

# Correlation between Corneal Topographic Indices and Higher-Order Aberrations in Keratoconus

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**Purpose:** To compare corneal higher-order aberrations (HOAs) between normal and keratoconic eyes, and to investigate the association between elevation-based corneal topographic indices and corneal wavefront data in the latter group.

**Methods:** In this cross-sectional comparative study, 77 normal right eyes of 77 control subjects and 66 eyes of 36 keratoconic patients were included. In each eye, elevation-based corneal topographic indices including mean keratometry readings, best-fit sphere, maximum elevation, and 3-mm and 5-mm zone irregularity indices were measured using Orbscan II. The Galilei Scheimpflug analyzer was used to measure HOAs of the corneal surface. The independent student t-test was used to compare HOAs between the study groups. Spearman correlation was used to investigate possible associations between Orbscan and Galilei data in the keratoconus group.

**Results:** All Zernike coefficients up to the 4<sup>th</sup> order except for horizontal trefoil, and vertical and horizontal tetrafoil were significantly greater in the keratoconus group than normal eyes ( $P < 0.05$ ). Root mean square (RMS) of HOAs up to the 6<sup>th</sup> order and total HOAs were significantly higher in the keratoconus group ( $P < 0.05$ ). In the keratoconus group, the strongest association was observed between vertical coma ( $r = -0.71$ ,  $P < 0.01$ ) and total RMS of HOAs ( $r = 0.94$ ,  $P < 0.01$ ) with irregularity in the 3-mm zone. Spherical and vertical coma aberrations were significantly correlated with mean keratometry ( $P < 0.05$  for both comparisons).

**Conclusion:** Centrally located corneal HOAs are significantly greater in keratoconic eyes than normal controls. Anterior and inferior displacement of the cornea causes the majority of higher-order aberrations observed in keratoconus.

**Keywords:** Keratoconus; Orbscan II; Galilei; Higher-order Aberrations

*J Ophthalmic Vis Res* 2013; 8 (2): 113-118.

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**Received:** December 20, 2012      **Accepted:** February 15, 2013

## INTRODUCTION

Keratoconus is a non-inflammatory, usually progressive disease of unknown etiology. It leads to thinning and bulging of the cornea and consequently produces irregular astigmatism and myopia. Detection of keratoconus among refractive surgery candidates is important because the prevalence of keratoconus is

higher in such eyes as compared to the general population<sup>1,2</sup> and operating on an undetected keratoconic cornea is a major cause of post-refractive surgery ectasia.<sup>3</sup>

The diagnosis of keratoconus is based on biomicroscopic findings, and additional tests, such as pachymetry, keratometry and corneal topography.<sup>4</sup> Measurement of Placido disk-based videokeratography and central corneal thickness

are widely used methods in the diagnosis of keratoconus.<sup>5-7</sup> However, Placido disk-based corneal topography only examines the central 7-8 mm of the anterior corneal surface and its results are sensitive to alterations in reference point or viewing angle.<sup>8,9</sup> Additionally, the accuracy of contact ultrasonic pachymetry is operator dependent.<sup>10</sup>

Other available diagnostic modalities, in particular, corneal elevation-based topography and wavefront analysis, have become more widely used in an effort to supplement videokeratographic data. The Orbscan II (Bausch & Lomb, Rochester, NY, USA) is a 3-dimensional scanning-slit topography system employed for analysis of the anterior and posterior corneal surfaces as well as pachymetry. It utilizes a scanning-slit system to measure 18,000 data points and also uses a Placido-based system to make necessary adjustments to yield topographic data.

The Galilei dual Scheimpflug system (Ziemer Ophthalmic Systems AG, Zurich, Switzerland) is a noninvasive diagnostic system designed for evaluating the anterior segment by analyzing corneal shape and thickness, pupil size, and anterior chamber size, volume and angle. It combines both technologies including Placido imaging which provides curvature data, and Scheimpflug imaging which is optimal for precise elevation data. The Galilei system can extrapolate corneal wavefront data from analysis of anterior and posterior corneal surfaces using mathematical analysis of height data.<sup>11</sup>

Some investigators have used higher order aberrations (HOAs) to distinguish early keratoconus from normal and others have used them to grade the severity of keratoconus.<sup>12,13</sup> The purpose of this study was to compare corneal HOAs, measured with the Galilei Scheimpflug analyzer, between normal and keratoconic corneas, and to evaluate the correlation between these data and topographic findings obtained with the Orbscan II in keratoconic corneas.

## METHODS

In this prospective comparative study, 36 consecutive patients (17 male subjects)

with keratoconus and 77 normal age-matched controls (34 male subjects) who were scheduled for refractive surgery were included. Only right eyes of the normal group were enrolled in the study.

The diagnosis of keratoconus was based on slit lamp findings (stromal thinning, conical protrusion, Fleischer ring and Vogt striae), and associated Placido-based topographic patterns described by Rabinowitz.<sup>5</sup> Eyes with previous acute corneal hydrops or history of ocular surgery were excluded. In the normal group, the only ocular abnormality was refractive errors and subjects with any ocular pathology such as dry eye, keratoconus, glaucoma, retinal disease, ocular surgery, or systemic conditions such as diabetes mellitus and connective tissue disorders were excluded. All participants were asked to stop wearing soft contact lenses for at least two weeks and rigid gas-permeable contact lenses for at least four weeks before obtaining measurements.

The Ethics Committee of the Ophthalmic Research Center approved the study and written informed consent was obtained from all participants after explaining the purpose of the study.

A complete ocular examination including slit lamp biomicroscopy, cycloplegic refraction, best spectacle-corrected visual acuity (BSCVA) using a Snellen chart, intraocular pressure measurement and dilated fundus examination was performed.

Data including mean keratometry readings, anterior and posterior elevation best-fit sphere, maximum anterior and posterior elevation, and 3-mm and 5-mm zone irregularity indices were obtained from Orbscan II measurements.

For measurements with the Galilei dual Scheimpflug analyzer, appropriate alignment of the scan center with the corneal apex was checked using an initial Scheimpflug image formed on the monitor. The measurement results were checked under a quality-specification window; only measurements with an "OK" reading were included.

HOAs were calculated for corneal diameter of 6 mm up to the eighth order in terms of Zernike polynomials. Zernike coefficients

were transformed to the standard form as recommended by the Optical Society of America.<sup>14</sup> Since both eyes were included in the keratoconus group, enantiomorphism was neutralized by inverting the sign of mirror-symmetric coefficients of left eyes as follows:<sup>15,16</sup>

For all  $Z_n^m$  if  $n = \text{even}$  and  $m < 0 \rightarrow Z_n^m = -(Z_n^m)$   
 For all  $Z_n^m$  if  $n = \text{odd}$  and  $m > 0 \rightarrow Z_n^m = -(Z_n^m)$

All measurements were obtained by an experienced operator using the same machines and procedures.

### Statistical Analysis

Data including age, spherical equivalent (SE) refraction, keratometry readings, Zernike coefficients, and root mean square (RMS) were expressed as mean  $\pm$  standard deviation using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). Independent student t-test was used to compare

HOAs between the study groups. In the keratoconus group, Spearman's correlation was used to investigate associations between Orbscan derived data including keratometry readings, anterior and posterior elevation best-fit sphere, maximum anterior and posterior elevation, and 3 and 5 mm zone irregularity indices against HOAs as determined by the Galilei. P values less than 0.05 were considered as statistically significant.

### RESULTS

Seventy-seven right eyes of 77 normal controls and 66 (30 right) eyes of 36 keratoconus patients were evaluated and analyzed. Mean age was  $28.6 \pm 4.7$  (range, 20-40) years in the normal group and  $31.1 \pm 5.5$  (range, 19-40) years in the keratoconus group ( $P=0.63$ ). Table 1 compares refractive data between the study groups.

All Zernike coefficients up to the 4<sup>th</sup> order

**Table 1.** Refraction and keratometry readings in the study groups

Characteristics	Normal group	Keratoconus group	P-value
Cycloplegic refraction (D)			
Sphere	-2.21 $\pm$ 1.85	-3.66 $\pm$ 4.86	0.02
Cylinder	-1.01 $\pm$ 1.10	-4.32 $\pm$ 2.67	0.006
Spherical equivalent	-2.72 $\pm$ 1.81 (-13.25 to -0.25)	-5.82 $\pm$ 4.91 (-22.0 to 0.0)	<0.001
Mean keratometry (D)	44.11 $\pm$ 1.25 (41.39 to 47.73)	50.36 $\pm$ 5.18 (48.7 to 64.55)	<0.001
Keratometric astigmatism (D)	1.28 $\pm$ 1.02 (0.0 to 4.25)	5.40 $\pm$ 2.84 (2.75 to 11.50)	<0.001

D, diopter

**Table 2.** Comparison of Zernike coefficients and root mean squares (RMS) of higher-order aberrations (HOAs) between the normal and keratoconic eyes

HOAs	Normal group ( $\mu\text{m}$ )	Keratoconus group ( $\mu\text{m}$ )	P-value
Vertical trefoil	-0.15 $\pm$ 0.22	0.48 $\pm$ 1.07	<0.001
Vertical coma	0.004 $\pm$ 0.37	-1.78 $\pm$ 1.73	<0.001
Horizontal coma	-0.11 $\pm$ 0.27	-0.70 $\pm$ 1.19	<0.001
Horizontal trefoil	-0.04 $\pm$ 0.24	-0.29 $\pm$ 1.40	0.12
Vertical tetrafoil	0.0 $\pm$ 0.14	-0.04 $\pm$ 0.51	0.56
Vertical secondary astigmatism	-0.01 $\pm$ 0.14	0.36 $\pm$ 0.61	<0.001
Spherical	0.23 $\pm$ 0.09	-0.59 $\pm$ 1.09	<0.001
Horizontal secondary astigmatism	-0.04 $\pm$ 0.12	0.11 $\pm$ 0.61	0.03
Horizontal tetrafoil	-0.11 $\pm$ 0.16	-0.04 $\pm$ 0.43	0.30
RMS of 3 <sup>rd</sup> order	0.49 $\pm$ 0.33	2.86 $\pm$ 1.81	<0.001
RMS of 4 <sup>th</sup> order	0.39 $\pm$ 0.43	1.14 $\pm$ 1.24	<0.001
RMS of 5 <sup>th</sup> order	0.11 $\pm$ 0.08	0.63 $\pm$ 1.49	0.002
RMS of 6 <sup>th</sup> order	0.05 $\pm$ 0.03	0.36 $\pm$ 1.26	0.037
RMS of 7 <sup>th</sup> order	0.0	0.15 $\pm$ 1.04	0.21
RMS of 8 <sup>th</sup> order	0.0 $\pm$ 0.01	0.10 $\pm$ 0.56	0.11
<b>RMS of total HOAs</b>	<b>1.55<math>\pm</math>0.94</b>	<b>5.94<math>\pm</math>3.91</b>	<b>&lt;0.001</b>

Higher order aberrations are reported for a 6 mm diameter

**Table 3.** Correlation coefficients between different Orbscan height data and higher-order aberrations

Higher-order aberrations	Elevation data						Mean keratometry
	Anterior elevation best-fit sphere	Posterior elevation best-fit sphere	Maximum anterior elevation	Maximum posterior elevation	3-mm zone irregularity	5-mm zone irregularity	
Vertical trefoil	-0.22	-0.16	0.32*	0.34*	0.53**	0.41**	0.22
Vertical coma	0.07	0.05	-0.59**	-0.64**	-0.71**	-0.59**	-0.32**
Horizontal coma	-0.24	-0.30*	-0.29*	-0.29*	-0.35**	-0.31*	-0.18
Horizontal trefoil	-0.04	-0.01	-0.16	-0.31*	-0.24	-0.18	-0.11
Vertical tetrafoil	-0.08	-0.15	-0.18	-0.24	-0.29*	-0.22	-0.13
Vertical secondary astigmatism	-0.11	-0.03	0.32*	0.27*	0.37**	0.23	0.18
Spherical	-0.13	-0.26	-0.60**	-0.62**	-0.60**	-0.59**	0.67**
Horizontal secondary astigmatism	0.12	0.20	0.19	0.14	0.18	0.26	0.30*
Horizontal tetrafoil	0.09	0.12	-0.20	-0.07	-0.21	-0.18	-0.04
Total RMS of higher-order aberrations	0.20	0.27*	0.86**	0.85**	0.94**	0.89**	0.78**

RMS: root mean square, \* P<0.05, \*\* P<0.01

except for horizontal trefoil, and vertical and horizontal tetrafoil were significantly greater in the keratoconus group as compared to the normal group. The RMS of HOAs up to the 6<sup>th</sup> order and total HOAs were also significantly higher in the keratoconus group (P<0.05). However, there was no statistically significant difference in terms of 7<sup>th</sup> or 8<sup>th</sup> order RMS between the study groups. (Table 2)

Spearman correlation indicated the strongest association to be between total RMS of HOAs and irregularity at the 3-mm zone. Among individual Zernike coefficients, the association between vertical coma and irregularity of the 3-mm zone was strongest (Table 3). Additionally, spherical and vertical coma aberrations were significantly correlated with mean keratometry readings (P<0.05). However, the correlation of spherical aberration was stronger (r=0.67, P<0.01). No aberration was significantly correlated with the anterior elevation best-fit sphere and only horizontal coma demonstrated a significant but weak association with the posterior elevation best-fit sphere (Table 3).

## DISCUSSION

This study reports the characteristics of individual Zernike coefficients in keratoconic eyes in comparison to normal controls. To the best of our knowledge, it is the first to investigate the correlation between height data and corneal

aberrations. The Orbscan II quantitatively depicts abnormalities of both anterior and posterior corneal surfaces, while the corneal wavefront determines the extent an abnormal cornea can distort the retinal image and also predicts the potential visual performance.

Although height map data could have been obtained with the Galilei Scheimpflug analyzer and this instrument has previously been found to have high repeatability for corneal wavefront measurement in normal unoperated eyes,<sup>11,17</sup> it utilizes a mathematical method to convert height data to corneal aberrations. Therefore, since these two variables are mathematically correlated, statistical analysis for association does not make sense. For this reason, we utilized independent data obtained by the Orbscan machine.

The results of our study demonstrated that all aberrations except for horizontal trefoil, and vertical and horizontal tetrafoil were significantly higher in the keratoconus group than normal eyes. Interestingly, these findings were supported by the results of Spearman correlation which demonstrated a significant association between spherical, coma and trefoil aberrations with topographic indices reflecting the severity of keratoconus such as mean keratometry, and 3- and 5-mm zone irregularity.

Additionally, the RMS of HOAs up to the sixth order was significantly higher in the keratoconus group. However, the RMS of remaining orders (7<sup>th</sup> and 8<sup>th</sup>) was comparable

between the study groups. It is possible that these aberrations are too coarse to represent subtle changes in irregular corneas.

Previous studies have reported that aberrations (especially coma-like aberrations) in keratoconic eyes are significantly different from normal eyes.<sup>13,18-21</sup>

Maeda et al<sup>18</sup> compared corneal aberrations in normal eyes and eyes with forme fruste or mild keratoconus and found that coma-like and spherical-like aberrations were significantly higher in the latter group. Additionally, they reported the dominance of coma-like aberrations over spherical-like aberrations in the keratoconus group. This observation indicates that the earliest manifestation of corneal asymmetry in keratoconus is vertical.<sup>22</sup> In the current study which included more severe cases, both vertical and horizontal coma were significantly greater in the keratoconus group than controls. However, vertical coma had a stronger association with irregularity in the 3-mm and 5-mm zones in keratoconic eyes, as compared to horizontal coma. In keratoconus, the cone is displaced inferiorly in most of the cases, resulting in an increase in topographic indices such as the inferior-superior (I-S) index or surface asymmetry index (SAI).<sup>23</sup> This explains why vertical aberrations were more prominent and why the Zernike coefficient of horizontal trefoil did not differ between the study groups.

The present study revealed that spherical aberration in keratoconic eyes had a stronger association with mean keratometry readings than did coma. In addition to inferior displacement, a keratoconic cornea also displaces anteriorly resulting in a hyperprolate profile, leading to an increase in spherical aberration.

The results of our study also demonstrated that both horizontal and vertical tetrafoil aberrations of keratoconic eyes were not significantly higher than controls. Furthermore, except for a weak association between vertical tetrafoil and irregularity in the 3-mm zone, both vertical and horizontal tetrafoil were not significantly correlated with any topographic parameter determined by Orbscan in the keratoconus group. These observations indicate that the peripheral portion of the corneal

wavefront may be less affected in keratoconic eyes.

In conclusion, centrally located corneal higher-order aberrations are significantly greater in keratoconic eyes as compared to controls. However, the peripheral portion of the corneal wavefront remains relatively spared in keratoconus. Characteristics of HOAs may be predicted from abnormalities in corneal shape as determined by height data.

### Conflicts of Interest

None.

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