Quantifying the Optical, Physical, and Predicted Visual Consequences of Daily Cleaning on Conventional and Wavefront-Guided Scleral Lenses

by

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ABSTRACT

Purpose: To test whether an equivalent of 12 months of manual cleaning alters optical aberrations, base curve or predicted visual performance of conventional and wavefront-guided scleral contact lenses.

Methods: Twelve scleral lenses (4 repeats of 3 designs, A-C) were manufactured in Boston XO material. Design A: –5.00 D defocus; Design B: –5.00 D defocus with –0.153 µm vertical coma; Design C: –5.00 D defocus with a full custom wavefront-guided (WFG) correction (2nd - 5th Zernike radial orders) of an eye with severe keratoconus. One lens of each design group served as a control and was not cleaned. To simulate a year of cleaning, 7 individuals cleaned 9 lenses (3 from each group) twice a day for 27 days using the palm technique and commercially available cleaners, resulting in 378 cleanings of each lens. Lens aberrations were optically profiled and base curve radii were measured at baseline and after every 42nd cleaning. Differences in higher order root mean square (HORMS) wavefront error (WFE) and base curve radii associated with cleaning were compared to clinical benchmarks using sign tests. Given that aberrations interact with one another, the change over time in the visual Strehl ratio was used to estimate the predicted change in visual acuity associated with manual cleaning.

Results: For the experimental lenses, median change in Seidel spherical dioptric power was +0.01D (range: +0.001D to +0.023D). Median change in HORMS WFE was 0.013 µm (range:0.008 to 0.019 µm). Median percent change in HORMS in the three wavefront-guided lenses was 0.96% (max = 1.25%). Median change in base curve radii was 0.00 mm, with all lenses exhibiting changes (P = .002), less than the ANSI tolerance of 0.05 mm. The predicted change in visual acuity derived from the visual Strehl ratio for all coma and wavefront-guided lenses was less than 2.5 letters.

Conclusion: Cleaning scleral contact lenses in a manner consistent with the method and number of cleanings that would occur over a 12-month period did not induce clinically significant changes in the optical properties, base curve radii of curvature or predicted changes in visual acuity of conventional or wavefront-guided scleral lenses.

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CHAPTER 1: BACKGROUND

The Eye and Refractive Error:

The human eye collects electromagnetic radiation from the external environment and transforms this radiation into action potentials that exit the eye via the optic nerve. This conversion of light into neural signals begins when light within the visible spectrum is absorbed by a photoreceptor found in the outer retina. The focusing of light from the environment onto the retina is accomplished by two main refractive elements in the eye: the cornea and the crystalline lens. The majority of the refractive power of the eye originates at the anterior surface of the cornea, resulting from the large change in refractive index that occurs moving across the curved air/tear interface. The air/tear interface accounts for about $^{2}/_{3}$rds of the dioptric power of the eye, with the posterior corneal surface and crystalline lens account for the remaining $^{1}/_{3}$rd of the focusing power of the eye.[1] In addition, the crystalline lens has the ability to change shape (a process known as accommodation) and add optical power to the eye. This is beneficial to vision, as it allows for a clear image to be formed on the retina for different object distances. Ideally, light from a distant object will be refracted through the optical elements of the eye and brought to a focus on the fovea (the area of the retina with the highest density of cone photoreceptors) when accommodation is relaxed, allowing for the resolution of fine visual detail. When this ideal condition occurs in an eye, the eye is said to be emmetropic. However, this condition does not always exist, and eyes that are not emmetropic exhibit some level of refractive error, or mismatch between the optical power of the elements of the eye and the eye's axial length.

Quantifying and Classifying Refractive Error:

The most common refractive errors (spherical and cylindrical errors) are classified clinically by the optical elements (or lenses) that are utilized to correct them. For instance, a 2D myope is an individual that needs a -2D spherical lens to correct their refractive error. This lens has the same power in all meridians and will result in the focus of light moving back from a location somewhere inside the globe to a location closer to or falling on the retina. Moving up in complexity from simple spherical error, an individual may exhibit astigmatic refractive error, or a focusing error that requires a cylinder lens (0 power in one meridian, + or – power in the orthogonal meridian). The majority of the typically sighted population is well-corrected (achieving 20/16 acuity) with some combination of spherical and cylindrical lenses.[2] This is not true of eyes that suffer from corneal ectasias, such as keratoconus, Pellucid Marginal Degeneration, and post-refractive surgery ectasia. While each of these conditions presents from their own unique etiology, the outcome is the same: refractive error that is not well corrected, or even described, in conventional dioptric terms.

The Zernike polynomial is a mathematical function that describes a 3-dimensional surface over a unit circle.[3] This feature makes the Zernike polynomial a good system for describing the optical performance of the eye because the limiting aperture of the eye is round. When applied to the eye's refractive error, individual components of the Zernike polynomial are commonly referred to as Zernike aberrations (denoted as Z), and the amount of each aberration term present is reported with a Zernike coefficient (denoted as C).

Zernike coefficients can be reported in several different ways, including a single-index notation and a double-index notation.[5] The single-index designation numbers the Zernike coefficients starting with piston designated with a 0, tip and tilt with 1 and 2 respectively, and continues with increasing numbers for each coefficient. For instance, vertical coma is designated as Z7, and the amount of vertical coma present would be denoted with C7. The double-index designation gives more information for each coefficient as it uses both the angular frequency and radial order to create a unique description. For instance, Z7, vertical coma, is denoted with Z^{-1}_{3}, with the superscript, -1, being the angular frequency (m) and the subscript, 3, being the radial order (n). This designation can be created for all the Zernike coefficients and makes identifying them easier. Similar nomenclature is used for all single- and double-index Zernike aberration terms.

Individual aberrations terms can be further classified as lower-order (radial order $n \leq 2$) or higher-order aberrations (radial order $n > 2$). The portion of the Zernike polynomial referred to as lower-order aberrations consist of piston, tip, tilt, astigmatism and defocus.[3,4] Piston (radial order, $n = 0$) is a mathematical constant which is applied equally to the entire wavefront error surface and does not affect optical quality. Tip and tilt (radial order, $n = 1$) also do not affect optical quality, but they do shift the image in the plane of the retina. Defocus and astigmatism (radial order, $n = 2$) describe focusing errors of the eye, and these focusing errors can be corrected with conventional sphero-cylindrical spectacle and soft contact lenses. Unlike lower-order aberrations, higher-order aberrations (radial order, $n > 2$) are not corrected with conventional optics available in the clinic.

Metrics:

The Zernike polynomial can be helpful in identifying how much of an individual aberration is present in an eye (e.g. defocus (C4) or vertical coma (C7)). However, interpreting the importance of individual aberration terms becomes more difficult when many aberration terms (which are necessary to describe the optical performance of the eye) are considered at once. Therefore, several summary metrics have been developed that take these individual Zernike coefficient terms and combine them mathematically into a single value. By far the most common single value metric is root mean square (RMS) wavefront error (WFE), which can be calculated by taking the square root of the sum of the squares of a given set of Zernike coefficients. Higher-order RMS (or HORMS) is calculated by taking the square root of the sum of the squares of terms in the 3^{rd} through the n^{th} radial orders. The benefit of HORMS is that it can easily be examined and compared to normative values available in the literature as a function of both pupil size and age. Thus, with a single measurement, an examiner can know if the level of aberration present is consistent with age and pupil-matched norms. However, while HORMS can be used to compare to normative values, it cannot be used to predict an individual's level of visual performance.[6]

The visual Strehl ratio (VSX) is another metric that uses the aberrations of the eye in its calculation.[7] Unlike HORMS, VSX contains an estimate of the neural processing capability of the eye. With this additional factor as an advantage, change in VSX has been shown in several studies to predict change in visual acuity and to find optimized spectacle refractions.[8,9] Ravikumar described a method that uses a change in logVSX to determine a predicted change in visual acuity.[9] These predictions are possible because VSX considers the manner in which interactions between the individual aberration terms affect vision. Other studies have also found that the interaction of the aberrations is important to determine visual quality.[10,11] VSX ranges from 0 to 1, with 1 being the best visual image quality. Hastings et al. found that VSX was higher in young eye and higher in smaller pupils, with the best VSX being in 20-29 years old with 3 mm pupils. VSX was shown to change more with pupil size than change in age. In the Hastings et al. study, the mean VSX of a normal eye with conventional sphere cylinder, and axis correction fora 3 mm pupil was 0.661+/-0.143.[12]

Keratoconus:

Keratoconus is a bilateral, yet asymmetric, ectatic disorder of the cornea that causes central or paracentral corneal thinning.[13] The onset of this disease is typically around puberty and progresses until the fourth decade of life, when progression tends to slow or halt altogether.[13,14] A common historical estimate of the prevalence of keratoconus was 1 in 2000 people in the general population[13], but more recent work from 2016 suggests that the prevalence is much higher, reporting that 1 in 375 people in a national health program had corneal characteristics consistent with keratoconus.[15] Like many other chronic illnesses, keratoconus has been shown to be associated with depression.[16] Disease progression in keratoconus leads to a thinning and protrusion in the central or para-central cornea. The cone-shape cornea can produce high myopia, high levels of astigmatism, and high levels of higher-order aberrations. Higher-order aberrations are present in all eyes (both typical and diseased). In conditions such as keratoconus, higher-order aberrations are elevated well-beyond the levels seen in typical eyes, and the presence of these elevated higher-order aberrations reduces visual acuity.[17] Further exacerbating the problem, higher-order aberrations are not correctable with commonly prescribed soft contact lenses and spectacles. Conventional spectacle lenses are not able to mask the higher-order aberrations as they do not rest on the cornea and only target the lower-order aberrations of defocus and cylinder. Sphero-cylinder soft contact lenses, similarly, only target lower-order aberrations. Instead, rigid gas permeable (RGP) lenses are used to reduce the deleterious impact of higher-order aberrations. RGP lenses use the lens and tear layer to create a new first refractive surface, reducing the higher-order aberrations created by the anterior cornea.[18]

Scleral Contact Lenses:

The scleral contact lens is a form of rigid contact lens that is enjoying a significant resurgence in popularity. Scleral contact lenses were first described in 1888 by Mueller, Fick, and Kalt, and demonstrated clinically as blown or ground glass shells.[19] Due to corneal hypoxia observed with these glass lenses and the emergence of other, smaller diameter contact lens designs, scleral lenses popularity diminished in the mid 1900's. In the 1980s, scleral lenses began to make a comeback, as they were now manufactured in gas permeable materials that allow significantly more oxygen to reach the cornea.[19] Scleral contact lenses have been shown to be primarily used to improve vision in corneal degeneration, corneal dystrophies (such as keratoconus), post-surgical ectasias, and high refractive errors.[20,21] They can also be used to restore and maintain the corneal integrity of ocular surface diseases such as corneal stem cell disorders and severe dry eye.[20]

As discussed before, patients with keratoconus and other corneal ectasias have decreased vision that is attributed to elevated higher-order aberrations caused by irregularities of both the anterior and posterior corneal surface.[1,22] Scleral lenses are able to partially mask the optical irregularities produced by the anterior cornea through the formation of a tear lens between the posterior surface of the lens and the anterior surface of the eye. However, due to the imperfect refractive index matching and the irregular posterior cornea, residual higher-order aberrations remain in addition to the aberrations originating at the posterior cornea and lens.[22,23,24] Thus, scleral lenses are not able to fully correct for the higher-order aberrations present in ectatic conditions.

The ability of rigid lenses to reduce aberrations originates from the fact that they retain their shape when placed on the eye, rather than conforming to the shape of the cornea as occurs with soft lenses. The rigidity (or hardness) of the lens is material-dependent and quantified as the hardness of the material. Hardness is quantified as the resilience of the plastic to resist change.[25] The plastics that scleral lenses are made from are tested using specifically the Shore D hardness test, which uses a pointed cone with a minimally rounded tip indenter to test the plastic's resilience.[25] The scale range is from 0 to 100, with 0 representing a less hard material and 100 representing a material that will not allow any deformation. Thus, the higher the shore D hardness value, the more resilient the plastic is to change.[25] Clinically common scleral lens materials range from 78 to 83 on the Shore D hardness scale, meaning they are relatively resistant to outside forces resulting in a change to the plastic.[26-29]

As scleral lenses have the potential for a long service life (on the order of a year or more), proper daily care is critical. Manual rubbing with a cleaning agent is a commonly prescribed method for cleaning the lenses. It has been shown in rigid gas permeable lenses that this manual cleaning of the lenses has the potential to cause warpage and power changes over time.[30]

Wavefront-guided Optics and Scleral Lenses:

Aberration measurements have been integrated with contact lenses to target the residual lower- and higher-order aberrations.[22,23] These optics, referred to as wavefront-guided corrections, are created with rotationally asymmetric submicron contours (lathed into the correcting lens. Wavefront-guided technology has been used in soft contact lenses, resulting in reduced higher-order aberrations.[31,32] However, scleral lenses offer more on-eye stability and an easier platform for customization. Like soft lenses, wavefront-guided scleral lenses have also been shown to reduce higher-order aberrations in patients and improve visual acuity.[22,23,31,32,33] Hasting et al. found that while the best correcting conventional, sphero-cylindrical scleral lens increased visual acuity as compared to the habitual correction that the patients had, they still did not decrease the average HORMS to within the 95% confidence interval around the mean higher-order aberrations experienced by typical eyes. However, with the wavefront-guided correction, average HORMS did decrease to within the 95% confidence interval experienced by typical eyes.[22]

Significance of this Thesis:

Successful implementation of a wavefront-guided scleral lens is the result of meticulous effort that goes into first fitting a conventional scleral lens, and then requires integration of wavefront-guided optics into the conventional lens design. This additional level of effort will be reflected in the price of the lenses as they become more commercially available to patients who need them most.

Due to the current replacement schedule of scleral lenses (lasting up to a year or longer) these lenses require a cleaning protocol that involves mechanical rubbing of the lens to break help down deposits on the lens surface. This type of cleaning protocol involves instilling a certain amount of cleaner, which can be a multipurpose solution, an extra strength cleaner, or an abrasive cleaner and then using the index finger to rub both sides of the lens for a certain length of time.

With the submicron correction designed into the wavefront-guided scleral lenses, little is known regarding how this mechanical cleaning process impacts the optical correction in the lens. Given the added expense associated with successfully fitting these lenses, clinicians and patients that are committing to them need to have a general understanding of the expected duration of time over which the lenses will function as designed, and thereby know a general replacement schedule.

As a step toward answering these questions, this study aims to test the resilience of both conventional and wavefront-guided scleral lenses to the manual daily cleaning process.

CHAPTER 2: QUANTIFYING THE OPTICAL AND PHYSICAL CONSEQUENCES OF DAILY CLEANING ON CONVENTIONAL AND WAVEFRONT-GUIDED SCLERAL LENSES

Reprinted with modifications from: Wilting SM, Hastings GD, Nguyen LC, Kauffman MJ, Bell ES, Hu C, Rijal S, Marsack JD. Quantifying the optical and physical consequences of daily cleaning on conventional and wavefront-guided scleral lenses. Optom Vis Sci. 2020 Sep;97(9):754-760. This paper is included with permission from the publisher; no formal license number is required for use by the author in a thesis.

Scleral lenses were the first successful form of contact lens correction and are currently undergoing a resurgence due to 1) the development of materials with high oxygen transmissibility and 2) the ability of the lenses to vault the cornea.[34] Scleral lenses are more commonly used with patients suffering from corneal ectasias and other ocular surface diseases, including dry eye, as they provide a smooth first refractive surface for the eye[34,35] and have also served as an effective vehicle for wavefront-guided corrections that target residual higher-order aberrations during conventional rigid lens wear.[22,23,24] Physical daily cleaning of scleral lenses is essential in limiting deposition on the lens surfaces.[36]
The efficacy of wavefront-guided scleral lenses depend on submicron non-rotationally-symmetric contours in the optical zone surface of the lens to correct both lower-order (defocus and astigmatism) and higher-order aberrations (e.g. coma, spherical aberration, secondary astigmatism).[23,24] While the short-term efficacy of wavefront-guided scleral lenses has been demonstrated by several [5,22,23,24] groups, there has yet to be an investigation looking at the resilience of the wavefront-guided correction to typical cleaning and degradation over long periods of time. The longevity of both conventional and wavefront-guided scleral lenses

leaves them vulnerable to possible changes in optical and physical properties including base curve, refractive power, etc. One source of this potential degradation is the manual daily rubbing of the lens surfaces with fluid-based cleaners. The purpose of this study was to investigate whether a simulated year of manual cleaning alters the optical corrections and physical properties of both conventional and wavefront-guided scleral lenses.

Methods:

SCLERAL LENS DESIGNS

Twelve scleral lenses were designed and manufactured in Boston XO material (Dk = 100, Bausch and Lomb, Rochester, New York) at the Visual Optics Institute, University of Houston College of Optometry (Houston, Texas) using a common macro lens design, with the only variation in design across the individual lenses being the intended optical corrections. All lenses had a 7.2 mm base curve radius and six posterior surface zones (curves). More detailed descriptions of lens design and manufacture processes have been reported previously.[22,24]

The 12 lenses comprised three optical corrections:

- Design A (four lenses): – 5.00 D of defocus (Figure 2.1a).
- Design B (four lenses): –5.00 D of defocus with -0.153 µm vertical coma over a 6 mm diameter centered on the geometric center of the lens (Figure 2.1b) (this was the median residual vertical coma correction of 20 eyes with keratoconus from a previous study [22,37]).
- Design C (four lenses): –5.00 D of defocus with a custom wavefront-guided correction (2^{nd} through 5^{th} Zernike radial orders[38] intended to correct one eye with

severe keratoconus, 3^{rd} – 5^{th} HORMS = 1.382 µm; 6 mm diameter) over a decentered optical zone (Figure 2.1c).

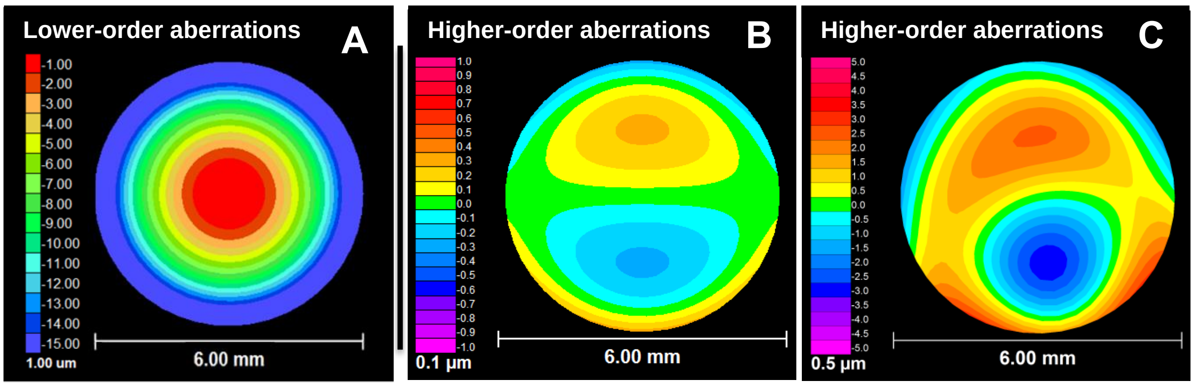

Figure 2.1. Aberration structures integrated into the three different designs. (A) Defocus (–5.00 D) common to all lenses manufactured and the only aberration designed into Group A. Note that a nonstandard color scheme is used here. Typically, the center of the map is referenced as green, and all other colors are referenced from that green area. We have chosen to keep the map in this format to be consistent with prior demonstrations of this map. (B) Vertical coma (–0.153 µm over a 6mm pupil) incorporated into Group B lenses. (C) Higher-order aberration structure incorporated into Group C lenses (a 2nd to 5th Zernike radial order correction, 3^{rd} – 5^{th} higher-order RMS wavefront error = 1.382 µm). The different aberration scales in Figures 2.1A-C were necessitated by the different aberration magnitudes across lens groups. Though all lenses were designed with defocus, Figures 2.1 B and C only show the higher-order aberrations designed with the lens. The defocus has been removed from the figure in order for the higher-order aberrations to be more visible.

Prior work found a mean displacement of -0.49 mm (inferior) in the horizontal direction and -0.48 mm (temporal) in the vertical direction when scleral lenses were worn on the eye.[22] To counteract this displacement of the scleral lens on-eye, in group C, the wavefront-guided correction patch in Design C was decentered by +0.49 mm in the horizontal direction and +0.48 mm in the vertical direction.

CLEANING PROTOCOL

One lens from each group was exempt from the cleaning protocol and served as a control. These three control lenses were optically profiled on the same schedule as the experimental lenses in each group. The nine experimental lenses (three lenses from each of the three groups) were cleaned in random order by seven masked individuals twice a day, three days a week for nine weeks, for a total of 378 cleaning sessions per lens. This equates to just over one year of cleaning under real world conditions (cleaned once a day for 365 days). The masked individuals consisted of 3 women and 4 men. All individuals followed a controlled cleaning procedure, as described below:

For every day of cleaning (14 cleanings of each individual lens), Unique pH daily cleaning solution (Menicon, North Billerica, MA) was used 10 times and Optimum Extra Strength Cleaning (ESC) solution (Lobob Laboratories, San Jose, CA) was used four times. Though Optimum ESC can be purchased and used as a "total care system" with other Lobob products, in this experiment only the ESC cleaner portion of the Optimum total care system was used. This ratio of Unique pH to ESC is a clinically representative ratio of using a stronger cleaning solution 1 to 2 times a week to remove deposits. The order of cleaning solutions used and order in which individuals performed the cleanings were randomized. Table 1 represents an example of a daily cleaning schedule.

Table 2.1. Example assignments for a day of cleaning.

Individual Performing Cleaning	Cleaning Solution Used	Experimental Lens Number								
Individual Cleaner 1	Unique pH	1	3	2	4	5	7	8	9	6
	Optimum	3	4	1	6	8	9	7	5	2
Individual Cleaner 2	Optimum	2	9	1	4	7	8	5	6	3
	Unique pH	1	5	8	4	6	9	7	2	3
Individual Cleaner 3	Unique pH	3	8	5	6	4	1	7	2	9
	Unique pH	7	1	8	2	6	5	3	9	4
Individual Cleaner 4	Unique pH	7	3	5	2	4	8	6	9	1
	Optimum	1	6	2	7	9	5	8	3	4
Individual Cleaner 5	Unique pH	1	3	2	4	5	7	8	9	6
	Unique pH	5	1	6	9	7	2	3	4	8
Individual Cleaner 6	Optimum	1	5	9	6	4	2	8	3	7
	Unique pH	8	9	1	7	5	4	3	6	2
Individual Cleaner 7	Unique pH	9	5	1	2	6	7	8	4	3
	Unique pH	4	2	7	3	9	5	8	1	6

The 9 experimental lenses (3 lenses from each of the 3 groups, labeled here as lenses 1-9) were cleaned in random order by 7 masked individuals twice a day. For every day of cleaning (14 cleanings of each individual lens), Unique pH daily cleaning solution (Menicon, North Billerica, MA) was used 10 times and Optimum ESC solution (Lobob Laboratories, San Jose, CA) was used 4 times. This process (including re-randomization of lens order and the type of cleaner used by individuals performing the cleaning) was repeated on 27 separate days, resulting in each lens being cleaned 378 times.

The seven individuals (labeled Individual Cleaner 1 – Individual Cleaner 7) were randomly assigned either Unique pH cleaning solution (Unique pH) or Optimum extra strength cleaning solution (Optimum) to clean the nine experimental lenses in a randomized order.

Each time a lens was cleaned, it was removed from the lens case and rinsed with saline solution. Lenses were cleaned using the *palm method*: while in the palm of one hand, either five drops of Unique pH or three drops of Optimum were applied onto the concave surface of the lens, after which the index finger of the fellow hand was used to rub the lens.[40] Cleanings were timed, so that both the concave and convex surfaces were rubbed for 15 seconds each. After each lens was cleaned, it was rinsed with saline solution and returned to the lens case. Between cleanings, lenses were stored in Unique pH, which was drained and replaced daily. For consistency across all lenses, control lenses were also stored in Unique pH, which was drained and replaced daily.

OPTICAL AND PHYSICAL CHARACTERIZATION OF LENSES

The optical aberration structure of each lens was profiled over a 6 mm pupil diameter after manufacture and prior to the initiation of the cleaning protocol, and after every 42nd cleaning (equivalent to once every six weeks of real-world cleaning) using a SHSOphthalmic Optical Profiler (Optocraft, Erlangen, Germany). Given the cleaning schedule, this corresponded to aberration measurement of the complete set of lenses once per week during the execution of the study. Using the 5 markings on the surface of the lenses, the intersession alignment tolerance of the optical profiler was set at 0.2° (rotation) and 0.1 mm (translation) which minimized the potential of differences due to misalignment of the lens during measurement (Figure 2.2). The absolute sensitivity of the Optocraft was previously reported to be 0.002 µm (total root mean square wavefront error) and 0.001 µm (higher-order root mean square wavefront error) over a 6 mm pupil diameter.[37]

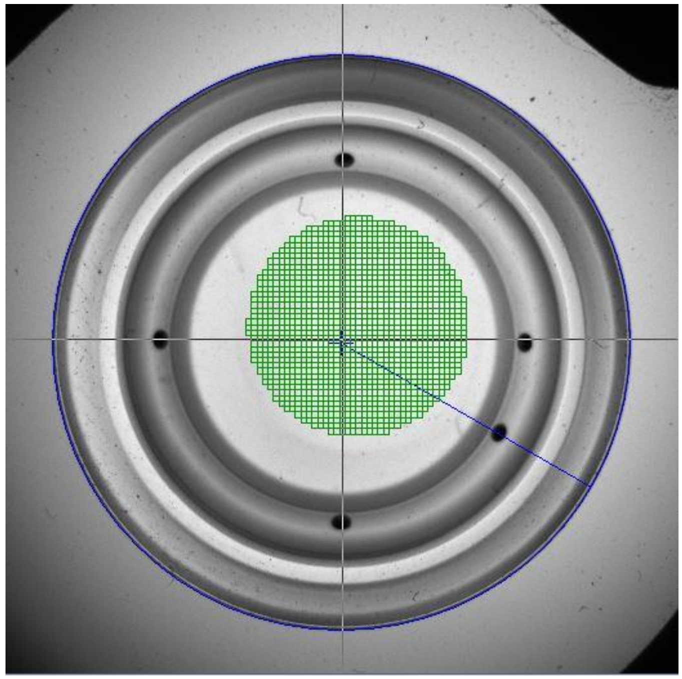

Figure 2.2. View of a lens from Group C (wavefront-guided (WFG) lens group) during measurement with the SHSOphthalmic Optical Profiler. The five black dots on the lens surface are aligned to within 0.2° (rotation) and 0.1 mm (translation). The green patch denotes the 6 mm diameter area of wavefront measurement, and in this example, is located over the offset WFG correction optics.

The higher-order root mean square wavefront error for each lens was calculated from the intra-lens aberration differences over time. The spherical dioptric power was calculated using the Seidel conversion, which considers the impact of spherical aberration.[7] The base curve of each lens was measured at baseline and after 378 cleanings using a M30195 radius gauge (Marco, Jacksonville, FL) equipped with a U30 digital-radius indicator (Sony, Tokyo, Japan).

The 378 cleanings occurred over a total of 64 days, which include the 27 days the lenses were cleaned and 37 days which the lenses were stored and not cleaned or were being measured, over the Summer of 2018. In order to differentiate the potential effects of cleaning from the passive aging of the lens material, the lenses were measured again during the Summer of 2019, after an actual year of dry storage.

ANALYSES

Sign tests were performed against clinical benchmarks on intra-lens aberrations and base curve changes observed between baseline and after 378 cleanings. The differences were considered significant if the *P*-value was less than 0.05. This is to say, that a statistically significant finding will be a finding that is different than the clinical benchmark.

Results:

CHANGE IN SPHERICAL POWER BETWEEN BASELINE AND AFTER ONE YEAR OF CLEANING

The median change after 378 cleanings in Seidel spherical dioptric power was +0.010 D (Figure 2.3) and values ranged from +0.001 D to +0.023 D. All experimental lenses experienced a positive shift in spherical power, however that shift was less than a benchmark of 1/8th diopter in all cases (P = .002). Changes observed in control lenses that were not cleaned are plotted for reference and are on the same order of magnitude as those observed for cleaned lenses.

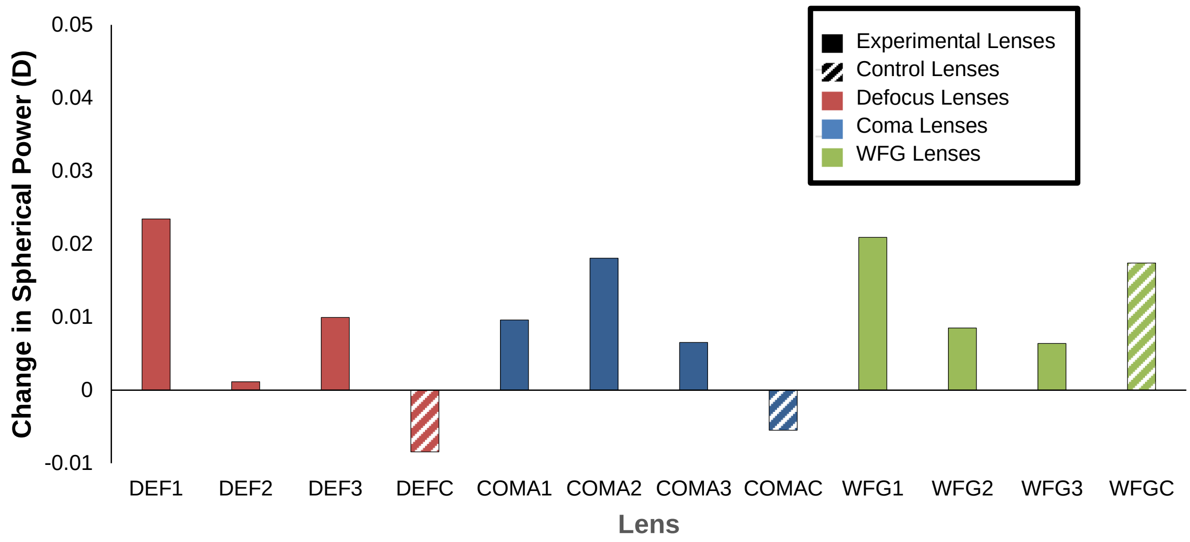

Figure 2.3. Change in spherical dioptric power for each lens between baseline and after one simulated year of cleanings. DEF1-3 (solid red), COMA1-3 (solid blue), and WFG1-3 (solid green) are the experimental lenses in groups A, B, and C respectively. DEFC, COMAC, and WFGC (hatched bars) are the controls that were not subject to cleaning.

CHANGE IN HIGHER-ORDER ROOT MEAN SQUARE WAVEFRONT ERROR BETWEEN BASELINE AND AFTER ONE YEAR OF CLEANING

The median change after 378 cleanings in higher-order root mean square wavefront error was 0.013 µm (Figure 2.4) and values ranged from 0.008 µm to 0.019 µm. All lenses exhibited HORMS changes less than a benchmark of 1/8th equivalent diopters (P = .002).[38] It is important to note that 'equivalent diopters' are not equivalent to 'diopters'. Changes observed in control lenses that were not cleaned are plotted for reference and are on the same order of magnitude as those observed for cleaned lenses. The median percentage change in HORMS seen in the three wavefront-guided lenses was 0.96%, with the maximum change being 1.25%.

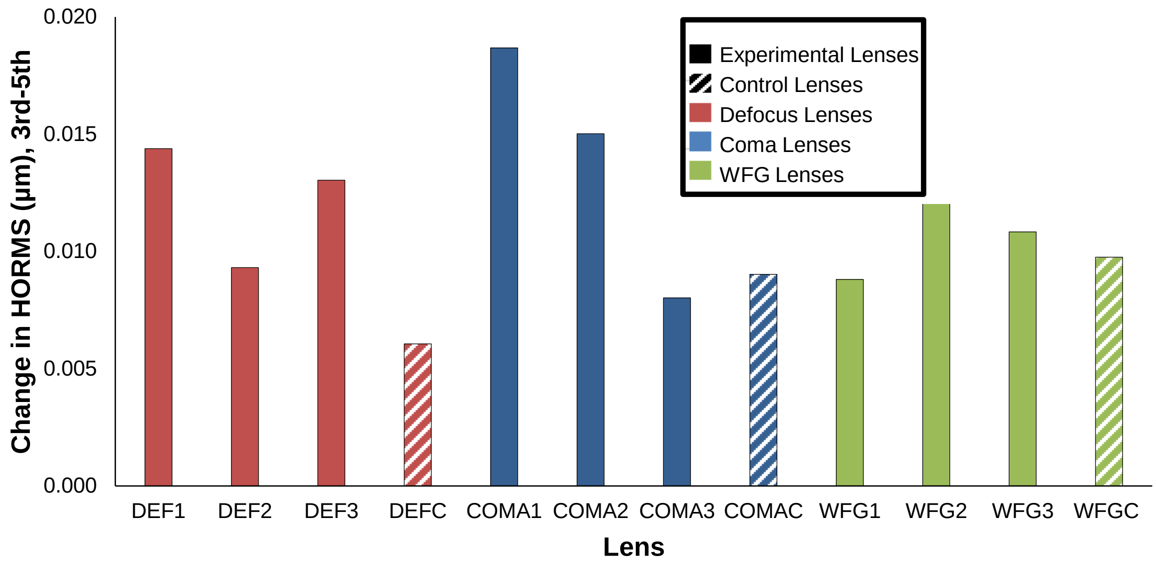

Figure 2.4. Change in higher-order root mean square wavefront error for each lens between baseline and after one simulated year of cleanings. DEF1-3 (solid red), COMA1-3 (solid blue), and WFG1-3 (solid green) are the experimental lenses in groups A, B, and C respectively. SPHC, COMAC, and WFGC (hatched bars) are the controls that were not subject to cleaning.

In addition to examination of change in higher-order root mean square wavefront error, individual 2nd – 5th order aberration terms were also examined after every 42nd cleaning, equating to once a week during the execution of the experiment. Figure 2.5 shows the trend in higher-order aberration terms for the lens that exhibited the largest change for any one higher-order aberration term from any lens over any period of time (WFG3, ΔC7 = 0.027 µm, week 1 to week 7).

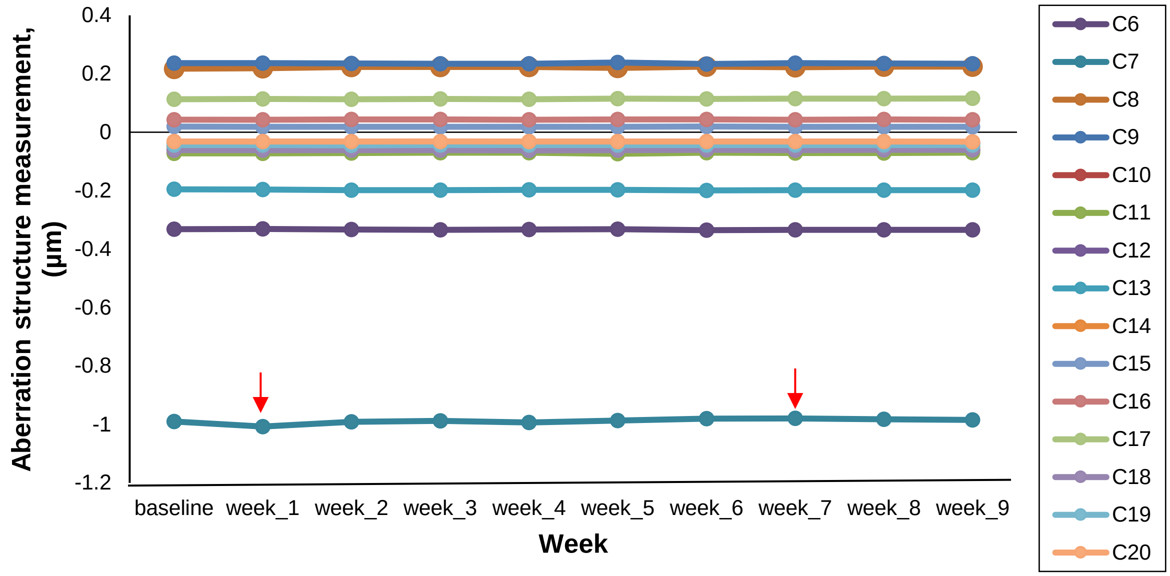

Figure 2.5: Individual 3rd – 5th order Zernike aberration terms by week (after every 42nd cleaning) for wavefront-guided lens WFG3. The largest change for any one higher-order aberration term from any lens cleaned during the study over any period of time was 0.027 μm (WFG3, ΔC7, week 1 to week 7), which is denoted by red arrows.

The measured change in a single lens over time due to cleaning was also compared to the repeatability of manufacturing the same design of the four lenses in each particular lens group (Figure 2.6). Repeatability here is defined as the standard deviation of the higher-order root mean square measured at baseline across the four lenses manufactured (three experimental lenses and one control lens). The observed changes for the three groups were all smaller than the changes seen across lenses due to manufacture and were all substantially lower than the ANSI tolerances for sphere and cylinder manufacture.

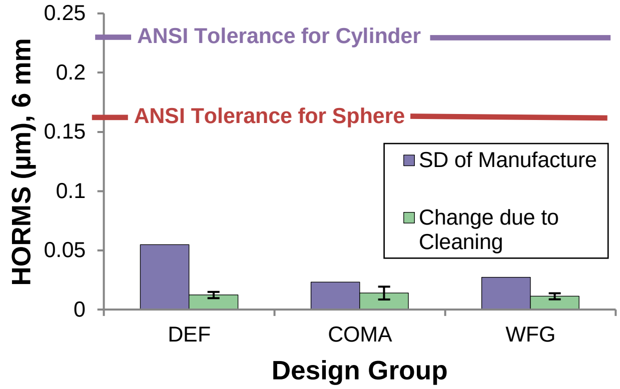

Figure 2.6. Change due to cleaning versus manufacturing. Standard deviations (SDs) of higher-order root mean square (HORMS) (3rd through 5th Zernike radial orders) wavefront error (WFE) for baseline measurements of each group and the average change of HORMS WFE due to cleaning. The red and purple horizontal lines denote the ANSI tolerance for defocus and cylinder manufacture (expressed in microns over a 6 mm pupil diameter) respectively.

CHANGE IN HIGHER-ORDER ROOT MEAN SQUARE WAVEFRONT ERROR BETWEEN BASELINE AND AFTER ONE YEAR OF DRY STORAGE

This experiment simulated 12 months of cleaning by compressing the cleanings into 64 days. Therefore, the change in lenses due to passive aging could not be measured during the initial summer. In an effort to examine the effect of passive aging of the lens over an actual 12-month period, the lenses were measured after an actual one year (time between first measure first summer and measures in second summer). The median change in sphere in all cleaned lenses was –0.003 D, with the largest change being +0.032 D and the median change in higher-order root mean square wavefront error in all cleaned lenses was 0.013 µm, with the largest change being 0.019 µm.

CHANGE IN BASE CURVE BETWEEN BASELINE AND ONE YEAR OF CLEANING

As seen in Figure 2.7, the median change in base curve radii was +0.00 mm (three of the experimental lenses exhibited this absence of change), with all lenses exhibiting change less than the ANSI tolerance benchmark of 0.05mm (P = .002). One experimental lens from Group A chipped after 16 weeks of simulated cleaning. The damage was limited to the periphery. As the chip did not involve the area over which aberrations were profiled or base curves measured, the lens continued to be cleaned and measured for the remaining cleanings.

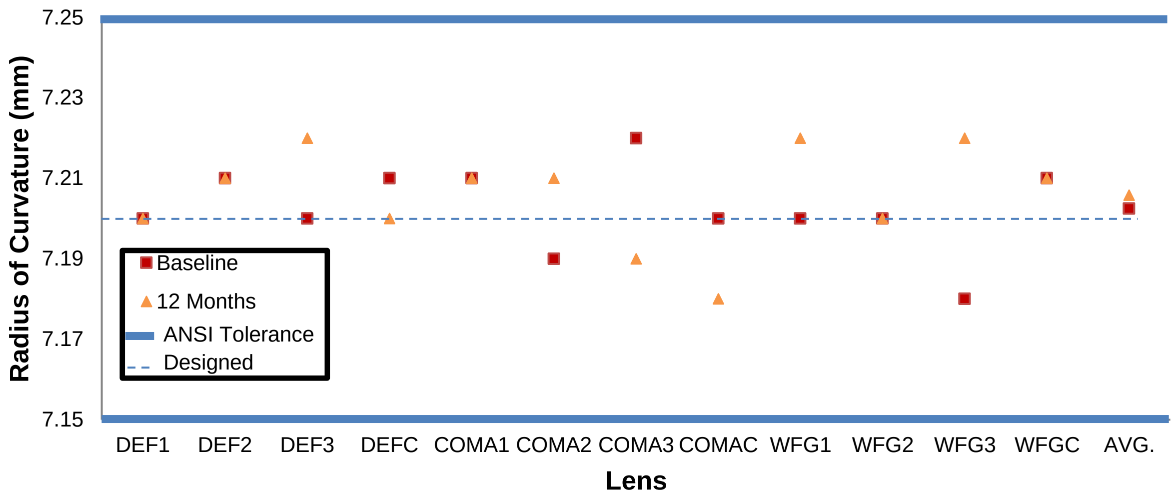

Figure 2.7. Base curve radius measurements for baseline and after the simulated 378 days of cleaning. ANSI tolerance for base curve manufacture is a difference of 0.05 mm from design denoted by the blue solid lines.[40]

Discussion:

We sought to examine whether one simulated year of manual cleaning would alter the aberration structure or base curve of conventional and wavefront-guided scleral lenses. To put the observed changes into a clinical context, spectacles and rigid gas permeable conventional contact lenses are prescribed in 0.25 D steps of defocus and cylinder powers.

None of the lenses in this study changed by more than 0.025 D (1/10th the clinical step size) in spherical power from baseline over the simulated one year of cleaning. Furthermore, none of the studied lenses had a change in base curve radius of greater than 0.03 mm.

Though the ability to manufacture a lens compared to the design or the ability to remake a lens was not explored in depth in this study, the change in cleaning for each lens group (A, B, and C) was compared to the standard deviation of HORMS wavefront error (3rd to 5th radial orders) of manufacture. This was done to investigate if the induced changes due to cleaning were within the variation of lens manufacture. Though both variability of manufacturing and changes due to cleaning were low, this comparison gives insight that the cleaning of the lenses had less impact on the optics of the lens than repeatedly making a lens, which in clinic would be done if the patient wanted a spare lens or if the patient broke a lens and needed a replacement.

Figure 2.3, illustrating the change in the Seidel spherical dioptric value, showed that all experimental lenses became more positive with cleaning while two out of the three control lenses became more negative. While two of the three controls became slightly more negative, the average change for the control lenses was positive. The changes reported are also very small (largest being <0.03D) and are visually insignificant.

As noted in the methodology section, this simulation of 12 months of cleaning took place over 64 days. By doing this, the lens changes due to passive aging of the lens material could not be measured during the initial summer. By measuring the lenses again after a year, the lens change due to passive aging of material can be examined and were found to be insignificant. However, by looking at the cleaning and aging of material separately, the possible synergistic result of aging while cleaning cannot be assessed. For instance, an older lens that has been cleaned for a longer duration may be more mutable than a lens that is newer and has been cleaned less often.

The cleaning protocol used in the study was clinically representative and was followed strictly, including timing the number of seconds rubbing each side. Real world patients typically do not follow the recommended protocol as strictly, for example, cleaning the lens for less than the recommended time. Thus, poorer compliance could result in varying changes in the optics and base curve of the lenses. It is also possible that other recommended cleaning protocols could lead to different levels of observed change in the optical profile and base curve of the lenses. Further, on-eye lens wear presents other sources of variability, such as lens movement, static misalignment, wetting issues, and potential change in the lens from use of the common devices for lens removal. Abrasive cleaning solutions may also affect the optics of the lenses differently to the solutions used here. Nothing can be said here about their optical consequences, as these aspects of lens performance were not studied.

In addition to only employing one cleaning technique, this study also only examined one contact lens material (Boston XO). The stiffness of plastic materials used to make scleral lenses is quantified on the Shore hardness scale, which ranges from 0 for a 2.5 mm penetration, to 100 for no penetration. Scleral lens materials are measured specifically using the Shore D hardness scale.[25] With the Shore D hardness of four other clinically common materials ranging from 78 to 83, Boston XO material is representative of most materials, with a Shore D hardness of 81.[26-29] Other materials used to manufacture scleral lenses are all similar in Shore D hardness, and Boston XO is one of the most commonly used material for scleral lenses manufacture. However, it remains that a different material with a lower Shore D hardness value may be altered differently by this cleaning regimen.

In addition, this study only accounted for the changes associated with cleaning and passive aging of the material and did not consider changes that may have arisen from physically wearing the lens, such as blinking, improper fit, and on-eye warpage. Vincent et al.[41] found that minimal permanent warpage occurred for lenses of 350 µm thickness (less than 0.05 D). However, those lenses were worn for shorter period of time than simulated in this study, and more wear could result in more warpage. Vincent et al.[41] also found a significant association between lens flexures and scleral toricity (for scleras with a >200 µm scleral toricity) for 150 µm and 250 µm lenses indicating that improper fit on a toric scleral could induce flexure that could affect vision, however they found that the flexure did not produce significant variations on the higher-order aberration profile. Also, the association was not significant for 350 µm lenses which was the designed thicknesses of the lenses in this experiment. Future research should be conducted to determine if lens wear, and the associated continual friction produced by the lids on the lens surface, the interactions associated with the biological components in tears or the formation of deposits on the lens surfaces, initiate any change in the optics or curvature of the lens, beyond what was observed here.

As the focus of this study was to assess the change in optical properties and base curve of scleral lenses due to manual cleaning, only aberrations and base curves were measured, however other properties of the lens may have changed such as surface integrity, wettability, edge thickness, and edge smoothness. Cho et al.[42] found that there was an increase in number of surface scratches with increased number of cleaning in rigid gas permeable lenses. These parameters could potentially have effects on the fit and comfort of lens wearing and the quality of vision which might affect the replacement schedule of scleral lenses.

Clinically representative daily cleaning over a simulated 12-month period did not induce clinically significant changes in the optical aberrations or base curves of conventional and wavefront-guided scleral lenses. Based on these negligible changes, conventional and wavefront-guided lenses should not have to be replaced due to changes to the optics or base curve of the lens induced by the manual cleaning process after having undergone a recommended cleaning schedule for a one-year time duration.

CHAPTER 3: SIMULATED CHANGES IN VISUAL ACUITY ASSOCIATED WITH MANUAL CLEANING OF SCLERAL LENSES

Chapter two of this thesis demonstrated that the changes associated with mechanical cleaning were relatively small, when judged as changes in HORMS and base curve. Figure 2.4 demonstrated that the median change after 378 cleanings in higher-order root mean square wavefront error was 0.013 µm. In addition, Figure 2.5 shows the change over time of individual aberration terms for one of the wavefront-guided lenses (WFG3). The largest change observed in any given aberration term was a change in vertical coma (C7) of 0.027um over a 6mm pupil.

Given the experimental design of Chapter 2, the observed intra-lens changes in HORMS and base curve describe optical and physical changes to the lens itself. However, it is well established that aberration terms interact with one another to influence resulting visual performance.[6] Therefore, the analysis in this Chapter takes an additional step of asking whether the small changes observed in Chapter 2 could manifest in visually relevant changes to the patient. To accomplish this aim, the investigators leveraged a visual image quality metric (the visual Strehl ratio (VSX)) that considers both an optical component and a neural component of seeing.[7,8,9,12] Studies have shown that changes in the visual Strehl ratio are predictive of changes in visual acuity.[9] Put in the context of the data collected in Chapter 2, the changes in visual Strehl observed over the 378 cleanings will be used to calculate changes in visual acuity that are predicted to arise due to the observed changes induced by mechanical cleaning. In this section, we calculated VSX according to the equation described by Thibos et al.[43] (equation A23), as shown here:

$$\mathrm{VSX} = \frac{\int\int_{\mathrm{psf}} \mathrm{PSF}(x,y)N(x,y)\mathrm{d}x\mathrm{d}y}{\int\int_{\mathrm{psf}} \mathrm{PSF}_{\mathrm{DL}}(x,y)N(x,y)\mathrm{d}x\mathrm{d}y}.$$

Methods:

Using the data previously collected in Chapter 2, the wavefront error data for both the wavefront-guided and coma-compensating lenses were further analyzed using the visual Strehl ratio (VSX).

Here, the intention was to calculate the predicted change in visual acuity that would occur over time when the lens was being worn on the eye. This optical condition (the lens being worn on the eye) is quite different than the condition experienced when the lens is optically profiled in the Optocraft system (the lens in a wet cell), therefore a series of mathematical steps were undertaken to move from a measurement of aberration in the Optocraft to an estimate of the residual aberrations that would be experienced when the lens was worn.

For this section, we wanted to look at the change in the aberrations as compared to the spherical carrier lens. In order to isolate these aberrations, we performed a two-part subtraction to target the residual aberrations in the coma and wavefront-guided lenses.

First, the average aberrations that were measured in the four sphere lenses were subtracted from each coma and wavefront-guided lens measurement. Since the underlying macro design of all lenses was identical (except for the wavefront aberration patch), this operation results in a measure of the aberrations that were cut into each lens (the coma patch for group B lenses and the 2^{nd} -5^{th} radial order wavefront patch for group C lenses). Second, in order to isolate the residual aberrations experienced while the lens was being worn on-eye, the wavefront error correction designed into the lens (coma for group B lenses and the 2^{nd}-5^{th} order wavefront patch for group C lenses) was subtracted. In an ideal condition, the result of these two operations (removing the average aberrations in the spherical lenses and the designed higher-order aberration correction of the lens) would result in a diffraction-limited system. However, under real-world conditions, every lens exhibited residual aberrations.

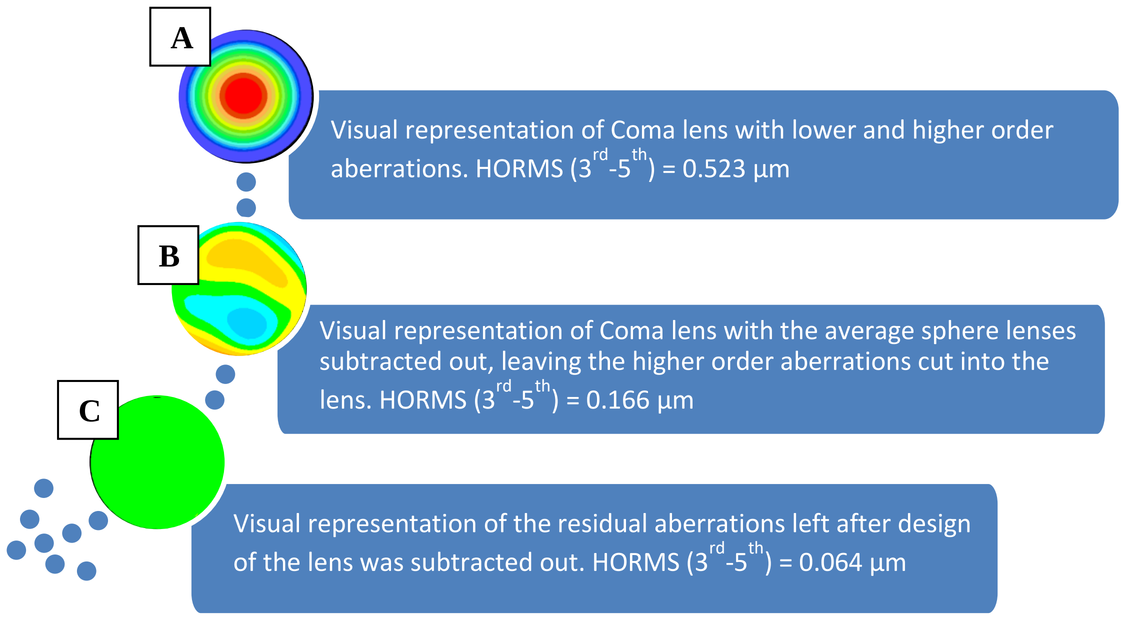

Figure 3.1. Estimating residual aberrations for each coma and wavefront-guided lens. This example uses the coma control lens to demonstrate how the residual aberrations were determined. Figure 3.1A shows a visual representation of the lower and higher-order aberration measured in the lens. At this time point, the HORMS of the coma control lens was 0.523 µm. Between 3.1A and 3.1B, the average of the sphere lenses was subtracted out leaving the measured higher-order aberrations cut into each lens. B is a visual representation of the higher-order aberrations cut into each lens. At this point, the HORMS of the coma control lens was 0.166 µm. Between 3.1B and 3.1C, the design of each lens was subtracted out leaving the residual aberrations of each lens. Figure 3.1C shows a visual representation of the coma control lens' residual aberrations. At this time point, the HORMS (representing an estimate of the residual aberration associated with the lens) was 0.064 µm.

The third and final step was to use these residual aberrations to calculate a change in VSX over time, and the change in VSX was used to predict a change in visual acuity. A modified version of the formula reported by Ravikumar, which refit her published data to eliminate the DC offset constant, was used in this experiment.[8,24] To calculate the predicted change in visual acuity, comparison at each week was made to the VSX value at baseline. A predicted change of 2.5 letters was chosen as a clinically meaningful change in acuity, based on the fact that Raasch et al. found that the standard deviation of the test-retest of visual acuity was around 2.5 letters. [44] Clinically speaking, this is equivalent to half a line of acuity.

ANALYSES

Sign tests were performed against our clinical benchmark on predicted change in visual acuity observed between baseline and after 378 cleanings. The differences were considered significant if the *P*-value was less than 0.05. This is to say, that a statistically significant finding will be a finding that is different than the clinical benchmark.

Results:

For the 4 coma lenses, the median change after 378 cleanings in predicted visual acuity was 0.26 Snellen letters. After an actual year of dry storage, the median change was 0.54 letters (Figure 3.2). The predicted changes in visual acuity ranged from less than 1 letter to 2 letters with the average change of all experimental lenses between baseline and week 9 being +0.32 letters. All lenses exhibited predicted visual acuity changes of less than 2.5 letters after 378 cleanings (P = .002).

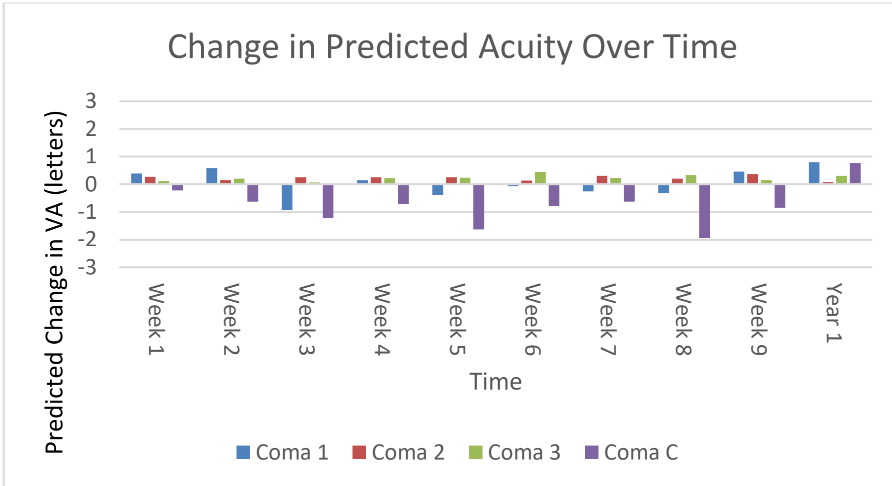

Figure 3.2. Predicted VA Changes in Coma Lenses. The predicted VA changes based on change in VSX for each lens from baseline to week 9 and after 1 year of dry storage. Coma 1, 2, and 3 are the experimental lenses and Coma C is the control lens. The predicted VA change is measured in letters gained or lost. None of the predicted changes in acuity met or exceeded the benchmark of 2.5 letters.

For the 4 wavefront-guided lenses, the median change after 378 cleanings in predicted visual acuity was less than 0.20 letters. After an actual year of dry storage, the median change was 0.36 letters (Figure 3.3). The predicted change in visual acuity ranged from less than 1 letter to 2 letters with the average change of all experimental lenses between baseline and week 9 being -0.11 letters. All lenses exhibited predicted visual acuity changes of less than 2.5 letters after 378 cleanings (P = .002).

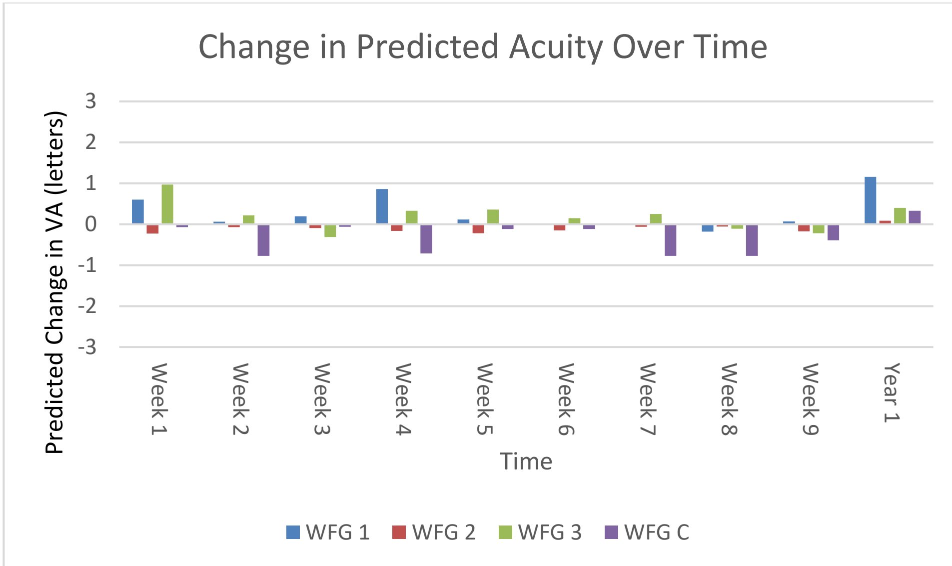

Figure 3.3. Predicted VA Changes in Wavefront-Guided Lenses. The predicted VA changes based on change in VSX for each lens from baseline to week 9 and after 1 year of dry storage. WFG 1, 2, and 3 are the experimental lenses and WFG C is the control lens. The predicted VA change is measured in letters gained or lost. None of the predicted changes in acuity met or exceeded the benchmark of 2.5 letters.

Discussion:

Though no clinical or significant changes were reported in HORMS and base curve due to cleaning, this chapter examined whether the small changes that were observed could interact in a manner that lead to changes in visual acuity. When judged against a clinical benchmark of 2.5 letters, no significant changes in predicted acuity were observed.

When comparing these findings to a misaligned wavefront-guided correction, cleaning the lenses created less change in acuity than the misaligned correction. Rijal et al. simulated the visual impact of a misaligned wavefront-guided scleral lens designed to correct an eye with keratoconus. According to their work, 35 out of the 36 eyes resulted in predicted loss of VA of three letters or greater if the correction was moved from the eye-specific pupil position to the geometric center of the lens.[45] Most eyes showed a reduction in vision greater than any simulated change in vision due to cleaning, thus stability of the lens and position of correction would be more important to proper performance of the lens than changes in the lens associated with 1 year of manual cleaning. This analysis is limited in that it only examines the changes due to the optical changes in the aberration structure of the lens. It does not consider the many other factors that may impact lens performance when the lens is worn on-eye. All of the limitations listed in Chapter 2 continue to be relevant, and unaccounted for, here. Some of these limitations include surface integrity or wettability of the lenses, warping of the lens shape over the optical zone or the landing zone (where the lens rests on the conjunctiva), scratches, chips or other defects in the lens and lens material clouding. Those changes notwithstanding, these results demonstrate that the changes observed due to mechanical cleaning of the lens are not predicted to lead to changes in visual acuity that would be noticeable to the individual.

CHAPTER 4: DISCUSSION AND FUTURE DIRECTIONS

In summary, Chapter 2 demonstrated that clinically representative daily cleaning over a simulated 12-month period did not induce clinically significant changes in the optical aberrations or base curves of conventional and wavefront-guided scleral lenses. Chapter 3 demonstrated that when judged against a clinical benchmark of 2.5 letters, no significant predicted changes in visual acuity were anticipated. Based on the negligible observed changes, it is hypothesized that conventional and wavefront-guided lenses should not have to be replaced due to changes to the optics or base curve of the lens induced by the manual cleaning process after having undergone the number of cleanings that would occur in a one-year time duration. However, a relatively limited set of aberrations were tested in this work. Future work may examine change due to cleaning in a more diverse set of aberrations.

Other important areas of this study that were not covered in this thesis, and that could be examined in the future include:

- Limitations
    - Other factors effecting the life span and wearability of the lenses that were not measured
        - surface integrity
        - wettability
        - edge thickness
        - edge smoothness

        - the impact of different lens materials
        - different cleaning agents and different cleaning regimens, lens deposits
    - Individual patient's characteristics that may change the outcome observed here
        - The way the patient removes the lens from its case
        - Rubbing the lens against the side of the case
        - Rough/callous fingers
        - Amount of pressure applied while cleaning the lens
        - Duration of the cleaning
        - Frequency and timing of cleanings other than those explored here
- Future research
    - Use of abrasive cleaners with abrasive particles
        - The cleaners used in this study did not have abrasive particles in them and more abrasive cleaners could have different affects than the cleaners used
    - An experiment designed to evaluate the lens that was worn on-eye, rather than just cleaned.
        - Biological interactions with the lens
            - Tear protein build up
            - Lid friction
            - Use of mechanical tools (suction cup) to remove the lens from the eye
    - Synergistic effect of cleaning and time
        - The study was not able to assess any synergistic effects of cleaning and time.

    - The study did look at lenses after 1 year of dry storage
  - Comparison of the time course of the studies reported here and proposed in future directions with current recommended replacement cycle

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