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Assessing the visual image quality provided by refractive corrections during keratoconus progression

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Keratoconus, refractive correction, keratoconus progression, statistical eye model, rigid lens, subjective refraction,

Running title
Refractive correction in progressive keratoconus

Competing interests
The University of Houston holds patent interests on using visual image quality metrics to determine refractions and on wavefront guided corrections, on which RAA is a listed inventor.

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Abstract

<u>Purpose</u>: To expand a SyntEyes keratoconus (KTC) model to assess the Visual Image Quality (VIQ) of sphero-cylindrical spectacle and rigid contact lens correction as keratoconus progresses.

<u>Methods</u>: The previously published SyntEyes KTC eye model to determine best sphero-cylindrical spectacle and rigid contact lens correction in keratoconic eyes was expanded to include the natural progression of keratoconus, thus allowing the assessment of corrected VIQ with disease progression.

<u>Results</u>: As keratoconus progresses, the pattern of visual Strehl ratio (VSX) in correction space for spectacles alters from a typical hourglass pattern into a shell pattern. The former would quickly guide the subjective refraction towards the optimal correction and the latter is relatively insensitive to large dioptric steps. In *15* out of the *20* SyntEyes, the shell pattern eventually produces two foci on opposite sides of correction space separated by a very large dioptric difference with a similar, albeit low VIQ. Wearing the best possible spectacle correction provided an average gain of up to *3.5* lines of logMAR acuity compared to the uncorrected cases, which increased to *5.5* lines for the best rigid contact lens correction. Continuing to wear an old spectacle correction as the disease progresses often leads to a VIQ nearly as bad as the uncorrected case. Continuing to wear an old rigid contact lens correction as the disease progresses still retains a relatively high level of VIQ, albeit in the low range for typical normal eyes.

<u>Conclusions</u>: The results presented reflect clinical experience that subjective refraction is difficult at best in highly-aberrated keratoconic eyes, the benefit of spectacle correction is short lived, rigid contact lenses provide better and more stable VIQ with disease progression. Other aspects, such as the presence and behavior of the second focus in some cases, remain to be confirmed clinically.

Key points

- The SyntEyes KTC eye model was used to analyze refractive correction of progressive keratoconus.
- The results reflect clinical experience, with short-lived spectacle corrections and better and more stable results for rigid contact lenses.
- Keratoconic eyes may have two regions of best correction, located at opposite sides of correction space, that provide a similar visual image quality.

Introduction

The best refractive correction is only as good as its ability to correct the optical errors of the eye in a manner that provides excellent visual image quality (VIQ). In healthy eyes, where relatively low levels of higher order aberrations are present and lower order aberrations of sphere and cylinder dominate,[1] good VIQ can typically be achieved with a sphero-cylindrical spectacle correction.[2] On the other hand, eyes with corneal diseases such as keratoconus, develop large amounts of higher order aberrations that are not correctable with sphero-cylindrical spectacles.[3] In such cases, rigid contact lenses may be used, which largely mask the higher order aberrations of the cornea by replacing the anterior corneal surface and refractive index matching.[4] Although such lenses cannot mask the aberrations of the distorted posterior cornea, they improve VIQ in keratoconus by reducing higher order aberrations by approximately *60%*.[5,6]

The story is not as simple as just reducing the magnitudes of higher order aberrations, however, as VIQ metrics consist of two interactive parts representing the optical and neural components of the eye.[7] Optically, the various aberrations can interact to increase or decrease VIQ,[8] while the neural component is subject to the sampling limits imposed by the photoreceptors[9] and processing of the visual pathways.[10]

The onset of keratoconus typically occurs in the second decade of life,[11] and its severity and progression rate can vary considerably between patients.[12] To best address the visual needs of these patients, it is clinically beneficial to understand how ophthalmic corrections interact with the visual image properties of keratoconic eyes as the disease progresses over time. However, such studies are rare and typically focus on documenting corneal changes, rather than on whether corrections provide the VIQ in best sphero-cylindrically corrected normal, healthy eyes.[13] The lack of studies is not surprising given that such studies are difficult for patients, time consuming for clinicians, expensive to organize and ideally require a large sample of eyes to be followed over a long period of time.

In recent years there have been great strides in developing statistical models of the optical properties of the normal[14] and keratoconic[15] eyes, and in transforming retinal image quality metrics into visual image quality metrics,[16,17] the changes of which are predictive of changes in visual acuity.[18] These metrics have in turn been used to objectively determine sphero-cylindrical corrections that provided visual acuity equal to or better than subjective refraction in typical myopic eyes.[2]

For such a model to be useful in highly aberrated eyes, it needs to provide objective quantification of clinical observations, corroborating patient complaints, and thereby providing new insights and options to meet the visual needs of the patients. To explore whether such models can be useful, existing tools were evolved and combined to model the optical progression of keratoconus and to assess how well and how long visual image quality is maintained with a given correction as the disease progresses.

Methods

The initial keratoconus correction model is described in detail elsewhere.[19] In brief, spherical and sphero-cylindrical spectacle and rigid contact lenses were used to simulate the corrected visual image quality of *20* synthetic eyes with keratoconus generated by the SyntEyes keratoconus (KTC) model.[14,15] To determine the correction needed, the front curvature of the correcting lens was varied to produce each possible sphero-cylindrical correction in the phoropter correction space[19] and ray tracing of the entire system was performed over a *5 mm* pupil diameter to assess VIQ based on the visual Strehl ratio (*VSX*).[16,17] The complexity of the optical errors in keratoconus means that two substantially different sphero-cylindrical corrections may exist in phoropter space, that each provide comparable (albeit not necessarily typical) levels of image quality for the highly aberrated eye.[19,20] Here, a sphero-cylindrical correction in phoropter space that optimizes (i.e. provides a maximum) *VSX* is referred to as a *"focus"*. Discrete points in the phoropter correction space are considered as distinct foci if the associated *VSX* values reach a threshold of *2/3·max*(*VSX*) and are separated (in phoropter space) by a region of corrections with *VSX* values below that threshold.

The newly developed model for longitudinal analysis utilized *20* keratoconic SyntEyes from a previous paper,[19] and calculated the optimal corrections at *12* time points during simulated keratoconus progression of those eyes. As progression varies widely between patients, these time points are to be considered as arbitrary, ranging from Time *0*, when the corneal shape is still within the normal range (sub-clinical), and Time *120*, corresponding to the end stage of keratoconus. The first *11* time points are equidistant between *0 – 60*, while the last point at *120* is after progression plateaus in later stages of the disease.[12] The method by which the keratoconus development was modeled is described elsewhere.[15] The model essentially generates a keratoconic SyntEye and runs an algorithm to find a healthy SyntEye[14] with matching non-corneal biometry (i.e. crystalline lens thickness and power, as well as vitreous depth). The progression is then modelled as an interpolation between the healthy eye and the diseased end state of the keratoconic eye (in varying levels of severity) using a non-linear Gompertz function,[15] which has been shown to be ideal for this purpose.[21]

For each SyntEye and each timepoint the optimal spherical and sphero-cylindrical corrections using both spectacles and rigid lenses were calculated for a *5 mm* pupil diameter, making a total of *20* (patients) x *12* (time points) x *4* (types of correction) = *960* calculations, each containing *> 10,000* ray tracing analyses (possible corrections in phoropter space). The resulting VIQ values were then plotted in sphero-cylindrical space and explored to compare the results with clinical experience and to determine where they help improve best clinical practice.

The long-term effectiveness of a given refractive correction during keratoconus progression was assessed by determining the *VSX* value at each subsequent time point for each model eye and correction method, assuming the previous correction was retained, thereby mirroring the situation in which a patient does not update their spectacle or rigid lens correction.

Results

Influence of keratoconus progression

As keratoconic eyes progress from normal or pre-clinical to manifest and eventually late-stage keratoconus, the *VSX* pattern in spectacle correction space gradually changes (Figure 1 and Supplement A). Initially, the spectacle correction of all SyntEyes show a *hourglass pattern* centered around the sphere axis in correction space found in healthy eyes[19] with an optimal *VSX* value at its narrowest point. Here the conical slopes of the hourglass shape are steep and VIQ changes quickly away from the optimal correction in the dioptric space. Consequently, each *0.25 D* step taken during the subjective refracting process will produce a difference in visual quality that could be easily detected by a patient, thus allowing the subjective refraction procedure to work effectively in finding the optimal correction, as routinely observed in clinical practice. After keratoconus onset, the compact typical pattern forms an asymmetric, disk-like extension that in *18/20* SyntEyes gradually deepens over time into a *shell-like pattern* (Figure 1); the two other SyntEyes formed a knot-like pattern.[19] The shell-like pattern means that the *0.25 D* or even larger steps taken during the subjective refracting process cause less change (flatter slope) in VIQ, thus the difference between the two lens options would be less distinct, making the subjective refraction less effective at finding the optimal correction, as observed in clinical practice with highly aberrated eyes.

For spectacle corrections, the formation of the shell pattern during keratoconus progression often results in the appearance of a second focus[19] between time points *12* and *30* (Figure 1 and Supplement A). This second focus was found in *15/20* SyntEyes and was typically associated with myopic corrections. When keratoconus progresses, the position of both foci within dioptric space can change in three ways, depending on the relative positions of the keratoconus with respect to the pupil: (*1*) an immediate, rapid myopic shift of the first focus without the formation of a second focus. This was seen in *3/20* SyntEyes and aligns best with what is clinically expected in keratoconus. (*2*) In *11/20* SyntEyes the first focus (the best initial correction) shifts towards hypermetropic corrections while a second focus forms (with disease progression) on the myopic side and becomes increasingly myopic. The initial hypermetropic shift may not manifest itself to the patient due to accommodation. Eventually, the second, myopic focus begins to offer the highest, albeit still below typical, VIQ (Figure 1, Supplement A). (*3*) The first focus makes a mild hypermetropic shift, as before, and it continues to offer the best VIQ. Even when the secondary myopic focus appears with progression, it never surpasses the VIQ of the first focus. In these six SyntEyes the dioptric distance between the foci increased faster than in the other two groups, mostly due to the large differences in cylinder.

The previous description shows that there is no uniform course of the refractive changes during keratoconus progression. Even so, it is possible to derive average curves for the hypermetropic and myopic foci to better illustrate the underlying processes. On average, the first focus will become more hypermetropic by about *+1.75D* between time points *0* and *30* (Figure 2a), while simultaneously the cylinder changes by *–2.4D* (Figure 2b), leading to minor increase in spherical equivalent by *+0.6D*. Generally, at approximately time point *12,* the second focus appears on the myopic side of correction space and rapidly becomes more myopic over time (red lines in Figure 2). Because it starts at a poorer level, the decrease in VIQ with progression occurs slower for the myopic focus than for the first, hypermetropic focus (Figure 2f), and from approximately time point *36* onwards, the best spectacle correction is associated with the myopic focus, as is known from clinical experience. Regardless of the case and the focus considered, the VIQ of spectacle corrections in a keratoconic SyntEye is well below typically best-corrected levels. Given the considerable dioptric distance between the two foci (on average 11.63 ± 3.91 *D* at the last stage; Figure 2e), a clinician performing subjective refraction (even using large dioptric steps) that starts near the second-best focus will not be able to find the better focus and vice versa.

The cylinder correction increased as disease severity progressed and comprised more of the vector component J_0 (i.e., with/against-the-rule astigmatism) than J_{45} (i.e., oblique astigmatism). Both vector components tended to increase and move in opposite directions, with the hypermetropic focus associated with against-the-rule astigmatism and the myopic focus with-the-rule astigmatism (Figure 2c). A similar split is seen in the oblique astigmatism (Figure 2d).

Rigid lens corrections also lead to gradual, albeit far less extensive distortions of the hourglass pattern. A double focus may occasionally occur, but these tend to remain in closer dioptric proximity to each other than the spectacle correction condition described above.[19]

Best achievable visual image quality

The best achievable *VSX* during keratoconus progression differs considerably between spectacle or rigid contact lens correction, regardless whether the correction is spherical or sphero-cylindrical (Figure 3). The *VSX* values of the uncorrected SyntEyes begin at a low level, where they remain throughout the disease progression. None of the uncorrected SyntEyes reached the range of typical best-corrected *VSX* values of healthy eyes[13] (blue area in Figure 3a) even at baseline due to uncorrected typical refractive errors. Similar patterns are seen for spherical and toric spectacle corrections. At the earliest timepoints, the optimal sphero-cylindrical spectacles corrected the keratoconic eyes to within normative *VSX* levels of well-corrected typical eyes, but this level could no longer be reached as the disease progressed in severity. Across all timepoints, best spherical spectacles could not correct the keratoconic eyes to within those normative *VSX* levels. The best rigid contact lens corrections provided much more stable *VSX* levels during disease progression. Spherical designs achieved an average *VSX* just below the normal range, but better than spectacle corrections across most timepoints. Conversely, sphero-cylindrical rigid lenses provided an average *VSX* within the best-corrected range of typical eyes over the entire course of the disease.

It is possible to estimate of the number of lines of logMAR visual acuity gained from the correction compared to the uncorrected situation through a regression of previously published data,[18] multiplied by -10 to convert from logMAR to lines of visual acuity:

$$logMAR\ change = -10\cdot(0.371*(log_{10}(VSX_{\text{corrected}}) - log_{10}(VSX_{\text{uncorrected}}))) \qquad (1)$$

Plotting the change in logMAR visual acuity as a function of keratoconus progression (Figure 3b), shows that the average predicted improvements of the best spectacle corrections over the uncorrected condition are stable at *1.75–2* lines of logMAR for spherical corrections and *3.5* lines for toric spectacle corrections. The value of rigid lenses in moderate and severe keratoconus can also be seen in Figure 3b, where the mean improvement from unaided increases from *2.5* to *4.75* lines for spherical lenses and from *3.25* to *5.5* lines for toric lenses as the severity of keratoconus progresses. Although these represent all major clinically significant improvements in VIQ, there are considerable differences between individual eyes, as is expected and clinically observed.

Long-term effectiveness of a given correction

The long-term effectiveness of any given refractive correction during keratoconus progression can be assessed by determining *VSX* at each time point of progression, assuming the previous best correction was retained, mirroring the situation in which a patient does not regularly update the spectacle or rigid lens correction. For spectacle corrections, it is seen (Figure 4) that sticking to old corrections would quickly reduce the *VSX* to values close to the uncorrected case, while for rigid lenses the resulting *VSX* values are considerably more stable over time.

Realistically, patients often cannot afford the costs of frequently updating their prescription, so instead they will seek a new prescription once they notice a significant drop in VIQ. This can be also be modelled, starting from the assumption that all SyntEye wear their best spectacle correction at time point *0*, or are uncorrected if their best correction is below *0.5D*. As the keratoconus progresses, the SyntEyes receive the best correction of the next correction modality (i.e., from uncorrected to spectacles to rigid lenses) each time the eye loses more than one line of logMAR. Applying this to all SyntEyes, *3/20* eyes will start without correction and receive spectacles by time point *18* and rigid lenses at a later point; in *1/20* the spectacle correction remained sufficient throughout the follow-up period. The other *16/20* SyntEyes started with their best spectacle correction and had to be updated to rigid lenses between time points *18* to *60* (Figure 5). Note that in reality some of these patients would initially have worn rigid contact lenses, which may obscure the early sign of keratoconus, thus delaying diagnosis. Instead, these people might have sought a new contact lens prescription to address an increasingly poor fit.

Discussion

The goal of this paper was to combine models of keratoconic disease progression and correction to capture the VIQ experienced by a corrected eye with progressive keratoconus. For the modeling to be effective, it needs to reflect common clinical experience, patient complaints, and provide new insights and future direction.

The model accurately and objectively reflects several common clinical experiences for various levels of disease severity, including the limitations of each type of correction in terms of VIQ. For example, it illustrates why the subjective refraction process works well in typical eyes, due to the monotonic decrease in *VSX* as the correction moves away from the optimal value in phoropter space.[19] This process is much more difficult to perform in highly aberrated keratoconic eyes, as can be seen from the lower *VSX* values and the smaller changes in *VSX* (i.e., flatter slopes) associated with steps of *0.25 D* or larger in any direction of phoropter space (Figure 1). The changes in the refractive components of the best correction (Figure 2) agree with the prevailing experience of correcting progressing keratoconus, such as, the relatively large contribution of cardinal astigmatism (J_0) attempting to correct the emerging vertical coma as best as possible.

Patients also become increasingly dependent on their refractive correction as keratoconus progresses and in later stages of the disease, they tend to require a contact lens correction (Figure 3a). The gain in VIQ provided by a spectacle correction for any given time point in disease progression is short lived and is less satisfactory with time. Meanwhile, rigid contact lenses provide better VIQ than a spectacle correction, which can be within the lower half of the normal range. Rigid contact lenses also provided more stable VIQ at any timepoint as the disease progresses (Figure 4). Finally, the model confirms that a failure to update sphero-cylindrical corrections, using any of the tested correction modalities, will lead to a greater loss in *VSX* compared to the best possible level (Figure 3b), albeit that this is far less critical in rigid contact lenses than in spectacles.

Beyond accurately reproducing known clinical experiences, the model also provides new insight about the optical correction of the keratoconus. For example, when two foci are present the subjective refraction process will not necessarily identify the best of these two foci, and it is highly unlikely that one can traverse a dioptric region of poorer focus to reach the other focus using the standard subjective refraction techniques.[19] This motivates starting subjective refraction from a new or recent objective measure of refractive state rather than the habitual correction.

Visual image quality metrics serve as an objective benchmark for comparison of different correction strategies or modalities. The model is also very flexible and modular and can be easily be adapted to include more accurate measures of the physical parameters of the eye, as well as better VIQ metrics, once they become available. These points make the model an ideal platform to develop and compare new refractive solutions for keratoconus in terms of VIQ.

Another important aspect is a better understanding of patient complaints. Since keratoconus typically onsets between the ages of *18–25* years, patients' visual systems had a chance to develop normally, both refractive and neurologically.[22,23] Consequently, patients will remember having had good vision, will quickly notice any loss in VIQ, and expect a correction that returns their vision to what they had before. The model of keratoconic progression and correction developed in this paper provides objective evidence of this percept in terms of VIQ (Figure 4).

Furthermore, changing or updating a refractive correction usually requires some adaptation by the wearer that is proportional to the difference in image quality between the old and new corrections.[24] Because healthy adult eyes generally exhibit a relatively stable refractive state, the adaptation required is typically small and rapidly performed by the visual neural system.[2] In progressive keratoconus, however, the best refraction can change substantially compared to typical eyes (Figure 1). While individuals with keratoconus do retain the ability to adapt their visual processing long after the sensitive and critical periods of neural development,[22] this adaptation process is gradual compared to the sudden adaptation that is required with a substantial change in correction power. Hence, updating the refractive correction frequently when noticeable visual quality changes occur is also advisable in terms of minimizing the burden of adaptation required – naturally, while balancing this against the economic burden of new corrections.

As illustrated by the large error bars in Figures 2 and 3, one cannot forecast the future progression of keratoconus in an individual patient as it is impossible to know at what stage of their keratoconus development they are at their first presentation. Some degree of short-term forecasting may be possible using machine learning,[25] but this requires tomographical information beyond what the present model provides. Another limitation is that the model does not consider the ocular changes due to physiological aging (e.g., changes in pupil size and exact pupil location, crystalline lens thickness, etc.). But as keratoconus is typically in its progressive phase between the ages of $15 - 30$ years, the expected ageing effects would be relatively minor. Moreover, this work only considers the most ideal situation, excluding the influence of manufacturing errors, the influence of pupil size and position, as well as the misalignment, tilts, or rotations of the corrections. It also assumed that the integrity of the rigid lens corrections remained intact over the course of their wear; this has been shown to be true over a one-year period with a typical cleaning regimen.[26] The current version of the model also uses rather brute force to accomplish its goals by searching the whole dioptric space, thus requiring long computation times. For the model to become clinically adopted, it will require intelligent search strategies that find the correction providing the best image quality in much shorter time, as well as the personalization of the biometry used in the model. Finally, The normative *VSX* values for typically health eyes are based on objectively optimized sphero-cylindrical corrections.[19] The *VSX* values from another, clinical dataset[27] suggest a slightly lower and broader range, which might have led more corrected SyntEyes to fall within to fall within the low end of the normal range, particularly when wearing rigid lenses.

The model can obviously be improved and made more computationally efficient to minimize the current limitations. Likewise, other correction strategies can be evaluated that might benefit individual patients, such as wavefront guided rigid lens corrections.

Conclusion

The model presented here integrates ocular biometry of progressive keratoconus and refractive correction to objectively quantify clinical experience in terms of visual image quality, illustrating the strengths, weaknesses, and longevity of four common correction strategies.

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Figure captions

Figure 1: Changes in logVSX for spectacle corrections with progression of the keratoconus stage for SyntEye KTC 15 plotted in cylindrical coordinates. Changes in the dioptric value of the sphere is plotted vertically. Changes in astigmatism plotted radially according to axis. Black markers indicate the foci; solid marker represents the focus with highest VSX, which are in the green part of the scale initially, but in the yellow part of the scale as the condition progresses.

Figure 2: Average parameter changes of the most hypermetropic (black line) and most myopic (red line) focus across 20 spectacle corrected SyntEyes: a. spherical refractive error; b. cylinder refractive error; c. with/against the rule astigmatism; d. oblique astigmatism; e. dioptric distance between foci; f. visual Strehl ratio VSX. Solid lines and filled markers indicate the focus with the highest VSX; dotted lines and open markers the focus with the lowest VSX. Error bars represent the 95% confidence interval.

Figure 3: a. Average best achievable image quality calculated for 20 SyntEyes KTC represented by the logarithm of VSX as a function of disease progression; b. average improvement in logMAR lines of visual acuity compared to uncorrected vision (zero on the abscissa) as a function of disease progression. Error bars represent the 95% confidence interval. Blue shaded area represents the range of healthy VSX values.

Figure 4: Average long-term stability of visual image quality for best corrections of each correction modality at each time point for 20 SyntEyes KTC as a function of disease progression using (a) spherical spectacles; (b) toric spectacles; (c) spherical rigid lenses; (d) toric rigid lenses. The thick solid and dashed lines represent the VSX of the best correction at each time point; thin lines represent the changes in VSX for earlier best corrections; blue area represents the range of well-corrected VSX values in typical eyes.

Figure 5: Change in best possible visual acuity for two specific case in which the initial spectacle wearer should change to rigid lenses (black and blue lines). Markers represent the correction modality changes for all 20 SyntEyes from spectacles to rigid lenses.

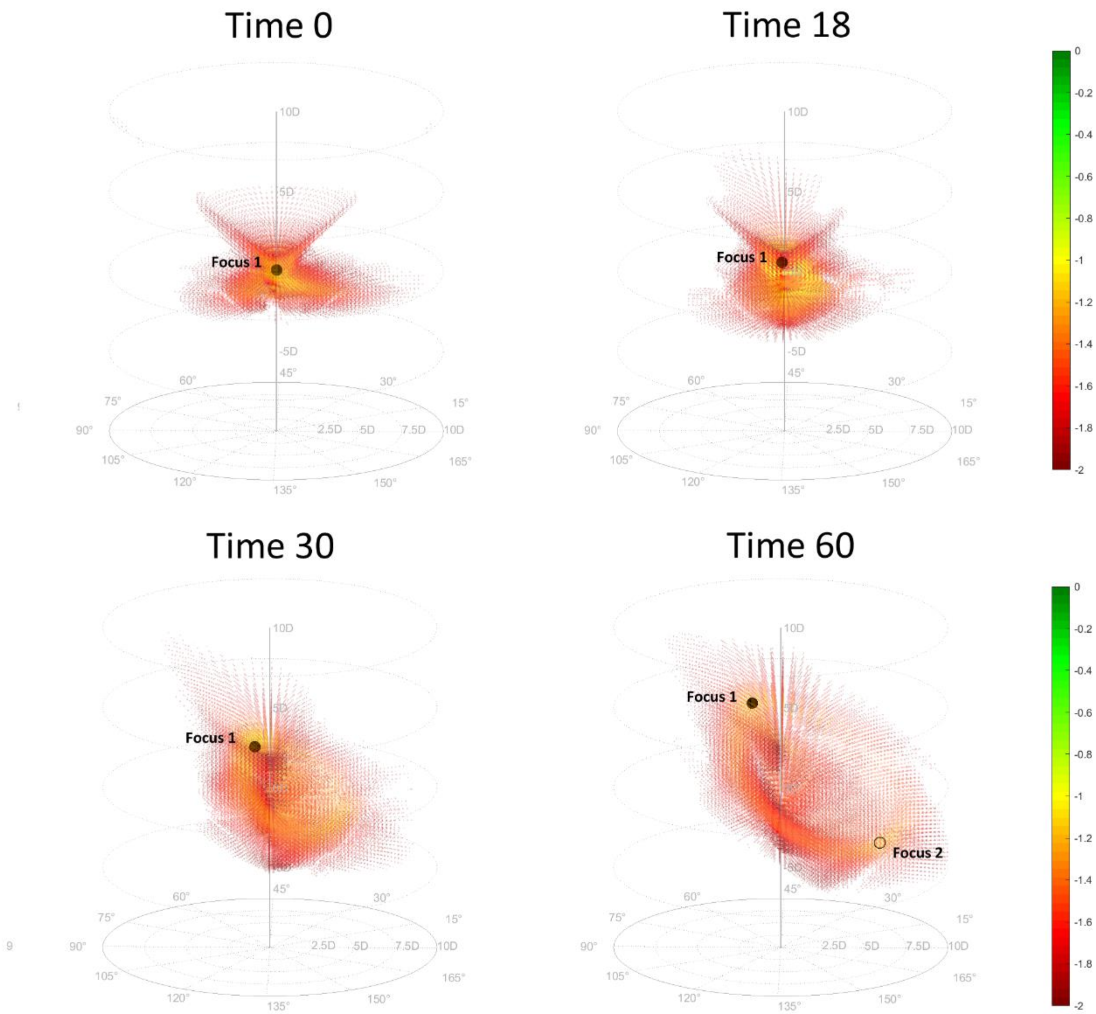
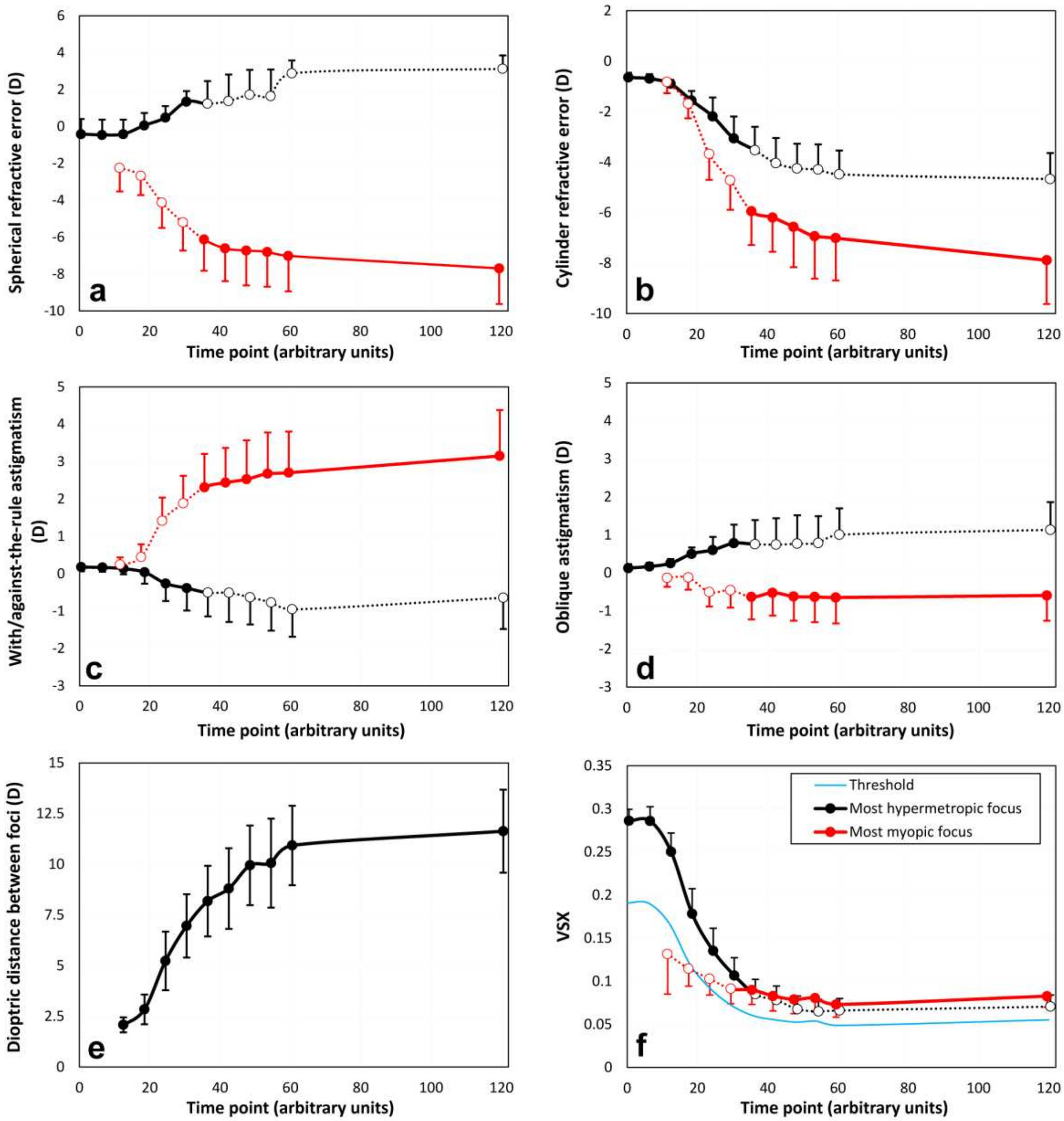

Time 0
Time 18
Time 30
Time 60
Focus 1
Focus 2
10D
5D
-5D
2.5D
5D
7.5D
10D
0
-0.2
-0.4
-0.6
-0.8
-1
-1.2
-1.4
-1.6
-1.8
-2

Figure 1



Spherical refractive error (D)
a
Time point (arbitrary units)
Cylinder refractive error (D)
b
Time point (arbitrary units)
With/against-the-rule astigmatism (D)
c
Time point (arbitrary units)
Oblique astigmatism (D)
d
Time point (arbitrary units)
Dioptric distance between foci (D)
e
Time point (arbitrary units)
Threshold
Most hypermetropic focus
Most myopic focus
VSX
f
Time point (arbitrary units)

Figure 2

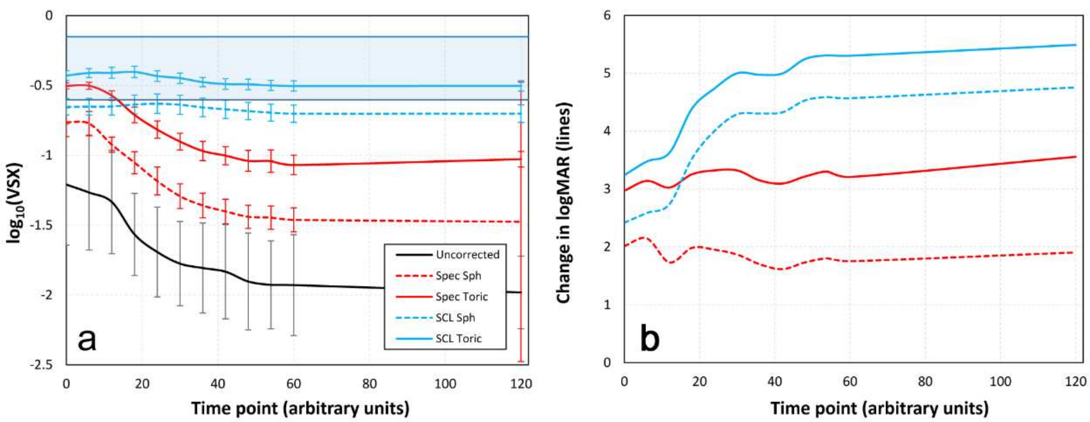


Figure 3

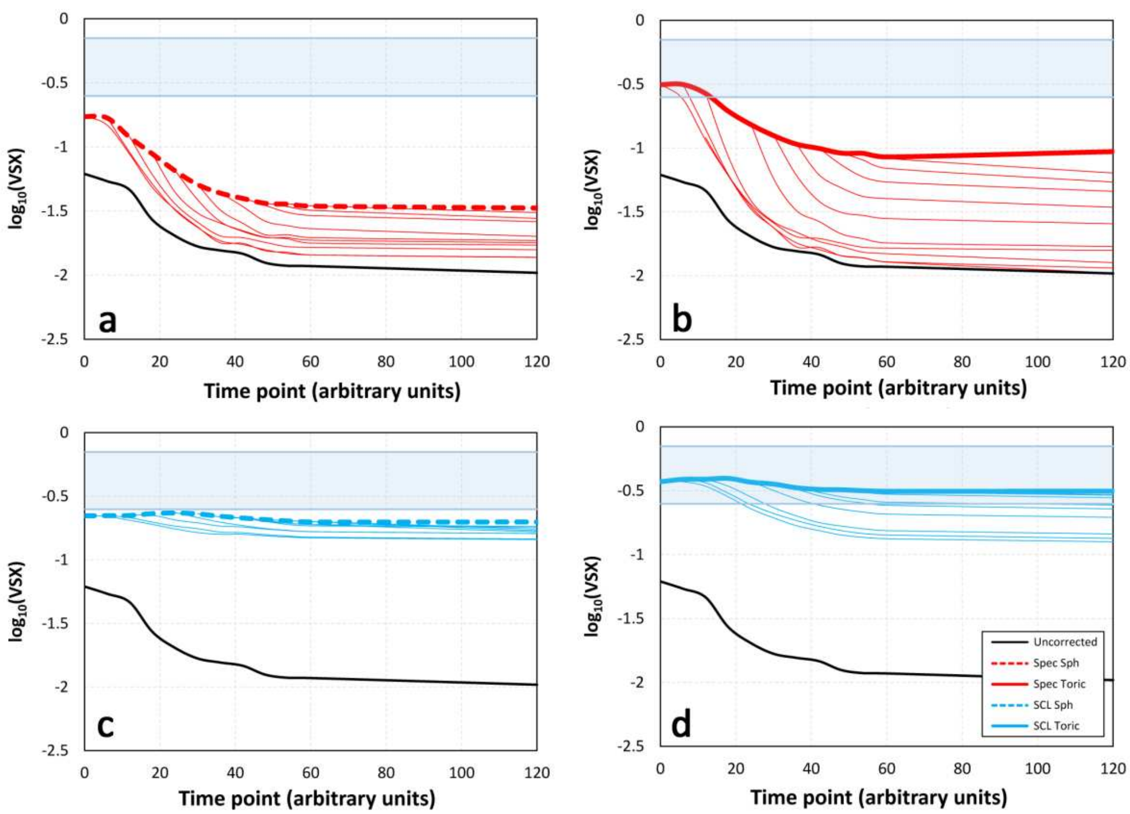


Figure 4

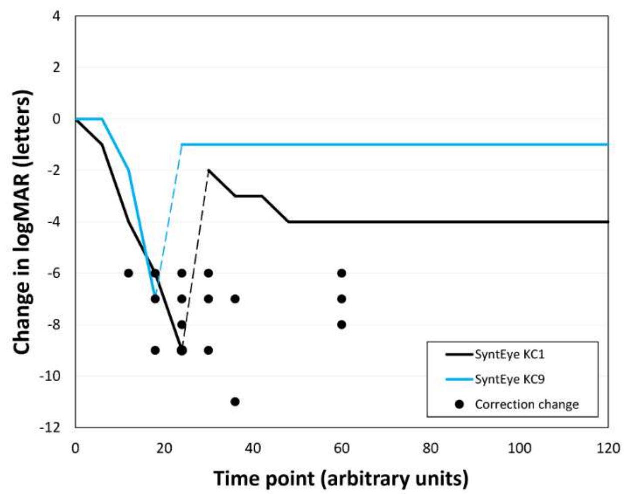

4
2
0
-2
-4
-6
-8
-10
-12
Change in logMAR (letters)
0
20
40
60
80
100
120
Time point (arbitrary units)
SyntEye KC1
SyntEye KC9
Correction change

Figure 5