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Peripheral ocular aberrations in mild and moderate keratoconus

Purpose: To investigate the influence of keratoconus on peripheral ocular aberrations.

Methods: Aberrations of 7 mild and 5 moderate keratoconics were determined over a 42° horizontal x 32° vertical visual field with a modified COAS-HD aberrometer. Control data were obtained from an emmetropic group.

Results: Most aberrations in keratoconics showed field dependence predominately along the vertical meridian. Mean spherical equivalent M, oblique astigmatism J45 and regular astigmatism J180 refraction components and total root mean square aberrations (excluding defocus) had high magnitudes in the inferior visual field. The rates of change of aberrations were higher in moderate than in mild keratoconics. Coma was the dominant peripheral higher-order aberration in both emmetropes and keratoconics; for the latter it had high magnitudes in the centre and periphery of the visual field.

Conclusion: Greater rates of change of aberrations across the visual field occurred for the keratoconic groups than for the emmetropic control group. Moderate keratoconics had more rapid changes in, and higher magnitudes of, aberrations across the visual field than
mild keratoconics. The dominant higher-order aberration for the keratoconics across the visual field was vertical coma.
Manuscript title: Peripheral ocular aberrations in mild to moderate keratoconus

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Short Title: Keratoconus and peripheral aberrations

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Abstract

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Conclusion: Greater rates of change of aberrations across the visual field occurred for the keratoconic groups than for the emmetropic control group. Moderate keratoconics had more rapid changes in, and higher magnitudes of, aberrations across the visual field than mild keratoconics. The dominant higher-order aberration for the keratoconics across the visual field was vertical coma.

Keywords: coma, keratoconus, peripheral aberrations, visual field
Introduction

Keratoconus is a progressive and usually bilateral condition affecting the cornea.\(^1\) Non-inflammatory progressive central thinning results in the cornea assuming a conical shape causing significant reductions in visual performance.\(^1\), \(^2\) The “irregular” astigmatism associated with keratoconus is difficult to correct with spectacles alone. Once visual acuity becomes unsatisfactory with spectacles, rigid gas permeable contact lenses are typically prescribed which better neutralize the corneal aberrations by providing a spherical refractive surface.\(^3\)

The concepts of wavefront guided corneal refractive surgery\(^4\) and aberration correcting contact lenses\(^5\), \(^6\) have sparked interest in higher-order aberration studies. Keratoconus patients are one population that has received attention, with the literature correlating their higher-order aberrations with visual performance.\(^7\), \(^8\) Some papers have addressed the issue of diagnosing keratoconus before clinical signs and symptoms develop by examining corneal\(^2\), \(^9\) or ocular higher-order aberrations.\(^10\) Thus, studies furthering our understanding of aberrations are fundamental to the future clinical management of keratoconic and other abnormal corneas.

Studies have shown significantly greater magnitudes of on-axis (those along the line of sight) higher-order and total eye aberrations, in particular coma-like aberrations, to be present in keratoconus patients compared with normals.\(^9\)-\(^13\) As an example, Pantanelli et al.\(^13\) used a large-dynamic range Hartmann-Shack wavefront sensor to characterize the on-axis aberrations of 32 eyes with keratoconus. Analysis over a 6 mm pupil showed vertical coma to be the dominant higher-order aberration followed by trefoil and then by spherical aberration. Every aberration coefficient up to the 5\(^{th}\)-order was between 2 and 7 times greater in the keratoconus population than in an emmetropic control group.
The majority of research into ocular aberrations both in normal eyes and in eyes with pathological conditions such as keratoconus has concentrated on the axial aberrations. So far, peripheral higher-order aberrations studies have been conducted by only a few groups. Peripheral vision is utilized for tasks such as detection, peripheral motion perception, mobility and postural balance and driving which, compared with visual acuity, have less demand for image quality. Peripheral vision is limited not only by image quality but also by the low resolution capacity of the eccentric retina. There are a number of reasons for investigating peripheral aberrations: best correcting eccentric fixation after central field loss, the possible adverse effects on peripheral tasks post LASIK, and the idea that peripheral defocus is a possible cause of myopia progression, have all generated interest in peripheral refraction. From the few studies measuring peripheral higher-order aberrations it is well established that second-order aberrations dominate in peripheral vision, but higher-order aberrations, in particular coma, can also be substantial. Mathur et al. investigated the variations in aberration coefficients across the visual field of young emmetropic subjects. Whilst many terms varied across the visual field, only a selection showed obvious trends. Increases in the second-order astigmatic coefficients $C_{2}^{-2}$ and $C_{2}^{2}$ from the centre to the periphery along 45-225° and 0-180° meridians, respectively, were noted, as were decreases in these terms along the meridians perpendicular to the above mentioned meridians. Vertical coma coefficient $C_{3}^{-1}$ increased linearly from the superior to inferior field, whilst horizontal coma coefficient $C_{3}^{1}$ increased linearly from nasal to temporal field. The rates of change of $C_{3}^{-1}$ across the visual field increased with myopia. The interventions of LASIK and orthokeratology changed the sign of the rate of change of coma across the field. Our study extends previous work by investigating peripheral aberrations in keratoconic eyes. We hypothesize that a greater rate of change of higher-order aberrations
across the visual field exists within a keratoconic population compared with emmetropes, and that the use of peripheral measures may amplify the differences in ocular aberrations between keratoconic and normal subjects.

Methods

This research was approved by the Queensland University of Technology’s Human Research Ethics Committee and conformed to the tenets of the Declaration of Helsinki. Information regarding the study was given to the subjects and written consent obtained prior to testing.

Twelve subjects with keratoconus were recruited from the University’s Optometry clinic, research department databases and specialist contact-lens private practices. Other ocular pathology and severe keratoconus complications including corneal scarring and acute hydrops were exclusion criteria. Rigid gas permeable contact lens wearers were also excluded. If a patient wore soft contact lenses, a period of one day and one night without lens wear was enforced prior to testing to ensure their effect on the cornea did not influence the results.

Keratoconus was confirmed by a scissoring reflex on retinoscopy, central or paracentral steepening on computerized topography with a Medmont E300 videokeratoscope (Medmont International Pty. Limited, Australia), and at least one of central or paracentral corneal thinning, Vogt’s striae, or a Fleischer ring. All subjects exhibited bilateral signs of keratoconus, with varying degrees of between eye symmetry. The Oculus Pentacam’s (Oculus Inc., Germany) keratoconus program offered further confirmation of the condition and was adopted to classify our subjects into 7 mild (3 male, 4 females) and 5 moderate (3 male, 2 female) cases. The Pentacam software provides a keratoconus severity classification (from pre-stage keratoconus and mild keratoconus “KK-1” through to advanced keratoconus “KK-4”) adapted from the Amsler grading system and based upon 8 indices derived from the
anterior surface topography, and corneal thickness progression.\textsuperscript{35} We used this classification in order to grade the severity of keratoconus for each subject, and defined “mild keratoconus” as being less than KK-2, and “moderate keratoconus” being KK-2 to 3. Most previous studies categorized keratoconus patients on their keratometry values.\textsuperscript{36, 37} Given the Pentacam’s recent popularity and demonstrated utility for detecting keratoconus\textsuperscript{38} we felt the use of its indices were justified as it provided an objective assessment of the severity of keratoconus.

Mean ages were 28 ± 5 years for the mild keratoconic group (21 to 34 years) and 30 ± 7 years for the moderate keratoconic group (22 to 37 years). Ocular aberration data from the keratoconic populations were compared with a control population, consisting of 10 young adult emmetropic subjects with a mean age of 25 ± 3 years (age range 20 to 30 years), that has been described in detail elsewhere.\textsuperscript{30, 32} Mean steep simulated keratometry (as measured by Medmont corneal topographer) was 44.2 ± 1.5 D (Range: 41.5 D to 47.6 D) for emmetropes, 46.8 ± 1.1 D (Range: 45.1 D to 48.3 D) for mild keratoconics and 46.8 ± 2.2 D (Range: 44.8 D to 50.0 D) for moderate keratoconics.

Each subject underwent an ophthalmic examination which included unaided vision, best-corrected visual acuity using both high and low contrast Bailey-Lovie charts, retinoscopy and subjective refraction. The spherical equivalent for the mild and moderate keratoconics was 0.00 ± 0.46 D and +1.30 ± 1.44 D, respectively. The best spectacle-corrected high (HCVA) and low (LCVA) contrast visual acuities for the keratoconics are described in Table 1. For emmetropes, only HCVA was measured, which was ≤ 0.00 logMAR for all subjects. The cone location relative to the pupil centre was determined from Medmont E300 topography; the ‘ruler’ function inbuilt in the Medmont E300’s software was used to measure the vertical and horizontal displacements from the pupil centre to the steepest anterior corneal curvature location on the tangential power map (Table 1).
Table 1. Best spectacle-corrected high (HCVA) and low (LCVA) contrast visual acuity and cone locations along horizontal (x) and vertical (y) corneal meridians for the keratoconic groups. Positive x and y values represent nasal and superior cornea, respectively.

<table>
<thead>
<tr>
<th>Group</th>
<th>HCVA (logMAR)</th>
<th>LCVA (logMAR)</th>
<th>Cone location x (mm)</th>
<th>y (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Keratoconics</td>
<td>0.02 ± 0.10</td>
<td>0.45 ± 0.17</td>
<td>0.5 ± 0.2</td>
<td>−1.6 ± 0.6</td>
</tr>
<tr>
<td>Moderate Keratoconics</td>
<td>0.07 ± 0.10</td>
<td>0.48 ± 0.08</td>
<td>0.3 ± 0.3</td>
<td>−2.0 ± 0.2</td>
</tr>
</tbody>
</table>

Each subject also had their corneal thickness and topography measured using the Oculus Pentacam HR rotating Scheimpflug camera. The Pentacam instrument has previously been found to provide highly repeatable measures of corneal thickness in patients with keratoconus.\textsuperscript{36, 39} The Complete Ophthalmic Analysis System – High Definition (AMO WaveFront Sciences LLC, USA; COAS-HD) Hartmann-Shack type aberrometer was used to determine peripheral aberrations of each subject’s right eye using a procedure that has been described in detail previously.\textsuperscript{31} A 100 cm x 75 cm rear projection screen was placed at a distance of 1.2 m, onto which the fixation targets were projected and viewed via a glass slide beam splitter. Targets were arranged in a 6 row x 7 column matrix to give a visual field of 42° x 32°. The centre of the fixation target array was aligned with the COAS-HD internal fixation target. Two images only for each fixation target were taken in order to reduce the subject’s total testing time to less than 2 hours. The dynamic range of the Hartmann-Shack sensor limits the measurement of highly aberrated corneas,\textsuperscript{13} and therefore more severe cases were not investigated. The quality of the images captured by the modified COAS-HD aberrometer was generally high. Only 10 of 916 images were unsuitable for analysis, which meant that only one image, rather than two images, was available for a particular subject and visual field position. For some images, the software of the COAS-HD was unable to determine the centroids of some of the points. In such cases, these were estimated by a manual procedure carried out by one of the authors. The number of points estimated manually was generally small (≤ 30 points) relative to about 766 points across a 5 mm pupil. Using a Matlab (The
MathWorks, Inc., USA) based algorithm, the image magnification and contrast was increased and the observer used a cursor to estimate the centroid. Further analysis was performed with custom software that “stretched” elliptical pupils to circular pupils and converted from the instrument’s 840 nm wavelength to 555 nm.\textsuperscript{40, 41} Aberration coefficients up to the 6th-order were estimated from the wavefront for a pupil diameter of 5 mm for all subjects. Aberration coefficients for the 2 images at each visual field position were averaged.

Because of the large inter-subject variations within the keratoconic groups, average group values for each aberration coefficient were used. We determined refractive components mean spherical equivalent \( M \), oblique astigmatism \( J_{45} \), and with/against the rule astigmatism \( J_{180} \) refraction components based on 2nd- to 6th-order aberration coefficients.\textsuperscript{40, 41} Total root mean square aberrations excluding defocus (TotalRMS), and higher-order root mean square aberrations (HORMS) values were also determined.

Contour plots were generated to represent refractive components, aberration coefficients, HORMS and TotalRMS across the visual field. Further analysis was done along the vertical visual field meridian by performing quadratic fits to the data. Quadratic fits were chosen because they most closely represented the change in most aberration coefficients.

The refractive components, 2nd, 3rd and 4th order aberration coefficients, HORMS and Total RMS were further analyzed using repeated measures analyses of variance (ANOVA) with field position (38 positions) as within-subjects factor and group as between-subject factor. Bonferroni post hoc analysis was also done for the 3 groups. ANOVA was performed using SPSS statistical package (SPSS Inc., USA).

Results

The average cone location relative to pupil centre with corneal topography was 1.60 ± 0.6 mm inferiorly and 0.45 ± 0.2 mm nasally for mild keratoconics and 1.97 ± 0.2 mm inferiorly.
and 0.34 ± 0.3 mm nasally for moderate keratoconics. The pupils during corneal topography were typically smaller than 5 mm, and for the larger pupil during aberrometry measurements there would likely be a mean absolute pupil shift of about 0.21 mm, but with mean changes in horizontal and vertical locations of less than 0.03 mm, so the estimate of mean cone position relative to the larger pupil would not be expected to change substantially.

Refraction components and aberration coefficients across the visual field were displayed as 2-D contour maps, with a common scale for a refraction component/aberration across all three groups. Negative (−) coordinates represent temporal and inferior visual fields. Figure 1 shows the refraction components across the visual field, Figure 2 shows higher-order wavefront maps across the eccentric pupil for each location in the visual field, Figure 3 shows the third-order coefficients and spherical aberration coefficient across the visual field, and Figure 4 shows higher-order root mean squared aberrations (HORMS) and total root means squared aberrations excluding defocus (TotalRMS) across the visual field.

The rates of change of refraction components and higher-order coefficients across the visual field were greater for the keratoconic groups than for the emmetropic control group for all aberration terms considered. The moderate keratoconics exhibited greater rates of change than the mild keratoconics for all aberrations.

For spherical equivalent M (Figure 1A), the emmetropes had little variation across the field, whereas mild keratoconics had high negative (myopic) values in the inferior field which became less negative into the superior field. Moderate keratoconics had a similar pattern to this, but magnitude in the inferior field and rate of change were higher.

Astigmatism J_{180} (Figure 1B), for emmetropes, decreased quadratically from the centre to the periphery along the 0°- 180° meridian and increased quadratically along the 90°- 270° meridian. The keratoconic groups had high negative J_{180} in the superior field that became less negative and eventually positive into the inferior field. The change was quadratic.
and greater in the inferior field than in the superior field. Moderate keratoconics had greater rate of change than mild keratoconics.

Oblique astigmatism $J_{45}$ (Figure 1C), for emmetropes, decreased from the central to the peripheral field along the $45^\circ$ - $225^\circ$ meridian, and increased along the $135^\circ$ - $315^\circ$ meridian. For mild and moderate keratoconics, it decreased linearly from the inferior nasal field to the superior temporal field along the $315^\circ$ - $135^\circ$ meridian. Moderate keratoconics exhibited a greater rate of change than mild keratoconics.

Figure 2 shows the mean higher-order wavefront maps across the pupil at each of the 38 visual field positions. For the emmetropes, coma dominated the peripheral visual field. Both keratoconic groups had larger aberrations than the emmetropes at any visual field position, with the moderate keratoconics having the highest aberrations. Aberrations were again dominated by the comas for the keratoconics, but with some influence of spherical aberration in the inferior visual fields as indicated by the increase in symmetry of the plots and with some influence of trefoil in the inferior-nasal fields as indicated by the three-lobed nature of the plots. Mild keratoconics had their most aberrated wavefronts in the superior-temporal field, and moderate keratoconics had their most aberrated wavefronts along the horizontal meridian. For the emmetropes, the axis of the combined horizontal and vertical comas approximately matched the visual field meridian. The axis of coma in keratoconics was mainly vertical across the visual field, indicating the dominance of vertical coma, although with some rotation from this in the superior visual field indicating the influence of horizontal coma.

Vertical coma $C_{3}^{-1}$ coefficient (Figure 3A) for emmetropes increased linearly from the superior to the inferior field. For mild keratoconics it increased quadratically from the superior to the inferior field. Moderate keratoconics had high negative $C_{3}^{-1}$ in the centre of the visual field and this became less negative both superiorly and inferiorly. Horizontal coma
$C_3^1$ coefficient (Figure 3B) increased linearly from the nasal to temporal fields for all 3 groups, with the variation for moderate keratoconics rotated towards the $135^\circ - 315^\circ$ meridian. The rates of change were similar for mild ($-0.018 \, \mu \text{m/deg}$) and moderate ($-0.016 \, \mu \text{m/deg}$) keratoconics, and these were approximately 2.5 times greater than for emmetropes ($-0.007 \, \mu \text{m/deg}$).

Vertical trefoil $C_3^{-3}$ and horizontal trefoil $C_3^3$ coefficients (Figures 3C, 3D) varied very little across the visual field for emmetropes. For keratoconics however, there was considerable variation in both coefficients, with high negative and high positive values evident in the peripheral fields, particularly for the moderate keratoconic group.

Spherical aberration coefficient $C_4^0$ (Figure 3E) for emmetropes varied little across the visual field. For keratoconics, it increased from the inferior to the superior field. Rates of change were greater for the moderate than for the mild keratoconics, with peak positive values for the moderate keratoconics in the mid-superior field.

Higher-order root mean square aberration $\text{HORMS}$ (Figure 4A) of all groups showed quadratic variation along the vertical meridian. The magnitudes and rates of change were more pronounced for the moderate keratoconics than for the other groups. As an estimation of variability in aberrations along the vertical field meridian, standard deviations of $\text{HORMS}$ and $\text{TotalRMS}$ were calculated for each subject. The average standard deviations of $\text{HORMS}$ for mild and moderate keratoconics ($0.20 \, \mu \text{m}$ and $0.30 \, \mu \text{m}$, respectively) were substantially larger than for emmetropes ($0.05 \, \mu \text{m}$). By noting the similarities between the magnitudes and variations of $\text{HORMS}$ and vertical coma (Figure 3A), it is clear that vertical coma was the dominant higher-order aberration across the field.

Total root mean squared aberrations excluding defocus $\text{TotalRMS}$ (Figure 4B) for emmetropes increased quadratically from the centre to the periphery. The keratoconics showed increase in $\text{TotalRMS}$ from the superior to the inferior of the visual field. The
vertical rates of change were similar for mild and moderate keratoconics (−0.041 μm/deg and
−0.052 μm/deg, respectively), but the magnitudes were greater for the latter at any visual field
position. The average standard deviations for mild and moderate keratoconics along the
vertical meridian (0.72 μm and 0.60 μm, respectively) were substantially larger than for
emmetropes (0.11 μm), indicating the high variability between the individuals within each
keratoconic group.

Table 2 shows the ANOVA results. Repeated measures ANOVA confirmed the
differences in refractive components, aberration coefficients, HORMS and Total RMS
between the 3 groups. Refractive group had a significant effect on all refractive components
and most aberration coefficients except $C_2^0, C_2^2, C_3^1, C_4^{-2}, C_4^{-4}$ and $C_4^0$. As expected, field
position had significant effect on all refractive components and aberration coefficients. There
were significant group-field interactions for all the terms, showing that group significantly
affected the pattern of aberrations across the field. Bonferroni post-hoc analysis showed that
most of the terms were significantly different between emmetropes and keratoconics. $RPRE$,
$J_{180}, C_3^{1}, C_4^2, C_4^4$ and HORMS differed significantly between mild and moderate
keratoconics.

Aberrations are affected by cone location. In our keratoconic groups, the cone
locations were usually more inferior than nasal. This resulted in higher aberrations for the
inferior than for the superior visual fields. We compared the anterior surface power derived
from the Medmont corneal topography data along the vertical corneal meridian (Figure 5)
(passing through the pupil centre) with the ocular refraction and aberrations along the vertical
visual field meridian (Figure 6). The corneal power changed little for emmetropes, but
showed considerable changes for the keratoconic groups (Figure 5). In the inferior field, the
corneal power was, as expected, highest for the moderate keratoconic group. In the superior
field, corneal power for moderate keratoconics was considerably lower than for the other groups.

Generally the refractive components and aberrations changed quadratically along the vertical meridian for the keratoconic groups. The astigmatic components $J_{45}$ and $J_{180}$ and $J_{45}$ became more positive (Figure 6a and 6c) and spherical equivalent $M$ became more negative (Figure 6b) in the inferior field compared with the respective results for the emmetropic group. The rates of change in the refractive components were highest in the moderate keratoconics followed by the mild keratoconics. Vertical trefoil coefficient $C_3^{-3}$ (Figure 6d) changed little for emmetropes and mild keratoconics, but was more positive overall across the field in mild keratoconics than in emmetropes. It increased linearly from superior to inferior field in moderate keratoconics. Vertical coma coefficient $C_3^{-1}$ (Figure 6e) showed the most prominent differences between the 3 groups. It changed linearly vertically for emmetropes and quadratically for mild and moderate keratoconics. Moderate keratoconics also had high negative vertical coma coefficient $C_3^{-1}$ across the vertical field meridian. Spherical aberration coefficient $C_4^0$ (Figure 6f) changed little for emmetropes, but changed linearly for mild keratoconics and quadratically for moderate keratoconics.

Higher-order root mean square aberrations ($HORMS$, Figure 6g) and total root mean square aberrations excluding defocus ($TotalRMS$, Figure 6h) were highest across the field for moderate keratoconics followed by mild keratoconics. $HORMS$ decreased away from the centre of the field for moderate keratoconics and increased towards the superior field for mild keratoconics, and was dominated by changes in vertical coma $C_3^{-1}$ in the 2 groups. $TotalRMS$ increased towards the inferior field because of increase in astigmatism in the inferior field. The mild and moderate keratoconic groups exhibited 5 and 9 times greater axial $TotalRMS$ respectively, than the emmetropic subjects. In the inferior field, $TotalRMS$ increased to be 6
(mild keratoconic) and 11 (moderate keratoconic) times greater in keratoconic than in control subjects. For the keratoconic subjects, a significant correlation was found between the quadratic component of the rate of change in aberrations along the vertical meridian and the corneal power at the cone apex for both vertical coma coefficient ($r^2 = 0.58$, $p < 0.001$) and HORMS ($r^2 = 0.41$, $p = 0.03$), indicative of a greater change in aberrations along the vertical meridian for greater corneal powers (Figure 7).

Discussion

This is the first study to investigate and quantify peripheral ocular aberrations in keratoconic subjects. The results support our hypothesis of greater rate of change of aberrations across the visual field for keratoconic than for normal eyes. The magnitudes of aberrations and rates of their change across the visual field were greater for a moderate than for a mild keratoconic group, and with considerable variation within the keratoconic groups. Second-order terms were the dominant aberrations across the visual field for both emmetropes and keratoconics. Rapid changes in $M$ and $J_{180}$ were noted in the inferior field for keratoconics with as much as $-8.00$ D of spherical error occurring in the moderate keratoconic group. For $5$ mm pupils, horizontal and vertical comas were the dominant higher-order aberrations for emmetropes across the visual field, but vertical coma alone was the dominant higher-order aberration for keratoconics across most of the visual field. The latter is consistent with on-axis studies on keratoconus.$^{10,13}$

The characteristics of the peripheral aberrations in our keratoconic population appeared to be related largely to the location and magnitude of the cone. Horizontal coma decreased from the temporal to the nasal field for all 3 groups. For the keratoconic groups the horizontal coma change appeared to be rotated towards the 135°-315° meridian. This is explained by the cone being typically located in the inferior-nasal quadrant. Furthermore the
cornea power at the cone apex was associated with the change in certain aberrations (i.e. vertical coma and HORMS) along the vertical field.

With the advent of laser refractive surgery, there has been considerable interest in identifying those patients with early or sub-clinical forms of keratoconus, as the presence of keratoconus even in a sub-clinical form is considered a major risk factor for the development of iatrogenic keratoectasia following refractive surgery.\(^{44}\) Whilst videokeratoscopy is still the most commonly used clinical tool for the diagnosis of keratoconus, a number of other novel methods may be potentially useful for detecting early keratoconus, including methods based upon measures of corneal thickness\(^ {38}\) posterior corneal topography,\(^ {39}\) and ‘on axis’ corneal\(^ {2, 9}\) and ocular\(^ {1, 45}\) aberrations. The aberrations are, of course, an indirect measure of the corneal topography. This study shows that substantial differences exist in the magnitude and rate of change of peripheral ocular aberrations between emmetropes and subjects with mild keratoconus. This suggests that metrics based upon peripheral ocular higher-order aberrations, or the rate of change in these aberrations across the field, could potentially be of use in identifying patients with early or sub-clinical forms of keratoconus; a complicating factor is that myopes tend to have greater rates of change of coma across the visual field than emmetropes.\(^ {30}\) Further research is required on a larger population of subjects to determine the optimum metrics and the clinical utility and sensitivity of peripheral aberration measurements in the diagnosis and screening of early keratoconus. The lengthy time taken for data collection and analysis with currently available clinical instruments probably precludes these measurements from being viable clinically at this stage. However, with further advancements in aberrometer designs it will likely be possible to measure peripheral aberrations in a few minutes.

It has been hypothesized that peripheral ocular aberrations may be an important factor influencing the growth of the eye and development of myopia.\(^ {46}\) and there has been
substantial increased interest in peripheral aberrations and refractive error in recent years.\textsuperscript{30, 47} Imposed defocus on the peripheral retina has been found to lead to myopic eye growth in monkeys.\textsuperscript{48, 49} Furthermore, defocus imposed on local retinal regions in chicks and primates has been found to lead to compensatory eye growth, localized to those regions of the retina.\textsuperscript{50-54} Recent work investigating peripheral aberrations in human myopes and emmetropes has demonstrated some difference in peripheral aberrations associated with refractive error (e.g. a greater rate of change in vertical coma across the field in myopes).\textsuperscript{30} While it is unknown at this time whether the increased peripheral aberrations measured in myopic eyes contribute to the development of myopia or are simply a consequence of the ocular biometric changes associated with myopia, the substantial peripheral aberrations evident in keratoconus (particularly vertical coma) might have implications for eye growth control in these subjects. If defocus of the peripheral retina is important for the control of eye growth in human subjects, and if the onset of keratoconus is at a time when the visual system is capable of undergoing axial eye growth in response to peripheral defocus, then the substantial asymmetry in defocus that we have observed across the vertical visual field in our keratoconic subjects could potentially lead to compensatory asymmetric growth of the peripheral regions of the eye in these subjects. Given the typical age of onset of keratoconus is often in the teenage years\textsuperscript{1, 55} and that previous studies of refractive error development have demonstrated the human eye is capable of undergoing axial eye growth at this age,\textsuperscript{56-59} future studies utilizing magnetic resonance imaging or peripheral ocular length measures (e.g. partial coherence interferometry) in keratoconic subjects may help to determine whether asymmetric axial eye growth occurs in response to the substantially asymmetric retinal defocus in these subjects.

In conclusion, we have described in detail the magnitude and pattern of peripheral low and high-order ocular aberrations in populations of mild and moderately advanced
keratoconic subjects, and compared these aberrations to those from an emmetropic control group. Consistent with previous studies of on-axis aberrations in keratoconus and with the measured corneal topographical changes, our keratoconic subjects exhibited higher magnitudes and rates of change in peripheral ocular aberrations compared to emmetropic controls, with comatic terms being the dominant higher-order peripheral aberrations.

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Figure captions
Figure 1. Mean refraction components across the visual field in dioptres (D) for a) emmetropes, b) mild keratoconics (Mild K’conus) and c) moderate keratoconics (Mod K’conus). A: spherical equivalent $M$; B: with/against the rule astigmatism $J_{180}$; C: oblique astigmatism $J_{45}$. Pupil size 5 mm. For any refraction component, the scale is the same for the three groups.

Figure 2. Wavefront maps across the elliptical pupil at 38 visual field locations for a) emmetropes, b) mild keratoconics (Mild K’conus) and c) moderate keratoconics (Mod K’conus). Pupil size 5 mm. The scale is the same for all three groups.

Figure 3. Mean aberration components across the visual field in micrometers ($\mu$m) for a) emmetropes, b) mild keratoconics (Mild K’conus) and c) moderate keratoconics (Mod K’conus). A: vertical coma coefficient $C_{3}^{-1}$; B: horizontal coma coefficient $C_{3}^{1}$; C: vertical trefoil coefficient $C_{3}^{-3}$; D: horizontal trefoil coefficient $C_{3}^{3}$; spherical aberration coefficient $C_{4}^{0}$. Pupil size 5 mm. For any coefficient, the scale is the same for the three groups.
Figure 4. Combined aberrations across the visual field in micrometers (µm) for a) emmetropes, b) mild keratoconics (Mild K’conus) and c) moderate keratoconics (Mod K’conus). A: Higher-order root mean square aberrations (HORMS); B Total root mean square aberrations excluding defocus (TotalRMS). Pupil size 5 mm. For any combined aberrations, the scale is the same for the three groups.

Figure 5. Axial anterior corneal power along vertical meridian (passing through pupil centre as estimated by Medmont corneal topographer) relative to the distance from the pupil centre for emmetropes, mild keratoconics and moderate keratoconics. The error bars represent standard deviations, I and S represent inferior and superior cornea.

Figure 6. Refraction and aberrations along the vertical visual field meridian. (a) oblique astigmatism $J_{45}$, (b) spherical equivalent $M$, (c) with/against the rule astigmatism $J_{180}$, (d) vertical trefoil coefficient $C_{3}^{-3}$, (e) vertical coma coefficient $C_{3}^{-1}$, (f) spherical aberration coefficient $C_{4}^{0}$, (g) Higher-order root mean square aberrations (HORMS) and (h) Total root mean square aberrations excluding defocus (TotalRMS). The lines represent quadratic fits to the data and error bars represent standard deviations. Different refractions and aberrations have different scales.

Figure 7. Second-order fitting coefficients along the vertical visual field, as a function of axial corneal power (in dioptres) at cone apex for mild and moderate keratoconics: (a) vertical coma $C_{3}^{-1}$ coefficient, (b) higher-order root mean square aberrations (HORMS).

References


http://www.iovs.org/


Figure 1

Figure 2

http://www.iovs.org/
Figure 3

A. Higher order root mean square (HORMS)
- (a) Emmetropes
- (b) Mild K’conus
- (c) Mod K’conus

B. Total root mean square (TotalRMS)
- (a) Emmetropes
- (b) Mild K’conus
- (c) Mod K’conus

Figure 4
Table 2. P-values of the repeated measures ANOVA for refraction components, Zernike aberration coefficients and root-mean-squared aberrations with within-subjects factor of field position and between-subjects variable of group. The defocus coefficient $C_{20}^0$ is relative to its central field value for each subject. Asterisks indicate significant effects ($p \leq 0.05$). $P < 0.005$ is given as 0.00.

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Figure 5

- Emmetropes
- Mild K'conus
- Mod K'conus

Figure 6

- Total RMS
- HORMS
- Visual field angle (degrees)

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Figure 7