Higher order aberrations in keratoconus

Optometry in Practice Vol 10 (2009) 141–160

Higher-Order Aberrations in Keratoconus: A Review

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Date of acceptance 29 June 2009

Introduction

Keratoconus causes a reduction in the optical quality of the eye as a result of corneal distortion, corneal scarring and higher-order aberrations. The correction of these optical aberrations would significantly improve the visual performance of keratoconic eyes. However the first step would be to measure the optical flaws in keratoconus accurately, which in itself presents a challenge. This paper will attempt to explain the optical aberrations typically found in keratoconic eyes, and will also review the progress made in attempting to correct them using soft contact lenses.

Pathogenesis

Keratoconus is a non-inflammatory ectatic (outward-bulging) disease of the cornea, typically characterised by stromal tissue thinning. The latter occurs mainly where the cornea protrudes maximally, causing the weakened cornea to take on a steepened, conical shape at the 'anterior' corneal surface. The condition is most usually bilateral in nature, predominantly affecting the inferior central two-thirds of the cornea. Reports of centrally, inferior nasally and inferiorly positioned cones have been made, suggesting that the nature of the corneal steepening is unique in each keratoconic eye (Kennedy *et al*. 1986, Krachmer 2004, Krachmer *et al*. 1984, Lafond *et al*. 2001, Wilson *et al*. 1991, Zadnik *et al*. 1996). Numerous studies show that the cone apex in keratoconus is most commonly displaced inferior temporally (Auffarth *et al*. 2000, Demirbas & Pflugfelder 1998, Doh *et al*. 2000, Núñez & Blanco 2008, Owens & Watters 1996).

Keratoconus causes visual problems which vary from large magnitudes of myopic astigmatism, with blurring and distortion, to ghosting and poor low-contrast acuity (Weed *et al*. 2008, Zadnik *et al*. 1998). In the severest form of the disease, corneal scarring is commonplace (Zadnik *et al*. 2000). In keratoconus it is believed that corneal thinning, protrusion and scarring help to cause the loss in visual performance (Edrington *et al*. 1995, Weed *et al*. 2007, Zadnik *et al*. 1996). The retina and the postretinal neural aspects of the visual system are unaffected in the aetiology of keratoconus, and so the visual degradation found compared to in normal eyes is purely due to the optical deficiencies at the cornea, such as higher-order aberrations (Tan *et al*. 2008).

The Lower- and Higher-Order Aberrations of the Eye

In an 'ideal' or 'perfect' eye light hits the retina at a succinct point, as shown in Figure 1A. Figure 1B shows that even in most normal eyes the optics will not produce a succinct point at the retina (even with the optimal refraction in place); this is usually due to higher-order aberrations. These cause light rays, upon entering the eye, to become deviated slightly from the ideal paths which are required to form the point image in Figure 1A.

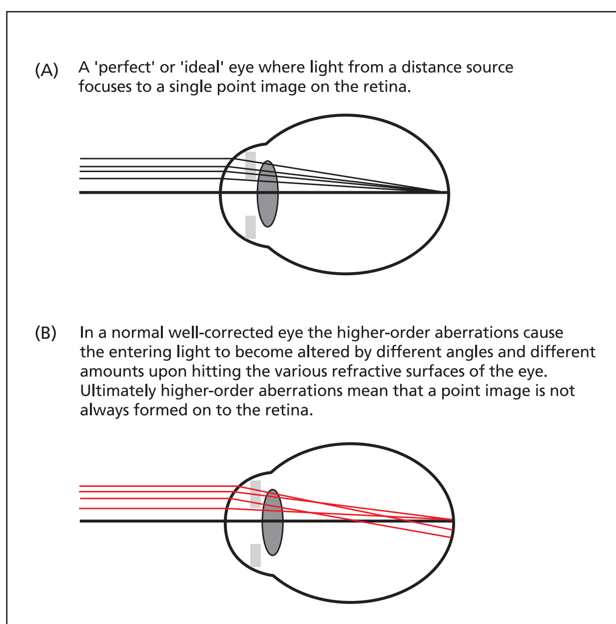

Figure 1 The 'ideal' eye versus a 'typical' normal eye. The diagrams show how light entering the eye is focused on to the retina in an 'ideal' (A) and a 'typical' normal eye (B).

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Ocular aberrations were classically described in Seidel terms, using functions such as oblique astigmatism, spherical aberration, field curvature and coma (Atchison & Smith 2000, Born & Wolf 1999). However these Seidel terms are limited, in that they cannot describe every single type of aberration found in the eye. As a result these have been replaced by Zernike's polynomials, which are complex mathematical formulae that are used to describe the intricate shapes of aberrations across the pupil (explained in the section on Zernike polynomials and wavefront aberrations, below).

As an alternative to ray aberrations, most modern aberrometers (instruments used to measure aberrations) today use wavefronts to describe the higher-order aberrations of the eye. In aberration terms, a wavefront is more specifically described as the shape of an optical disturbance as it leaves a refractive surface such as a lens, as shown in Figure 2. The wavefront will essentially connect all the different points on the propagating light wave which have an equal phase. The wavefront surface includes all the points reached by a light wave at the same instant as it travels. In isotropic media wavefronts are always perpendicular to the corresponding rays. Thus in Figure 2 we can either think in terms of parallel rays being refracted by the lens to form a point image, or plane wavefronts incident on the lens being refracted as concentric spherical wavefronts centred at the image point.

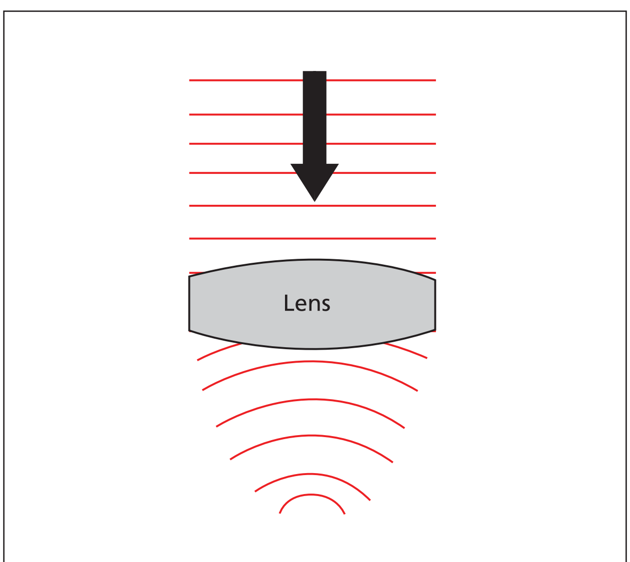


Figure 2 A diagrammatic representation of a wavefront. Lenses can be used to change the shape of a wavefront. In this illustration planar wavefronts become spherical after passing through the lens.

Measuring Higher-Order Aberrations

There are several options available to enable the measurement of the optical quality of the eye.

Measuring total ocular aberrations

With the optical instruments available on the market today, we can measure both total ocular aberrations and corneal aberrations. The total ocular aberrations include the optical effects of the anterior and posterior cornea as well as the crystalline lens. The Shack–Hartmann method is the most common and accepted method of measuring total ocular aberrations in clinical research and in the field of laser vision correction. The basic principle of the Shack–Hartmann aberrometer is to send a narrow collimated beam of light (around 1mm wide) into the eye (Figure 3A) to create a reflection (essentially a point source) off the retina outwards, which is then focused by a lenslet array of identical small lenses on to a charged couple device (CCD) sensor (Figure 3B) (Platt & Shack 2001). The 'ideal' aberration-free, emmetropic eye would produce a regular lattice array of point images, as in Figure 4A, since each lenslet would receive a small area of the plane wavefront emerging from the eye and image this on axis in the lenslet's focal plane.

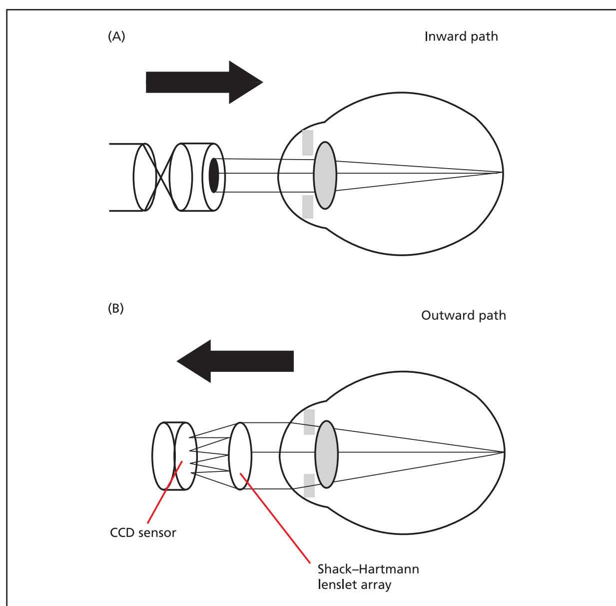


Figure 3 Simplified diagrams of the inward and outward light paths in Shack–Hartmann aberrometry.

(A) The path that light takes into the eye;
(B) The path that light reflecting from the retina takes outwards on to the lenslet array before hitting the charged couple device sensor.

However, if the wavefronts leaving the eye are not planar, the portion of the wavefront entering each microlenslet will be tilted with respect to the lenslet's axis. This means that the spot image no longer lies on the lenslet's optical axis; it will be displaced by an amount and a direction depending on the unique nature of the tilt of the wavefront leaving the eye (Figure 4B). Mathematical integration of the slopes of the deviated spots from their 'ideal' or chief ray gives the aberrant wavefront's shape.

As will be described later, these measurements can prove to be very difficult in patients with the poor optical quality found in keratoconus (Thibos & Hong 1999).

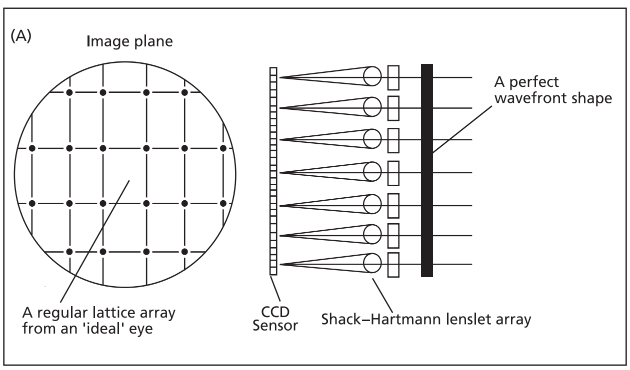
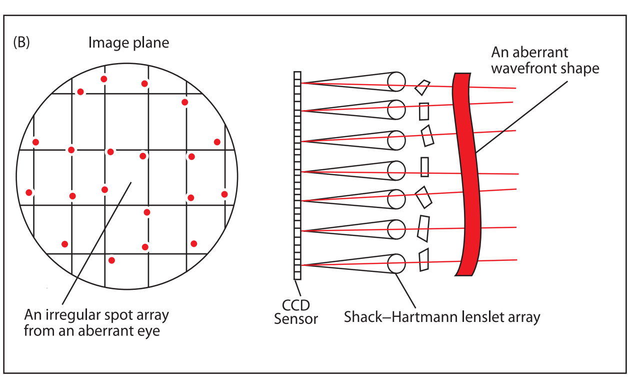


Figure 4 The principles of Shack–Hartmann aberrometry for a perfect (A) and an aberrated eye (B).

(A) A micro-lenslet array (each lens is typically 0.4mm in diameter) subdivides the wavefront into multiple beams. The local slope of the wavefront over each lenslet aperture determines the location of the spot on the video charged couple device (CCD) sensor (the image above portrays an 'ideal' eye). The solid black line shows an 'ideal' wavefront.



(B) An aberrated wavefront produces an irregular pattern of spots on the video sensor. Displacement of each spot from the corresponding lenslet axis gives a measure of the slope of the wavefront (the image above shows an aberrated eye). The wavy red line shows an aberrant wavefront.

Other less common methods of measuring total ocular aberrations in keratoconus include the Tscherning aberrometer (Mrochen *et al.* 2000) and the laser ray tracing (LRT) method (Navarro & Losada 1997).

Measuring corneal aberrations

There are numerous techniques for measuring corneal higher-order aberrations derived from corneal topography data. Briefly these include:

- Placido ring method, eg the TMS-1 topographer (Tomey Technology, Waltham, MA, USA) (Schwiegerling *et al.* 1995)
- Combined slit-scanning and Placido ring technology, eg the Orbscan II topographer (Bausch & Lomb, Rochester, NY, USA) (Bühren *et al.* 2007)
- Scheimpflug photography, eg the Oculus Pentacam (Wetzlar, Germany) (Miranda *et al.* 2009)

Of these instruments, the TMS-1 will only measure anterior corneal surface aberrations, whereas the Orbscan II and the Pentacam can measure both anterior and posterior corneal surface aberrations.

Zernike Polynomials and Wavefront Aberrations

The shape of the wavefront is often altered if the waves emanating from a source hit an irregular optical surface, such as a keratoconic cornea (Atchison 2004). The resultant wavefront is often referred to as an 'aberrant' wavefront, as in Figure 4B. 'Wavefront aberration' refers to the difference in separation between two surfaces: the ideal plane (Figure 4A) and the aberrant wavefront (Figure 4B) (Thibos *et al.* 2003a). The larger the separation between these two surfaces, the greater the magnitude of the wavefront aberration error. Differences in the separation of these two surfaces at the retina will mean that aberrations have a detrimental effect on visual performance. The larger the magnitude of the wavefront aberration, the poorer the optical image quality; these separations are normally measured in microns (µm).

Wave aberrations are fitted with a mathematical modelling system to help describe their often complex shapes across the pupil. The Optical Society of America recommends describing wave aberrations using Zernike decomposition polynomials (Thibos *et al.* 2002a). Each Zernike polynomial coefficient term is arranged and recognised by two features: its angular frequency and its radial order (see Equation 1, below). The coefficient values have both a magnitude and a sign which describes how that particular term makes up a certain proportion of the total wave aberration. The coefficients can tell us the variation in magnitude for each Zernike term used to describe the aberrations. These properties have made Zernike polynomials very attractive in optics. The ordering system for Zernike polynomials starts from 0 (the 0th order) upwards, with most aberrometers calculating up to the 10th radial order.

The values for 'piston' (the 0th radial order coefficient term) and 'tip' and 'tilt' (the 1st radial order coefficient terms) are most often ignored when analysing aberrometry data for normal and abnormal eyes. This is because these terms relate to the displacement of the image only; consideration of these with respect to image quality is therefore not usually relevant (Applegate *et al*. 2001, 2002, Charman 2005b, Iskander *et al*. 2002, Thibos 2001, Thibos & Applegate 2001, Thibos *et al*. 2002a). Another useful property of Zernike aberrations is that some of the coefficient terms of the Zernike polynomial expansion series are related to known types of optical aberrations such as defocus and astigmatism (2nd order), coma (3rd order) and spherical aberration (4th order) (Noll 1976).

Equation 1

$$\text{Total wavefront aberration } W(\rho,\theta) = \sum_{n}^{k} \sum_{m=-n}^{n} C_n^m Z_n^m (\rho,\theta)$$

where: (Thibos & Applegate 2001)

- n = radial order (the vertical axis of the Zernike pyramid)
- m = angular frequency (the horizontal axis of the Zernike pyramid)
- Z = Zernike polynomial term (which represents the shape of the distorted wavefront)
- C = Zernike coefficient (the proportion of the polynomial present in the subject's eye)
- k = the polynomial order of the expansion
- ρ = the normalised radial distance in the pupil, ie $\rho = r/r_{max}$, where r_{max} is the maximum pupil diameter for the measured wavefront aberration
- r = radial coordinate in the pupil
- θ = the azimuthal angle

The most significant optical aberrations are usually manifest in the form of sphere and cylinder, which are known as the lower-order aberration terms of the eye (where $Z(2,0)$ and $Z(2, \pm 2)$ represent sphere and cylinder respectively). The Zernike pyramid (Figure 5) provides a useful diagrammatic approach to the systematic method of ordering and naming the different Zernike polynomial aberration terms that can be used to describe the complex optical flaws of the eye. As we go further down the Zernike pyramid (past the 2nd radial order), we move to the components known as the higher-order aberrations. Figure 5 clearly shows that the higher the order, the more complex the shape of the coefficient term; compare, for example the simple shape of 2nd-order sphere with the more complex shape of 5th-order secondary coma. This is also the case as we move from the centre of the pyramid laterally to its edges (ie moving from a low to high angular frequency).

Finally a collective quantitative term which is used to represent the magnitude of aberration is the root-mean-square wavefront error (RMS error). This term is defined as the square root of the mean of the squared differences between the wavefront error at each point in the pupil, and the mean error across the whole of the pupil for all Zernike aberration terms. The magnitude of the RMS error is dependent on the size of the pupil being investigated, and the amount of wavefront RMS error found will increase as the pupil size increases (Charman 2005a). The wavefront RMS error value allows a brief comparison between different eyes, but the limitation of the RMS error is that it is only a single number, which does not give information about the actual shape of the aberrant wavefront itself. Additionally, this number is not directly linked to the retinal image quality of the eye being investigated (Marsack *et al*. 2004). The higher-order RMS error is the vector sum of all the Zernike terms from the 3rd order and above.

Aberrations have either negative or positive signs as well as a magnitude. A positive sign means that the aberrated wavefront is in front of the ideal plane, whereas a negative sign means that the aberrated wavefront is behind the ideal plane. These sign differences are normally depicted by different colours, as shown in Figure 5 (also see the section on the higher-order aberrations of the keratoconic eye, below).

Higher-Order Aberrations in Normal Eyes

Before describing how optical aberrations change in keratoconus, it is necessary to appreciate what is 'normal'. Several studies have shown that beyond the 2nd order, all the Zernike terms come to an average of almost zero (Porter *et al*. 2001, Radhakrishnan & Charman 2007, Thibos *et al*. 2002b, c). However this does not mean that most normal human eyes are generally free from higher-order aberrations; some eyes have positive Zernike coefficient values and some eyes have negative values. As shown in Figure 6, only in the case of 4th-order spherical aberration is there a tendency for eyes to have non-zero mean positive values (spherical aberration is represented in Figure 6 by the Zernike notation $Z(4,0)$).

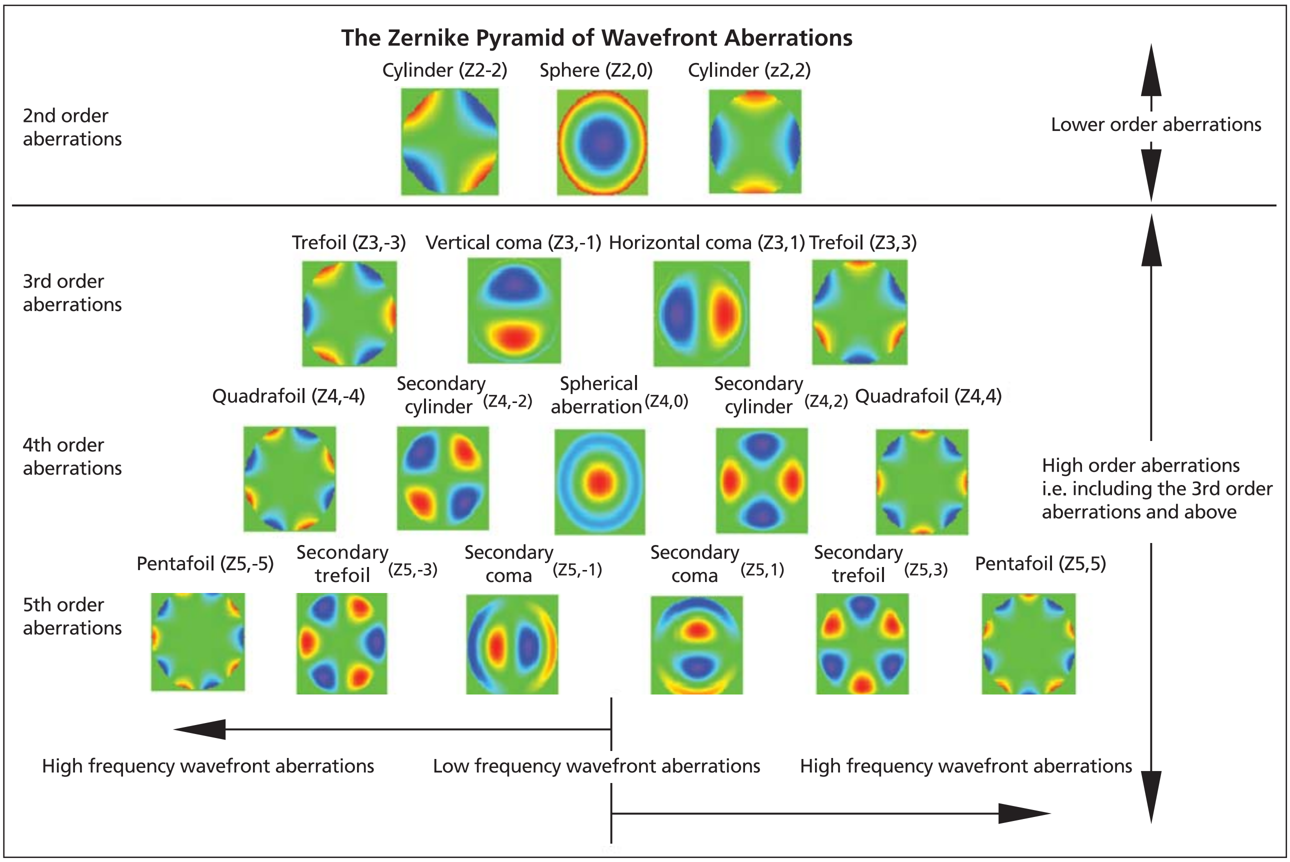


Figure 5 A pictorial representation of the Zernike pyramid from the 2nd up to the 5th radial order only. The red colours here represent positive aberrations, and the blue colours represent negative aberrations.

Higher-Order Aberrations in Keratoconus

In keratoconus, corneal thinning causes marked shape changes which create large amounts of higher-order optical aberration, which differ significantly from the aberrations found in normal eyes.

Challenges in measuring higher-order aberrations in keratoconus

Accurately measuring the higher-order aberrations is more challenging in keratoconic eyes. This is because the cornea is often very distorted and/or scarred in severe disease, leading to gross spot image irregularities at the CCD sensor (Figure 7). The irregularities cause data calculation problems:

1. Some spots will overlap or cross over on to each other; when this occurs the sensor will register only one image instead of two.
2. Some spots will be deviated greatly and will not land on their own corresponding lenslet, but will land on a neighbouring spot's lenslet, causing computational errors.
3. Some spots in the extreme case will even become so deviated that they do not land on the CCD sensor at all, resulting in 'lost' data.

Figure 7 compares the raw Shack–Hartmann images from a normal eye (A) to that of a keratoconic eye (B), as well as depicting how these irregularities arise as the outward light from a keratoconic eye hits the microlenslet array (C). The disruptive effect of keratoconus at the CCD sensor (image plane) is apparent when comparing Figure 4A with Figure 7C.

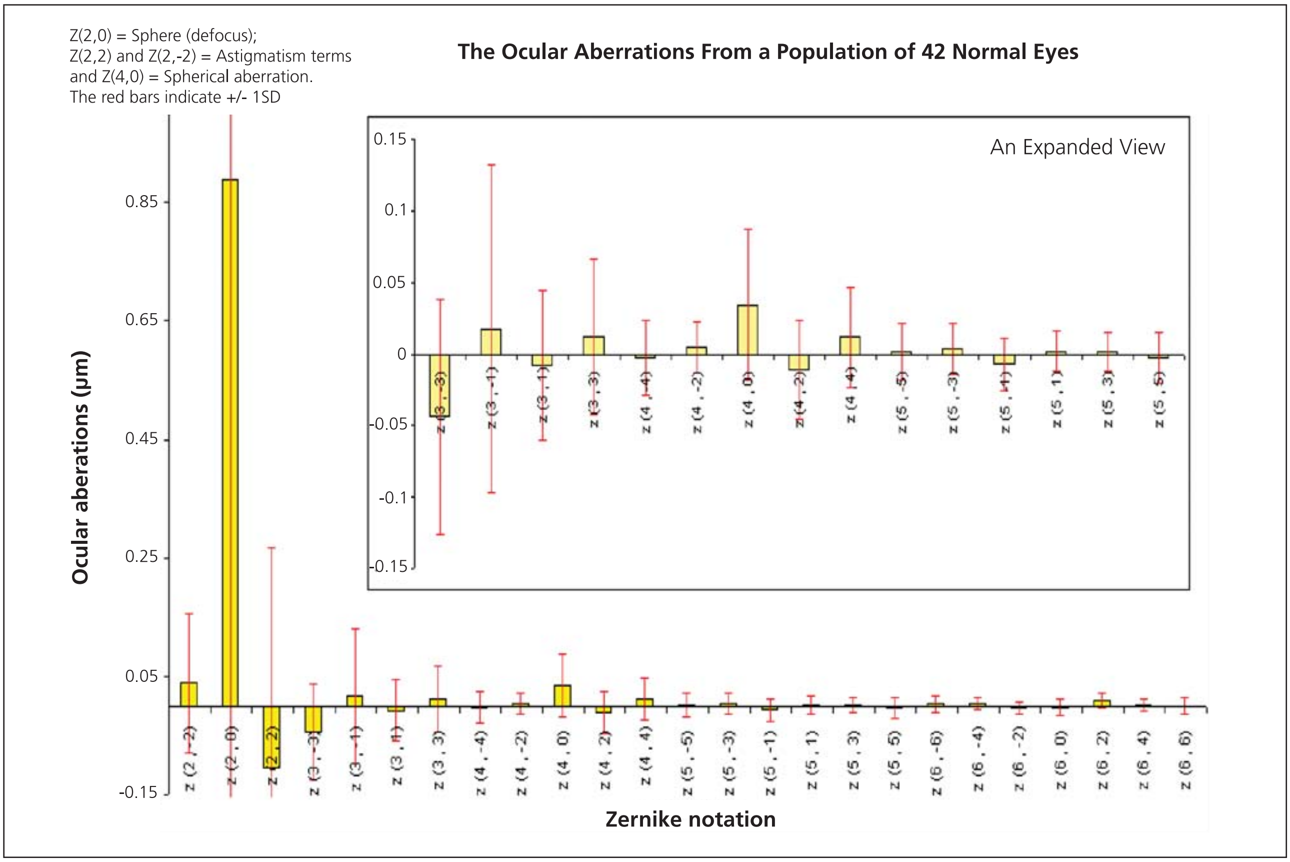


Figure 6 The mean total ocular aberrations from a population of 42 normal eyes for 4.5mm pupil diameter, up to the 6th Zernike order (Radhakrishnan and Charman, 2007). The data show that the majority component of the optical aberrations in normal eyes are from the 2nd-order terms for sphere (Z(2,0)) and cylinder (Z(−2,2)/Z(2,2)). The error bars represent ±1 standard deviation from the mean value. The data in the expanded ordinate exclude 2nd-order terms and show that spherical aberration, Z(4,0), is positively skewed from zero.

Several studies have investigated the use of complicated specialised adaptations to the Shack–Hartmann method in order to improve the accuracy of aberrometry measurements obtained from keratoconic eyes (Lindlein *et al*. 2000, 2001, Pantanelli *et al*. 2007, Pfund *et al*. 1998, Yoon *et al*. 2006). These various techniques have their own advantages and disadvantages. At present no recognised technique exists that allows a Shack–Hartmann aberrometer to overcome all of the difficulties faced when measuring the optical aberrations of highly aberrated, keratoconic eyes.

The studies by Moreno-Barriuso & Navarro (2000) and Moreno-Barriuso *et al*. (2001) compared the LRT method to the Shack–Hartmann method. Briefly, in LRT, parallel pencils of laser rays are sequentially sent into the pupil in a series of steps using multiple sample rays in a hexagonal arrangement. For a given pencil of ray beams, the eye's local aberrations will cause a focal shift of the retinal images with respect to the initial central reference or 'chief' ray. Similar to the Shack–Hartmann method, the retinal image is captured on to an array of photodetectors. The instrument's scanners are then used to move the laser to fire sequentially more pencils into different pupil entry positions, until a spread of aberration measurements is made for the whole of the pupil.

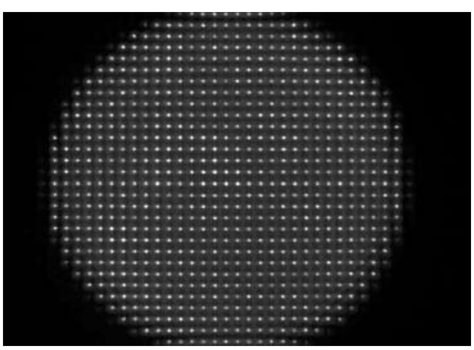
Moreno-Barriuso *et al*.'s (2001) data suggested that the LRT method would be more accurate than the Shack–Hartmann when measuring highly aberrated, keratoconic eyes because it can be programmed for any desired sampling pattern. However the authors make these assumptions about highly aberrated eyes based on measurements taken from two normal subjects only.

Disadvantages of the LRT method include longer acquisition and data computation times; the longer the measurements take, the greater the inaccuracies with respect to time-related factors such as small eye movements, accommodation microfluctuations and laser scanner movement. In general the LRT method has fewer measuring points in comparison to the Shack–Hartmann method, thus reducing precision (Applegate *et al.* 2001, Thibos 2000, Thibos & Hong 1999).

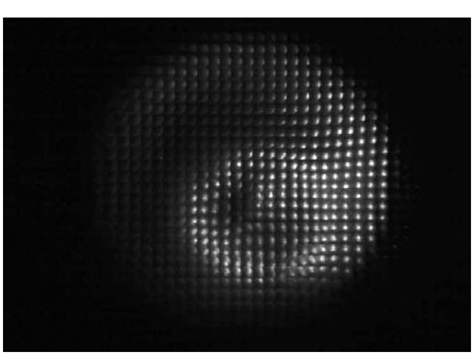
The higher-order aberrations of the keratoconic eye

Vertical coma (*Z* 3,–1) is most commonly found to be elevated in keratoconic eyes (Figure 8) because corneal thinning classically occurs at the inferior temporal position. This means that light waves from a distant source arriving at the keratoconic eye will be distorted by comparatively different amounts at the superior (flatter) and inferior (steeper) cornea. Keratoconic eyes typically show negative vertical coma aberration. The cone will also distort incoming light waves by tilting them, inducing trefoil (or triangular astigmatism), and finally the steepened cone induces spherical aberration (Figures 9 and 10).

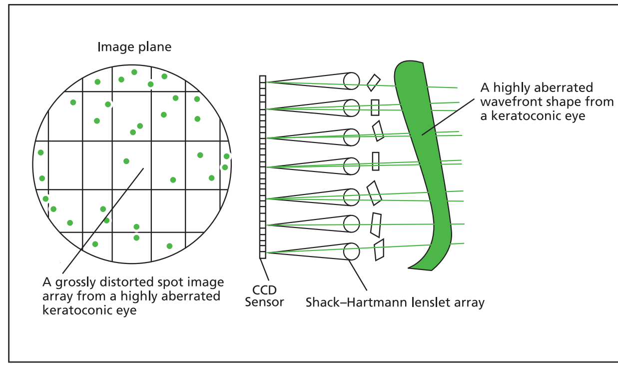
Figure 7 The difficulties in measuring the higher-order aberrations of the keratoconic eye.



(A) A regular series of spots on the raw Shack–Hartmann image from a normal eye.



(B) Gross spot distortion on the raw Shack–Hartmann image from a keratoconic eye.



(C) Light leaving a keratoconic eye results in gross spot distortion in Shack–Hartmann aberrometry.

In Figure 9 the illustrations A and B demonstrate how inferior temporal corneal thinning and steepening of the keratoconic cornea induce higher-order aberrations. The red, green and blue colours depict areas on the cornea that all show different magnitudes of higher-order aberration errors; redder colours represent positive wavefront aberration, whereas bluer colours represent negative wavefront aberration.

Figure 10 shows how a point source (A) becomes affected by coma (B), trefoil (C) and spherical aberration (D), using the point spread function (PSF). The PSF is a complex mathematical function whose image shows the optical quality of the eyes' retinal image. The PSFs in Figure 10 represent the optical distortion of the image of a point source once the light has passed through all the major refractive components of the eye. Each PSF image overall subtends about 50min of arc square.

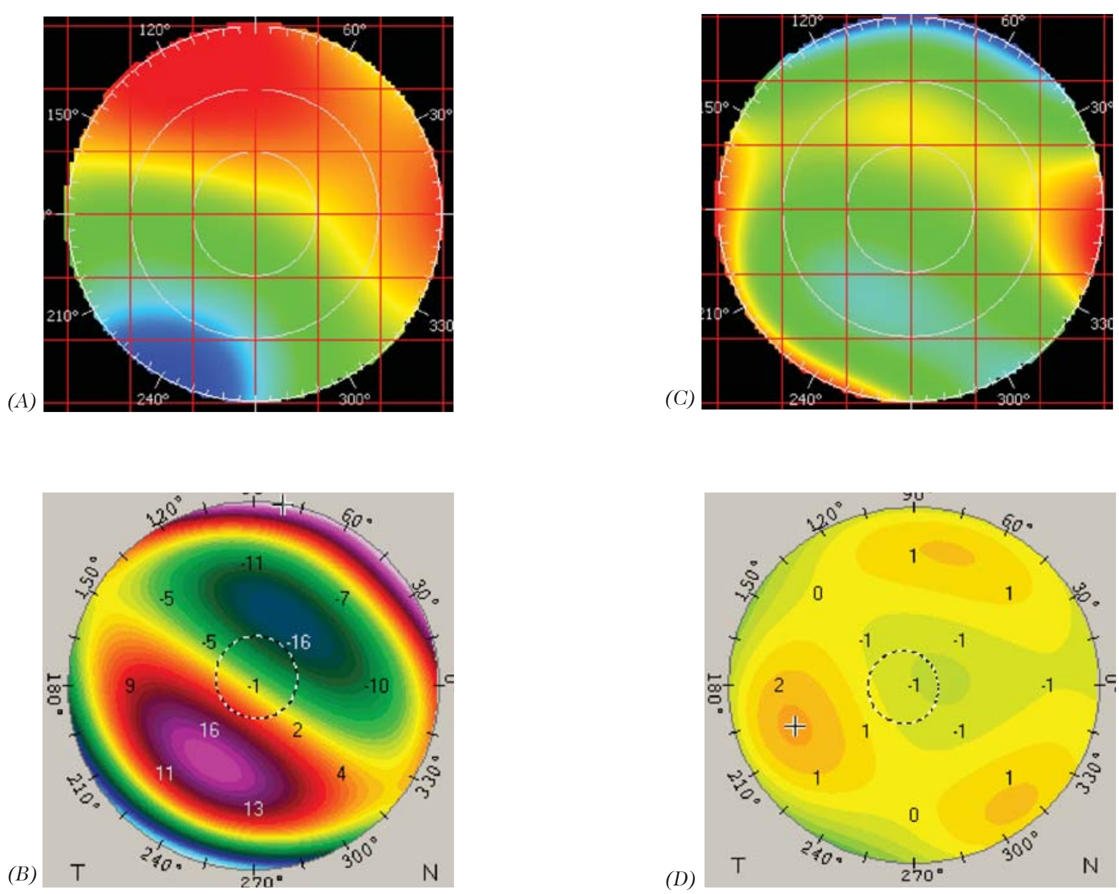
Several groups have measured either corneal or total ocular higher-order aberrations in keratoconic patients and compared them to normal eyes (Table 1). However these results are not always exactly comparable because of the different criteria used in selecting the keratoconic patients.

Table 1 Summary of the findings from four studies comparing the higher-order aberrations seen in normal (N) and keratoconic (KC) eyes. (All values are calculated at a 6mm corneal/pupil diameter).

Measurement statistic	Measurement type	Study	Keratoconic eyes	Normal eyes	Number of eyes
Average 3rd-order RMS error	Corneal	Gobbe and Guillon (2005)	3.10±2.28μm	0.28±0.15μm	870 N, 92 KC
Average 3rd-order RMS error	Corneal	Maeda *et al.* (2002)	1.99μm	0.26μm	38 N, 35 KC
Average 3rd-order RMS error	Total ocular	Maeda *et al.* (2002)	1.83μm	0.25μm	38 N, 35 KC
Average vertical coma	Corneal	Bühren *et al.* (2007)	(−)1.35μm	(−) 0.17μm	127 N, 23 KC

RMS, root mean square

Figure 8 The ocular and corneal higher-order wavefront aberration maps of a moderate keratoconic and normal eye for a fixed 6mm pupil/corneal diameter (all illustrations include a spherocylindrical correction). The vertical coma coefficient in the moderate keratoconic eye was measured at –1.87μm for the ocular aberrations (A) and –2.91μm for the corneal aberrations (B). On these maps the coloured contours join points in the pupil (for ocular aberrations) or in the corneal area (for corneal aberrations) which have the same amount of wavefront aberration. (A) and (B) show a classic vertical difference in coma aberration, which is portrayed by the superior and inferior parts of these two images showing marked differences in contour colours. Such a marked difference in contours is not found in normal eyes (C and D). The redder colours show positive aberrations, the bluer colours show negative aberrations and the yellower colours show neutral aberrations. All measurements were taken from right eyes. (A) The total ocular aberrations of a keratoconic eye; (B) the anterior corneal aberrations of a keratoconic eye; (C) the total ocular aberrations of a normal eye; (D) the anterior corneal aberrations of a normal eye.



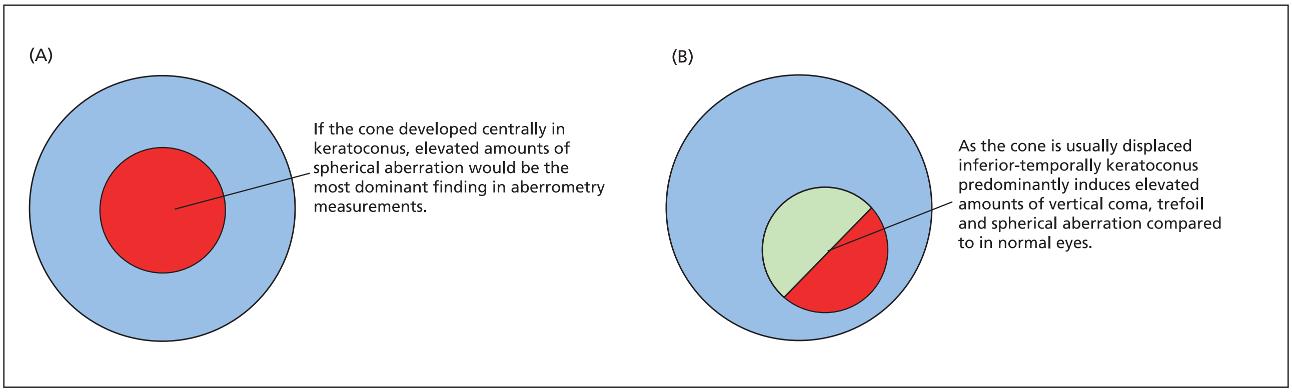
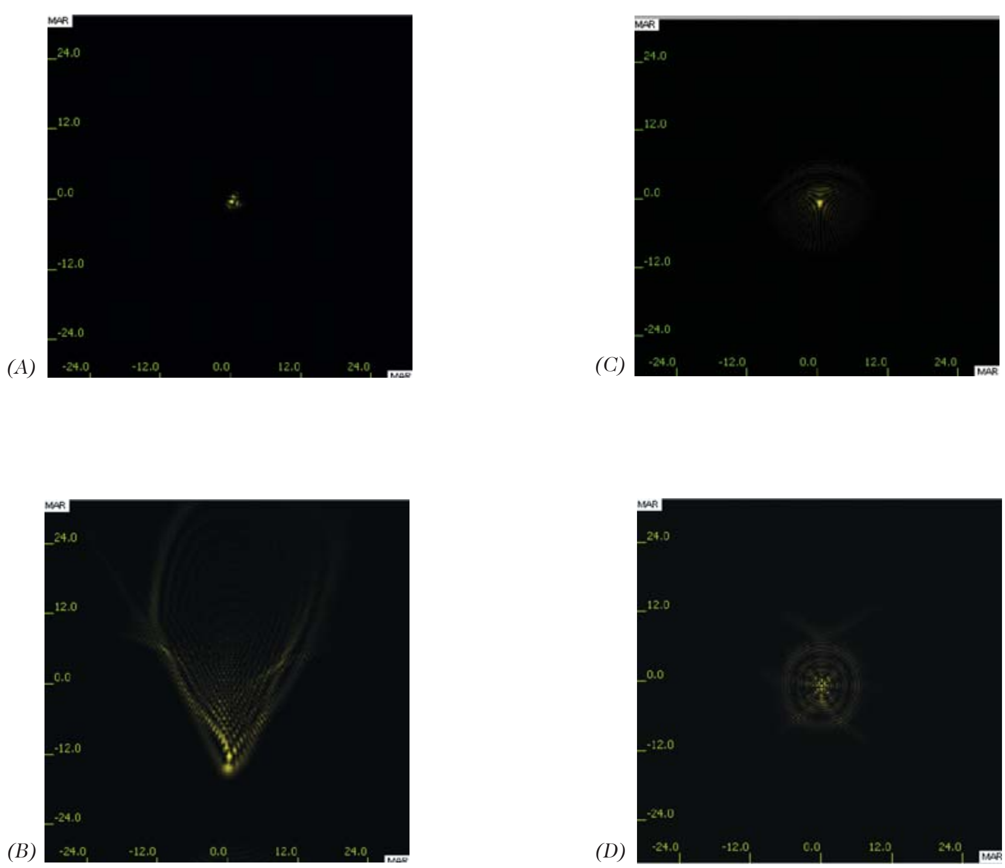


Figure 9 A diagrammatic representation of how keratoconus induces higher-order aberrations.

Figure 10 The images show the point spread functions (PSFs) for a range of optical aberrations in model, moderate and severe keratoconic eyes (5mm pupil diameter). For the purpose of illustrating the effects of coma, trefoil and spherical aberration, all other aberrations affecting the PSF have been excluded in images B, C and D. Each PSF image overall subtends about 50min of arc square. (A) shows the PSF of a model eye showing an almost perfect spot image; (B) shows the PSF from a moderate keratoconic eye showing –1.30μm of vertical coma; (C) shows the PSF from a moderate keratoconic eye with –1.00μm of trefoil (or triangular astigmatism) and (D) shows the PSF from a severe keratoconic eye with +0.47μm of spherical aberration.



Howland *et al*. (1992) first suggested that measuring and assessing the higher-order aberrations derived from corneal topography data may help to distinguish between normal and abnormal corneas. The studies by Schwiegerling *et al*. (1995) and Schwiegerling & Greivenkamp (1996) both derived corneal aberrations by expanding their collected data into Zernike terms from videokeratoscopic measurements made using the Placido-based TMS-1 topographer. Schwiegerling & Greivenkamp found elevated absolute values for the 3rd-order Zernike terms coma and trefoil in 15 keratoconic eyes, compared to 61 normal eyes. The data showed that the average keratoconic values for coma and trefoil were significantly different from normal mean values.

Gobbe & Guillon's (2005) data for corneal aberrations using the Keraton keratoscope (Optikon, Rome, Italy) and CTView software supported Schwiegerling & Greivenkamp's (1996) results. They too found statistically significantly elevated amounts of 3rd-order coma and trefoil in keratoconic eyes compared to normals, as well as elevated spherical aberration. The average total 3rd-order RMS value for a 6mm corneal aperture was 0.28 ± 0.15μm in 870 normal eyes and 3.10 ± 2.28μm in 73 keratoconic eyes. Their results showed that the best differentiator of keratoconus was negative vertical coma, which showed a specificity of 71.9% and a sensitivity of 89.3%. To be deemed 'abnormal' (or forme fruste), the value of vertical coma should be lower than –0.12μm; to be deemed 'keratoconic' the vertical coma value should be lower than –0.30μm.

Unlike in Schwiegerling & Greivenkamp's (1996) study, which was conducted on prediagnosed keratoconic eyes, Gobbe & Guillon were the first to use the aberration values of vertical coma as a diagnostic tool on undiagnosed patients to help detect keratoconus with a high level of sensitivity.

Maeda *et al*. (2002) compared total ocular (from Shack–Hartmann data) and corneal aberrations (from videokeratographic data) measured using the combined Wavefront Analyzer KR-9000 (Topcon, Tokyo, Japan). Both sets of data were measured simultaneously in normal and keratoconic eyes. Maeda *et al*. also found that, compared to normals, keratoconic patients had significantly higher levels of 3rd-order RMS error in both corneal (0.26μm in normals versus 1.99μm in keratoconics) and ocular aberration measurements (0.25μm in normals versus 1.83μm in keratoconics). Maeda *et al*. found good correlation between the anterior corneal aberrations and the total ocular aberrations for keratoconic eyes, and suggested that the anterior surface of the cornea was therefore the major contributor of total eye aberrations in keratoconus. In this study 38 normal eyes were compared to 35 keratoconic eyes; however the keratoconic eyes investigated ranged from 'suspect' (or forme fruste) to 'mild' keratoconus cases only.

Barbero *et al*. (2002) investigated three keratoconic eyes using the LRT method and found that the mean 3rd-order RMS values were 3.74 times larger in keratoconic eyes (2.02 ± 0.41μm) than in 22 normal eyes (0.54 ± 0.30μm). The subjects investigated included two mild and one severe case of keratoconus. Barbero *et al*. used two different pupil sizes (6.51mm for two eyes, and 5.5mm for one eye) when calculating the Zernike polynomials for these keratoconic eyes, meaning that the data for the three eyes should not be directly compared to each other.

In what was deemed to be the clinically normal fellow eye of 10 newly diagnosed keratoconic patients, Bühren *et al*. (2007), using the Orbscan II, found statistically significant elevated levels of vertical coma (–0.300μm; $P < 0.001$), secondary vertical coma (Z 5,–1) (0.037μm; $P < 0.05$) and 3rd-order RMS error (0.476μm; $P < 0.01$), compared to in 127 normal control eyes. Bühren *et al*.'s results supported Gobbe & Guillon's (2005) previous study suggesting that corneal aberration data (as well as corneal height and curvature/shape data) can be useful to help detect forme fruste keratoconus. Bühren *et al*. found that for vertical coma the Orbscan gave a cut-off value of –0.20μm (or less) in order to be deemed 'abnormal' (or forme fruste). Bühren *et al*. showed that 23 mild keratoconic eyes had an average vertical coma value of –1.35μm compared to –0.17μm from 127 normal eyes.

In summary, Schwiegerling & Greivenkamp (1996), Gobbe & Guillon (2005), Barbero *et al*. (2002), Maeda *et al*. (2002) and Bühren *et al*. (2007) all found increased higher-order aberrations in keratoconic corneas, suggesting that these eyes will have a poorer retinal image than a normal eye, leading to reduced visual acuity.

Correcting Higher-Order Aberrations in Keratoconus

The visual benefit of correcting the higher-order aberrations

Several studies have investigated the visual benefit of correcting higher-order aberrations using adaptive optics in both normal and abnormal eyes (Bara *et al*. 2000, Jeong & Yoon 2006, Liang *et al*. 1997, Navarro *et al*. 2000, Sabesan *et al*. 2007a, Williams *et al*. 2000, 2001, Yoon *et al*. 2004, Yoon & Williams 2002). Adaptive optics include both deformable mirrors and liquid crystal phase plates; these are complex laboratory-based optical devices that can be accurately manipulated by bending the light at each point in the pupil plane in just the right way to correct wavefront aberrations with high levels of precision.

Williams *et al.* (2000) report considerable improvements in visual performance in four keratoconic eyes: however the authors do not state the severity classifications of their keratoconic patients. In Sabesan *et al.*'s (2007a) study, a deformable mirror was used to reduce the total RMS error from 2.73 ± 1.75μm to 0.10 ± 0.001μm for a moderate keratoconic eye.

Yoon & Williams (2002) compared the effects of monochromatic and chromatic aberration correction using a deformable mirror for 17 normal subjects. They discovered better visual performances when higher-order monochromatic aberrations were corrected in white light, compared with chromatic aberration correction alone. They hypothesised that correcting both chromatic and monochromatic aberrations will give the optimal visual performance; at present no optical device allows such corrections to be made.

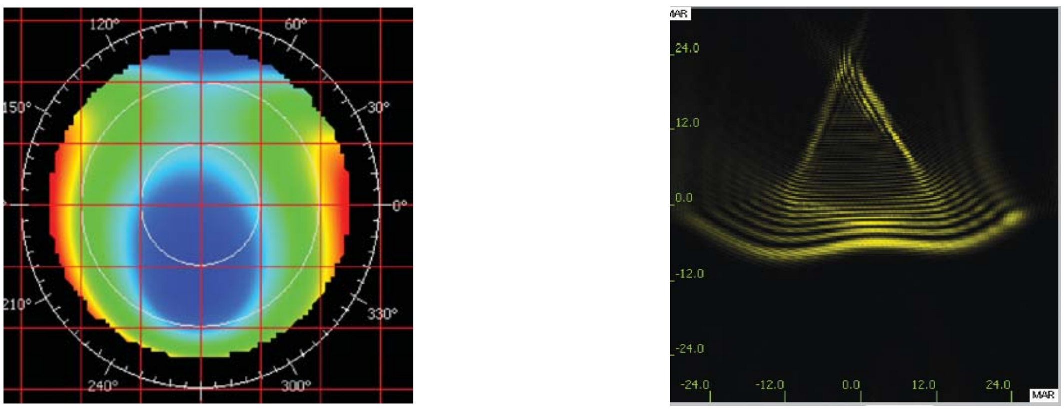
Correcting higher-order aberrations in keratoconus

The options that have been used to correct the higher-order aberrations found in keratoconic eyes include adaptive optics, customised contact lenses, rigid gas-permeable (RGP) contact lenses and aberration-controlling soft contact lenses. In the literature reviewed, conventional soft contact lenses do not appear to be as popular a method of correcting higher-order aberrations in keratoconic eyes. This is perhaps because they do not correct the keratoconic cornea as effectively as RGP lenses (Zadnik & Mutti 1987). Also, unlike aberration-controlling soft lenses or adaptive optics, studies have shown that conventional soft contact lenses are poorer at correcting higher-order aberrations (De Brabander *et al.* 2003, Hong *et al.* 2001, Marsack *et al.* 2007a, Sabesan *et al.* 2007b, Yoon *et al.* 2004).

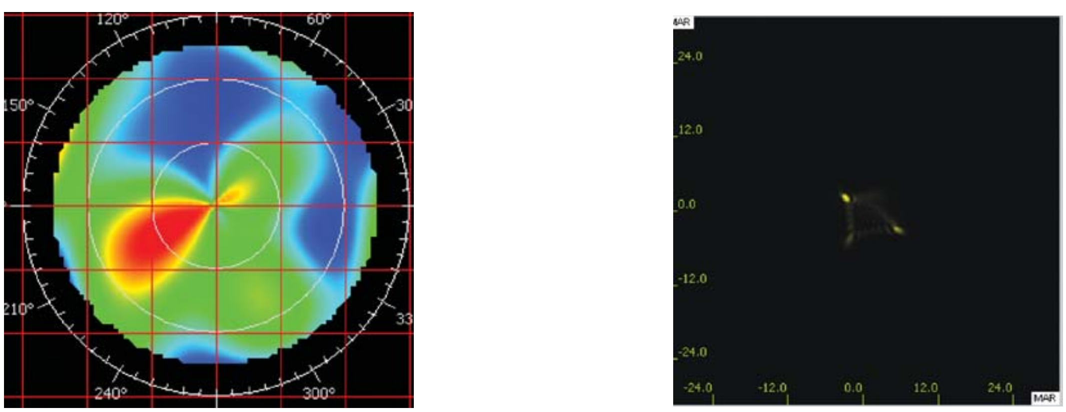
Adaptive optics systems are, at the present time, essentially laboratory devices which are not designed to meet the daily needs of patients. A more suitable device to correct higher-order aberration would be the customised contact lens, which is discreet, simple to use and relatively inexpensive to manufacture compared to adaptive optics. The ideal lens would have its local thickness modified so that it introduces variations in optical path which are opposite in sign to the wavefront aberration of the individual eye. This idea for aberration correction was first proposed by Smirnov (1962), who suggested: 'in principle it is possible to manufacture a lens compensating for the wave aberrations of the eye'. Aware of the fact that a spectacle lens will not conjugately follow the movements of the eye, Smirnov explains that 'these lenses must obviously be contact ones'. The major problem of using such customised contact lens corrections is that any rotation or translation of the lens on the eye causes a loss of correction of the wavefront aberration.

At present, the most common method of correcting vision in keratoconic patients is via non-customised, conventional RGP contact lenses (Kapur *et al.* 2003, Szczotka *et al.* 2001, Weed *et al.* 2007, Zadnik *et al.* 1998). Although such lenses may translate and rotate, several studies have shown that RGP lenses will reduce many of the higher-order aberrations found in keratoconic eyes (Kosaki *et al.* 2007, Marsack *et al.* 2007b, Negishi *et al.* 2007, Radhakrishnan & O'Donnell 2008). Figure 11 shows the higher-order aberrations of a moderate keratoconic right eye with and without a keratoconic RGP lens (Dyna Z Cone, Boston XO, base curve 7.00mm, diameter 9.00mm, power –1.50D, Bausch & Lomb, NY, USA) in situ at a 5mm pupil diameter. The lens helped to reduce the eye's most dominant aberration, vertical coma, from –1.22μm (Figure 11A) to –0.64μm (Figure 11B). The dark blue area in the lower part of the aberration map in Figure 11A corresponds to the large magnitude of uncorrected negative vertical coma; this dark blue area is essentially 'smoothed over' by the RGP lens and is less pronounced in Figure 11B.

Figure 11 Comparisons of the higher-order ocular wavefront aberration maps and point spread functions (PSFs) with and without a rigid gas-permeable (RGP) lens (Dyna Z Cone, Boston XO, base curve 7.00mm, diameter 9.00mm, power –1.50D, Bausch and Lomb, NY, USA) in situ for a moderate keratoconic right eye at a 5mm pupil diameter. The redder colours show positive aberrations, the bluer colours show negative aberrations and the yellower colours show neutral aberrations (all illustrations include a spherocylindrical correction). Each PSF image overall subtends about 50min of arc square.



(A) The higher-order ocular wavefront aberration map (left) before fitting an RGP lens to a keratoconic right eye. The resulting PSF shows a reduced optical quality (right). The most dominant aberration vertical coma (–1.22µm) is depicted by the dark blue area in the lower part of the aberration map.



(B) The higher-order ocular wavefront aberration map (left) of the higher-order ocular aberrations of a keratoconic right eye with the RGP lens in situ. The RGP lens helped to reduce the eye's higher-order aberrations, leading to a sharper and crisper PSF and better optical quality (right). Vertical coma with the RGP lens was measured at –0.64µm.

Challenges in correcting higher-order aberrations with soft aberration-controlling contact lenses in keratoconus

A more stable alternative to an RGP lens would be a soft lens, which moves much less in comparison (Tomlinson *et al.* 1994). The use of computer packages has allowed researchers to predict the visual outcome (and decentration effects) of an 'ideal' aberration-correcting (or customised) soft contact lens on-eye (De Brabander *et al.* 2003, Guirao *et al.* 2001, 2002). Guirao *et al.* (2001) carried out simulations of on-eye customised soft contact lens decentrations for 10 normal eyes and investigated their corrective effects on the measured wavefront aberrations. The decentrations found were a combination of rotation and translation (vertical or lateral displacement), just as in normal soft contact lens wear (Tomlinson *et al.* 1994). Guirao *et al.* (2001) explain that a contact lens purely correcting spherical aberration only will induce coma-like aberrations when it translates on the eye. Guirao *et al.* showed that the effect of decentration was different for each particular aberration term corrected, and that the benefits yielded were reduced as the decentrations increased in magnitude. Guirao *et al.* (2002) hypothesised that perhaps not all aberrations are therefore worth correcting, as some coefficient terms will be particularly sensitive to decentrations, thus inducing more aberration than actually correcting; potentially this may cause a loss in visual performance in an extreme case of on-eye lens decentration.

De Brabander *et al*. (2003) simulated the visual performance of nine moderate keratoconic eyes, and found that large improvements in retinal image contrast were possible with the perfect alignment of a custom lens. De Brabander *et al*., like Guirao *et al*. (2001), computed that decentrations of a custom lens led to partial loss of the visual benefit gained. Nevertheless De Brabander *et al*. showed that rotations up to a maximum of 5° and decentrations to a maximum of 1mm on blinking would be permissible to yield a visual benefit from a customised lens in moderate keratoconic eyes. How much tolerance is possible for mild or severe keratoconic eyes remained unexplored in this paper.

Most clinical research in this field has concentrated on attempting to make aberration-controlling contact lenses. However, some of the early work looked at aberration-generating contact lenses, comparing the aberrations measured with and without the contact lenses, as well as comparing in vivo and in vitro lens aberration measurements (López-Gil *et al*. 1998, 2002). The data from López-Gil *et al*.'s (2002) study suggested that the inducement of aberrations was possible with contact lenses, meaning that the converse situation of correcting aberrations with contact lenses was plausible. López-Gil *et al*. (2003) trialled lathe-cut, front surface aberration-controlling soft contact lenses, which were made for normal, postpenetrating keratoplasty and keratoconic eyes. Their results showed no statistically significant difference in visual acuity or contrast sensitivity between with the customised lenses and with spectacles in either the postpenetrating keratoplasty or normal groups. López-Gil *et al*. reported that keratoconic eyes achieved better visual acuity and contrast sensitivity with the custom lenses than with spectacles; however, the authors did not indicate if these differences were significant.

Jeong & Yoon (2006) used the Hartmann–Shack method to make a front-surface, customised, aberration-controlling soft lens for an advanced keratoconic subject. In this study the authors accounted for on-eye lens decentration by fitting a –1.50DS conventional soft contact lens of a fixed base curve (the value was not disclosed) and monitoring its centration on the pupil camera of their aberrometer. The final customised soft lens in this study had the same base curve as this –1.50DS trial lens. The aberrations were then transferred on to the customised lens accounting for the decentration that had occurred with the trial lens in situ. The customised lens successfully reduced the eye's higher-order RMS error from 3.89 to 1.28μm. The lens gave the patient a subjective improvement in vision; however the authors did not measure the visual acuity for this patient. Jeong & Yoon (2006) found that some Zernike coefficient terms showed small residual errors even with the customised lens in situ. The authors suggested that tear film changes, accommodation microfluctuations or small eye movements could all possibly induce these unwanted residual higher-order aberrations. Also in this study the authors monitored the customised lens movements on the eye, finding that typical vertical translations and small rotations occurred with blinks. The authors stated that decentrations of the customised lens could also have contributed to the residual error found.

Sabesan *et al*. (2007b) used the Hartmann–Shack method to carry out a comparison study for three keratoconic eyes (two severe and one moderate case) using front-surface, customised, soft lenses versus conventional soft and RGP lenses. The authors accounted for decentration by trialling three different base curves, and assessed their fitting to see which was the most stable for each eye, before manufacturing their customised soft lenses. In the most successful case the total RMS error was only reduced from an uncorrected 3.97μm to 3.28μm with a conventional lens; but with the customised lens this was significantly lowered to 0.97μm. The customised soft lenses gave improved visual performances at the lower contrast acuities (20%), compared to conventional soft lenses, by an average of 2.1 lines of logMAR acuity. For one subject the customised lens gave three lines of low-contrast logMAR acuity improvement, compared to their habitual RGP lens. The authors explain that these significant improvements in low contrast acuity could be due to the differences in magnitude of any residual spherical aberration, with the different lens types in place. Their rationale for this is that spherical aberration has a high impact on visual performance (Applegate *et al*. 2002, 2003). For high contrast acuity (100%) there was very little difference between the subject's own habitual RGP lens and the soft custom lens: the custom lens still performed the best, however. Finally, like Jeong & Yoon (2006), Sabesan *et al*. also noted that some small residual errors persisted even with the aberration-correcting custom contact lenses in situ.

Marsack *et al*. (2007a) manufactured a front-surface custom aberration-controlling soft lens using Shack–Hartmann data for a moderate keratoconic and compared this to the patient's habitual conventional soft lens. The results showed that both high and low contrast acuity were improved with the customised lens compared with the habitual lens. However, in contrast to Sabesan *et al*. (2007b), Marsack *et al*. found that the high-contrast acuity was improved more (by 1.5 lines; $P = 0.03$) than the low-contrast acuity (by one line of letters; $P = 0.11$). Marsack *et al*. noted that the habitual lens translated on the eye with blinks, but did not incorporate this into their lens design for the final custom lens. Nevertheless, the lens designed by Marsack *et al*. reduced the higher-order RMS error by 50%, suggesting that the lens was successful.

Chen *et al*. (2007) experimented with a method of enhancing the lens fit by custom designing the back surface of the lens (using the Orbscan II) in an attempt to reduce the residual higher-order aberration errors due to decentration. They found that the stability of their back-surface, aberration-controlling soft lenses was better than that of conventional lenses. These lenses reduced horizontal and vertical decentration by a factor of two and reduced rotation by a factor of five. The customised lenses helped to reduce the higher-order RMS error for two of the moderate keratoconic subjects investigated. For one subject the higher-order RMS error was reduced from 1.17 ± 0.04 to 0.61 ± 0.04μm and for another from 1.66 ± 0.06 to 1.30 ± 0.1μm. Chen *et al*. found, as with previous studies by Jeong & Yoon (2006) and Sabesan *et al*. (2007b), that some residual higher-order aberrations still persisted even with their aberration-controlling lenses in situ. Chen *et al*. measured both anterior and posterior corneal aberrations using the Orbscan II; from these data they performed calculations to model the internal optics of their subjects. Their results suggested that the internal optics (the posterior corneal surface and the crystalline lens) were largely responsible for the residual aberrations measured with the customised lenses.

Marsack *et al*. (2008) compared the visual performance and higher-order RMS error correction achieved using customised wavefront-guided soft contact lenses versus the subject's own habitual RGP lenses. The authors made customised lenses for three keratoconic eyes (two moderate and one severe) and found that all three customised lenses gave a better visual acuity than with the RGP lenses. For the subject with severe keratoconus, the habitual RGP lens gave a high-contrast logMAR visual acuity of 0.04 ± 0.09, whereas the customised lens gave –0.05 ± 0.05. For this same subject, the average higher-order RMS error was reduced from an uncorrected value of 1.57 ± 0.027 to 0.76 ± 0.033μm with the customised lens, and down to 0.50 ± 0.15μm by the habitual RGP lens. For one subject with moderate keratoconus the uncorrected higher-order RMS error was reduced from an uncorrected value of 0.61 ± 0.018 to 0.39 ± 0.018μm using their habitual RGP lens, and to 0.38 ± 0.074μm with the customised lens. The high-contrast logMAR visual acuity for this same subject was 0.20 ± 0.02 with the RGP lens and 0.14 ± 0.02 with the customised lens in situ. These two cases help to demonstrate that customised soft contact lenses have the potential to give comparable results to RGP lenses in terms of high-contrast visual acuity performance and higher-order RMS error correction.

It is evident from the literature reviewed that soft contact lenses can be used to correct higher-order aberrations via wavefront customisation. This seems to have been successful in previous studies. Nevertheless, soft lenses will suffer from particular disadvantages that will limit the potential visual benefit from being a 100% success (Thibos *et al*. 2003b). These include:

- Contact lens dehydration
- Lens flexure
- Decentration (rotation and/or translation) of the aberration-controlling lens inducing unwanted higher-order aberrations
- Errors in the manufacturing process of transferring the required aberration correction on to the lens
- Light scattering from the lens material at the areas where the lens will be customised
- The tear film inducing unwanted higher-order aberrations (Montés-Micó *et al*. 2004)
- Changes in higher-order aberrations due to disease progression or ageing mean that the aberration-controlling lenses will need upgrading from time to time
- Poor lens handling (ie damage during cleaning)

Summary

In normal eyes there are some drawbacks to correcting higher-order aberrations, including the fact that the eye is a dynamic optical and biological system, and as a consequence the optical aberrations measured and corrected one day may not yield the same level of visual improvement on another day (Cheng *et al*. 2004). Several studies also report that variability in aberration measurements can come from accommodation fluctuations, tear film fluctuations, small eye movements and pupil size changes (Cheng *et al*. 2003, Liang &

Williams 1997, Mirshahi *et al*. 2003). Put more simply, aberration correction in normal eyes equates to attempting to correct a small fluctuating value. Despite the drawbacks for normal eyes, the use of contact lenses to correct higher-order aberrations could still be very useful at improving the visual performance in keratoconic eyes, due to the large magnitudes of optical aberration found in these patients. Research into the feasibility of aberration-controlling contact lenses for keratoconic eyes is ongoing.

However, as described in the previous section, at present these customised lenses are found to correct only partially the higher-order aberrations found in keratoconic eyes.

This paper describes the challenges in measuring and correcting the optical aberrations in keratoconic eyes, and reviews what has been learned from studies investigating the use of aberration-controlling contact lenses in keratoconus. At present the idea of aberration-controlling contact lenses is plausible. If contact lens designers can manufacture customised lenses with accuracy and good movement stability, then aberration-controlling contact lenses could possibly prove to be a very useful tool for those involved in managing keratoconic patients.

Acknowledgements

Amit Jinabhai's PhD is funded by the College of Optometrists. We would also like to thank Julie Anne Theobalds for proof-reading the article.

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Multiple Choice Questions

This paper is reference C-12272. Three points are available for optometrists and contact lens opticians. Please use the inserted answer sheet. Copies can be obtained from Optometry in Practice Administration, PO Box 6, Skelmersdale, Lancashire WN8 9FW. There is only one correct answer for each question.

1. Which of the following higher-order Zernike aberration terms has been found to be most commonly elevated in keratoconic eyes, compared to in normal eyes?
(a) Pentafoil
(b) Quadrafoil
(c) Vertical coma
(d) Secondary trefoil

2. What is the most common type of aberrometer used to measure total ocular aberrations in clinical research and in the field of laser vision correction?
(a) The laser ray tracing (LRT) method
(b) The Tscherning aberrometer
(c) The Shack–Hartmann method
(d) Scheimpflug photography

3. Which authors were the first to use their corneal aberration values as a diagnostic tool on undiagnosed patients to help detect keratoconus with a high level of sensitivity?
(a) Gobbe & Guillon (2005)
(b) Schwiegerling & Greivenkamp (1996)
(c) Kosaki *et al.* (2007)
(d) Thibos & Hong (1999)

4. In the Shack–Hartmann experimental set-up the light in the pupil plane emerging from the retina outwards is focused on to the CCD sensor using which type of lenses?
(a) Orthogonal lenses
(b) Shack–Hartmann lenslets
(c) Astigmatic lenses
(d) Contact lenses

5. In the normal population, which Zernike aberration term is positively skewed from zero?
(a) Vertical coma
(b) Pentafoil
(c) Quadrafoil
(d) Spherical aberration

6. Which of the following statements is false?
(a) Any undercorrected sphere and/or cylinder will drastically reduce (if not cancel out) any visual benefits gained by correcting the comparatively smaller coma or spherical aberration terms
(b) Changes in higher-order aberrations due to disease progression or ageing mean that the aberration-controlling lenses will need upgrading from time to time
(c) Decentration (rotation and/or translation) of the aberration-controlling lenses could induce unwanted higher-order aberrations reducing the potential visual benefit
(d) RGP lenses do not help to reduce the higher-order aberrations of the keratoconic eye

7. Which authors found a good correlation between the anterior corneal aberrations and the total ocular aberrations for keratoconic eyes, and suggested that the anterior surface of the cornea was therefore the major contributor of the total eye aberrations in keratoconus?
(a) Chen *et al.* (2007)
(b) Kosaki *et al.* (2007)
(c) Maeda *et al.* (2002)
(d) Hong *et al.* (2001)

8. Which of the following instruments cannot be used for measuring corneal aberrations?
(a) The Pentacam
(b) The corneal aesthesiometer
(c) The Orbscan II
(d) The TMS-1

9. Which of the following is the collective quantitative term which represents the distortion of a wavefront that is given by all aberrometers?
(a) RMS error
(b) PSF
(c) CCD
(d) TMS-1

10. In keratoconus the cone is classically displaced in which position?
(a) Superiorly to the line of sight
(b) Inferior-temporally to the line of sight
(c) Nasally to the line of sight
(d) Temporally to the line of sight

11. Wavefront aberrations are normally measured in units of which size?
(a) Micrometers
(b) Picometres
(c) Millimetres
(d) Nanometres

12. A 'wavefront' can be described as a surface over which an optical disturbance leaves its source; the surface will essentially connect all the different points on the propagating light wave, which have an equal …
(a) Frequency
(b) Intensity
(c) Duration
(d) Phase

13. In keratoconic eyes the fundamental problem lies in actually measuring the optical aberrations present using aberrometry. Which of the following problems leads to gross spot image irregularities at the CCD sensor?
(a) The cornea can often be very dry
(b) The cornea can often be very soft
(c) The cornea can often be very distorted and/or scarred
(d) The cornea can often be thickened

14. Which of the following statements regarding root mean square wavefront error (RMS error) is incorrect?
(a) The higher-order RMS error is the vector sum of all the Zernike terms from the 3rd order and above
(b) The RMS error does not give information about the shape of the aberrant wavefront itself
(c) The RMS error is directly linked to the retinal image quality of the eye under investigation
(d) RMS error increases as pupil size increases

15. Kosaki *et al*. (2007) found that, in keratoconic eyes, the average axis of 3rd-order trefoil aberration differed compared to the average axis found in normal eyes. By how many degrees did these average values differ in this study?
(a) 39.1
(b) 49.8
(c) 58.4
(d) 69.3