Total, Corneal, and Internal Ocular Optical Aberrations in Patients With Keratoconus

Zuzana Schlegel, MD; Yara Lteif, MD; Harkaran S. Bains; Damien Gatinel, MD, PhD

ABSTRACT

PURPOSE: To measure and compare total, corneal, and internal ocular aberrations using combined wavefront analysis and corneal topography in eyes with keratoconus and eyes with normal corneas.

METHODS: This prospective study comprised eyes of patients with keratoconus and myopic patients seeking refractive surgery. Patients diagnosed with keratoconus and with a classification of "normal" or "keratoconus" on the NIDEK Corneal Navigator corneal disease screening software were selected for inclusion in this study. The normal group comprised eyes with a "normal" classification with 99% similarity. In the normal group, only one eye per patient was randomly selected based on a randomization schedule. Corneal, internal, and total wavefront measurements were provided by the NIDEK OPD-Scan II.

RESULTS: One hundred eyes with keratoconus and 155 normal eyes were enrolled in the study. Statistically significant higher corneal and internal higher order aberrations were observed in the eyes with keratoconus ($P<.05$). However, an increase in ocular higher order aberrations proportional to corneal higher order aberrations was not observed in the keratoconus group.

CONCLUSIONS: A compensatory effect of increased anterior corneal aberrations by internal aberrations in keratoconic eyes was present for some aberrations. The origin of this compensation and the optical mechanism behind it requires further study. [*J Refract Surg*. 2009;25:S951-S957.] doi:10.3928/1081597X-20090915-10

The front corneal surface is a major refracting component of the eye and is considerably distorted in patients with keratoconus.[1] Asymmetric corneal protrusion is the primary cause of irregular astigmatism in keratoconus.[2] This deformity affects both the anterior and posterior corneal surfaces.[3-5] Recent studies have investigated the contribution of the posterior surface to the overall corneal optical performance by analyzing data obtained with slit-scanning[6] or Scheimpflug topography.[7] Significantly larger amounts of posterior corneal aberrations and higher compensation effects were observed in keratoconic eyes compared to normal eyes.[6,7] Both the posterior corneal aberrations and crystalline lens aberrations contribute to the internal aberration component.

Recent studies have found that in pre-presbyopic patients, the magnitude of higher order aberrations for the cornea or the lens individually are larger than for the entire eye.[8-12] Despite variation in size and shape, the average magnitude of aberrations in emmetropic eyes is similar to that found in eyes with mild to moderate myopia and hyperopia.[12] Artal et al[13] propose a passive, simple geometric model for the ocular compensation of aberrations. They suggest that the components of the eye are similar to an autocompensating design producing similar overall average optical quality for different refractive errors, despite large structural variations. Keratoconus represents an acquired structural change, and currently, no study has investigated the ocular, anterior corneal, and internal higher order wavefront aberrations in a large number of eyes with keratoconus using a combined anterior corneal topographer and aberrometer (OPD-Scan II; NIDEK Co Ltd, Gamagori, Japan).

From the Department of Ophthalmology, Rothschild Foundation; AP-HP Bichat-Claude Bernard Hospital; and Center for Expertise and Research in Optics for Clinicians, Paris, France (Schlegel, Lteif, Gatinel).

Mr Bains is a consultant to NIDEK Co Ltd. The remaining authors have no proprietary interest in the materials presented herein.

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Correspondence: Damien Gatinel, MD, PhD, Rothschild Foundation, 25 rue Manin, 75019 Paris, France. Tel: 33 1 48 03 64 82; Fax: 33 1 48 03 64 87; E-mail: gatinel@aol.com

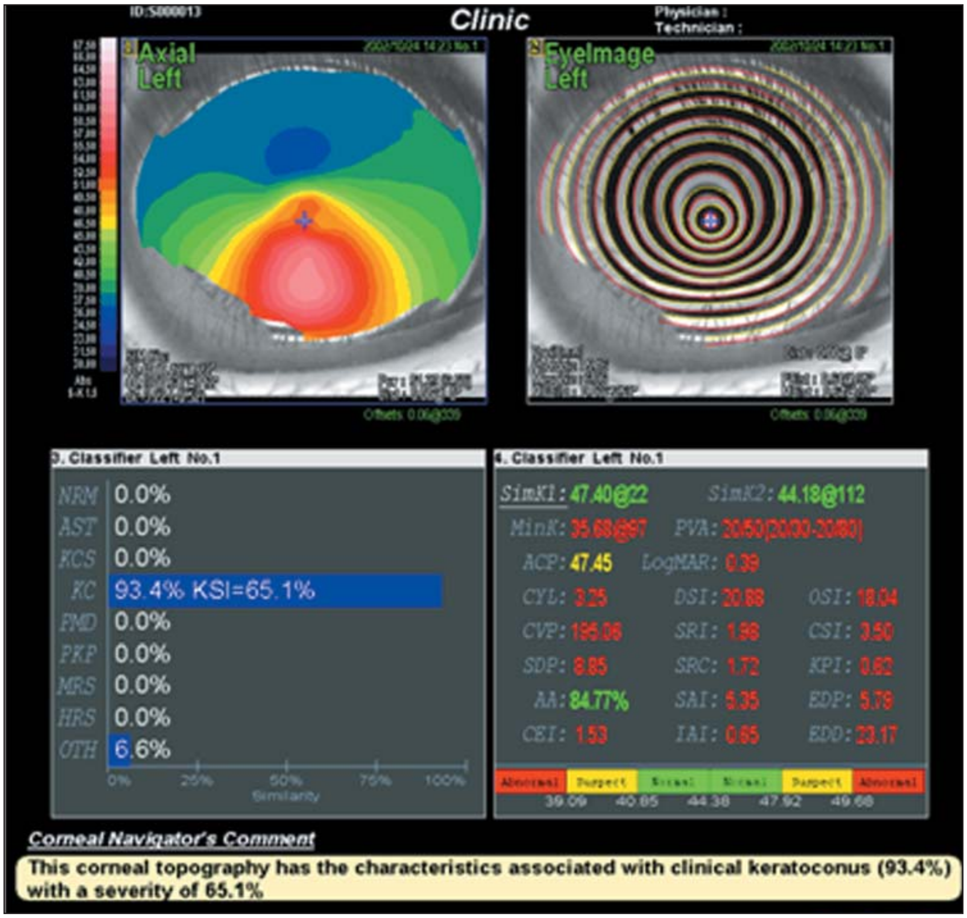

Figure 1. Screen image of the Corneal Navigator (NIDEK Co Ltd, Gamagori, Japan) software of an eye with keratoconus. KC = keratoconus, KSI = keratoconus severity index

PATIENTS AND METHODS

This prospective study included eyes of patients with keratoconus and eyes of myopic patients seeking refractive surgery at the outpatient clinic of the Department of Ophthalmology at the Rothschild Foundation, Paris, France, between October 2007 and October 2008. This research adhered to the tenets of the Declaration of Helsinki. Verbal informed consent was obtained from all patients after an explanation of the risks and benefits of the study.

The Corneal Navigator (NIDEK Co Ltd) software was used to analyze the data obtained via the OPD-Scan II anterior Placido-based topographer. The Corneal Navigator uses artificial intelligence to train a computer neural network to recognize specific classifications of corneal topography. The Corneal Navigator first calculates various indices representing the characteristics of corneal shape and then classifies the cornea into one of the following nine types: “normal,” “astigmatism,” “keratoconus suspect,” “keratoconus,” “pellucid marginal degeneration,” “post-keratoplasty,” “myopic refractive surgery,” “hyperopic refractive surgery,” and “unclassified variation” (Fig 1). These diagnostic results are estimated based on the relationship between many corneal indices and cases. For each diagnostic condition, the percentage of similarity is indicated, and the value can vary from 0 to 99%. The result for each topography classification is independent of other categories. Only eyes classified as “normal” or “keratoconus” by the Corneal Navigator were selected for inclusion in this study (see Fig 1).

Inclusion and Exclusion Criteria for Eyes With Keratoconus

For patients with keratoconus, bilateral data were used when available; however, in some cases, keratoconus was more advanced in one eye compared to the fellow eye. Inclusion criteria were a positive (>80%) score for manifest keratoconus similarity using the Corneal Navigator with no previous eye disease, injury, contact lens wear, or surgery. Other inclusion criteria were one or more of the following obtained with OPD-Scan II or Orbscan IIz (Bausch & Lomb, Rochester, NY) corneal topography: an area of central, inferior, or superior marked steepening; topographic asymmetry; oblique cylinder >1.50 diopters (D); steep keratometric curvature >47.00 D; or minimal central corneal thickness <500 µm. All eyes with a positive keratoconus classification with the Corneal Navigator were examined by an ophthalmologist for central thinning of the stroma, with a Fleischer’s ring, Vogt’s striae, or both observed on slit-lamp examination, which were considered confirmatory criteria, not required criteria, for inclusion in this study. Patients with corneal scarring, cataract, or other ocular diseases and eyes with advanced keratoconus from which reliable topography or wavefront measurements could not be obtained were excluded from the study. Patients classified as “keratoconus suspect” by the Corneal Navigator and those with a forme fruste keratoconus pattern on Orbscan IIz topography were excluded. A forme fruste pattern on the Orbscan IIz included focal or inferior corneal steepening and/or central keratometry >47.00 D on the keratometric map. Orbscan IIz was used as a secondary confirmation of the topography patterns associated with suspicious or forme fruste topographies. We routinely use corneal topography measurements from two different topographers (OPD-Scan II and Orbscan IIz) to confirm topographic patterns. If both topography measurements gave a similar pattern indicative of forme fruste, the patient was excluded from the study. Additionally, the Orbscan IIz provides elevation topography of the posterior corneal surface, which could indicate early changes associated with keratoconus. Such patients were also excluded. Using this method, we ensured that the corneas were considered normal based on currently available technology.

To be included in the study, measurements before any surgery using the OPD-Scan and Orbscan IIz (Bausch & Lomb) had to be acquired successfully. The Orbscan and OPD-Scan measurements were performed by two experienced operators (Jacques Munck, OD; Maud Thévenot, OD).

Inclusion and Exclusion Criteria for Normal Eyes

The normal group comprised eyes with a "Normal" classification with 99% similarity and without a forme fruste keratoconus pattern on Orbscan IIz topography maps. In the normal group, only one eye per patient was randomly selected based on a randomization schedule.

Patients with a physiologic pupil diameter <5 mm in mesopic conditions and preoperative central corneal thickness <490 µm were excluded. Patients with corneal thickness <490 µm were excluded due to inadequate residual stromal bed thickness after LASIK, which could be a risk factor for ectasia (as normal eyes were selected from the prospective refractive surgery candidates).

Procedure

All eyes underwent a baseline ophthalmic examination that included slit-lamp microscopy, corneal pachymetry, and simultaneous measurement of corneal topography, wavefront aberrometry, and photopic and mesopic pupil size using the OPD-Scan II.

Combined Aberrometry and Corneal Measurements

The mean central keratometry and total, corneal, and internal optical aberrations were measured using the OPD-Scan II. This device measures the autorefraction, keratometry, photopic and mesopic pupil diameters, corneal topography, and wavefront aberrations simultaneously on the same axis without moving the patient.

All wavefront data were measured using the OPD-Scan II. The wavefront error is calculated using time-based aberrometry as opposed to position-based aberrometry. This allows the instrument to have a broader dynamic range, higher resolution, increased accuracy, and is particularly adapted to the measurement of highly aberrated eyes compared to position-based aberrometers such as Hartmann-Shack aberrometers.[14-17] The corneal topography is measured using Placido-disk technology and the ocular wavefront is measured using the principle of skiascopic phase difference. The retina is scanned with an infrared light slit beam and the reflected light is captured by an array of rotating photodetectors over a 360° area. Measurements are taken within 0.5 seconds for 1440 pupil positions. It is particularly adapted to the measurement of highly aberrated eyes partly due to the semi-sequential acquisition (meridian by meridian), which reduces the risk of error in wavefront reconstruction. The OPD-Scan II has similarities with Placido-disk type keratographers in that measurement at any pupil position is in a radial direction only.

Corneal topography measurements provide the simulated keratometry, average corneal asphericity, and color-coded maps of the corneal surface and elevation. Placido-disk–based corneal topography measures the precise characteristics of the corneal surface, transforming shape into color-coded dioptric power maps. Virtual ray tracing is performed using the OPD Station software (NIDEK Co Ltd) to obtain the corneal wavefront aberrations, expressed at the pupil plane through a 6th order Zernike expansion. Coupling corneal topography measurements with aberrometry measurements permits the display of the internal aberrations of the eye. Internal wavefront aberrations are computed from direct term-by-term subtraction between the total (ocular) and corneal wavefront Zernike terms. All wavefront aberrations are calculated and plotted with respect to the corneal vertex.

All OPD-Scan II measurements were acquired under dim illumination (2.2 lux) after 2 minutes of dark adaptation and were repeated at least three consecutive times before calculating the average with dark adaptation between each measurement. Total, corneal, and internal wavefront aberrations were reconstructed using a 6th order Zernike polynomial decomposition for a 5-mm pupil, centered on the corneal vertex for a physiologically dilated pupil.

Data Analysis

The following data were compared between the two groups: objective refraction (spherical equivalent, and spherical refraction and astigmatism) and root-mean-square (RMS) of the total, corneal, and internal wavefront. From the Zernike coefficients, of the 27 terms

TABLE 1

Demographics and Refraction of Normal Eyes and Eyes With Keratoconus

	Mean±Standard Deviation		
	Normal Eyes	Eyes With Keratoconus	*P* Value
Sex (M/F)	85/70	64/48	.09
Age (y)	33.4±8.7	31.7±9.3	.21
Sphere (D)	−3.67±2.73	−4.72±4.12	.004
Cylinder (D)	−3.23±2.60	−4.12±4.43	.0006

of the Zernike pyramid included in the 6th order decomposition (excluding the 0th=Z_0^0 piston term), the following groups were examined:

Tilt group (1st=Z_1^{-1} and 2nd=Z_1^1 terms);

Lower order astigmatism group (3rd=Z_2^{-2} and 5th=Z_2^2 terms);

Higher order group (all terms included in the 3rd, 4th, 5th, and 6th order);

Total coma group (7th=Z_3^{-1}, 8th=Z_3^1, 17th=Z_5^{-1}, and 18th=Z_5^1 terms);

Total trefoil group (6th=Z_3^{-3}, 9th=Z_3^3, 16th=Z_5^{-3}, and 19th=Z_5^3 terms);

Total spherical aberration group (12th=Z_4^0 and 24th=Z_6^0 terms);

Total tetrafoil group (10th=Z_4^{-4}, 14th=Z_4^4, 22nd=Z_6^{-4}, and 26th=Z_6^4 terms);

Higher order astigmatism (11th=Z_4^{-2}, 13th=Z_4^2, 23rd=Z_6^{-2}, and 25th=Z_6^2 terms).

These aberration term groups were used to describe the corneal aberrations, internal aberrations, and total eye aberrations.

Statistical comparison between the two group measurements was performed using the Student *t* test (independent samples). A *P* value <.05 was considered statistically significant.

RESULTS

One hundred eyes with keratoconus were included in the keratoconus group, and 155 eyes, classified as normal, were included in the normal group. The demographics and mean objective refraction (spherical and cylindrical refractive error measured by the OPD-Scan II at the spectacle plane) are presented in Table 1.The lower and higher order total ocular aberrations were statistically significantly different between groups (Table 2). All corneal aberrations were statistically significantly higher in the keratoconus group (Table 3). All internal aberrations were statistically significantly higher in the keratoconus group compared to the normal group (Table 4).

TABLE 2

Total Ocular Aberrations in Normal Eyes and Eyes With Keratoconus

	Root-Mean-Square±SD (μm)		
Aberration	Normal Eyes	Eyes With Keratoconus	*P* Value
Tilt	0.28±0.23	2.00±1.74	.000
Lower order astigmatism	0.41±0.47	1.26±1.00	<.0001
Higher order total	0.27±0.27	1.18±0.85	<.0001
Total coma	0.11±0.10	0.72±0.61	.000
Total trefoil	0.20±0.24	0.73±0.54	<.005
Total quadrafoil	0.07±0.10	0.18±0.38	<.0004
Total spherical aberration	0.06±0.05	0.22±0.22	<.001
Total higher order astigmatism	0.04±0.04	0.14±0.12	<.001

Note. All aberrations were measured to the 6th order Zernike polynomial for a 5-mm pupil centered on the corneal vertex.

Except for lower order astigmatism and total trefoil, the magnitudes of the various ocular aberrations were proportionally lower than their respective corneal components in the keratoconus group (Fig 2). This indicates a partial balancing effect of corneal aberrations by internal aberrations.

DISCUSSION

This study found differences in total, anterior corneal, and internal ocular aberrations among normal and keratoconic eyes. Corneal aberrations were calculated from corneal data with respect to the corneal vertex. To allow direct calculation of the internal aberration, corneal and total aberrations must be plotted on a common axis to avoid calculation errors. In the current study, both the total and corneal aberrations were calculated with regards to the corneal vertex, and no realignment procedures were required before comparing corneal and total aberrations. Unlike our measurements, most methods plot aberrations on the line of sight, which is defined as the line joining the fovea to the pupil center.[18] However, the location of the pupil center can deviate with differing pupil diameters causing ambiguity in the reference plane.[19] Salmon and Thibos[20] reported the consequences of incorrect misalignment when measuring corneal and total aberrations separately. In the current study, corneal and total aberrations were measured on a common axis (videokeratometric axis), which differs from the line of

TABLE 3

Corneal Aberrations in Normal Eyes and Eyes With Keratoconus

	Root-Mean-Square±SD (μm)		
Indices	Normal Eyes	Eyes With Keratoconus	*P* Value*
Tilt	0.34±0.26	3.86±2.77	.000
Lower order astigmatism	0.70±0.55	1.17±1.33	<.0006
Higher order total aberrations	0.26±0.26	1.63±1.98	.00001
Total coma	0.14±0.12	1.35±0.95	.000
Total trefoil	0.12±0.12	0.57±0.38	<.0001
Total quadrafoil	0.06±0.12	0.20±0.20	<.0004
Total spherical aberration	0.14±0.09	0.33±0.30	<.0003
Total higher order astigmatism	0.05±0.10	0.28±0.21	<.0001

**Student t test.*
Note. All aberrations were measured to the 6th order Zernike polynomial for a 5-mm pupil centered on the corneal vertex.

TABLE 4

Internal Aberrations in Normal Eyes and Eyes With Keratoconus

	Root-Mean-Square±SD (μm)		
Indices	Normal Eyes	Eyes With Keratoconus	*P* Value*
Tilt	0.28±0.17	2.09±1.52	.0001
Lower order astigmatism	0.42±0.23	0.91±0.61	.0001
Higher order total aberrations	0.29±0.24	0.93±0.68	.0001
Total coma	0.11±0.10	0.72±0.51	.0001
Total trefoil	0.14±0.11	0.30±0.35	.0001
Total quadrafoil	0.08±0.11	0.17±0.25	.001
Total spherical aberration	0.16±0.09	0.21±0.17	.0055
Total higher order astigmatism	0.05±0.09	0.22±0.24	.0001

**Student t test.*
Note. All aberrations were measured to the 6th order Zernike polynomial for a 5-mm pupil centered on the corneal vertex.

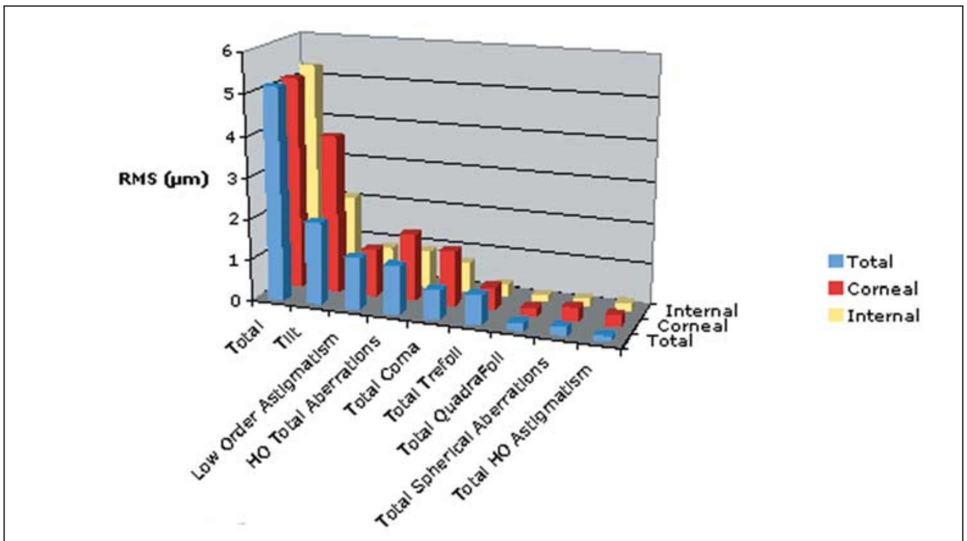

Figure 2. Total, corneal, and internal higher order (HO) aberrations in 100 eyes with keratoconus. All aberrations were measured to the 6th order Zernike polynomial for a 5-mm pupil, centered on the corneal vertex. RMS = root-mean-square

sight and is not affected by pupil diameter. Given the frank level of increase in the magnitude of higher order aberrations in eyes with keratoconus, we postulate that a shift of the reference plane would not significantly alter the broad conclusions of our study. In a previous study of aberration compensation of LASIK patients, we calculated the differences in plotting aberration on the line of sight and corneal vertex and found them to be clinically negligible.[21]

The keratoconic group in this study consisted of moderate to advanced cases of keratoconus. Root-mean-square values were higher for keratoconic eyes than normal eyes, with a significant difference of total, anterior, and internal aberrations ($P<.05$) (Tables 2-4). In the keratoconic group, we found a reduction in total ocular aberrations compared to anterior corneal aberrations for all higher order aberration groups except trefoil. For the lower order aberrations, some compensatory effect was found for the tilt aberration, but not for lower order astigmatism.

The attenuation of corneal aberrations by internal aberrations may be due to the posterior corneal surface when its geometrical deformation adopts a mirror image of the anterior surface, inducing an optical deviation of approximately equal yet opposite sign due to the inversion of refractive index gradient between the stroma and aqueous humor. The anterior cornea generated lower order astigmatism (2nd order) and trefoil-type aberrations that were not compensated internally. One explanation could be due to the nature of the keratoconus distortion, which may induce some specific difference in the azimuthal correspondence between the anterior and posterior corneal surfaces for specific aberrations, making aberrations with azimuthal frequency of 2 and 3 less prone to compensating effects from the posterior surface. However, recent studies have found some posterior compensation for these aberrations when they arise at the anterior surface.[6,7] An alternate explanation might be that the lens sutures may become unmasked due to the corneal deformation giving rise to excess trefoil and a breakdown of the compensation mechanism. Subtle alterations in the tilt of the crystalline lens, by changing the relative alignment of the anterior and posterior lens sutures, could change the magnitude of trefoil.[12,22,23]

Rigid gas permeable lenses are a treatment option for keratoconus. These lenses can mask the anterior corneal aberrations by regularizing the anterior corneal surface, thereby reducing higher order aberrations. However, visual performance is still not the same as after correction of a normal myopic or regular astigmatic eye.[24-26] This suggests that some internal structure, presumably the posterior surface of the cornea, may induce a larger amount of aberrations in eyes with keratoconus.

Barbero et al[27] measured total and corneal wave aberrations of three eyes diagnosed with keratoconus by slit-lamp microscopy and corneal topography: two eyes from one patient with early keratoconus and one eye with more advanced keratoconus. Total aberrations were measured with laser ray tracing. Corneal aberrations were obtained from corneal elevation data measured with a corneal videokeratoscope using custom software that performs virtual ray tracing on the measured front corneal surface. A dramatic increase in aberrations (both corneal and total), particularly coma-like terms, was found in the eyes with keratoconus. The similarity between anterior corneal surface aberrations and total aberrations was greater for the patient with early keratoconus, suggesting a possible implication of the posterior corneal surface in advanced keratoconus.

To date, this internal compensation for keratoconus anterior corneal induced aberrations has not been reported on such a large subset of patients. This is primarily due to the inability of Hartmann-Shack aberrometers to measure highly aberrated eyes and relative lack of commercially available instruments, such as the OPD-Scan II, that can measure both corneal and total aberrations on the same axis. However, studies on the reliability of OPD-Scan II data from highly aberrated eyes are not available and therefore our data should be interpreted with caution. Another limitation of the data in this study is that change in axis and orientation of the aberrations were not analyzed, as we used only grouped aberrations compared to individual Zernike coefficients. We elected to report aberrations for a 5-mm pupil diameter rather than a 6-mm pupil diameter to ensure no artifacts were present from pupil reflection, as all measurements were performed on physiologically dilated pupils.

A compensatory effect was observed of increased anterior corneal aberrations by internal aberrations in keratoconic eyes for certain higher order aberrations. Although the posterior corneal surface may account for most of this compensation, further study is required to identify the exact mechanisms.

AUTHOR CONTRIBUTIONS

Study concept and design (D.G.); data collection (Z.S., Y.L., D.G.); interpretation and analysis of data (Z.S., D.G., H.S.B.); drafting of the manuscript (Y.L., H.S.B.); critical revision of the manuscript (Z.S., D.G., H.S.B.); statistical expertise (D.G.)

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