

1 **Regional changes in corneal shape over a 6 month follow-up**
2 **period post FS-LASIK**

3

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20 **Conflict of Interest**

21 The authors indicate no financial conflict of interest.

22

1 **Running title**

2 Regional changes in corneal shape post FS-LASIK

3

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8 **Synopsis:**

9 Corneal shape changes after LASIK followed different trends in different regions (from
10 central to peripheral area). Over the follow-up period, the shape changes were small
11 and followed a reverse trend.

12

13 Number of words: 3639

1 **Abstract**

2 **PURPOSE:** To assess the regional changes in corneal shape following FS-LASIK in
3 patients with different myopia extents.

4 **SETTING:** Eye Hospital, WenZhou Medical University, WenZhou, China.

5 **DESIGN:** Retrospective case series.

6 **METHODS:** A retrospective study of 608 myopic eyes treated with FS-LASIK was
7 conducted to assess the shape changes within different corneal regions following
8 surgery. Corneal curvature was measured in the central region (0-3mm diameter),
9 pericentral region (3-6mm diameter) and peripheral region (6-9 mm diameter) before
10 (pre) and after surgery (1 week: pos1w to 6 months: pos6m).

11 **RESULTS:** During the 6 month follow-up, the anterior cornea became steeper in
12 central and pericentral regions, but flatter in the peripheral region ($p < 0.01$),
13 representing a partial, gradual, yet significant reversal of the immediate change in
14 corneal shape after laser ablation. In contrast, the posterior surface experienced much
15 less change than the anterior surface, with the cornea becoming slightly flatter ($p < 0.01$)
16 in the central region at pos1w, and steeper elsewhere ($p < 0.05$), and remaining stable in
17 the rest of follow-up. On the other hand, anterior astigmatism experienced significant
18 decreases in the central region (pos1w, $p < 0.01$) and slight increases in the peripheral
19 region (pos1w, $p < 0.01$), and that remained stable over the follow-up period. In contrast,
20 posterior astigmatism experienced little and non-significant changes throughout follow-
21 up ($p > 0.05$).

22 **CONCLUSIONS:** Post-surgery shape changes that were different in different regions,
23 the follow-up period saw shape changes in individual corneal regions that represented
24 reverse trends but were much smaller than the short-term changes observed 1 week after
25 surgery.

26

27 **Keywords:** FS-LASIK, Corneal topography

28

1 **Introduction**

2 Most Refractive surgeries (RS), which reshape the anterior corneal surface to adjust the
3 refractive power of the eye, are becoming increasingly popular worldwide. Laser in situ
4 keratomileusis (LASIK) is currently the most common refractive surgery procedure,
5 known to be relatively safe and effective ¹⁻⁴. The refractive outcome of LASIK, which
6 depends on the post-operative corneal shape, is affected by several factors including the
7 surgery parameters (flap thickness and diameter, and ablation depth and profile), the
8 value of intraocular pressure (IOP), wound healing (causing alteration in corneal tissue
9 ultrastructure and hence mechanical stiffness) ⁵, and possible post-operative
10 inflammation.

11
12 The introduction of new technologies has enabled better control of the ablation profile,
13 improved energy delivery to corneal tissue and development of more effective ablation
14 algorithms. With these developments, 93% of eyes undergoing LASIK achieve a ± 1.00
15 D refractive outcome ⁶, and reach an acceptable visual acuity with few debilitating
16 visual complaints ⁷. Further, while current surgery planning is largely based on a
17 population-based normative response, corneal reaction to surgical ablation is
18 individualized, possibly causing residual refractive error, refractive regression, and
19 even corneal ectasia ⁸. The current increasing emphasis on customization of treatment
20 make it important to characterize corneal shape changes caused by the surgery.

21
22 Several earlier studies sought to evaluate the topographical changes after LASIK and
23 predict corneal response to surgical tissue subtraction ⁹⁻¹². These studies relied on
24 interpretation of corneal topography to analyze the changes in curvature, asphericity,
25 aberrations, whole corneal thickness, epithelium thickness and elevation of posterior
26 cornea ¹²⁻¹⁷. In these studies, the cornea was covered as one region without considering
27 that different sub-regions could be affected differently. This study attempts to address
28 this shortfall through a retrospective analysis of topography data with emphasis on the
29 regional variation in response to surgery, and with attention given to the shape changes

1 in a 6 months follow up period. The analysis covers separately the central, pericentral
2 and peripheral regions of both the anterior and posterior surfaces, and considers the
3 induced, and sometimes unexpected, modifications of corneal shape caused by LASIK.

4 5 **Materials and Methods**

6 7 *Study participants*

8 Patients who had undergone femtosecond assisted LASIK for myopia between -0.75
9 and -10.75 D and/or astigmatism between 0.00 and -3.00 D were evaluated
10 retrospectively, and records were included if the patients had completed a 6 month-long
11 post-operative follow-up including ophthalmologic examinations before surgery (pre),
12 and 1 week (pos1w), 1 month (pos1m), 3 months (pos3m) and 6 months (pos6m) post-
13 LASIK. 608 patients (303 male and 305 female, age: 22.8 ± 5.5 years) who had
14 undergone LASIK were included in the study. Since bilateral corneas are correlated
15 with each other and behave with mirror symmetry as reported in our earlier study ¹⁸,
16 only the right eyes were selected for analysis to avoid this confounding effect.

17
18 The protocol for the retrospective analysis was reviewed and approved by the ethic
19 Committee of the Eye Hospital, WenZhou Medical University. The LASIK procedure,
20 and pre-operative and post-operative ophthalmologic examinations were performed at
21 the Refractive Surgery Center of the Eye Hospital. In the LASIK procedure, 90-110 μm
22 thick, 8.0-9.0 mm diameter flap with a superior hinge was created using two
23 femtosecond laser machines (FEMTO LDV, Ziemer Ophthalmic Systems AG, Port,
24 Switzerland) or (IntraLase iFS150, Abbott Medical Optics, CA, USA). A 0.4-mm-thick
25 flap hinge was chosen in the former, and a 45° hinge with a 70° side-cut angle was set
26 up in the latter. This step was followed by tissue ablation using the Schwind Amaris
27 750 excimer laser (Schwind eye-tech-solutions, Kleinostheim, Germany).

1 ***Data Acquisition***

2 The following clinical observations were recorded before surgery and after by 1 week,
3 1 month, 3 months and 6 months: refractive error (RE), corneal thickness data, and
4 elevation data of corneal anterior and posterior surfaces. Surgical parameters including
5 refractive error correction (REC), which consists of spherical (S) and cylindrical (C)
6 corrections, spherical equivalent (SE), astigmatism axis, and optical/transition zones
7 (OZ/TZ) were excerpted from medical records. Manifest RE before and 1 week and 6
8 months after surgery was measured with a phoropter (Nidek RT-2100; Nidek Inc,
9 Gamagori, Japan) and converted to SE. According to SE measured pre-surgery,
10 participants were divided into three groups with low myopia ($-0.50D > SE \geq -3.00D$, 59
11 eyes), moderate myopia ($-3.00D > SE \geq -6.00D$, 323 eyes) and high myopia group ($-$
12 $6.00D > SE$, 226 eyes). Corneal thickness and elevation were provided by a Pentacam
13 HR (OCULUS Optikgerate GmbH, Wetzlar, Germany; Software Version 6.02r23). The
14 best Pentacam measurement in each follow-up stage, with an instrument-generated
15 quality factor of at least 95% and 90% for the anterior and posterior surfaces,
16 respectively, was selected for analysis.

17

18 Elevation data with reference to a plane that is tangential to the corneal surface at the
19 apex and perpendicular to the ocular longitudinal axis was exported from Pentacam. As
20 some of the peripheral data were missing because of the eyelids and eyelashes, only
21 elevation data within the 9mm diameter central region were used in analysis. This
22 region included approximately 6400 data points with 0.1mm spacing in the horizontal
23 (temporal-nasal) and vertical (inferior-superior) directions. The elevation data $z(x, y)$ at
24 each point (x, y) on either the anterior or posterior corneal surface with Cartesian
25 coordinates was defined as the Z distance from corneal surface to an XOY plane passing
26 through the origin point, at which the instrument axis intercepts the cornea, which was
27 described in a previous study¹⁸ (Figure 1).

28

1 ***Computation of corneal curvature***

2 The elevation data of corneal topography within an aperture of 9 mm diameter was
3 imported into a bespoke Matlab code for surface fitting with a set of Zernike
4 polynomials up to order 10. The first and second derivatives of this Zernike expression
5 were then derived to calculate the principal curvatures and their corresponding principal
6 directions at each point on corneal surface, based on the differential geometry theory ¹⁹.
7 The local power of corneal surface was obtained as

8
$$P_i(x, y) = (n' - n) \cdot \kappa_i(x, y), \quad i = 1, 2$$

9 where $\kappa_i(x, y)$ is the principal curvature at the location (x, y) , κ_1 and κ_2 are the min and
10 max principal curvatures, respectively, n and n' are the refractive indexes of the medium
11 separated by corneal surface. Then, the local corneal surface astigmatism $A(x, y)$ was
12 given by

13
$$A(x, y) = P_2(x, y) - P_1(x, y)$$

14 we converted the local corneal surface power to local power vector form ²⁰ by using the
15 following equations:

16
$$M(x, y) = \frac{P_2(x, y) + P_1(x, y)}{2}$$
$$J_0(x, y) = -\frac{A(x, y)}{2} \cos 2\alpha_1(x, y)$$
$$J_{45}(x, y) = -\frac{A(x, y)}{2} \sin 2\alpha_1(x, y)$$

17 where $\alpha_1(x, y)$ is the principal direction of the min principal curvature, $M(x, y)$ is the
18 local spherical equivalent, and $J_0(x, y)$ and $J_{45}(x, y)$ are the local astigmatism at 0-degree
19 and 45-degree meridians, respectively. Numerical integration was used to determine the
20 mean values of the power components M , J_0 and J_{45} over three corneal sub-regions;
21 central 0-3mm, pericentral 3-6 mm and peripheral 6-9 mm.

22

23 Keratometry, normally calculated based on topography data obtained in the central 3

1 mm diameter zone, is used to describe the central corneal shape ²¹. Further, most
2 refractive surgery procedures (such as LASIK and SMILE) consider the optical zone to
3 be around the 6 mm diameter area. In addition, there is high likelihood of peripheral
4 data beyond the 9 mm diameter region being missed due to interference by eyelids and
5 eyelashes ^{18,22}. For these reasons, the cornea's topography data was divided in this study
6 into three regions with diameters 0-3, 3-6 and 6-9 mm, respectively.

7

8 ***Statistical analysis***

9 Commercial software SPSS Statistics (version 20.0, IBM, Inc.) was utilized for all
10 statistical analyses. Analysis of variance (ANOVA) was carried out to compare the
11 shape parameters among the three groups with different myopia severity, while
12 MANOVA of repeated measurements was employed in the analysis of data obtained at
13 different follow-up periods for the same participant. Correlation analyses were assessed
14 using the Pearson's or Spearman linear correlation factor according to a normal
15 distribution test.

16

17 **Results**

18

19 Before surgery, SE was -2.38 ± 0.55 D, -4.62 ± 0.86 D and -7.73 ± 1.23 D in low, moderate
20 and high myopia groups, respectively. After the surgery procedure, RE showed some
21 limited hyperopia (pos1w: 0.09 ± 0.40 D, 0.23 ± 0.41 D and 0.32 ± 0.54 D for the three
22 myopia groups), and this hyperopia decreased during the follow-up period in moderate
23 and high myopia groups (pos6m: 0.12 ± 0.30 D, 0.19 ± 0.38 D and 0.13 ± 0.58 D). The
24 change in RE at pos6m compared with pos1w was statistically significant in high
25 myopia group (-0.19 ± 0.53 D, $p < 0.01$), while not significant in low and moderate
26 myopia groups (0.02 ± 0.39 D, $p = 0.806$; -0.04 ± 0.41 D, $p = 0.078$).

27

28 ***Changes in spherical refractive power***

29 Within the 0-3mm diameter anterior central region, the cornea became flatter with
30 surgery (42.67 ± 2.29 D vs 48.18 ± 1.58 D; $p < 0.01$), then gradually steeper post-surgery

1 in all three myopic groups (43.03 ± 2.13 D for pos6m; $p < 0.01$, Table 1), Figure 2A,C,E
2 (black lines). The steepening at pos6m compared with pos1w was statistically
3 significant: 0.14 ± 0.24 D (45.37 ± 1.54 D vs 45.22 ± 1.61 D; $p < 0.01$), 0.21 ± 0.31 D
4 (43.54 ± 1.86 D vs 43.33 ± 1.89 D; $p < 0.01$) and 0.63 ± 0.45 D (41.68 ± 1.75 D vs
5 41.07 ± 1.86 D; $p < 0.01$) in low, moderate and high myopia groups, respectively, and
6 these curvature changes showed significant increases with myopic correction ($r = -0.537$,
7 $p < 0.01$).

8

9 In contrast, the anterior peripheral annulus region (6-9mm diameter) showed the
10 opposite trends as curvature became steeper after surgery (48.54 ± 2.12 D vs 44.94 ± 1.65
11 D for pos6m and pos1w, respectively; $p < 0.01$), then flatter gradually from pos1w to
12 pos6m in all myopic groups (47.90 ± 2.04 D; $p < 0.01$, Table 1), Figure 2A,C,E (blue
13 lines). Corneal curvature became flatter at pos6m compared with pos1w by -0.45 ± 0.73
14 D (46.15 ± 1.79 D vs 46.59 ± 1.71 D; $p < 0.01$), -0.62 ± 0.92 D (47.56 ± 1.86 D vs
15 48.19 ± 1.89 D; $p < 0.01$) and -0.71 ± 1.12 D (48.85 ± 1.88 D vs 49.54 ± 2.02 D; $p < 0.01$) in
16 low, moderate and high myopia groups, respectively, while no correlation was found
17 with REC (Total: $r = 0.078$, $p = 0.058$).

18

19 The red lines in Figure 2A,C,E show that the anterior surface shape changes within the
20 pericentral annulus region (with diameter between 3 and 6 mm) were similar to the
21 central regions (Table 1). The steepening at pos6m compared with pos1w was
22 statistically significant; 0.31 ± 0.25 D (45.47 ± 1.46 D vs 45.15 ± 1.49 D; $p < 0.01$), 0.38
23 ± 0.41 D (44.69 ± 1.72 D vs 44.33 ± 1.73 D; $p < 0.01$) and 0.35 ± 0.35 D (44.74 ± 1.64 D
24 vs 44.40 ± 1.66 D; $p < 0.01$) from low to high myopia groups, respectively. However,
25 these curvature changes were not correlated with REC ($r = 0.016$, $p = 0.690$).

26

27 Compared with anterior corneal surface, the curvature of posterior surface in all three
28 regions experienced much less change (Table 2). In all groups, posterior corneal
29 curvature became slightly flatter (-6.26 ± 0.24 D vs -6.29 ± 0.23 D; $p < 0.01$) in the central
30 region (0-3mm diameter), and slightly steeper in both the pericentral (-6.25 ± 0.23 D vs

1 -6.24±0.22 D; p< 0.05) and peripheral regions (-5.70±0.28 D vs -5.65±0.25 D; p< 0.05)
2 after surgery (pos1w) compared with pre-operation period (pre), then remained almost
3 unchanged in the remainder of the follow-up period (Figure 2B,D,F). The difference in
4 posterior curvature between pre-surgery and pos1w increased with REC in the central
5 region (r= -0.12, p< 0.01) but not the pericentral and peripheral regions (p> 0.05).

6 7 ***Changes in astigmatic refractive power*** 8

9 The anterior central region with 0-3mm diameter experienced significant changes (p<
10 0.01) in corneal astigmatism, from J₀: -0.60±0.39 D and J₄₅: -0.04±0.23 D pre-surgery
11 to J₀: -0.26±0.27 D and J₄₅: 0.04±0.19 D at pos1w, then remained stable in the follow-
12 up period compared to pos1w (p> 0.05), Figures 3A,C,E; 4A,C,E (black lines), Table
13 3, 5. The small differences in astigmatic curvature between pos1w and pos6m were not
14 correlated with REC (J₀: r= -0.039, p= 0.338; J₄₅: r= -0.071, p= 0.084).

15
16 On the other hand, the anterior peripheral annulus region (6-9mm diameter) exhibited
17 slight increases in corneal astigmatism at pos1w (J₀: -0.85±0.82 D, p< 0.01; J₄₅: -
18 0.22±0.46 D, p< 0.01) compared with pre surgery (J₀: -0.58±0.54 D and J₄₅: -0.13±0.26
19 D), then remained stable in the rest of the follow up period (p> 0.05), Figures 3A,C,E;
20 4A,C,E (blue lines), Table 3, 5. In contrast, the anterior pericentral region (with 3-6 mm
21 diameter) had stable J₀ at all stages (p> 0.05), while J₄₅ changed slightly (p <0.01) until
22 pos1m (-0.10±0.23 D) vs pre stage (-0.13±0.21 D), then remained stable afterwards (p>
23 0.05), Figures 3A,C,E; 4A,C,E (red lines), Table 3, 5. As for the posterior surface,
24 corneal astigmatism J₀ and J₄₅ experienced little and non-significant changes (p> 0.05)
25 between groups with different myopia extents, over the follow up period and in all three
26 surface regions considered, Figures 3B,D,F; 4B,D,F (black lines) , Table 4, 6.

27 28 ***Changes in corneal thickness*** 29

30 Corneal thickness at 0.7mm radial distance from apex (taken to represent the cornea's

1 central 0-3mm region) experienced large reductions following surgery of -52.8 ± 14.9
2 μm , $-85.4\pm 18.9 \mu\text{m}$ and $-117.1\pm 16.8 \mu\text{m}$ in the low, moderate and high myopia groups,
3 respectively. These values reduced significantly to $-36.6\pm 13.4 \mu\text{m}$, $-54.2\pm 15.1 \mu\text{m}$ and
4 $-69.3\pm 14.1 \mu\text{m}$ at 2.2mm radial distance (representing the pericentral 3-6mm region)
5 and then $-10.6\pm 17.4 \mu\text{m}$, $-8.4\pm 11.4 \mu\text{m}$ and $-11.8\pm 12.3 \mu\text{m}$ at 3.7mm distance
6 (representing the peripheral 6-9mm region).

7
8 Over the rest of the follow-up period, the thickness experienced gradual small recovery
9 in the central and pericentral regions ($p < 0.01$). The increase in thickness at 0.7mm
10 radial distance was less in low ($3.7\pm 7.3 \mu\text{m}$, $p < 0.01$) and moderate ($5.2\pm 7.6 \mu\text{m}$, $p <$
11 0.01) myopia groups than that in high myopia group ($9.3\pm 8.6 \mu\text{m}$). These values
12 reduced significantly to $2.1\pm 8.1 \mu\text{m}$, $3.0\pm 8.0 \mu\text{m}$ and $4.6\pm 9.1 \mu\text{m}$ ($p < 0.05$) at 2.2mm
13 radial distance. Further, the differences in thickness between pos1w and pos6m were
14 significantly correlated with REC (0.7mm: $r = -0.244$, $p < 0.01$, Figure 5A; 2.2mm: $r = -$
15 0.089 , $p < 0.05$, Figure 5B). On the other hand, the peripheral region experienced small
16 and insignificant decreases in thickness at pos6m compared with pos1w of -0.7 ± 11.4
17 μm , $-1.7\pm 12.0 \mu\text{m}$ and $-1.5\pm 12.8 \mu\text{m}$ ($p > 0.05$), which were not significantly correlated
18 with REC (3.7 mm: $r = -0.001$, $p > 0.05$, Figure 5C).

20 Discussion

21 Despite the significant corneal tissue loss in laser refractive surgeries, the planning of
22 the procedures still ignores the resulting effect on corneal biomechanics, and hence on
23 surgical outcome^{8, 23}. This effect is made complex by the microstructure of the cornea,
24 in which the cornea has mainly horizontal and vertical collagen fibrils at the centre,
25 circumferential fibres at the limbus and intermediate fibrils in between²⁴. Since
26 collagen fibrils are the main load carrying components of the stroma, this variation in
27 microstructure is expected to lead to variations in the cornea's response to refractive
28 surgery from one region to another. This paper aims to quantify these variations, with
29 particular emphasis on the topography change over a long, 6 month follow-up period.

30

1 In the central corneal region (0-3mm diameter), the central corneal surface undergoes
2 significant changes following surgery, becoming flatter and less astigmatic while the
3 posterior surface undergoes a smaller change in both spherical curvature and
4 astigmatism. This trend became more evident with deeper ablation, in groups with
5 moderate and high myopia, where the flattening trend was stronger in both anterior and
6 posterior surfaces than in the low myopia group. Compared with the anterior surface,
7 the posterior surface continued to undergo lower but still significant changes. A similar
8 but less clear trend was observed in the anterior pericentral annulus region (3-6mm
9 diameter), where ablation made the anterior cornea flatter while astigmatism remained
10 stable, and this trend was stronger with moderate and high myopia, it was weaker than
11 in the central region. Meanwhile, the posterior cornea continued to undergo little but
12 still significant steepening regardless of the extent of myopia, similar to what has been
13 reported in a previous study ²⁵. This trend was partly reversed in the peripheral region
14 (6-9mm diameter) where both the anterior and posterior surfaces became steeper and
15 more astigmatic following surgery. Such trend became stronger from low to high
16 myopia in the anterior surface, as well as the posterior surface but with smaller changes,
17 which were not correlated with the degree of refractive error correction.

18

19 The extended follow-up (up to 6 months) in this study enabled analysis of the long-term
20 shape changes following LASIK and the subsequent wound healing process. The results
21 point clearly at the reversal of the short-term trends discussed above, with the anterior
22 cornea becoming steeper in the central region and flatter in the peripheral region, albeit
23 with much less change compared with that observed immediately after surgery. The
24 same observation was repeated with thickness measurements, where the immediate
25 reductions, caused by ablation, was followed by slight increases over the 6 month
26 follow up period. The increase in corneal thickness was correlated with refractive error
27 correction in both central and pericentral regions. Meanwhile, the astigmatic corneal
28 refractive power in anterior surface, and both spherical and astigmatic refractive power
29 in posterior surface remained stable during the follow-up period.

30

1 The reshaping of the cornea is undoubtedly influenced by a combination of flap
2 separation, tissue ablation, associated biomechanical weakening and later wound
3 healing. In the short term, immediately after surgery, tissue ablation should lead to
4 flattening of the anterior central surface. However, the associated mechanical
5 weakening, due to tissue ablation and flap separation, will cause shape changes that can
6 follow one of the two options depicted in Figures 6A and C, or the intermediate behavior
7 illustrated in Figure 6B. In option A, weakening of the central cornea leads to easier
8 pushing out of the peripheral region under intraocular pressure (IOP), and flattening of
9 anterior central region. In contrast, in option C, the weaker central region is further
10 curved under IOP, pulling the peripheral region towards the center. The result is that the
11 central cornea becomes steeper while the periphery becomes flatter. Considering the
12 hyperopia outcome at one week after surgery ($0.25 \pm 0.46D$), it is expected that Option
13 A was more plausible. Then over the rest of the follow up period, up to 6 months after
14 surgery, it is expected that the wound healing would take effect in anterior stroma, and
15 this possibly was responsible for most if not all the reverse changes in corneal shape to
16 account for the decrease in hyperopia according to the mechanism depicted in Figure
17 6C ($0.16 \pm 0.46D$).

18

19 Therefore, the immediate changes in corneal topography observed after surgery are
20 caused by both the geometric effects and biomechanical weakening of corneal structure
21 associated with tissue ablation and flap separation. On the other hand, the long-term
22 changes, observed in this study between pos1w and pos6m stages, are expected to be
23 related to the biomechanical effect of wound healing. Since wound healing is expected
24 to lead to tissue stiffening²⁶, it is logic to cause some reversal of the immediate effects
25 of surgery, which leads to mechanical softening and weakening of the cornea. These
26 progressive changes will continue according to a previous study²⁷, which indicated that
27 manifest refraction continued to regress up to 5 years after surgery, but the variation
28 amplitude would become significantly small beyond 6 months.

29

30 Epithelial and stromal remodeling may play a further role in post-surgery changes in

1 corneal shape, but this role remains controversial ²⁸. While epithelial response to
2 myopic ablation was found greater in the central sub-region than in pericentral in some
3 studies with very high-frequency (VKH) digital ultrasound ^{29, 30}, others reported the
4 opposite trend ¹⁶. Erie reported no change in stromal thickness between pos1m and
5 pos12m after LASIK ³¹, while it was found to be significantly higher at pos1m ³² in
6 Avunduk's study. The change in manifest refractive error was much lower than the
7 steepening effect of anterior central cornea for the three levels of correction at pos6m
8 compared with pos1w. The calculation of post-operative corneal refraction assumed the
9 shape change only took place in the stroma. However, the shape change in anterior
10 central corneal surface during the follow up after LASIK is mainly due to regrowth of
11 both the epithelium and stroma ³³, which meant that the actual change in corneal
12 refraction was lower than that calculated for the corneal anterior surface.

13

14 The apex in Pentacam topography maps, which coincides with corneal vertex where the
15 instrument axis intersects the cornea, was close to the corneal purkinjie reflex ³⁴ used
16 as the ablation center in this study. Therefore, the changes in angle kappa would not be
17 expected to lead to any notable change in analysis results. However, as laser ablation
18 instruments vary in their cutting algorithms, these variations may have an effect on the
19 topography results obtained for different corneal regions. Further, the thickness
20 information on epithelium and stroma could not be assessed in our study due to
21 limitations in the instrument used (Pentacam). All above indicated were considered as
22 the shortcomings of the study.

23

24 While there is agreement among most studies on the significant trends of anterior
25 topography changes following refractive surgery, there is still disagreement on the
26 posterior changes – apart from the fact that they are much smaller than those observed
27 in the anterior surface. A number of earlier studies reported increased posterior corneal
28 elevation after surgery ^{9, 35-37} that grew with smaller corneal thickness, lower residual
29 thickness, higher myopic correction and higher IOP ^{9, 35}. However, these findings,
30 which are not compatible with the results of the present study, were derived from

1 Orbscan measurements (Bausch & Lomb, Rochester, NY), whose accuracy post corneal
2 refractive surgery, especially for posterior corneal surface assessment, has been largely
3 contested ³⁸.

4
5 Other studies, based on scheinpflug or OCT technology, reported insignificant changes
6 in posterior corneal elevation and curvature ^{14, 22, 39-42}, including slight central flattening
7 and peripheral steepening ¹⁷ (in agreement with the present study), followed by further
8 longer-term overall flattening ^{25, 43-46} or small fluctuations ^{11, 12}. Similar inconsistent
9 findings were reported following other forms of corneal refractive surgery; PRK,
10 SMILE and LASEK ^{39, 46-49}. The posterior surface showed a slight backward shift
11 during the post SMILE period ⁵⁰.

12
13 In order to evaluate the changes in corneal elevation caused by surgery, it would be
14 ideal to use a reference surface that remains stable throughout all pre and post-surgery
15 stages, possibly located on the limbus (with 11-12mm diameter). However, since the
16 accuracy of topography maps reduced progressively towards corneal periphery, only
17 data located within the 8-9 mm diameter region were included in analysis ^{11, 18, 22}. For
18 this data, the reference surface, such as the best-fit sphere (BFS), varied between pre
19 and post-surgery, even if the same data region and surface setting were chosen ^{11, 49},
20 since the change in corneal apex location post-surgery introduced changes in the
21 coordinate system used. These possible alterations in the reference surface may make
22 the elevation changes at specific points, caused by refractive surgery, appear to undergo
23 fluctuations as described in earlier studies ^{14, 42, 11, 12, 25, 43}. For this reason, tangential
24 curvature, which depends on the relative position of adjacent points and is not
25 influenced by the change in reference plane, was used in this study instead of elevation
26 data. This was considered more reliable than the BFS, which could not be used
27 accurately to characterize corneal astigmatism especially in the peripheral sub-region.

28
29 To conclude, the study used a large, gender-balanced database of topography maps

1 obtained before and up to 6 months after LASIK refractive procedure. The database
2 was analyzed to determine the shape changes in both anterior and posterior topography
3 at central, pericentral and peripheral regions, and in groups with low ($-0.50D > SE \geq -$
4 $3.00D$), moderate ($-3.00D > SE \geq -6.00D$) and high myopia ($-6.00D > SE$). The analysis
5 showed immediate steepening and increased astigmatism in the anterior peripheral
6 regions, opposite trends in the central and pericentral anterior region, and smaller yet
7 significant similar changes in the posterior surface. Over a 6 month follow-up period,
8 shape changes in most anterior regions followed a reverse trend with amplitudes that
9 were much smaller than the short-term changes observed 1 week post-surgery, yet
10 significantly correlated with refractive error correction in the central anterior region.
11 Meanwhile corneal astigmatism and posterior surface curvature in the three sub-regions
12 remained stable during the follow up period. The results observed in this study are
13 expected to lead to better understanding of the shape changes – both short and long term
14 – following refractive surgery, and to assist in efforts to improve the prediction and
15 planning of the procedures.

16

17 **WHAT WAS KNOWN**

- 18 ● Most earlier studies, sought to evaluate the topographical changes after LASIK, in
19 which the cornea was covered as one region without considering that different sub-
20 regions may respond differently to surgery.
- 21 ● Central anterior cornea becomes flatter after myopic refractive surgery.
- 22 ● Change in posterior corneal surface remain controversial.

23 **WHAT THIS PAPER ADDS**

- 24 ● Evidence has been presented that different corneal regions and different corneal
25 surfaces respond differently to LASIK surgery.
- 26 ● Analysis results based on a large, gender-balanced database of topography maps
27 obtained before and up to 6 months after FS-LASIK showed immediate steepening
28 and increased astigmatism in the anterior peripheral regions, opposite trends in the
29 central and pericentral anterior region, and smaller yet significant similar changes

1 in the posterior surface.

- 2 ● Over a 6 month follow-up period, shape changes in most regions followed a reverse
3 trend with amplitudes that were much smaller than the short-term changes observed
4 1 week post-surgery, these curvature changes showed significant increases with
5 myopic correction in central anterior region.
- 6 ● Corneal astigmatism and posterior surface curvature in the three sub-regions
7 remained stable during the follow up region.

8

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39

1 **Figure Captions:**

2 **Figure 1** Corneal regions including, central 0-3mm, pericentral 3-6 mm and peripheral
3 6-9 mm regions

4 **Figure 2** Changes in mean corneal curvature in different corneal regions and in eyes
5 with low, moderate and high myopia

6 **Figure 3** Change in astigmatic corneal curvature at 0-degree (J_0) in different corneal
7 regions and in eyes with low, moderate and high myopia

8 **Figure 4** Change in astigmatic corneal curvature at 45-degree (J_{45}) in different corneal
9 regions and in eyes with low, moderate and high myopia

10 **Figure 5** Correlation between the changes in corneal thickness between pos1w and
11 pos6m among different corneal regions with refractive error correction

12 **Figure 6** Conceptual models that depict possible corneal shape changes in response to
13 the LASIK procedure

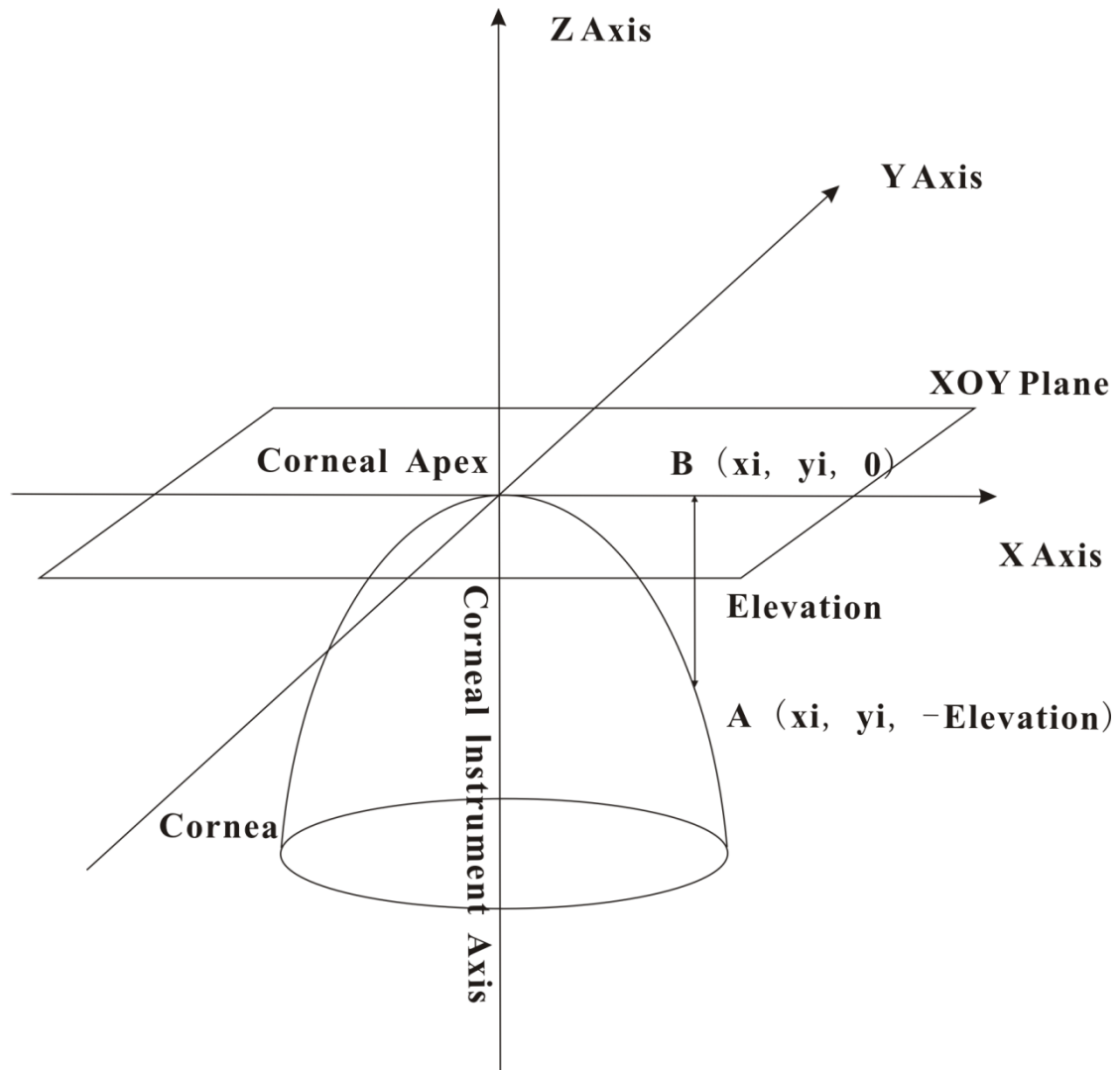


Figure 1 Elevation data obtained from the Pentacam. Elevation z_i is defined as the z axis distance between Point i and the XOY plane

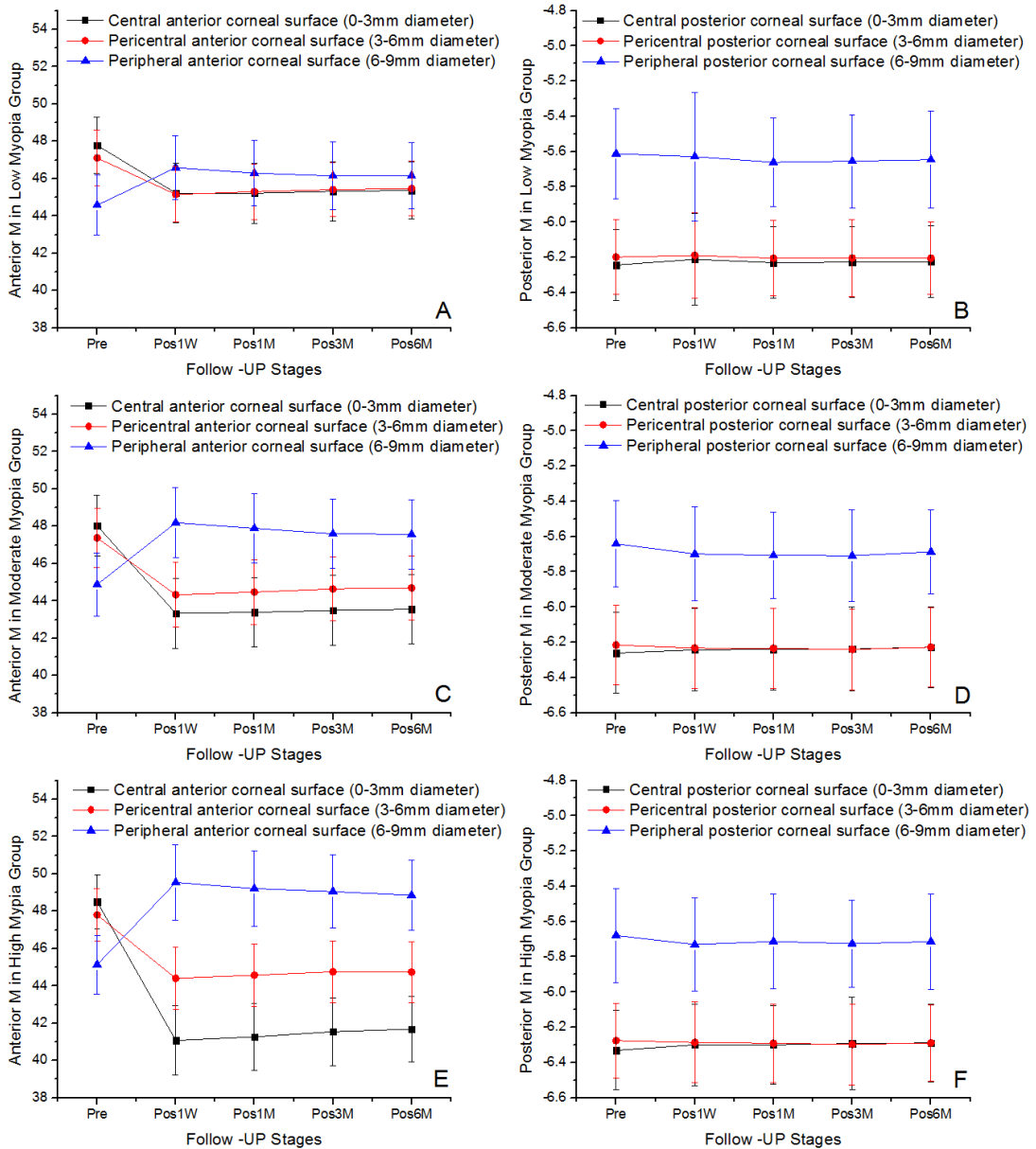


Figure 2 Changes in mean corneal curvature (M) in different corneal regions and in eyes with low, moderate and high myopia

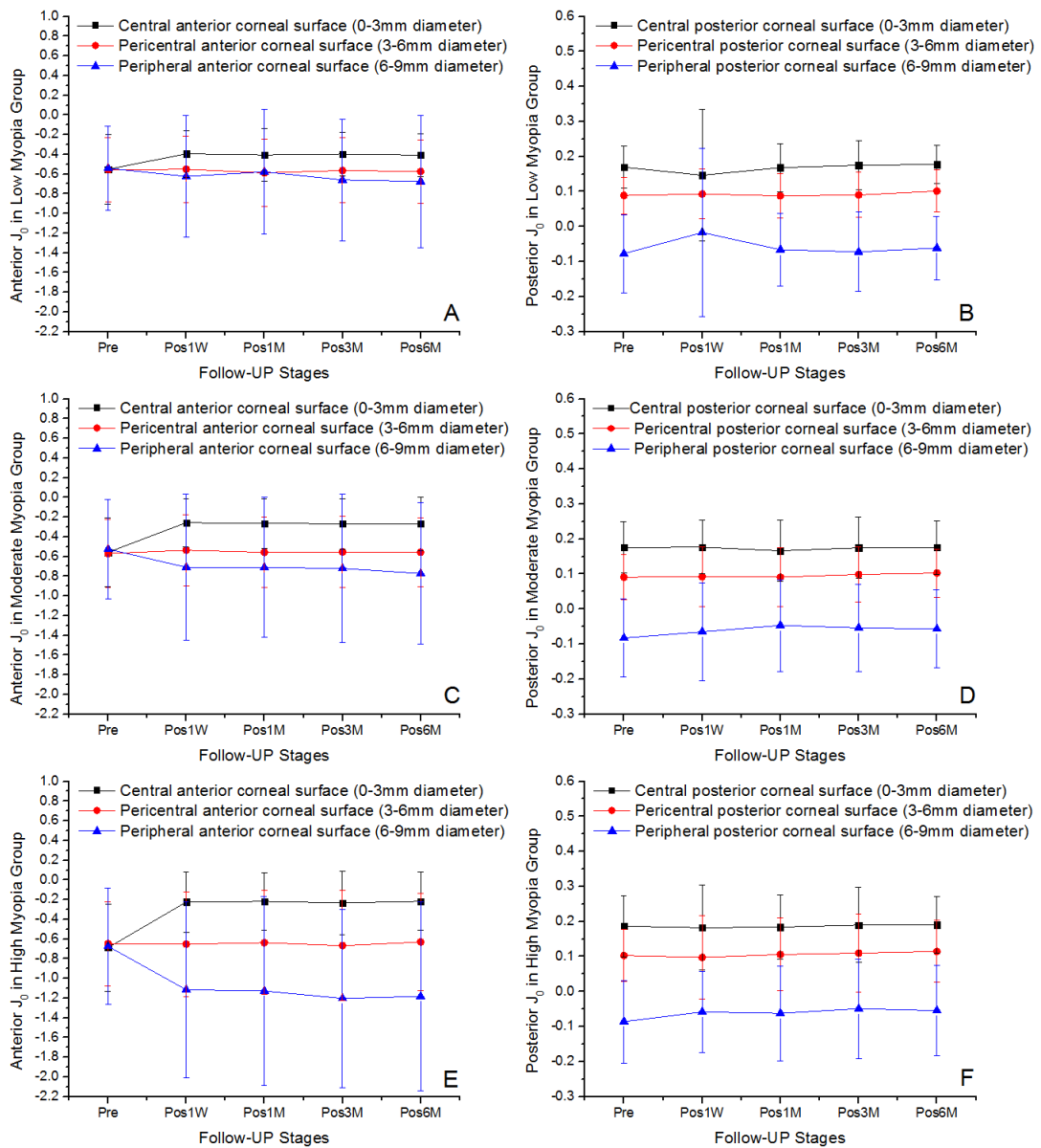


Figure 3 Change in astigmatic corneal curvature at 0-degree (J_0) in different corneal regions and in eyes with low, moderate and high myopia

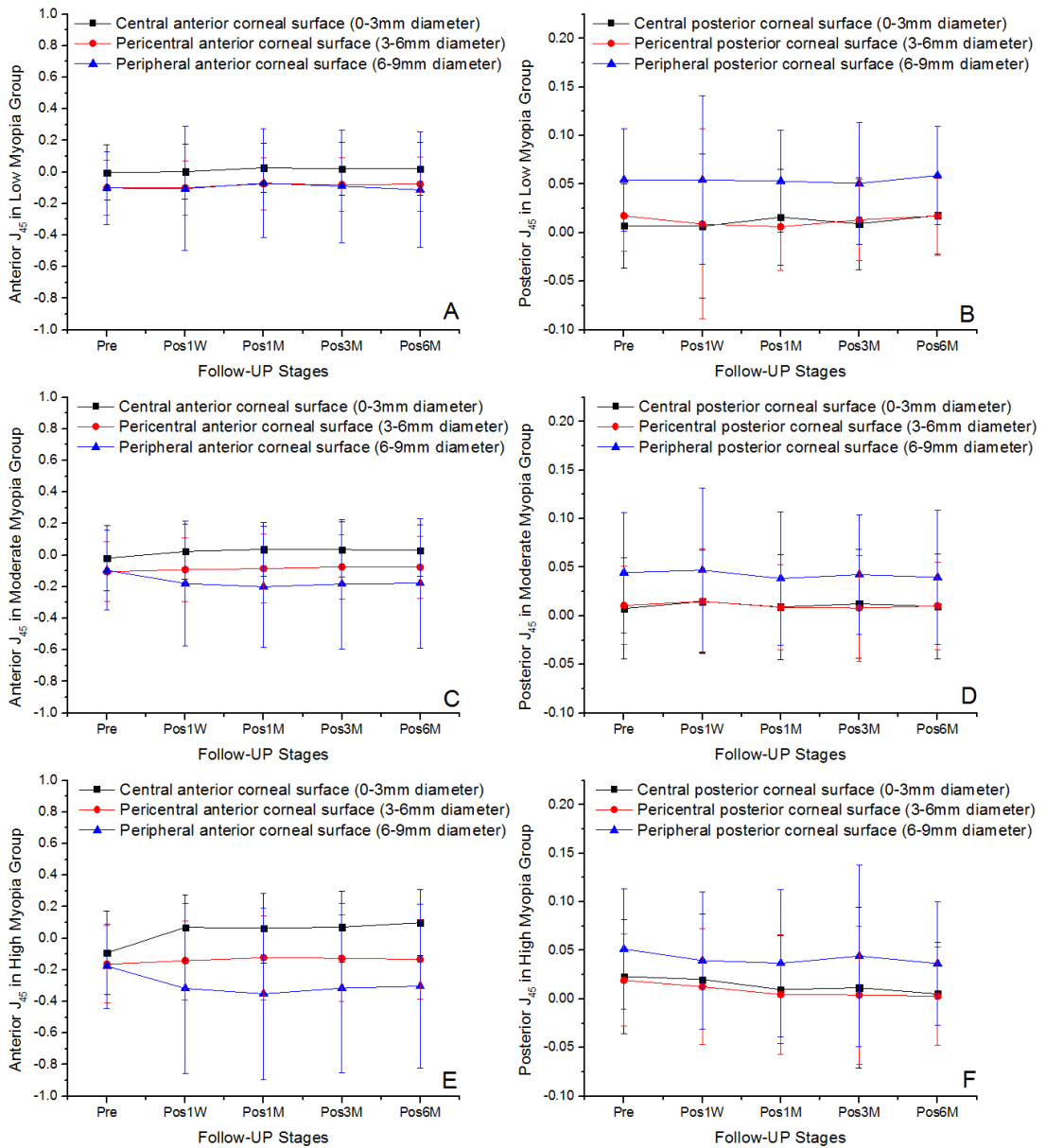


Figure 4 Change in astigmatic corneal curvature at 45-degree (J_{45}) in different corneal regions and in eyes with low, moderate and high myopia

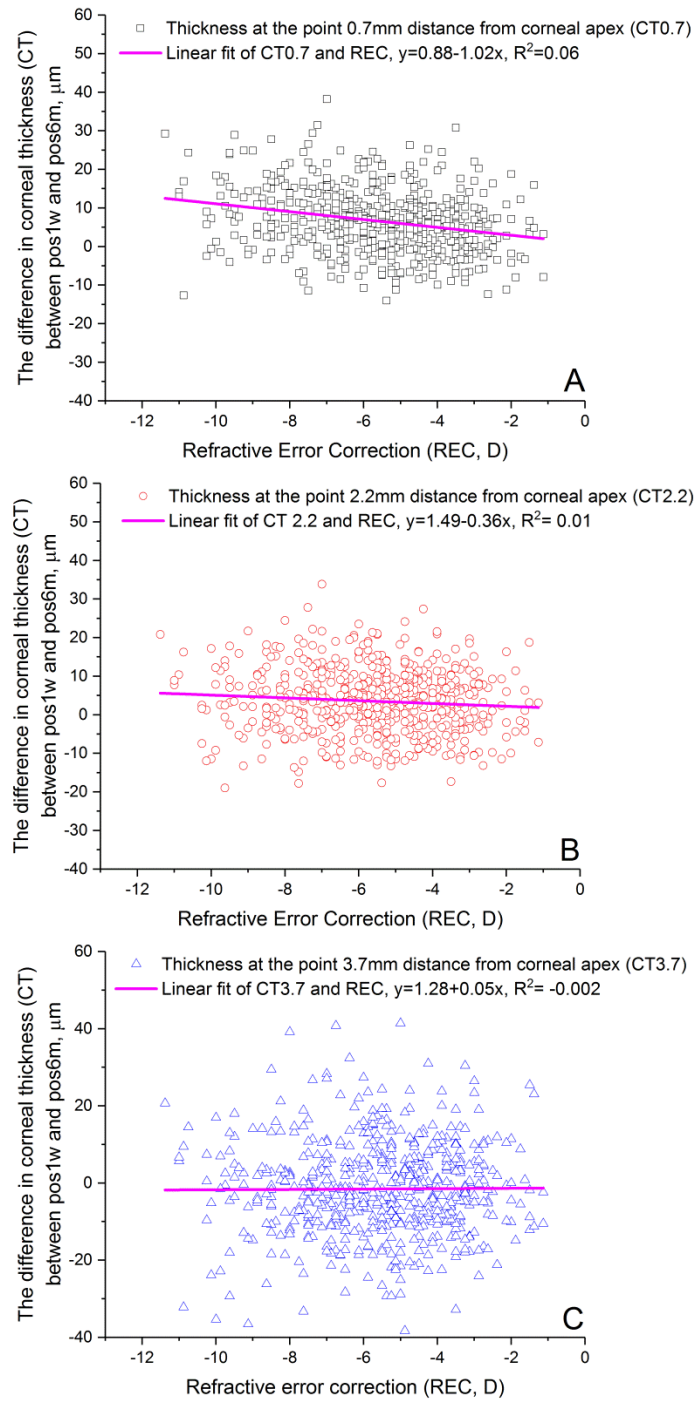


Figure 5 Correlation between the changes in corneal thickness between pos1w and pos6m among different corneal regions with refractive error correction

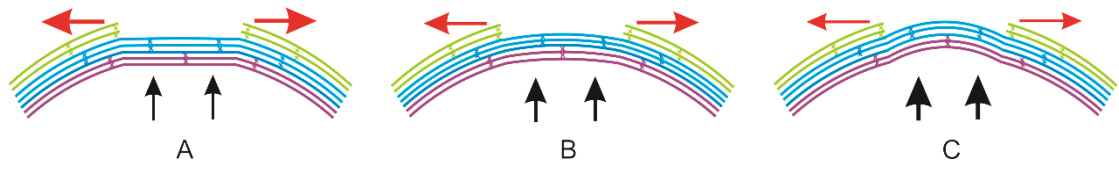


Figure 6 Conceptual models that depict possible corneal shape changes in response to the LASIK procedure

Table Captions:

Table 1: Changes in mean local spherical equivalent curvature (M) of anterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

Table 2: Changes in mean local spherical equivalent curvature (M) of posterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

Table 3: Changes in local astigmatism at 0-degree (J_0) of anterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

Table 4: Changes in local astigmatism at 0-degree (J_0) of posterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

Table 5: Changes in local astigmatism at 45-degree (J_{45}) of anterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

Table 6: Changes in local astigmatism at 45-degree (J_{45}) of posterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

Table 1: Changes in mean local spherical equivalent curvature (M) of anterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

| Changes between pre and post surgery stages | Central Area (0-3 mm) | | | Pericentral Area (3-6 mm) | | | Peripheral Area (6-9 mm) | | |
|---------------------------------------------------|-----------------------|--------------------|----------------|---------------------------|--------------------|----------------|--------------------------|--------------------|----------------|
| | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia |
| Pos1W - Pre | -2.55±0.59 | -4.69±0.96 | -7.43±1.21 | -1.95±0.61 | -3.05±0.79 | -3.39±0.79 | 2.01±0.72 | 3.32±0.9 | 4.41±1.04 |
| Pos1M - Pre | -2.57±0.56 | -4.64±0.92 | -7.24±1.08 | -1.81±0.59 | -2.90±0.75 | -3.22±0.77 | 1.72±0.76 | 3.01±0.84 | 4.07±1.07 |
| Pos3M - Pre | -2.46±0.59 | -4.54±0.91 | -6.97±1.13 | -1.70±0.63 | -2.74±0.7 | -3.04±0.76 | 1.57±0.89 | 2.72±0.87 | 3.91±1.08 |
| Pos6M - Pre | -2.41±0.58 | -4.48±0.89 | -6.83±1.01 | -1.64±0.62 | -2.68±0.74 | -3.06±0.66 | 1.57±0.85 | 2.68±1.02 | 3.72±1.08 |

Table 2: Changes in mean local spherical equivalent curvature (M) of posterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

| Changes between pre and post surgery stages | Central Area (0-3 mm) | | | Pericentral Area (3-6 mm) | | | Peripheral Area (6-9 mm) | | |
|---------------------------------------------------|-----------------------|--------------------|----------------|---------------------------|--------------------|----------------|--------------------------|--------------------|----------------|
| | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia |
| Pos1W - Pre | 0.03±0.15 | 0.02±0.05 | 0.03±0.06 | 0.01±0.09 | -0.02±0.07 | -0.01±0.07 | -0.02±0.28 | -0.06±0.16 | -0.05±0.14 |
| Pos1M - Pre | 0.01±0.04 | 0.02±0.05 | 0.03±0.06 | -0.01±0.05 | -0.02±0.05 | -0.02±0.08 | -0.04±0.15 | -0.07±0.12 | -0.03±0.14 |
| Pos3M - Pre | 0.02±0.05 | 0.02±0.08 | 0.04±0.14 | -0.01±0.06 | -0.02±0.06 | -0.02±0.10 | -0.04±0.15 | -0.07±0.14 | -0.05±0.16 |
| Pos6M - Pre | 0.02±0.05 | 0.03±0.05 | 0.04±0.06 | -0.01±0.06 | -0.01±0.06 | -0.01±0.07 | -0.03±0.16 | -0.05±0.14 | -0.04±0.16 |

Table 3: Changes in local astigmatism at 0-degree (J_0) of anterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

| Changes between pre and post surgery stages | Central Area (0-3 mm) | | | Pericentral Area (3-6 mm) | | | Peripheral Area (6-9 mm) | | |
|---------------------------------------------------|-----------------------|--------------------|----------------|---------------------------|--------------------|----------------|--------------------------|--------------------|----------------|
| | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia |
| Pos1W - Pre | 0.16±0.29 | 0.30±0.33 | 0.46±0.45 | 0.01±0.14 | 0.03±0.21 | 0.00±0.25 | -0.08±0.5 | -0.19±0.55 | -0.44±0.68 |
| Pos1M - Pre | 0.15±0.29 | 0.29±0.35 | 0.47±0.44 | -0.03±0.14 | 0.01±0.21 | 0.01±0.27 | -0.04±0.49 | -0.19±0.54 | -0.45±0.73 |
| Pos3M - Pre | 0.15±0.30 | 0.29±0.33 | 0.45±0.43 | -0.01±0.14 | 0.02±0.20 | -0.02±0.32 | -0.12±0.55 | -0.20±0.56 | -0.53±0.66 |
| Pos6M - Pre | 0.14±0.28 | 0.29±0.31 | 0.47±0.41 | -0.02±0.16 | 0.01±0.20 | 0.02±0.24 | -0.13±0.48 | -0.25±0.53 | -0.51±0.67 |

Table 4: Changes in local astigmatism at 0-degree (J_0) of posterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

| Changes between pre and post surgery stages | Central Area (0-3 mm) | | | Pericentral Area (3-6 mm) | | | Peripheral Area (6-9 mm) | | |
|---------------------------------------------------|-----------------------|--------------------|----------------|---------------------------|--------------------|----------------|--------------------------|--------------------|----------------|
| | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia |
| Pos1W - Pre | -0.02±0.18 | 0.00±0.05 | 0.00±0.1 | 0.00±0.05 | 0.00±0.07 | -0.01±0.1 | 0.06±0.23 | 0.02±0.14 | 0.03±0.11 |
| Pos1M - Pre | 0.00±0.04 | -0.01±0.07 | 0.00±0.07 | 0.00±0.03 | 0.00±0.07 | 0.00±0.09 | 0.01±0.10 | 0.04±0.11 | 0.02±0.14 |
| Pos3M - Pre | 0.01±0.05 | 0.00±0.07 | 0.00±0.09 | 0.00±0.04 | 0.01±0.06 | 0.01±0.10 | 0.00±0.11 | 0.03±0.12 | 0.04±0.14 |
| Pos6M - Pre | 0.01±0.05 | 0.00±0.05 | 0.00±0.05 | 0.01±0.04 | 0.01±0.05 | 0.01±0.06 | 0.02±0.1 | 0.03±0.11 | 0.03±0.12 |

Table 5: Changes in local astigmatism at 45-degree (J_{45}) of anterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

| Changes between pre and post surgery stages | Central Area (0-3 mm) | | | Pericentral Area (3-6 mm) | | | Peripheral Area (6-9 mm) | | |
|---------------------------------------------------|-----------------------|--------------------|----------------|---------------------------|--------------------|----------------|--------------------------|--------------------|----------------|
| | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia |
| Pos1W - Pre | 0.01±0.18 | 0.04±0.21 | 0.16±0.31 | 0.00±0.11 | 0.01±0.12 | 0.02±0.15 | 0.00±0.28 | -0.08±0.29 | -0.14±0.42 |
| Pos1M - Pre | 0.03±0.18 | 0.06±0.21 | 0.16±0.29 | 0.02±0.09 | 0.02±0.14 | 0.04±0.14 | 0.03±0.26 | -0.11±0.29 | -0.18±0.41 |
| Pos3M - Pre | 0.02±0.18 | 0.05±0.21 | 0.16±0.28 | 0.02±0.11 | 0.03±0.14 | 0.04±0.17 | 0.01±0.26 | -0.09±0.32 | -0.14±0.41 |
| Pos6M - Pre | 0.02±0.19 | 0.05±0.19 | 0.19±0.25 | 0.02±0.12 | 0.03±0.12 | 0.03±0.14 | -0.01±0.28 | -0.08±0.31 | -0.13±0.40 |

Table 6: Changes in local astigmatism at 45-degree (J_{45}) of posterior corneal surface between pre and post-surgery stages (1 week: pos1w, 1 month: pos1m, 3 months: pos3m and 6 months: pos6m) in different corneal regions and in eyes with low, moderate and high myopia

| Changes between pre and post surgery stages | Central Area (0-3 mm) | | | Pericentral Area (3-6 mm) | | | Peripheral Area (6-9 mm) | | |
|---------------------------------------------------|-----------------------|--------------------|----------------|---------------------------|--------------------|----------------|--------------------------|--------------------|----------------|
| | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia | Low Myopia | Moderate Myopia | High Myopia |
| Pos1W - Pre | 0.00±0.07 | 0.01±0.04 | 0.00±0.06 | -0.01±0.1 | 0.00±0.04 | -0.01±0.05 | 0.00±0.09 | 0.00±0.08 | -0.01±0.07 |
| Pos1M - Pre | 0.01±0.05 | 0.00±0.05 | -0.01±0.05 | -0.01±0.04 | 0.00±0.04 | -0.01±0.05 | 0.00±0.06 | -0.01±0.07 | -0.01±0.08 |
| Pos3M - Pre | 0.00±0.05 | 0.00±0.05 | -0.01±0.08 | 0.00±0.03 | 0.00±0.05 | -0.02±0.06 | 0.00±0.07 | 0.00±0.06 | -0.01±0.09 |
| Pos6M - Pre | 0.01±0.04 | 0.00±0.04 | -0.02±0.05 | 0.00±0.03 | 0.00±0.03 | -0.02±0.04 | 0.00±0.05 | 0.00±0.07 | -0.01±0.07 |