



Changes in biomechanically corrected intraocular pressure and dynamic corneal response parameters before and after transepithelial photorefractive keratectomy and femtosecond laser–assisted laser in situ keratomileusis

Hun Lee, MD, Cynthia J. Roberts, PhD, Tae-im Kim, MD, PhD, Renato Ambrósio Jr, MD, PhD, Ahmed Elsheikh, PhD, David Sung Yong Kang, MD

Purpose: To evaluate the changes in biomechanically corrected intraocular pressure (IOP) and new dynamic corneal response parameters measured by a dynamic Scheimpflug analyzer before and after transepithelial photorefractive keratectomy (PRK) and femtosecond laser–assisted laser in situ keratomileusis (LASIK).

Setting: Yonsei University College of Medicine and Eyereum Eye Clinic, Seoul, South Korea.

Design: Retrospective case series.

Methods: Medical records of patients having transepithelial PRK or femtosecond-assisted LASIK were examined. The primary outcome variables were biomechanically corrected IOP and dynamic corneal response parameters, including deformation amplitude ratio 2.0 mm, stiffness parameter at first applanation, Ambrósio relational thickness through the horizontal meridian, and integrated inverse radius before the procedure and 6 months postoperatively.

Results: Of the 129 patients (129 eyes) in the study, 65 had transepithelial PRK and 64 had femtosecond-assisted LASIK. No

significant differences in biomechanically corrected IOP were noted before and after surgery. The deformation amplitude ratio 2.0 mm and integrated inverse radius increased, whereas the stiffness parameter at first applanation and the Ambrósio relational thickness through the horizontal meridian decreased after surgery ($P < .001$). The changes in deformation amplitude ratio 2.0 mm and integrated inverse radius were smaller in transepithelial PRK than femtosecond-assisted LASIK ($P < .001$). Using analysis of covariance, with refractive error change or corneal thickness change as a covariate, the changes in deformation amplitude ratio 2.0 mm and integrated inverse radius were smaller in transepithelial PRK than femtosecond-assisted LASIK ($P < .001$).

Conclusions: The dynamic Scheimpflug analyzer showed stable biomechanically corrected IOP measurement before and after surgery. The changes in dynamic corneal response parameters were smaller with transepithelial PRK than with femtosecond-assisted LASIK, indicating less of a biomechanical effect with transepithelial PRK.

J Cataract Refract Surg 2017; 43:1495–1503 © 2017 ASCRS and ESCRS

Corneal biomechanics is the response of corneal tissue to an applied force that involves interactions between the externally applied force, the intrinsic viscoelastic properties of the cornea, and the intraocular

pressure (IOP).^{1–3} Biomechanical response parameters of the cornea, although not classic properties, might be useful clinically for many purposes including identification of corneal disease, characterization of susceptibility to ectasia

Submitted: May 26, 2017 | Final revision submitted: August 25, 2017 | Accepted: August 28, 2017

From the Department of Ophthalmology (Lee), International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, the Eyereum Eye Clinic (Kang), Seoul, and the Institute of Vision Research (Lee, Kim), Department of Ophthalmology, Yonsei University College of Medicine, Seoul, South Korea; the Department of Ophthalmology & Visual Science and Department of Biomedical Engineering (Roberts), Ohio State University, Columbus, Ohio, USA; Rio de Janeiro Corneal Tomography and Biomechanics Study Group (Ambrósio), Rio de Janeiro, Brazil; the School of Engineering (Elsheikh), University of Liverpool, Liverpool, United Kingdom.

Supported in part by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology (NRF-2016R1A2B4009626) and by the research fund of Catholic Kwandong University International St. Mary's Hospital (CKURF-201604900001), Incheon, South Korea. The funding agency had no role in the design or conduct of this study, collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or in the decision to submit the manuscript for publication.

Corresponding author: David Sung Yong Kang, MD, Eyereum Eye Clinic, Kangnam Center Building 7 Floor 825-13, Yeoksam-dong, Gangnam-gu, Seoul 06232, South Korea. E-mail: kangeye@eyereum.com.

progression, and assistance with predicting refractive outcomes after corneal refractive surgery.^{4–6} Moreover, corneal biomechanical properties are known to influence the measurement of IOP alongside the central corneal thickness (CCT), and both CCT and biomechanical response parameters are recognized as important factors in the susceptibility to the development of glaucomatous damage.^{7–9}

The dynamic Scheimpflug analyzer (Corvis ST, Oculus Optikgeräte GmbH), which allows in vivo characterization of corneal biomechanical deformation response to an applied air puff, has become a useful instrument for evaluating biomechanical response parameters of the cornea clinically.^{10,11} The dynamic Scheimpflug analyzer captures the dynamic process of corneal deformation caused by an air puff of consistent spatial and temporal profiles using an ultra-high-speed camera that operates at 4300 frames per second to capture a series of 140 sequential horizontal Scheimpflug images of corneal deformation. The dynamic Scheimpflug analyzer enables the calculation of a variety of dynamic corneal response parameters to characterize biomechanical response by analyzing patterns of deformation at highest concavity and applanation, during inward deformation (loading) and during outward recovery (unloading), which have been reported to be influenced predominantly by IOP, as well as CCT and age.^{12–14} Recently, new corneal biomechanical response parameters have been introduced, including deformation amplitude ratio 2.0 mm (DA ratio 2.0 mm), integrated inverse radius (IntInvRad), stiffness parameter at first applanation (SP-A1), and Ambrósio relational thickness through the horizontal meridian (ARTh).¹⁵ In addition, the dynamic Scheimpflug analyzer provides a measurement of a biomechanically corrected IOP that is intended to be free of effects from changes in corneal geometric and material stiffness parameters.¹⁵

Although the dynamic Scheimpflug analyzer has been previously used to measure changes in corneal biomechanical response parameters after laser vision correction procedures such as photorefractive keratectomy (PRK), laser in situ keratomileusis (LASIK), and small-incision lenticule extraction (SMILE), as well as corneal crosslinking, the stability of biomechanically corrected IOP measurements and the significance of new dynamic corneal response parameters have not yet been studied.^{16–20} Moreover, knowledge remains limited with respect to understanding how corneal biomechanical parameters are modified according to surgical techniques.

The present study aimed to assess the stability of the recently introduced biomechanically corrected IOP and evaluate the changes in new dynamic corneal response parameters obtained from the dynamic Scheimpflug analyzer after transepithelial PRK and femtosecond laser-assisted LASIK procedures.

PATIENTS AND METHODS

The medical records of patients who met the inclusion and exclusion criteria were reviewed. A retrospective comparative

observational case series was performed with the approval of the Institutional Review Board of Yonsei University College of Medicine (Seoul, South Korea). The study adhered to the tenets of the Declaration of Helsinki and followed good clinical practices. All patients provided written informed consent for their medical information to be included in the study.

Patients included in the study were older than 20 years of age and had transepithelial PRK or femtosecond-assisted LASIK using standardized techniques performed by the same surgeon (D.S.Y.K.) between May 2014 and April 2015. Patients with previous ocular or intraocular surgery, ocular abnormalities other than myopia or myopic astigmatism with a corrected distance visual acuity (CDVA) of 1.00 (20/20 Snellen) or better in both eyes, corneal endothelial cell density of less than 2000 cells/mm², cataract, ocular inflammation, infection, or moderate and severe dry eye were excluded. Also excluded were patients with signs of keratoconus on Scheimpflug tomography (displacement of the corneal apex, decrease in thinnest-point pachymetry, and asymmetric topographic pattern). One eye from each patient was included in the analysis via randomization between the 2 eyes to avoid the bias of the relationship between bilateral eyes that could influence the analysis result. A randomization sequence was created using a spreadsheet (Excel 2007, Microsoft Corp.) with random block sizes of 2 and 4.

Examinations and Measurements

Preoperatively and 6 months postoperatively, all patients had complete ophthalmic examinations, including uncorrected distance visual acuity and CDVA, manifest refraction, slitlamp evaluation (Haag-Streit AG), corneal volume (Pentacam, Oculus Optikgeräte GmbH), IOP with a noncontact tonometer (NT-530, Nidek Co., Ltd.), and fundus examination. In addition, the dynamic corneal response parameters were measured using the dynamic Scheimpflug analyzer. All measurements were performed by the same investigator to eliminate possible interobserver variability and taken at approximately the same time of day. Each measurement was performed 3 times and the average value was used in the analysis. The dynamic corneal response parameters from each measurement were exported to a spreadsheet.

The dynamic Scheimpflug analyzer provides a new and validated biomechanically corrected IOP value that is intended to offer an estimate of true IOP or the corrected value of measured IOP, which considers the biomechanical response of the cornea to air pressure including the effects of variation in CCT and material behavior.^{15,21,22} The algorithm for biomechanically corrected IOP is based on numerical simulation of the dynamic Scheimpflug analyzer procedure, as applied on human eye models with different tomographies (including thickness profiles), material properties, and true IOPs.^{21,22} The eye models were developed for analysis using the finite element method and designed to simulate important biomechanical features of the eye, including the cornea's aspheric topography, the cornea's variable thickness, low stiffness of epithelium and endothelium, the cornea's weak interlamellar adhesion, and the tissue's hyperelasticity, hysteresis, and age-related stiffening.^{21,22} The biomechanically corrected IOP formula used in the dynamic Scheimpflug analyzer was a modified algorithm of the published formula.^{15,21}

New dynamic corneal response parameters include the DA ratio 2.0 mm, IntInvRad, ARTh, and SP-A1. The DA ratio 2.0 mm represents the ratio between the deformation amplitude of the apex and the average of 2 points located 2.0 mm on either side of the apex. A larger value indicates a more compliant cornea that is less resistant to deformation. The IntInvRad parameter was calculated as the integration of the inverse radius values, which are the reciprocals of radius of curvature at the highest concavity between inward and outward applanation. A greater concave radius is associated with greater resistance to deformation or a stiffer cornea. Conversely, a higher integrated inverse radius is associated with greater compliance or a softer cornea. The dynamic Scheimpflug

analyzer provides data for calculating the rate of increase of corneal thickness from the apex toward the nasal and temporal sides.¹¹ Via the characterization of the thickness data on the horizontal Scheimpflug image, the dynamic Scheimpflug analyzer enables the calculation of the new corneal thickness index, ARTh.^{11,23} Lower ARTh indicates a thinner cornea and/or a faster thickness increase toward the periphery.²³ The SP-A1 parameter is defined as resultant pressure divided by displacement in an analogous manner to 1-dimensional stiffness.²⁴ The resultant pressure is defined as the adjusted pressure at A1 minus the biomechanically corrected IOP. The displacement is the distance the corneal apex moves from the pre-deformation state to A1.¹⁵ Therefore, SP-A1 = (adjusted API - biomechanically corrected IOP)/A1 deflection amplitude.²³ A larger value indicates a stiffer response.

Surgical Techniques

Transepithelial Photorefractive Keratectomy Photoablation was performed using an excimer laser (Amaris 1050RS excimer laser platform, Schwind eye-tech-solutions GmbH & Co. KG), which uses a flying-spot laser with a repetition rate of 1050 Hz. Ablation profile planning was carried out using the integrated Optimized Refractive Keratectomy-Custom Ablation Manager software (version 5.1, Schwind eye-tech-solutions GmbH & Co. KG). Mitomycin 0.02% was applied to all corneas for 20 seconds followed by thorough rinsing with a chilled balanced salt solution. Postoperatively, 1 drop of topical levofloxacin 0.5% (Cravit) was instilled at the surgical site and a bandage contact lens (Acuvue Oasys, Johnson & Johnson Vision Care, Inc.) was placed on the cornea and then removed 4 days later after complete healing of the corneal epithelium. Topical levofloxacin 0.5% and fluorometholone 0.1% (Flumetholon) were applied 4 times per day for 1 month. The dosage was tapered over 3 months.

Femtosecond Laser-Assisted Laser In Situ Keratomileusis The Visumax femtosecond laser system with a repetition rate of 500 kHz was used to create the flap. The flaps had diameters of 8.1 mm and thicknesses of 100 μm with standard 90-degree hinges and 90-degree side-cut angles. The lamellar and side cuts were achieved with energies of 185 nJ. Stromal tissue ablation was performed with the Amaris 1050RS excimer laser platform with a repetition rate of 1050 kHz. Flaps were repositioned after the excimer laser treatment and a bandage contact lens was placed on the cornea for 1 day. Topical fluorometholone 0.1% was used initially 8 times daily and tapered for 20 days. Topical levofloxacin 0.5% was used 4 times daily for 7 days.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 22.0, IBM Corp.). Differences were considered statistically significant when the P values were less than 0.05. The results are

expressed as means ± SD. The Kolmogorov-Smirnov test was used to confirm data normality. The independent t test for continuous variables and the chi-squared test for categorical variables were used to statistically compare preoperative with postoperative data between transepithelial PRK and femtosecond-assisted LASIK. The paired t test was performed to evaluate the differences between preoperative and 6-month postoperative parameters, including IOP with a noncontact tonometer, biomechanically corrected IOP, CCT, corneal volume, and dynamic corneal response parameters in each group. Simple linear regression analysis was used to determine the relationship between changes (Δ) in dynamic corneal response parameters or biomechanically corrected IOP, and Δmanifest refraction spherical equivalent (MRSE), ΔCCT, Δcorneal volume, or ΔARTh in each group. Furthermore, analysis of covariance (ANCOVA) was performed to compare changes in dynamic corneal response parameters between transepithelial PRK and femtosecond-assisted LASIK, with the ΔMRSE, ΔCCT, Δcorneal volume, or ΔARTh as a covariate.

RESULTS

Data were collected from 129 normal healthy participants (129 eyes) with a mean age of 28.1 ± 5.4 years (range 20 to 41 years). The percentage of women was 72.3% and 56.3% in the transepithelial PRK group and the femtosecond-assisted LASIK group, respectively (P = .057). Table 1 shows the preoperative characteristics of the 2 groups with no significant statistical differences between them regarding age, preoperative sphere, cylinder, spherical equivalent, CCT, optical zone, and ablation depth.

Table 2 shows the changes in IOP with a noncontact tonometer, biomechanically corrected IOP, CCT, and corneal volume before and after transepithelial PRK or femtosecond-assisted LASIK. The biomechanically corrected IOP was stable before and after transepithelial PRK and femtosecond-assisted LASIK (P = .101 and P = .138, respectively). In each group, differences in biomechanically corrected IOP before and after surgery were significantly smaller than those in IOP with a noncontact tonometer before and after surgery (all P < .001). When combining the 2 forms of laser vision surgery, the difference in biomechanically corrected IOP before and after surgery was slight (P = .875). These values were significantly smaller than those for IOP with a noncontact tonometer (P < .001)

Table 1. Baseline characteristics of eyes that had transepithelial PRK or femtosecond-assisted LASIK.

Parameter	Transepithelial PRK (n = 65)		Femtosecond-assisted LASIK (n = 64)		P Value
	Mean ± SD	Range	Mean ± SD	Range	
Age (y)	27.2 ± 4.7	20, 41	29.0 ± 5.9	20, 40	.060
Refractive error (D)					
Sphere	-3.95 ± 1.55	-7.25, -0.75	-3.81 ± 1.35	-7.37, -1.37	.588
Cylinder	-0.82 ± 0.69	-3.62, 0.00	-0.94 ± 0.88	-4.75, 0.00	.353
SE	-4.36 ± 1.60	-7.69, -1.06	-4.28 ± 1.36	-7.81, -1.50	.777
Preop rotating Scheimpflug camera-CCT	550.7 ± 30.2	487.0, 618.0	557.0 ± 22.7	518.0, 623.0	.187
Preop dynamic Scheimpflug analyzer-CCT	557.9 ± 31.4	503.0, 631.0	561.8 ± 23.8	525.0, 624.0	.428
Optical zone (mm)	6.76 ± 0.27	6.26, 7.26	6.77 ± 0.21	6.20, 7.26	.842
Ablation depth (μm)	96.3 ± 25.9	36.0, 149.0	89.3 ± 23.1	44.0, 140.0	.107

CCT = central corneal thickness; LASIK = laser-assisted laser in situ keratomileusis; PRK = photorefractive keratectomy; SE = spherical equivalent

Table 2. Changes in IOP with a noncontact tonometer, biomechanically corrected IOP, CCT (dynamic Scheimpflug analyzer), and corneal volume (rotating Scheimpflug camera) before and after transepithelial PRK or femtosecond-assisted LASIK.

Parameter	Transepithelial PRK (n = 65)		Femtosecond-assisted LASIK (n = 64)		Total (N = 129)	
	Mean ± SD	P Value	Mean ± SD	P Value	Mean ± SD	P Value
IOP-NCT (mm Hg)		<.001		<.001		<.001
Preop	16.88 ± 1.86		16.81 ± 1.87		16.84 ± 1.85	
Postop	14.84 ± 1.57		14.19 ± 1.34		14.52 ± 1.49	
Δ	-2.04 ± 1.44		-2.63 ± 1.60		-2.33 ± 1.54	
biOP (mm Hg)		.101		.138		.875
Preop	16.30 ± 1.68		16.12 ± 1.66		16.21 ± 1.66	
Postop	16.60 ± 1.29		15.86 ± 1.32		16.23 ± 1.35	
Δ	0.30 ± 1.45		-89.3 ± 23.1		0.02 ± 1.45	
CCT (μm)		<.001		<.001		<.001
Preop	557.9 ± 31.4		561.8 ± 23.8		559.9 ± 27.8	
Postop	461.6 ± 38.0		472.5 ± 26.9		467.0 ± 33.3	
Δ	-96.3 ± 25.9		-89.3 ± 23.1		-92.8 ± 24.7	
Corneal volume		<.001		<.001		<.001
Preop	62.9 ± 3.0		62.8 ± 3.2		62.9 ± 3.1	
Postop	60.4 ± 3.1		61.0 ± 3.5		60.7 ± 3.3	
Δ	-2.6 ± 1.3		-1.7 ± 1.3		-2.2 ± 1.4	

Δ = change from preop to postop; biOP = biomechanically corrected intraocular pressure; CCT = central corneal thickness; IOP = intraocular pressure; LASIK = laser in situ keratomileusis; NCT = noncontact tonometer; PRK = photorefractive keratectomy

Table 3 shows the changes in the new dynamic corneal response parameters before and after transepithelial PRK and femtosecond-assisted LASIK. There were no significant differences in preoperative dynamic corneal response parameters between the 2 groups. The differences between

preoperative and postoperative parameter values were significant in the 2 groups (all $P < .001$). The DA ratio 2.0 mm and IntInvRad significantly increased, whereas SP-A1 and ARTh significantly decreased after surgery. Results showed that ΔDA ratio 2.0 mm and ΔIntInvRad

Table 3. Changes in dynamic corneal response parameters before and after transepithelial PRK and femtosecond-assisted LASIK.

Parameter	Transepithelial PRK (n = 65)		Femtosecond-assisted LASIK (n = 64)			Total (N = 129)	
	Mean ± SD	P Value	Mean ± SD	P Value	P Value*	Mean ± SD	P Value
DA ratio 2.0 mm		<.001		<.001	<.001		<.001
Preop	4.30 ± 0.40		4.23 ± 0.29			4.27 ± 0.35	
Postop	5.12 ± 0.64		5.45 ± 0.51			5.28 ± 0.60	
Δ	0.82 ± 0.43		1.21 ± 0.46			1.01 ± 0.49	
Change (%)	19		29			—	
SP-A1		.001		<.001	.710		<.001
Preop	95.2 ± 18.5		94.2 ± 15.4			94.7 ± 17.0	
Postop	65.9 ± 16.7		63.9 ± 12.7			64.9 ± 14.8	
Δ	-29.3 ± 15.1		-30.2 ± 14.1			-29.7 ± 14.5	
Change (%)	-31		-32			—	
ARTh		<.001		<.001	.095		<.001
Preop	465 ± 86		452 ± 114			459 ± 101	
Postop	176 ± 51		192 ± 45			184 ± 48	
Δ	289 ± 80		260 ± 108			-275 ± 95	
Change (%)	-62		-58			—	
IntInvRad		<.001		<.001	<.001		<.001
Preop	8.26 ± 0.90		8.13 ± 0.91			8.20 ± 0.90	
Postop	10.15 ± 1.30		10.74 ± 1.11			10.44 ± 1.24	
Δ	1.88 ± 0.92		2.61 ± 0.80			2.24 ± 0.94	
Change (%)	23		32			—	

Δ = change from preop to postop; ARTh = Ambrósio relational thickness through the horizontal meridian; DA ratio 2.0 mm = deformation amplitude ratio 2.0 mm; IntInvRad = integrated inverse radius; LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy; SP-A1 = stiffness parameter at first appplanation

*Independent *t* test between the 2 groups regarding changes in the dynamic corneal response parameter before and after surgery

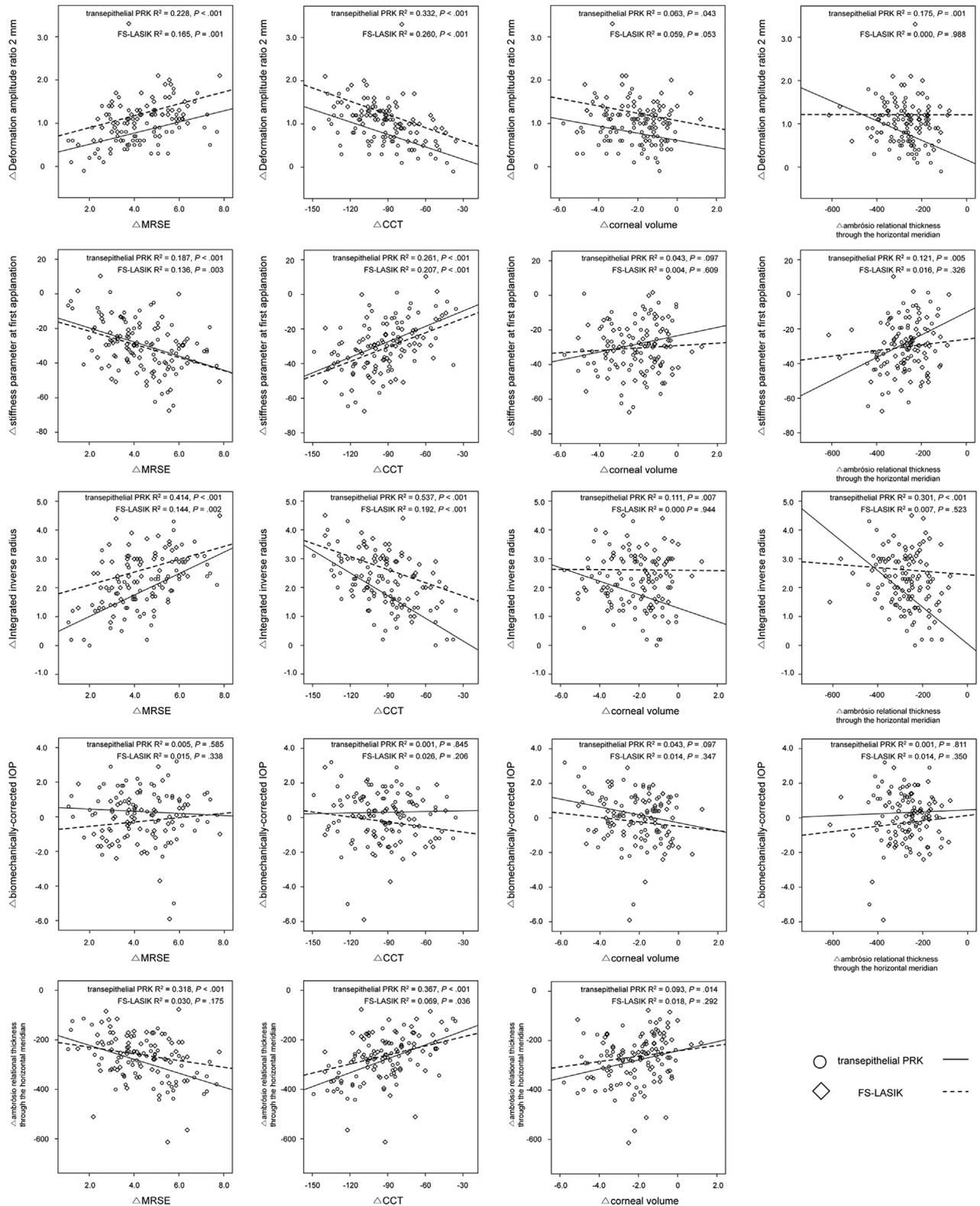


Figure 1. Scatterplots and results for simple linear regression analysis between changes in dynamic corneal response parameters or biomechanically corrected IOP and changes in refractive error change, corneal thickness change, corneal volume change, or Ambrósio relational thickness through the horizontal meridian change between transepithelial PRK and femtosecond laser–assisted LASIK (Δ = change from pre-operatively to postoperatively; CCT = central corneal thickness; IOP = intraocular pressure; FS-LASIK = femtosecond laser–assisted laser in situ keratomileusis; MRSE = manifest refraction spherical equivalent; PRK = photorefractive keratectomy).

were significantly smaller with transepithelial PRK than with femtosecond-assisted LASIK (all $P < .001$).

Figure 1 shows the scatterplots and results for simple linear regression analysis between changes (Δ) in dynamic corneal response parameters or biomechanically corrected IOP, and Δ MRSE, Δ CCT, Δ corneal volume, or Δ ARTh between the 2 groups. The parameter showing the strongest relationships with Δ MRSE, indicated by the r^2 values, was Δ IntInvRad, followed by Δ ARTh, Δ DA ratio 2.0 mm, and finally Δ SP-A1 in the transepithelial PRK group. For the femtosecond-assisted LASIK group, the parameter showing the strongest relationships with Δ MRSE was Δ DA ratio 2.0 mm, followed by Δ IntInvRad and Δ SP-A1. The parameter showing the strongest relationships with Δ CCT was Δ IntInvRad, followed by Δ ARTh, Δ DA ratio 2.0 mm, and finally Δ SP-A1 in the transepithelial PRK group, whereas it was Δ DA ratio 2.0 mm, followed by Δ SP-A1, Δ IntInvRad, and finally Δ ARTh in the femtosecond-assisted LASIK group.

In comparing the changes in dynamic corneal response parameters between the 2 groups with ANCOVA and Δ MRSE, Δ CCT, Δ corneal volume, or Δ ARTh as a covariate, there were significant differences in Δ DA ratio 2.0 mm and Δ IntInvRad (all $P < .001$) (Table 4). The Δ DA ratio 2.0 mm and Δ IntInvRad were significantly smaller in transepithelial PRK than femtosecond-assisted LASIK (all $P < .001$). No significant differences were found in Δ SP-A1 or Δ ARTh between the 2 groups.

DISCUSSION

In the present study, we evaluated the changes in biomechanically corrected IOP and newly developed dynamic corneal response parameters before and after transepithelial PRK and femtosecond-assisted LASIK. Most notably, the biomechanically corrected IOP obtained from the dynamic Scheimpflug analyzer was stable before and after laser vision correction surgery, without a clinically or statistically significant difference in the mean. Previous

studies have shown that variations in CCT can introduce inaccuracies in IOP measurements using different forms of tonometry,^{25,26} and that corneal biomechanical properties might have a greater effect on IOP measurements than CCT.^{3,7} The tangent modulus (a measure of material stiffness) has been reported to determine the relationship between the CCT and IOP measurement error in applanation tonometry, with stiffer corneas having the strongest relationship between CCT and IOP measurement error.^{3,7}

With laser vision surgery, in addition to the CCT reduction caused by tissue removal, softening of tissue would be expected because of structural alteration by severing tension-bearing lamellae in both groups as well as separation of the flap in femtosecond-assisted LASIK. However, that biomechanically corrected IOP measurements remained almost unaltered after surgery is an indication that biomechanically corrected IOP estimates are less influenced by changes in CCT and material properties than the uncorrected IOP measurements.¹⁵ These results are compatible with an earlier study using a database involving 634 healthy eyes in which application of the biomechanically corrected IOP algorithm led to weaker associations of IOP measurements with CCT (from $r^2 = 0.204$, 3.06 mm Hg/100 μ m to $r^2 = 0.005$, 0.04 mm Hg/100 μ m) and age (from $r^2 = 0.009$, 0.24 mm Hg/decade to $r^2 = 0.002$, 0.09 mm Hg/decade).²¹

In the present study, postoperative changes in DA ratio 2.0 mm and IntInvRad after transepithelial PRK are significantly smaller than those for femtosecond-assisted LASIK. The original parameter deformation amplitude is defined as the maximum amplitude when the cornea is deformed to its greatest concave curvature by an air puff and is influenced predominantly by IOP and secondarily by corneal stiffness.²⁷ It is well known that thinner corneas have a tendency to show higher deformation amplitude than thicker corneas with similar IOP readings.²⁷ In a previous study that evaluated the differences in corneal deformation parameters after small-incision lenticule extraction,

Table 4. Changes in dynamic corneal response parameters before and after transepithelial PRK and femtosecond-assisted LASIK using the ANCOVA analysis with changes in MRSE, CCT, corneal volume, or ARTh as a covariate.

Parameter	Mean \pm SD		P Value			
	Transepithelial PRK (n = 65)	Femtosecond-assisted LASIK (n = 64)	P^*	P^\dagger	P^\ddagger	P^\S
DA ratio 2.0 mm	0.82 \pm 0.43	1.21 \pm 0.46	<.001	<.001	<.001	<.001
SP-A1	-29.3 \pm 15.1	-30.2 \pm 14.1	.596	.193	.412	.453
ARTh	-289 \pm 80	-260 \pm 108	.095	.274	.346	—
IntInvRad	1.88 \pm 0.92	2.61 \pm 0.80	<.001	<.001	<.001	<.001

ARTh = Ambrósio relational thickness through the horizontal meridian; DA ratio 2.0 mm = deformation amplitude ratio 2.0 mm; IntInvRad = integrated inverse radius; LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy; SP-A1 = stiffness parameter at first applanation

*P value between the 2 groups regarding changes in dynamic corneal response parameters with analysis of covariance (ANCOVA) with the refractive error change as a covariate

[†]P value between the 2 groups regarding changes in dynamic corneal response parameters with ANCOVA with the corneal thickness change as a covariate

[‡]P value between the 2 groups regarding changes in dynamic corneal response parameters with ANCOVA with the corneal volume change as a covariate

[§]P value between the 2 groups regarding changes in dynamic corneal response parameters with ANCOVA with the Ambrósio relational thickness through the horizontal meridian change as a covariate

laser-assisted subepithelial keratectomy (LASEK), and femtosecond-assisted LASIK with adjustment for age, preoperative CCT and MRSE, postoperative deformation amplitude with the femtosecond-assisted LASIK was significantly higher than with LASEK.¹⁶ Considering that DA ratio 2.0 mm represents the ratio between deformation amplitude at the apex and the average of 2 points located 2.0 mm on either side of the apex, our current results—which show that changes in DA ratio 2.0 mm after adjustment for changes in refractive error, corneal thickness, corneal volume, or ARTh are significantly smaller in transepithelial PRK than femtosecond-assisted LASIK—are in line with the previous study. Both studies indicate that the corneas after femtosecond-assisted LASIK were less resistant to deformation than those after surface ablations such as PRK and LASEK. Because PRK did not create a flap (as in LASIK), its effect on the corneal structural integrity is less than with LASIK.^{28–30}

On the other hand, in a recent study that evaluated the postoperative tensile strength of the cornea after LASIK, PRK, or small-incision lenticule extraction using a mathematical model derived from depth-dependent stromal tensile strength data, Reinstein et al.²⁸ found that postoperative relative total tensile strength was greatest after small-incision lenticule extraction, followed by PRK, and was lowest after LASIK.³¹ Although we did not include data on the small-incision lenticule extraction procedure, our results are in line with those of previous studies in that transepithelial PRK causes a smaller reduction in corneal stiffness relative to femtosecond-assisted LASIK based on the result that changes in dynamic corneal response parameters such as DA ratio 2.0 mm and IntInvRad before and after transepithelial PRK were smaller than those before and after femtosecond-assisted LASIK. Further study comparing transepithelial PRK, small-incision lenticule extraction, and LASIK was necessary to show whether flap or any other phenomenon was associated with differences in the Δ dynamic corneal response parameter.

The major biomechanical effect of laser vision surgery is the amount of tissue removed to generate the change in refraction, which is similar between transepithelial PRK and femtosecond-assisted LASIK with similar intended corrections. This is shown in the preoperative to postoperative changes reported. Biomechanical differences between tissue removed from the surface or under a flap, however, are secondary and smaller. The current study indicates that surface ablation has the smallest additional effect on corneal biomechanics, consistent with the literature and evidenced by the smaller changes in DA ratio 2.0 mm and IntInvRad. Moreover, in the case of transepithelial PRK, there were strong relationships between new dynamic corneal response parameters (Δ DA ratio 2.0 mm, Δ SP-A1, Δ ARTh, and Δ IntInvRad) and refractive error change or corneal thickness change when compared with the femtosecond-assisted LASIK. Regression analysis showed that significant positive linear relationship between Δ MRSE and Δ DA ratio 2.0 mm

($r^2 = 0.228$) and Δ IntInvRad ($r^2 = 0.414$), and a negative linear relationship between Δ MRSE and Δ SP-A1 ($r^2 = 0.187$) and Δ ARTh ($r^2 = 0.318$) in the transepithelial PRK group. In the femtosecond-assisted LASIK group, there was significant positive linear relationship between Δ MRSE and Δ DA ratio 2.0 mm ($r^2 = 0.165$) and Δ IntInvRad ($r^2 = 0.144$), and a negative linear relationship between Δ MRSE and Δ SP-A1 ($r^2 = 0.136$). Interestingly, there was no relationship in the femtosecond-assisted LASIK group in the regression of changes in MRSE to changes in ARTh ($r^2 = 0.030$, $P = .175$). We suspect that there might be not only a greater variability in the measurement of ARTh, but also much weaker correlation between Δ MRSE and Δ ARTh in the femtosecond-assisted LASIK group. When compared with the transepithelial PRK group, effects of flap creation during LASIK on the corneal structural integrity are relatively larger than those in transepithelial PRK with no requirement to create corneal flap, evidenced by the smaller changes in DA ratio 2.0 mm and IntInvRad. Thus, 1 possible explanation is the added biomechanical consequences of flap creation in the femtosecond-assisted LASIK group. Further study evaluating the effect of flap creation performed by the femtosecond laser or microkeratome on corneal biomechanics is necessary to understand more thoroughly our results using new dynamic corneal response parameters. Although SP-A1 and ARTh were significantly different between the preoperative and postoperative states, they were not different between the 2 groups. Therefore, they more strongly reflect the major biomechanical effect of tissue removal and are less sensitive to the secondary differences with regard to whether the tissue is removed from the surface or under a flap.

We performed the ANCOVA with corneal thickness change as a cofactor because corneal thickness is known to be a crucial factor affecting the biomechanical response of the cornea.^{14,32} In our study, corneal thickness change was found to be a moderate but significant confounder. In terms of IOP, we showed that biomechanically corrected IOP obtained with the dynamic Scheimpflug analyzer, which is already adjusted for corneal thickness and corneal biomechanical response, was stable before and after transepithelial PRK and femtosecond-assisted LASIK, showing no significant difference. Thus, we did not include changes in biomechanically corrected IOP as a cofactor during the ANCOVA analysis.

The present study had limitations in its retrospective design and the relatively short 6-month follow-up. Although the study presented significant evidence on the stability of biomechanically corrected IOP and validity of dynamic corneal response parameters, a larger sample size and longer follow-up would allow a more thorough biomechanical comparison between laser vision surgery procedures. This will be done within a prospective controlled comparative paired-eye study comparing several laser vision surgeries.

In summary, we showed the reliability of the biomechanically corrected IOP estimates obtained by the dynamic

Scheimpflug analyzer through the stability of its measurement after a surface ablation or lamellar procedure. This result indicated the reduced effect of changes in corneal thickness and material behavior on biomechanically corrected IOP measurements compared with uncorrected IOP estimates. Most notably, changes in corneal structural integrity in transepithelial PRK are significantly less than those in femtosecond-assisted LASIK likely because of the additional effect of the flap on corneal structure. The study also showed that new dynamic corneal response parameters, such as DA ratio 2.0 mm, SP-A1, ARTh, and IntInvRad can be helpful as reliable measures of the biomechanical changes in the cornea caused by laser vision surgery.

WHAT WAS KNOWN

- There is no well-organized study comparing transepithelial PRK and femtosecond-assisted LASIK in terms of biomechanically corrected IOP measurements and new dynamic corneal response parameters obtained from the dynamic Scheimpflug analyzer.

WHAT THIS PAPER ADDS

- The dynamic Scheimpflug analyzer showed stable biomechanically corrected IOP measurements after transepithelial PRK and femtosecond-assisted LASIK.
- Corneas after femtosecond-assisted LASIK were less resistant to deformation than those after transepithelial PRK based on smaller changes in new dynamic corneal response parameters after transepithelial PRK.

REFERENCES

1. Soergel F, Jean B, Seiler T, Bende T, Mücke S, Pechhold W, Pels L. Dynamic mechanical spectroscopy of the cornea for measurement of its viscoelastic properties in vitro. *Ger J Ophthalmol* 1995; 4:151–156
2. Dupps WJ Jr, Wilson SE. Biomechanics and wound healing in the cornea. *Exp Eye Res* 2006; 83:709–720
3. Roberts CJ. Importance of accurately assessing biomechanics of the cornea. *Curr Opin Ophthalmol* 2016; 27:285–291
4. Schweitzer C, Roberts CJ, Mahmoud AM, Colin J, Maurice-Tison S, Kerautret J. Screening of forme fruste keratoconus with the Ocular Response Analyzer. *Invest Ophthalmol Vis Sci* 2010; 51:2403–2410. Available at: <http://iovs.arvojournals.org/article.aspx?articleid=2185897>. Accessed September 27, 2017
5. Roberts C. Biomechanics of the cornea and wavefront-guided laser refractive surgery. *J Refract Surg* 2002; 18:S589–S592
6. Ambrósio R Jr, Nogueira LP, Caldas DL, Fontes BM, Luz A, Cazal JO, Ruiz Alves M, Belin MW. Evaluation of corneal shape and biomechanics before LASIK. *Int Ophthalmol Clin* 2011; 51:11–38
7. Liu J, Roberts CJ. Influence of corneal biomechanical properties on intraocular pressure measurement; quantitative analysis. *J Cataract Refract Surg* 2005; 31:146–155
8. Wells AP, Garway-Heath DF, Poostchi A, Wong T, Chan KCY, Sachdev N. Corneal hysteresis but not corneal thickness correlates with optic nerve surface compliance in glaucoma patients. *Invest Ophthalmol Vis Sci* 2008; 49:3262–3268. Available at: <http://iovs.arvojournals.org/article.aspx?articleid=2125576>. Accessed September 27, 2017
9. Lee H, Kang DSY, Ha BJ, Choi JY, Kim EK, Seo KY, Kim HY, Kim TI. Biomechanical properties of the cornea measured with the dynamic Scheimpflug analyzer in young healthy adults. *Cornea* 2017; 36:53–58
10. Ambrósio R Jr, Ramos I, Luz A, Correa Faria F, Steinmueller A, Krug M, Belin MW, Roberts CJ. Dynamic ultra high speed Scheimpflug imaging for assessing corneal biomechanical properties. *Rev Bras Oftalmol* 2013; 72:99–102. Available at: <http://www.scielo.br/pdf/rbof/v72n2/05.pdf>. Accessed September 27, 2017
11. Luz A, Faria-Correia F, Salomão MQ, Lopes BT, Ambrósio R Jr. Corneal biomechanics: where are we? [editorial]. *J Curr Ophthalmol* 2016; 28:97–98. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4992120/pdf/main.pdf>. Accessed September 27, 2017
12. Bao F, Deng M, Wang Q, Huang J, Yang J, Whitford C, Geraghty B, Yu A, Elsheikh A. Evaluation of the relationship of corneal biomechanical metrics with physical intraocular pressure and central corneal thickness in ex vivo rabbit eye globes. *Exp Eye Res* 2015; 137:11–17
13. Valbon BF, Ambrósio R Jr, Fontes BM, Luz A, Roberts CJ, Alves MR. Ocular biomechanical metrics by CorVis ST in healthy Brazilian patients. *J Refract Surg* 2014; 30:468–473
14. Huseynova T, Waring GO IV, Roberts C, Krueger RR, Tomita M. Corneal biomechanics as a function of intraocular pressure and pachymetry by dynamic infrared signal and Scheimpflug imaging analysis in normal eyes. *Am J Ophthalmol* 2014; 157:885–893
15. Vinciguerra R, Elsheikh A, Roberts CJ, Kang DSY, Lopes BT, Morengi E, Azzolini C, Vinciguerra P. Influence of pachymetry and intraocular pressure on dynamic corneal response parameters in healthy patients. *J Refract Surg* 2016; 32:550–561. Available at: <http://www.healio.com/ophthalmology/journals/jrs/2016-8-32-8/%7B78250870-3d63-4f32-846b-d4fb65f8070f%7D/influence-of-pachymetry-and-intraocular-pressure-on-dynamic-corneal-response-parameters-in-healthy-patients>. Accessed September 27, 2017
16. Shen Y, Chen Z, Knorz MC, Li M, Zhao J, Zhou X. Comparison of corneal deformation parameters after SMILE, LASEK, and femtosecond laser-assisted LASIK. *J Refract Surg* 2014; 30:310–318
17. Lee H, Roberts CJ, Ambrósio R Jr, Elsheikh A, Kang DSY, Kim T-i. Effect of accelerated corneal crosslinking combined with transepithelial photorefractive keratectomy on dynamic corneal response parameters and biomechanically corrected intraocular pressure measured with a dynamic Scheimpflug analyzer in healthy myopic patients. *J Cataract Refract Surg* 2017; 43:937–945
18. Tomita M, Mita M, Huseynova T. Accelerated versus conventional corneal collagen crosslinking. *J Cataract Refract Surg* 2014; 40:1013–1020
19. Osman IM, Helaly HA, Abdalla M, Shousha MA. Corneal biomechanical changes in eyes with small incision lenticule extraction and laser assisted in situ keratomileusis. *BMC Ophthalmol* 2016; 16:123. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4960872/pdf/12886_2016_Article_304.pdf. Accessed September 27, 2017
20. Pedersen IB, Bak-Nielsen S, Vestergaard AH, Ivarsen A, Hjortdal J. Corneal biomechanical properties after LASIK, ReLEx flex, and ReLEx smile by Scheimpflug-based dynamic tonometry. *Graefes Arch Clin Exp Ophthalmol* 2014; 252:1329–1335
21. Joda AA, Shervin MMS, Kook D, Elsheikh A. Development and validation of a correction equation for Corvis tonometry. *Comput Methods Biomech Biomed Engin* 2016; 19:943–953
22. Elsheikh A. Finite element modeling of corneal biomechanical behavior. *J Refract Surg* 2010; 26:289–300
23. Vinciguerra R, Ambrósio R Jr, Elsheikh A, Roberts CJ, Lopes B, Morengi E, Azzolini C, Vinciguerra P. Detection of keratoconus with a new biomechanical index. *J Refract Surg* 2016; 32:803–810. Available at: <https://www.healio.com/ophthalmology/journals/jrs/2016-12-32-12/%7B150935e4-10b3-4720-9313-0ea017c74ac8%7D/detection-of-keratoconus-with-a-new-biomechanical-index>. Accessed September 27, 2017
24. Roberts CJ, Mahmoud AM, Bons JP, Hossain A, Elsheikh A, Vinciguerra R, Vinciguerra P, Ambrósio R Jr. Introduction of two novel stiffness parameters and interpretation of air puff induced biomechanical deformation parameters with a dynamic Scheimpflug analyzer. *J Refract Surg* 2017; 33:266–273
25. Brandt JD. Corneal thickness in glaucoma screening, diagnosis, and management. *Curr Opin Ophthalmol* 2004; 15:85–89
26. Brandt JD, Beiser JA, Kass MA, Gordon MO. Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS); the Ocular Hypertension Study (OHTS) Group. *Ophthalmology* 2001; 108:1779–1788
27. Hon Y, Lam AKC. Corneal deformation measurement using Scheimpflug noncontact tonometry. *Optom Vis Sci* 2013; 90:e1–e8. Available at: http://journals.lww.com/optvissci/Fulltext/2013/01000/Corneal_Deformation_Measurement_Using_Scheimpflug.17.aspx. Accessed September 27, 2017
28. Reinstein DZ, Archer TJ, Randleman JB. Mathematical model to compare the relative tensile strength of the cornea after PRK, LASIK, and small incision lenticule extraction. *J Refract Surg* 2013; 29:454–460. Available at: http://www.choeye.co.kr/webi_board/upFile/mathematical_model_to_compare_the_reletive_tensile_strength_of_the_cornea_after_PRK_Lasik_Smile.pdf. Accessed September 27, 2017

29. Qazi MA, Sanderson JP, Mahmoud AM, Yoon EY, Roberts CJ, Pepose JS. Postoperative changes in intraocular pressure and corneal biomechanical metrics; laser in situ keratomileusis versus laser-assisted subepithelial keratectomy. *J Cataract Refract Surg* 2009; 35:1774–1788
30. Dong Z, Zhou X, Wu J, Zhang Z, Li T, Zhou Z, Zhang S, Li G. Small incision lenticule extraction (SMILE) and femtosecond laser LASIK: comparison of corneal wound healing and inflammation. *Br J Ophthalmol* 2014; 98:263–269. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3913294/pdf/bjophthalmol-2013-303415.pdf>. Accessed September 27, 2017
31. Randleman JB, Dawson DG, Grossniklaus HE, McCarey BE, Edelhauser HF. Depth-dependent cohesive tensile strength in human donor corneas: implications for refractive surgery. *J Refract Surg* 2008; 24:S85–S89
32. Elsheikh A, Gunvant P, Jones SW, Pye D, Garway-Heath D. Correction factors for Goldmann tonometry. *J Glaucoma* 2013; 22:156–163

Disclosures: Drs. Ambrósio and Roberts are consultants to and Dr. Elsheikh has received research funding from Oculus Optikgeräte GmbH. Dr. Kang is a consultant to Avedro, Inc. and Schwind eye-tech solutions GmbH & Co. KG. None of the other authors has a financial or proprietary interest in any material or method mentioned.



First author:

Hun Lee, MD

*Department of Ophthalmology,
International St. Mary's Hospital, Catholic
Kwandong University College of Medicine,
Incheon, South Korea*