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Dynamics of ocular aberrations in keratoconus

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Background: The aim was to investigate the fluctuations in monochromatic ocular aberrations with accommodation and tear-film changes in moderate keratoconic eyes.

Methods: We measured the changes in ocular higher-order aberrations in 10 moderate keratoconic and 10 visually normal eyes to accommodative stimuli ranging from zero to 5.00 DS using a Hartmann-Shack aberrometer. In addition, the changes in ocular higher-order aberrations were measured for up to 15 seconds after a blink in eight keratoconic and eight visually normal eyes.

Results: These results show that ocular spherical ($p = 0.68$) and coma-like ($p = 0.71$) aberrations did not change significantly with accommodation from zero to 5.00 DS in keratoconic eyes. In contrast to normal eyes, the ocular higher-order RMS error tended to decrease in magnitude after a blink in keratoconic eyes. Vertical coma became less negative with time after a blink in the keratoconic group, therefore, reducing the manifest ocular higher order RMS error by counteracting the negative vertical coma of the cornea.

Conclusions: Compared to the manifest monochromatic higher-order aberrations, any dynamic fluctuations in ocular aberrations with accommodation and tear film changes are relatively small in moderate keratoconic eyes. This implies that the correction of monochromatic higher-order aberrations in keratoconus using customised soft contact lenses will not be significantly hindered by such dynamic aberrational changes.

Key words: aberrations, accommodation, keratoconus, tear film

Ocular aberrations play a key role in influencing retinal image quality. Corneal disorders such as keratoconus produce significantly higher levels of ocular aberrations in comparison to the normal population.[1–7] The reduction in visual quality in keratoconus is largely explained by the high levels of higher-order aberrations of the eye.[8] Therefore correcting higher-order aberrations in patients with keratoconus is likely to improve the quality of vision significantly.

It has been suggested that by correcting ocular aberrations it may be possible to obtain 'supernormal' vision in patients with normal levels of ocular aberrations.[9–11] An important factor influencing the degree to which these aberrations can be corrected is the stability of ocular aberrations. Ocular aberrations differ significantly between individual patients and vary throughout the day due to changes in the tear film and accommodation.[12–21]

The tear film is the most powerful ocular refractive surface as it is at the boundary of the largest difference in refractive indices of the optics of the eye. Németh, Erdélyi and Csákány[22] reported that while recording corneal topography using a videokeratoscope, the 'breaking up' of the tear film made the anterior corneal surface asymmetric and irregular. Several other studies have shown that the tear film disruptions measured while holding a blink can reduce the optical quality of the eye.[23–26] A recent study by Montés-Micó and colleagues[21] evaluated changes in corneal and ocular aberrations due to post-blink changes in the tear film, showing significant changes in aberrations over a 20-second time scale after a blink. They[21] showed that the higher-order RMS error increases with time post-blink for both corneal and total ocular aberrations due to the changes in the tear film. In a subsequent study, Montés-Micó and associates[27] report that changes in the post-blink total RMS error in normal patients could be accounted for by changes in the component aberrations. Spherical aberration terms (Z_0^4 and Z_0^6) tended to increase monotonically with time after a blink, whereas the coma-like aberrations passed through a minimum. Montés-Micó and associates[27] suggested that the minimum values for the total aberrations were due to the changes in coma-like aberration.

In addition to the changes in optics caused by instability of the tear film, ocular aberrations are also affected by changes caused as a result of accommodation. As accommodation is achieved by changes in the shape and position of the crystalline lens, the aberrations of the eye are expected to change with accommodation.[28,29] Several studies[12–20,30] have shown systematic changes in spherical and coma-like aberrations of the eye with accommodation.

The large variability in ocular aberrations caused by factors such as tear film instability and accommodation make correction of ocular aberrations in the normal population to produce 'supernormal' vision a difficult task. Keratoconic patients have significantly high levels of third-order coma-like aberrations in comparison to normals.[1–6,31] Maeda and co-workers,[4] Gobbe and Guillon[2] and Bühren, Kühne and Kohnen[31] also show a significant difference in spherical-like aberrations between keratoconic and normal eyes for both corneal and ocular aberrations. Correcting these aberrations is likely to improve the visual image quality in keratoconic eyes significantly. To be able to correct these aberrations appropriately, it is essential to understand the changes in aberrations produced by changes in the tear film and accommodation in keratoconic eyes. There are relatively few published studies investigating how keratoconus alters the pre-ocular tear film. Some authors report that the disease causes increased tear instability, squamous cell metaplasia and goblet cell loss,[32] while others suggest that some of these changes may be attributed to contact lens wear rather than keratoconus per se.[33] The levels of inflammatory cytokines also appear to be increased in the keratoconic tear film[34] and perhaps may be related to disease severity.[35] There are no published studies addressing how the ocular aberrations of the eye are influenced by possible alterations to the pre-ocular tear film or with accommodation in keratoconic individuals.

This study investigates the dynamics of higher-order aberrations in keratoconic eyes by assessing the changes in aberrations post-blink and with accommodation in patients with keratoconus and in visually normal subjects.

METHODS

Nineteen subjects took part in the study including seven moderate keratoconic and 12 visually normal control subjects. Five of the seven keratoconic participants had been diagnosed previously with bilateral keratoconus, whereas two participants had been diagnosed with unilateral keratoconus. These unilateral keratoconic subjects both showed normal topography and no clinical signs of keratoconus in their contralateral eyes on slitlamp examination. The subjects were recruited from the University of Manchester's Vision Centre optometry clinics. Aberrometry data were collected from 12 keratoconic eyes and 12 left normal eyes. Data were collected from both eyes of the bilateral keratoconic patients as the disease tends to be asymmetric in the two eyes.[36–39] Three of the keratoconic patients habitually wore rigid gas permeable (RGP) contact lenses. Patient 1 wore Rose K lenses (David Thomas Contact Lenses Ltd, Northampton, UK), Patient 3 wore a Dyna-Z cone lens (Number 7, Contact Lenses, Hastings, UK) and Patient 6 wore Jack Allen Aspheri-KD lenses (Jack Allen Contact lenses, Middlesex, UK). The other four keratoconic patients were habitually corrected using spectacles only and still achieved reasonable visual acuity. None of the normal subjects wore contact lenses, six wore spectacles and six required no visual correction. No subject enrolled in this study had been diagnosed with dry eyes.

The mean age and standard deviation of the 12 keratoconic patients was 34.1 ± 9.0 years (with a range of 25 to 53 years) and 31.9 ± 10.6 years (with a range of 23 to 55 years) for the 12 normal subjects. None of the keratoconic patients in this study showed corneal scarring detectable on slitlamp examination. The study inclusion criteria required that all participants had a visual acuity of 6/12 or better, to allow them to view the aberrometer's target, and no history of previous ocular surgery or dry eye. The study followed the tenets of the Declaration of Helsinki. All subjects gave informed consent after being told the purpose of the experiment. The project protocol was approved by the Senate Committee on the Ethics of Research on Human Beings of the University of Manchester.

Baseline measurements were taken of the visual acuity of all subjects with their habitual spectacles or contact lenses in place. A slitlamp bio-microscope was used to conduct an examination of the subject's external eye and measure the tear break-up time using sodium fluorescein in the form of a saline wetted 1 mg fluoret. Tables 1 and 2 show the times at which the tear film just began to destabilise for the keratoconic and normal subjects, respectively. The Oculus Pentacam (Oculus, Wetzlar, Germany) was used to measure the subject's keratometric readings and corneal thickness. Topographic data from the Pentacam were also acquired. The rotating Scheimpflug camera (and a monochromatic slit-light source; a blue LED at 475 nm) provides 25 images during a one-second scan; with 500 true elevation points per image.[40] During measurements the patients positioned their chins on the chin-rest and their foreheads against the head support bar, while fixing on the central black circle against the blue

Patient number	Eye	Age (years)	CLEK severity	Flat K (D)	Steep K (D)	Corneal thickness (microns)	Fleischer's ring	Vogt's striae	Fluorescein tear break-up time(s)
1	R	53	Moderate	48.5	50.4	392	Present	Present	10
1	L	53	Moderate	48.9	49.9	419	Present	Absent	10
2	R	34	Moderate	47.9	48.8	448	Present	Absent	9
2	L	34	Moderate	47.7	46.8	470	Absent	Absent	9
3	R	29	Moderate	46.9	48.6	462	Present	Absent	10
4	L	30	Moderate	42.4	46.8	474	Absent	Absent	10
5	R	25	Moderate	42.7	47.1	445	Present	Present	11
5	L	25	Moderate	42.9	45.4	466	Absent	Absent	11
6	R	32	Moderate	47.7	51.1	425	Present	Present	9
6	L	32	Moderate	48.2	50.9	420	Present	Absent	11
7	R	36	Moderate	43.5	46.0	435	Present	Absent	11
7	L	36	Moderate	43.3	46.9	418	Present	Present	9

Table 1. A summary of the seven keratoconic patients' corneal data. Patient 3 and Patient 4 were unilateral keratoconic participants.

Patient number	Age (years)	Steep K (D)	Flat K (D)	Corneal thickness (microns)	Fleischer's ring	Vogt's striae	Fluorescein tear break-up time(s)
1	27	45.5	44.5	533	Absent	Absent	10
2	26	41.2	40.2	534	Absent	Absent	14
3	28	42.2	41.5	523	Absent	Absent	10
4	23	45.2	44.8	593	Absent	Absent	12
5	24	41.9	39.7	517	Absent	Absent	12
6	32	44.3	43.8	514	Absent	Absent	12
7	34	44.2	43.4	558	Absent	Absent	10
8	25	40.5	40.0	538	Absent	Absent	14
9	27	40.9	40.8	579	Absent	Absent	12
10	55	42.3	40.3	598	Absent	Absent	10
11	52	41.0	40.2	576	Absent	Absent	12
12	30	44.5	44.0	537	Absent	Absent	12

Table 2. A summary of the twelve normal subjects' corneal data.

LED slit light. The severity of the subjects' keratoconus was graded using the CLEK study group's criteria, where steep keratometric readings less than 45 D were graded as mild keratoconus, steep keratometric readings between 45 and 52 D were moderate keratoconus and finally steep keratometric readings greater than 52 D were graded as severe keratoconus.[41] In addition to corneal curvature, corneal thickness and the presence or absence of Fleischer's ring, Vogt's striae and a scissored retinoscopic reflex were also recorded.

Total ocular aberrations were measured using a Hartmann-Shack aberrometer (IRX-3, Imagine Eyes, Paris, France) with a 32×32 sampling array and wavelength of 780 nm. Wavefront errors were recorded under monocular conditions. The instrument records pupil diameter at the same time as the aberrations and normally uses a dynamic fogging method to relax accommodation to the far point. It also contains an internal Badal system, which allows the vergence of the fixation target to be systematically altered with respect to the subject's far point (that is, the far point target vergence providing a zero dioptre accommodative stimulus). Recordings were made with the stimulus, a black 6/12 Snellen letter 'E' in an elliptical white background field subtending about $0.7 \times 1.0°$ and having a luminance of about 85 cd/m^2.

Changes in ocular aberrations with accommodation were measured with 1.00 D intervals, to provide accommodative stimuli over the range zero to 5.00 D, in 10 keratoconic eyes (from six patients, with an average age and standard deviation of 31.0 ± 3.9 years, from a range of

25 to 36 years) and 10 normal eyes (from 10 subjects, with an average age and standard deviation of 27.6 ± 3.5 years, from a range of 23 to 34 years). One keratoconic patient (aged 53 years) and two normal participants (aged 55 and 52 years, respectively) were excluded from these measurements in view of their presbyopic status. The subjects were encouraged to try to keep the letter as clear as possible at all times, so that both reflex and voluntary accommodation were employed. If the keratoconic subject habitually wore RGP lenses, then these were worn during the measurements (n = 3 eyes). In the case of spectacle wearers, no refractive corrections were worn; instead the measurements started with the determination of the aberrometer target position corresponding to the far point of the eye, followed by the measurement of the associated ocular aberrations. The accommodative demand was then increased in 1.00 D intervals up to 5.00 D with the built-in Badal system. Axial changes in target position took place approximately every 0.75 seconds, with the target being kept at a constant vergence for approximately one second, after which a measurement of the wavefront aberration was made. The initial interval of one second was sufficient for any pupil constriction to be completed[42,43] and for the subject's accommodation to reach its new level.[44–47] The target was then moved again. Subjects were given two practise runs to familiarise them with the task, after which three complete runs were recorded. As expected, the contact lenses did move over the measurement period, however, the instrument was kept aligned with the lens-eye combination as far as possible.

Changes in ocular aberrations over time due to tear film break-up were also measured with the Shack-Hartmann aberrometer. These measurements were taken without the participant's contact lenses in place. Changes in higher-order ocular aberrations, induced by the tear film 'breaking up', were measured for up to 15 seconds after a blink. Some participants failed to keep their eye open for the full 15 seconds without blinking and the data acquisition was terminated when the subject blinked. For each 15 second run the fixation target was kept at the far point of the eye. The sampling frequency of the post-blink ocular aberration measurements was set to 1.0 Hz with one measurement being taken every second for the duration of 15 seconds. Each 15-second measurement run was repeated four times per eye with a five-minute interval between runs.

Data analysis

CHANGES WITH ACCOMMODATION

The 'refraction' for each accommodative stimulus was deduced with the manufacturer's software (Version 1.2, Imagine Eyes, Paris, France), which effectively fits the wavefront (using the least-squares fitting method) for the natural or any chosen pupil diameter with an appropriately tilted sphero-cylinder.[48] The wavefront-derived refractive results for the natural pupil size were then vector averaged.[49] The accommodative response to any near stimulus was taken as the difference between the mean-spherical refraction measured with the near stimulus and that at the far point, with the negative sign reversed to make the responses positive.

Both third-order coma and fourth-order spherical aberration were expressed in their alternative dioptric forms using equations (1)[14] and (2),[14] where r = the pupil radius in mm:

$$\text{Coma (D/mm)} = \frac{9\sqrt{8}}{r^3}\cdot\sqrt{(C_3^{-1})^2 + (C_3^{+1})^2} \qquad (1)$$

$$\text{Spherical aberration (D/mm}^2\text{)} = \frac{24\sqrt{5}}{r^4}\cdot(C_4^0) \qquad (2)$$

The accommodative response and pupil size data were found to be normally distributed using a Shapiro-Wilk's normal distribution test. Therefore, parametric tests were used for the data analysis.

POST-BLINK ABERRATIONS

As some patients were unable to keep their eyes open, without blinking, for a period of 15 seconds during the measurements with the aberrometer, post-blink aberrations were measured for only eight keratoconic and eight normal eyes.

Zernike wavefront aberration coefficients were calculated using the manufacturer's software for a 4.0 mm pupil diameter (up to the sixth order). Four sets of measurements were taken from each patient. The average standard deviation was calculated as the square root of the average variance after all the standard deviation values were converted into variances.

RESULTS

In some keratoconic patients both eyes were used to collect the data as keratoconus is often an asymmetric disease in bilateral cases,[36–39] however, only one eye was used to collect data from the normal participants in all of the experiments conducted. Table 1 shows that the left and right eyes of the bilateral keratoconic subjects were not equivalent in terms of the steepest k-readings, corneal thicknesses and slitlamp signs of keratoconus.

In comparison, Table 2 shows a summary of the normal subject's corneal findings.

Changes in ocular aberrations with accommodation

The mean accommodative response gradient to altering distance stimuli (up to 5.00 D) was found to be 0.96 in normal eyes and 0.90 in keratoconic eyes. Analysis of variance showed that normal subjects had significantly higher accommodative response values (ANOVA: $F_{1,119} = 90.28$; $p < 0.00001$) when compared to the keratoconic subjects, as found in a previous report by Ohmi and colleagues.[50] Figure 1 shows the changes in accommodative response and pupil size with accommodative demand in keratoconic and normal participants.

As expected, pupil size changed significantly with accommodation in both groups (ANOVA: $F_{5,119} = 1.35$; $p = 0.017$), however, there were no significant differences in the pupil size between the two subject groups (ANOVA: $F_{1,119} = 0.50$; p =

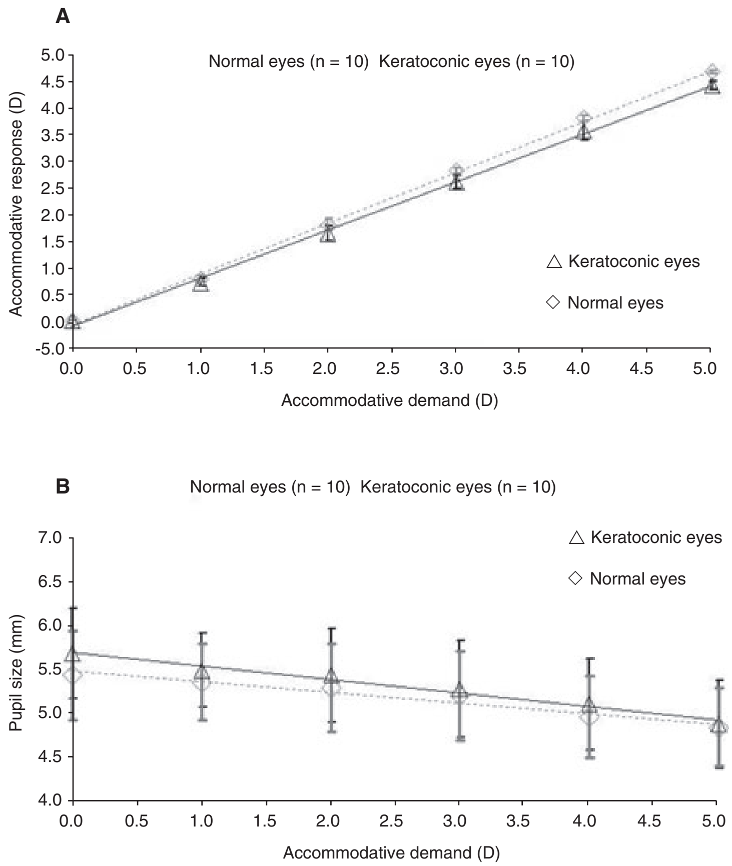

Figure 1. Changes in the accommodative response (A) and pupil size (B) with accommodative demand in normal and keratoconic eyes. The error bars represent ±1 standard deviation.

0.30). In addition, there was also no significant interaction between pupil size in the two groups and accommodative stimulus level (ANOVA: $F_{5,119} = 0.58$; p = 0.99).

SPHERICAL ABERRATION

On taking into consideration the individual pupil sizes at various levels of accommodation, the spherical aberration values were calculated in dioptric equivalents and in D/mm^2. Figure 2 shows the changes in spherical aberration (in D/mm^2) as a function of accommodative response for the 10 normal (A) and 10 keratoconic eyes (B) over 5.00 D of accommodation. At all accommodative levels, spherical aberration varied considerably between individuals in the keratoconic group.

Spherical aberration showed a significant shift in a negative direction with increased accommodation in the normal group ($R^2 = 0.070$; p = 0.043—from the average slope for the 10 subjects). In comparison, the larger variability in the keratoconic group led to no consistent trends being apparent with accommodation ($R^2 = 0.0029$; p = 0.68—from the average slope for the 10 subjects). The individual slope values of the lines of best fit, for the averaged spherical aberration data collected over three runs for each participant, were compared between the normal and keratoconic groups using the non-parametric Mann-Whitney test. This showed that the changes in spherical aberration with accommodation were not significantly different between the keratoconic and normal groups (p = 0.65).

COMA-LIKE ABERRATIONS

Coma-like aberrations showed minimal changes with accommodation in both subject groups. Figure 3 shows the changes in coma-like aberrations (in D/mm) as a function of accommodative response for the 10 normal (A) and 10 keratoconic eyes (B) over 5.00 D of accommodation. These measurements take into account the individual pupil diameter of the participants at each accommodative state. In general, the keratoconic eyes had considerably higher levels of coma aberration in comparison to normal eyes. Although coma showed a small positive increase on accommodation in the normal subjects (an average slope value for the 10 subjects of 0.017 D/mm per dioptre of accommodation), this shift was not found to be significant ($R^2 = 0.030$, p = 0.19). A larger positive increase in coma-like aberrations with accommodation was found for the keratoconic eyes (an average slope value for the 10 subjects of 0.030 D/mm per dioptre of accommodation), however, the data collected showed a larger magnitude of change with accommodation when compared to the normal eyes but there was no significant difference ($R^2 = 0.0025$, p = 0.71). The individual slope values of the lines of best fit for the averaged coma-like aberration data, collected over three runs for each participant, were compared between normal and keratoconic groups, using the Mann-Whitney test. This test showed that the changes in coma-like aberrations with accommodation were not significantly different between the keratoconic and normal groups (p = 0.94).

The changes in spherical and coma-like aberrations with accommodation were plotted separately for the seven keratoconic eyes not wearing lenses (KC-NRGP group) and the three keratoconic eyes wearing RGP lenses (KC-RGP group). Both groups of keratoconic patients showed no significant changes in spherical aberration with accommodation (KC-NRGP group $R^2 = 0.0038$, p = 0.70 and the KC-RGP group $R^2 = 0.0023$, p = 0.85), or coma (KC-NRGP group $R^2 = 0.0042$, p = 0.68 and the KC-RGP group $R^2 = 0.021$, p = 0.57). Finally, the slope values calculated

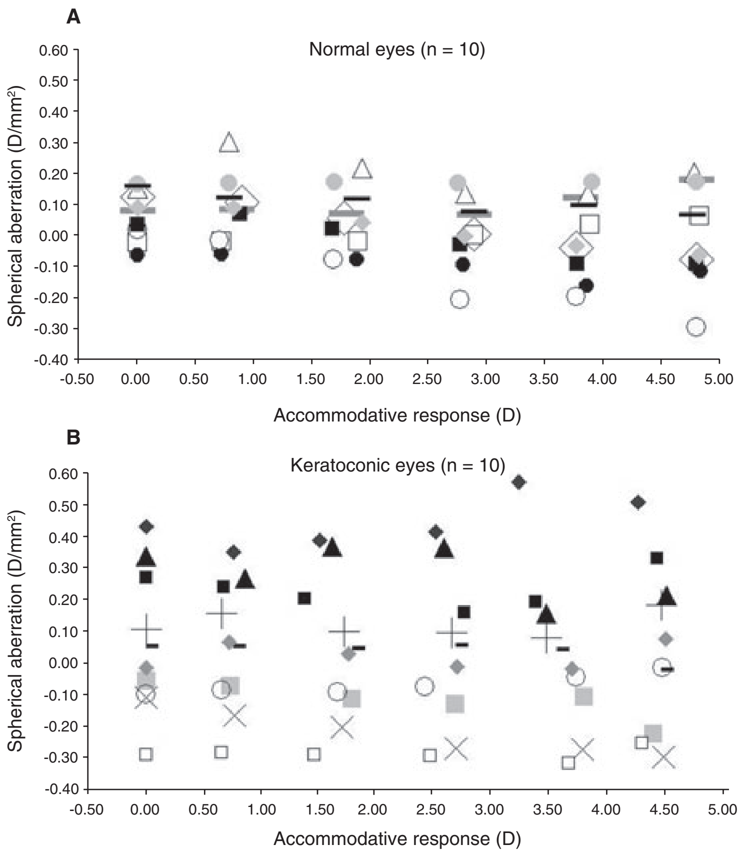

Figure 2. Changes in spherical aberration with accommodation in normal (A) and keratoconic (B) eyes using the dioptric form in D/mm²

for the changes in spherical and coma-like aberrations with accommodation for the KC-NRGP and KC-RGP group were also compared using the Mann-Whitney test. No significant differences were found between the two groups for either the spherical aberration (p = 0.43) or the coma-like aberration (p = 0.73) slope values.

POST-BLINK CHANGES IN OCULAR ABERRATIONS

Figure 4 shows that higher-order aberrations changed in magnitude following a blink in both the normal and keratoconus groups. Figure 4B shows that the higher-order RMS error typically increased in the first four to five seconds after blinking in most keratoconic eyes and following this increase, there was a trend towards a reduction in the magnitude of higher-order RMS error back to almost the baseline value. In contrast, most normal eyes showed a decrease in RMS higher-order aberrations in the first few seconds after blinking, followed by a subsequent increase in the magnitude of aberrations thereafter (Figure 4A). This increase in higher-order aberrations was linked to modest changes in third- and fourth-order aberrations.

On the other hand, the keratoconic eyes showed a decrease in higher-order RMS error over time after a blink. This was perhaps linked to an increase in vertical coma which shifted from a negative value to a less negative value after a blink. The mean changes in vertical coma (with time after a blink) in normal and keratoconic eyes are shown in Figure 5.

Visual image quality is partly dependent on the magnitude and changes in higher-order aberrations after a blink. The average post-blink higher-order RMS error in normal eyes over the 15 seconds of measurement time was 0.13 µm with a mean standard deviation of 0.018 µm for all the normal subjects. The keratoconic eyes had a significantly higher (ANOVA: $F_{1,31} = 55073$; $p < 0.00001$) average post-blink higher-order RMS error of 0.66 µm and the mean standard deviation for all the keratoconic patients was 0.022 µm.

DISCUSSION

As found in previous studies,[12–15,18,19,30,51,52] these results show that spherical aberration tended to show a significant shift in a negative direction with accommodation in normal eyes. In contrast, the keratoconic group showed large changes in spherical aberration with accommodation, and no obvious trend was apparent. The changes in both coma-like and spherical aberrations seen among the keratoconic subjects are in line with those reported in previous literature and are believed to be linked to the severity of keratoconus, corneal thickness, corneal curvature and the position of the cone.[53–56] Given this large variability in aberrations seen in keratoconic patients, the systematic changes in higher-order aberrations caused by accommodation appear to be relatively inconsequential.

Another possible reason for the higher magnitude of changes in spherical and coma-like aberrations in the keratoconic population could be that the shape of the cornea in keratoconus can cause computational errors during Hartmann-Shack aberrometry data acquisition.[23,57] To help overcome this issue, all the aberrometric measurements made in this investigation were repeated several times as suggested by Cheng and associates.[58] Other studies have suggested that the laser ray tracing method of measuring aberrations may help to reduce some of these computational errors,[59,60] however, this method of measurement takes longer to perform and compute when compared to Hartmann-Shack aberrometry. Therefore, this technique would not be suitable for measuring dynamic changes in aberrations.

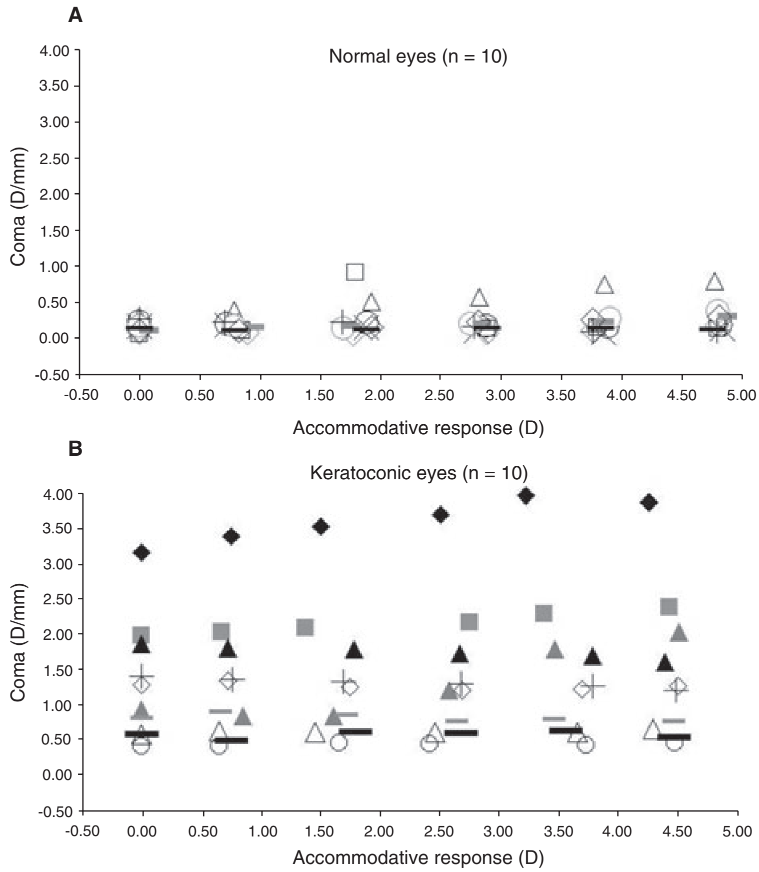

Figure 3. Changes in coma with accommodation in normal (A) and keratoconic (B) eyes using the dioptric form in D/mm.

Keratoconus causes a significantly large increase in ocular coma-like aberrations compared to a normal eye. Data from both groups show that each individual subject's coma-like aberrations vary in both direction and magnitude with accommodation, as has been found in normal participants in some previous studies.[13,14,16–20] Although the changes in coma-like aberrations with accommodation were larger in the keratoconic group than in the normal subjects, they did not differ significantly from the normal eyes.

Our results imply that keratoconus may have no significant influence on the way in which spherical and coma-like aberrations change on accommodation. This concurs with previous published research, which leads us to believe that during accommodation coma-like aberrations change due to alterations in the tilt and vertical positioning of the crystalline lens.[61] Similarly the changes in spherical aberration that occur during accommodation are believed to be due to the changes in the curvatures of the crystalline lens surfaces. The crystalline lens shows an increase in the anterior lens curvature centrally and possibly a flattening of the lens peripherally during accommodation.[62–65] A negative shift in spherical aberration has also been observed in the *in vitro* lenses of both young humans[66] and monkeys.[67] The data presented show no statistically significant linear effect of the mean accommodative response on either spherical or coma-like aberrations among the keratoconic participants. Additionally, this investigation found that the slopes of the spherical and coma-like aberration curves were not significantly different between the normal and keratoconic groups. These findings could indicate that the optics of keratoconic eyes do not have a mechanism to add negative spherical aberration with increased accommodation. Previous studies explain that the crystalline lens is principally responsible for the negative shift in spherical aberration with accommodation found in normal eyes. At present, no studies have investigated the accommodative mechanisms of the crystalline lens in keratoconus. Keratoconus is widely accepted as an ectasia of the cornea with no recognised effects on the crystalline lens.[68–71] To date only one isolated report describes anterior lenticonus, a bulging of the anterior crystalline lens capsule (most commonly associated with Alport's syndrome[72–75]) in a keratoconic patient.[76] Consequently, it is perhaps more likely that the keratoconic crystalline lens does have a mechanism to add negative spherical aberration with increased accommodation, however such changes may be masked by other sources of higher-order aberrations and so are harder to identify than in normal subjects.

The purpose of this investigation was to evaluate how higher-order aberrations changed with accommodation, during habitual viewing conditions in keratoconic eyes. Therefore, measurements of accommodation were made with contact lenses for some keratoconic participants who habitually wore RGP lenses (n = 3 eyes). For all the other keratoconic participants, their habitual spectacle refraction was inputted into the aberrometer to correct them for distance viewing. RGP lens movements during the measurements of accommodation could have influenced the changes in aberrations measured. Leaving these subjects uncorrected would have left large amounts of residual blur that may have caused the subject to over- or under-accommodate, perhaps skewing the results. To avoid the possibility of contact lens movements from confounding the results, the IRX-3 device was kept aligned with the eye as far as possible. Additionally, the statistical analysis shows that there were no significant differences in the magnitudes of coma-like or spheri-

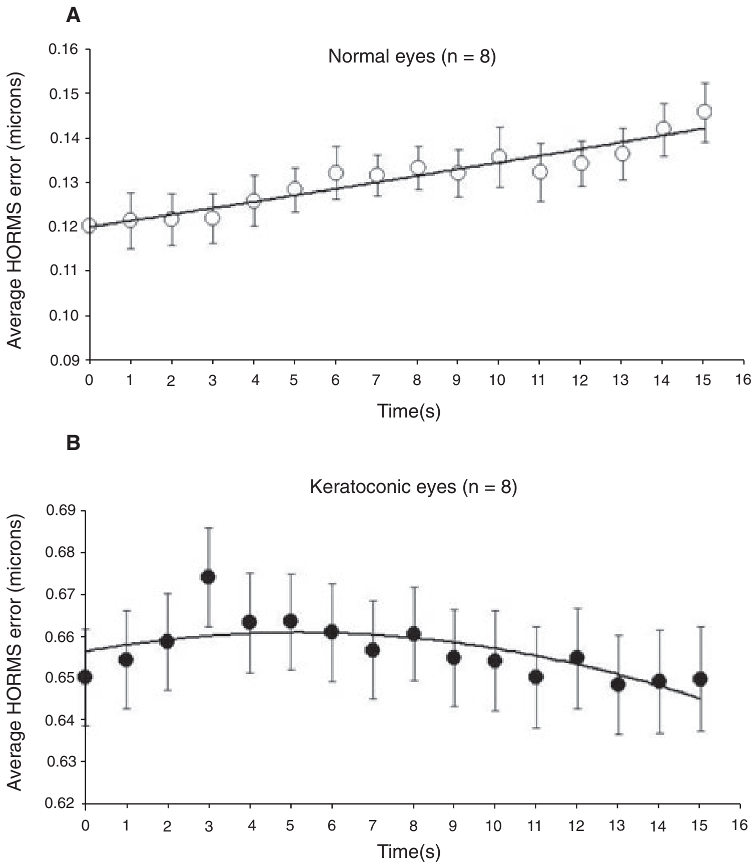

Figure 4. Average higher-order RMS errors with time after blink in normal (A) and keratoconic (B) eyes. The solid lines show the best-fit second-order polynomial curves. The error bars represent ±1 standard error. Note the magnitude of aberrations in keratoconic eyes in comparison to the normal eyes.

cal aberration, with accommodation between keratoconic eyes wearing RGP lenses and those not wearing lenses.

In this study, the corneal curvature data were acquired using the Oculus Pentacam within approximately five to 10 minutes of the RGP lens-wearing keratoconic patients (five out of the 12 eyes) removing their lenses (average flat k-reading = 7.34 ± 0.43 mm, average steep k-reading = 6.96 ± 0.32 mm). With this in mind, the corneal curvature data recorded in this investigation may have been flatter, compared to those of previous studies, where RGP lenses may have been left out for longer periods or where larger sample sizes were evaluated. In addition, all the keratoconic patients included in the study had moderate keratoconus only, showing no signs of anterior corneal scarring or hydrops.

Previous studies show that tear film changes affect the higher-order aberrations after a blink in normal eyes, which alter the optical quality of the eye dynamically.[21,23–27] In normal eyes the RMS higher-order aberrations decreased in the first few seconds after blink, followed by a subsequent increase in the magnitude thereafter. These results agree with these previous reports.

The present study also shows that the higher-order RMS error in keratoconic eyes initially increases in the first few seconds after a blink followed by a subsequent reduction. This reduction appears to be linked to changes in vertical coma aberrations, which occur after a blink. In the normal subjects, the vertical coma coefficient showed a positive shift as the tears began to break up ($R^2 = 0.73$), a finding in support of Montés-Micó and co-workers' earlier study.[21] A similar positive shift was also found in keratoconic eyes after a blink ($R^2 = 0.61$). The positive vertical coma aberration induced by the tear film after a blink effectively reduced the magnitude of the negative vertical coma aberration caused by the patient's keratoconus. Previously, the positive increase in vertical coma after a blink has been attributed to vertical gravitational effects on the pre-corneal tear film, which may induce this type of aberration.[21,77] Other reports suggest that the keratoconic tear film contains elevated amounts of inflammatory cytokines compared to normal eyes.[34,35] These inflammatory molecules may also be responsible for these changes in higher-order aberrations after a blink.

The changes over time in post-blink higher-order RMS aberrations were found to be similar in both normal and keratoconic eyes. The average standard deviations of the tear film aberrations in the two groups were found to be within 0.04 µm of each other, although the magnitudes of the higher-order aberrations were significantly higher in the keratoconic group in comparison to normal participants. This difference in magnitude between the two populations is expected as several studies have shown that keratoconic eyes manifest significantly larger amounts of ocular aberrations when compared to normal eyes.[3,5,6]

The average higher-order RMS error (or HORMS) measured in this study is comparable to values found in other published reports. To allow such comparisons to be made between different studies using different pupil sizes, the HORMS values (in microns) are converted into dioptric equivalents (in D), as outlined by Thibos and associates.[78] The present study, which includes 12 moderate keratoconic eyes, found an average HORMS dioptric equivalent value of 1.17 D compared to 1.12 D from three moderately keratoconic eyes by

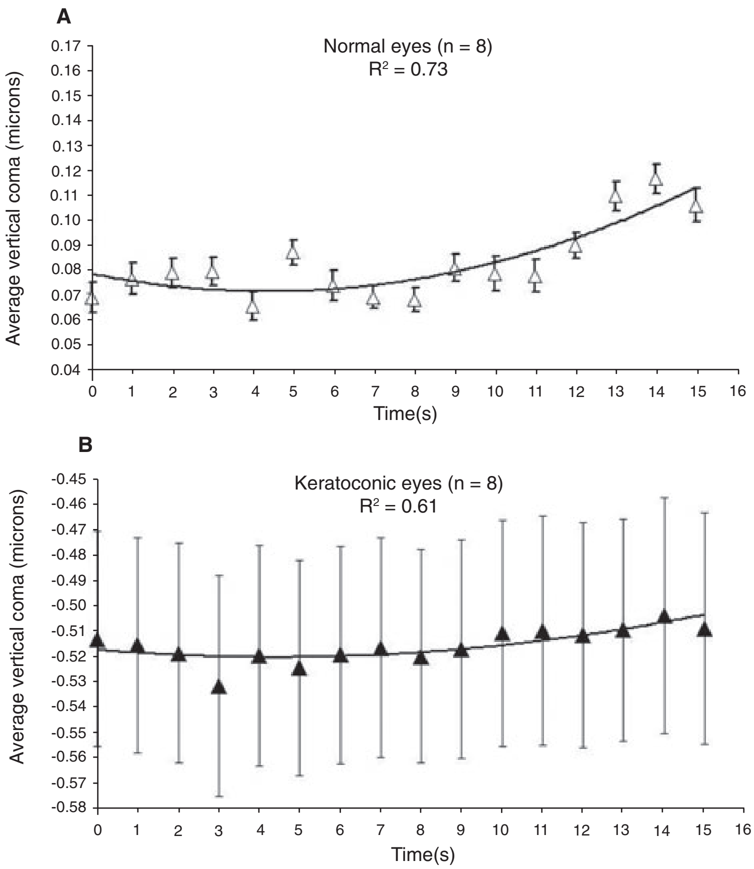

Figure 5. Average changes in vertical coma aberration with time after blink in normal (A) and keratoconic (B) eyes. The solid lines show the best fit second-order polynomial curves. The error bars represent ±1 standard error. Note the magnitude of aberrations in keratoconic eyes in comparison to the normal eyes.

Chen and colleagues[79] and 1.33 D by Lim and co-workers[6] for 35 keratoconic eyes, whose disease severity ranged from mild to severe according to CLEK guidelines.[41] In addition, Marsack, Parker and Applegate[80] reported lower values of HORMS in two moderate keratoconic subjects with dioptric equivalent values of 0.33 D and 0.93 D.

Several studies have suggested that the correction of higher-order aberrations in normal eyes, to help give a better visual performance, will be limited by tear film and accommodative changes.[81–84] On the other hand, keratoconic eyes manifest large magnitudes of higher-order aberrations[1–4,6,31] and for these patients, correction of aberration gives significant improvements in visual performance.[79,80,85–91] Overall, the present study of a limited number of keratoconic participants shows that the changes in aberrations with accommodation and tear film changes are of a similar magnitude in keratoconic patients and normal participants, despite the higher absolute levels of aberrations found in keratoconic eyes. A large study including patients with severe keratoconus is required to assess these effects further. Nonetheless, these results indicate that correcting the higher-order aberrations in keratoconic eyes will not be hindered by dynamic changes in ocular aberrations, which occur due to tear film changes or increased accommodation.

In summary, the purpose of this study was to explore the changes in higher-order aberrations that occur with accommodation and post-blink in keratoconic eyes. These results show that spherical and coma-like aberrations did not change significantly with accommodation in keratoconic eyes. In contrast to normal eyes, these results show that the higher-order RMS error tended to decrease after a blink in keratoconic eyes.

This investigation shows that compared to the manifest higher-order aberrations, any dynamic changes in ocular aberrations with accommodation and tear film changes are relatively small in keratoconic eyes. It is possible that such changes in aberrations are present but are relatively small in comparison to the magnitude of the manifest higher-order aberrations in keratoconus. On the other hand, there is no evidence to show that the changes in aberrations due to alterations in the pre-corneal tear film and accommodation are smaller than those measured in normal eyes. In summary, our results imply that the correction of higher-order aberrations in keratoconus using a customised soft contact lens will not be hindered by dynamic accommodation or tear film changes.

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CONFLICT OF INTEREST

None of the authors has any financial interest in the instruments mentioned.

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