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Influence of Programmed Optical Zone Diameter on Corneal Higher-Order Aberrations After Small Incision Lenticule Extraction: A Retrospective Comparative Study

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Abstract

Purpose

To evaluate whether programmed optical zone diameter (OZD) influences postoperative corneal higher-order aberrations (HOAs) after small incision lenticule extraction (SMILE), with a particular focus on responses that may vary with analysis diameter and type of aberration.

Methods

This retrospective study enrolled patients with myopia who underwent SMILE. Patients were analyzed in two programmed OZD comparison cohorts: 6.7 vs. 6.5 mm and 6.5 vs. 6.3 mm. Corneal HOAs, including trefoil, coma, spherical aberration (SA), and total HOA, were measured using Pentacam at 1 day, 1 month, and 3 months postoperatively and analyzed at 3-, 4-, 5-, and 6-mm diameters. Induced changes in each HOA component were calculated as the postoperative value minus the corresponding preoperative value and analyzed longitudinally using generalized estimating equations. OZD group and postoperative time were entered as categorical factors, with adjustment for age, gender, spherical equivalent refraction, preoperative apex corneal thickness, and the corresponding preoperative HOA value; a group × time interaction term was included. Because multiple models were fitted across two cohorts, four aberration components, and four analysis diameters, interaction P values were adjusted using the Benjamini-Hochberg false discovery rate, with $q < 0.05$ considered statistically significant.

Results

In the 6.7- vs. 6.5-mm comparison, overall group effects were observed for several HOA components, but no significant group × time interactions were found at any analysis diameter. In the 6.5- vs. 6.3-mm comparison, no significant group × time interactions were detected for any aberration component at any analysis diameter. After BH-FDR adjustment across all 32 interaction tests, none of the interactions remained statistically significant.

Conclusions

These findings suggest that a larger programmed OZD does not necessarily reduce induced HOAs after SMILE, and routine enlargement of the OZD solely for optical-quality benefit is not supported by the present data. Routine selection of a larger OZD for optical-quality benefit is therefore not supported, and OZD should be individualized according to refractive and corneal characteristics.

Introduction

SMILE is an established procedure for the correction of myopia and myopic astigmatism. Although favorable uncorrected visual acuity, refractive predictability, and safety are routinely achieved, postoperative visual quality is not determined by Snellen acuity or manifest refraction alone. Glare, halos, starbursts, and fluctuating vision may still occur, particularly under mesopic conditions or in eyes with larger pupils, and may be related to residual refractive error, pupil size, and surgically induced HOAs, including coma, trefoil, and SA [1–3]. Thus, optimization of SMILE planning should consider both refractive outcomes and corneal optical quality.

The programmed OZD is an important adjustable surgical planning parameter in SMILE. A larger programmed OZD may enlarge the postoperative functional or effective optical zone and reduce optical degradation when the pupil dilates [4–9]. However, a larger OZD requires greater stromal tissue removal for the same refractive correction, which may limit its use in

eyes with higher myopia or thinner corneas [7,10]. Therefore, OZD selection represents a balance between optical quality and tissue conservation, and the optimal programmed OZD remains a matter of ongoing clinical investigation.

Recent studies have shown that the programmed OZD does not equal the achieved postoperative optical zone. After SMILE, the effective or functional optical zone is usually smaller than planned and may be influenced by attempted correction, astigmatism, corneal curvature, decentration, and wound healing [5–9]. Postoperative effective or functional optical zone has been associated with SA, total HOA, and visual quality [4,9,11]. However, whether modest differences in programmed OZD independently affect these outcomes remains uncertain. In routine practice, smaller OZDs are often selected for eyes requiring higher myopic corrections or with thinner corneas to conserve stromal tissue, which may confound direct comparisons between programmed OZD groups.

Moreover, corneal HOAs are pupil-size dependent [12], and different HOA components may respond differently to optical-zone design [11]. SA may mainly reflect the corneal power transition across the treatment boundary, whereas coma and trefoil may also be affected by decentration [13], astigmatic correction, and early postoperative corneal remodeling. Therefore, a multi-diameter and longitudinal assessment is needed to characterize the optical consequences of different programmed OZD settings after SMILE.

In this study, patients were analyzed in two clinically relevant programmed OZD comparisons: 6.7 versus 6.5 mm and 6.5 versus 6.3 mm. Trefoil, coma, SA, and total HOA were evaluated at 3-, 4-, 5-, and 6-mm analysis diameters at 1 day, 1 month, and 3 months postoperatively. The study aimed to determine whether modest differences in programmed OZD were associated with differences in surgically induced corneal HOAs and, in particular, whether the longitudinal patterns of these changes differed between OZD groups according to aberration component and analysis diameter.

Patients and Methods

Patients

This retrospective comparative study included patients who underwent SMILE surgery for the correction of myopia and astigmatism. The study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional ethics committee. Patients were analyzed in two programmed OZD comparison cohorts: 6.7 versus 6.5 mm and 6.5 versus 6.3 mm.

Programmed OZD was selected by the same surgeon (HW) before surgery based on the attempted spherical equivalent correction and corneal tissue availability. The 6.7- versus 6.5-mm cohort comprised eyes undergoing lower myopic corrections, whereas the 6.5- versus 6.3-mm cohort comprised eyes undergoing higher myopic corrections. To compare adjacent 0.2-mm OZD differences, patients were grouped into these two non-overlapping cohorts. Although both cohorts included a 6.5-mm group, the eyes were not shared between cohorts. One eye was included per patient.

The requirements for inclusion were as follows: (1) age between 18 and 45 years; (2) preoperative spherical equivalent refraction (SER) < − 0.50 D; (3) stable refraction (annual progression ≤ 0.50 D) for more than two years; (4) minimum central corneal thickness (CCT) of 480 μm or greater, and calculated residual stromal thickness greater than 280 μm; and (5) stopping the use of rigid gas-permeable lenses for more than three weeks or soft contact lenses for more than one week. The exclusion criteria included: (1) pellucid marginal degeneration or suspected or clinical keratoconus; (2) a history of ocular trauma or surgery; (3) active ocular surface diseases; and (4) systemic connective tissue disorders. Postoperative follow-up was performed at 1 day, 1 month, and 3 months.

Surgical Techniques

All SMILE procedures were performed by the same experienced surgeon (HW) with the VisuMax femtosecond laser system (Carl Zeiss Meditec AG, Jena, Germany) at a repetition rate of 500 kHz. Topical anesthesia was induced with 0.5%

proparacaine hydrochloride eyedrops (Alcaine; Alcon-Couvreur n.v., Puurs, Belgium), administered 2 to 3 times before surgery. The laser pulse energy was set at 155 nJ. The intended cap thickness was 120 μm. After creation of the lenticule, a corneal side-cut incision approximately 2 mm in length was made at the 12-o'clock position, through which the lenticule was dissected and extracted. At the end of surgery, one drop of tobramycin/dexamethasone combination eyedrops (Tobradex, Alcon Laboratories, Fort Worth, TX, USA) was instilled into each eye.

Corneal Aberration Measurements

Corneal HOAs were measured using the Pentacam system (Oculus Optikgeräte GmbH, Wetzlar, Germany). Measurements were obtained preoperatively and at 1 day, 1 month, and 3 months postoperatively, and only high-quality scans were included. Zernike coefficients were exported according to the OSA standard. Coma was expressed as the RMS of the paired third-order coma terms Z(3,−1) and Z(3,1); trefoil as the RMS of Z(3,−3) and Z(3,3); SA as the Z(4,0) coefficient; and total HOA as the RMS of third- and higher-order Zernike terms. Aberrations were analyzed at fixed 3-, 4-, 5-, and 6-mm analysis diameters, and values were expressed in micrometers (μm).

Outcome Measures

Outcome Measures
The outcome measures included the induced changes in corneal trefoil, coma, SA, and total HOA, calculated as the postoperative value minus the corresponding preoperative value. Postoperative absolute HOA values and visual and refractive outcomes, including UDVA, CDVA, refractive accuracy, refractive astigmatism, and refractive stability, were also assessed. Because this retrospective study did not prespecify a single primary outcome and multiple aberration components and analysis diameters were evaluated, all analyses were considered exploratory.

Statistical Analyses

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as frequencies or percentages, as appropriate. Baseline analyses were performed using IBM SPSS Statistics, and GEE analyses were performed using R version 4.6.1. Baseline between-group comparisons were performed using the independent-samples t test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher exact test for categorical variables, as appropriate.

Induced changes in trefoil, coma, SA, and total HOA were analyzed longitudinally using generalized estimating equations (GEE), separately for each analysis diameter and each OZD comparison. A normal distribution with an identity link function and an exchangeable working correlation structure were specified, with robust covariance estimation. OZD group and postoperative time were entered as categorical factors, whereas age, gender, spherical equivalent refraction (SER), preoperative apex corneal thickness (ACT), and the corresponding preoperative HOA value were included as covariates. A group × time interaction term was included to assess whether longitudinal changes differed between OZD groups. Because no single primary outcome was prespecified and multiple aberration components and analysis diameters were evaluated, all analyses were considered exploratory. P values for the 32 group × time interaction tests were adjusted using the Benjamini-Hochberg false discovery rate (FDR), with $q < 0.05$ considered statistically significant. As no interaction remained significant after global FDR adjustment, no visit-specific group comparisons were formally performed. All tests were two-sided.

Results

Baseline Characteristics and Refractive Outcomes

A total of 84 eyes were included in the analyses. The 6.7- vs. 6.5-mm comparison included 22 eyes in each group, whereas the 6.5- vs. 6.3-mm comparison included 20 eyes in each group (Table 1). Baseline characteristics were comparable between the 6.7- and 6.5-mm groups. In the 6.5- vs. 6.3-mm comparison, most baseline characteristics were comparable; however, preoperative apex corneal thickness (ACT) was greater in the 6.5-mm group than in the 6.3-mm group (575.45 ± 25.56 vs. 543.15 ± 18.15 μm, P < 0.001).

Table 1
Preoperative Baseline Characteristics in the Two Programmed OZD Comparison Cohorts

Characteristics	**OZD**			**OZD**		
	6.7mm	**6.5mm**		**6.5mm**	**6.3mm**	
	(n = 22)	(n = 22)	P	(n = 20)	(n = 20)	P
Age (years)	23.23 ± 5.24	25.05 ± 7.00	0.444	26.10 ± 5.53	24.25 ± 5.00	0.274
Gender, % female	44%	56%	0.361	75%	55.00%	0.185
Sphere(D)	-3.66 ± 1.66	-3.78 ± 1.66	0.807	-7.06 ± 1.22	-7.00 ± 0.97	0.859
Cylinder(D)	-0.84 ± 0.64	-0.63 ± 0.48	0.243	-1.23 ± 0.89	-1.44 ± 0.85	0.444
SE (D)	-4.08 ± 1.71	-4.09 ± 1.71	0.979	-7.68 ± 1.26	-7.72 ± 1.20	0.911
Km (D)	42.50 ± 1.03	43.05 ± 1.46	0.250	43.73 ± 1.34	43.2 ± 0.89	0.129
Ablated depth (μm)	99.40 ± 29.22	92.41 ± 25.78	0.404	149.30 ± 19.09	139.40 ± 16.93	0.091
UDVA(logMAR)	1.13 ± 0.36	1.08 ± 0.36	0.511	1.40 ± 0.31	1.50 ± 0.25	0.094
CDVA(logMAR)	-0.01 ± 0.03	-0.01 ± 0.05	0.517	-0.01 ± 0.03	0.01 ± 0.03	0.091
ACT (μm)	558.18 ± 21.06	551.77 ± 22.11	0.331	575.45 ± 25.56	543.15 ± 18.15	< 0.001***
IOP (mmHg)	17.18 ± 2.36	16.36 ± 2.38	0.259	18.50 ± 1.47	17.20 ± 3.17	0.108

Data are presented as mean ± SD or percentage, as appropriate. P values represent between-group comparisons within each OZD comparison cohort. D = diopters; SE = spherical equivalent; ACT = apex corneal thickness; Km = mean keratometry of the anterior corneal surface; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; IOP = intraocular pressure; OZD = optical zone diameter.*P < 0.05, **P < 0.01, ***P < 0.001

SMILE demonstrated favorable visual and refractive outcomes at 3 months (Fig. 1). Overall, 98% of eyes achieved UDVA of 20/20 or better and 100% achieved 20/25 or better. No eye lost two or more lines of CDVA; 5% lost one line, 36% had no change, 46% gained one line, and 13% gained two or more lines. The attempted and achieved SER values were strongly correlated ($R^2 = 0.9809$). At 3 months, 98% of eyes were within ± 0.50 D and 100% within ± 1.00 D of the target refraction. Postoperative refractive astigmatism was ≤ 0.50 D in 98% of eyes and ≤ 1.00 D in 100%.

Effect of 6.7-mm Versus 6.5-mm OZD on Induced Corneal Aberrations

After adjustment for the corresponding preoperative HOA, overall OZD group effects were observed for coma and total HOA at all 3-, 4-, 5-, and 6-mm analysis diameters. Overall group effects for SA were present at 4, 5, and 6 mm but not at 3 mm (P = 0.065), whereas no group effect was observed for trefoil at any analysis diameter (Table 2; Fig. 2). As shown in Fig. 2, trefoil remained close to zero in both groups throughout follow-up. Coma and total HOA increased modestly over time in both groups, whereas SA showed a small early decrease that tended to return toward baseline by 3 months. The between-group trajectories were broadly similar across the three postoperative visits. No group × time interaction remained statistically

significant after global BH-FDR correction across the 32 interaction tests. Although the unadjusted interaction for total HOA at 3 mm reached nominal significance (P = 0.049), it did not survive global FDR adjustment (q > 0.05).[Table 2 near here]

Table 2
GEE Analysis of Induced Changes in Corneal Higher-Order Aberrations at 3–6-mm Analysis Diameters in the 6.7-mm versus 6.5-mm Programmed OZD Groups

	Trefoil			Coma			SA			HOA		
	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P
Model term												
3mm												
Group(6.5mm,6.7mm)	3.321	1	0.068	10.312	1	0.001	3.416	1	0.065	8.531	1	0.003
Gemder	0.289	1	0.591	1.149	1	0.284	1.690	1	0.194	0.043	1	0.835
Age	0.015	1	0.902	10.110	1	0.001	0.043	1	0.836	7.110	1	0.008
SER	0.250	1	0.617	7.670	1	0.006	43.572	1	< 0.001	7.301	1	0.007
ACT	1.405	1	0.236	1.038	1	0.308	0.748	1	0.387	0.003	1	0.953
Baseline HOA	17.640	1	< 0.001	14.921	1	< 0.001	0.268	1	0.605	17.379	1	< 0.001
Time	5.425	2	0.066	2.831	2	0.243	1.724	2	0.422	7.209	2	0.027
Group*Time	3.622	2	0.164	2.390	2	0.303	1.302	2	0.522	6.034	2	0.049
4mm												
Group(6.5mm,6.7mm)	2.963	1	0.085	9.831	1	0.002	6.214	1	0.013	6.461	1	0.011
Gender	0.780	1	0.377	7.597	1	0.006	1.546	1	0.214	1.142	1	0.285
Age	0.068	1	0.794	8.817	1	0.003	0.015	1	0.904	7.743	1	0.005
SER	0.224	1	0.636	13.846	1	< 0.001	27.859	1	< 0.001	8.220	1	0.004
ACT	2.700	1	0.100	3.829	1	0.050	1.373	1	0.241	0.306	1	0.580
Baseline HOA	43.157	1	< 0.001	11.280	1	< 0.001	0.734	1	0.392	22.690	1	< 0.001
Time	5.265	2	0.072	0.376	2	0.829	2.885	2	0.236	4.412	2	0.110
Group*Time	5.216	2	0.074	1.584	2	0.453	2.041	2	0.360	4.203	2	0.122
5mm												
Group(6.5mm,6.7mm)	2.715	1	0.099	12.723	1	< 0.001	5.714	1	0.017	6.038	1	0.014
Gender	0.845	1	0.358	15.602	1	< 0.001	3.514	1	0.061	3.326	1	0.068
Age	3.622	1	0.057	3.243	1	0.072	0.003	1	0.959	5.690	1	0.017

Induced changes (Δ) for each aberration component were calculated as the postoperative value minus the corresponding preoperative value. GEE models were fitted separately at each analysis diameter. OZD group and postoperative time were entered as categorical factors; age, gender, spherical equivalent refraction (SER), preoperative apex corneal thickness (ACT), and the corresponding preoperative HOA value were included as covariates; and a group × time interaction term was included. An exchangeable working correlation structure and a robust covariance estimator were used. P values are raw GEE P values. After BH-FDR correction across all 32 group × time interaction tests, no interaction remained statistically significant. SA = spherical aberration; HOA = higher-order aberration; OZD = optical zone diameter; SER = spherical equivalent refraction; ACT = apex corneal thickness.

	Trefoil			Coma			SA			HOA		
	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P
SER	2.336	1	0.126	17.790	1	< 0.001	1.535	1	0.215	7.854	1	0.005
ACT	7.232	1	0.007	0.898	1	0.343	2.317	1	0.128	1.529	1	0.216
Baseline HOA	39.400	1	< 0.001	14.791	1	< 0.001	1.557	1	0.212	26.903	1	< 0.001
Time	6.273	2	0.043	0.953	2	0.621	6.953	2	0.031	1.015	2	0.602
Group*Time	5.034	2	0.081	0.682	2	0.711	0.919	2	0.632	2.453	2	0.293
6mm												
Group(6.5mm,6.7mm)	1.876	1	0.171	7.434	1	0.006	7.723	1	0.006	8.247	1	0.004
Gender	2.162	1	0.142	6.539	1	0.011	3.958	1	0.047	1.716	1	0.190
Age	2.885	1	0.089	0.388	1	0.533	0.007	1	0.932	2.393	1	0.122
SER	1.414	1	0.235	8.178	1	0.004	15.918	1	< 0.001	13.523	1	< 0.001
ACT	10.455	1	0.001	2.508	1	0.113	6.095	1	0.014	7.857	1	0.005
Baseline HOA	26.772	1	< 0.001	15.638	1	< 0.001	2.526	1	0.112	18.986	1	< 0.001
Time	7.266	2	0.026	1.665	2	0.435	14.154	2	< 0.001	0.639	2	0.726
Group*Time	3.039	2	0.219	0.389	2	0.823	1.278	2	0.528	1.220	2	0.543

Induced changes (Δ) for each aberration component were calculated as the postoperative value minus the corresponding preoperative value. GEE models were fitted separately at each analysis diameter. OZD group and postoperative time were entered as categorical factors; age, gender, spherical equivalent refraction (SER), preoperative apex corneal thickness (ACT), and the corresponding preoperative HOA value were included as covariates; and a group × time interaction term was included. An exchangeable working correlation structure and a robust covariance estimator were used. P values are raw GEE P values. After BH-FDR correction across all 32 group × time interaction tests, no interaction remained statistically significant. SA = spherical aberration; HOA = higher-order aberration; OZD = optical zone diameter; SER = spherical equivalent refraction; ACT = apex corneal thickness.

Effect of 6.5-mm Versus 6.3-mm OZD on Induced Corneal Aberrations

In the 6.5- versus 6.3-mm comparison, most overall group effects did not reach statistical significance after adjustment for the corresponding preoperative HOA; only coma at the 6-mm analysis diameter showed an unadjusted group effect (P = 0.025) (Table 3; Fig. 3). As shown in Fig. 3, trefoil remained near zero in both groups. Coma and total HOA increased over time in both groups, with numerically higher values in the 6.3-mm group at several visits, whereas SA showed an early negative change that gradually moved toward zero. No significant group × time interactions were observed for any aberration component at any analysis diameter after adjustment (all raw P > 0.05). The corresponding preoperative HOA value was a significant covariate in most models, particularly for trefoil, coma, and total HOA, suggesting that baseline HOA differences contributed substantially to the variation in induced changes. Because no interaction reached statistical significance, visit-specific Bonferroni-adjusted post hoc comparisons were not formally performed.[Table 3 near here]

Table 3
GEE Analysis of Induced Changes in Corneal Higher-Order Aberrations at 3–6-mm Analysis Diameters in the 6.5-mm versus 6.3-mm Programmed OZD Groups

	Trefoil			Coma			SA			HOA		
	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P
Model term												
3mm												
Group(6.5mm,6.3mm)	2.841	1	0.092	0.378	1	0.539	0.896	1	0.344	0.473	1	0.492
Gender	10.359	1	0.001	0.904	1	0.342	0.058	1	0.810	0.014	1	0.907
Age	3.268	1	0.071	0.532	1	0.466	0.163	1	0.687	2.499	1	0.114
SER	4.285	1	0.038	0.416	1	0.519	8.432	1	0.004	0.002	1	0.964
ACT	6.656	1	0.010	0.756	1	0.385	10.348	1	0.001	1.427	1	0.232
Baseline HOA	34.399	1	< 0.001	20.600	1	< 0.001	10.017	1	0.002	21.578	1	< 0.001
Time	5.162	2	0.076	3.855	2	0.146	4.811	2	0.090	2.272	2	0.321
Group*Time	2.120	2	0.346	0.304	2	0.859	0.111	2	0.946	0.875	2	0.646
4mm												
Group(6.5mm,6.3mm)	0.973	1	0.324	0.105	1	0.746	0.328	1	0.567	0.019	1	0.889
Gender	11.977	1	< 0.001	0.150	1	0.698	0.130	1	0.718	0.363	1	0.547
Age	0.842	1	0.359	0.030	1	0.863	3.810	1	0.051	2.638	1	0.104
SER	1.169	1	0.280	0.086	1	0.769	6.352	1	0.012	0.011	1	0.916
ACT	1.530	1	0.216	0.394	1	0.530	12.441	1	< 0.001	0.792	1	0.373
Baseline HOA	49.413	1	< 0.001	36.246	1	< 0.001	4.929	1	0.026	17.191	1	< 0.001
Time	5.222	2	0.073	0.954	2	0.621	10.022	2	0.007	0.929	2	0.628
Group*Time	3.185	2	0.203	3.179	2	0.204	1.273	2	0.529	1.800	2	0.407
5mm												
Group(6.5mm,6.3mm)	0.094	1	0.759	0.319	1	0.572	0.171	1	0.679	0.046	1	0.830
Gender	3.143	1	0.076	0.377	1	0.539	0.001	1	0.976	0.591	1	0.442
Age	0.094	1	0.759	1.151	1	0.283	3.235	1	0.072	0.081	1	0.776
SER	0.278	1	0.598	0.777	1	0.378	3.066	1	0.080	0.000	1	0.992

Induced changes (Δ) for each aberration component were calculated as the postoperative value minus the corresponding preoperative value. GEE models were fitted separately at each analysis diameter. OZD group and postoperative time were entered as categorical factors; age, gender, spherical equivalent refraction (SER), preoperative apex corneal thickness (ACT), and the corresponding preoperative HOA value were included as covariates; and a group × time interaction term was included. An exchangeable working correlation structure and a robust covariance estimator were used. P values are raw GEE P values. After BH-FDR correction across all 32 group × time interaction tests, no interaction remained statistically significant. SA = spherical aberration; HOA = higher-order aberration; OZD = optical zone diameter; SER = spherical equivalent refraction; ACT = apex corneal thickness.

	Trefoil			Coma			SA			HOA		
	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P	Wald χ^2	df	P
ACT	0.203	1	0.652	0.371	1	0.543	15.056	1	< 0.001	0.161	1	0.688
Baseline HOA	82.306	1	< 0.001	34.788	1	< 0.001	0.812	1	0.368	27.078	1	< 0.001
Time	1.730	2	0.421	10.945	2	0.004	17.518	2	< 0.001	9.022	2	0.011
Group*Time	1.328	2	0.515	4.336	2	0.114	1.594	2	0.451	3.577	2	0.167
6mm												
Group(6.5mm,6.3mm)	0.619	1	0.432	5.036	1	0.025	2.840	1	0.092	0.372	1	0.542
Gender	0.131	1	0.717	0.073	1	0.787	0.043	1	0.836	0.001	1	0.977
Age	0.471	1	0.492	1.374	1	0.241	1.027	1	0.311	0.616	1	0.433
SER	0.656	1	0.418	2.631	1	0.105	0.102	1	0.749	0.209	1	0.647
ACT	0.816	1	0.366	4.044	1	0.044	3.263	1	0.071	1.023	1	0.312
Baseline HOA	26.245	1	< 0.001	14.582	1	< 0.001	0.016	1	0.898	7.222	1	0.007
Time	0.354	2	0.838	16.046	2	< 0.001	21.012	2	< 0.001	30.095	2	< 0.001
Group*Time	0.399	2	0.819	2.496	2	0.287	0.387	2	0.824	3.678	2	0.159

Induced changes (Δ) for each aberration component were calculated as the postoperative value minus the corresponding preoperative value. GEE models were fitted separately at each analysis diameter. OZD group and postoperative time were entered as categorical factors; age, gender, spherical equivalent refraction (SER), preoperative apex corneal thickness (ACT), and the corresponding preoperative HOA value were included as covariates; and a group × time interaction term was included. An exchangeable working correlation structure and a robust covariance estimator were used. P values are raw GEE P values. After BH-FDR correction across all 32 group × time interaction tests, no interaction remained statistically significant. SA = spherical aberration; HOA = higher-order aberration; OZD = optical zone diameter; SER = spherical equivalent refraction; ACT = apex corneal thickness.

Influence of Analysis Diameter on OZD-Related Aberration Differences

OZD-related differences did not increase monotonically with analysis diameter. In the 6.7- versus 6.5-mm comparison, some overall group effects were observed for coma and total HOA at both smaller and larger analysis diameters, but these effects were not accompanied by significant group × time interactions. In the 6.5- versus 6.3-mm comparison, no significant group × time interaction was observed at any analysis diameter after adjustment for the corresponding preoperative HOA.After global FDR correction, no significant differences in induced corneal HOAs were found between programmed OZD groups. These results suggest that, within the OZD range evaluated, a larger programmed OZD does not necessarily reduce induced corneal HOAs after SMILE.

Discussion

Two main findings emerged from this study. In the 6.7- versus 6.5-mm comparison, overall group effects were observed for several HOA components, particularly coma and total HOA; however, no significant group × time interactions were found at any analysis diameter, indicating that the two groups showed similar longitudinal patterns of induced HOA changes during the 3-month follow-up. In the 6.5- versus 6.3-mm comparison, after adjustment for the corresponding preoperative HOA, no significant group × time interactions were detected for any aberration component at any analysis diameter. After global FDR

correction across all 32 interaction tests, none of the interactions remained statistically significant. Thus, within the OZD range evaluated in this study, the data did not provide robust evidence that modest differences in programmed OZD produce component-, diameter-, or time-specific changes in postoperative corneal HOAs; Increasing the programmed OZD was not accompanied by a corresponding reduction in induced HOAs.

The favorable visual and refractive outcomes obtained in this cohort, in line with previously reported SMILE outcomes [2,3], allowed the influence of programmed OZD to be interpreted in terms of postoperative optical quality rather than residual refractive error. Even in eyes with excellent uncorrected visual acuity, patients may still report glare, halos, or reduced visual quality under mesopic conditions [2,3]. Corneal HOAs are therefore clinically relevant, and previous studies have linked specific HOA components to visual symptoms and visual function: Zhao et al. [14] reported that halo radius was correlated with ocular HOAs and coma, whereas Li et al. [15] found that greater postoperative horizontal coma was associated with poorer mesopic contrast performance. These findings suggest that HOA measurements provide complementary information on postoperative optical quality beyond that reflected by conventional high-contrast visual acuity.Corneal epithelial thickening and remodeling may further modulate corneal aberrations and visual quality after SMILE [16,17], and larger effective or functional optical zones have been associated with better postoperative visual quality [5,18]. Together, these observations provide a clear rationale for evaluating programmed OZD effects on corneal optical quality when favorable refractive outcomes are achieved.

The overall group effects observed in the 6.7- versus 6.5-mm OZD comparison are optically plausible. A broader treatment profile, including larger optical and transition zones, has been proposed to reduce the stromal surface curvature gradient [19]. Such optical-zone-related effects may differ among individual HOA components [11]. However, the absence of significant group × time interactions indicates that the temporal evolution of induced HOAs was not significantly different between the 6.7- and 6.5-mm OZD groups during the 3-month follow-up period. Therefore, the larger programmed OZD did not demonstrate a consistent advantage in postoperative HOAs in this study.

The influence of programmed OZD did not increase monotonically with analysis diameter. In the 6.7- versus 6.5-mm comparison, overall group effects for coma and total HOA were present at both smaller and larger analysis diameters, whereas no group effect was observed for trefoil. In the 6.5- versus 6.3-mm comparison, after adjustment for the corresponding preoperative HOA, no significant group × time interactions remained at any analysis diameter. Therefore, the present data did not detect any consistent effect of programmed OZD on induced corneal HOAs, and this effect was neither component-specific nor dependent on analysis diameter. The absence of such a pattern may partly reflect the difference between the programmed and achieved postoperative optical zone: Wang et al. [20] demonstrated that the effective optical zone after SMILE was significantly smaller than the programmed OZD, and previous studies have shown that the effective or functional optical zone is more directly associated with postoperative HOAs and visual quality [4,5,7,9,18,21]. These findings suggest that the programmed OZD alone may not fully determine the achieved optical zone or its optical consequences. The present results extend this evidence by showing that a 0.2-mm difference in programmed OZD was not associated with robust diameter-specific differences in induced corneal HOAs after baseline adjustment.

The findings from the 6.5- versus 6.3-mm comparison should be interpreted cautiously, as the sample size was modest and no group × time interaction remained significant after baseline adjustment and global FDR correction. The present results extend those of Ladi et al. [22], who found no significant differences in postoperative HOAs or glare between eyes treated with 5.0- and 6.5-mm optical zones. Whereas that study compared a relatively large difference in optical zone size, the present comparison focused on a clinically common adjacent 0.2-mm difference in programmed OZD within a higher myopic correction range. Our findings add to this evidence by showing that, even after adjustment for preoperative HOA and correction for multiple testing, the 6.5- and 6.3-mm groups did not show robust differences in induced corneal HOAs. Together with Ladi et al. [22], these data suggest that programmed OZD within the evaluated range may not be a major determinant of induced corneal HOAs after SMILE.

The present study adds to the existing literature by comparing two adjacent and clinically relevant programmed OZD pairs, 6.7 versus 6.5 mm and 6.5 versus 6.3 mm, within different myopic correction ranges under a common longitudinal framework. More importantly, the analyses adjusted for the corresponding preoperative HOA and applied global FDR correction across multiple aberration components and analysis diameters. These methodological features reduce the likelihood that the null findings reflect baseline differences or chance results from multiple testing. Although a larger optical zone is generally expected to provide better optical quality, the present results showed that a larger programmed OZD did not necessarily reduce postoperative corneal HOAs. From a tissue-preservation perspective, this suggests that routine enlargement of the programmed OZD may not be justified solely on the basis of HOA reduction, because it requires additional stromal tissue removal without a demonstrated optical benefit. Conversely, in eyes requiring higher myopic corrections or with limited corneal tissue, choosing a smaller programmed OZD may preserve more stromal tissue without necessarily increasing induced corneal HOAs.

This study has several limitations. First, the retrospective design and small sample size (20–22 eyes per group) may limit the applicability of our findings to broader populations. Because no formal sample size or power calculation was performed, and because the GEE analyses involved multiple aberration components, analysis diameters, and postoperative time points, the study may be underpowered to detect small between-group differences; therefore, non-significant results should not be interpreted as evidence of equivalence between OZD groups. Second, baseline apex corneal thickness differed significantly between the 6.5- and 6.3-mm groups. Because programmed OZD was not randomly assigned, smaller OZDs tended to be used in eyes with higher myopic corrections or more limited corneal tissue; therefore, adjustment for age, gender, spherical equivalent refraction, preoperative apex corneal thickness, and the corresponding preoperative HOA in the GEE models may reduce but cannot fully eliminate residual indication bias. Other unmeasured confounders, including lenticule thickness and corneal curvature, could not be excluded. Third, the two OZD comparisons were analyzed as separate cohorts; therefore, the present data should not be interpreted as a direct three-group dose-response comparison across 6.3, 6.5, and 6.7 mm. Fourth, because coma and trefoil were expressed as RMS magnitudes of paired Zernike terms, their induced changes represent changes in aberration magnitude rather than vector changes in the wavefront; therefore, direction-specific changes could not be evaluated. Finally, achieved effective optical zone, treatment decentration, mesopic pupil diameter, contrast sensitivity, and patient-reported visual quality were not quantitatively assessed. Larger prospective studies incorporating these parameters are needed to clarify the independent effect of programmed OZD on postoperative optical quality.

Conclusion

No significant OZD-related differences in induced corneal HOAs were found. These findings do not support routine enlargement of programmed OZD for optical benefit; OZD selection should be based on refractive correction and corneal tissue availability.

Declarations

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Competing interests:

The authors declare no conflicts of interest.

Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of The First Affiliatde Hospital of Fujian Medical University and adhered to the tenets of the Declaration of Helsinki. Because of the retrospective design, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Author Contribution

J.Z. and H.W. conceived and designed the study and provided project supervision. P.D., as the first author, led the data collection, data validation, preliminary statistical analyses, and drafting of the original manuscript, and was also responsible for the systematic organization of clinical data, preparation of key figures, and revision of tables. M.Z. assisted with data entry and auxiliary figure processing. Z.C. participated in the cross-verification of clinical data. J.G. and H.W. contributed to the in-depth interpretation of the results, critical revision of the manuscript, acquisition of funding, and overall accountability for the work. All authors reviewed and approved the final manuscript.

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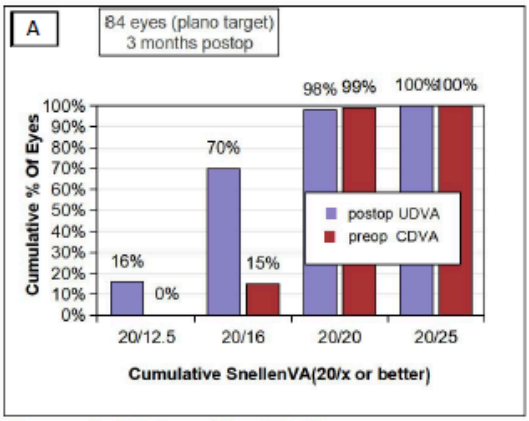
Not applicable.

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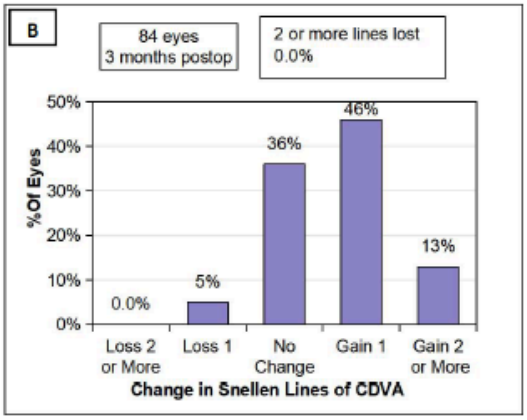
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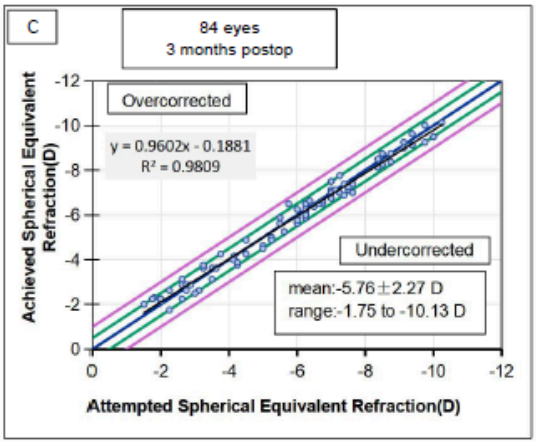
Figures



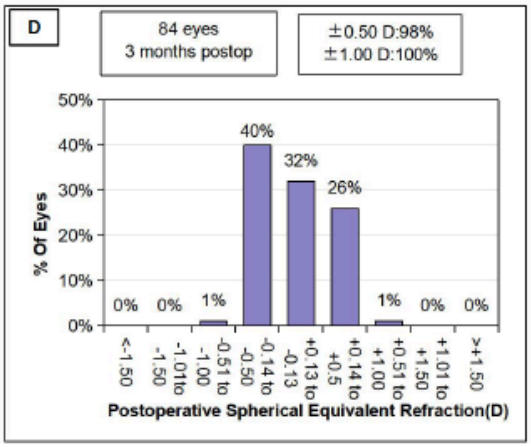
Uncorrected Distance Visual Acuity



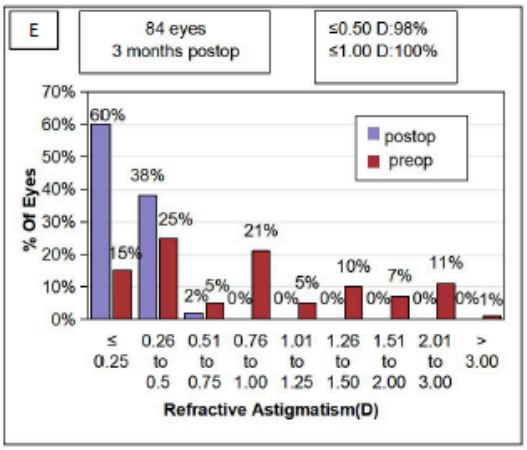
Change in Corrected Distance Visual Acuity



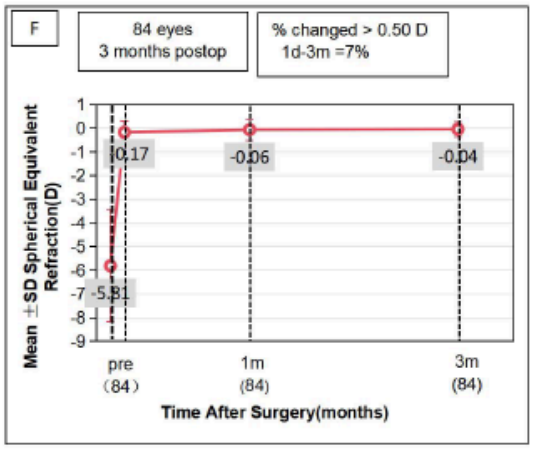
Spherical Equivalent Refraction Attempted vs Achieved



Spherical Equivalent Refractive Accuracy



Refractive Astigmatism



Stability of Spherical Equivalent Refraction

Figure 1

Standard refractive outcomes at 3 months after SMILE. (A) Uncorrected distance visual acuity. (B) Change in corrected distance visual acuity. (C) Attempted versus achieved SER. (D) Spherical equivalent refractive accuracy. (E) Refractive astigmatism. (F) Stability of SER. D = diopters; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; SER = spherical equivalent refraction.

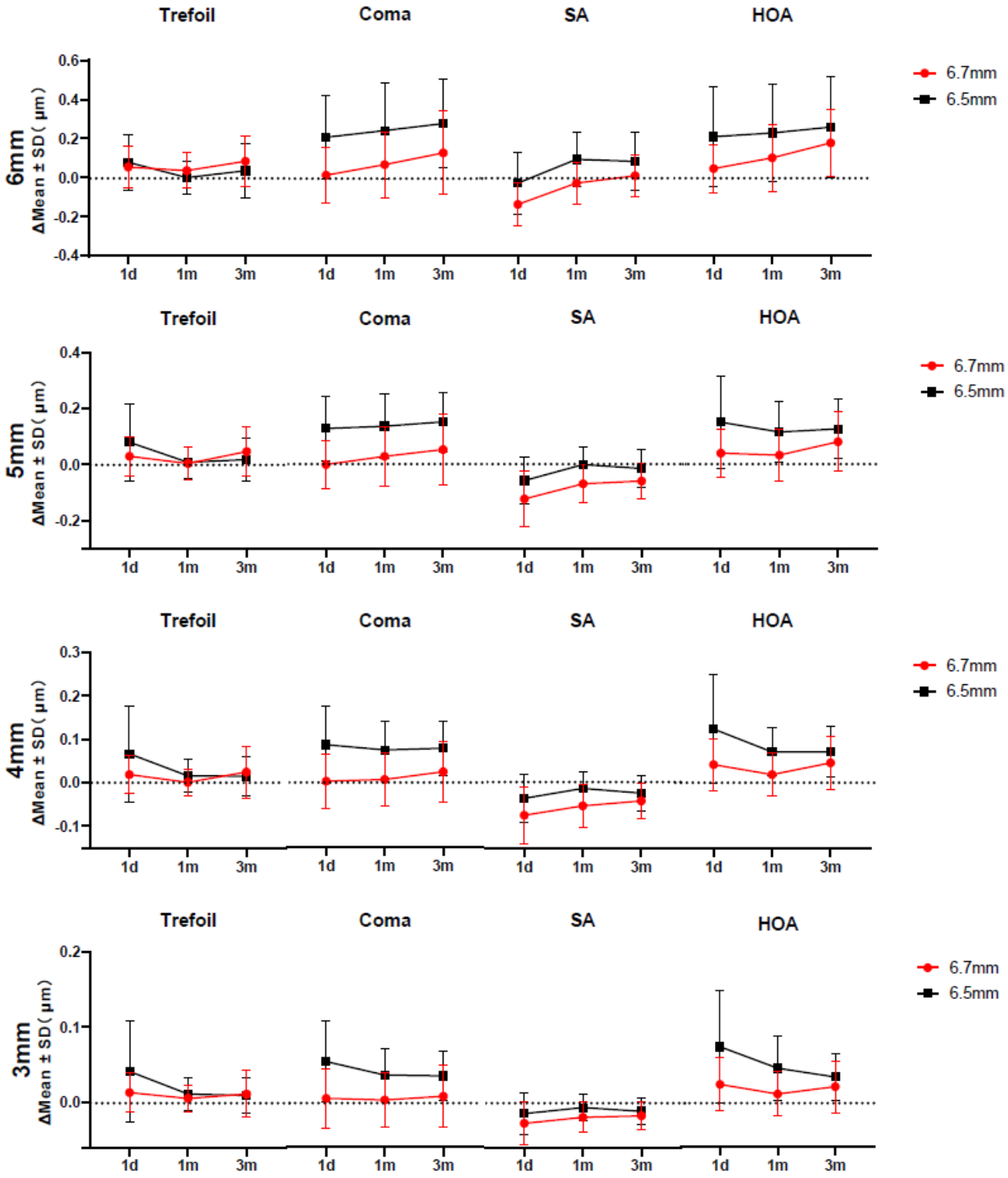


Figure 2

Induced changes (Δ) in corneal HOAs after SMILE in the 6.7- and 6.5-mm programmed OZD groups. Induced changes in trefoil, coma, spherical aberration (SA), and total higher-order aberration (HOA) are shown at 3-, 4-, 5-, and 6-mm analysis diameters at 1 day, 1 month, and 3 months postoperatively. Δ was calculated as the postoperative value minus the corresponding preoperative value. Data are presented as mean ± SD. OZD = optical zone diameter; SA = spherical aberration; HOA = higher-order aberration.

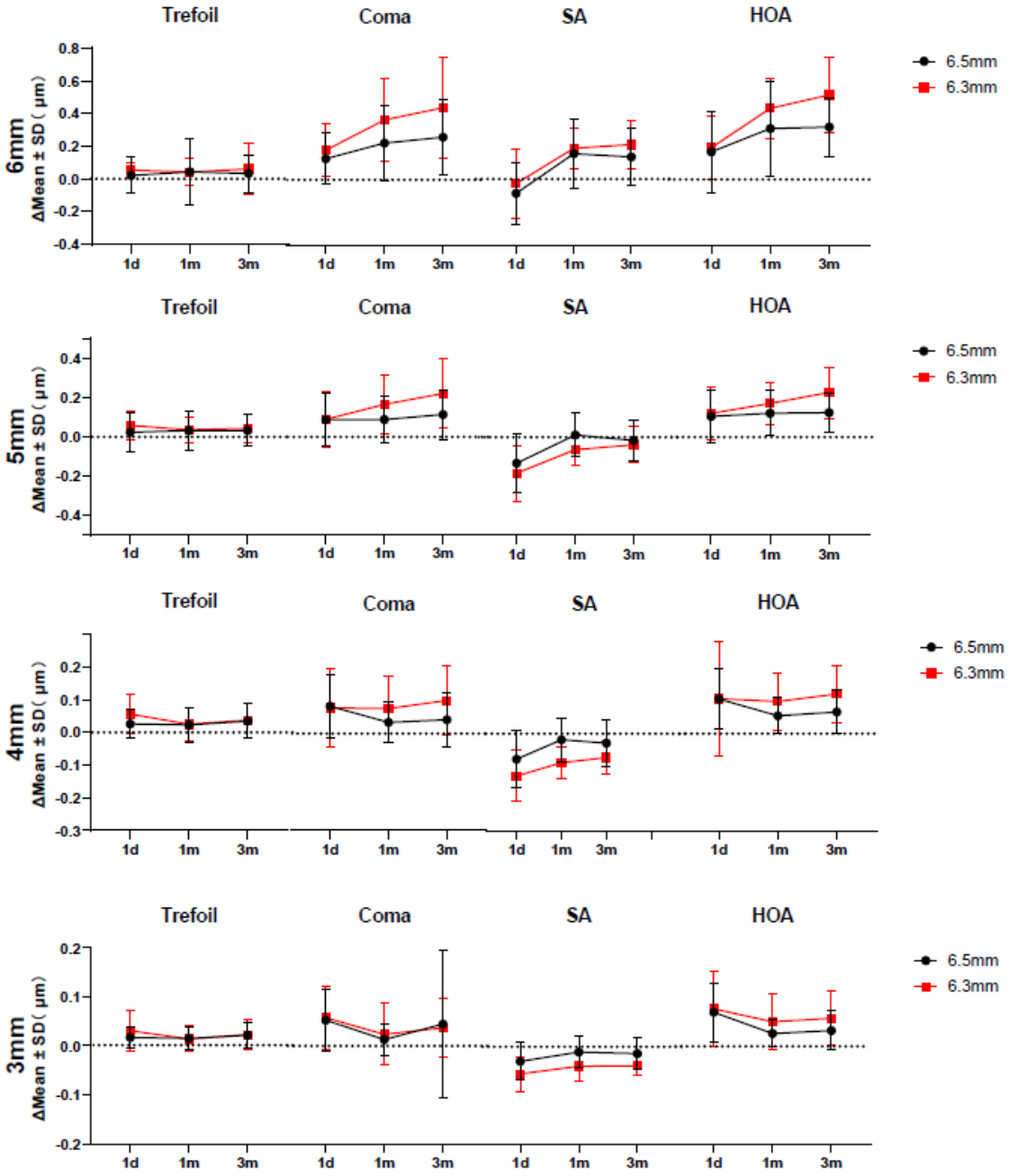


Figure 3

Induced changes (Δ) in corneal HOAs after SMILE in the 6.5- and 6.3-mm programmed OZD groups. Induced changes in trefoil, coma, spherical aberration (SA), and total higher-order aberration (HOA) are shown at 3-, 4-, 5-, and 6-mm analysis diameters at 1 day, 1 month, and 3 months postoperatively. Δ was calculated as the postoperative value minus the corresponding preoperative value. Data are presented as mean ± SD. OZD = optical zone diameter; SA = spherical aberration; HOA = higher-order aberration.

Supplementary Files

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- SupplementaryTableS2.docx