. It is generally believed that such remodeling is associated with preoperative refractive error and changes in corneal curvature. Among the consequences of epithelial remodeling, myopic regression following refractive surgery is considered a major concern. However, only a limited number of studies have focused on the impact of epithelial remodeling on visual quality.

Diplopia, glare, halos, starbursts, and reduced night vision quality are common postoperative adverse effects following FS-LASIK and SMILE. The decline in visual quality is primarily attributed to an increase in higher-order aberrations (HOAs), which are believed to result from the reduction of lower-order spherical and cylindrical aberrations during the surgical correction process [5]. Xia et al. [6] observed that total HOAs and vertical coma aberration were notably elevated after SMILE compared to the preoperative period. Both SMILE and FS-LASIK have been shown to induce a considerable amount of HOAs; however, the specific types of HOAs induced by each procedure and the mechanisms underlying these changes remain uncertain. As the primary refractive surface of the eye, the cornea plays a pivotal role in determining the eye's overall wavefront aberrations. Corneal epithelial remodeling may influence corneal morphology, thereby contributing to alterations in corneal HOAs [7, 8].

To date, few studies have specifically investigated the effects of regional corneal epithelial remodeling on HOAs following SMILE and FS-LASIK, and detailed descriptions remain lacking. Spectral-domain optical coherence tomography (SD-OCT) enables reliable evaluation of postoperative corneal epithelial remodeling through standardized epithelial thickness measurements.

In this study, SD-OCT (RTVue100-xr, Optovue Inc., USA) was employed to assess postoperative epithelial thickness changes in the central, paracentral, and mid-peripheral zones. Corneal HOAs were measured using the Pentacam HR (Pentacam, OCULUS, Germany). The objective was to explore the remodeling patterns of the corneal epithelium after SMILE and FS-LASIK, and to investigate the relationship between epithelial thickness changes and alterations in anterior corneal surface HOAs. The present study aims to explore the early patterns of epithelial remodeling and its correlation with HOAs within 3 months postoperatively, providing evidence for short-term clinical management.

Method

Patient

In this study, a total of 138 patients who underwent SMILE surgery (only the right eyes, 138 eyes) and 107 patients who underwent FS-LASIK surgery (only the right eyes, 107 eyes) were included for analysis. Exclusion criteria: (1) history of other ocular diseases or ocular surgeries; (2) systemic autoimmune diseases or long-term use of systemic medications that could affect the study outcomes; (3) pregnant women.

All surgeries were performed at Beijing Mingshiguang Ophthalmology Hospital between March 2024 and August 2024. Inclusion criteria: (1) refractive stability with a change of no more than 0.5 diopters per year; (2) best corrected visual acuity (BCVA) of 20/25 or better; (3) meeting other surgical requirements for FS-LASIK or SMILE.

This study protocol was approved by the Ethics Committee of Yinhai Ophthalmology Hospital, Chengdu University of Traditional Chinese Medicine (approval number: 2021yh-025), and conducted in accordance with the principles of the Declaration of Helsinki (2013 revision). The study commenced after obtaining ethical approval from the hospital ethics committee, and informed consent was obtained from all participants.

All enrolled patients underwent comprehensive preoperative ophthalmic examinations prior to FS-LASIK or SMILE surgery and met the corresponding surgical criteria. The ophthalmic assessments included best corrected visual acuity (BCVA), corrected distance visual acuity (CDVA), uncorrected distance visual acuity (UDVA), subjective and objective refraction, non-contact intraocular pressure measurement, dry eye evaluation, corneal topography analysis, Pentacam imaging, optical coherence tomography (OCT), slit-lamp biomicroscopy, and indirect fundoscopy.

Surgery

Keratorefractive Lenticule Extraction (KLEx) is used as the umbrella term for corneal refractive procedures in which an intrastromal refractive lenticule is created and removed; the specific KLEx technique used in this study was SMILE.

All SMILE procedures were performed by an experienced ophthalmologist (ZYH) using the VisuMax 500 kHz femtosecond laser system (Carl Zeiss

Meditec AG, Jena, Germany) under topical anesthesia with 0.01% proparacaine hydrochloride. Standard surgical parameters were set as follows: laser pulse energy of 110 to 120 nJ, spot spacing of 4.5 μm, optical zone ranging from 6.0 to 6.8 mm, cap diameter between 6.8 and 7.6 mm, cap thickness of 110 μm, and a 2 mm small incision located at the 90° position. After femtosecond laser treatment, the lenticule was dissected and extracted through the incision using a fine scraper. The interface was irrigated with balanced salt solution.

All FS-LASIK surgeries were also performed by the same experienced ophthalmologist (ZYH) under topical anesthesia with 0.01% proparacaine hydrochloride. The VisuMax 500 kHz femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) was used to create the corneal flap with the following parameters: flap diameter of 7.9 mm; flap thickness customized based on corneal thickness and ablation depth, ranging from 90 to 110 μm; hinge length of 4 mm located at 90°; flap side-cut angle of 60°. Stromal ablation was performed using the VISX STAR S4 IR excimer laser (AMO Manufacturing USA, LLC, USA) with an ablation diameter of 6.3 to 6.8 mm. The surgeon instructed patients to maintain proper fixation during the ablation process. After ablation, the eye was irrigated with balanced salt solution, and the corneal flap was repositioned. A bandage contact lens (Bausch, NY, USA) was placed to prevent flap displacement and promote epithelial healing; the contact lens was removed one day postoperatively.

Postoperative medications were administered immediately after surgery as follows: 0.5% loteprednol etabonate suspension eye drops, 1% sodium hyaluronate eye drops, and 0.5% levofloxacin eye drops, each applied four times every 2 hours with at least 10 minutes interval between each type of drop. From the first postoperative day, patients continued with 0.5% levofloxacin eye drops four times daily for one month, 0.1% sodium hyaluronate eye drops four times daily for one month, and 0.5% loteprednol etabonate suspension eye drops with dosage adjusted according to computerized refraction results. The frequency of loteprednol etabonate was tapered by one drop every three days starting one week postoperatively, with a total duration of 28 days.

Corneal Aberration Measurement

The Pentacam anterior segment analysis and diagnostic system utilizes a 3D Scheimpflug rotating camera to acquire three-dimensional anterior segment data. It can measure and analyze 25,000 to 138,000 data points of the anterior segment within less than 2 seconds, with an automatic eye-tracking system to compensate for ocular movement. This allows for precise measurement of corneal HOAs within a 6 mm diameter zone, including total anterior corneal HOAs, spherical aberrations (Z_4^0 and $Z6^0$) ，coma aberrations (Z_3^{-1}，Z_3^1，Z_5^1) and trefoil aberrations (Z_3^3，$Z3^{-3}$，$Z5^3$) . All aberration outcomes in this study refer to anterior corneal higher-order aberrations derived from Pentacam analysis over a 6.0-mm zone. Individual Zernike terms are reported as Zernike coefficients (μm), whereas RMS values (μm) are used only for summary HOA metrics when applicable.

Epithelial Thickness Measurement

Spectral-domain optical coherence tomography (SD-OCT) was used to measure corneal epithelial thickness (CET). An automated algorithm generated epithelial thickness maps divided into 17 regions, including superior, superonasal, nasal, inferior, inferonasal, inferotemporal, temporal, and superotemporal sectors. In this study, the central 2-mm diameter zone was defined as the central zone; the corneal area within the 2-5 mm annulus was defined as the paracentral zone; and the 5-6 mm annulus was defined as the mid-peripheral zone.

Postoperative examinations were performed at 1 day, 1 week, 1 month, and 3 months to assess UDVA, intraocular pressure (IOP), and refraction. CET and Pentacam measurements were conducted at 1 and 3 months postoperatively. The change in CET (ΔCET) was calculated as postoperative CET minus preoperative CET.

Data Analysis

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., NY, USA). The Shapiro–Wilk test was used to assess the normality of continuous variables. As most variables did not follow a normal distribution ($P < 0.05$), nonparametric statistical methods were applied throughout the analysis. The Mann–Whitney U test was used for descriptive inter-cohort contrasts. Analyses focused on within-cohort longitudinal changes and within-cohort correlations. Given the marked baseline refractive differences between cohorts, any inter-cohort contrasts (including P values) are presented descriptively and should not be interpreted as isolated procedure effects. For repeated measurements at different time points, nonparametric repeated-measures comparisons were performed using the Friedman test, and the corresponding chi-square (χ^2) values and P values were reported. Spearman's rank correlation coefficient was used to evaluate associations between variables. A P value < 0.05 was considered statistically significant. For 5th-order aberrations, the analysis was limited to selected Zernike terms available from the Pentacam output (e.g., Z_5^1, Z_5^3, Z_5^5), rather than a complete 5th-order RMS summary.

Results

Repeated-measures analyses across time points were performed using the Friedman test. All surgeries were completed successfully without intraoperative complications. The baseline characteristics and surgical parameters of the two groups are summarized in Table 1. One patient (0.4%) in the right eye developed stromal haze, which did not affect visual acuity and resolved during the follow-up period. No other postoperative complications were observed throughout the entire follow-up.

Table 1. Patient characteristics and average preoperative values

Parameter	FS-LASIK	SMILE

Age (years)	25.56±7.12	25.01±7.82
Gender (Male/Female)	44/64	57/80
Spherical (D)	−7.94±2.86	−4.29±1.68
Cylinder (D)	−1.85±1.42	−0.95±0.75
SE (D)	−8.87±2.95	−4.76±1.75
Central cornea thickness (μm)	527.57±27.23	549.56±54.81
Central Epithelial thickness (μm)	53.92±3.76	54.31±3.57
IOP	14.99±2.54	16.19±2.59
AL (μm)	26.90±1.36	25.70±0.98
Flat curvature (D)	42.69±1.45	42.51±1.33
Steep curvature (D)	44.61±1.55	43.91±1.46
Mean curvature (D)	43.65±1.42	43.21±1.36
Pupil diameter (mm)	3.12±0.57	3.21±0.75
Depth of cut (μm)	97.56±18.09	107.38±26.98

SE= spherical equivalent；IOP= intraocular pressure; AL= Axial Length

Note: Preoperative spherical equivalent differed markedly between cohorts, indicating substantial baseline imbalance; therefore, inter-cohort differences are presented descriptively.

Regional Distribution of Epithelial Thickness

In the SMILE group, the preoperative central corneal epithelial thickness was 54.3 ± 3.6 μm. The central epithelial thickness showed statistically significant increases at both 1 month and 3 months postoperatively compared to baseline (1 month: $X^2 = 5.588$, $P < 0.001$; 3 months: $X^2 = 8.820$, $P < 0.001$), and the difference between the 1-month and 3-month postoperative measurements was also statistically significant ($X^2 = 3.232$, $P = 0.004$). In the FS-LASIK group, the preoperative central epithelial thickness was 53.9 ± 3.8 μm. Significant increases in central epithelial thickness were also observed at both 1 month and 3 months postoperatively compared to baseline (1 month: $X^2 = 9.297$, $P < 0.001$; 3 months: $X^2 = 11.621$, $P < 0.001$). However, the change between the 1-month and 3-month measurements was not statistically significant ($X^2 = 2.324$, $P = 0.06$).

In the SMILE group, the paracentral corneal epithelial thickness at both 1 month and 3 months postoperatively was significantly increased compared to the preoperative measurements (1 month: $X^2 = 8.850$, $P < 0.001$; 3 months: X^2

= 9.726, P < 0.001). However, no statistically significant difference was observed between the 1-month and 3-month postoperative values (X^2 = 0.876, P = 1.000). Similarly, in the FS-LASIK group, the paracentral epithelial thickness was significantly greater at both 1 and 3 months postoperatively compared to baseline (1 month: X^2 = 9.458, P< 0.001; 3 months: X^2 = 11.771, P< 0.001), with no significant change between 1 and 3 months postoperatively (X^2 = 2.313, P = 0.062). These results indicate that both surgical techniques led to varying degrees of corneal epithelial remodeling in the central and paracentral zones, as illustrated in Figure 1.

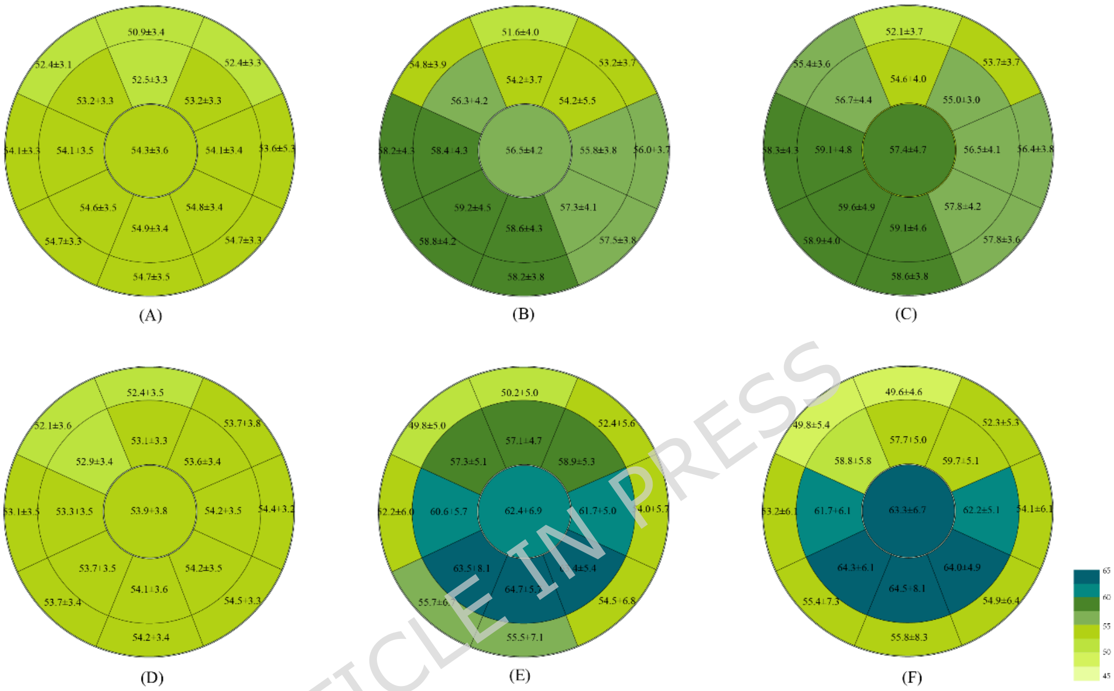

Figure 1. Distribution of corneal epithelial thickness in different regions (A–C) represent the corneal epithelial thickness changes in the SMILE group at preoperative, 1 month postoperative, and 3 months postoperative time points, respectively. (D–F) represent the corresponding changes in the FS-LASIK group at preoperative, 1 month postoperative, and 3 months postoperative time points, respectively.

In mid-peripheral region, the SMILE group exhibited significant increases in epithelial thickness at both 1 month and 3 months postoperatively compared to preoperative values (1 month: X^2 = 8.669, P< 0.001; 3 months: X^2 = 9.726, P< 0.001), with no significant difference observed between the 1-month and 3-month values (X^2 = 1.057, P = 0.871). In the FS-LASIK group, epithelial thickness in the mid-peripheral zone did not show significant changes at any time point (X^2 = 1.064, P= 0.587).

The overall mean corneal epithelial thickness in the SMILE group also showed statistically significant increases at 1 and 3 months postoperatively compared to preoperative measurements (1 month: X^2 = 9.696, P< 0.001; 3 months: X^2 = 10.421, P < 0.001), with no significant difference between the two postoperative time points (X^2 = 0.725, P= 1.000). Similarly, in the FS-LASIK group, the overall mean epithelial thickness increased significantly at 1 month and 3 months after surgery (1 month: X^2 = 8.845, $P < 0.001$; 3 months: X^2 = 10.648, $P < 0.001$), with no statistically significant difference between the two postoperative measurements (X^2 = 1.803, $P = 0.214$). Postoperative epithelial thickness in various regions for both surgical procedures is presented in Table 2 and Table 3, with corresponding changes shown in Table 4.

Table 2. Corneal epithelial thickness in different regions in the SMILE cohort

Zone	Preoperative	Postoperative 1 Month	Postoperative 3 Months
Central	54.31±3.572	56.49±4.243[a]	57.44±4.749[ab]
Paracentral	53.922±3.234	56.746±3.778[a]	57.298±4.093[a]
Mid-peripheral	53.437±2.992	56.025±3.330[a]	56.395±3.279[a]
Overall Average	53.717±3.061	56.392±3.445[a]	56.881±3.628[a]

Note: [a] P < 0.05 vs. preoperative values in the same group; [b] P < 0.05 vs. 1-month postoperative values in the same group. "Overall average" refers to the mean epithelial thickness within the 0–6 mm corneal diameter range.

Table 3. Corneal epithelial thickness in different zones in the FS-LASIK cohort

Zone	Preoperative	Postoperative 1 Month	Postoperative 3 Months
Central	53.92±3.762	62.35±6.883 [a]	63.3±6.663 [a]
Paracentral	53.656±3.27	60.894±4.242[a]	61.036±7.440[a]
Mid-peripheral	53.508±3.037	53.031±3.556	52.641±6.284
Overall Average	53.602±3.081	57.279±3.499[a]	57.184±6.597[a]

Note: **[a]** P < 0.05 vs. preoperative values in the same group; **[b]** P < 0.05 vs. 1-month postoperative values in the same group. "Overall average" refers to the mean epithelial thickness within the 0–6 mm corneal diameter range.

Table 4. Within-cohort changes in corneal epithelial thickness in two clinical cohorts (SMILE and FS-LASIK)

	SMILE		FS-LASIK	
Zone	**Postoperative 1 Month**	**Postoperative 3 Months**	**Postoperative 1 Month**	**Postoperative 3 Months**
Central	2.175±3.115[a]	3.124±3.741[a b]	8.435±4.988[a]	9.336±4.949[a]
Paracentral	2.824±2.615[a]	3.376±3.112[a]	7.237±2.978[a]	7.380±6.346[a]
Mid-peripheral	2.588±2.458[a]	2.958±2.577[a]	-0.477±2.865	-0.867±5.560
Overall Average	2.675±2.345[a]	3.164±2.706[a]	3.678±2.444[a]	3.582±5.695[a]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group. “Overall average” refers to the mean epithelial thickness within the 0–6 mm corneal diameter range.

Changes in Corneal Aberrations at Different Postoperative Time Points

HOAs

In the SMILE group, the HOAs at 1 month and 3 months postoperatively were both significantly different compared to preoperative values (1 month: $X^2 = 9.666$, $P < 0.001$; 3 months: $X^2 = 9.545$, $P < 0.001$), while no significant difference was observed between the 1-month and 3-month postoperative time points ($X^2 = 0.121$, $P = 1.0$). In the FS-LASIK group, HOAs showed significant differences at 1 month and 3 months postoperatively compared to preoperative measurements (1 month: $X^2 = 12.315$, $P < 0.001$; 3 months: $X^2 = 9.118$, $P < 0.001$), and there was also a statistically significant difference between the 1-month and 3-month postoperative values ($X^2 = 3.198$, $P = 0.04$).

Z_3^{-1}

In the SMILE group, the postoperative Z_3^{-1} values at 1 month and 3 months showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 6.494$, $P < 0.001$; 3 months: $X^2 = 6.917$, $P < 0.001$), whereas the change between 1 month and 3 months postoperatively was not statistically significant ($X^2 = 0.423$, $P = 1.0$). In the FS-LASIK group, Z_3^{-1} at 1 month postoperatively showed a significant difference compared to the preoperative value ($X^2 = 2.858$, $P = 0.013$), while the difference at 3 months postoperatively was not statistically significant ($X^2 = 2.245$, $P = 0.074$). The change between 1 month and 3 months postoperatively was also not statistically significant ($X^2 = 0.612$, $P = 1.0$).

Z_3^{1}

For the SMILE group, there were no statistically significant differences in Z_3^{1} across all time points ($X^2 = 4.429$, $P = 0.109$). In the FS-LASIK group, Z_3^{1} at 1 month postoperatively showed a significant difference compared to the preoperative value ($X^2 = 3.266$, $P = 0.003$), while the difference at 3 months postoperatively was not statistically significant ($X^2 = 2.347$, $P = 0.057$). The change between 1 month and 3 months postoperatively was also not statistically significant ($X^2 = 0.919$, $P = 1.0$).

Z_3^{-3}

In the SMILE group, Z_3^{-3} at both 1 month and 3 months postoperatively showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 3.625$, $P = 0.001$; 3 months: $X^2 = 3.353$, $P = 0.002$), while the change between 1 month and 3 months postoperatively was not statistically significant ($X^2 = 0.272$, $P = 1.0$). In the FS-LASIK group, the postoperative Z_3^{-3} values at both 1 month and 3 months also showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 2.654$, $P = 0.024$; 3 months: $X^2 = 2.654$, $P = 0.024$), and the change between 1 month and 3 months postoperatively was not statistically significant ($X^2 =0.000$, $P = 1.0$).

Z_3^3

For the SMILE group, there were no statistically significant differences in Z_3^3 across all time points ($X^2 = 0.739$, P = 0.691). In the FS-LASIK group, Z_3^3 at 1 month postoperatively showed a statistically significant difference compared to the preoperative value ($X^2 = 2.790$, P = 0.016), while the difference at 3 months was not statistically significant ($X^2 = 1.089$, P = 0.829). The change between 1 month and 3 months postoperatively was also not statistically significant ($X^2 = 1.701$, P = 0.267).

Z_4^0

In the SMILE group, Z_4^0 values at both 1 month and 3 months postoperatively showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 8.428$, $P < 0.001$; 3 months: $X^2 = 7.703$, $P < 0.001$), while the change between 1 month and 3 months was not statistically significant ($X^2 = 0.725$, P = 1.0). In the FS-LASIK group, Z_4^0 at both postoperative time points showed significant differences compared to the preoperative value (1 month: $X^2 = 11.975$, $P < 0.001$; 3 months: $X^2 = 9.050$, $P < 0.001$), and the change between 1 month and 3 months postoperatively was also statistically significant ($X^2 = 2.926$, P = 0.010).

Z_5^1

In the SMILE group, Z_5^1 at 1 month postoperatively showed a statistically significant difference compared to the preoperative value ($X^2 = 5.075$, $P < 0.001$), while the difference at 3 months was not statistically significant ($X^2 = 1.541$, P = 0.370). However, the change between 1 month and 3 months postoperatively was statistically significant ($X^2 = 3.534$, P = 0.001). In the FS-LASIK group, there were no statistically significant differences in Z_5^1 across all time points ($X^2 = 3.019$, P = 0.221).

Z_5^3

In the SMILE group, Z_5^3 at both 1 month and 3 months postoperatively showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 2.598$, P = 0.028; 3 months: $X^2 = 3.111$, P = 0.006), while the change between 1 month and 3 months was not statistically significant ($X^2 = 0.514$, P = 1.0). In the FS-LASIK group, there were no statistically significant differences in Z_5^3 across all time points ($X^2 = 0.200$, P = 0.905).

Z_5^5

In the SMILE group, Z_5^5 at both 1 month and 3 months postoperatively showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 2.598$, P = 0.028; 3 months: $X^2 = 3.111$, P = 0.006), and the change between 1 month and 3 months was not statistically significant ($X^2 = 1.873$, P = 0.183). In the FS-LASIK group, Z_5^5 at both 1 month and 3 months postoperatively showed significant differences compared to the preoperative values (1 month: $X^2 = 3.572$, P = 0.010; 3 months: $X^2 = 3.776$, $P < 0.001$), while the change between 1 month and 3 months was not statistically significant ($X^2 = 0.204$, P = 1.0).

Z_6^0

In the SMILE group, Z_6^0 at both 1 month and 3 months postoperatively showed statistically significant differences compared to the preoperative values (1 month: $X^2 = 11.478$, $P < 0.001$; 3 months: $X^2 = 10.451$, $P < 0.001$), while the change between 1 month and 3 months was not statistically significant ($X^2 = 1.027$, P = 0.913). In the FS-LASIK group, Z_6^0 at both 1 month and 3 months postoperatively showed significant differences compared to the preoperative values (1 month: $X^2 = 8.573$, $P < 0.001$; 3 months: $X^2 = 11.635$, $P < 0.001$), and the change between 1 month and 3 months was also statistically significant ($X^2 = 3.062$, P = 0.007).

Table 5 and Table 6 present anterior corneal aberration metrics at each postoperative time point and the corresponding within-cohort changes for the SMILE and FS-LASIK cohorts, respectively. Inter-cohort contrasts are descriptive only due to baseline refractive differences.

Table 5. Anterior corneal aberrations at postoperative time points in two clinical cohorts (SMILE and FS-LASIK)

	SMILE			**FS-LASIK**		
	Preoperative	**Postoperative 1 Month**	**Postoperative 3 Months**	**Preoperative**	**Postoperative 1 Month**	**Postoperative 3 Months**
HOAs	0.419±0.09	0.645±0.200[a]	0.649±0.216[a]	0.416±0.135	1.861±0.700[a]	1.750±0.680[ab]
Z_3^{-1}	0.004±0.2	-0.146±0.321[a]	-0.145±0.330[a]	-0.022±0.192	-0.174±0.985[a]	-0.130±0.931
Z_3^{1}	-0.108±0.114	-0.135±0.217	-0.133±0.216	0.036±0.117	0.242±0.843[a]	0.274±0.813
Z_3^{-3}	-0.067±0.118	-0.021±0.131[a]	-0.028±0.147[a]	-0.055±0.120	0.0003±0.254	0.011±0.216
Z_3^{3}	-0.034±0.105	-0.038±0.111	-0.035±0.114	0.001±0.099	-0.059±0.230[a]	-0.009±0.185
Z_4^{0}	0.289±0.361	0.390±0.140[a]	0.388±0.135[a]	0.264±0.094	1.204±0.522[a]	1.167±0.508[ab]

Z_5^1	0.020±0.021	-0.003±0.055[a]	0.005±0.057[b]	0.019±0.023	0.036±0.157	0.047±0.157
Z_5^3	-0.03±0.21	-0.009±0.028[a]	-0.011±0.031[a]	-0.004±0.021	-0.004±0.057	-0.007±0.062
Z_5^5	0.02±0.03	0.005±0.041[a]	-0.005±0.050[a]	0.01±0.04	-0.009±0.067[a]	-0.015±0.071[a]
Z_6^0	-0.011±0.021	0.063±0.050[a]	0.061±0.051[a]	-0.017±0.025	0.162±0.095[a]	0.178±0.105[ab]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group.

Table 6. Within-cohort changes in higher-order aberration metrics in two clinical cohorts (SMILE and FS-LASIK)

	SMILE		FS-LASIK	
	Postoperative 1 Month	**Postoperative 3 Months**	**Postoperative 1 Month**	**Postoperative 3 Months**
HOAs	0.225±0.224[a]	0.23±0.238[a]	1.444±0.690[a]	1.333±0.675[ab]
Z_3^{-1}	-0.150±0.262[a]	-0.149±0.270[a]	-0.151±1.000[a]	-0.108±0.949
Z_3^1	-0.025±0.203	-0.024±0.205	0.278±0.836[a]	0.31±0.813
Z_3^{-3}	0.044±0.137[a]	0.037±0.149[a]	0.055±0.265	0.066±0.238
Z_3^3	-0.005±0.112	-0.001±0.12	-0.059±0.224[a]	-0.01±0.186
Z_4^0	0.100±0.378[a]	0.098±0.379[a]	0.939±0.505[a]	0.902±0.493[ab]
Z_5^1	-0.023±0.058[a]	-0.015±0.059[b]	0.017±0.161	0.028±0.160
Z_5^3	-0.007±0.029[a]	-0.011±0.031[a]	0.000±0.053	-0.007±0.062
Z_5^5	-0.014±0.052[a]	-0.024±0.059[a]	-0.019±0.071[a]	-0.003±0.060[a]
Z_6^0	0.074±0.049[a]	0.072±0.050[a]	0.180±0.091[a]	0.195±0.098[ab]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group.

Correlation Analysis Between Corneal Epithelial Thickness and

Corneal Aberrations

At 3 months postoperatively in the SMILE group, changes in central, paracentral, mid-peripheral, and overall average corneal epithelial thickness (ΔCET) were positively correlated with changes in higher-order aberrations (ΔHOAs) (central: r = 0.308, $P < 0.001$; paracentral: r = 0.410, $P < 0.001$; mid-peripheral: r = 0.181, $P = 0.034$; average: r = 0.321, $P < 0.001$) , indicating weak to moderate associations in magnitude. ΔCET in the paracentral, mid-peripheral, and average zones was negatively correlated with ΔZ_3^{-1} (r = -0.195, $P = 0.022$; r = -0.216, $P = 0.011$; r = -0.217, $P = 0.011$, respectively). ΔCET in the central, paracentral, and average zones was negatively correlated with ΔZ_3^{1} (r = -0.209, $P = 0.014$; r = -0.215, $P = 0.012$; r = -0.200, $P = 0.019$, respectively). ΔCET in the central, paracentral, and average zones was positively correlated with ΔZ_4^{0} (r = 0.314, $P < 0.001$; r = 0.320, $P < 0.001$; r = 0.203, $P = 0.018$, respectively). Similarly, ΔCET in the central, paracentral, and average zones was positively correlated with ΔZ_6^{0} (r = 0.324, $P < 0.001$; r = 0.402, $P < 0.001$; r = 0.357, $P < 0.001$, respectively).

In the FS-LASIK group, central ΔCET at 3 months postoperatively was positively correlated with ΔHOAs (r = 0.234, $P = 0.015$), while mid-peripheral ΔCET was negatively correlated with ΔHOAs (r = -0.232, $P = 0.016$), reflecting weak associations in magnitude.ΔCET in the paracentral and mid-peripheral zones was negatively correlated with ΔZ_3^{-1} (r = -0.196, $P = 0.042$; r = -0.194, $P = 0.045$, respectively). Central ΔCET was positively correlated with ΔZ_4^{0} (r = 0.271, $P = 0.005$), while mid-peripheral ΔCET was negatively correlated with ΔZ_4^{0} (r = -0.221, $P = 0.021$). ΔCET in the paracentral, mid-peripheral, and average zones was positively correlated with ΔZ_6^{0} (r = 0.220, $P = 0.022$; r = 0.252, $P = 0.009$; r = 0.283, $P = 0.003$, respectively). Table 7 and Table 8 summarize the correlation coefficients and statistical significance for the SMILE and FS-LASIK groups. The corresponding heatmaps are illustrated in Figure 2 and Figure 3.

Table 7. Correlation Analysis Between ΔCET and ΔCorneal Aberrations in the SMILE cohort

	Δ3m Central		**Δ 3m Paracentral**		**Δ 3m Mid-peripheral**		**Δ 3m Grand average**	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
ΔHOAs	0.308	<0.001*	0.41	<0.001*	0.181	0.034*	0.321	<0.001*
ΔZ_3^{-1}	-0.129	0.134	-0.195	0.022*	-0.216	0.011*	-0.217	0.011*
ΔZ_3^{1}	-	0.014*	-	0.012*	-	0.076	-0.2	0.019*

	0.209		0.215		0.152			
ΔZ_3^{-3}	0.018	0.813	0.051	0.557	0.104	0.224	0.083	0.337
ΔZ_3^{3}	0.142	0.098	0.129	0.133	0.142	0.098	0.141	0.099
ΔZ_4^{0}	0.314	<0.001*	0.32	<0.001*	0.028	0.741	0.203	0.018*
ΔZ_5^{1}	-0.032	0.708	-0.127	0.139	-0.148	0.083	-0.147	0.087
ΔZ_5^{3}	0.024	0.784	0.024	0.779	0.00	0.999	0.008	0.929
ΔZ_5^{5}	0.005	0.952	0.001	0.993	-0.024	0.779	-0.01	0.903
ΔZ_6^{0}	0.324	<0.001*	0.402	<0.001*	0.239	0.005	0.357	<0.001*

Note: * $P < 0.05$.

Table 8. Correlation Analysis Between ΔCET and ΔCorneal Aberrations in the FS-LASIK cohort

	Δ 3m Central		**Δ 3m Paracentral**		**Δ 3m Mid-peripheral**		**Δ 3m Grand average**	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
Δ **HOAs**	0.234	0.015*	0.055	0.571	-0.232	0.016*	-0.047	0.628
ΔZ_3^{-1}	0.011	0.907	-0.196	0.042*	-0.095	0.326	-0.194	0.045*
ΔZ_3^{1}	0.01	0.91	-	0.33	-0.096	0.322	-0.096	0.322

		4	0.095					
ΔZ_3^{-3}	0.009	0.923	0.097	0.319	0.152	0.117	0.147	0.129
ΔZ_3^{3}	0.027	0.781	0.055	0.569	0.076	0.432	0.072	0.462
ΔZ_4^{0}	0.271	0.005*	0.177	0.067	-0.221	0.021*	0.029	0.767
ΔZ_5^{1}	-0.185	0.056	-0.1	0.304	-0.047	0.631	-0.123	0.206
ΔZ_5^{3}	0.095	0.326	0.181	0.061	0.09	0.355	0.177	0.067
ΔZ_5^{5}	0.051	0.598	-0.046	0.633	-0.048	0.62	-0.066	0.494
ΔZ_6^{0}	-0.122	0.208	0.22	0.022*	0.252	0.009*	0.283	0.003*

Note: * $P < 0.05$.

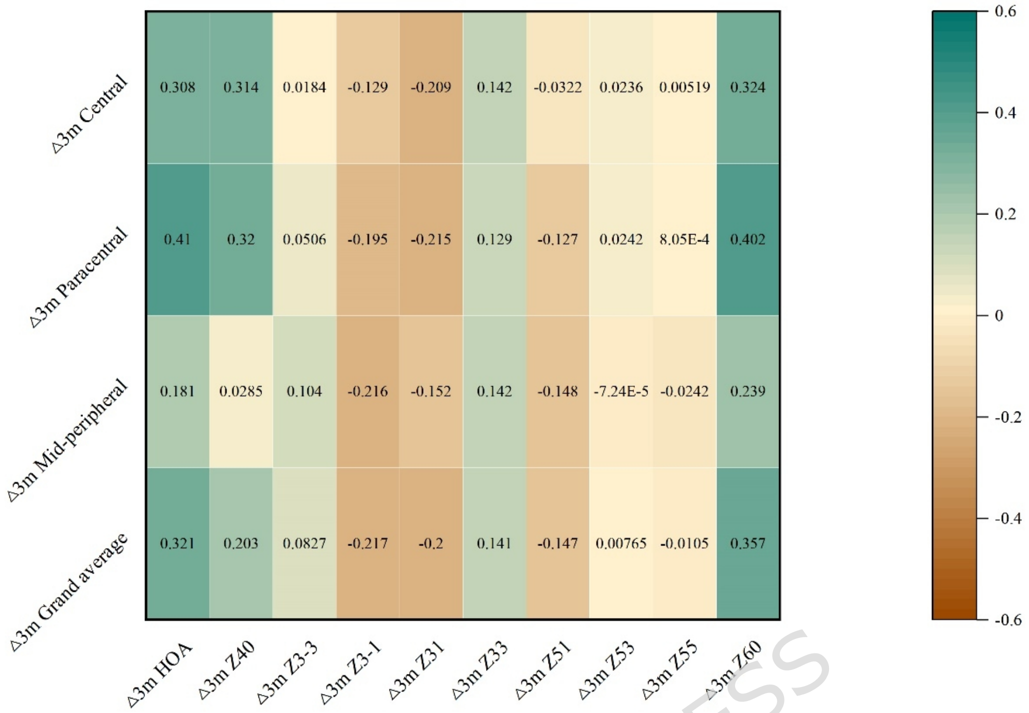

Figure 2. Heatmap of the Correlation Between ΔCET and ΔCorneal Aberrations in the SMILE cohort. Color intensity represents the magnitude of Spearman’s correlation coefficient.

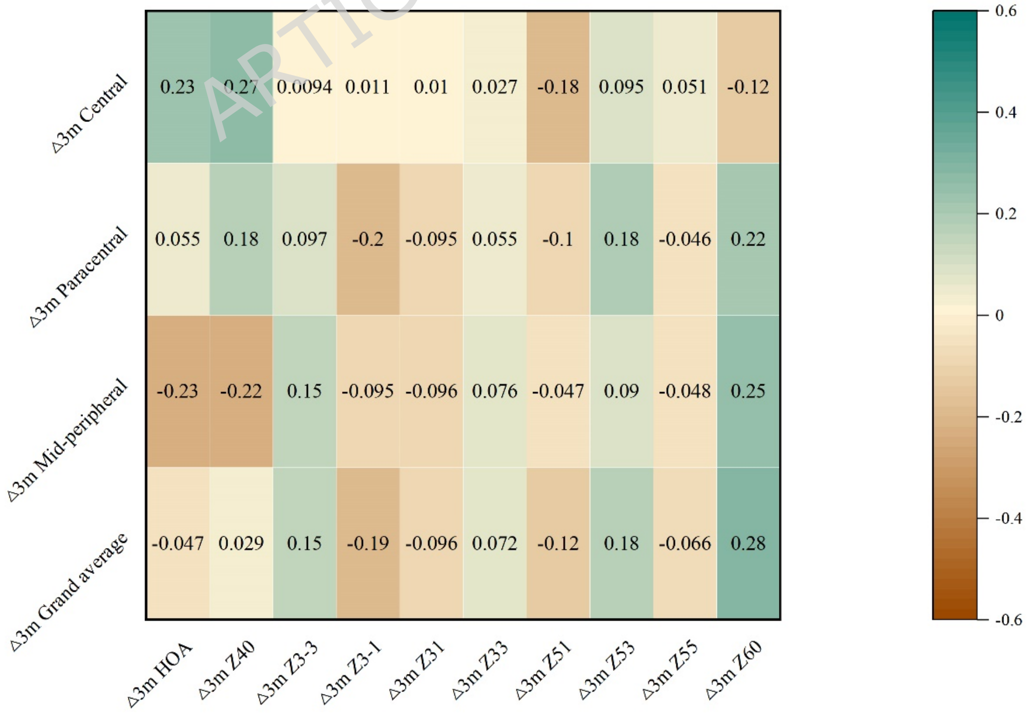

Figure 3. Heatmap of the Correlation Between ΔCET and ΔCorneal Aberrations in the FS-LASIK cohort. Color intensity represents the magnitude of Spearman's correlation coefficient.

Discussion

Previous studies have shown that corneal epithelial remodeling occurs after corneal cross-linking, corneal transplantation, phakic intraocular lens implantation, and corneal refractive surgery [9-14], Such postoperative epithelial remodeling may potentially affect visual quality. Currently, the mechanisms underlying epithelial remodeling remain controversial. Reinstein et al. suggested that epithelial remodeling acts as a compensatory mechanism, with changes in corneal curvature possibly being one of the inducing factors [15]. In contrast, other studies have proposed that the remodeling is related to alterations in corneal biomechanics [16]. Epithelial remodeling has been hypothesized to contribute to optical surface regularity, which may partially explain reported associations with corneal curvature. Regarding remodeling outcomes, Ye et al.[1] used widefield OCT scanning and found that epithelial thickness increased in both the central and paracentral zones, which is consistent with our findings. In both the KLEx (SMILE) and FS-LASIK groups, significant epithelial thickening was observed in the central and paracentral areas at 3 months postoperatively. Although KLEx was performed using the SMILE platform in this study, the magnitude and pattern of epithelial remodeling after lenticule extraction may vary slightly across other platforms due to differences in laser energy settings and incision geometry. Moreover, an asymmetric distribution of epithelial remodeling was observed within the 6-mm optical zone. Postoperative epithelial healing and the mechanical pressure exerted by the upper eyelid during blinking may contribute to this asymmetric distribution [17], which is similar to the findings reported by Luft et al. Ryu et al. [4] and Kanellopoulos et al. [18] compared epithelial thickness changes between SMILE and LASIK, reporting a meniscus-shaped thickening pattern of the epithelium in both procedures. In our study, epithelial remodeling in the SMILE group was biased toward the inferotemporal region, while in the FS-LASIK group, it was more pronounced inferiorly. However, this does not necessarily indicate an inherent difference between SMILE and FS-LASIK, as the indications for the two procedures differ and the baseline characteristics were not identical. It should be noted that this baseline imbalance is inherent to the non-randomized clinical setting and represents a major limitation and confounding factor for inter-cohort interpretation. The selection of SMILE or FS-LASIK is inherently based on individual surgical indications, including refractive magnitude, corneal thickness, and biomechanical considerations, rather than random allocation. Similar baseline differences between SMILE and LASIK cohorts have been reported in previous comparative studies[4, 13, 18], in which analyses focused primarily on longitudinal intra-group changes rather than direct baseline-matched comparisons. Accordingly, the present study primarily emphasized postoperative changes relative to baseline (Δ values) and correlation analyses, which help mitigate the potential influence of baseline differences on outcome interpretation.

A major limitation of this study is the marked difference in preoperative spherical equivalent between the two cohorts. This substantial baseline imbalance represents a significant confounding factor inherent to the non-randomized design and confounds any attempt to isolate the independent effect of the surgical procedure itself. The magnitude of refractive correction is known to be a key determinant of postoperative corneal shape changes, epithelial remodeling, and higher-order aberrations. Therefore, any observed inter-cohort differences in the magnitude or pattern of postoperative epithelial thickening or HOA changes are likely to be substantially influenced by differences in correction amount, rather than reflecting isolated or intrinsic effects of SMILE or FS-LASIK. Accordingly, inter-cohort differences should be interpreted with caution and viewed as descriptive observations, while the primary value of the present study lies in characterizing within-cohort postoperative patterns and associations between epithelial remodeling and anterior corneal HOAs.

Some studies have reported that such remodeling may persist for up to 7 years postoperatively, which could be a major factor affecting long-term stability [19-21]. In the SMILE group, epithelial remodeling in the central zone continued to show statistically significant differences between 1 and 3 months postoperatively, suggesting that remodeling may still be ongoing during this period. In contrast, the FS-LASIK group showed no significant change in epithelial thickness between 1 and 3 months, and no difference was observed in the mid-peripheral zone compared to preoperative values, suggesting that, within the 1–3-month follow-up of this study, epithelial thickness changes in the FS-LASIK cohort showed no statistically significant differences between 1 and 3 months, consistent with previous reports [3, 4]. In the FS-LASIK group, central epithelial thickening was more pronounced than in the peripheral zones, forming a "convex lens" pattern. This is similar to the findings of Li et al. [22]. This pattern may be influenced by procedure-related factors (e.g., ablation profile and wound-healing response) as well as by correction magnitude and baseline refractive status.In the SMILE cohort, the observed paracentral remodeling pattern may similarly reflect multiple influences, including surgical characteristics and correction magnitude; procedure-specific effects cannot be isolated in the present design. In summary, epithelial remodeling following corneal refractive surgery is not driven by a single mechanism, but rather results from the interplay of multiple factors.

At present, there appear to be relatively few studies on the relationship between corneal epithelial remodeling and corneal aberrations following refractive surgery. Although refractive procedures effectively correct lower-order aberrations such as astigmatism and defocus, postoperative symptoms like glare, ghosting, starbursts, and reduced night vision remain significant issues, which are believed to be associated with HOAs. In our study, we also observed a significant increase in HOAs after surgery compared to preoperative values. The sources of HOAs may be related to changes in corneal asphericity and biomechanics after corneal refractive surgery [23], Early postoperative HOAs may also stem from factors such as corneal flap striae, intraoperative manipulation, inflammatory responses, or even corneal epithelial remodeling. This study analyzed the changes in epithelial thickness and their correlation with changes in HOAs, aiming to reveal their interrelationship.

In the SMILE group, HOAs showed statistically significant but weak to moderate associations with epithelial remodeling across all regions. In contrast, in the FS-LASIK group, significant correlations were observed only in the central and paracentral regions. We speculate that this pattern may be related to asynchronous epithelial thickening across regions; however, causal mechanisms cannot be determined from the present observational design. In the SMILE group, indices showing significant changes at 3 months postoperatively compared to preoperative values included HOAs, Z_3^{-1}, Z_3^{-3}, Z_4^0, Z_5^3, Z_5^5 and Z_6^0. In the FS-LASIK group, significantly changed indices included HOAs, Z_4^0, Z_5^5 and Z_6^0. The introduction of vertical coma (Z_3^{-1}) may be associated with asymmetric epithelial healing between the superior and inferior cornea. Ablation of the stromal layer alters the corneal asphericity, which primarily leads to an increase in spherical aberrations (Z_4^0 and Z_6^0).

Epithelial remodeling may contribute to postoperative changes in anterior corneal HOAs; however, the present non-randomized two-cohort design with marked baseline refractive differences does not allow isolation of procedure-specific mechanisms. Therefore, the observed associations between epithelial thickness changes and spherical aberration should be interpreted as within-cohort relationships that may be influenced by correction magnitude and other factors (e.g., wound healing responses and biomechanical changes), rather than definitive evidence of mechanism attributable to a specific procedure.

Additional contributors to HOAs may include intraoperative transection of corneal nerve fibers, resulting in reduced tear film stability, shortened tear breakup time, and the formation of an irregular optical surface. Changes in corneal biomechanics may also cause forward protrusion of the posterior corneal surface to varying degrees. Our study further revealed that in the SMILE group, epithelial thickening was positively correlated with changes in spherical aberration (ΔZ_4^0) and higher-order spherical aberration (ΔZ_6^0), and negatively correlated with coma (ΔZ_3^{-1} and ΔZ_3^{-3}). This pattern may indicate an association between epithelial thickening and changes in “symmetric” aberration metrics (e.g., spherical aberration) and an inverse association with coma-related terms, without implying a directional mechanistic effect. It is worth noting that in the FS-LASIK group, the correlation between epithelial remodeling and HOAs was weaker and regionally inconsistent. While central epithelial thickening was associated with increased spherical aberrations, the paracentral region showed a negative correlation. These region-dependent associations may be influenced by multiple factors, including flap-related structural changes, tear film stability, wound healing, and biomechanical responses, in addition to correction magnitude. The morphological recovery of the cornea after FS-LASIK may involve more “asymmetry”, leading to region-specific compensatory epithelial remodeling and may contribute to region-dependent HOA patterns observed during follow-up. Overall, we observed region-dependent epithelial thickening patterns in the FS-LASIK cohort alongside region-dependent changes in HOA metrics. These findings suggest that postoperative epithelial remodeling and anterior corneal HOAs are associated within this cohort; however, the present design does not support causal inference regarding compensatory mechanisms or visual quality outcomes. In addition, given baseline refractive differences between cohorts, any inter-cohort contrasts should be interpreted descriptively rather than as isolated procedure effects.

Differences in the observed within-cohort associations between epithelial remodeling and HOA metrics across the two cohorts may reflect multiple influences, particularly the marked imbalance in preoperative spherical equivalent and correction magnitude. Accordingly, any inter-cohort differences in the magnitude or pattern of change should be interpreted descriptively and should not be used to infer isolated procedure effects.

Another set of indices worth close attention are coma (Z_3^1, Z_3^{-1}) and spherical aberration (Z_4^0□Z_6^0). Some reports suggest that coma and spherical aberration play important roles in visual quality and have shown correlations between starburst and spherical aberration, as well as glare and spherical aberration [24, 25]. Coma can be induced by the corneal flap, an irregular stromal bed, and the wound healing response of the cornea [26-28]. In the present study, we also confirmed the correlation between corneal epithelial remodeling and coma. In the FS-LASIK group, only Z_3^{-1} showed a correlation with paracentral epithelial remodeling. Previous studies have indicated that postoperative spherical aberration may be caused by the "cosine effect," and that the ablation procedure changes the corneal shape from a prolate ellipse to an oblate ellipse. Corneal epithelial remodeling alters the corneal curvature and asphericity [2]. Some studies have shown a positive correlation between corneal spherical aberration and asphericity [29]. Clearly, there is a relationship between epithelial remodeling and corneal spherical aberration, which is consistent with our findings.

Asymmetric aberrations such as coma are more closely associated with localized surface irregularities and decentration. The observed inverse relationship between epithelial thickening and coma in the SMILE group suggests that epithelial remodeling may exert a compensatory smoothing effect on micro-irregularities of the anterior corneal surface. By partially regularizing local surface asymmetries, epithelial remodeling may help reduce certain asymmetric aberrations, may be associated with reduced coma-related terms in the SMILE cohort.

Limitations

This study has certain limitations. First, the 3-month follow-up period only reflects early postoperative changes. Long-term follow-up is needed to confirm whether epithelial remodeling and HOAs will stabilize or further evolve, as previous studies have reported that epithelial remodeling may persist for up to 7 years. Second, corneal epithelial measurements rely on devices such as OCT, which have resolution and algorithmic limitations that may introduce deviations in certain regions. Additionally, we did not further analyze the impact of HOAs changes on subjective visual quality (e.g., glare, night vision). Future studies should integrate both subjective and objective indicators to systematically assess the clinical significance of epithelial remodeling.

The evaluation of 5th-order HOAs was limited to the horizontal/oblique Zernike components available from the measurement output, and the corresponding vertical terms were not included in the analysis. Therefore, the 5th-order results should not be interpreted as a comprehensive assessment of all 5th-order aberrations. This exclusion also limits our ability to fully evaluate potential vertical coma coupling mechanisms that may be induced by eyelid pressure; future studies using full 5th-order decomposition including both horizontal and vertical terms are warranted.

Conclusions

Across two clinical cohorts undergoing SMILE or FS-LASIK, postoperative epithelial thickening and changes in anterior corneal HOAs were observed, with measurable within-cohort associations between epithelial remodeling and HOA metrics. Given the marked baseline differences in preoperative spherical equivalent and correction magnitude between cohorts, these findings should be interpreted as descriptive patterns and within-cohort associations, and direct between-procedure inference should be avoided.

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Data availability: The datasets generated and/or analysed during the current study are not publicly available due to restrictions imposed by institutional ethics approval and patient confidentiality agreements, but are available from the corresponding author on reasonable request.

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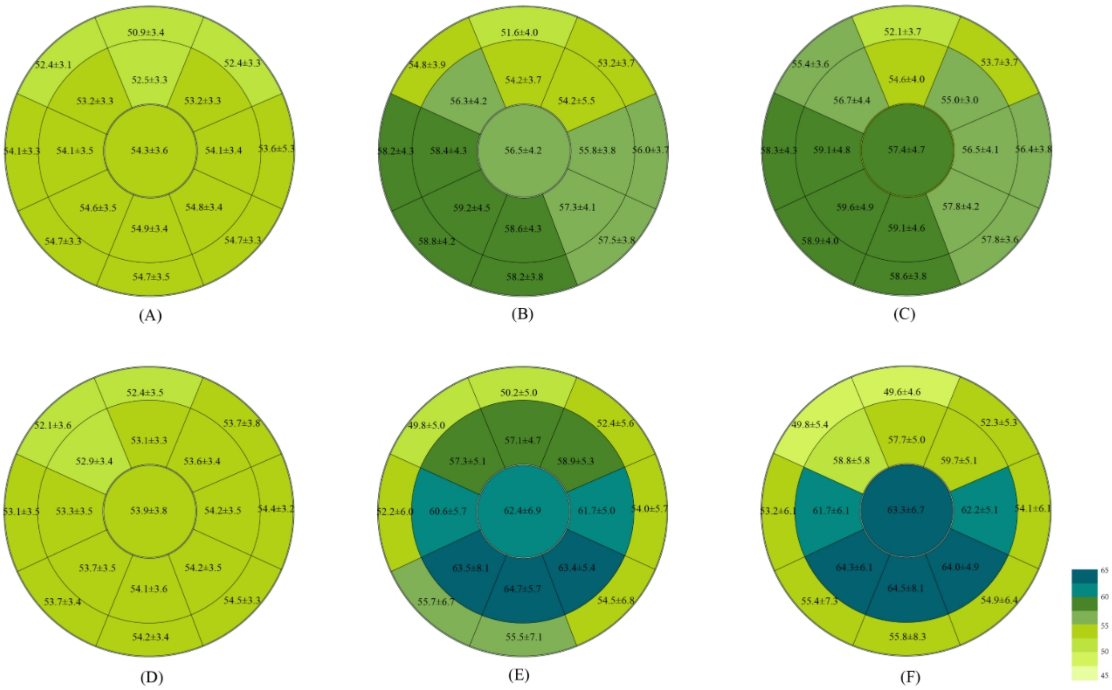

Figure 1. Distribution of corneal epithelial thickness in different regions

(A–C) represent the corneal epithelial thickness changes in the SMILE group at preoperative, 1 month postoperative, and 3 months postoperative time points, respectively. (D–F) represent the corresponding changes in the FS-LASIK group at preoperative, 1 month postoperative, and 3 months postoperative time points, respectively.

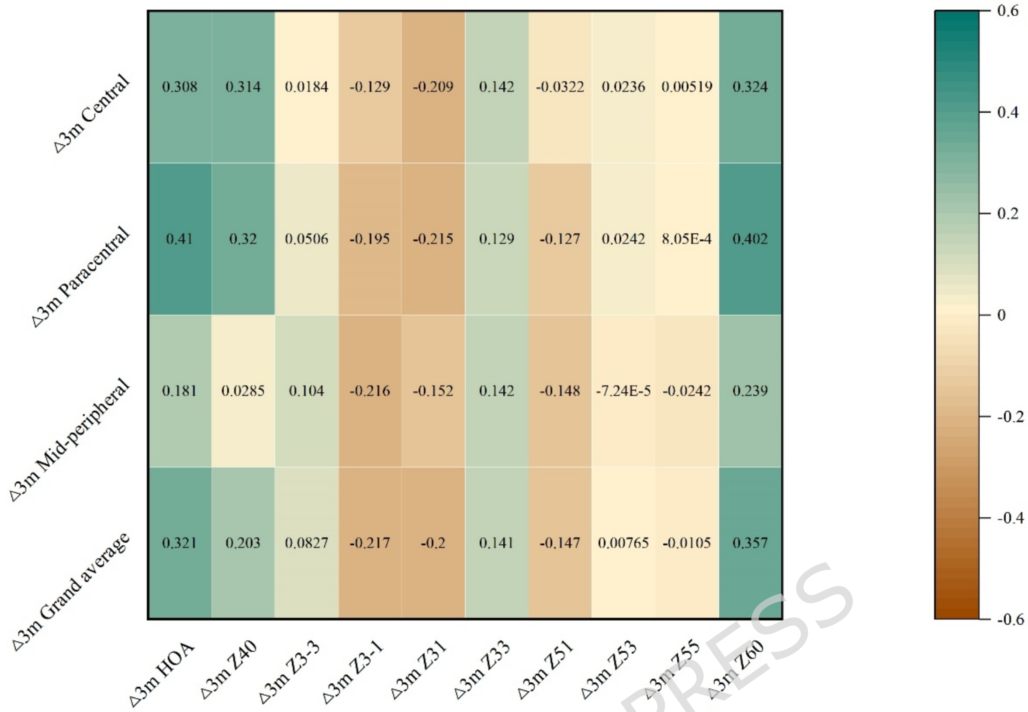

Figure 2. Heatmap of the Correlation Between △CET and △Corneal Aberrations in the SMILE Group cohort

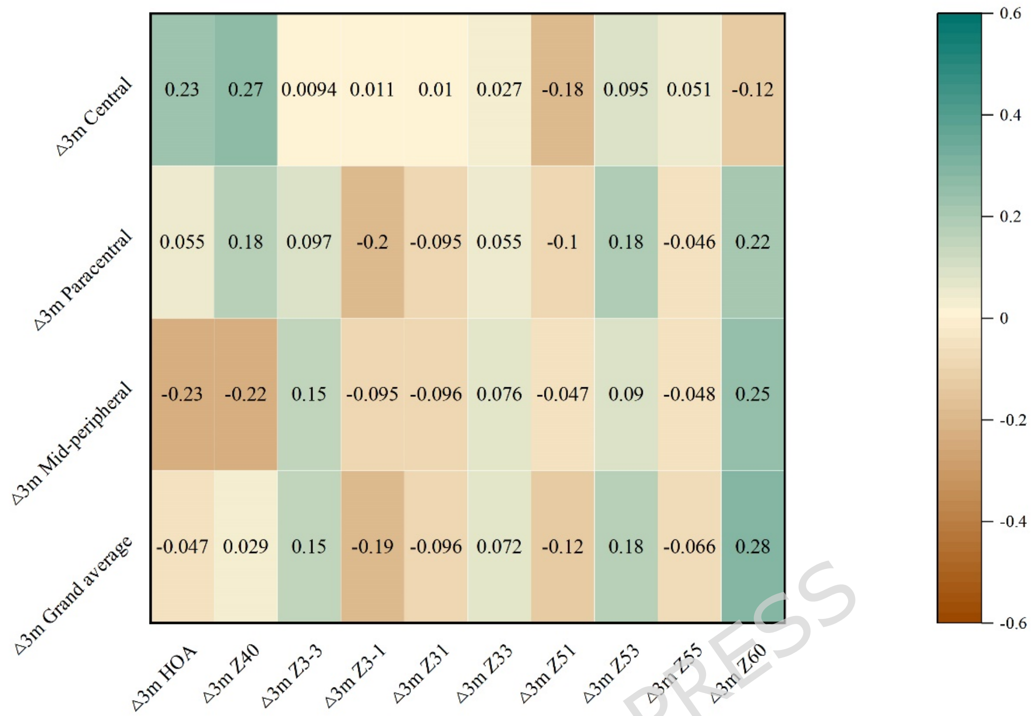

Figure 3. Heatmap of the Correlation Between △CET and △Corneal Aberrations in the FS-LASIK Group cohort

Table 1. Patient characteristics and average preoperative values

Parameter	FS-LASIK	SMILE
Age (years)	25.56±7.12	25.01±7.82
Gender (Male/Female)	44/64	57/80
Spherical (D)	−7.94±2.86	−4.29±1.68
Cylinder (D)	−1.85±1.42	−0.95±0.75
SE (D)	−8.87±2.95	−4.76±1.75
Central cornea thickness (µm)	527.57±27.23	549.56±54.81
Central Epithelial thickness (µm)	53.92±3.76	54.31±3.57
IOP	14.99±2.54	16.19±2.59
AL (µm)	26.90±1.36	25.70±0.98
Flat curvature (D)	42.69±1.45	42.51±1.33
Steep curvature (D)	44.61±1.55	43.91±1.46
Mean curvature (D)	43.65±1.42	43.21±1.36
Pupil diameter (mm)	3.12±0.57	3.21±0.75
Depth of cut (µm)	97.56±18.09	107.38±26.98

SE= spherical equivalent；IOP= intraocular pressure; AL= Axial Length

Note: Preoperative spherical equivalent differed markedly between cohorts, indicating substantial baseline imbalance; therefore, inter-cohort differences are presented descriptively.

Table 2. Corneal epithelial thickness in different regions in the SMILE cohort

Zone	**Preoperative**	**Postoperative 1 Month**	**Postoperative 3 Months**
Central	54.31±3.572	56.49±4.243[a]	57.44±4.749[ab]
Paracentral	53.922±3.234	56.746±3.778[a]	57.298±4.093[a]
Mid-peripheral	53.437±2.992	56.025±3.330[a]	56.395±3.279[a]
Overall Average	53.717±3.061	56.392±3.445[a]	56.881±3.628[a]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group. "Overall average" refers to the mean epithelial thickness within the 0–6 mm corneal diameter range.

Table 3. Corneal epithelial thickness in different zones in the FS-LASIK cohort

Zone	**Preoperative**	**Postoperative 1 Month**	**Postoperative 3 Months**
Central	53.92±3.762	62.35±6.883 [a]	63.3±6.663 [a]
Paracentral	53.656±3.27	60.894±4.242[a]	61.036±7.440[a]
Mid-peripheral	53.508±3.037	53.031±3.556	52.641±6.284
Overall Average	53.602±3.081	57.279±3.499[a]	57.184±6.597[a]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group. "Overall average" refers to the mean epithelial thickness within the 0–6 mm corneal diameter range.

Table 4. Within-cohort changes in corneal epithelial thickness in two clinical cohorts (SMILE and FS-LASIK)

	SMILE		**FS-LASIK**	
Zone	**Postoperative 1 Month**	**Postoperative 3 Months**	**Postoperative 1 Month**	**Postoperative 3 Months**
Central	2.175±3.115[a]	3.124±3.741[ab]	8.435±4.988[a]	9.336±4.949[a]
Paracentral	2.824±2.615[a]	3.376±3.112[a]	7.237±2.978[a]	7.380±6.346[a]
Mid-peripheral	2.588±2.458[a]	2.958±2.577[a]	-0.477±2.865	-0.867±5.560
Overall Average	2.675±2.345[a]	3.164±2.706[a]	3.678±2.444[a]	3.582±5.695[a]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group. “Overall average” refers to the mean epithelial thickness within the 0–6 mm corneal diameter range.

Table 5. Anterior corneal aberrations at postoperative time points in two clinical cohorts (SMILE and FS-LASIK)

	SMILE			FS-LASIK		
	Preoperative	**Postoperative 1 Month**	**Postoperative 3 Months**	**Preoperative**	**Postoperative 1 Month**	**Postoperative 3 Months**
HOAs	0.419±0.09	0.645±0.200[a]	0.649±0.216[a]	0.416±0.135	1.861±0.700[a]	1.750±0.680[ab]
Z_3^{-1}	0.004±0.2	-0.146±0.321[a]	-0.145±0.330[a]	-0.022±0.192	-0.174±0.985[a]	-0.130±0.931
Z_3^{1}	-0.108±0.114	-0.135±0.217	-0.133±0.216	0.036±0.117	0.242±0.843[a]	0.274±0.813
Z_3^{-3}	-0.067±0.118	-0.021±0.131[a]	-0.028±0.147[a]	-0.055±0.120	0.0003±0.254	0.011±0.216
Z_3^{3}	-0.034±0.105	-0.038±0.111	-0.035±0.114	0.001±0.099	-0.059±0.230[a]	-0.009±0.185
Z_4^{0}	0.289±0.361	0.390±0.140[a]	0.388±0.135[a]	0.264±0.094	1.204±0.522[a]	1.167±0.508[ab]
Z_5^{1}	0.020±0.021	-0.003±0.055[a]	0.005±0.057[b]	0.019±0.023	0.036±0.157	0.047±0.157
Z_5^{3}	-0.03±0.21	-0.009±0.028[a]	-0.011±0.031[a]	-0.004±0.021	-0.004±0.057	-0.007±0.062
Z_5^{5}	0.02±0.03	0.005±0.041[a]	-0.005±0.050[a]	0.01±0.04	-0.009±0.067[a]	-0.015±0.071[a]
Z_6^{0}	-0.011±0.021	0.063±0.050[a]	0.061±0.051[a]	-0.017±0.025	0.162±0.095[a]	0.178±0.105[ab]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group.

Table 6. Within-cohort changes in higher-order aberration metrics in two clinical cohorts (SMILE and FS-LASIK)

	SMILE		**FS-LASIK**	
	Postoperative 1 Month	**Postoperative 3 Months**	**Postoperative 1 Month**	**Postoperative 3 Months**
HOAs	0.225±0.224[a]	0.23±0.238[a]	1.444±0.690[a]	1.333±0.675[ab]
Z_3^{-1}	-0.150±0.262[a]	-0.149±0.270[a]	-0.151±1.000[a]	-0.108±0.949
Z_3^{1}	-0.025±0.203	-0.024±0.205	0.278±0.836[a]	0.31±0.813
Z_3^{-3}	0.044±0.137[a]	0.037±0.149[a]	0.055±0.265	0.066±0.238
Z_3^{3}	-0.005±0.112	-0.001±0.12	-0.059±0.224[a]	-0.01±0.186
Z_4^{0}	0.100±0.378[a]	0.098±0.379[a]	0.939±0.505[a]	0.902±0.493[ab]
Z_5^{1}	-0.023±0.058[a]	-0.015±0.059[b]	0.017±0.161	0.028±0.160
Z_5^{3}	-0.007±0.029[a]	-0.011±0.031[a]	0.000±0.053	-0.007±0.062
Z_5^{5}	-0.014±0.052[a]	-0.024±0.059[a]	-0.019±0.071[a]	-0.003±0.060[a]
Z_6^{0}	0.074±0.049[a]	0.072±0.050[a]	0.180±0.091[a]	0.195±0.098[ab]

Note: [a] $P < 0.05$ vs. preoperative values in the same group; [b] $P < 0.05$ vs. 1-month postoperative values in the same group.

Table 7. Correlation Analysis Between ΔCET and ΔCorneal Aberrations in the SMILE cohort

	Δ3m Central		Δ3m Paracentral		Δ3m Mid-peripheral		Δ3m Grand average	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
Δ HOAs	0.308	<0.001*	0.41	<0.001*	0.181	0.034*	0.321	<0.001*
ΔZ_3^{-1}	-0.129	0.134	-0.195	0.022*	-0.216	0.011*	-0.217	0.011*
ΔZ_3^{1}	-0.209	0.014*	-0.215	0.012*	-0.152	0.076	-0.2	0.019*
ΔZ_3^{-3}	0.018	0.813	0.051	0.557	0.104	0.224	0.083	0.337
ΔZ_3^{3}	0.142	0.098	0.129	0.133	0.142	0.098	0.141	0.099
ΔZ_4^{0}	0.314	<0.001*	0.32	<0.001*	0.028	0.741	0.203	0.018*
ΔZ_5^{1}	-0.032	0.708	-0.127	0.139	-0.148	0.083	-0.147	0.087
ΔZ_5^{3}	0.024	0.784	0.024	0.779	0.00	0.999	0.008	0.929
ΔZ_5^{5}	0.005	0.952	0.001	0.993	-0.024	0.779	-0.01	0.903
ΔZ_6^{0}	0.324	<0.001*	0.402	<0.001*	0.239	0.005	0.357	<0.001*

Note: * $P < 0.05$.

Table 8. Correlation Analysis Between ΔCET and ΔCorneal Aberrations in the FS-LASIK cohort

	△3m Central		**△3m Paracentral**		**△3m Mid-peripheral**		**△3m Grand average**	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
△HOAs	0.234	0.015*	0.055	0.571	-0.232	0.016*	-0.047	0.628
△Z_3^{-1}	0.011	0.907	-0.196	0.042*	-0.095	0.326	-0.194	0.045*
△Z_3^{1}	0.01	0.914	-0.095	0.33	-0.096	0.322	-0.096	0.322
△Z_3^{-3}	0.009	0.923	0.097	0.319	0.152	0.117	0.147	0.129
△Z_3^{3}	0.027	0.781	0.055	0.569	0.076	0.432	0.072	0.462
△Z_4^{0}	0.271	0.005*	0.177	0.067	-0.221	0.021*	0.029	0.767
△Z_5^{1}	-0.185	0.056	-0.1	0.304	-0.047	0.631	-0.123	0.206
△Z_5^{3}	0.095	0.326	0.181	0.061	0.09	0.355	0.177	0.067
△Z_5^{5}	0.051	0.598	-0.046	0.633	-0.048	0.62	-0.066	0.494
△Z_6^{0}	-0.122	0.208	0.22	0.022*	0.252	0.009*	0.283	0.003*

Note: * $P < 0.05$.