TEAR EXCHANGE AND MIDDAY FOGGING

By

Kelsea Skidmore, B.S.

THESIS

In partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in

PHYSIOLOGICAL OPTICS

Presented to the Graduate Faculty of the

College of Optometry
University of Houston

May, 2017

Approved:

_____
Jan Bergmanson, O.D., Ph.D. (Chair)

_____
William Miller, O.D., Ph.D.

_____
Jason Marsack, Ph.D.

Committee in Charge

Abstract

Purpose: Approximately 30% of scleral gas-permeable lens (SGP) wearing patients are affected by midday fogging (MDF). The purpose of this study was to determine the influence of post-lens tear exchange and other fitting characteristics on the presence or absence of MDF.

Methods: 33 subjects were recruited for this study. 23 subjects were habitual SGP wearers (11 MDF, 12 non-MDF subjects), and 10 were non-SGP wearing normal controls. At the study visit, dry eye symptoms were quantified (TERTC Dry Eye Questionnaire), and lens-fitting characteristics were evaluated using ocular coherence tomography and biomicroscopy. Tear exchange rates were measured using the Fluorotron fluorophotometer. The procedure was to instill high molecular weight fluorescein (FITC) Dextran into the tear film reservoir beneath the SGP, and measure the tear fluid fluorescein concentration every 5-30 minutes over a period of 4 hours. The tear reservoir fluorescein concentrations were plotted to measure the fluorescein decay from within the tear fluid, which was used to calculate the tear exchange rate. Statistical analysis was done using student t-test and ANOVA.

Results: In this study, there was less tear exchange in the MDF group (mean: 0.111%) when compared to the nonMDF group (mean: 0.417%), although statistical significance was not reached due to the high variability of the exchange rates ($p = 0.26$). There was no significant difference between the tear film reservoir thickness in the MDF (283um) and nonMDF (326um) groups ($p = 0.53$), or with dry eye scores (mean of 29.5 in MDF, 30.4 in nonMDF) ($p = 0.91$).

Conclusions: In this study, there is no clear relationship between the amount of tear exchange during SGP wear and the incidence of MDF. Tear exchange may indeed be a factor, although additional studies are needed to clarify its role, and to further explore other contributing factors that may be involved in modulating the occurrence of MDF.

Table of Contents

List of Figures

List of Tables

Introduction

Background and clinical indications for scleral lenses

The origins of the scleral lens (SGP) date back to the late 1880s, with the works of Müller, Fick, and Kalt. This first contact lens was made of blown glass, and was used for correcting high ametropia and corneal irregularities.[1,2] Fick designed a lens to neutralize the optics of a keratoconic cornea, while Müller developed lenses with specified powers for myopic patients.[3] Both Fick and Müller built upon the expertise of Himmler, an optician, to manufacture their lenses from blown glass which were remarkably accurate for the technology available at that time.[4]

While these lenses offered great promise, they were not without their limitations. One of the most significant drawbacks was the limited oxygen availability to the cornea secondary to large lens diameter, impermeable material, and the essentially sealed environment that severely limited oxygen availability to the cornea (which receives approximately 80% of its oxygen requirement exogenously). Even as the technology advanced from glass to plastic, the first generation of plastics (poly-methyl methacrylate, PMMA) were also impermeable to oxygen, causing the contact lens market to favor the smaller diameter corneal lenses as the primary modality of rigid lens choices in the 20th century. In 1978, Polymer Technology came out with the first gas permeable (GP) corneal lens material (Boston II), which allowed oxygen permeation through the lenses, drastically reducing complications associated with hypoxia and revolutionizing the application of rigid lenses.[5] The scleral lens then became a more viable option, and in

1983 Ezekiel described the first scleral lens fabricated from a rigid gas permeable material.[6] According to Fatt, a leading corneal physiologist at the time, a 100 Dk/t lens material would enable the practitioner to provide sufficient oxygen to the scleral lens wearing cornea.[7]

Over the past 20 years, scleral lenses have resurfaced abundantly with advanced materials, complex, multicurve designs, and innovative optics, and are now used for a wide range of indications. They are one of the fastest growing segments of the contact lens industry, with one in five gas permeable contact lens fittings being a scleral design.[8] Today, an SGP is typically manufactured in highly oxygen permeable materials with Dk values of 100 or greater in order to minimize extreme hypoxic environments that were seen with earlier materials.[9,10] Figure 1 illustrates a modern scleral lens on the eye of a patient. The common indication for scleral lenses is keratoconus, but they are used to fit less common conditions that induce irregular astigmatism, such as pellucid marginal degeneration, and neurotrophic disease.[11–13] They are becoming the lens of choice for managing post-surgical corneal transplantation and refractive surgeries (i.e. post-radial keratotomy, post-PRK, and post-LASIK ectasia),[14–19] and are also now being utilized to manage ocular surface diseases such as, Sjögren's, Stevens-Johnson Syndrome, and chronic graft versus host disease.[12,20,21] In addition, they can be used acutely and chronically in the management of exposure-based situations like neural palsies and severe periorbital burns.[22] The SGP is considered medically necessary for most of these situations in which they are indicated due to their unique ability to provide comfortable

and usable vision through a diseased ocular surface, and they can even delay the need for surgical intervention.[23]

Complications of Scleral Lenses

SGP lenses possess a unique relationship with the ocular surface, as compared to other RGP lenses. The SGP vaults over the cornea, landing on the conjunctival tissue covering the sclera, maintaining apposition to the eye through negative suction forces. The tear reservoir between the cornea and the SGP is on average approximately 200 microns, but can be as thick as 700 microns in certain areas of the reservoir due to the unique irregularities of the cornea. Since the majority of corneal oxygen supply originates exogenously, a thick tear reservoir poses the risk of inducing corneal hypoxia.[24,25,26] In addition, a lack of tear exchange due to the large diameter and lens settling into the conjunctival tissue may lead to stagnation of the tears under the lens, and potential inflammatory complications due to the accumulation and stagnation of metabolic waste products.[24,27,28]

Midday Fogging

One of the most common SGP complications is a phenomenon known as “mid-day fogging” (MDF), which affects 20-33% of SGP wearers.[29,30] Particulate matter accumulates in the post lens tear reservoir, creating a fog-like veil over the patient’s vision. The severity of this complication ranges from mild blur at the end of the day, to immediate blur soon after lens application. Research has shown that wear time for patients with MDF

ranges from 1.75 to 6 hours with an average of 4.45 hours before lens removal.[31] (Figures 2-4) This accumulation of debris in the post-lens tear reservoir causes a significant reduction in visual acuity in many individuals, necessitating removal of the SGP and reapplication with fresh solution.[32,33] It is important to differentiate between true debris in the post-lens tear reservoir, versus the "fog" that patients sometimes use to describe poor lens wettability, or corneal edema that can occur due to hypoxia. Up until recently, the origin and composition of the tear reservoir debris in MDF has been entirely unknown. Recent studies have analyzed tear samples from the lens reservoir in individuals with and without MDF. The studies indicated that the lipid component may be cholesterol-based in some patients.[34] It is likely that there are different components of debris, including lipids, proteins, cell fragments, and other tear film components, that are present in variable amounts in each individual that experiences MDF.

The two major known risk factors for MDF are excessive lens clearance and ocular surface disease.[29,31,35,36,37] It has been hypothesized that abnormal lipid profiles in dry eye disease and allergies may contribute to MDF. [34,38] In relation to the fit of the lens, many practitioners have found that MDF can be reduced by decreasing apical and limbal clearance, thus decreasing the overall vault.[31,39]

The exact etiology of MDF has yet to be established. Previous studies have shown that a post-lens tear thicknesses greater than 300 microns, along with a tight fit, may contribute to MDF and decreased wear time.[31] A theoretical study proposed that the sagittal depth should be less than 200 microns for an optimal SGP fit.[24] In general, clinical experience supports designing a lens with minimal apical clearance, without creating corneal bearing on the diseased or post-surgical cornea. While lens fit

manipulation is not always sufficient to eliminate the occurrence of MDF in susceptible individuals, careful fitting technique can improve visual function by reducing the thickness of the layer of debris.[38]

In addition, some clinicians have found that the shape of the tear reservoir beneath the scleral lens can influence the presence and severity of MDF, with less MDF observed with a relatively plano shaped (uniform in thickness over the cornea) tear reservoir than with a plus or minus shape.[39] Unfortunately, creating a uniform tear reservoir is difficult in many patients due to their highly irregular corneal shapes.[30] As of yet, a single variable has not been shown to eliminate MDF in all individuals affected, which indicates that this is a multifactorial complication.

The specific origin of the debris seen in MDF is still unknown, specifically whether or not there are differences in secretions or the tear film components that are abundant in MDF. Some hypothesize that excessive tear exchange can lead to debris accumulation and entrapment under the lens, and that the debris is the result of secretions or diffusion through the perilimbal conjunctival tissue. This theory has been tested at Pacific University, where subjects who exhibited MDF were fitted with SGP devices that sealed the peripheral zone and eliminated the presence of conjunctival tissue beneath the lens. This type of fitting relationship eliminated fogging in the subjects, indicating that perilimbal conjunctival tissue may be the source of entry for the MDF precipitate.[38] This theory implies that reducing tear exchange would reduce the incidence of MDF; however, most experts agree that tear exchange is essential for proper oxygen transmission and that limited tear exchange will also cause prolonged corneal exposure to toxic metabolic waste.[27,17]

Current Understanding of Tear Exchange Beneath SGP

Scleral contact lenses are fitted to closely align the conjunctiva and vault over the cornea, leading to entrapment of tears. Most SGP lenses are fitted with slight to no movement of the lens with blink. This is believed to cause a reduction, or in some cases a lack of tear exchange entirely. Subjective measure of the fluorescein under the SGP when applied before insertion has shown little to no movement of tear fluid over an 8-hour period.[40] In addition, when fluorescein has been applied to the superior bulbar conjunctiva after application of the lens, little to no fluorescein is observed under the lens, implying a lack of tear exchange.[41] Early scleral lenses had fenestrations in order to deliver oxygen to the cornea, and for tear exchange. However, with the modern high Dk materials available, fenestrations are rarely used in clinical practice.[42] Literature varies when it comes to the role of tear exchange with scleral lenses. If tear exchange is hindered, it is believed that metabolic byproducts accumulate in the tear reservoir, forming what has been referred to as a "toxic swamp".[27,28]

Measuring Tear Exchange with Contact Lenses

Historically, tear exchange estimates have been calculated by fluorophotometry. This method was first established in 1882 when the use of fluorescein in ophthalmological research was introduced.[43,44] The technique became extremely useful for investigation of fluid exchange in the various structures of the eye, both anterior and posterior segment.[45–49] Fluorophotometry has been further modified through the years to be utilized in

measurements of tear flow under contact lenses.[47,50] Using this method, researchers are able to determine the fluorescein concentration in the pre-corneal tear film without having to collect tear specimens. Figure 5 depicts the set-up of the Fluoroton Master (FM2) Fluorophotometer (Ocumetrics, Mountain Vew, CA). High molecular weight FITC Dextran is typically utilized in order to simulate natural tear consistency and eliminate penetration into the corneal epithelium.[51] By measuring the decay in fluorescein concentration over time, a tear exchange rate may be calculated. It is important to remember that what is actually measured is the elimination of fluorescein dye from under the lens, not tear exchange directly. This measure is then mathematically extrapolated to calculate tear exchange rate. While there are flaws in this method, results are relatively consistent across the literature and it is considered the gold standard to determine tear turnover, or exchange rates.[27,49]

Fluorophotometry has been utilized throughout the literature to measure exchange rates in corneal RGP wear, as well as both hydrogel and silicon hydrogel soft lens wear; however, limited data exists for exchange rates in SGP lenses. Tear exchange rates for soft contact lenses are considerably lower than for RGP lenses. Exchange rates for RGP lenses range from 10 to 20 percent per blink, while soft lenses are as low are 1 to 2 percent.[52–55] This increase in tear replenishment associated with RGP lenses is thought to provide a protective effect over soft contact lenses with regards to expulsion of microbes and metabolic waste products.[53] Mathematical models of the post-lens tear film under a soft contact lens in response to the mechanical suction pressure of a contact lens have been established, and can predict the amount of exchange of fluid beneath the lens.[56] Studies have found that fenestration in lenses lead to greater tear mixing, as they allow the post-

lens tear fluid to escape through the holes, rather than limited strictly to the lens periphery.[57] The amount of tear mixing was found to be dependent on the post-lens tear film tthickness under the SCL. Minimal data regarding tear exchange with SGP lenses exists, but early studies on fenestrated and channeled PMMA scleral lenses reveal variable amounts of tear exchange between subjects when measured with fluorophotometry, with some subjects exhibiting seal off of the lens despite these modifications.[58] Fenestrations in SGPs are rarely used today secondary to bubble formation.

The purpose of this study was to evaluate tear exchange beneath a scleral lens in a population of individuals who experience MDF, compare these rates to individuals who do not experience MDF, and analyze the influence of dry eye characteristics and tear film reservoir depth on the incidence of MDF.

Methods

Experimental Eye Model of Fluorophotometry Measurement

To our knowledge, there is limited and unverified data on the reliability of fluorophotometry to measure tear exchange in a SGP system. Therefore, a model eye was designed to collect objective control data using known tear reservoir thicknesses, eye rotations, and fluorescein concentrations, to develop a better understanding of the data outputs in this study. We used rubber model eyes of approximate human dimensions (Figure 6), and secured scleral lenses with three difference sagittal depths and two difference fluorescein concentrations, in order to evaluate fluorescein concentrations with varying environments with our system (SAG values: 340, 400, 500 μm). In addition, various angles of incidence were measured to mimic the effect of head tilt during subject examination. The lenses were marked in millimeter increments in order to precisely evaluate each position.

To develop the control eye model, small 1.5mm holes were cauterized into each scleral lens in the superior region (Figure 7), and the lenses were adhered to the rubber eye models. The holes were designed to facilitate pipetting of a specified FITC-Dextran concentration (two concentrations were used) for each measurement session. Each of the three simulator eye-lenses combinations underwent a two separate series of measurements with the fluorophotometer. During the first session, 2 μL of FITC-Dextran was instilled under the lens, with the remaining portion consisting of saline. The concentration of fluorescein was then measured using six different eye orientations: central, central-right tilt, central-left tilt, inferior, inferior-right tilt, and inferior-left tilt.

Figure 8 depicts the set-up of the simulator system for primary gaze. In order to obtain measurements off axis, the simulator eye was rotated either left or right to orient the measurement axis with a specific mark on the lens 2mm from central. During the second session, 4 μL of FITC-Dextran was instilled under the lens and the same measurements were repeated. By collecting this control data, which inherently is measured without the added variables of tear exchange and other dynamic human variables, we were able to better understand the precision and accuracy of the instrument at measuring the concentration of fluorescein in an SGP system.

Primary Tear Exchange Study

All experimental study protocols were done in accordance with the International Review Board at the University of Houston and all subjects gave informed consent and signed an informed content document. Subjects were recruited from the University Eye Institute's Cornea and Contact Lens Service. Inclusion criteria included an eye examination within the last 2 years, and current habitual SGP wear; in addition, approximately 50% of patients had to have a subjective complaint on MDF. Exclusion criteria included active anterior segment infection or known hypersensitivity to solutions used in the study. In order to further eliminate possible confounding factors, subjects were instructed to refrain from topical ophthalmic medications, including artificial tears on the day of their appointment. Thirty-three subjects were included in the study. Group one consisted of subjects that experienced interrupted wear time (<8hours of continuous

wear on an average day) in their current scleral contact lenses due to MDF, and the second group were subjects that exhibited uninterrupted scleral contact lens wear (>8 hours), and thus represent the more successful lens wearers. All subjects in these two groups were adapted SGP wearers, with a SGP fit deemed to be acceptable by an experienced clinician at the time of enrollment in the study.

The third group consisted of ten subjects without the presence of any corneal pathology, who were recruited to serve as a control group, allowing us to compare tear exchange between regular and irregular corneas. These subjects were fitted in trial scleral lenses, followed by fluorophotometry measurements using the same protocol as the habitual wearers.

Our approach to quantifying the exchange rate was to utilize the Fluorotron Fluorophotometer (Fluorotron Master FS2). We applied this technique to the post-lens tear layer of scleral lens patients. The Fluorophotometer measures the fluorescein concentration levels of the different layers of the cornea and the lens, and there is a graphical, as well as tabulated, output of the data to show the fluorescein concentrations at different anterior segment depths (Figures 9, 10). We first took a measurement of the natural florescence of the cornea with no scleral lens in place in order to obtain baseline data for each patient, as seen in Figure 11. The concave portion of the lens was then filled with non-preserved solution (Unisol, Alcon Laboratories, Fort Worth, TX) along with high molecular weight fluorescein (FITC Dextran, Sigma-Greenway Pharmacy), then applied the lens to the subject's eye. Sterile saline was used because it is the most commonly used application solution for scleral lenses. Fluorotron measurements with the lens in place were taken immediately following lens application, and at twenty additional

time points over a four-hour period. These data points were graphed, and the rate of fluorescein decay in post-lens tear layer was calculated for each subject.

At visit 1, the subject reported to the University Eye Institute wearing their habitual SGP, at which time they underwent the consent process, and a thorough medical and visual history was taken. Visual acuity and anterior segment evaluation was completed to establish eligibility for the study. Individuals in the control group were fitted in a trial SGP (either CustomStable, manufactured by Valley Contax, or Zenlens, manufactured by Alden Optical). Next, their contact lens fit was assessed with bimicroscopy, and the subjects completed the TERTC dry eye questionnaire to evaluate ocular dryness and lens comfort.[59]

After the completion of the survey, the Fluorophotometry section of the visit began. The protocol for imaging was as follows: prior to lens removal, a baseline concentration of the natural fluorescence of the cornea was measured, without Fluorescein dye instilled in the eye. The patient's lenses were removed, cleaned, filled with sterile saline solution (Unisol) along with 2µl of FITC Dextran Fluorescein (administered with a pipette), and placed back on the patient's eye. Using the fluorophotometer, regular measurements were made to assess the concentration of fluorescein (ng/ml) beneath the lens. During the first hour, fluorescein was measured every five minutes. The second hour comprised of measurements taken every fifteen minutes, and for the remaining two hours, every thirty minutes, for a total of twenty concentration readings. The study also included Visante ocular coherence tomography (OCT) imaging in order to visualize and quantify the post-tear lens depth, or sagittal

depth (Figure 12). This factor may be important in the fitting relationship leading to decreased tear exchange. A final visual acuity was obtained on exit from the study.

Once the twenty fluorescein concentrations were obtained, the fluorescein decay over the four-hour period was calculated by measuring the slope of the change in fluorescein concentration. This represents the post-lens tear exchange rate. Data was analyzed first by graphing each individual subject's fluorescein concentration decline as a function of time.

Analysis Method

Historically, the peak fluorescein concentration point of the cornea/contact lens area of the data has been used to calculate the decline of fluorescein over time, representing the tear exchange/tear elimination value. While this method works well for soft lenses and corneal GP lenses that have a relatively negligible post lens tear reservoir, the scleral lens may have anywhere from 200-600 microns of central corneal clearance, leading to variability in tear lens volume. In order to account for this variability in the tear lens volume between subjects, a custom MatLab algorithm was written to calculate the fluorescein concentration under the central portion of the lens. The subject's natural corneal fluorescence was subtracted and the data normalized for comparison. Tear exchange is the percentage decrease per minute of fluorescein concentration measured over a period of time, four hours in our case. From this, the concentration of FITC was plotted over time to transform into a tear decay plot, with the slope representing the exchange rate.

Results

Simulator Experiment Results

Results of the model eye experiments indicate that flow of fluorescein under the lens, as well as misalignment, may lead to data outliers, but they are of mild consequence given the large volume of measurements.

In the model eye experiments, there is a significantly greater mean concentration of FITC Dextran in the inferior zone of the post-lens tear reservoir when compared to the central zone. Figure 13 depicts average values from the three simulator lens models for the central lens zone. The average fluorescein concentration in the central zone was 1,961 ng/ml for the low FITC Dextran fluid reservoir, and 3,855 ng/ml for the higher amount. Figure 14 depicts average values from the three simulator lens models for the inferior lens zone. The average fluorescein concentration in the inferior zone for the low FITC Dextran fluid reservoir was 2,751 ng/ml, while the average for the higher amount was 6,611 ng/ml. The superior zone of the model eye was not assessed because the lens was modified to allow filling with NaFl solution for testing (Figure 7).

We also analyzed the variation in measurements when the eye is in central position, but tilted 2mm to the left or to the right of central (Figure 15). Results indicated that central tilt causes less variation than measuring 2mm inferior to the central zone. Figure 16 and 17 display results of all positions of gaze for each of the three simulator models.

Primary Tear Exchange Experiment Results

The study included thirty-three subjects: twenty-three habitual scleral lens wearers and ten scleral neophytes. Of the twenty-three habitual wearers, eleven were categorized as interrupted wearers secondary to MDF, and twelve subjects did not experience MDF. The additional ten subjects with no anterior segment pathology were fitted into scleral lenses as a control. The demographics of the subjects are shown in Table 1.

There was less tear exchange in the MDF group (mean exchange rate: 0.111%/min with standard deviation of 0.589) when compared to the non-MDF group (mean: 0.417%/min with standard deviation of 0.665), although statistical significance was not reached due to high variability of the exchange rates ($p=0.26$). (Figure 18,19). The control group had a mean tear exchange rate of 0.65%/min, but high variability with standard deviation of 1.3%/min.

Subjects who experienced MDF tended to have a smaller diameter lens on average (mean: 16.91mm) when compared to non-MDF subjects (mean: 17.46mm), but it did not reach statistical significance ($p=0.26$). There was no significant difference between the tear film reservoir thickness in the MDF (mean: 283 μm) and the non-MDF (mean: 326 μm) groups ($p=0.53$). In addition, there was no correlation found between the dry eye scores of the MDF (mean: 29.5) and non-MDF (mean: 30.4) groups ($p=0.91$).

Discussion

The cause of MDF has historically been hypothesized to be a multifactorial phenomenon. For this reason, we analyzed several variables and their effect on debris accumulation, including: subjective dry eye symptoms, post-lens tear reservoir depth, lens diameter, and tear turnover rate.

The TERTC dry eye questionnaire was utilized to subjectively assess the dry eye status of each patient.[59] Our data revealed no association between the calculated dry eye score and the presence of MDF. This contrasts the vast majority of previously published material, as many studies and clinical reports have observed that patients who experience post-lens tear debris also exhibit dry eye signs and symptoms.[34,35,38,60,61] It is important to consider the differences in how the subject is classified with dry eye syndrome. Our study looked just at subjective responses via a validated questionnaire, rather than objective clinical findings. In addition, our relatively small sample size was not recruited form a population of patients wearing SGPs for dry eye management. If we had specifically recruited subjects from a population of individuals wearing SGPs to manage their dry eye disease, there may have been a stronger prevalence of MDF observed.

In regards to the fitting elements between both groups of subjects, sagittal depth and lens diameter did not play a statistically significant role. Clinical experience suggests that one method to tackle MDF is to decrease the sagittal depth of the lens to alleviate fogging.[38,61,29,31,39] This may not always mitigate tear film debris, but it will narrow the depth of the tear lens reservoir, less thickness for accumulation of debris, thereby allowing less deterioration of visual acuity. Figure 20 illustrates a decrease in density and thickness

of tear film debris when sagittal depth is lowered. It is crucial that future studies measure the density of the particulate matter in the post-lens tear film with OCT to better categorize the amount of MDF based on a turbidity score.[34,30]

The subject of tear exchange under a scleral lens has led to varied responses in the literature and clinical settings. This study suggested that tear exchange may have a role in preventing MDF and allowing a longer wear time for patients. Historically, tear exchange with contact lenses has been considered necessary in order to provide adequate oxygen to the cornea, and prevent toxic metabolic products from accumulating under the lens.[24,37,52,63] Other clinical experience has proposed that excessive tear exchange may be the culprit behind MDF by drawing debris and metabolic byproducts under the lens.[64,65] These wide-ranging theories support the premise that MDF is multifactorial, and tear exchange is not the only factor implicated. The general consensus remains that while there is much unknown regarding the necessity of tear exchange with SGP lenses, it is imperative to consider each patient and their unique corneal healthy requirements individually.

Fluorophotometry is considered the gold standard method for measuring tear exchange with contact lens wear, but it is not without its limitations. The terminology of "tear exchange" implies a bidirectional circulation of tears, but the fluorophotometer essentially measures the decrease in fluorescence from beneath the lens over time, providing no knowledge of the replenishment of tears from the ocular surface outside the lens. This method determines the tear expulsion from behind the lens rather than a true tear exchange value, formulating an inferential measurement rather than direct. While substantial published data is available concerning RGP and soft lenses, little is known about the application of this technique with SGP lenses.

This study aimed to explore the normal variation in the data collected by designing simulator eyes with absent tear exchange. The control experiment revealed considerable disparities in the quantified fluorescence of various regions of the post-lens tear reservoir. Measurements off-axis, especially inferior, varied significantly from those measured in the central region of the eye. The inferior concentrations of NaFl were greater than central, which we attribute to be partially due to the particles dropping inferior in the lens, but also attributable to greater post-lens tear depth inferiorly. Results of this control experiment indicate that flow of fluorescein under the lens, we well as patient misalignment may lead to data outliers. This may be of little consequence given the large volume of measurements that help to account for these variations, but highlights a unique difference in SGP lenses from other lens designs—there is a highly variable range of tear layer depths in each subject, as well as between subjects (Figure 21). Future studies in SGP tear exchange should aim to formulate improved fluorophotometer protocol including optimal patient alignment and standardized measurement zone in order to yield improved accuracy in measurements and minimize variation.

As of yet, there are no peer-reviewed, large clinical studies that dictate treatment and management of MDF. Most literature gives suggestions of management options based on their individual clinical experiences. Decreasing the sagittal depth of the lens is a common troubleshooting decision that sometimes eliminates, or at least minimizes patient fogging.[29,31,61,65] Many practitioners find that some patients benefit from instilling several drops of a viscous artificial tear in the lens reservoir, in addition to non-preserved saline.[30,66,67]

If MDF cannot be eliminated altogether, frequent breaks in lens wear are recommended to prevent excessive buildup of the particulate matter.[29,36,37,61,65] It has been shown that breaks throughout the day can improve patients' success in SGP lenses. With recent advances in scleral topography, it has been hypothesized that designing lenses with back surface toricity to improve alignment may contribute to a reduction in MDF.[29,66,68] The scleral shape in the majority of eyes is toric in nature, with the nasal sclera tending to be flatter than the temporal region.[69] Proper alignment of the peripheral curves can be instrumental in achieving a successful scleral lens fit of both optimal comfort, ocular health, and vision.[68,70,71] However, this perfect alignment has the potential to create seal off in the periphery of the lens, which can lead to inadequate tear exchange and instigate further problems.[30] Fitting approach for practitioners varies from patient to patient based on their individual needs, and will continue to evolve based on research.

Limitations of the Study

This study was a novel use of an established technology, fluorophotometry, to measure the amount of tear exchange beneath a SGP. To date there are no publications that report measuring the rate of tear exchange beneath an SGP. Using this technology presented some unique challenges for data collection and interpretation.

The primary limitation of this study was that we did not grade the MDF for severity, and rather categorized subjects based on subjective reports of MDF. However, we are confident that these subjects were in fact experiencing MDF (rather than other causes of interrupted wear), due to their clinical diagnoses from the attending clinicians. While it was

not done in this study, it is critical that future studies measure the density of the particulate matter in the post-lens tear film with OCT to more precisely grade the level of MDF using a turbidity score.[34]

Conclusion

The reemergence of scleral lenses has revolutionized the treatment and management options available for corneal and ocular surface disease. There is no doubt that this lens modality has facilitated improved vision, comfort, enhanced clinical outcomes, and quality of life to a vast population of patients who have failed with previous treatment strategies. Nevertheless, as with all new advancements, complications and limitations follow suit. Midday fogging is among these complications, and while progress has been made to overcome this limitation, its existence still appears to be multifactorial in nature. As this lens modality continues to have an expanding role in patient care, it becomes even more important that SGP complications be better understood and addressed. It is essential that clinical and basic research strive to identify, understand, and resolve these complications as they arise.

Figures

Figure 1: Scleral lens on the eye of a patient. The scleral lens vaults over the cornea, landing on the conjunctiva overlying the sclera.

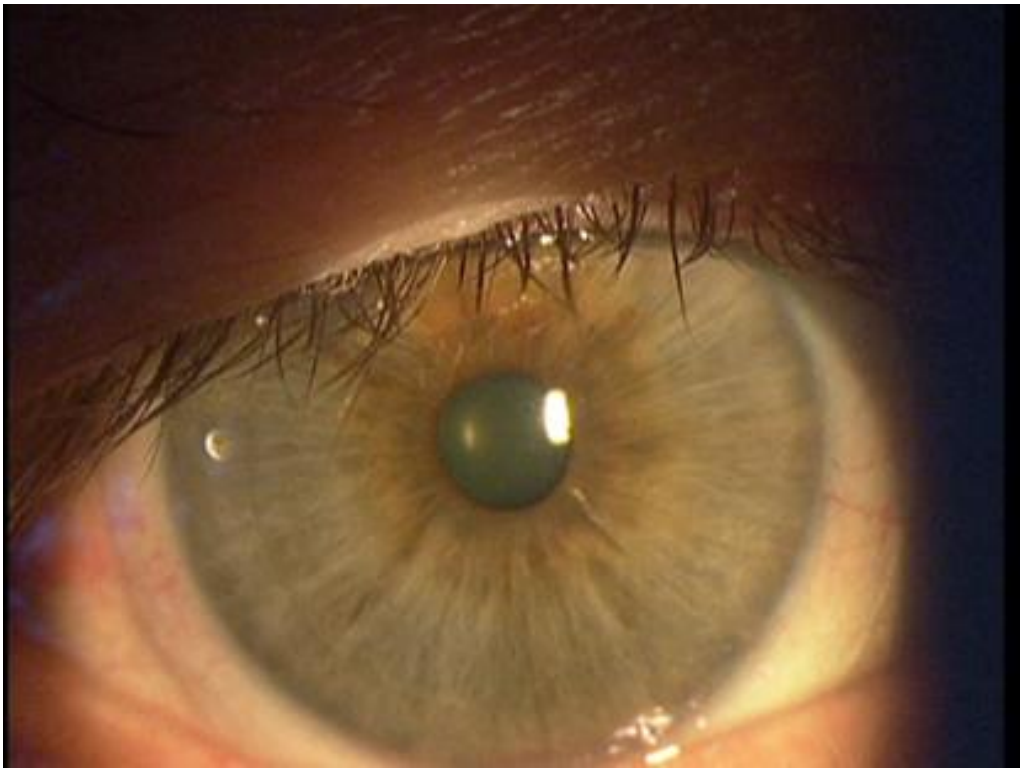


Figure 2: Midday fogging in a patient with scleral lens in place. Instead of being clear, the post-lens tear reservoir exhibits a dense layer of particulate matter.

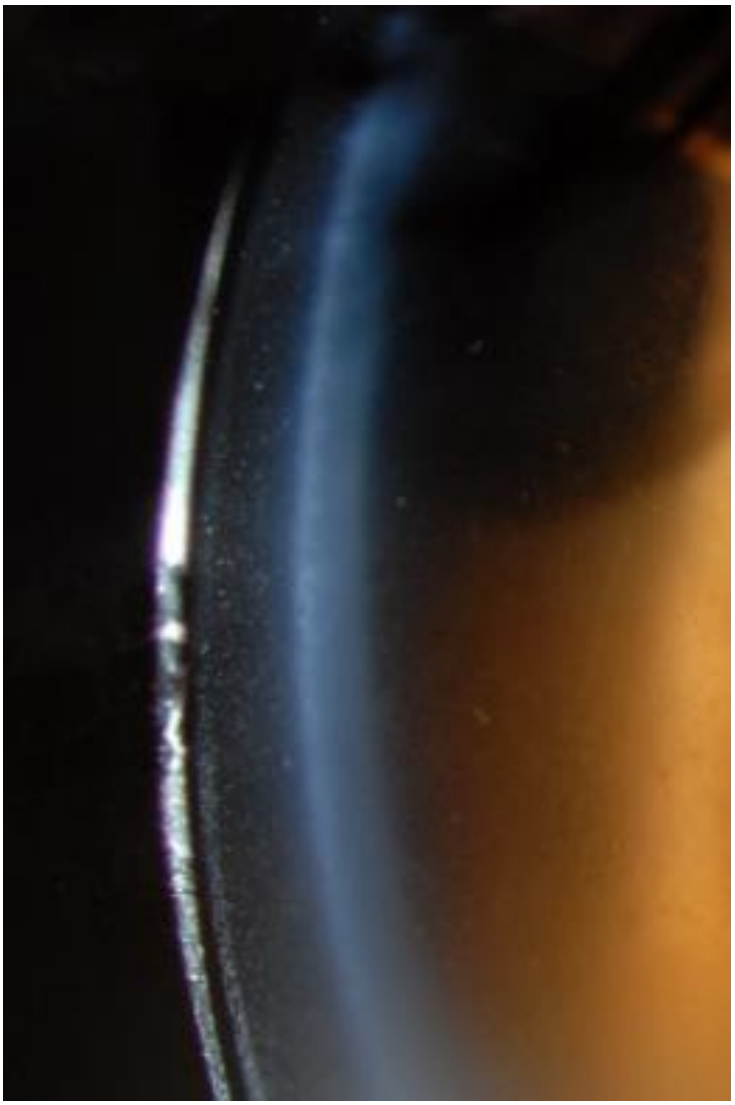


Figure 3: Visante OCT image of cornea and scleral lens, with layer of debris in post-lens tear reservoir.

Figure 4: Optic section illustrating a layer of foggy post-lens tear reservoir between the cornea and contact lens.

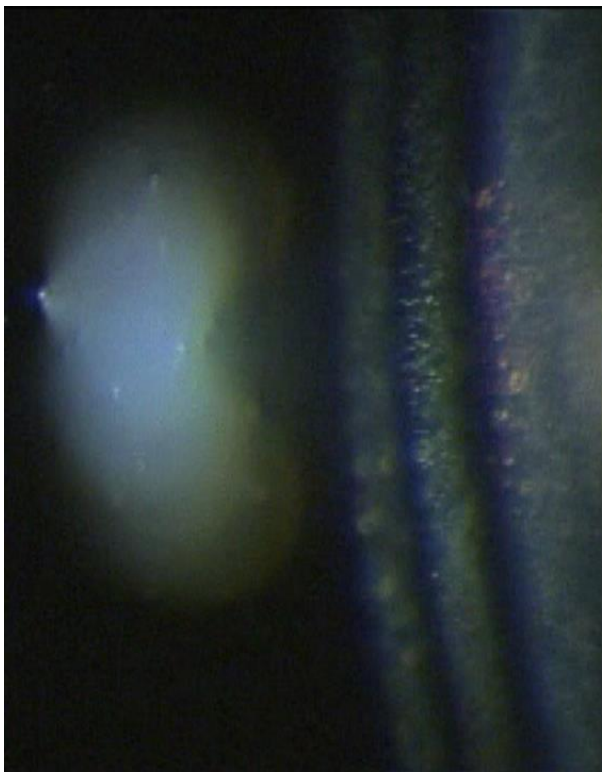


Figure 5: Fluorotron Master Fluorophotometer setup.

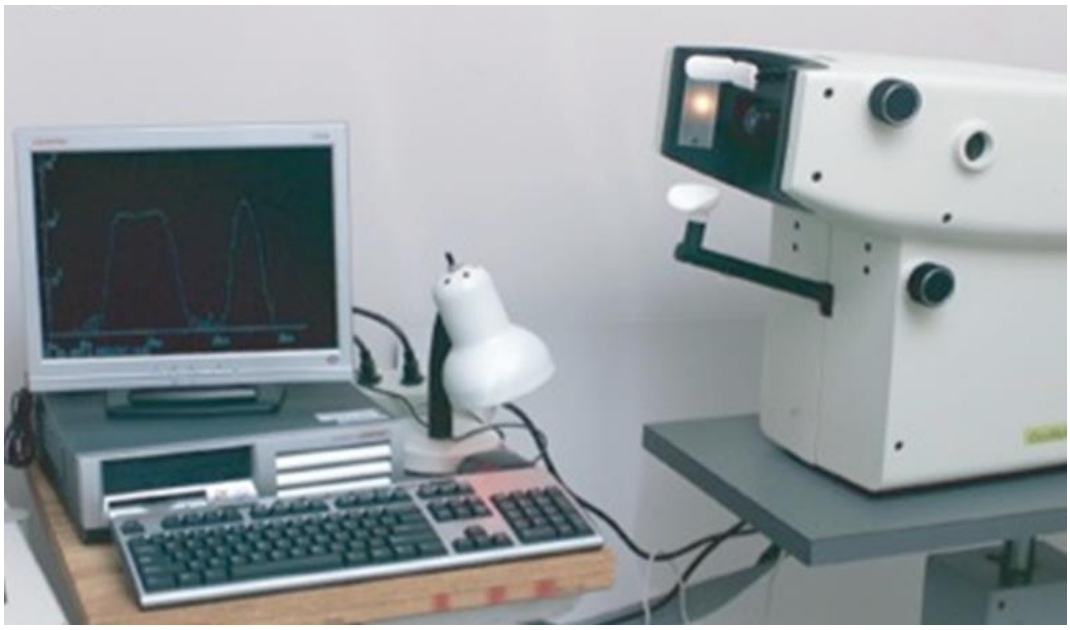


Figure 6: Rubber simulator eyeball of approximately human dimensions without scleral lens attached.

Figure 7: Scleral lens with two holes (approximately 1.5mm diameter) cauterized in superior region in order to pipette FITC Dextran solution into tear reservoir

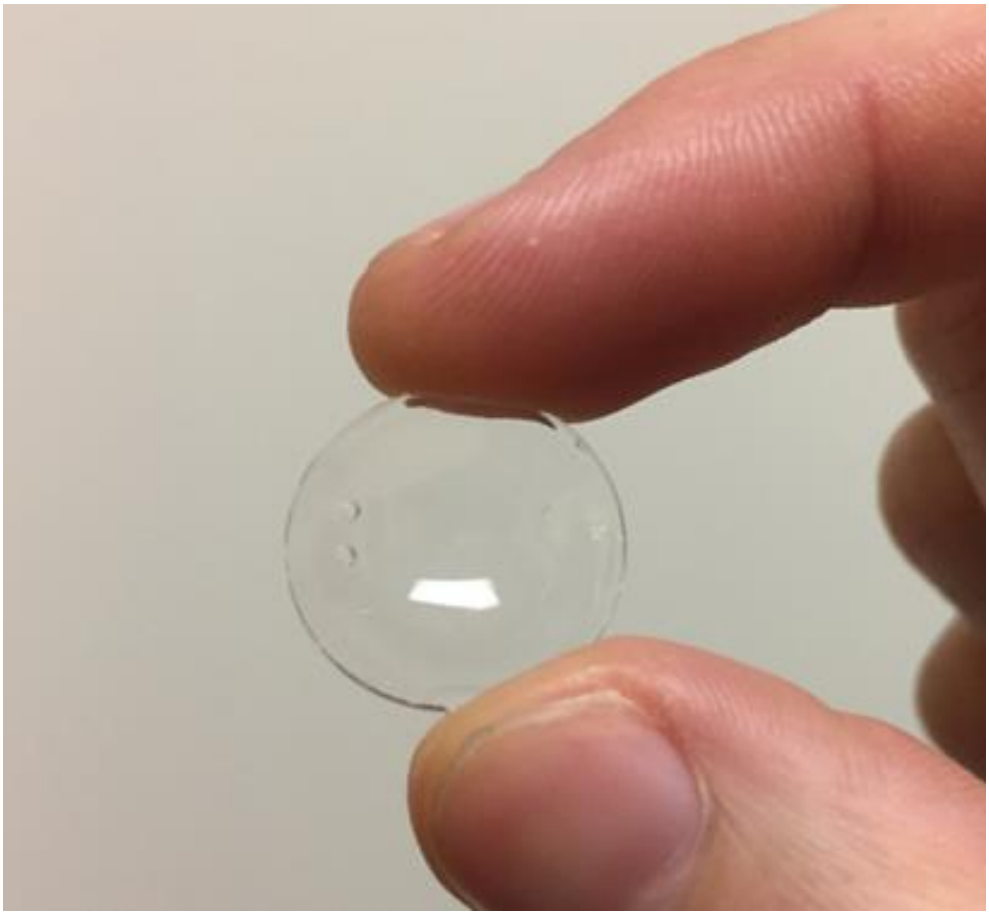


Figure 8: Simulator eye with attached scleral lens and fluorescein in lens bowl, setup on the fluorophotometer in central orientation.

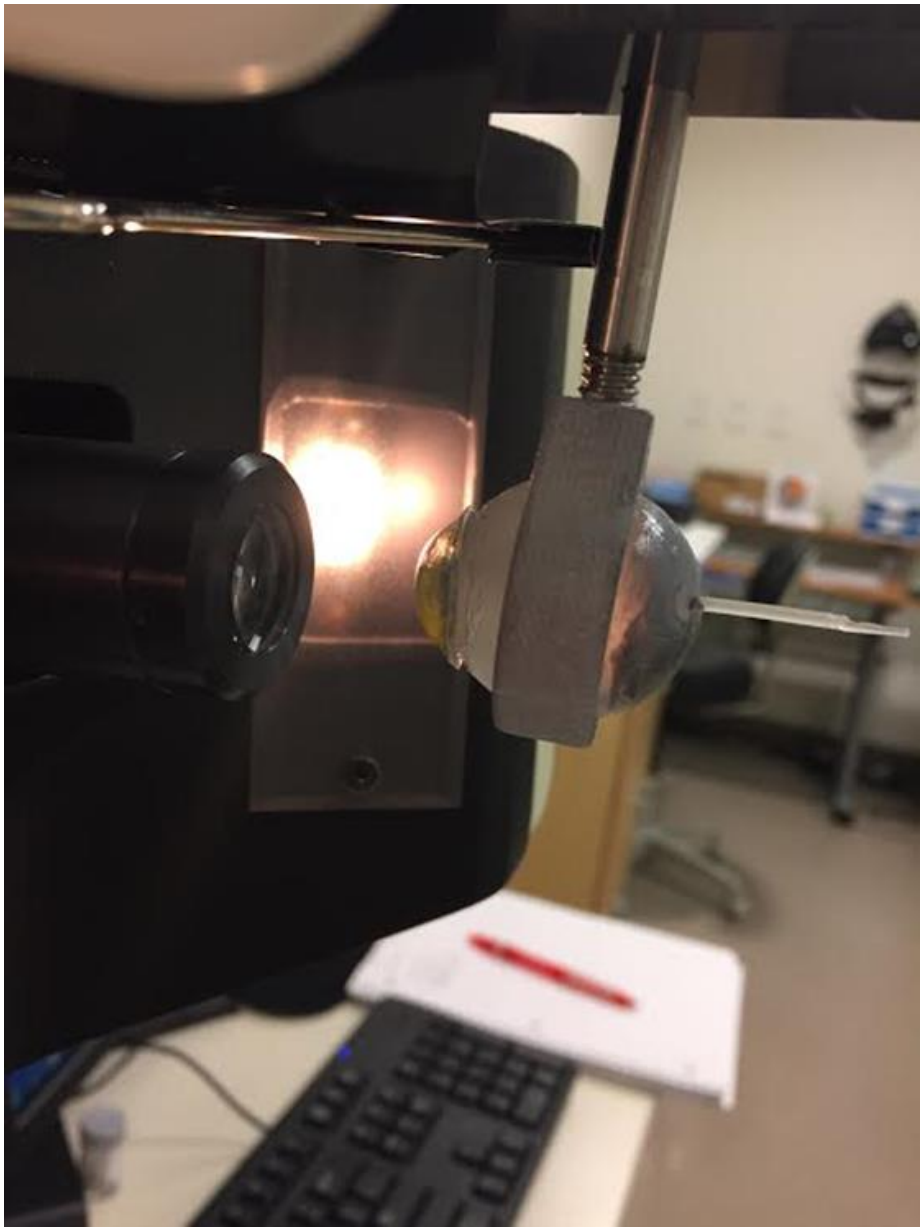
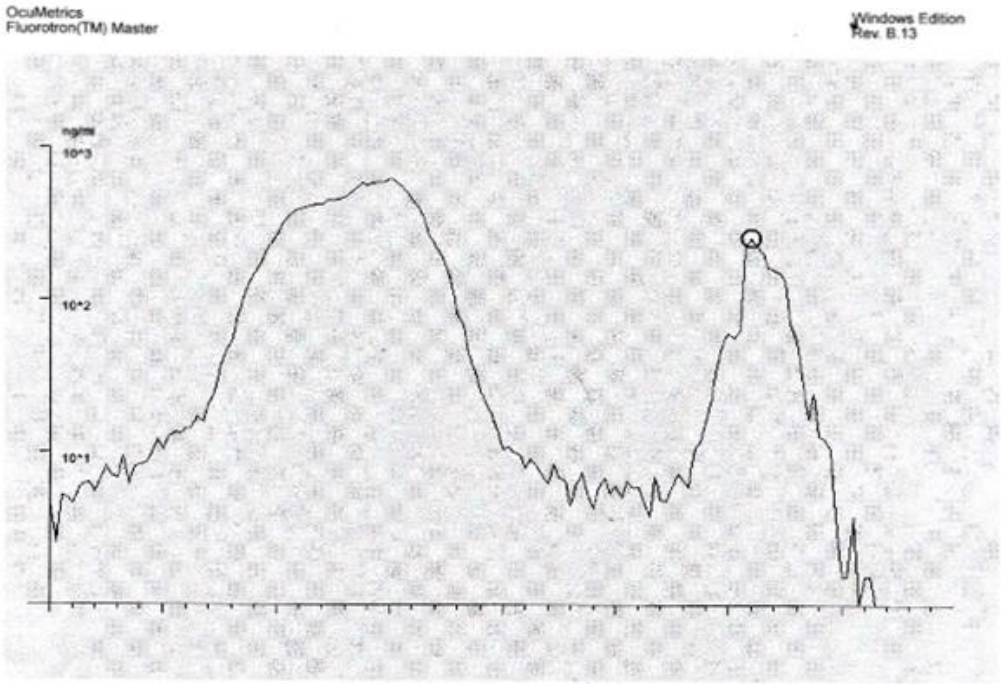


Figure 9: Subject setup for fluorophotometry measurements.

Figure 10: Raw data from the Fluorotron Master. The y-axis represents fluorescein concentration in ng/ml units. The x-axis represents distance into the visual system, beginning posterior to anterior.



Patient: Segel, Eugenia
Patient Comment: N/A
7/18/2012 1:42:24 PM

Step Size: 1
Cornea Location: 26mm
Cornea Value: 262.74
Side: Right Eye
Lens Type: Anterior Chamber
Ref: 190114
Dark: 14
Calibration: 1470
Gate Time: 100
Comment: FITC 0 min

	+ 0 steps	+ 1 steps	+ 2 steps	+ 3 steps	
0 steps	4.6393	2.5516	5.1606	5.1033	ng/ml
4 steps	4.6393	5.6445	6.2631	6.3404	ng/ml
8 steps	5.5672	6.8043	8.1961	7.1136	ng/ml
12 steps	6.8043	9.4333	6.1858	8.0415	ng/ml
16 steps	8.3508	8.6601	9.5479	12.372	ng/ml
20 steps	10.516	12.661	13.686	13.454	ng/ml
24 steps	14.382	14.537	17.475	15.928	ng/ml
28 steps	20.677	25.13	36.419	45.001	ng/ml
32 steps	53.352	74.848	99.513	127.58	ng/ml
36 steps	148.77	171.81	206.3	234.44	ng/ml
40 steps	267.84	320.96	359.16	383.83	ng/ml
44 steps	400.84	407.02	421.56	426.35	ng/ml
48 steps	426.51	456.35	454.42	466.72	ng/ml
52 steps	481.25	510.63	546.82	589.35	ng/ml
56 steps	573.42	591.05	605.9	603.58	ng/ml
60 steps	632.8	615.02	573.42	520.84	ng/ml
64 steps	467.9	414.14	350.81	274.03	ng/ml
68 steps	229.8	206.45	167.87	126.65	ng/ml
72 steps	82.425	69.435	44.947	34.563	ng/ml
76 steps	25.439	21.65	17.909	14.15	ng/ml
80 steps	10.438	10.902	10.052	9.8199	ng/ml
84 steps	7.9642	9.124	8.1961	7.1136	ng/ml
88 steps	6.3404	6.4281	6.8817	6.6497	ng/ml
92 steps	4.562	6.3404	7.4229	5.5672	ng/ml
96 steps	4.33	6.0311	6.8043	5.3352	ng/ml
100 steps	6.1084	5.1033	6.4951	5.8765	ng/ml
104 steps	6.0311	4.8713	3.8661	6.959	ng/ml
108 steps	4.9486	4.8713	5.9536	7.2683	ng/ml
112 steps	6.6497	6.0311	10.825	11.906	ng/ml
116 steps	16.382	23.274	37.81	54.048	ng/ml
120 steps	81.733	98.6	65.492	221.76	ng/ml
124 steps	262.74	231.73	208.23	166.09	ng/ml
128 steps	160.83	153.87	137.63	71.136	ng/ml
132 steps	54.125	32.475	17.011	24.743	ng/ml
136 steps	13.145	12.372	10.825	3.0929	ng/ml
140 steps	1.5464	1.5464	3.8661	0	ng/ml
144 steps	1.5464	1.5464	0	0	ng/ml
148 steps	0				ng/ml

Figure 11: Fluorotron graphs displaying before and after lens application with fluorescein.

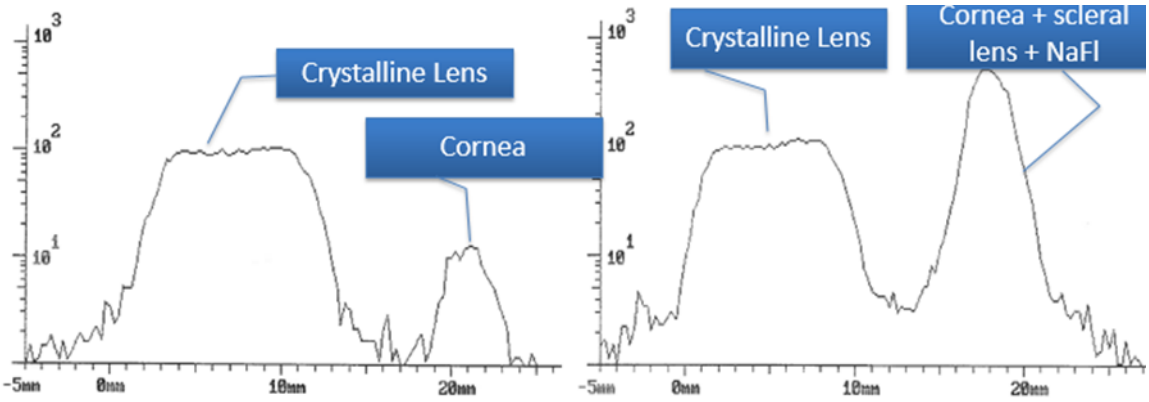


Figure 12: Visante OCT, utilized to image post-tear lens depth.

Figure 13: Mean concentration of fluorescein in central zone, for low and high concentration trials.

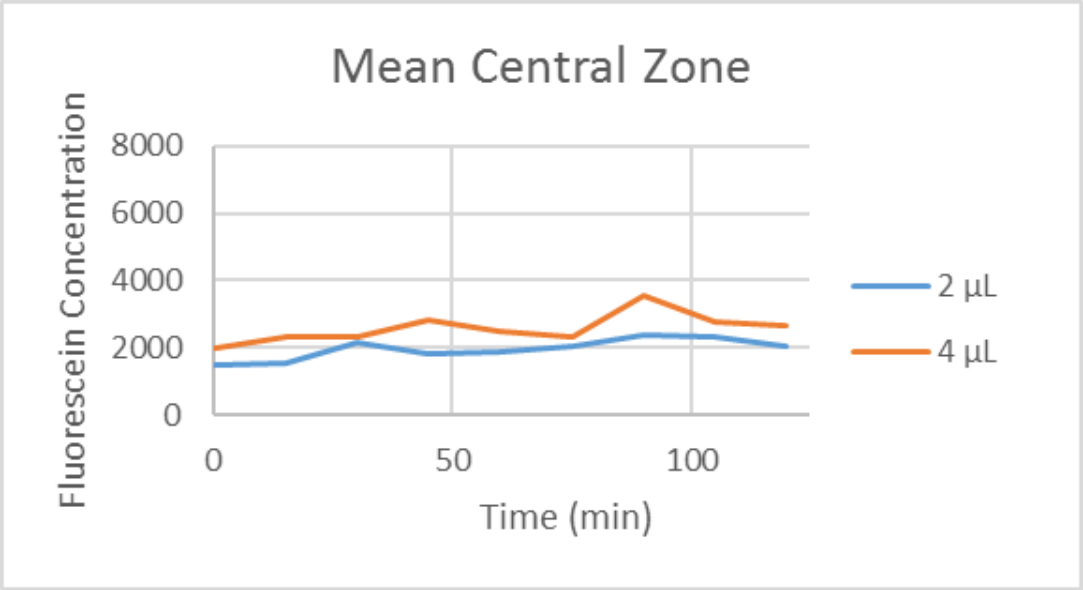


Figure 14: Mean concentration of fluorescein in the inferior zone, for low and high concentration trials.

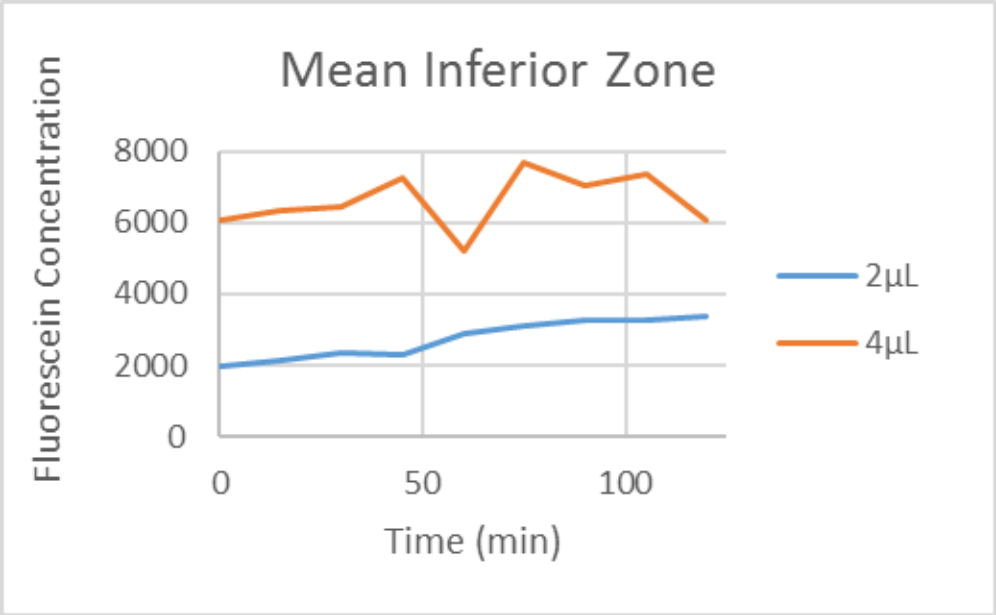


Figure 15: Combined mean of the central, central with right tilt, and central with left tilt fluorescein concentrations for each sagittal depth. The error bars denote the standard deviation.

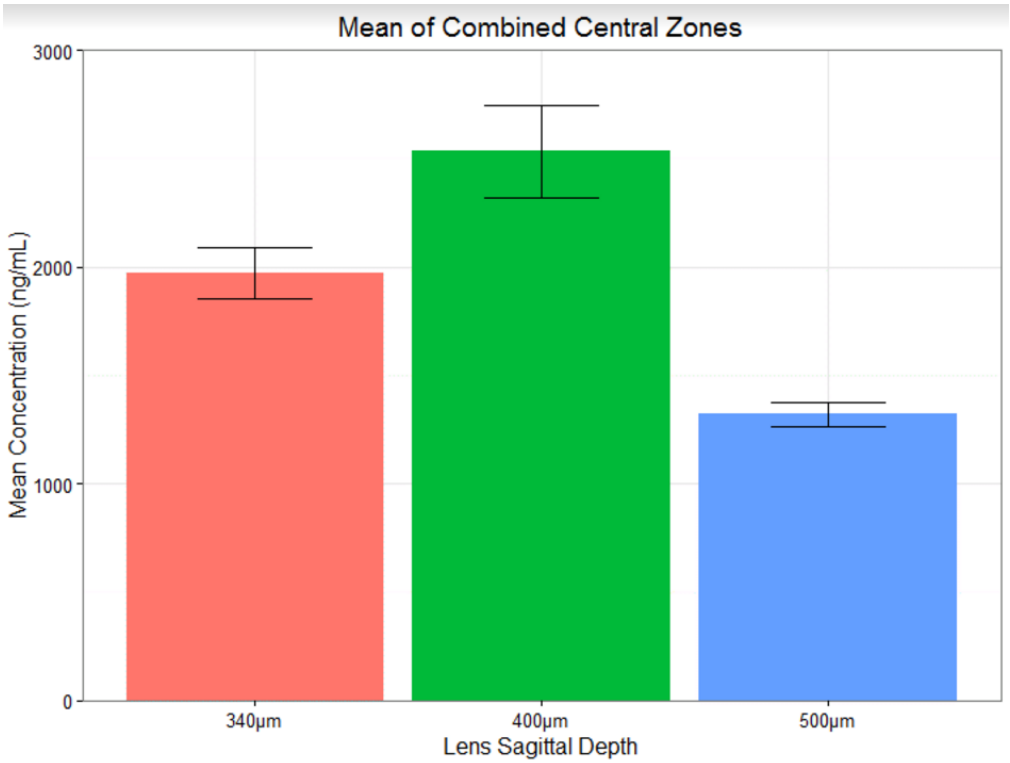


Table 1: Table shows overview of each subject including lens indication, dry eye diagnosis based on questionnaire score, central lens clearance (sag), study group, SGP type, and lens diameter.

Subject	Age	Indication	Dry Eye Dx	Sag	Group	Lens Type	Diameter
001	25	Other	Normal	140	Uninterrupted	Digiform	18
003	30	Kc	Suspect	530	Uninterrupted	MSD	15.8
004	45	Post-Sx	Suspect	690	Uninterrupted	Jupiter	18
005	41	Kc	Dry Eye	230	Interrupted	Jupiter	18.8
006	33	Kc	Suspect	430	Interrupted	MSD	15.8
007	30	Kc	Dry Eye	310	Uninterrupted	Jupiter	18.2
008	27	Kc	Dry Eye	300	Interrupted	MSD	18
009	43	Kc	Normal	220	Uninterrupted	Digiform	18
010	25	Kc	Dry Eye	170	Uninterrupted	Jupiter	18.2
011	47	Kc	Suspect	480	Interrupted	Digiform	18
013	29	Kc	Dry Eye	550	Uninterrupted	Jupiter	16.6
014	37	Kc	N/A	70	Interrupted	Digiform	18
015	32	Control	Normal	260	Control	Custom Stable	16.8
016	30	Kc	Suspect	290	Uninterrupted	Digiform	18
017	30	Kc	Suspect	230	Interrupted	Custom Stable	16.7
018	26	Control	Normal	230	Control	Zen Lens	16
019	24	Control	Dry Eye	N/A	Control	Custom Stable	16.8
020	24	Control	Dry Eye	210	Control	Custom Stable	16.8
021	24	Control	Suspect	120	Control	Custom Stable	16.8
022	31	Kc	Suspect	50	Uninterrupted	Digiform	18
025	25	Control	Suspect	250	Control	Zen Lens	16
026	25	Control	Normal	150	Control	Zen Lens	16
027	25	Control	Suspect	100	Control	Zen Lens	16
028	24	Control	Normal	160	Control	Zen Lens	16
029	25	Control	Normal	390	Control	Zen Lens	17
030	30	Kc	Dry Eye	450	Uninterrupted	Zen Lens	17
031	31	Post-Sx	Dry Eye	200	Uninterrupted	Custom Stable	16.8
033	20	Kc	Normal	320	Uninterrupted	Zen Lens	17
034	69	Kc	Suspect	170	Interrupted	Jupiter Reverse	18.2
035	31	Other	Dry Eye	420	Interrupted	Zen Lens	16
036	25	Other	Normal	270	Interrupted	Zen Lens	16
037	50	Kc	Normal	250	Interrupted	Zen Lens	17
038	29	Other	Dry Eye	270	Interrupted	OneFit	14.9

Figure 16: Summary of simulator data for 2 µL concentration. The error bars represent the standard deviation.

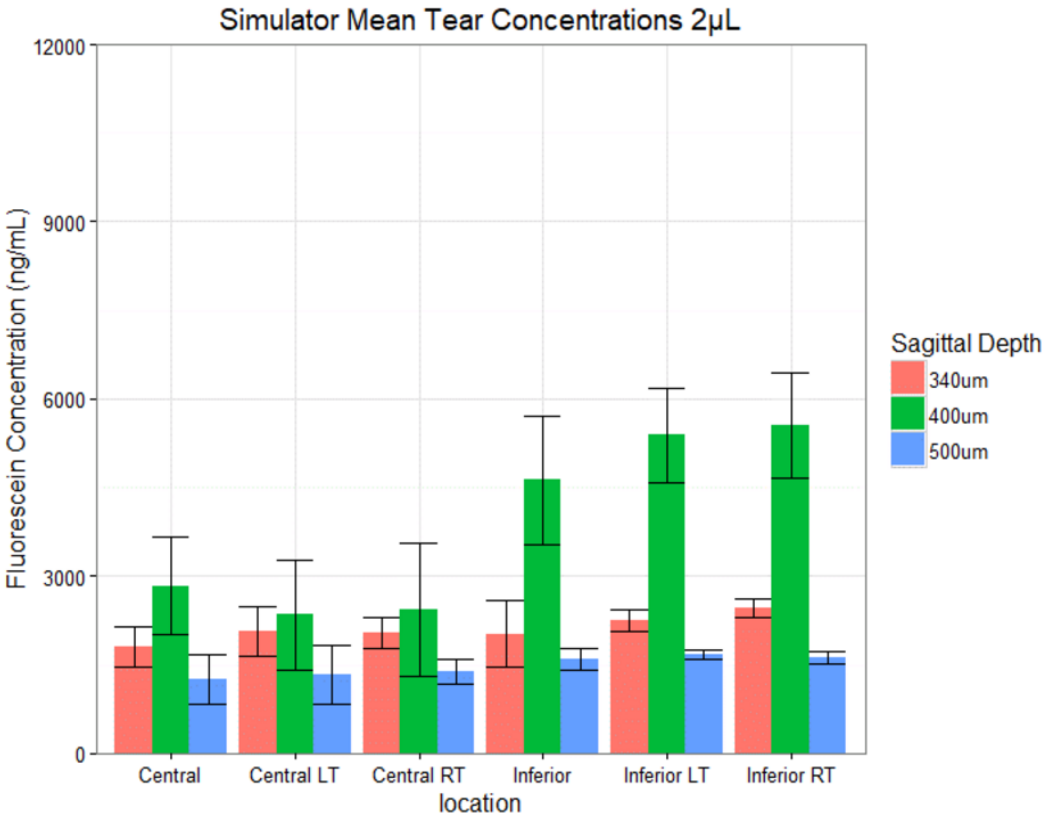


Figure 17: Summary of simulator data for 4 µL concentration. The error bars represent the standard deviation.

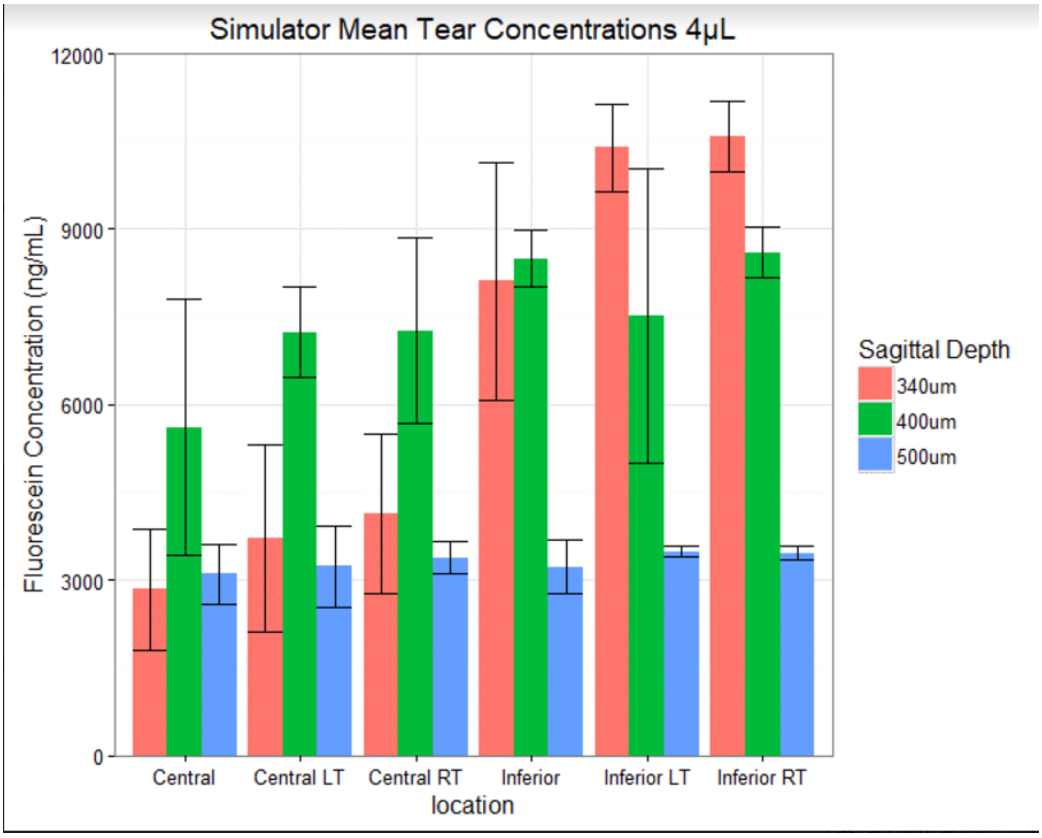
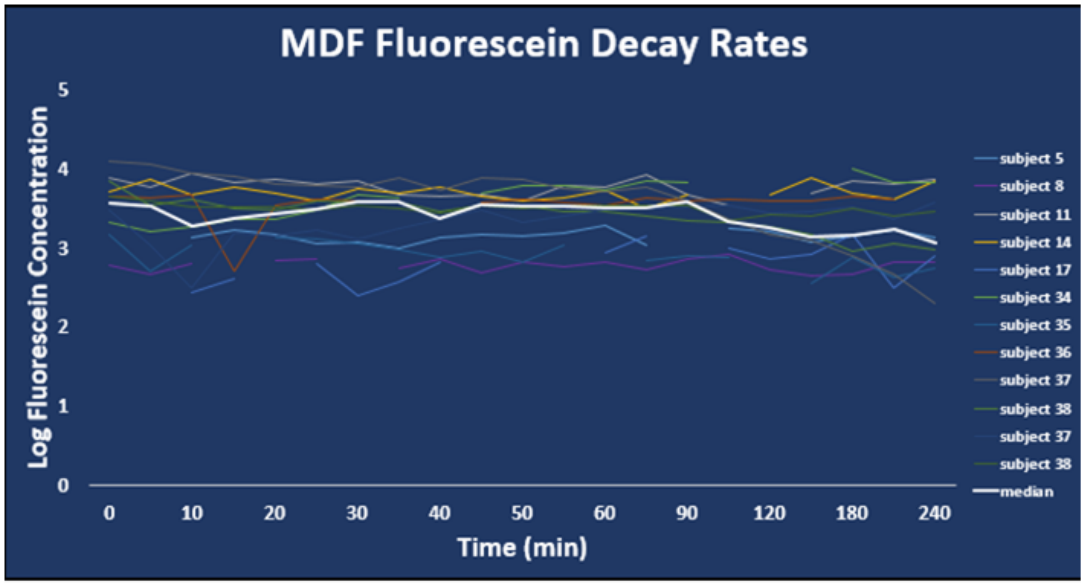


Figure 18: The fluorescein decay rates (change in fluorescein concentration over time) for the MDF (top) and non-MDF (bottom) subjects. Most subjects show slow rates of decay over the 240-minute study session, indicating limited tear exchange. The graphs depict the log of the concentration over time in minutes. The median values for each group are shown by the white lines.



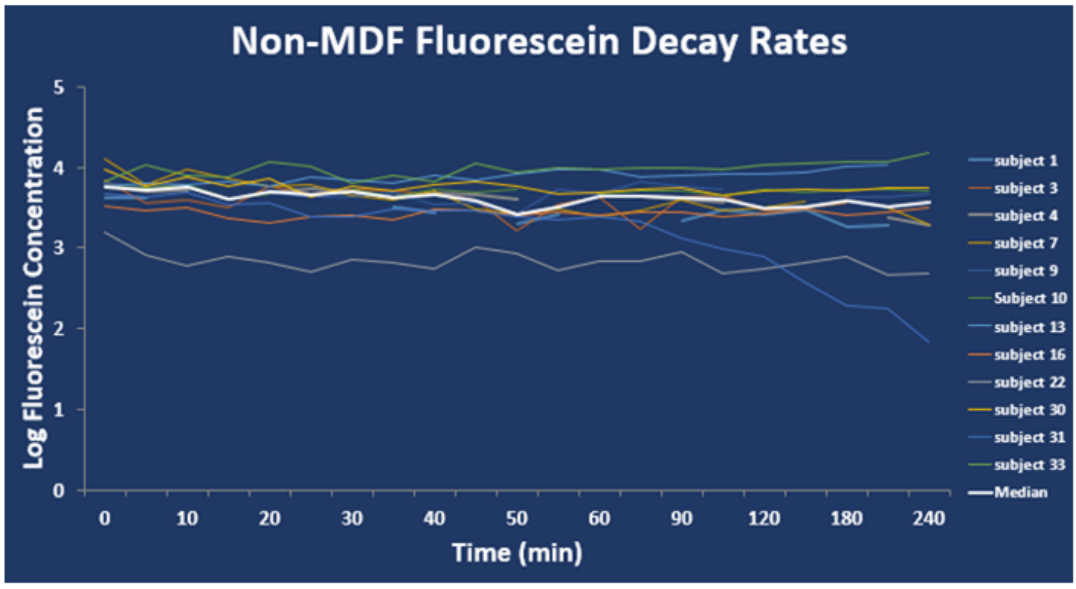


Figure 19: Mean tear exchange rates for MDF, Non-MDF, and control groups.

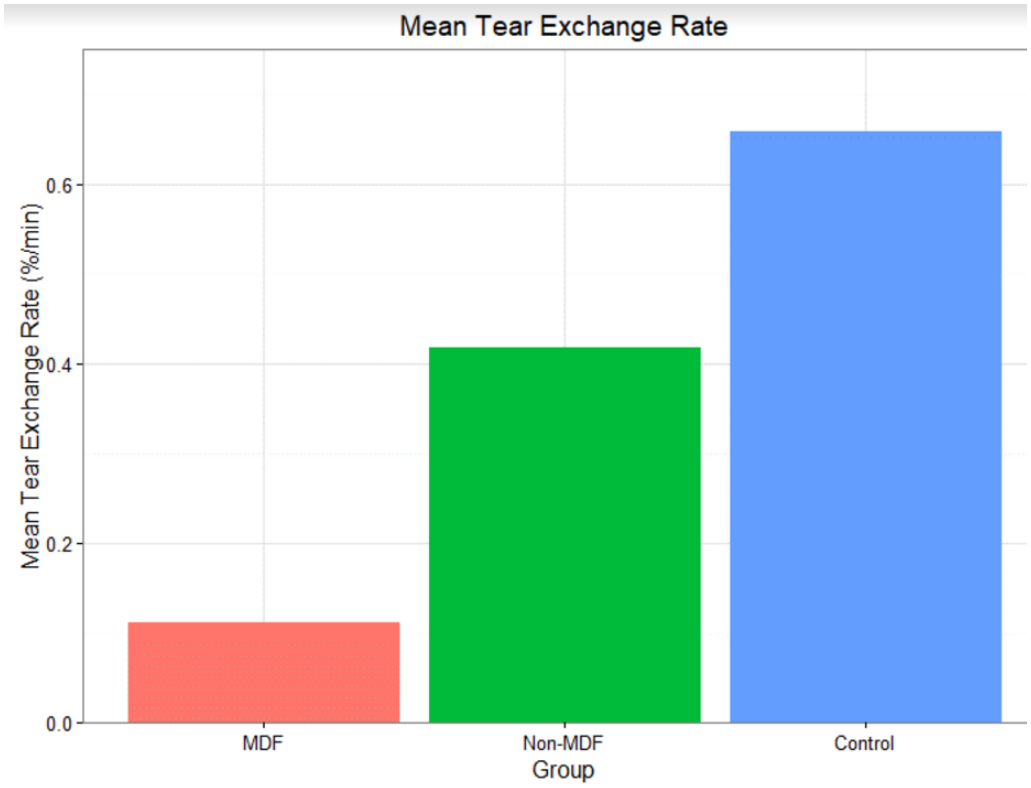


Figure 20: Illustrates decrease in density and thickness of tear film debris when sagittal depth is lowered.

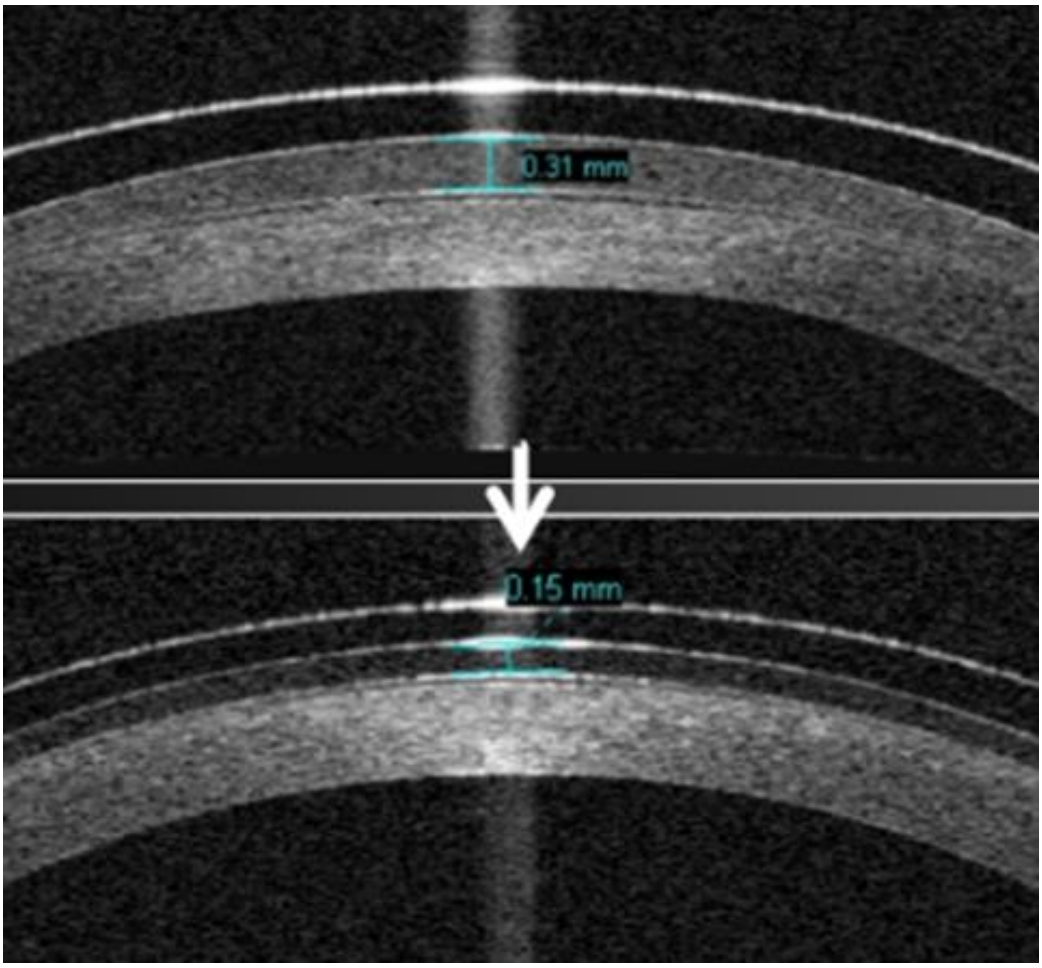
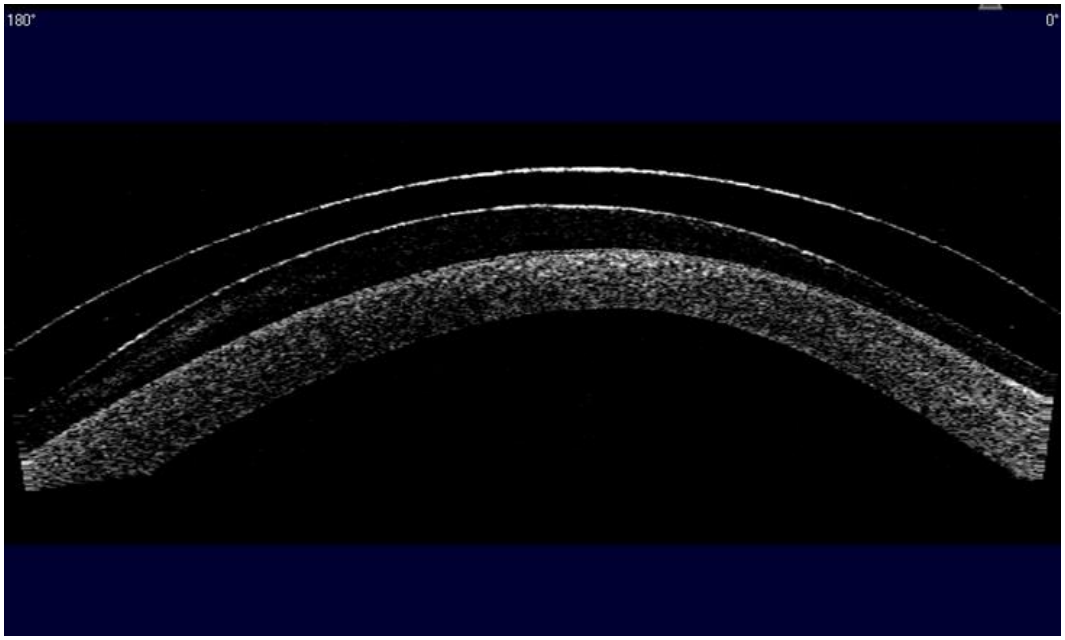


Figure 21: OCT scan of SGP on a subject. Note the variation in post-lens tear layer depth across the ocular surface. Measurements through off-axis may cause falsely elevated or depressed concentration measurements.



References

1. Pearson RM. The centenary of the contact lens. *J Br Contact Lens Assoc*. 1988;11(2):12-16. doi:10.1016/S0141-7037(88)80003-X.

2. Pearson R. The Samisch Case and the Mullers of Wiesbaden. *Optom Vis Sci*. 2009;86(2):157-164.

3. Pearson RM, Efron N. Hundredth anniversary of August Muller's inaugural dissertation on contact lenses. *Surv Ophthalmol*. 1989;34(2):133-141. doi:10.1016/0039-6257(89)90041-6.

4. Pearson RM. Karl Otto Himmler, manufacturer of the first contact lens. *Contact Lens Anterior Eye*. 2007;30(1):11-16. doi:10.1016/j.clae.2006.10.003.

5. Ezekiel D. Gas permeable haptic lenses. *J Br Contact Lens Assoc*. 1983;6(4):158-161. doi:10.1016/S0141-7037(83)80064-0.

6. Mountford J, Carkeet N, Carney L. Corneal thickness changes during scleral lens wear: Effect of gas permeability. *Int Contact Lens Clin*. 1994;21(1-2):19-22. doi:10.1016/0892-8967(94)90036-1.

7. Bergmanson JPG, Ezekiel DF, van der Worp E. Scleral contact lenses and hypoxia: Theory versus practice. *Contact Lens Anterior Eye*. 2015;38(3):145-147. doi:10.1016/j.clae.2015.03.007.

8. Bennett E. GP Annual Report 2015. *Contact Lens Spectr*. 2015;30(October 2015):24-27.

9. Bleshoy H, Pullum KW. Corneal response to gas-permeable impression scleral lenses. *J Br Contact Lens Assoc*. 1988;11(2):31-34. doi:10.1016/S0141-7037(88)80006-5.

10. Efron N, Brennan NA, Holden BA. The Oxygen Permeability of Rigid Gas Permeable Contact Lens Materials : Reaching a Concensus. 1987:62-66.

11. Dimit R, Gire A, Pflugfelder SC, Bergmanson JPG. Patient ocular conditions and clinical outcomes using a PROSE scleral device. *Contact Lens Anterior Eye*. 2013;36:159-163.

12. Dalton K, Sorbara L. Fitting an MSD (mini scleral design) rigid contact lens in advanced keratoconus with INTACS. *Contact lens Anterior Eye*. 2011;34(6):274-281. doi:10.1016/j.clae.2011.05.001.

13. Grey F, Carley F, Biswas S, Tromans C. Scleral contact lens management of bilateral exposure and neurotrophic keratopathy. *Contact Lens Anterior Eye*. 2012;35(6):288-291. doi:10.1016/j.clae.2012.07.009.

14. Downie LE, Lindsay RG. Contact lens management of keratoconus. *Clin Exp Optom*. 2015;98(4):299-311. doi:10.1111/cxo.12300.

15. Schornack MM, Patel S V. Scleral Lenses in the Management of Keratoconus. *Eye Contact Lens Sci Clin Pract*. 2010. doi:10.1097/ICL.0b013e3181c786a6.

16. Alipour F, Kheirkhah A, Jabarvand Behrouz M. Use of mini scleral contact lenses in moderate to severe dry eye. *Contact Lens Anterior Eye*. 2012. doi:10.1016/j.clae.2012.07.006.

17. Sonsino J, Mathe DS. Central Vault in Dry Eye Patients Successfully Wearing Scleral Lens. *Optom Vis Sci*. 2013;90.

18. Heur M, Bach D, Theophanous C, Chiu GB. Prosthetic replacement of the ocular surface ecosystem scleral lens therapy for patients with ocular symptoms of chronic Stevens-Johnson syndrome. *Am J Ophthalmol*. 2014. doi:10.1016/j.ajo.2014.03.012.

19. Schornack MM, Baratz KH, Patel S V, Maguire LJ. Jupiter scleral lenses in the management of chronic graft versus host disease. *Eye Contact Lens*. 2008. doi:10.1097/ICL.0b013e318188e205.

20. Severinsky B, Behrman S, Frucht-Pery J, Solomon A. Scleral contact lenses for visual rehabilitation after penetrating keratoplasty: long term outcomes. *Contact lens Anterior Eye*. 2014;37(3):196-202. doi:10.1016/j.clae.2013.11.001.

21. Mahadevan R, Jagadeesh D, Rajan R, Arumugam AO. Unique Hard Scleral Lens Post-LASIK Ectasia Fitting. *Optom Vis Sci*. 2014;73(2):136-142. doi:10.1097/OPX.0000000000000170.

22. Kalwerisky K, Davies B, Mihora L, Czyz CN, Foster JA, Demartelaere S. Use of the Boston ocular surface prosthesis in the management of severe periorbital thermal injuries: A case series of 10 patients. *Ophthalmology*. 2012. doi:10.1016/j.ophtha.2011.08.027.

23. Takahide K, Parker PM, Wu M, et al. Use of Fluid-Ventilated, Gas-Permeable Scleral Lens for Management of Severe Keratoconjunctivitis Sicca Secondary to Chronic Graft-versus-Host Disease. *Biol Blood Marrow Transplant*. 2007;13.

doi:10.1016/j.bbmt.2007.05.006.

24. Michaud L, van der Worp E, Brazeau D, Warde R, Giasson CJ. Predicting estimates of oxygen transmissibility for scleral lenses. *Contact lens Anterior Eye*. 2012;35(6):266-271. doi:10.1016/j.clae.2012.07.004.

25. Florkey L, Fink BA, Ph D, Mitchell GL, Hill RM. Tear Exchange and Oxygen Reservoir Effects in Silicone Hydrogel Systems. 2003;29:90-92. doi:10.1097/01.ICL.0000042380.42931.01.

26. Fatt I. Gas-to-Gas oxygen permeability measurements on RGP and silicone rubber lens materials. *Int Contact Lens Clin*. 1991;18(9):192-199. doi:10.1016/0892-8967(91)90007-M.

27. Muntz A, Subbaraman LN, Sorbara L, Jones L. Tear exchange and contact lenses: a review. *J Optom*. 2015;8(1):2-11. doi:10.1016/j.optom.2014.12.001.

28. Eiden B. Scleral lenses: We don't know what we don't know. *Contact Lens Spectr*. 2016;31(October 2016):14, 15.

29. Caroline P, Andre M. Cloudy Vision with Sclerals. *Contact Lens Spectr*. 2012;27(June 2012):56. http://www.clspectrum.com/articleviewer.aspx?articleID=107081.

30. Walker MK, Bergmanson JP, Miller WL, Marsack JD, Johnson LA. Complications and fitting challenges associated with scleral contact lenses: A review. *Cont Lens Anterior Eye*. 2015;39(2):88-96. doi:10.1016/j.clae.2015.08.003.

31. Leach N, Miller W, Mckinney A, Polizzi C, can der Worp E, Bergmanson J. *Midday Visual Fogging in Scleral Lens Wearers – Does Fit Matter*. Vol 54. 2012.

32. Rathi VM, Mandathara PS, Vaddavalli PK, Srikanth D, Sangwan VS. Fluid filled scleral contact lens in pediatric patients: challenges and outcome. *Cont Lens Anterior Eye*. 2012;35(4):189-192. doi:10.1016/j.clae.2012.03.001.

33. Pecego M, Barnett M, Mannis MJ, Durbin-Johnson B. Jupiter Scleral Lenses: the UC Davis Eye Center experience. *Eye Contact Lens*. 2012;38(3):179-182. doi:10.1097/ICL.0b013e31824daa5e.

34. Hemmati RT, Walker MK, Bergmanson J. Scleral Lens Tear Film Reservoir Analysis: Protein and Lipid Concentrations in Midday Fogging. 2014;4:1.

35. McKinney A, Miller W, Leach N, Polizzi C, van der Worp E, Bergmanson J. The Cause of Midday Visual Fogging in Scleral Gas Permeable Lens Wearers. *Invest Ophthalmol Vis Sci* . 2013:ARVO E-Abstract 5483.

36. Barequet IS, Ortenberg L, Geraisy W, Behrman S. Wearing Time as a Measure of Success of Scleral Lenses for Patients with Irregular Astigmatism. *Eye Contact Lens*. 2013;39(6):381-384. doi:10.1097/ICL.0b013e31829e8faa.

37. Visser E, Sc M, Visser R, Lier HJJ Van, Otten HM, Sc B. Modern Scleral Lenses Part II : Patient Satisfaction. *Eye Contact Lens Sci Clin Pract*. 2007;33(1):21-25. doi:10.1097/01.icl.0000228964.74647.25.

38. Walker M. Scleral lenses, clearing the fog. *ISITE online J*. 2014;(October):2014.

39. Miller BYWL. Scleral Contact Lens Fog Optimizing the Tear Reservoir. *Contact*

Lens Spectr. 2013;28(September 2013):52.

40. Morrison S, Walker M, Caroline P, Lampa M, Andre M, Kojima R. *Tear Exchange Beneath Scleral Lenses?*

41. Caroline P, Andre M. How Much Tear Exchange Occurs Beneath Scleral Lenses. *Contact Lens Spectr*. 2014;29(July 2014):64. http://www.clspectrum.com/articleviewer.aspx?articleID=111360.

42. Rathi VM, Mandathara PS, Taneja M, Dumpati S, Sangwan VS. Scleral lens for keratoconus: Technology update. *Clin Ophthalmol*. 2015;9:2013-2018. doi:10.2147/OPTH.S52483.

43. Cunha-Vaz J. History of fluorophotometry. *Grafe's Arch Clinc Exp Ophthalmol*. 1985;222:168.

44. Langham M, Wybar KC. Fluorophotometric Apparatus for the Objective Determination of Fluorescence in the Anterior Chamber of the Living Eye. *Brit J Ophthal*. 1954;38(52):52-57.

45. Smith AT, Jones DP, Sturrock GD, Wright P. An improved objective slit-lamp fluorophotometer using tungsten-halogen lamp excitation and synchronous detection. 1977:722-725.

46. Munnerlyn CR, Gray JR, Hennings DR. Design considerations for a fluorophotometer for ocular research. *Graefe's Arch Clin Exp Ophthalmol*. 1985;222(4-5):209-211. doi:10.1007/BF02133676.

47. Mishima S, Gasset A, Klyce SD, Baum JL. Determination of Tear Volume and

Tear Flow. 1966;5(3):264-276.

48. Maus TL, Brubaker RF. Measurement of Aqueous Humor Flow by Fluorophotometry in the Presence of a Dilated Pupil. *IOVS*. 1999;40(2):542-546.

49. Pearce EI, Keenan BP, McRory C. An improved fluorophotometric method for tear turnover assessment. *Optom Vis Sci*. 2001;78(1):30-36. http://www.ncbi.nlm.nih.gov/pubmed/11233332.

50. Eter N, Gobbels M. A New Technique for tear film fluorophotometry. *Br J Ophthalmol*. 2002;86(6):616-619. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1771146/.

51. Sorbara L, Simpson T, Vaccari S, Jones L, Fonn D. Tear turnover rate is reduced in patients with symptomatic dry eye. *Cont Lens Anterior Eye*. 2004;27(1):15-20. doi:10.1016/j.clae.2003.10.001.

52. Paugh JR, Stapleton F, Keay L, Ho A. Tear exchange under hydrogel contact lenses: Methodological considerations. *Investig Ophthalmol Vis Sci*. 2001;42(12):2813-2820.

53. Quinn T. GP Versus Soft Lenses. *Contact Lens Spectr*. 2012;27(March 2012):34-39.

54. McNamara NA, Polse KA, Bonnano J. Fluorophotometry in Contact Lens Research: The Next Step. *Optom Vis Sci*. 1998;75(5):316-322. doi:10.1097/00006324-199805000-00020.

55. Berger RE, Corrsin S. A surface tension gradient mechanism for driving the pre-

corneal tear film after a blink. *J Biomech*. 1974;7(3):225-238. doi:10.1016/0021-9290(74)90013-X.

56. Maki KL, Ross DS. Exchange of Tears under a Contact Lens Is Driven by Distortions of Contact Lens. *Integr Comp Biol*. 2014;54(6):1043-1050. doi:10.1093/icb/icu092.

57. Miller K, Polse K, Radke C. Fenestrations Enhance Tear Mixing under Silicone-hydrogel Contact Lenses. *Invest Ophthalmol Vis Sci* . 2003;44:60-67.

58. Marice, Ruben M. Fluid exchange under scleral contact lenses in relation to wearing time. *Br J Ophthalmol*. 1970;54(486).

59. Narayanan S, Miller W, Prager T, et al. The Diagnosis and Characteristics of Dry Eye. *Eye Contact Lens*. 2005;31(3):96-104. http://ovidsp.tx.ovid.com/sp-3.15.1b/ovidweb.cgi?QS2=434f4e1a73d37e8c94f3b1572.

60. Walker M, Bergmanson JP, Marsack JD, Miller W, Johnson L. Complications and Fitting Challenges Assocaited with Scleral Contact Lenses: A Review. *Contact Lens Anterior Eye*. 2016;39(2):88-96.

61. Mathew JH, Building JDA. Scleral Contact Lens - Managing the Midday Fog.

62. van der Worp E, Bornman D, Ferreira DL, Faria-Ribeiro M, Garcia-Porta N, González-Meijome JM. Modern scleral contact lenses: A review. *Cont Lens Anterior Eye*. 2014;37(4):240-250. doi:10.1016/j.clae.2014.02.002.

63. Sonsino J, Schornack M. Troubleshooting Scleral Lenses. *Contact Lens Spectr*. 2013;28(May 2013):26-33.

64. Hill G, Michaud L, Jedlicka J. Addressing scleral lens clinical concerns. *Optom Times*. 2016:2016-2018.

65. Jedlicka J. Solving Scleral Lens Complications. *Contact Lens Spectr*. 2012;27(October 2012):40-44.

66. Nichols JJ, Bennett ES, Starcher L. Education Highlights from the 2015 GSLS. *Contact Lens Spectr*. 2015;30(April 2015):22-30.

67. Taylor-Westt S. Top 10 complications of scleral lenses. *Optician*. 2014:34-39.

68. Jedlicka J, Johns L, Brynes S. Scleral Contact Lens Fitting Guide. *Contact Lens Spectr*. 2010;(October 2010).

69. Van der Worp E. *A Guide to Scleral Lens Fitting, Version 2.0*. Forest Grove: Pacfici University; 2015. http://commons.pacificu.edu/mono/4/%0Ahttp://commons.pacificu.edu/cgi/viewcontent.cgi?article=1003&context=mono.

70. Watanabe R. All Sclerals Are Not the Same. *Contact Lens Spectr*. (January 2013).

71. Gupta N, Kaur M. Scleral Contact Lenses. *Alllied Ophthalmic Sci*. 2017:1-9.