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Customised aberration-controlling corrections for keratoconic patients using contact lenses

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Technological advancements in the design of soft and scleral contact lenses have led to the development of customised, aberration-controlling corrections for patients with keratoconus. As the number of contact lens manufacturers producing wavefront-guided corrections continues to expand, clinical interest in this customisable technology is also increasing among both patients and practitioners. This review outlines key issues surrounding the measurement of ocular aberrations for patients with keratoconus, with a particular focus on the possible factors affecting the repeatability of Hartmann-Shack aberrometry measurements. This review also discusses and compares the relative successes of studies investigating the design and fitting of soft and scleral customised contact lenses for patients with keratoconus. A series of key limitations that should be considered before designing customised contact lens corrections is also described. Despite the challenges of producing and fitting customised lenses, improvements in visual performance and comfortable wearing times, as provided by these lenses, could help to reduce the rate of keratoplasty in keratoconic patients, thereby significantly reducing clinical issues related to corneal graft surgery. Furthermore, enhancements in optical correction, provided by customised lenses, could lead to increased independence, particularly among young adult keratoconic patients, therefore leading to improvements in quality of life.

Key words: aberration-controlling lenses, customised scleral lenses, customised soft lenses, higher-order aberrations, keratoconus, vertical coma

Keratoconus is an ectatic disease of the cornea, typically characterised by stromal tissue thinning causing the cornea to take on a steepened, conical shape. Such alterations occur due to significant changes in the biomechanical properties of the cornea, resulting in the stromal lamellar matrix no longer following a highly regularised, orthogonal pattern. Instead, there are distinct areas of poorly aligned collagen intermixed with collagen that is arranged in the conventional quasiregular fashion. Subsequently, the keratoconic corneal shape becomes more easily distorted and typically shows a high degree of protrusion. The keratoconic cornea can also develop apical scarring, which may typically be attributed to rigid corneal contact lens wear and/or disease progression over time. As the retina usually remains unaffected in keratoconus, the reduced visual performance found, compared to normal eyes, is directly attributable to a combination of irregular astigmatism, higher-order aberrations (HOAs) and, where present, corneal scarring, which induces unwanted light scatter.

Although keratoconus is most usually bilateral, inter-ocular asymmetry is common, with Nichols et al. reporting that the degree of asymmetry is usually largest in patients with more advanced disease. Unlike other ectatic conditions, such as pellucid marginal corneal degeneration, keratoconus characteristically affects the inferior-central two-thirds of the cornea; however, reports of centrally, inferiorly, inferior-nasally and superiorly positioned cone apices have also been published. Other studies indicate that the cone apex is most commonly displaced inferior-temporally in keratoconus. Overall, the nature and exact location of the corneal steepening is unique for each keratoconic eye.

Alterations in the profile of the keratoconic cornea (Figure 1) induce large magnitudes of HOAs which differ significantly from those measured in healthy eyes. Vertical coma (Z (3,-1)) is most commonly found to be significantly elevated in keratoconic eyes, as the maximal stromal thinning classically occurs at either the inferior or inferior-temporal position. Light waves arriving at the keratoconic eye, from a distant source, will be distorted by comparatively differing amounts at the (flatter) superior and (steeper) inferior cornea. The keratoconic cone apex also distorts incoming light waves by ‘rotating’ them, thereby inducing trefoil (or triangular astigmatic) aberrations. Furthermore, the steepened cone also induces spherical aberration. These notable differences in HOA terms, compared to normal eyes, have supported the use of aberrometry measurements as a useful tool to detect subclinical keratoconus as well as to grade its severity.

Despite these uses, a debatable issue, in relation to the measurement of HOAs in keratoconic patients, is their repeatability, particularly when compared to repeated aberration measurements made in normal
eyes. Using a Scheimpflug-based topographer, both Shankar et al.\textsuperscript{29} and Sideroudi et al.\textsuperscript{31} have previously reported poor repeatability of anterior and posterior corneal surface aberrations, respectively. This finding was further supported by Jinabhai et al.,\textsuperscript{32} who reported poor repeatability of ocular HOA measurements made using the Hartmann-Shack technique. In contrast, Bayhan et al.\textsuperscript{33} reported comparable levels of intra-examiner repeatability between anterior corneal aberrations measured in 41 keratoconic eyes and 31 normal eyes using a combined Scheimpflug-Placido topographer. However, the authors’ data indicate that the repeatability of their posterior corneal aberration measurements was comparatively poorer in the same group of keratoconic patients. Interestingly, Ortiz-Toquero et al.\textsuperscript{34} have reported that anterior corneal HOA measurements, made using a Placido-based topographer, were actually more repeatable in 36 keratoconic eyes than measurements made in 36 normal eyes. Correspondingly, Shetty et al.\textsuperscript{35} suggested that using a programmable, liquid-crystal-on-silicon phase modulating adaptive optics set-up, to evaluate ocular HOAs, yielded a high intra-session repeatability for eyes with mild to moderate keratoconus.

As the broad aim of this review is to consider HOA measurements with respect to their potential optical correction, discussion of the issues surrounding the measurement of ocular aberrations would be of greater importance than just anterior corneal surface aberrations alone. This is due to the fact that the eye’s internal optics (the posterior corneal surface and the crystalline lens) are known to partly compensate for the aberrations of the anterior cornea in both normal\textsuperscript{36,37} and keratoconic eyes\textsuperscript{19,22,38,39} In fact, Chen and Yoon\textsuperscript{38} proposed that in keratoconus, some level of compensation exists between the coma root-mean-square (RMS) error aberrations of the anterior and posterior corneal surfaces. Their results indicated that the level of compensation seemed to vary with the severity of disease; on average 22, 24 and 14 per cent of the anterior surface’s coma RMS error
aberrations were compensated for by the posterior surface in severe, moderate and mild keratoconic eyes, respectively. In contrast, no such compensatory effects for coma RMS error were found in their normal subjects.

The majority of the studies that have explored the correction of ocular HOAs in keratoconic patients, using either soft, rigid corneal or rigid scleral contact lenses, have used the Hartmann-Shack principle to measure their patient’s aberrations, whereas comparatively fewer studies have used either skiascopic methods or the laser ray-tracing method.

Due to its comparative popularity, some key contributors that are likely to impact on the repeatability of ocular aberration measurements made using the Hartmann-Shack technique, in keratoconic patients, include:

- spot-imaging errors at the wavefront sensor
- computational limitations
- small (fixational) eye movements during measurements
- changes in aberrations due to microfluctuations in accommodation and/or changes in the tear film during measurements.

### Spot-imaging issues

For the Hartmann-Shack technique, the aberrated wavefront emerging from the eye is relayed onto a micro-lenslet array (Figure 2, lower image) thereby generating a pattern of multiple spot images, which is then analysed by computerised software. By measuring the displacement of the spot image, with respect to a fixed ‘reference’ point (Figure 3), the software then attempts to reconstruct the original aberrated wavefront falling onto the lenslet array (Figure 4, lower image).

When attempting to evaluate the optical quality of the keratoconic eye using the Hartmann-Shack technique, the fundamental problem lies in acquiring the spot images at the wavefront sensor, as the cornea may often be very distorted or even scarred (particularly in severe cases of keratoconus). The measurement performance of the wavefront sensor directly depends on how accurately the centre of each spot can be detected by the sensor’s centroiding algorithm. In general, data derived from a Hartmann-Shack sensor does not consider the ‘optical quality’ of the individual spots formed by the lenslet array.
Only the degree of their ‘displacement’ is needed to compute the local wavefront slope over each lenslet aperture (Figure 3). However, it is important to note that the optical quality of these spot images can vary greatly between normal and keratoconic eyes.\textsuperscript{62,63}

A fundamental limitation of the Hartmann–Shack sensor is the requirement that each spot image, generated by any given micro-lenslet, must land within the ‘virtual sub-aperture’ of a certain photon detector at the charge-coupled device (CCD). To this end, the ‘dynamic range’ of a Hartmann–Shack aberrometer is somewhat restricted by the diameter of each individual micro-lenslet, which typically ranges somewhere between 0.3 to 0.5 mm,\textsuperscript{64} but can be as large as 0.75 mm.\textsuperscript{65}

The computerised software typically used in commercially available Hartmann-Shack aberrometers is not usually capable of correctly identifying the following spot image registration issues:\textsuperscript{56,61,66}

- when two (or more) separate spot images are formed at the same CCD photon detector sub-aperture (Figure 5A)
- a spot image which perfectly overlaps with another, formed by an adjacent micro-lenslet (Figure 5B)
- a spot image that ‘crosses over’ the allocated path of another spot (Figure 5C)
- missing spot images – when one or more spot images are formed in an area that falls entirely outside of the CCD sensor (Figure 5D).

While a ‘displaced’ spot image is obviously aberrant from the ‘chief’ or ‘reference’ ray, the magnitude of this displacement provides no indication of the image’s quality. On the other hand, a blurry spot image may actually contain more aberration, optical scatter and refractive blur compared to a sharper spot image.\textsuperscript{62,63} Figure 6 shows a typical example of the appearance of the Hartmann–Shack spot images captured from an eye with severe keratoconus, while Figure 7 depicts the reconstruction of a highly aberrated wavefront derived from a grossly distorted spot image array formed at the CCD array, as is typically found in patients with keratoconus.

With the Hartmann–Shack technique, the CCD sensor assumes that all of the spot images will lie ‘flat’ over the finite diameter of the lenslet in question.\textsuperscript{67} This assumption begins to break down even for coarse, lower-order aberrations when the magnitude of those aberrations is large. In such cases, the wavefront is significantly curved over the lenslet’s aperture, resulting in a

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**Figure 4.** The imaging principles underpinning the Hartmann–Shack aberrometry technique for a perfect (upper) and an aberrated eye (lower). Upper: the Hartmann–Shack device’s micro-lenslet array (where individual lenslets are typically between 0.3 to 0.5 mm in diameter) effectively subdivides the wavefront into multiple beams. The ‘local slope’ of the wavefront, over each individual lenslet’s aperture, will determine the location of each individual spot image on the charge-coupled device (CCD) sensor. The upper illustration depicts the results for an ‘ideal’ eye, where the solid red line shows a ‘perfect’ wavefront. Lower: an aberrated wavefront produces an irregular pattern of spots on the CCD sensor. Displacement of each spot from the corresponding lenslet’s axis gives a measure of the ‘local slope’ of the wavefront. The lower illustration depicts the results of an ‘aberrated’ eye where the wavy purple line shows an ‘aberrated’ wavefront.
blurry spots, which is difficult to localise because its centre cannot always be accurately located. However, if the aberrations are large enough, these blurry spots can even overlap, which considerably complicates the analysis.

It is also possible that ‘micro-aberrations’ may exist within the spot images, which are too small to be detected by the wavefront sensor’s detector. These micro-aberrations could still be detrimental to the retinal image quality as they may contribute to the

inducement of a ‘hazy’ image of the spot, rather than a true geographical deviation of the spot image. Although these blurry spot images are problematic, they contain useful information about the degree and location of optical scatter sources within the eye.

Fundamentally, a simple solution to help decrease the amount of ‘crossover’ or ‘overlapping’ of the aberrated spot images would be to reduce the physical amount of spot displacement possible. This may be achieved simply by using a micro-array of lenslets with a shorter second focal length. However, this concept is somewhat flawed, as higher-powered micro-lenses would result in a reduction in sensitivity, that is, a decrease in the sensor’s ability to detect differences between differing magnitudes of aberration. Conversely, increasing the micro-lenses’ second focal length could provide permissible sensitivity, which may still be clinically useful; however, this adjustment limits the sensor’s dynamic range. Another option would be to rearrange the physical spacing of the lenslets to allow maximum resolution; however, this is not easily achieved with most commercially available Hartmann-Shack aberrometers and would likely impact on the spatial resolution of the wavefront.

Rarer and more complex methods have been suggested to help reduce the loss of data for the Hartmann-Shack technique, which include using:

- complex ‘unwrapping’ algorithms in the computational spot detection process; mathematical modifications to assign spots to their corresponding lenslet, even if deviated outside their sub-aperture.
- astigmatic lenses in the micro-lenslet array, which produce ‘line’ rather than ‘spot’ images, all the cylindrical lenses are orientated at a multitude of different angles allowing simpler recognition of the line image from a given cylindrical aperture lens.
- a spatial modulator array; this device is placed in front of the lenslet array and allows the selective switching ‘on’ and ‘off’ of certain sub-apertures, allowing a definite assignment of the spots to their corresponding sub-apertures onto the CCD sensor.
- an image-processing algorithm, alongside an astigmatic lenslet array, that is capable of tracing line foci which fall outside the bounds of the conventional search.
- a ‘spot searching’ method, which involves fitting an astigmatic micro-lenslet to the centre of every group of 2-×-2 spherical micro-lenslets within the overall array (also known as a dual micro-lenslet array). This optical set-up allows the generation of both spot and line images, which creates a unique discernible pattern which is then processed using binary computations and mask processing.

However, it is worth noting that most commercially available Hartmann-Shack aberrometers do not easily allow any of the

Figure 5. Examples of spot-imaging issues impacting on the Hartmann-Shack technique, including: A: ‘multiple’ spot images, B: ‘overlapping’ spot images, C: ‘crossed-over’ spot images and D: a ‘missing’ spot image

Figure 6. A comparison of the raw Hartmann-Shack spot images (formed at the charge-coupled device) between a healthy normal eye (left) and an eye with severe keratoconus (right). While the left-hand image shows a regular series of spot images arranged into a lattice-like array, the right-hand image shows substantial spot image irregularities, such as missing spot images as well as fainter, blurrier spot images.

Micro-lens array

Virtual sub-aperture for ‘centroiding’ algorithm

A. ‘Multiple’ spot images formed at the same section of the CCD sensor

B. ‘Overlapping’ spot images formed at the same section of the CCD sensor

C. ‘Crossed-over’ spot images formed at the CCD sensor

D. ‘Missing’ spot image, essentially formed away from the CCD sensor entirely

Charge-coupled device (CCD) sensor

Incident aberrated wavefront

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Aberration-controlling lenses for keratoconus

Figure 7. A highly aberrated wavefront produces a grossly distorted pattern of spots on the charge-coupled device (CCD) sensor (left-hand image). Displacement of each spot from the corresponding lenslet’s axis gives a measure of the ‘local slope’ of the wavefront. The illustration above depicts the results from a ‘highly aberrated’ keratoconic eye, where the wavy green line shows a highly aberrated wavefront (right-hand image).

Analysis, primarily due to their orthogonality over a circular pupil and their representation of ‘classic’ Seidel aberration terms such as coma and spherical aberration. Computation of the Zernike co-efficients requires a set of discrete orthogonal polynomials to be constructed using the Gram-Schmidt method, where the co-efficients are calculated by ‘fitting’ the wavefront slope gradients and orthogonal polynomials using a ‘least-squares’ method. This methodology essentially describes how each aberration coefficient makes up a proportion of the total wavefront and aims to minimise the absolute error between the measured sampled points and the Zernike terms which are fitted to the data. However, investigators should be wary that the number of sampling points available from the Hartmann-Shack aberrometer will typically be far greater than the number of Zernike polynomial terms that can be fitted to the wavefront to describe its shape. This has led to other research exploring newer methods to reconstruct and compute HOAs.

Unfortunately, the direct subtraction or comparison of ‘corneal’ and ‘total ocular’ aberrations is not usually possible and can give rise to major inaccuracies, purely because different reference axes may have been used during the topography and aberrometry measurements. Most commercially available wavefront aberrometers measuring the total ocular aberrations tend to use the patient’s line of sight as the reference axis. Aberrations measured with respect to this axis therefore have the pupil centre as the Cartesian origin. On the other hand, corneal topographers generally align the videokeratographic axis with the corneal sighting centre (the intersection of the line of sight with the corneal surface). Such inaccuracies in comparing corneal versus ocular aberrations may be accounted for (both mathematically and geometrically) and may be minimised by using an instrument that can take simultaneous corneal and ocular aberration measurements.
such small eye movements during the measurement stage would induce larger variations in aberrations. This point is of particular importance as the magnitude of fixational eye movements are likely to be larger in keratoconic patients, than in normal subjects, due to poorer levels of acuity. While this suggestion currently remains unexplored, it is worth noting that both Mihaltz et al.82 and Tan et al.83 have demonstrated that the magnitude of the lower-order and HOAs measured in keratoconic eyes will be greatly influenced by the location of the cone apex.

Changes in aberrations due to micro-fluctuations in accommodation or changes in the tear film

In normal eyes, other possible sources of variance in HOA measurements include changes in aberrations due to micro-fluctuations in accommodation83 or variations in the tear film84 during the measurement process. However, in patients with moderate keratoconus, Radhakrishnan et al.59 found that while HOAs did alter with accommodation and tear film changes immediately post-blink; the magnitude of these changes were relatively small compared to their patients' manifest aberrations. In support of these results, Chen et al.85 proposed that tear film-induced variations in aberrations could be somewhat countered by standardising aberration measurements, by ensuring that all readings are taken two seconds post-blink.

Correcting ocular aberrations in keratoconic patients

VISUAL BENEFIT

Despite potential issues regarding their repeatability, Williams et al.86 have proposed there is usually an identifiable and significant 'visual benefit' (VB) to correcting the ocular HOAs of the keratoconic eye measured using the Hartmann-Shack method. The authors calculated their VB scores as the ratio of the modulation transfer function (MTF) measured with a 'customised aberration correction' in place (that is, a correction that specifically corrected for all lower-order and HOA terms), to the MTF found with just the second-order aberrations corrected – all of their MTFs were computed for a pupil diameter of 5.7 mm and a spatial frequency of 16 cycles/degree.86 Accordingly, their VB scores indicated the potential increase in retinal image contrast by correcting all of the monochromatic HOAs (in white light), rather than just defocus and astigmatism alone. Scores of > 1.0 represent a positive VB, indicating a gain in visual performance through aberration correction, whereas eyes with a score of 1.0 would gain no VB from correction. Williams et al.86 found that the VB in 109 normal eyes ranged from 1.5 to 8.0, whereas the VB for their four keratoconic eyes varied between 2.5 to 25.0. Similar magnitudes of positive VB scores were also found for four keratoconic patients by Guiaro et al.,87 at MTF spatial frequencies of 16 and 32 cycles/degree. Furthermore, using their translatable grid-integrated Hartmann-Shack wavefront aberrometer to increase dynamic range,73 Pantanelli et al.73 also reported encouraging VB scores (ranging from 2.5 to 10.5) for 15 keratoconic patients. The authors calculated their VB scores using the metric of volume under the MTF across 16 and 32 cycles/degree. Overall, these three studies each highlighted that the theoretical benefit of using customised correction methods for keratoconic eyes was far superior to that of normal eyes.

DO ALL ABERRATION TERMS NEED CORRECTING?

The literature indicates that correcting every single aberration term may not be beneficial, as lens decentrations are likely to hinder the VB yielded for both normal87,88 and keratoconic eyes.40,89,90 Furthermore, due to changes with accommodation and variations in the tear film, it is also widely accepted that very few HOA terms are completely stable in either normal81,83,84,91 or keratoconic eyes.32,51,85 Nonetheless, López-Gil et al.92 reported that the aberrations created through decentration of customised lenses were likely to be smaller than the difference between the total RMS error measured with and without customised lenses in place for two normal eyes. Thus López-Gil et al.92 hypothesised that, 'wearing a customised contact lens over a course of time will show a clear benefit... especially for patients with moderate to high amounts of aberration'. On the other hand, Marsack et al.75 proposed that correction of all the HOA terms of the keratoconic eye are not worthwhile. The authors suggested that only correcting between the third and up to the fifth Zernike orders would give most keratoconic eyes better visual performance and lessen the likelihood of inducing superfluous aberrations due to lens decentrations. However, when interpreting the data presented by Marsack et al.,75 it is important to note that the authors assumed a 'perfect' on-eye alignment of their 'customised lens' correction (that is, a contact lens that was custom-designed to correct lower-order aberrations, while also simultaneously reducing some of the HOAs associated with keratoconus). However, this is an unrealistic assumption for even a prism-ballasted toric soft lens, which typically moves vertically by 0.3 to 1.0 mm upon blink,93,94 with approximately 2–15 degrees of rotation.95 The results of modelling simulation by Marsack et al.75 showed that mild and moderate cases of keratoconus would theoretically benefit more than those with severe keratoconus if the number of Zernike radial orders that are corrected are truncated. This finding was perhaps to be expected, as severe to advanced keratoconic patients are more likely to show larger magnitudes of aberrations at the higher radial orders. Therefore, in order to successfully correct aberrations in keratoconus, with aberration-controlling customised lenses, it may be necessary to modify the strategy of correction depending on each individual patient’s disease severity.

The use of non-customised contact lenses to correct aberrations

To date, a number of studies have investigated the use of non-customised soft lenses,43,57,58 rigid corneal lenses,7,23,40,42,46,47,54,57 and rigid scleral lenses51,55,59 to reduce the magnitude of manifest HOAs in keratoconic patients, with each demonstrating varying degrees of success, as well as revealing some important findings.

Perhaps rather predictably, both Jinabhai et al.43 and Abdu et al.57 agreed that non-customised corneal lenses provided better visual performance and superior aberration correction than non-customised soft contact lenses. Compared to soft lenses, corneal lenses can mask the manifest corneal aberrations, induced through keratoconus, by effectively ‘replacing’ the irregular corneal surface with smooth and regular refractive surfaces.96,97 However, both Jinabhai et al.43 and Abdu et al.57 confirmed that even with corneal lenses in situ, there were still some residual HOAs present, which were typically larger in magnitude than the aberrations measured in normal, healthy eyes.91,98 These findings corroborated the results of other previous studies of keratoconic patients habitually wearing corneal lenses2,23,46,47 or scleral lenses7,23,46,47.
lenses. Other authors have proposed that these residual aberrations are most likely attributable to irregularities of the posterior corneal surface, which is also known to become significantly distorted in keratoconus.

To investigate the potential impact of correcting such residual aberrations on visual performance, Yang et al. used a customised adaptive optics virtual simulator (a 37-actuator deformable mirror) to measure contrast sensitivity function (using sine-wave gratings, presented at five different spatial frequencies) with corneal contact lenses in situ for 20 eyes of 19 keratoconic patients. Compared to without it, the authors reported improved contrast sensitivity function with their simulator, particularly at low (two cycles/degree) and intermediate spatial frequencies (four, eight and 16 cycles/degree). Overall, the results from this study highlighted that better correction of residual aberrations could likely improve visual performance in keratoconic patients.

The use of customised corrections for keratoconic patients

Ahead of discussing individual studies, it is important to acknowledge that the majority of the literature regarding the design and use of customised lenses, phase plates or adaptive optics (typically in the form of a deformable mirror) is largely limited to ‘non-surgical’ keratoconic corneas only, which typically show no apical scarring. While this is not representative of the full spectrum of keratoconic patients, such studies provide key information about the impact of correcting optical aberrations without the confounding factor of ‘optical scattering’ due to the presence of corneal scarring.

Contact lenses are discrete, simple to use and relatively inexpensive to manufacture, and therefore represent a suitable device with which to correct HOAs. This idea was first proposed by Smirnov, who acknowledged that “it is possible to manufacture a lens compensating for the wavefront aberrations of the eye” and that “these lenses must obviously be contact ones”. As corneal lenses will typically show significant magnitudes of on-eye decentration with blinking, a number of studies have investigated the use of soft contact lenses for providing a customised correction of aberrations. A soft lens design, which could achieve maximum on-eye lens comfort as well as providing optimal visual performance, would be appealing to many keratoconic patients and practitioners alike. Ideally, this hydrogel contact lens would be silicone-based, of a regular thickness and would have the capabilities to reduce the manifest ocular HOAs associated with keratoconus.

SIMULATIONS

de Brabander et al. simulated the visual performance achieved by using a customised soft lens to correct HOAs in nine moderate keratoconic eyes and reported that their model visual performance was transferred onto the wavefront aberrations of the eye.

Like the results of Guirao et al., de Brabander et al. reported that decentrations of their customised soft lens led to a partial loss in the VB gained for keratoconic patients. However, it should be noted that the authors calculated the effects of rotation and translation separately from each other. Clinically, it is widely accepted that soft lenses will translate and rotate upon blinking, simultaneously, and that these movements are not mutually exclusive. Nonetheless, the results of de Brabander et al. showed that rotations up to a maximum of five degrees and translations up to a maximum of 1 mm, upon blinking, would be permissible to still yield a benefit from a customised lens.

Yoon and Jeong simulated the decentration of customised contact lenses for two post-penetrating keratoplasty and two keratoconic eyes. They found that compared to normal eyes (VB = 3), a customised correction gave their highly aberrated eyes a threefold improvement in visual performance (VB = 9).

The authors’ results also suggested that highly aberrated eyes were more tolerant to decentrations than normal eyes; for a 0.2 mm translation vertically, the VB gained was reduced by only a third for highly aberrated eyes, but by half in normal eyes.

CUSTOMISED SOFT LENSES

Jeong and Yoon manufactured a front-surface, customised aberration-controlling soft lens for a patient with advanced keratoconus. On-eye lens decentration was accounted for by first fitting a conventional soft ‘trial’ lens and monitoring its centration using an infrared pupil camera linked to their aberrometer. The aberration correction was transferred onto the final customised lens, accounting for any on-eye lens translation/rotation observed with the ‘trial’ lens. Their customised lens reduced uncorrected higher-order RMS (HORMS) error by 67 per cent; however, the authors did not measure visual acuity as part of their experiment. The authors proposed that their residual aberrations could have been induced by variations in the tear film, or even on-eye vertical translation and/or rotation of the customised lens with blinks.

Sabesan et al. conducted a comparison study for three keratoconic eyes (two severe and one moderate) investigating the effectiveness of front-surface, customised soft lenses versus conventional soft and corneal lenses. The authors accounted for possible soft lens decentrations by fitting ‘trial’ lenses with three different base curves and assessed their fittings to ascertain which was the most stable for each eye, ahead of manufacturing their customised soft lenses.

In the most successful case, the uncorrected HORMS error was reduced by 75 per cent with the customised lens, but only by 17 per cent with a conventional soft lens. Compared to the conventional lenses, the customised lenses gave improved low-contrast (20 per cent) logarithm of the minimum angle of resolution (logMAR) acuities, by an average of 2.1 lines. For one of their severe cases, the customised lens gave an improvement of three lines of low-contrast logMAR acuity compared to the patient’s habitual corneal lens. For high-contrast (100 per cent) acuity there was very little difference between the subject’s corneal lens and the customised lens; however, the customised lens still performed best. In agreement with Jeong and Yoon, Sabesan et al. also noted that some small residual errors persisted even with their customised lenses in situ.

Marsack et al. produced a front-surface, customised aberration-controlling soft lens for a patient with moderate keratoconus and compared this to the patient’s habitual, conventional soft contact lens. The results showed that both high-contrast (87 per cent) and low-contrast (4 per cent) logMAR acuity were improved with the customised lenses compared to with the habitual soft lens. In contrast to the results of Sabesan et al., Marsack et al. found that high-contrast logMAR acuity was improved by 1.5 lines; p = 0.03) more than low-contrast logMAR acuity (which only improved by one line of letters; p = 0.11); however, such differences may be due to the differing contrast levels used between these two studies.
Interestingly, although Marsack et al.\textsuperscript{45} noted that the habitual lenses typically translated on-eye with blinks, they did not incorporate this factor into the design of their final customised lenses. Nonetheless, their customised lens successfully reduced the uncorrected HORMS error from 0.99 μm to 0.37 μm over a 5 mm pupil (compared to 0.77 μm found with the habitual conventional soft lens).

Chen et al.\textsuperscript{48} proposed a method of enhancing the fitting of aberration-controlling soft lenses by custom-designing the lens’ back surface (using topographical data) to help reduce residual aberrations induced through lens translations/rotations. The authors reported that compared to conventional lenses, their customised lenses reduced both horizontal and vertical translations by a factor of two and reduced rotations by a factor of five. However, the authors’ customised lenses only successfully reduced uncorrected HORMS error for one of their three patients with moderate keratoconus, from 1.66 ± 0.06 μm to 0.61 ± 0.04 μm, whereas for one patient, the author’s customised lens actually induced a significant increase in HORMS error, from 1.17 ± 0.04 μm (when uncorrected) to 1.30 ± 0.10 μm, which was largely attributed to overcorrection of a majority of Zernike terms with their customised lens in situ. For the remaining patient, there was no significant change in HORMS error (uncorrected: 0.70 ± 0.03 μm, versus with the customised lens: 0.69 ± 0.08 μm).

Unfortunately, Chen et al.\textsuperscript{48} did not measure either high- or low-contrast visual acuity in their study. However, because they measured both corneal surfaces’ aberrations as well as the total ocular aberrations, they were able to partly model the magnitude of the aberrations of the eye's internal optics. Their modelling results indicated that the posterior corneal surface and crystalline lens were also responsible for some of the residual aberrations measured with their customised lenses on-eye for their three keratoconic patients. Chen et al.\textsuperscript{48} also acknowledged that their customised lenses only had a central 5 mm optical zone of aberration correction, which would likely cause problems with glare if the lenses were worn in scotopic conditions.

Marsack et al.\textsuperscript{44} compared visual performance and ocular aberrations using bespoke wavefront-guided soft contact lenses versus the subject’s own habitual corneal lenses. The authors produced customised lenses for three keratoconic eyes (one severe and two moderate cases) and reported that all three customised lenses provided better logMAR acuities compared to the patients’ habitual corneal lenses. For their patient with severe keratoconus, their habitual corneal lens provided a high-contrast (91 per cent) acuity of 0.04 ± 0.09 log units, whereas their customised lens gave an improved acuity of −0.05 ± 0.05 log units. Conversely, the patient’s habitual corneal lens provided a low-contrast (52 per cent) acuity of 0.58 ± 0.04 log units, whereas the customised lens yielded an acuity of 0.61 ± 0.04 log units. Encouragingly, the mean uncorrected HORMS error was reduced from 1.57 ± 0.03 μm to 0.76 ± 0.03 μm with the customised lens, and to 0.50 ± 0.15 μm with the habitual corneal lens. Similarly, for one of their moderate cases, the uncorrected HORMS error was reduced from 0.61 ± 0.02 μm to 0.39 ± 0.02 μm using their habitual corneal lens, and to 0.38 ± 0.07 μm with the customised lens. The high-contrast (91 per cent) acuity for this particular patient was 0.20 ± 0.02 log units with their habitual corneal lens, which reduced to 0.14 ± 0.02 log units with the customised lens. However, the patient’s habitual corneal lens provided a low-contrast (37 per cent) acuity of 0.58 ± 0.04 log units, whereas the customised lens yielded an acuity of 0.59 ± 0.04 log units. Nonetheless, these two cases highlighted that customised soft lenses have the potential to provide comparable results to corneal lenses in terms of low-contrast acuity, yet superior results in terms of high-contrast acuity.

Katsoulos et al.\textsuperscript{26} used a rather different approach to producing customised soft lenses for eight mild to moderate keratoconic eyes; their lenses were designed to correct for around 75 per cent of the eye’s manifest third-order negative vertical coma aberration, as well the second-order Zernike terms extracted directly from their aberrometry data for a 4 mm pupil diameter. In all eight cases, a reduction in uncorrected HORMS error was seen (the largest reduction was from 0.86 μm to 0.42 μm); however, the authors did not explain if the mean differences were significant. On the other hand, Katsoulos et al.\textsuperscript{26} reported a significant reduction in the magnitude of uncorrected vertical coma aberration with their customised lenses (p < 0.005). The largest reduction reported was from −0.56 μm to −0.15 μm. These reductions in HOAs were believed to have contributed to the improvements in high-contrast (100 per cent) logMAR visual acuities measured with the customised lenses, compared to the patient’s best-corrected spectacle acuities (the largest improvement reported was from 0.52 to 0.06 log units). In broad agreement with the results of Sabesan et al.,\textsuperscript{50} Katsoulos et al.\textsuperscript{26} also found greater improvements in low-contrast (50 per cent) logMAR visual acuities compared to best-corrected spectacle acuities (the largest improvement was from 1.00 to 0.10 log units). The authors’ rationale for using a 75 per cent correction was based on previous studies which had shown that decenterations of a partial wavefront aberration correction, rather than the full correction, would still yield a helpful VB compared to conventional contact lenses.\textsuperscript{105} Acknowledging that not all keratoconic cones are always decentred in the same position away from the individual eye’s line of sight,\textsuperscript{6,82} Katsoulos et al.\textsuperscript{26} also proposed that more centrally located cones could require the correction of spherical aberration in order to achieve optimal visual performance.

Building on the approach used by Katsoulos et al.\textsuperscript{26} and Jinabhai et al.\textsuperscript{41} explored the effectiveness of aberration correction provided by customised lenses that gave either a 50 per cent or a 100 per cent correction of both vertical and horizontal third-order coma, over a natural 4 mm pupil. The authors’ rationale for using a ‘partial’ correction was based on previous studies which confirmed that decenteration of a ‘full’ wavefront-guided correction (through either rotation and/or translation) induces superfluous residual aberrations,\textsuperscript{40,60,89,90} thereby diminishing visual performance. Jinabhai et al.\textsuperscript{41} compared their two customised lenses to noncustomised, conventional toric soft lenses and the patient’s habitual corneal lenses. Unlike in previous studies, the authors used a subjective over-refraction result to determine the lower-power orders of both their customised and noncustomised soft toric lenses. This was because both Katsoulos et al.\textsuperscript{26} and Jinabhai et al.\textsuperscript{8} had previously demonstrated that the lower-order sphere and cylinder terms, measured objectively using Hartmann-Shack aberrometry, did not readily correspond with the sphere and cylinder powers measured during a subjective refraction for keratoconic patients. Such variability between these methods may be attributable to errors at the wavefront sensor.\textsuperscript{61}
Jinabhai et al.\textsuperscript{41} reported significant changes in mean third-order vertical coma aberration for 12 keratoconic eyes, from −0.93 ± 0.34 μm when uncorrected, to +0.18 ± 0.39 μm with the ‘100 per cent lenses’ (p = 0.002); to −0.17 ± 0.30 μm with the ‘50 per cent lenses’ (p = 0.002) and to +0.39 ± 0.14 μm with the patient’s habitual corneal lenses (p = 0.002). In contrast, their non-customised toric lenses did not significantly reduce vertical coma (−0.66 ± 0.43 μm). While both the ‘100 per cent lenses’ and the habitual corneal lenses produced a ‘positive shift’ in vertical coma, the differences between these two modes of correction were not statistically significant. The authors also found no significant differences in horizontal third-order coma measurements between these five measurement conditions.

In spite of the apparent improvements in vertical coma aberration with their two customised lenses, Jinabhai et al.\textsuperscript{41} reported that the patient’s habitual corneal lenses provided significantly better distance high-contrast (95 per cent) logMAR acuity, distance low-contrast (15 per cent) logMAR acuity and near vision SKILL card\textsuperscript{107} scores compared to the ‘100 per cent lenses’ (p ≤ 0.002). However, the authors found no significant differences in high-contrast, low-contrast or SKILL card scores measured with the ‘50 per cent lenses’, versus either the habitual corneal lenses or the ‘100 per cent lenses’. While it was clear that the corneal lenses provided the best visual performance scores of all the possible lens options that were investigated, the authors also noted that the ‘50 per cent lenses’ generally provided better visual performance scores compared to the ‘100 per cent lenses’.

The authors acknowledged that their customised lenses’ visual performance results were likely to have been affected by small on-eye lens translations (despite on-eye rotations being accounted for during the manufacturing process), as well as differences between the patient’s natural pupil size (during the visual performance measurements) and the size of the zone of customisation of both their ‘50 per cent’ and ‘100 per cent’ lenses. These clinical findings corroborated the results of the authors’ previous study,\textsuperscript{40} which modelled the effects of customised lens translations and rotations on the correction of aberrations in keratoconic patients, where the theoretical customised lens was designed to fully correct all high-order Zernike terms, up to the fifth order. Using computerised simulations, Jinabhai et al.\textsuperscript{40} demonstrated that, depending on their magnitude as well as the eye’s inherent wavefront error, superfluous lower-order and HOAs, induced through unwanted customised lens decenterations, can reduce the effectiveness of the wavefront correction. These induced, residual aberrations are typically proportional to the amount of displacement, as well the magnitude of the displaced aberration.\textsuperscript{88,108} Of particular importance, Jinabhai et al.\textsuperscript{40} reported that vertical translations typically induced larger residual spherical and cylindrical errors than horizontal translations. The authors’ results suggested that vertical translations of a full, customised HOA correction might be limited to no more than 0.1 mm.

**CUSTOMISED SCLERAL LENSES**

Compared to customised soft lenses, which typically induce superfluous aberrations due to their unavoidable degree of ‘on-eye’ movement and their variable conformity to the keratoconic corneal profile, customised scleral contact lenses are likely to offer a greater degree of on-eye stability for keratoconic patients.\textsuperscript{52,52,109} Moreover, scleral lenses also have the added benefit of improving optical performance, by providing a ‘regular’, rigid first optical surface, while also simultaneously increasing lens wear comfort by allowing a majority of the lens’ weight to bear onto the conjunctiva.\textsuperscript{110}

Sabesan et al.\textsuperscript{52} designed customised scleral lenses, for six keratoconic patients (11 eyes), by first identifying their ‘best-fitting’ conventional lenses. These ‘best-fitting’ lenses each had a ‘central optic’, the corrective properties of which were purely spherical, and a ‘customisable periphery’ which had toric properties, and also allowed quadrant-specific adjustments to be made (where necessary) to stabilise the lens while simultaneously minimising compression/impingement on the conjunctiva. With these ‘best-fitting’ lenses in situ, the authors carefully evaluated and accounted for both on-eye rotation and translations after measuring ocular lower-order and HOAs (via Hartmann-Shack aberrometer) through the lenses. Using the ‘best-fitting’ lens parameters as a starting point, the authors used their aberration measurements to create front-surface, customised scleral lenses, manufactured using a sub-micron-precision lathe. Once verified and fitted on-eye, the customised scleral lenses were found to provide good temporal stability, showing no more than two degrees of on-eye rotation and less than 200 μm of on-eye translations with blinks over a 20-second period. Sabesan et al.\textsuperscript{52} found that, compared with the ‘best-fitting’ spherical optic lenses (1.17 ± 0.57 μm), the customised scleral lenses significantly reduced the mean HORMS error (to 0.37 ± 0.19 μm; p < 0.05) for their keratoconic patients. Equally, the authors also reported a significant improvement in mean monocular, distance high-contrast logMAR visual acuity between the study lenses, by an average of 1.9 lines (p < 0.05), in addition to significant improvements in sinusoidal grating-based contrast sensitivities at four (increased by a factor of 2.4), eight (increased by a factor of 1.8) and 12 cycles/degree (increased by a factor of 1.4), respectively. While these results indicate that the reduction of aberrations was fairly successful, it is worth noting that residual aberrations still remained even with the customised scleral lenses in situ; these were most likely due to the small lens movements observed immediately after blinking, or even due to keratoconus-induced distortions at the posterior corneal surface and/or the crystalline lens.\textsuperscript{38} Another contributing factor could have been the slight mismatch between the pupil size at which the HOAs were measured with the Hartmann-Shack aberrometer (6 mm) and the actual size of the zone of customisation within the scleral lenses (which varied between patients, from 7.0 to 8.5 mm).

In accordance with Sabesan et al.\textsuperscript{52} Marsack et al.\textsuperscript{53} also utilised a posterior surface scleral toric landing zone in their peripheral lens designs to help provide on-eye rotational stability. However, in contrast to the approach used by Sabesan et al.,\textsuperscript{52} Marsack et al.\textsuperscript{53} designed their ‘best-fitting’ conventional, or ‘intermediate’, scleral lenses to incorporate a ‘spherical equivalent’ defocus power within the central optic, which was derived from a subjective refraction routine; this was to produce a starting lens the weight of which would be more closely matched to that of the ‘final’ customised lens. This allowed for more accurate measurements of ‘on-eye’ lens rotation and/or translations of the ‘intermediate’ lens ahead of designing and manufacturing the customisation zone of their ‘final’ lenses. Marsack et al.\textsuperscript{53} used this approach to design lenses for seven keratoconic patients (14 eyes). Once the ‘intermediate’ lens had settled, a Hartmann-Shack aberrometer was used to evaluate...
aberrations through the lens, over a 7 mm pupil diameter, from the second to the fifth order (inclusive); these measurements were then used to design the final customised lens optic. Specifically, Marsack et al.\textsuperscript{53} explained that the ‘final’ customised scleral lenses contained the baseline level of defocus correction that was previously incorporated into the ‘intermediate’ lens, plus compensation for the residual objective lower-order and HOAs measured via aberrometry. Measurements of the ‘intermediate’ lens on-eye decentrations were made using a customised camera system; however, unlike Sabesan et al.,\textsuperscript{52} Marsack et al.\textsuperscript{53} only measured their lens’ decentrations over a period of 10 seconds.

Overall, Marsack et al.\textsuperscript{53} reported that, compared to the ‘intermediate’ lenses, the ‘final’ customised lenses provided significantly lower magnitudes of residual mean lower-order RMS error ($p < 0.001$) and residual mean HORMS error ($p < 0.02$), over a 6 mm pupil, for all 14 eyes. However, the authors’ individual patient data revealed that three (designed for two patients) of their 14 ‘final’ customised lenses actually induced more residual aberrations than the ‘intermediate’ lenses. The most likely reason for these anomalies was proposed to be on-eye lens decentration, resulting in the wavefront-compensating optical zone becoming misaligned with respect to the patient’s pupil. Nonetheless, the authors reported that, on average, 10 of the 14 eyes achieved a mean improvement of 1.5 lines of high-contrast monocular logMAR acuity, compared to their habitual mode of correction, which was similar to the findings of Sabesan et al.\textsuperscript{52}

Even with their customised scleral lenses in situ, both Sabesan et al.\textsuperscript{52} and Marsack et al.\textsuperscript{53} noted that a significant reduction in HOAs did not always yield a significant improvement in visual performance. This key finding suggests there might be a degree of post-receptoral neural deficit present in keratoconic patients, which limits the degree of visual improvement possible, even with the near-normal or better than normal levels of optical quality, as is provided by wearing a well-aligned customised wavefront correction. Such a deficit may be attributable to long-term exposure to an asymmetrically blurry retinal image.\textsuperscript{103} Further studies are needed to explore this concept; for example, it is currently unclear if the degree of neural deficit is related to the severity of the patient’s disease and/or age, or whether such deficits could be overcome through regular perceptual learning/training.\textsuperscript{111} At present, only one study has explored the impact of allowing keratoconic patients to habituate to a wavefront-guided, customised scleral lens correction for a substantial time period.\textsuperscript{109} Using the customisation methodology outlined in their previous investigation, Hastings et al.\textsuperscript{109} conducted a randomised study, which included a crossover design, allowing comparisons between ‘conventional’ scleral lenses (acting as a control) and ‘customised’ scleral lenses, over two eight-week (approximate) periods, for eight patients with keratoconus. Although the authors reported that both sets of lenses were worn on a ‘daily’ basis, for each eight-week period, specific data on how many hours of lens wear per day were not presented in their paper. Expectedly, Hastings et al.\textsuperscript{109} found that the mean HORMS error reduced from $+0.46 \pm 0.24$ μm with the conventional lenses, to $+0.26 \pm 0.08$ μm with the customised lenses ($p = 0.004$). However, although improved, the difference in the mean area under the log contrast sensitivity function did not reach statistical significance between the two lens types (conventional lenses = $13.91 \pm 2.20$ log units, customised lenses $15.82 \pm 2.34$ log units ($p = 0.09$)). Similarly, a non-significant improvement was also reported for mean high-contrast logMAR acuity (conventional lenses = $-0.03 \pm 0.09$ log units, customised lenses $-0.09 \pm 0.10$ log units ($p = 0.07$)).

**FURTHER LIMITATIONS TO THE USE OF CUSTOMISED LENSES**

While some limitations of using either soft or scleral customised contact lenses have already been discussed in this review (for example, on-eye lens decentration), there are other more general limitations that also need to be considered, with respect to the correction of HOAs, which include:

- optical limits that are set by diffraction; these are related to the patient’s pupil size
- the limit of the photoreceptors’ ‘packing density’ at the foveola centralis
- any errors in the manufacturing process of incorporating the required aberration magnitudes onto the customised lenses\textsuperscript{48,52}
- potential light scattering and/or glare effects from the boundaries of the lens’ customisation zone (more likely to be noticeable in scotopic conditions)
- changes in the patient’s habitual lower-order and/or HOAs due to disease progression would mean that the customised lenses need to be redesigned/modified and refitted on a regular basis, which could prove to be financially inconvenient to the patient, while also requiring substantial clinical chair time
- poor customised lens care by the patient (for example damage to the contact lenses during cleaning, storing or handling)
- customised contact lenses can only optimally correct HOAs at one given pupil size. When the patient’s pupil increases beyond this size, the effectiveness of the aberration control will begin to reduce; however, the patient might still experience some degree of benefit.

Another issue to overcome in manufacturing customised scleral/soft contact lenses is the need for highly specialised equipment. The cost of buying and maintaining microprecision lathe machines is typically high, which therefore significantly increases the cost of producing customised lenses. A further challenge is the requirement of specialist training for practitioners, to enable them to carry out the assessment, fitting and subsequent modification of these complex lens designs.

In order to gain the maximum benefit from HOA customised corrections, another difficulty to overcome is the need to improve the efficacy of correcting lower-order terms with customised lenses, as any under- or overcorrection of these terms may potentially diminish, or even eliminate, any benefits gained by correcting the comparatively smaller-magnitude HOA terms.

Nonetheless, further technological advances in the field of scleral/soft lens design are likely to promote the emergence of customised aberration-controlling lenses for keratoconic patients, particularly as improvements in visual performance and comfortable wearing times, provided by such lenses, could reduce the rate of keratoplasty in keratoconic patients, thereby significantly reducing clinical issues related to corneal graft surgery. Additionally, enhancements in optical correction, provided by customised lenses, could lead to increased independence, particularly among young adult keratoconic patients, thereby contributing to improvements in quality of life.

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