Characterizing the Wave Aberration in Eyes with Keratoconus or Penetrating Keratoplasty Using a High–Dynamic Range Wavefront Sensor

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Purpose: The purpose of this study was to characterize aberrations in 2 populations of eyes, namely those with keratoconus (KC) and those having undergone penetrating keratoplasty (PK), using a large–dynamic range Shack-Hartmann wavefront sensor.

Design: Prospective comparative case series.

Participants: Twenty-one people with ocular pathologic features (either KC or PK) were recruited for this study. A previously compiled population of 190 people with no pathologic features other than refractive error was used as a means for comparison.

Methods: Thirty-three abnormal eyes (19 with KC and 14 PK) were measured using a high–dynamic range wavefront sensor, and Zernike coefficients were computed over a 6-mm pupil. The data then were used to characterize the populations by themselves, as well as to compare them with the population of normal eyes.

Main Outcome Measures: Root mean square (RMS) higher-order aberration (HOA), percent of higher-order or total aberration variance, and magnitude of individual Zernike modes (in micrometers). Visual benefit of correcting higher-order aberrations was used when comparing pathologic and normal populations.

Results: The keratoconic eyes exhibited 2.24 μm of HOA RMS on average. Vertical coma accounted for 53 ± 32% (mean ± standard deviation [SD]) of the HOA variance and was the most dominant higher-order aberration. The PK subjects had an average higher-order RMS of 2.25 μm, and trefoil dominated in this population with an average HOA variance contribution of 38 ± 23% (mean ± SD). The KC and PK higher-order aberrations represented 16 ± 20% and 16 ± 13% (mean ± SD) of the total aberration variance, whereas the ratio was only 1 ± 1% in the normal population. A visual benefit calculation on 15 KC eyes and 14 PK eyes yielded a result of 4.4 ± 2.0 and 6.0 ± 1.5 (mean ± SD), respectively, whereas the normal population had a visual benefit of only 2.1 ± 0.4.

Conclusions: Eyes with KC and PK have higher-order aberrations that are approximately 5.5 times more than what is typical in normal eyes. Vertical coma is the dominant higher-order aberration in people with KC, whereas PK eyes are dominated by trefoil, spherical aberration, and coma. Correcting these aberrations may provide substantial improvements in vision beyond what is possible with conventional correction methods. Ophthalmology 2007;114:2013–2021 © 2007 by the American Academy of Ophthalmology.

Since Liang1 and Liang et al2 introduced the Shack-Hartmann aberrometer to vision science, wavefront sensing has become widely accepted as a tool for quantifying the aberrations in human eyes. The technology also has provided new information on individual lower- and higher-order aberrations in a normal population. The distribution of both lower- and higher-order aberrations in the normal human eye is well documented.3 It is also known that some of these aberrations fluctuate both from second-to-second (as with the heartbeat)4 and over the lifetime of the patient.5,6

Despite its adoption into clinical practice for measurement of normal eyes,3 wavefront sensors have had more difficulty measuring eyes with highly irregular corneas, such as those having keratoconus (KC) or those that have undergone penetrating keratoplasty (PK). In KC, there can be a substantial increase in higher-order aberrations resulting in visual acuity...
loss that is not correctable with conventional spectacles or soft contact lenses. Penetrating keratoplasty may induce a large amount of astigmatism and higher-order aberrations similar in scale to keratoconic patients. The lack of dynamic range in wavefront sensors needed to measure these aberrations accurately makes it difficult to correct them using customized ablation. This in turn leaves some eyes that have undergone corneal transplantation with a clear graft but suboptimal vision.

In 2002, Maeda et al. evaluated eyes with mild and moderate KC (n = 35) using a KR-9000 aberrometer (Topcon, Tokyo, Japan). The study was one of the first to look at a population of people with KC and to identify dominant higher-order aberrations (i.e., coma). Similarly, in 2003, Shah et al. also published measurements and comparisons of KC and PK eyes with those of normals. In both of these analyses, however, physical limitations of the wavefront sensor used prevented measurement of the wavefront aberration in eyes with various stages of KC over a large pupil size (>6 mm). The same limitation on dynamic range also prevented measuring the PK eyes over a large pupil in the study of Shah et al. This constraint limits the value of the measurement, because correction with customized contact lenses or laser refractive surgery may require characterization of the aberration outside an optical zone size of 6.00 mm or more, depending on their scotopic pupil sizes.

The limit in dynamic range mentioned above occurs because of constraints, namely a tradeoff between the dynamic range and measurement sensitivity, in the design of a conventional Shack-Hartmann wavefront sensor. Increased dynamic range of a Shack-Hartmann system can be obtained by using a shorter focal length lenslet array, but this causes a decrease in measurement sensitivity. Many methods, which are described elsewhere, have been proposed for overcoming the shortcomings that limit a wavefront sensors ability to measure KC and PK eyes. These methods, however, usually come at a cost. We previously reported a newly developed Shack-Hartmann wavefront sensor that has a large dynamic range and no sacrifice of measurement sensitivity (Pantanelli S, et al. Large dynamic range Shack-Hartmann wavefront sensor for highly aberrated eyes. Abstract presented at: Association for Research in Vision and Ophthalmology Annual Meeting, April 2003, Fort Lauderdale, Florida). The goal of this study was to use this system to investigate dominant higher-order aberrations in eyes with KC and those that have undergone PK over a pupil size of 6.00 mm or more. In addition, the wavefront aberration and theoretical visual benefit of correcting higher-order aberrations in these populations was studied and compared with a population of normal eyes.

Patients and Methods

The protocol for this study received institutional review board approval from the University of Rochester School of Medicine and Dentistry. The populations used included 14 PK eyes from 11 patients, 19 eyes with KC from 10 patients, and 378 pre-LASIK normal eyes from 190 patients. None of the normal eyes had any ocular pathologic features, aside from refractive errors. The measurement accuracy of the large–dynamic range wavefront sensor was verified previously by direct comparison with results obtained from a conventional Shack-Hartmann wavefront sensor; no significant difference in measuring higher-order aberration was found.

Wavefront aberrations in the pre-LASIK normal population were obtained from a previously existing database provided by Bausch & Lomb, Inc. (Rochester, NY). These aberrations were measured using a Bausch & Lomb Zywave I2 Shack-Hartmann–based wavefront sensor. Subjects in this control population had an average refractive error of -3.69±1.62 diopters (D; mean±standard deviation [SD]) sphere and 0.55±0.46 D cylinder. No subject had more than -7.74 D and -3.58 D of sphere or cylinder, respectively. The Zernike aberrations, up to the fifth order, were calculated for each subject based on the central 6.0 mm of the pupil. Informed written consent was obtained from the 21 participants with abnormal eyes. All of the subjects underwent dilation with 1.0% tropicamide. Aberrations in the abnormal groups were measured using a large–dynamic range Shack-Hartmann wavefront sensor described previously. A minimum of 10 measurements were obtained for each eye, and each measurement contained 145 spots over a 6.00-mm pupil. To ensure adequate dynamic range of the wavefront sensor, it was verified that each spot fell within its respective subaperture on the charge-coupled device. The Zernike coefficients for up to tenth-order aberrations were determined for each picture over the central 6.0-mm portion of the pupil. The 5 best measurements were chosen based on the quality of the wavefront sensing spot pattern.

The subjects were then averaged to produce a single set of Zernike coefficients, reported in the Optical Society of America standard format, for each abnormal eye. Finally, to compensate for the enantiomorphism that is present when comparing the aberrations in left and right eyes, the sign of Zernike modes that are not symmetric about the vertical axis was reversed in all data sets acquired from left eyes (i.e., Z3 Z1, Z3 Z1, etc.). A Student t test (α, 0.05) was used to determine which Zernike modes in the KC and PK populations were statistically different from normal.

The magnitude of individual Zernike aberrations and the root mean square (RMS) of the Zernike coefficients were used to compare the normal, KC, and PK populations. However, it is important to remember that RMS is not an ideal predictor of image quality, nor is it mathematically appropriate to use when assessing the proportion an individual aberration has on the total magnitude of aberration (Chen L, Porter J, Singer B, et al. Predicting subjective image quality from the eye’s wave aberration. Abstract presented at: Association for Research in Vision and Ophthalmology Annual Meeting, April 2003, Fort Lauderdale, Florida). In stead, the total variance (sum of the square of all Zernike coefficients second order and above) and higher-order variance (sum of the square of all Zernike coefficients third order and above) are used when calculating the contribution an individual aberration has on the total measured aberration. Therefore, the contribution an individual Zernike mode with radial index n and azimuthal frequency m has on the total aberration (P(TOT)) and higher-order aberration (P(HOAN)) is defined by

\[ P_{TOT} = \frac{(Z^m_n)^2}{\sum_{n=1}^{\infty} (Z^m_n)^2} \]

and

\[ P_{HOAN} = \frac{(Z^m_n)^2}{\sum_{i=3}^{\infty} (Z^m_i)^2} \]

where i is the highest radial index recorded for the population (i = 5 for normals and i = 10 for abnormals).

From the measured wave aberration, the RMS, point spread function, and modulation transfer function (MTF) can be calculated. All of these can be used as image quality metrics, although
one is usually better than the other, depending on the application. For instance, retinal plane-based metrics such as the point spread function and MTF provide a better prediction of retinal image quality compared with a metric based on the pupil plane, such as RMS. To quantify the benefit that these 3 populations might experience from perfect correction of their higher-order aberrations, a metric called visual benefit was used. This metric is based on another function mentioned above, the volume MTF (vMTF), which quantifies the optical quality of a system over the broad range of spatial frequencies that it encounters. To calculate visual benefit for each eye, the volume under the MTF was calculated for spatial frequencies between 0 and 60 cycles/degree under white light conditions. First, this was carried out assuming optimized correction of second-order aberrations only, where sphere, cylinder, and axis values were chosen that maximized the vMTF. Second, the vMTF was calculated assuming correction of all second-order and higher-order aberrations up to the tenth order for abnormal eyes. Higher-order aberrations up to only the fifth order were used for normal eyes because the aberration data higher than the fifth order were not available. However, as mentioned below, it is insignificant in normal eyes because of the small contribution of higher-order aberrations above the fifth order to degradation of image quality. The ratio of the second- and higher-order corrected vMTF (vMTF custom) over the second-order corrected vMTF (vMTF 2nd order) provides the estimate of visual benefit for correcting the higher-order aberrations. Therefore, a visual benefit of 1 indicates no benefit of correcting the higher-order aberration. This calculation is summarized by:

\[
\text{visual benefit} = \frac{\text{vMTF custom}}{\text{vMTF 2nd Order}}
\]

**Results**

**Keratoconic Population**

Figure 1 plots both the average second-order and higher-order aberrations of this abnormal population. In all of the eyes except for 2, the defocus was positive (5.15±4.20 μm or 3.96±3.23 D sphere, mean±SD) for a 6-mm pupil, which corresponded to the need for myopic correction. The astigmatism terms for the population when taking into account the sign were Z2 = −0.59±1.09 μm (mean±SD) and Z2 = 0.14±1.82 μm (mean±SD), equivalent to 2.06±1.15 D cylinder (mean±SD) for a 6-mm pupil. Higher-order aberrations were significantly larger than those typically found in the normal population; the keratoconic eyes had an average higher-order RMS of 2.24±1.22 μm (mean±SD) over a 6.00-mm pupil, which was 5.5 times more than the 0.41±0.16 μm (mean±SD) found in the normal eyes (P = 0.0). The most dominant higher-order aberrations in the keratoconic group were vertical coma, trefoil, and spherical aberration, in that respective order. Most notably, the vertical coma was negative in all of the eyes except for 1 of the 19 and accounted for 53±32% (mean±SD) of the higher-order variance. This average vertical coma was more than 1000% more than that found in normal eyes (P = 0.0). When both horizontal and vertical coma terms were considered, they accounted for 62±30% (mean±SD) of the higher-order variance. Trefoil and spherical aberration accounted for 18±27% and 6±13% (mean±SD) of the higher-order variance, respectively. Secondary astigmatism also was statistically different from normal (magnitude = 0.18±0.16 μm [mean±SD]; P = 0.005) in this population. Finally, 16±20% of the total variance in keratoconic eyes was due to higher-order aberrations, whereas only 12±12% (mean±SD) of this variance came from astigmatism.  

Penetrating Keratoplasty Population

Fourteen eyes that had undergone PK were measured using the large–dynamic range Shack-Hartmann wavefront sensor. The data were processed using the method described above for the keratoconic eyes and are presented in Figure 2. The PK subjects had second-order astigmatism values of Z2 = −1.69±2.61 μm and Z2 = −0.54±2.65 μm, or 4.24±1.48 D of cylinder (mean±SD). All except for 2 of the eyes had positive defocus (3.95±3.12 μm or 3.04±2.40 D sphere [mean±SD]) and were myopic. The corneal transplant eyes also had 5.5 times more higher-order RMS (2.25±0.75 μm, mean±SD) than normal eyes (0.41 μm) over a

![Figure 1](image)
6.0-mm pupil ($P = 0$). The most dominant higher-order aberrations were trefoil, coma, and spherical aberration, which accounted for $38 \pm 23\%$, $20 \pm 17\%$, and $12 \pm 14\%$ (mean \pm SD) of the higher-order variance, respectively. These eyes had a higher-order variance-to-total variance ratio of $16 \pm 13\%$; however, this time the percentage was smaller than the contribution of cylinder to the total variance: $41 \pm 21\%$ (mean \pm SD).

Comparison with Normal Eyes

Figure 3 plots the magnitude of the higher-order Zernike coefficients for keratoconic (n = 19), PK (n = 14), and normal eyes (n = 378) over a 6.0-mm pupil. The plot reinforces what has been mentioned previously: that abnormal eyes have larger amounts of higher-order aberrations when compared with normal eyes. In fact, the average magnitude of every aberration up to the fifth order in abnormal eyes was between 2 and 7 times the magnitude found in normal eyes. Dominant higher-order aberrations in each population are labeled; keratoconic eyes have the greatest magnitude of coma of the 3 populations and PK eyes have the greatest magnitude of trefoil and spherical aberration. Perhaps the clearest objective indication that higher-order aberrations are more severe in abnormal eyes than in normal eyes is the ratio of the higher-order aberration variance over the total aberration variance. In KC and PK eyes, the higher-order aberration contributed $16 \pm 20\%$ and $16 \pm 13\%$ (mean \pm SD), respectively, to the amount of total aberration in the eyes. In the normal population, the higher-order aberration was only $1 \pm 1\%$ (mean \pm SD) of the

![Figure 2](image-url)

**Figure 2.** Graphs demonstrating the average Zernike coefficient values for a population of penetrating keratoplasty (PK) eyes. The most dominant higher-order aberrations were trefoil, coma, and spherical aberration. Two penetrating keratoplasty eyes were not included in this plot because a lack of left–right designation prevented compensation for enantiomorphism. Zernike modes that were statistically different from normal ($P<0.05$) are designated by an asterisk (*).

![Figure 3](image-url)

**Figure 3.** Graph demonstrating comparison of abnormal and normal eyes. Abnormal eyes have greater amounts of higher-order aberrations when compared with normal eyes.
total aberration. Moreover, the comparison is underappreciated because the KC and PK populations also had 70% and 48%, respectively, more second-order variance than the normal population.

To determine which aberrations play a significant role in image quality degradation, the magnitude of the RMS versus Zernike order was plotted. Figure 4 plots the higher-order RMS for each Zernike order in the normal, KC, and PK populations over a 6.0-mm pupil.

The differences between the abnormal and normal populations also are evident when looking qualitatively at the wavefront maps. In Figure 5, 2 representative higher-order wavefront maps from individual eyes of each of the 3 populations are shown. The same color scale was used for all 6 of the maps so that they could be compared directly. One can note qualitatively what has already been demonstrated objectively: coma dominates the KC population and trefoil dominates in the PK population. Most notably, the sheer magnitude of the phase advances and phase lags seen in the KC and PK populations dwarf the higher-order aberrations of representative eyes from the normal population.

Visual Benefit

Figure 6 plots the predicted visual benefit on 15 of the KC eyes, all 14 PK eyes, and the mean of 32 of the normal eyes measured above. The KC, PK, and normal eyes had mean (±SD) estimated visual benefits of 4.4±2.0, 6.0±1.5, and 2.1±0.42, respectively.

Discussion

It was found previously that the KC population had the Zernike equivalent of 2.06±1.15 D (mean±SD) of astigmatism over a 6-mm pupil. From a clinical standpoint, this average value seems small because KC patients are, in general, thought to have much larger amounts of astigmatism. The reason for this discrepancy may be that the reported astigmatism is not based on a subjective refraction, but instead on only the Zernike astigmatism terms. Additional astigmatism may be needed to optimize retinal image quality or to refract these subjects subjectively. For instance, a larger manifest refraction magnitude may result because of interaction between higher- and lower-order
Zernike modes that may occur between astigmatism and coma or secondary astigmatism.

In this study, negative vertical coma was present in 18 of the 19 keratoconic (KC) eyes studied and was the most dominant of the higher-order aberrations in the KC group. Figure 5 illustrates this with 2 examples of higher-order aberration wavefront maps from 2 different KC subjects. The cause of this aberration can be attributed directly to the characteristic cone shape and inferior shift of this cone’s apex developing on the cornea as it degenerates. The cause of this could be attributed directly to the characteristic cone shape and inferior shift of this cone’s apex developing on the cornea as it degenerates. Figure 7A illustrates this point. A model of the actual cornea from a keratoconic eye is represented by the solid line, whereas the ideal spherical corneal shape is shown as a dashed line. When the aberrations are being measured using a Shack-Hartmann wavefront sensor, light leaving the eye crosses the cornea–air interface on the superior half of the cornea first. The refractive index difference between the cornea and air indicates that this light also will travel faster as soon as it encounters air. Therefore, a relative phase advance of the wavefront in the superior cornea occurs with respect to the inferior half of the cornea. This is exactly what is observed with negative vertical coma.

The most dominant aberration in the PK population was trefoil, but coma and spherical aberration also played significant roles in the degradation of image quality. The presence of trefoil in this population is visible in Figure 5, which illustrates 2 examples of higher-order aberration wavefront maps from 2 PK subjects. The trefoil is not completely unexpected and may be explained by the corneal tension of a single tight suture that also may be counteracted by firm counter pressure from sutures 120° away. Likewise, if there is firm counter pressure from a tight suture 180° away, one may expect astigmatism to dominate. This concept is illustrated in Figure 7B. The variable tensions in the stitches cause local deformations of the transplanted cornea, which in turn can result in local phase advances and phase lags in the wavefront. Trefoil is an aberration that has a greater effect on the peripheral portion of the wavefront; therefore, it plays its biggest role in image quality degradation only when the pupil is relatively large. Other dominant higher-order aberrations like spherical aberration and coma, however, dominate centrally and can degrade image quality at small pupil sizes.

The average magnitude of the spherical aberration found by Calver et al. in their study of young and old eyes was 0.38 μm for older subjects. The PK population measured in our study had an average spherical aberration value of 0.65 μm, and some patients even exceeded 1.0 μm, which is roughly 2 to 3 times that found in normal eyes. The spherical aberration comes, in part, from the inherent amount of spherical aberration present in the transplanted cornea; however, the increase when compared with the normal population again may be attributed to the stitching process. Spherical aberration may be the result of midperipheral steepening, which may be inherent to the wound initially caused by the sutures. The sutures may compress the wound and may be followed by stromal contracture after the sutures are removed. The steep curvatures peripherally in turn would induce positive spherical aberration—what was seen in our PK population data. Because decentered fourth-order spherical aberration results in third-order coma, slight decentration of the transplant during surgery may cause any spherical aberration to result in coma, which was what we observed in the PK population data.

In 1997, Liang and Williams demonstrated that they could measure the higher-order aberrations reproducibly in normal eyes out to the tenth order. They did this for 14 normal human eyes over a 7.3-mm pupil and found that the
sixth- to tenth-order RMS (i.e., the RMS for the sixth-order terms, fourth-order terms, fifth-order terms, etc.) were approximately 0.08, 0.05, 0.05, 0.035, and 0.035 μm, respectively. The second- to tenth-order RMS values also were all approximately equal to or more than an RMS error of λ/14 at 633 nm (a common value used to signify the tolerance of a diffraction limited optical system).26 Ninth-order through tenth-order RMS values were below this value and therefore did not contribute significantly to image quality degradation. In the study presented here, where abnormal eyes were measured out to the tenth order, the results were dramatically different. Despite a significantly smaller pupil size compared with that of the Liang and Williams study (6.0 mm vs. 7.3 mm), the magnitude of the RMS for each of the sixth through tenth orders was much larger in both abnormal KC and PK populations. In addition, both abnormal populations had tenth-order RMS Zernike contributions of more than the λ/14 diffraction-limited criterion.

To date, there are no reports out to the tenth order for a 6.0-mm pupil in a normal population. However, Thibos et al27 previously reported a sixth- through seventh-order higher-order RMS of less than 0.05 μm (variance, <0.002) for a 6.0-mm pupil on 200 normal eyes. The KC and PK populations in the present study had sixth- through seventh-order RMS values of 0.33±0.42 μm and 0.57±0.36 μm (mean±SD), respectively. These RMS values are nearly 7 and 12 times more than those found in the study of Thibos et al. Both abnormal populations have significant amounts of higher-order aberration beyond the fifth-order Zernike modes that contribute to the detriment in their visual acuity. Therefore, it may be necessary to measure up to the tenth order to truly represent the complex wavefronts of abnormal eyes.

Visual Benefit

As mentioned above, in Figure 6, the KC and normal eyes have estimated visual benefits of 4.4±2.0 and 2.1±0.42 (mean±SD), respectively. The visual benefit metric, derived from the vMTF described above, was used to predict the visual benefit that normal and abnormal eyes may experience above and beyond conventional correction. These visual benefit predictions, as well as the higher-order total variance ratios presented earlier, are consistent with the findings of Guirao et al28 from 2002. Guirao et al showed that the higher-order aberrations in normal eyes account for only a small percentage of the total variance of the wave aberration; however, these higher-order aberrations also have a disproportionately large contribution to degradation of the MTF.28 The current study shows that higher-order variance accounts for only 1% of the total variance in normal eyes, whereas the study by Guirao et al noted that higher-order variance accounts for approximately 8%. Our underrepresentation with respect to his result is likely attributed to the selection of a pre-LASIK myopic eye population as normal eye data used in this study. Because the eyes in this study were more myopic than those in the Guirao et al study, the myopia reduced the percentage attributable to higher-order aberration. Despite this, Guirao et al’s assessment of normal eyes at 16 cycles/degree and a 5.7-mm pupil revealed visual benefit of approximately 2.5 with customized correction, which is similar to the current study, which notes a visual benefit of 2.1 in the normal eye population.28 Guirao et al also claimed an average visual benefit of 12 for the 4 keratoconic eyes they measured.
whereas the average calculated visual benefit in our study of 15 keratoconic eyes was 4.2±2.0 (mean±SD). The difference between these results may be the result of the differing definitions of visual benefit used in the studies, namely, Guirao et al identified visual benefit at discrete spatial frequency values (16 and 32 cycles/degree), whereas our study considered the vMTF covering spatial frequencies ranging from 0 to 60 cycles/degree. Because there was no previous work on visual benefit in PK patients, a comparison with other results for this population was not possible. Nevertheless, the plot in Figure 6 illustrates the dramatic improvement that may be expected from correcting the higher-order aberrations in these eyes. It is important to note that this calculation assumes perfect correction of higher-order aberrations and that any decentration or rotation of a customized correction would reduce this theoretical benefit.

Implications

Wavefront sensing has renewed interest in correcting the higher-order aberrations of the eye and improving human visual acuity. Earlier strategies came with the shift from conventional spectacles and soft contact lenses to rigid gas permeable contact lenses. These lenses effectively correct higher-order aberrations by reducing the effect of corneal surface irregularities using the tear film to fill the gap between the cornea and the back surface of the lens. Wavefront sensing may allow for a new approach to customized vision correction (i.e., customized refractive surgery and customized contact lenses).

Keratoconic and PK eyes experience higher-order aberrations that are nearly 5.5 times more than those found in normal eyes. The most dominant of these aberrations in keratoconic eyes is negative vertical coma, whereas that in PK eyes is trefoil. The findings indicate that higher-dynamic range wavefront sensors will be necessary to describe the more complex shapes. In the future, higher-dynamic range wavefront sensors, when used with customized correction techniques, such as phase plates, customized contact lenses, customized intraocular lenses, and laser refractive surgery, may provide superior image quality for people with ocular pathologic features beyond what is considered the standard of care today.

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