Corneal Higher-Order Aberrations Following Small-Incision Lenticule Extraction Procedure

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PURPOSE. To investigate the amount of lenticule decentration following small-incision lenticule extraction (SMILE) by using the Keratron Scout tangential topography difference map, and the relationship between the magnitudes of total decentration and induced corneal higher-order aberrations (HOAs).

METHODS. This retrospective observational case series study analyzed decentration values obtained from the Keratron Scout tangential topography difference map of 360 eyes (360 patients) that underwent SMILE. Root mean square total HOAs, third order coma aberration, fourth order spherical aberration, as well as individual coefficients for vertical and horizontal coma were measured preoperatively and 3-months postoperatively. Simple linear regression analysis and piecewise regression models were used to determine the relationship between the magnitudes of total decentration and induced corneal HOAs.

RESULTS. The mean total decentration distance from the corneal vertex was 0.36 ± 0.22 mm (range, 0.02–1.27 mm). There were significant differences in total HOAs, coma, vertical and horizontal comas, and spherical aberration between preoperative and 3-month postoperative assessments. Significant relationships between the magnitudes of total decentration and induced corneal HOAs were noted. Subgroup analysis according to the degree of total decentration (group I, total centered displacement ≤0.335 mm; and group II, total centered displacement >0.335 mm) revealed that induced changes in total HOAs, coma, vertical coma, and spherical aberration were significantly larger in group II than in group I.

CONCLUSIONS. A minimal degree of decentration was closely related to a smaller induction of corneal HOAs. Efforts to optimize centration are critical for achieving better surgical outcomes in SMILE.

Keywords: small-incision lenticule extraction, decentration, corneal higher-order aberrations

Small-incision lenticule extraction (SMILE) using only a femtosecond laser is a new technique for the correction of myopia and myopic astigmatism.1,2 This procedure extracts the refractive lenticule through a small corneal incision ranging from 2 to 5 mm, with the absence of a flap and the preservation of the anterior-most stromal lamellae and Bowman’s layer.1,2 Thus, SMILE provides many benefits over laser-assisted in situ keratomileusis (LASIK), because it has no risk for traumatic flap displacement and reduces postoperative dry eye symptoms due to reduced damage to corneal subbasal nerve density.4,5 Although two studies reported that topography-guided or wavefront-guided LASIK provided superior results with regard to visual acuity and refractive errors over SMILE for myopic correction,6,7 clinical outcomes with respect to safety and efficacy were comparable between the two procedures.8–10

The SMILE procedure takes place under mild suction and does not involve an eye tracking system.11,12 Currently, the alignment of the refractive lenticule relies much on the patients’ cooperation, which enables a coaxial fixation to the light at the moment of application of suction, resulting in lenticule formation centered on the corneal vertex of the coaxially fixating eye. That is, optical zone centration in myopic SMILE is targeted to the coaxial corneal light reflex, also known as the first Purkinje image, which is a major advantage in SMILE.13,14
Accurate centration of the treatment zone during corneal refractive procedures plays a crucial role for achieving good visual outcomes. Visual axis, pupil center, and corneal vertex were suggested as the treatment center for refractive surgery. Although the corneal intercept of the visual axis has been recommended as the ideal centration point, it is difficult to precisely locate this point in practice. The pupil center is the corneal intercept of the line of sight, defined as the line joining the fixation point to the center of the entrance pupil. However, the pupil center is unstable because it shifts with changes in pupil size. The corneal vertex is the other major choice as the centration reference in other modalities. Corneal vertex measured using videokeratoscopy is regarded as a morphological reference to center corneal refractive procedures. The most extensively used way to determine corneal vertex is to determine the corneal coaxial light reflex (first Purkinje image). The coaxially sighted corneal light reflex is the corneal intercept of the line joining the fixation point to the corneal center of curvature. Pandé and Hillman recommended that the corneal coaxial light reflex should be centered during refractive surgery because it is closer to the corneal intercept of the visual axis than the pupil center and, as such, demonstrates superior optical results to entrance pupil centration. Furthermore, corneal vertex centration has been reported to be superior than entrance pupil centration regarding the induced ocular aberrations and asphericity.

With regards to SMILE, decentrations have been reported in the literature due to presumed difficult patient cooperation and docking.

In the current study, we aimed to investigate the amount of lenticule decentration following SMILE and to evaluate the relationship between the magnitudes of decentration and preoperative pupillary offset (angle kappa) on tangential topography difference maps obtained with the Keratron Scout (Optikon, Rome, Italy). Furthermore, because no established studies have been published investigating the relationship of the amount of decentration with tangential maps derived from small cone Placido-based topography to induced corneal aberrations, we wanted to determine whether the rate of induction of aberrations is comparable between small and large decentrations. Finally, we compared corneal higher-order aberrations (HOAs) between the two subgroups based upon segmented regression analysis and investigated the relationship between the magnitudes of total decentration and induced corneal HOAs in each subgroup.

**PATIENTS AND METHODS**

This was a retrospective observational case series of consecutive SMILE patients treated between May 2015 and December 2016. The study was performed with the approval of the Institutional Review Board of Yonsei University College of Medicine (Seoul, South Korea). All study conduct adhered to the tenets of the Declaration of Helsinki and followed good clinical practices. All patients provided written informed consent to allow their medical information to be included for analysis and publication.

Patients were included in the analyses if they had stable refraction at least 1 year prior to surgery, preoperative corrected distance visual acuity (CDVA) of 20/25 or better, and a normal preoperative corneal topography. Patients were excluded from analyses if they had any optical opacities or pathology on slit-lamp examination, previous corneal surgeries, ocular trauma, or intraocular surgery, severe dry eye, corneal disease, or ocular infection, and collagen vascular/autoimmune diseases. One eye from each patient was included in the analysis via randomization between the two eyes.

**Small-Incision Lenticule Extraction**

All SMILE treatments were performed using the 500-kHz VisuMax femtosecond laser (software version 2.4.0; Carl Zeiss Meditec, Jena, Germany) by the same surgeon (DSYK). Intended depth of the superior cap was set between 120 and 140 μm, and the length of the side cut was set to 2 mm. The optical zone diameter used was between 6.2 and 7.2 mm.

During the SMILE procedure, optical zone centration is targeted to the coaxial corneal light reflex. At the moment of contact between the curved contact lens and the cornea, a meniscus tear film appears, at which point the patient is able to see the fixation target clearly because the vergence of the fixation beam is adjusted according to the individual eye's refraction. At this point, the surgeon instructs the patient to look directly at the green light and, once in position, the corneal suction ports are activated to fixate the eye in this position. In this way, the patient aligns the visual axis and, hence, the corneal vertex to the vertex of the contact lens, which is centered to the laser system and the center of the lenticule to be created. All procedures were carried out with spot spacing of 4.5 μm and pulse energies between 100 to 115 nJ. After successful femtosecond laser cutting, the refractive lenticule of the intrastromal corneal tissue was extracted through the side-cut opening by using forceps.

**Measurements**

All patients underwent a preoperative ophthalmic examination that included uncorrected distance visual acuity (UDVA) and CDVA, autorefraction, manifest refraction, slit-lamp examination (Haag-Streit, Gartenstadtstrasse, Koniz, Switzerland), IOP measurement (noncontact tonometer, NT-530; NCT Nidek Co., Ltd., Aichi, Japan), dilated fundus examination, corneal thickness by using the Scheimpflug camera (Pentacam; OCULUS Optikgeräte GmbH, Wetzlar, Germany), and corneal topography and derived corneal wavefront aberrations by using the Keratron Scout (Optikon).

Changes in the corneal wavefront aberration at pupil diameter of 6 mm were implemented using the Keratron Scout software, based on corneal topographic data obtained with the Keratron Scout topographer. The root mean square (RMS) values of the third order coma aberration, fourth order spherical aberration, and total HOAs were calculated. The RMS value of total HOAs was analyzed up to the seventh order by expanding the set of Zernike polynomials. The individual coefficients of vertical and horizontal coma were also analyzed.

Follow-up examinations were performed 3 months postoperatively with UDVA, CDVA, Scheimpflug camera, Keratron Scout, and slit-lamp examination. All measurements were performed by a single experienced operator. The illumination in front of the Keratron Scout corresponded to the illuminance under the femtosecond laser and was measured with the IL-1700 Radiometer to be 6 lux (low-light conditions).

**Centration Analysis**

A difference map of the tangential curvature was generated for each eye by using the preoperative and 6-month postoperative Keratron Scout exams. The method used in this study is similar to the method that Reinstein et al. used in their recent published study investigating optical zone centration accuracy. The difference maps were imported into Microsoft PowerPoint 2010 (Microsoft Corporation, Redmond, WA), and a previously prepared grid and set of concentric circles was overlaid. The lines of the grid were distributed equally with 0.1-mm steps and the concentric circles had radii increasing in 0.1-mm steps, between 2.5- and 3.5-mm radii. The difference
map was magnified on the screen and made as large as possible so that the center of the optical zone could be confidently visualized within half a step. The optical zone was defined on the tangential topography difference map as the central zone up to the midperipheral power inflection point. The best-fitting circle and central grid were superimposed on the optical zone to determine the location of the optical zone center with reference to the corneal vertex. The topographic graph displayed the (0, 0) point as the corneal vertex and a coordinate (x, y) in millimeters for any point relative to the (0, 0) point. The x coordinates obtained for left eyes were reflected in the vertical axis (multiplied by −1), so that nasal/temporal characteristics of right and left eyes could be combined. Positive x values indicated nasal decentration, and negative x values indicated temporal decentration. The x and y coordinates of the optical zone centration were plotted on a 360° polar plot to show the location of the center of the optical zone relative to the corneal vertex. Centration was analyzed in terms of horizontal, vertical, and total decentration. Furthermore, we measured preoperative pupillary offset (angle kappa), which was generated by subtracting the pupil center coordinate from corneal vertex.

**Statistical Analyses**

Statistical analysis was performed using the R statistical software version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria). Differences were considered statistically significant when the *P* values were less than 0.05. The Kolmogorov-Smirnov test was used to confirm data normality. Piecewise regression models were used to determine the inflection points at which slope changes abruptly and to estimate level and trend between those having decentred distances greater than the breakpoint and those less than the breakpoint by determining the breakpoint between the magnitudes of total decentration and induced total HOAs, coma, and spherical aberrations. Subgroups were split according to the value (estimated breakpoint) suggested by piecewise regression analysis. Independent *t*-tests were used to compare clinical variables, preoperative pupillary offset, and induced corneal HOAs between the two subgroups. Paired *t*-tests were used to evaluate the differences between preoperative and 3-month-postoperative corneal HOAs in each subgroup. Simple linear regression analyses were used to determine the associations between the preoperative pupillary offset and decentration, between the magnitudes of total decentration and induced corneal HOAs, and between clinical variables (optical zone diameter and change in manifest refraction spherical equivalent [ΔMRSE]) and induced corneal HOAs in each subgroup.

**RESULTS**

A total of 360 eyes of 360 patients satisfied the inclusion criteria and were included in analyses. Table 1 summarizes baseline characteristics and results for the preoperative pupillary offset and decentration. All surgical procedures were uneventful, and no postoperative complications affecting vision were observed during the observation period.

The results of piecewise linear regression analysis revealed the estimated breakpoint between the total decentration and induced spherical aberration to be 0.335 mm, as evident from the locally weighted scatterplot smoothing plot (Fig. 1, left). A decentration amount of 0.335 mm was used to differentiate group I and group II (group I, total decentred displacement ≤0.335 mm; and group II, total decentred displacement >0.335 mm). No significant relationship between the magnitude of total decentration and induced spherical aberration was noted when decentration was smaller than 0.335 mm, whereas there was a significant positive relationship when decentration was larger than 0.335 mm (Fig. 1, right).

According to the results of the piecewise linear regression analysis, regression coefficients below and above the estimated breakpoint were −0.033 and 0.225, respectively. Accordingly, the slope of the linear fit above 0.335 mm was 0.192. No clear breakpoints were detected between the total decentration and induced total HOAs or between the total decentration and induced coma.

Table 2 shows results for subgroup analysis, according to degree of the total decentred displacement. There were no significant differences in all parameters between the subgroups, with the exception of preoperative pupillary offset (angle kappa), preoperative pupillary offset (y-axis), and decentred displacement (horizontal, vertical, and total). In the subgroup analysis of corneal aberrations, induced changes in total HOAs, coma, vertical coma, and spherical aberration were significantly larger in group II than group I (*P* < 0.001 for total HOAs; *P* = 0.001 for coma; *P* = 0.001 for vertical coma; and *P* = 0.001 for spherical aberration) (Table 3).

There was a significant relationship between the preoperative pupillary offset and decentration (*R*^2^ = 0.017, *P* = 0.012 for preoperative offset [x-axis] versus horizontal decentred displacement; and *R*^2^ = 0.024, *P* = 0.003 for preoperative offset [y-axis] versus vertical decentred displacement). Preoperative offset (x-axis) in group II was related with horizontal decentred displacement (*R*^2^ = 0.024, *P* = 0.046), whereas preoperative offset (y-axis) in group I was related with vertical decentred displacement (*R*^2^ = 0.021, *P* = 0.045) (Fig. 2).

Regression analysis found a significant relationship between the magnitudes of total decentration and induced total HOAs, coma, spherical aberrations, vertical coma, and horizontal coma (*P* < 0.001 for total HOAs, coma, spherical aberration, and vertical coma; and *P* = 0.006 for horizontal coma). In the subgroup analysis, no associations were found between the total decentration and induced corneal total HOAs in group I (*P* = 0.454 for total HOAs; *P* = 0.697 for coma; *P* = 0.451 for spherical aberration; *P* = 0.193 for vertical coma; and *P* = 0.210 for horizontal coma) (Fig. 3). On the other hand, there was a significant relationship between the total decentration and induced corneal aberations in group II (*R*^2^ = 0.053, *P* = 0.003 for total HOAs; *R*^2^ = 0.058, *P* = 0.002 for coma; *R*^2^ = 0.049, *P* = 0.005 for spherical aberration; and *R* = 0.122, *P* < 0.001 for vertical coma), with the exception of horizontal coma (*R*^2^ = 0.016, *P* = 0.110).

Figure 4 and 5 depict scatter plots between variables (optical zone diameter and ΔMRSE) and induced corneal HOAs in each subgroup.

**DISCUSSION**

In the current study, the mean total decentred distance from the corneal vertex on the tangential topography difference map of the Keratron Scout was 0.36 ± 0.22 mm (range, 0.02–1.27 mm). Regarding the optical zone centration in myopic SMILE, recently published articles have shown that the achieved centration of SMILE was relatively good. The decentred distance from the corneal vertex was 0.20 ± 0.11 mm (range, 0.00–0.50 mm) by using the tangential topography difference maps with Atlas topography (Carl Zeiss Medite AG, Jena, Germany). In another study, the decentred distance from the corneal vertex by using the pachymetry difference maps with the Scheimpflug Camera was 0.52 ± 0.21 mm (range, 0.00–1.13 mm) when evaluating the centra-
Corneal thickness difference maps may not be accurate because the anterior surface has been substantially altered after refractive surgery, and thus, the normal-to-the-surface calculation and direction in which corneal thickness is calculated are not comparable between preoperative and postoperative displays. The use of elevation maps is problematic because a reference is required, which must be fit to the surface and does not require centration of that reference relative to the surface in the fitting protocols. In addition, determining centration with the sagittal curvature difference maps obtained from the Scheimpflug camera may be a source bias, especially if the line of sight has changed between the preoperative and postoperative scans due to the modification of the anterior surface. Different centration references should also be considered when comparing the decentration after surgery, because the pupil center shifts with changes in pupil size under photopic, mesopic, and pharmacologically dilated conditions. On the other hand, analyzing a tangential curvature difference maps, such as in our study, avoids the limitations related to the direction of the subtraction or noncentered references. Reinstein et al. used the same tangential curvature difference map methodology and the same grid and concentric circle overlay. The only difference was that they used the Atlas, whereas the Keratron Scout was used in the present study. The Keratron Scout, one of the small-cone Placido disc topographers, has a shorter working distance and projects a greater number of rings onto the cornea compared with the Atlas topographer, one of the large-cone Placido disc topographers. A prospective agreement study comparing the Atlas and Keratron Scout would allow a more thorough investigation of the centration analysis method.

We evaluated the relationship between the magnitudes of decentration and pupillary offset (angle kappa) on tangential topography difference maps obtained with the Keratron Scout. Significant relationships were noted between the pupilary offset and decentration (preoperative offset \([x-axis]\) versus horizontal centered displacement, and preoperative offset \([y-axis]\) versus vertical centered displacement). According to one previous study presenting a theory to transform Zernike coefficients analytically with regard to the translation of the pupil center, the authors theoretically analyzed the impact of applying a translational pupillary offset in various aberration measurements and calculated the theoretical interrelationship between various higher and lower order aberrations after offset implementation. Furthermore, because aberrations are measured on the pupil and not on the corneal vertex, investigating the relationship between the pupillary offset and decentration is crucial during the SMILE procedure.

In the present study, we demonstrated the estimated breakpoint between the total decentration and induced spherical aberration, which was 0.335 mm. After categoriza-
Decentration of Optical Zone and Induced HOAs Following SMILE

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Abstract

The purpose of this study was to evaluate the decentration of optical zone and induced corneal HOAs in eyes that underwent SMILE. The study included 360 eyes of 184 patients. The study group was divided into two groups: group I, total decentered displacement \( \leq 0.335 \text{ mm} \); and group II, total decentered displacement \( > 0.335 \text{ mm} \). The average optical zone size was 6.7 \text{ mm}, and the analysis diameter for corneal aberrations was 6.0 \text{ mm}. The average preoperative pupillary offset was 0.13 \text{ mm} in the y-axis and 0.12 \text{ mm} in the x-axis. The study results showed a significant relationship between the optical zone diameter and induced corneal HOAs, with the exception of horizontal coma. In group I, there were significant relationships between the optical zone diameter and induced corneal HOAs, with the exception of horizontal coma. Furthermore, an optical zone of 6.7 \text{ mm} was not selected during treatment in all cases; thus, although the tolerance to decentration would likely be just 0.1 \text{ mm} for a small optical zone treatment (6.2 \text{ mm}), it may be up to 0.6 \text{ mm} for a large optical zone treatment (7.2 \text{ mm}), with an average close to 0.35 \text{ mm}.

Keywords: SMILE, corneal HOAs, decentration.
≤0.335 mm showed more stable behavior with regards to induced corneal HOAs against the optical zone diameter and refractive error changes than eyes that had a total decentered displacement >0.335 mm.

In one study evaluating the effects of ablation decentration on the induction of HOAs in active eye-tracker-assisted myopic photorefractive keratectomy, large decentration from the center of the entrance pupil was associated with greater induction of total HOA, coma, and spherical aberration.34 Consistent with our study, ablation decentration >0.30 mm induced significantly more total HOAs, coma, and spherical aberration, when compared with decentration <0.15 mm during photorefractive keratectomy.34 Even subclinical decentrations <1.0 mm can cause increased coma-like and spherical-like HOAs, along with increased lower-order aberrations, indicating some correlation between decentration and induced wavefront aberrations.16 Concerning LASIK, greater HOAs induction is associated with ablation decentration, which could be dependent on the excimer laser platform, variation in the transition zone, or different centration references.25,32,35,36 Myopic LASIK centered on the coaxially sighted corneal light reflex was more effective and safe than LASIK centered on the pupil, with a significantly lower induction of RMS coma and RMS total HOAs.26 On the other hand, one recent study evaluating the centration following the SMILE procedure found no statistically significant difference in induced ocular aberrations, rather than purely corneal aberrations.25

### TABLE 3. Subgroup Analysis of Corneal HOAs in Eyes That Underwent SMILE, According to Degree of Total Decentered Displacement

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I (196 Eyes, Total Decentered Displacement ≤0.335 mm)</th>
<th>Group II (164 Eyes, Total Decentered Displacement &gt;0.335 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>RMS total HOAs, µm</td>
<td>0.50±0.12</td>
<td>0.54±0.15</td>
</tr>
<tr>
<td>RMS coma, µm</td>
<td>0.28±0.13</td>
<td>0.29±0.16</td>
</tr>
<tr>
<td>Vertical coma, µm</td>
<td>−0.001±0.23</td>
<td>−0.09±0.23</td>
</tr>
<tr>
<td>Horizontal coma, µm</td>
<td>0.01±0.21</td>
<td>−0.01±0.22</td>
</tr>
<tr>
<td>RMS spherical aberration, µm</td>
<td>0.29±0.11</td>
<td>0.31±0.13</td>
</tr>
</tbody>
</table>

Results are expressed as means ± standard deviation. Δ, change (Post – Pre); RMS, root mean square; HOAs, higher-order aberrations (3rd to 7th order).

* Comparison between preoperative and postoperative corneal aberrations.
† Comparison between the two groups regarding changes in corneal aberrations.

### FIGURE 3. Simple linear regression of changes in corneal aberrations with total decentered displacement in eyes that underwent SMILE, according to degree of the total decentered displacement. Group I, total decentered displacement ≤0.335 mm; and group II, total decentered displacement >0.335 mm.
FIGURE 4. Simple linear regression of changes in corneal aberrations with optical zone diameter. Group I, total decentered displacement ≤0.335 mm; and group II, total decentered displacement >0.335 mm.

FIGURE 5. Simple linear regression of changes in corneal aberrations with change in manifest refraction spherical equivalent. Group I, total decentered displacement ≤0.335 mm; and group II, total decentered displacement >0.335 mm.
Decentration of Optical Zone and Induced HOAs Following SMILE

eyes with decentered distances greater than 0.30 mm to those within 0.30 mm.12

Although the present study had several limitations, including its retrospective design, it is the first study to investigate lenticule decentration following the SMILE procedure on the tangential topography difference map of the Keratron Scout. On the basis of the current results, we concluded that minimal decentration in myopic SMILE is related to smaller induction of total HOAs, coma, vertical coma, horizontal coma, and spherical aberration. Furthermore, having decentered distances less than 0.335 mm could yield more satisfactory results with regard to total HOAs, coma, vertical coma, and spherical aberration. Additionally, considering that preoperative pupillary offset was significantly positively related with decentration, surgeons should be cautious when performing SMILE for patients with relatively higher preoperative pupillary offset. Because the lenticule thickness and volume (excise cornea) increased quadratically and with the fourth power of the optical zone, respectively, aiming for manual, semiautomated, and automated improvements in centration would help to ameliorate induction of aberrations in SMILE, thus resulting in improvement in visual quality.

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