Custom Anterior Surfacing of Scleral Lens for Vision Quality Improvement in Patients with Keratoconus

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I. PURPOSE OF THE STUDY AND BACKGROUND

1. Purpose of the study

The goal of the study is to examine the effects of custom front-surface wavefront correction on visual performance, and on neutralization of higher order aberrations, in patients wearing a scleral lens device. We will study patients with keratoconus, the most common type of corneal ectasia, who have already been fitted with the BostonSight BSS (Boston Sight Scleral) for improved visual function.

2. Background

Despite the increasing pace of innovation in vision care, there are many vision ailments, which do not yet have effective therapies. These eye conditions can result in moderate to severe vision impairment or blindness, which have severe impacts on an individual's quality of life. One such condition is corneal ectasia which is characterized by a progressive thinning of the cornea causing a distortion in its shape and consequential visual impairment[1]. Many specific conditions fall within this category include keratoconus, keratoglobus, pellucid marginal degeneration[2], Terrien's marginal degeneration, and post-operative complications related to LASIK, RK, PRK, or corneal transplantation[3].

Distortions of the cornea from these corneal ectasias can result in increased levels of higher order aberrations[4, 5]. Higher order aberrations are types of optical defocus that cannot be corrected by conventional spherical and astigmatic spectacle correction. This makes standard spectacle and contact lens vision correction inadequate for all but mild corneal ectasias. More advanced corrections such as scleral lenses can help mask higher order aberration content using a fluid reservoir, but some higher order aberrations can remain uncorrected and contribute to the degradation of visual performance[6]. These remaining aberrations following correction are termed residual aberrations. Interest in corneal aberrations has increased with the development of customized contact lenses[7] and customized corrective refractive surgery[8, 9].

The goal of these treatment options is to improve visual performance beyond the results gained by only correcting lower order aberrations, namely the spherical and cylindrical refractive errors. These customized techniques require the reliable determination of both overall higher order corneal aberrations and specific higher order aberration terms.

Measurement of residual higher order aberrations after correction of lower order aberrations with a scleral lens is a necessary step towards aberration correction and visual performance improvement. The amount of aberration present in an eye can be quantified using a wavefront analyzer. This method allows for quick, noninvasive, objective assessment of the quality of the optics of the eye[10].

Several previous studies have been conducted to study and correct the effects of residual aberration with scleral lenses. Rigid gas permeable corneal contact lenses with aspheric optics offer improved visual acuity. Studies, including one from this center, have found that aspheric front surface contact lenses improved visual acuity when compared to conventional spherical contact lenses.[11, 12, 13] Earlier work at Boston Sight, Flaum Eye Institute, and elsewhere, has established that it is possible to reduce higher-order aberrations in patients wearing a scleral lens device with custom wavefront correction; in this early work, visual performance did not achieve levels typical of the normal population.[14, 15] This study is designed to allow for further refinement of customized correction for patients with aberrated optical systems.

The current study is another collaboration between Flaum Eye Institute and Boston Sight with the addition of Ovitz Corporation. The goal of the study is to examine the effects of custom front-surface wavefront correction on visual performance, and on neutralization of higher order aberrations, in patients wearing a scleral lens device. Ovitz manufactures an FDA-registered wavefront sensing device capable of measuring the residual higher order aberrations being studied. BostonSight provides the capability of manufacturing the standard and Higher Order Aberration (HOA)-customized scleral lenses being studied. The study will use the BostonSight Scleral (BSS) lens which is similar to the PROSE device used in previous collaborative studies. The BSS lens is FDA-cleared and provides a commercial solution with a standardized fitting process.

II. CHARACTERISTICS OF THE RESEARCH POPULATION

1. Number of subjects

Up to 40 subjects may be enrolled in the study. This number has been chosen based on the limited number of patients that fulfill the eligibility for participation.

2. Gender of Subjects

Inclusion in the study will not be gender specific and will not necessarily be equally men and women.

3. Age of Subjects

The subjects must be 18 or older to participate in this study.

4. Racial and Ethnic Origin
Subjects will not be selected based on racial or ethnic origin.

5. Inclusion Criteria
A person will be included in the study if he/she:

- Is 18 years or older and has full legal capacity to volunteer.
- Has been diagnosed with Keratoconus;
- Has no other active ocular disease;
- Is currently wearing the BostonSight BSS in at least one eye;
- Has non-spherical BostonSight BSS haptic design in the study eye;
- Has 20/400 or better best corrected visual acuity with pinhole 20/60 or better in the study eye;
- Is not pregnant or nursing;
- Has voluntarily agreed to participate in the study by signing the statement of informed consent;

6. Exclusion Criteria
A person will be excluded from the study if he/she:

- Is under the age of 18;
- Has best corrected visual acuity outside 20/400;
- Pregnant or nursing at the time of enrollment in the study;

7. Vulnerable Subjects

There are no vulnerable subjects for this study. All subjects will be notified that their participation is voluntary and that they are free to withdraw from the study at any time.

III. METHODS AND PROCEDURES

1. Overview

This study will be a single center, double-masked collection of data taking place at the Flaum Eye Institute. Informed consent will be obtained from all subjects after a thorough explanation of the nature and possible risks of the study. Flaum Eye Institute electronic health records of existing patients will first be screened by an optometrist or ophthalmologist to verify that they do not fall under the exclusion criteria. Some study communication regarding scheduling will be done over the phone or email. The screening will be similar to a standard

eye exam (without eye dilation) and will include a slit lamp examination as well as visual acuity and basic vision evaluation.
The study eye will be chosen based on inclusion criteria; if both eyes qualify, the eye with worse best corrected acuity will be chosen. A new scleral lens that incorporates peripheral etched markings is needed for the second visit. These markings are used to determine the exact rotational and positional orientation of the lens on the eye when performing the HOA measurement in the second visit. If screening evaluation reveals that the current lens does not fully neutralize spherical refractive error or that the current lens is not positionally stable, a design of this new lens will be updated to these new optimized parameters. If no optimization is required, then an identical lens will be created with the orientation markings added. The subject will keep his or her original lens and wear it between study visits until the end of the study. The new scleral lenses that will be made for each subject will be kept at the Flaum Eye Institute between subject visits. The principle investigator along with the study team will be responsible for storage, dispensing, collection, accountability and disposal. BostonSight will be responsible for the creation of the lenses.

At the second visit, the patient's vision and fit will be evaluated with the optimized baseline BSS lens. Visual acuity and device fit will be evaluated and recorded. If the BSS device fit is still not optimized, then a new device will be made, and the second visit evaluation will be rescheduled. Once the baseline lens design is determined to be satisfactory, the patient will have their wavefront aberration measured with a wavefront sensor. We will dilate the pupil pharmacologically with phenylephrine (2.5%) and tropicamide (1%) and take wavefront measurements of the optical aberrations of the subject's eye wearing the baseline lens using a portable, non-invasive wavefront analyzer designed to measure highly aberrated eyes (Ovitz, P10/EyeProfiler). We will then design and manufacture a study lens that is identical in design to the baseline BostonSight BSS lens except for a custom front surface designed to neutralize the optical aberrations measured with the wavefront analyzer. This HOA-optimized lens will be created prior to the third visit.

At the third visit the patient's vision and fit will be evaluated with the new HOA-optimized lens. A designated study team member will measure visual acuity and over-refraction of the patient. If an adjustment is needed for the lens, then a new device will be made, and the third visit evaluation will be rescheduled.

Once well-fitting baseline and HOA-optimized test lenses are established, both lenses will be remade and presented to the designated study team member in charge of evaluation and subject together in a masked fashion. During a fourth visit, the patient's vision will be extensively evaluated using standard non-invasive optometric measurements with each of the two lenses. First the patient's will undergo a basic evaluation with each lens to ensure that the fit is correct. The patient will then undergo basic visual acuity; high and low contrast visual acuity, contrast sensitivity, and subjective vision scoring with each lens. The subject's wavefront aberration will also be measured again with each lens.

The wide variety of visual assessments have been chosen to properly evaluate keratoconic eyes with heavy high order aberration presence. The inadequacy of high contrast visual acuity measurements as an index of visual quality has been previously discussed[16]. Therefore, studies have investigated other measures of vision in keratoconus, such as contrast sensitivity measurements[17-19]. It has been revealed that the loss of contrast sensitivity in keratoconus cannot be predicted from standard visual acuity measurements[17, 20, 21].

The relationship between contrast sensitivity, visual performance and aberrations has been researched. One study reported that while coma aberrations were correlated with letter contrast sensitivity, spherical aberrations were not.[22] Another study reported that following LASIK, the induced changes in contrast sensitivity were associated with changes in total higher-order and spherical aberrations and that the changes in low-contrast visual acuity resulting from surgery were correlated with the changes in total higher-order, coma, and spherical aberrations[23]. Due to these considerations, a wide mix of different vision evaluations was included in the study to better understand the differences between the test and control lens.

As noted in each description, study visits may be repeated if the lens being tested at that visit is found to have a suboptimal fit. Visits that find suboptimal fitting lenses will take 30 minutes or less. Each visit can be rescheduled a maximum of 3 times. The highest number of visits a patient can undergo is 10. Patients that require more than this number will be removed from the study as BostonSight is only willing to provide up to 10 lenses free of charge per subject; however, their collected data may be maintained with their continued consent.

Table listing all procedures that will be completed and the expected duration of each visit.

	Visit 1:Screening	**Visit 2:** **Study Visit 1**	**Visit 3:** **Study Visit 2**	**Visit 4:** **Study Visit 3**
Visit Duration	*30-60 min*	*60-120 min*	*30 min*	*120-180 min*
Visit Description	Screening and current BSS fit evaluation. A lens will be manufactured following the visit.	The new baseline lens is evaluated. If the fit is suboptimal another lens will be made and visit 2 rescheduled. Once the baseline fit is optimized then a wavefront measurement is done.	The HOA-optimized lens is given to the subject. If the fit is suboptimal another lens will be made and visit 3 rescheduled.	Baseline and HOA-optimized lenses are made anew. If the fit is suboptimal another lens will be made and visit 4 rescheduled.
Consent Process	X			
Demographic Information Questionnaire	X			
Slit Lamp Exam for Lens Fit	X	X	X	X
Visual Acuity and Basic Vision Evaluation	X	X	X	X
Wavefront Sensor HOA Measurement		X		X
Pharmacological Dilation		X		X
Extended Vision Evaluation (High and Low Contrast VA; Contrast Sensitivity)				X
Subjective Preference Evaluation				X

2. Instruments

Portable Wavefront Sensor (P10/EyeProfiler) - Subjects will be sitting or standing in front of the trained member of the study team. The member of the study team will hold the Wavefront Sensor up to the subject's eye where the orbit of the eye will make contact with a soft rubber eyecup. The subject will be asked to look forward at chart across the room and blink naturally while keeping the dim red spot (laser) "as clear as possible" throughout the measurement. The light reflected back out of the subjects' eye is collected to obtain measurements of wavefront aberrations of the eye. The measurement and light exposure will take an average of 6 seconds with a maximum of 15 seconds.

3. **Study Timeline:**
Each subject will undergo 4-6 study sessions taking 4-7 ½ hours. However, some subjects may require up to 9 ½ hours if unexpected refitting and repeated visits are required. A subject will not have more than 10 visits.

4. **Data Analysis and Monitoring**
Data from each of the subjects will be analyzed individually.

Statistical analyses will be performed using conventional software package such as SPSS.

At the end of each study visit, a team member will verify that the data obtained is readable and of sufficient quality for analysis. If the data is not usable, the subject may be asked to repeat the study on the same day or return on another day.

5. **Data Storage and Confidentiality**
After individuals are consented and enrolled in the study, they will be assigned a de-identified number. The file containing their personal health information (PHI) will reside on a limited-access shared drive with firewall and password protection and is restricted to individuals in the research team named on this application. The measurement data is transported on portable hard drives and analyzed on an encrypted, password-protected computer in the secured lab area. This data will be stored on desktops and portable hard drives that remain in offices in the limited access research area and are used for analysis on password-protected personal computers by members of the research team. Despite these measures, there is always some risk that patient information is unintentionally disclosed.

Screening exam results, ethnicity/race form and other printed PHI will be maintained in a locked office in the limited-access research area.

Identifiable PHI will be shared with BostonSight for the purposes of manufacturing the scleral lenses throughout the study. This will use the same Fit Connect secure computer system that is already used by Flaum Eye Institute and BostonSight for ordering Boston Sight Scleral lenses prescribed to regular patients. Data shared through this system is limited to name, date of birth, and lens parameters.

De-identified study information will be shared with Ovitz Corporation for the purposes of scientific analysis.

IV. RISK/BENEFIT ASSESSMENT

1. Risk Category

Minimal risk is involved.

2. Potential Risk

When taking measurements, the subject's eyes will be exposed to light or light flashes that are about the same or lesser intensity than those in a routine eye exam in an ophthalmologist's office. Subjects may get tired from having measurements taken in their eyes.

- For wavefront sensor measurement, subjects will require the use of eye drops that dilate the pupil. The eye drops we will use, Phenylephrine 2.5% and Tropicamide 1%, are routinely prescribed by ophthalmologists. The dilation drop may cause mild discomfort, stinging, and temporary redness in the eye. Exposure to light may be uncomfortable and vision may be blurred while the eye remains dilated for at least 5-7 hours. Before the use of eye drops subjects will receive a screening exam in order to make sure that their eyes are not at risk for closed-angle glaucoma. Subjects recruited from the Flaum Eye Institute practices will already have been evaluated for closed-angle glaucoma risk and therefore this step of recruitment may be waived. A small proportion of the population can develop an allergic conjunctivitis in response to topically applied eye drops. This is a benign condition that is self-limited upon discontinuing the drops and will either spontaneously resolve in one to three days without treatment or can be treated with mild anti-inflammatory medications if needed. If the eye drops are contaminated, however, they could cause an infection, which could be treated with mild anti-inflammatory or antibiotic eye drop medication, or the subject may be referred for additional medical care. Study staff will administer the eye drops. The drops are instilled in the lower portion of the eye, and dilation occurs in approximately 20 minutes.
  The effects of the eye drops used in this experiment have not been studied on pregnant women or fetuses; therefore pregnant women will be excluded from this study.
- For wavefront sensor measurement, the intensity of the laser diode is eye-safe according to the maximal permissible exposures allowed by the ANSI Standards. The light source will emit between 800-850nm of light. In this wavelength range, the eye can tolerate constant exposure of up to 400µW. The laser diode will operate at up to 25µW output, which is more than 15 times less than the maximal permissible exposure. All light sources used in this study are less than the Maximum Permissible Exposure (MPE) specified by the American National Standard for the Safe use of Lasers (ANSI Z136.1-2000)].
- Subjects in this study will already be wearers of BostonSight Scleral lenses and will have already been made aware of and exposed to the risks of their use. These risks can include but are not limited to discomfort, pain, tearing, redness, burning, sensitivity to light, and blurred vision when initially wearing the lenses. There is also a small chance of infection and corneal abrasion from normal usage.

Participation in this study requires subjects to undergo a new fitting process which carries an increased risk of corneal abrasion beyond normal use. This is because the lenses are applied and removed more frequently during the fitting process. Serious adverse events or infections attributable to the scleral lens device are rare.[24-28] Patients will be evaluated at every screening and study visit to ensure that all lenses being tested on the eye fit properly and are not causing corneal abrasions or other discomfort. Even when an identical lens is manufactured to one previously fit on the same patient, the lens fit will be re-evaluated. If any of the discussed complications arise an on-site Flaum Eye Institute optometrist will provide treatment.

3. Protection Against Risks

Care will be taken such that all screening and measurement procedures will be performed in a fashion consistent with best clinical practice. All potential risks of the study will be minimized as best as possible. A study team member will remain with the subject for the screening and measurement visits to allow the team to identify and appropriately manage any unexpected developments.

An optometrist will either monitor the subject or be available when the subject is at the study site. Subjects will be provided with a phone number for the study team available for 24 hours. In the unlikely circumstance that a subject has an issue after leaving the study site, he or she can contact the study team. The subject will be managed appropriately by an attending ophthalmologist at the University of Rochester Flaum Eye Institute.

The research team will bring adverse events, unanticipated problems or other study-related safety information, and protocol deviations and amendments to the Principle Investigator's attention as they occur during the study. The Principle Investigator will bring all of these issues and changes to the attention of the RSRB with amendments submitted appropriately as they arise.

4. Potential Benefits to the Subjects

If the patient prefers the optimized test lens created during the trial, then they will be provided with is lens free of charge. There are no other benefits from being in this study.

5. Alternatives to Participation

Participation is entirely voluntary. The subject may choose to not participate at any time.

V. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT

1. Method of Subject Identification and Recruitment

Subjects will be recruited through their medical records and will either be approached by their optometrist at their next regularly scheduled appointment or by a designated study team member over the phone. The study will be explained in detail to the potential subject and any questions that the subject may have about the study will be answered. Patients may also be recruited when they come to their optometrist for their eye exam checkup without prior review of their records. If the subjects express interest in the study, they will be put in contact with the member of the study team who will then answer further questions or set up a screening visit for the potential subject.

2. Process of Consent

Prior to enrollment subjects will have ample time to review the consent form, and any questions or concerns will be addressed. Prior to the first study session, the designated study team member obtaining consent will explain the procedures for the visit in detail and address any additional questions. Details of each study session will be explained greater detail before subjects start interventions. The participant will be explicitly told that he/she may stop participation at any time. Written consent will be obtained on the appropriate RSRB-stamped consent forms. The subject will be offered a copy of the signed consent form.

3. Subject Capacity

Only subjects with the capacity to give informed consent will be recruited into this study.

4. Consent Forms

The Principle Investigator, together with the team members, is responsible for ensuring that valid consent is obtained and documented for all subjects on the stamped consent form prior to start of study procedures.

5. Documentation of Consent

The subject signs the consent and a copy is offered to the subject. The original consent form will be housed in an office file cabinet in a locked office of the limited access research area.

6. Costs to the Subject

The subject will incur no costs a result of participating in the study.

7. Payment for Participation

Study patients will not be compensated for their participation in the study.

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