TITLE: **Pilot study**
to investigate the feasibility, reliability and efficiency of utilizing ocular surface optical coherence tomography to automate PROSE fitting

SPONSOR:

Self-funded (BostonSight)

ADDITIONAL SUPPORT:

Access to EYEdeal Scanning Ophthalmic Instrument (EYEdeal Scanning, LLC)

PRINCIPAL INVESTIGATOR:

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1.0 Objectives:

To evaluate the feasibility, reliability and efficiency of utilizing ocular surface optical coherence tomography to automate the PROSE (Prosthetic Replacement of the Ocular Surface Ecosystem) fitting process.

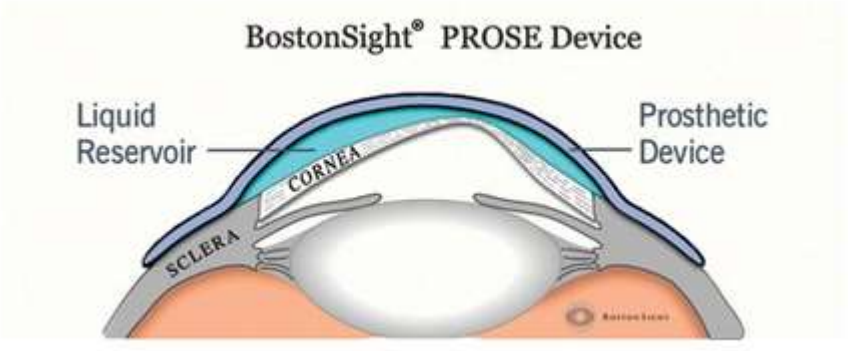
2.0 Background

Scleral lenses are contact lenses manufactured from a rigid gas permeable material (fluorosilicone acrylates) which are prescribed for several indications, including:

- improve best corrected visual acuity, such as for patients with ectasia or other corneal irregularities[1]
- provide comfort, such as to address pain and photophobia associated with ocular surface disease
- support the health of the ocular surface to address acute and chronic ocular surface breakdown secondary to disease processes such as Dry Eye Syndrome, Stevens-Johnson Syndrome, Sjogren's Syndrome, Rheumatoid Arthritis, and Graft Versus Host Disease.[2]

The PROSE device is similar to a scleral lens in theory though it allows for unique customizations of the fit that are unavailable in currently commercially marketed scleral lens designs.

The fluid which fills a PROSE device serves as a liquid cushion between the back surface of the rigid gas permeable lens material and the front surface of the cornea. As such, a PROSE device serves as both a healing liquid bandage lens and as a refractive lens for improving vision by masking corneal irregularities.



(BostonSight.org)

PROSE device manufacture and customization is currently an iterative time-intensive process often requiring at least 5-10 office visits and trials of multiple prosthetic devices that incrementally approach the final, dispensed design.

The entire PROSE device sits on the sclera, referred to as the lens bearing surface and vaults over the cornea. This bearing surface must properly match the topography of each patient's eye to achieve proper lens orientation, optical performance and patient comfort. Custom fitting is currently performed manually and is often a protracted process that requires multiple fitting sessions. Training for new practitioners is a long process.

Automated methods to measure the complete corneal and scleral topography would provide a valuable tool for both clinicians and PROSE device manufacturers.

EYEdeal Scanning technology could enable rapid measurement of the corneal and scleral topography. By accurately measuring the ocular surface the current iterative fitting method required to fit scleral contact lenses can be replaced with a rapid, automated fitting sequence. This could considerably reduce the time needed per visit, the number of visits, and the number of devices needed to be manufactured to reach the endpoint. Additionally, the scanning technology may afford the opportunity to successfully fit some pathology that were previously treatment failures. The automated technology may as well reduce the clinician intensive training time needed to fit PROSE devices, therefore increasing the availability and access to patients.

The goal of this research is to evaluate this automated technology that will allow for precise real-time measurement of the human eye anterior segment topography, with the data to be used to fabricate a prosthetic lens to reliably and efficiently treat corneal and ocular surface disease.

3.0 Inclusion and Exclusion Criteria

<u>The participant will be eligible to participate if the following criteria apply:</u>

1. Written Informed Consent has been obtained prior to any study-related procedures
2. Male or female, 18 years of age and older prior to the initial visit
3. Established wearer of PROSE in the study eye with an optimized fit in the opinion of the clinician
4. No medical need for a PROSE retreatment or replacement lens at the time of enrollment in the study eye, in the opinion of the clinician
5. Initial PROSE fitting was initiated and completed at BostonSight, Needham
6. Current PROSE device does not have channels or fenestrations

7. Currently wears a PROSE device in the study eye primarily for an irregular ocular surface /irregular cornea (including but not limited to Keratoconus, Pellucid Marginal Degeneration, Ectasia, Post-Penetrating Keratoplasty, Corneal Scar, Trauma) **AND/OR** ocular surface disease
8. Has the ability to NOT wear the current PROSE device in the study eye for 3 days prior to scan and 3 days prior to first fitting appointment in the opinion of the investigator and subject

9. In the opinion of the investigator, the subject has the ability to follow study instructions
10. In the opinion of the investigator, the subject has the ability to complete all study procedures and visits

The participant would **NOT** be eligible to participate if at least one of the following criteria is met:

1. Is currently participating in any other type of eye-related clinical or research study
2. Is pregnant or nursing as reported by the subject
3. Has a condition or is in a situation which, in the investigator's opinion, may put the subject at significant risk, may confound study outcomes, or may significantly interfere with the subject's participation in the study
4. Has had previous ocular surgery within the past 12 weeks
5. Intolerance to PROSE wear
6. Inability to maintain stable fixation and exposure for ocular surface imaging
7. Corneal touch by the posterior surface of the device in current PROSE device
8. Allergy to sodium fluorescein
9. Patient is an employee of BostonSight
10. Subject is currently incarcerated.

4.0 Vulnerable Populations

The following special populations will be excluded from this study:

- Adults unable to consent (including adults unable to read and understand English)
- Individuals who are not yet adults (infants, children, teenagers)
- Pregnant women
- Prisoners
- Employees of BostonSight

5.0 Number of Subjects

A minimum of 10 current PROSE patients with a primary PROSE treatment indication of an irregular ocular surface/irregular cornea (including but not limited to Keratoconus, Pellucid Marginal Degeneration, Ectasia, Post-Penetrating Keratoplasty, Corneal Scar, Trauma) **AND/OR** ocular surface disease will be enrolled in the study. We can approximate a 10-20% drop-out rate, so we will expect to recruit 12 patients total. The first 10 patients to be eligible and complete the study will be used for data analysis.

6.0 Recruitment Methods

Recruitment will begin once IRB approval has been received and will occur through BostonSight. The subject pool will consist of patients who are actively coming through the clinic. We anticipate that all our subjects will be from the current patient population at BostonSight. Patients will be recruited via our website, mailing and/or email and at office visits. If a patient is interested in participating in the study, they will be directed to the principal investigator or the study coordinator who will go over the study and ask the screening questions. If they are eligible based on the screening criteria, they will be invited for participation in the study. If the person calls to learn about the study, the investigator or coordinator will use the outline to determine initial eligibility. Current patients of BostonSight may also be recruited as a result of a search of the patient database.

7.0 Multi-Site Research Communication – N/A

8.0 Study Timelines

It is anticipated that to enroll all study subjects, it will take approximately 3 months. The estimated date for completion of this study is 6 months after the start of recruitment.

The total duration of the subjects' participation in the study will be approximately 1-2 months (to complete all 3-4 visits). The visits include:

- Initial screening visit/baseline evaluation at BostonSight
- Scanning visit at EYEdeal Scanning, LLC (Needham, MA)
- One additional follow up scanning visit at EYEdeal Scanning, LLC (as necessary)
- Lens fitting evaluation visit

Study Visits:

Initial Visit at BostonSight (present wearing PROSE device for at least 45 minutes)

Pre-visit calls:

- COVID-19 screening and travel forms:
  -Contact subject one week before visit to complete COVID-19 travel form
  -Contact subject one day before visit to complete COVID-19 screening form

Visit 1:

- Complete Informed Consent
- Complete patient screening checklist
- Complete medical and ocular history intake
- Document information about current PROSE device in the study eye
  - Current PROSE device parameters
  - Number of cuts needed to dispense initial standard PROSE lens in study eye (chart review)
- Current PROSE device performance questionnaire (0-10 scale)
  - Awareness
  - Comfort
- Check current VA with PROSE (logMAR, Appendix D)
- PROSE fit evaluation
  - Slit Lamp Biomicroscopy evaluation of current PROSE device fit in study eye
  - Confirm acceptable fit, no further customizations, replacement or retreatment required at this time (inclusion criteria requirement)
- Baseline Slit Lamp Biomicroscopy **without PROSE device or any contact lens applied** in the study eye

EYEdeal Scanning, LLC Visit(s) (Needham, MA) (within 4 weeks of Initial BostonSight Visit, no lens for 3 days prior to visit):

Pre-visit calls:

- Contact subject one week before visit to complete COVID-19 travel form
- Contact subject 4 days before visit to remind them not to wear lenses for the next three days.
- Contact subject one day before visit to complete COVID-19 screening form

Visit 2/3:

Visit Location and Subject Preparation

This visit for the scanning of the ocular surface will take place at EYEdeal, Scanning, LLC (124 Crescent Rd, Needham, MA 02494) under the oversight of Dr. Robert Bishop and under an additional IRB approved protocol and consent (submitted separately by Dr. Robert Bishop).

The measurements taken with the "EYEdeal Scanning ophthalmic instrument" are performed non-mydriatic (pupil dilation drops will not be administered). Scanning tomography measurements will be performed at the EYEdeal Scanning facility by an EYEdeal engineer, with the assistance of a licensed optometrist or ophthalmologist from BostonSight who will carefully expose the ocular surface by holding the eyelids open in a suitable position for scan acquisition. The EYEdeal Engineer will be in charge of and completely controlling all aspects of the "EYEdeal Scanning Ophthalmic Instrument". The EYEdeal engineer will have no contact and will not perform any examination or procedure on the patient. The licensed BostonSight optometrist or ophthalmologist will have no interaction and no control of the "EYEdeal Scanning Ophthalmic Instrument". The licensed BostonSight optometrist will interact with the patient and perform the eyelid maneuvers as described above.

Methodology

The volunteer will be asked to look into a 25 mm half silvered alignment mirror located in the center of the scanning instrument. A stationary TV camera located behind the partially transmissive alignment mirror monitors eye position throughout the scan. A fixation target may also be added to the instrument. A resting mechanism is provided to both support the head and place the eye within the measurement range of the instrument. At no time is the instrument closer than 76mm (3 inches) to the surface of the eye. The initial alignment will be performed using the alignment TV camera such that the eye pupil is imaged in the center of the camera picture. The scanning beams will be directed toward the eye as the volunteer is instructed to keep looking at the reflection of their eye in the alignment mirror and or the fixation target. Once the subject is aligned, the license optometrist or ophthalmologist will hold the lids open with their fingers or cotton tipped applicators for adequate exposure and the scan of the central cornea and scleral region is recorded. This lid holding procedure is routinely used by doctors in an ophthalmic office during eye examinations. The laser scan will last about 2-3 seconds and might need to be repeated due to eye motion, exposure, blinks, or saccades during the scan. This visit will last a maximum of one hour or maximum of 10 scans on the study eye, whichever occurs first.

Data Collection and Security

Data to be collected in the investigation includes eye images and videos, and electronic data files containing various representations of eye topography. Subject identity cannot be directly determined from any of the images or videos. Subject confidentiality is assured with

procedures and protections in place at EYEdeal Scanning. Images, video, and data collected on the subjects are maintained on a single computer according to subject identification numbers. The randomly-chosen identification numbers are assigned during the first subject visit and will be stored separately from all other data. The identification numbers can only be linked to the subject via a single password-protected encrypted data file maintained by the PI. Password protected de-identified scan data will be provided to BostonSight on a flash drive or via email.

Data Analysis

The laser scan will produce a series of eye surface height data along each scanned meridian. This data will be processed by an algorithm to determine the shape of the measured meridian. All meridians will then be stitched together to generate a large area topography map and image of the eye. If the data is deemed inadequate or unreliable scans are obtained or optimal scans are not achieved within 1 hour, or if in excess of 10 scans are required, the subject may return on a future date for one additional visit to EYEdeal Scanning, LLC with the same time and scan number constraints.

BostonSight Fitting Visit (no lens for 3 days prior to visit)

Pre-visit calls:

- Contact subject one week before visit to complete COVID-19 travel form
- Contact subject 4 days before visit to remind them not to wear lenses for the next three days.
- Contact subject one day before visit to complete COVID-19 screening form

Visit 4:

- Update medical and ocular history
- Baseline Slit Lamp Biomicroscopy **without PROSE device or any contact lens applied** in the study eye
- Image-guided PROSE* fit evaluation
    - Slit Lamp Biomicroscopy evaluation of image-guided PROSE device fit in study eye.
    - BCVA (over-refraction as needed) – prescription will be based on current optimized standard PROSE lens
- PROSE device performance questionnaire (after 45 minutes of wear, if able/tolerable)
    - Awareness
    - Comfort
- Post 45 minutes wear time evaluation:

- Slit Lamp Biomicroscopy evaluation of image-guided PROSE device fit
- Optical Coherence Tomography imaging of central corneal clearance
- iTRACE imaging of lens rotation and decentration
- Clinician determination if image-guided initial fit could be dispensed after initial fitting visit

**Note: all manufactured PROSE devices will use standard materials and coatings. Lens material and Hydra-PEG coating will match patient's current habitual standard lens.*

9.0 Study Endpoints

The primary endpoints in this study are as follows:

1. Fit evaluation of image-guided PROSE device
    a) Overall fit parameters (slit lamp)
    b) Central clearance ordered vs central clearance observed (slit lamp and OCT)
    c) iTRACE (rotation and decentration)
2. Evaluate ability to dispense after manufacturing one PROSE device with image guided system (YES/NO)
3. PROSE device performance questionnaire (awareness and comfort both graded 0 to 10)

10.0 Procedures Involved

Once a subject has been identified, the initial visit will be scheduled.

See Appendix A **"PROSE/EYEdeal ophthalmic scanning instrument: Schedule of Assessments"** which reviews the list of procedures during each visit and the length of time expected per procedure and per visit.

The testing descriptions are summarized in the table below:

Test	Description
General History and Medications	Participants will be asked questions about their general medical, ocular and medication use histories along with contact lens use history if applicable.
Lens Evaluation	The PROSE device fit will be evaluated via traditional methods utilizing a slit lamp microscope and standard fluorescein dye.
Visual Acuity	The participant's vision in each eye will be measured with a high contrast visual acuity chart. The participant will be asked to cover

	one eye and read the chart, and this procedure will be repeated for the other eye.
Slit-lamp Examination	The participant's front portion of each eye and PROSE devices will be examined with a lighted microscope. The participant will be asked to place his/her chin on the chinrest and place his/her forehead against the bar and look straight ahead. The instrument's light will be shined onto the eye to visualize the ocular surface for approximately 4 minutes per eye.
Sodium Fluorescein	Sodium fluorescein staining will be used to evaluate ocular surface damage indicated by cell damage or death.
EYEdeal Scanning Ophthalmic Instrument	The EYEdeal Scanning Ophthalmic Instrument is a non-invasive laser product (see 12.0 for more details). The participant will be asked to place his/her chin on the chinrest of the instrument. The forehead is placed against the bar and he/she will be asked to look straight ahead. The investigator will perform a scan of the eye to obtain data relating to the shape of the anterior surface of the eye. Data obtained from these scans at baseline can then be used to manufacture a customized image guided PROSE device.
Optical Coherence Tomography	Optical Coherence Tomography is an imaging procedure that is used in standard ophthalmic care which uses low-coherence light that can capture resolution down to the micrometer and is commonly used to obtain two and three dimensional images of optical scattering media such as contact lenses and biological tissue. The participant will be asked to place his/her chin on the chinrest of the OCT instrument. The forehead is placed against the bar and he/she will be asked to look straight ahead. The investigator will perform a scan of the eye to obtain an image of the PROSE device on the eye that will allow the measurement of central corneal clearance (the distance between the lens posterior surface and the corneal anterior surface).

iTRACE Visual Function Analyzer	iTRACE Visual Function Analyzer is a non-invasive class I laser product which contains two laser diodes, one a Class IIIb laser diode with a 785 nm wavelength, and one a Class IIIa laser diode with a 655 nm wavelength used to image aberrations in the movement of a wavefront of light transmitted through the optical system (the eye). It is a standard instrument used in ophthalmic care. The participant will be asked to place his/her chin on the chinrest of the instrument. The forehead is placed against the bar and he/she will be asked to look straight ahead. The investigator will perform a scan of the eye. The scan data will then be used by the iTRACE software to evaluate the amount of rotation and decentration of the study lens on the eye.

Table 3. Descriptions of tests

11.0 Setting

Subjects will be asked to complete 1-2 study visits at the offices of EYEdeal (Needham, MA) and 2 visits at the clinical facilities at BostonSight.

12.0 Drugs or Devices

PROSE device (BostonSight): The PROSE device is an FDA class II medical device. All rigid lens materials are FDA approved for use in a rigid contact lens, and they are not investigational devices.

Vistane OCT (Zeiss): The Visante OCT is a standard instrument used in ophthalmic clinical practice to image the ocular surface. It is a group 1 Instrument – Per EN ISO 15004–2. Group 1 instruments are ophthalmic instruments for which no potential light hazard exists.

iTRACE Visual Function Analyzer (Tracey Technologies)- The iTrace is a 510K exempt medical device used as a tool in ophthalmology clinical practice to measure the refractive, wavefront and corneal topographic data of the human optical system. The FDA has reviewed the premarket notification submission for the Tracey-VFA Visual Function Analyzer (iTrace) and has found this device to be exempt from premarket notification requirements.

The Tracey iTrace Visual Function Analyzer is a Class 1 laser product. It contains two laser diodes:
1) Class IIIb laser diode with a 785 nm wavelength, with maximum
power of ≈50 mW and collimated beam with a maximum attenuated

power of 4.6 mW; and
2) Class IIIa laser diode with a 655 nm wavelength, with maximum power of less than or equal to 2.5mw, and 2mrad beam divergence.

EYEdeal Scanning ophthalmic instrument –
Unlike currently used anterior segment topographers which typically only evaluate corneal contours, the EYEdeal Scanning ophthalmic instrument is concerned with contour measurements of both the sclera and corneal contour. To accomplish this measurement, a slightly modified, off-the-shelf 'displacement' type laser distance measuring device is leveraged. This commercial displacement distance measuring instrument functions by emitting a laser beam in one direction and viewing the position of the returned (scattered) light from a position off-axis with a CCD strip detector. In this manner, the instrument is calibrated to determine change in distance based on a change in the position of the returned signal. This laser distance measurement instrument is built into the EYEdeal scanner in such a manner that its laser and returned optical signal are both scanned across the eye via a single axis galvanometer scanner. The scanner moves the location of the measurement beam (the laser spot) from one side of the cornea, up across the apex of the cornea, then down the other side across the full radius of the cornea and well out on to the sclera. This single axis radial scanner oscillates with a triangle wave pattern. As the patient looks into the instrument, the radial scanner is rotated 360 degrees to scan the entire eye. In this manner, radial measurements ('meridians') are taken around the axis of the eye every few degrees to completely measure the entire front portion of the eye (anterior segment). This motion can be easily visualized as staring into a large clock face at a short distance. The laser beam scan originates from one end of the minute hand and scans back and forth along the minute hand as the hand sweeps around the clock. Except in this case, the minute hand sweeps the entire 360 degree clock face in 2 to 3 seconds rather than a full hour. Because instrument rotation takes place concurrently with the radial scans, each meridian's path is somewhat spiral in nature. The total scan time is 2 or 3 seconds and requires just one rotation of the instrument to fully characterize the exposed ocular surface in primary gaze.

Medical Risks and Safety of the EYEdeal Scanning Instrument

Ophthalmic imaging diagnostics such as those to be conducted during this protocol are regarded as non-significant risk (NSR) procedures, and an IRB approved protocol is sufficient (for a properly labeled device) for FDA Investigational Device Exemption (IDE) without FDA review.[3] The risks are minimal for testing the imaging instrument. In general, the main risks from laser-based imaging diagnostics are from retinal damage from light exposure to focused (ANSI) Class II or higher laser power levels. However, in this case, the beam is not focused on the retina and is insufficient in power to cause any ocular tissue damage.

Laser Safety Analysis Summary

To insure that the EYEdeal Scannning instrument meets FDA laser safety requirements and general guidelines for such instruments, EYEdeal Scanning hired "Laser Compliance", a third party company to perform a detailed analysis of the topology measurement instrument and prepare the attached Laser Safety Report (see Appendix B). Laser Compliance has worked with numerous manufacturers of ophthalmic instruments that incorporate lasers for scanning and surgical procedures, to obtain FDA certification for their products.

Highlights from the attached Laser Safety Report are provided below:

- This instrument as described, does not exceed the published international safety values for the following 3 applicable standards covering laser products, laser eye safety and ophthalmic instrument safety:

  1. The MPE (maximum permissible exposure) for retinal eye safety. IEC 60825-1, edition 2, 2007:03 (now correlated with the ANSI Z136.1)

  2. Corneal & Scleral exposure analysis under the ANSI (American National Standards Institute) Z136.1-2007 E., "American National Standard for the Safe Use of Lasers".

  3. Retinal exposure analysis specific to ocular instruments under the ISO 15004-2 first edition, 02-2007, "Ophthalmic Instruments - Fundamental requirements and test methods - Part 2: Light Hazard Protection"

- This instrument as described, also clearly qualifies as Class 1 in the US and internationally, and its exposure parameters would not exceed indicated limits for eye and skin exposure in applicable U.S. and international standards under the terms of the international EN/IEC 60825-1:2007 edition 2, 2007:03.

The Executive Summary from the Laser Compliance Report is provided (Appendix B).

In addition to Laser Compliance, EYEdeal Scanning also hired Dr. David Sliney, a leading world authority in the field of laser eye safety to work with Laser Compliance and review the Laser Safety Report. Dr. Sliney served as the Safety Director of the American Society for Laser Medicine and Surgery from 1996 – 2011 (15 years). Dr. Sliney's credentials are summarized below:

Dr. Sliney received his B.S. in physics from Virginia Polytechnic Institute, his M.S. in physics and radiological health from Emory University, and his Ph.D. in biophysics and medical physics from the University of London, Institute of Ophthalmology. He was the Manager of the Laser/Optical Radiation Program at the US Army Center for Health Promotion and Preventive Medicine for many years until retiring in 2007. His research interests focus on subjects related to UV effects upon the eye, laser-tissue interactions, laser hazards and laser applications in medicine and surgery. He served as member, advisor and chairman of numerous committees and institutions, which are active in the establishment of safety standards for protection against non-ionizing radiation in particular from lasers and other high-intensity optical sources (ANSI, ISO, ACGIH, IEC, WHO, NCRP, and ICNIRP). He was a Fulbright Scholar to Yugoslavia in 1977 and received the Schawlow Award from the LIA in 2005 and the Wilkening Award in 2004. He co-authored the 1000-page handbook, "Safety with Lasers and Other Optical Sources," Plenum Publishing Corp., New York, 1980. He served as President of the American Society for Photobiology, 2008-2009.

His complete curriculum vitae is provided in Appendix C.

Dr. Sliney confirmed in his attached letter (Appendix B) that the instrument meets all of the above stated safety requirements and states on page 1 of his letter “The EYEdeal Scanner meets all requirements of ISO 15004-2, which applies to the ocular safety of the patient. The safety assessment is summarized in the table below:

Page Break

(From Dr. Sliney’s letter)

SUMMARY TABLE OF EYEDEAL SCANNER COMPLIANCE WITH ISO 15004-2:2007

ISO §	Limit	405-nm laser scanned beam	Alignment laser	LED Fixation Target	Combination
5.4.1.1	**CW: UV-B Lens**	N/A	N/A	N/A	N/A
5.4.1.2	**CW: UV-A Lens**	N/A	N/A	N/A	N/A
5.4.1.3	**CW: Photochemical**	SAFE Meets limit with time restriction	N/A	SAFE Meets limit	SAFE Meets limit with time restriction*
5.4.1.4	**CW: IR Lens**	SAFE	SAFE Emission adhering to ICNIRP	N/A	SAFE

			Limit!		
5.4.1.5	**CW: VIR Lens**	SAFE	SAFE	SAFE	SAFE
5.4.1.6	**CW: Thermal Retina**	SAFE	SAFE	SAFE	SAFE
5.4.2.1	**Pulsed: Thermal Retina**	SAFE	SAFE	SAFE	SAFE
5.4.2.2	**Pulsed: IR Lens**	N/A	N/A	N/A	N/A
5.4.2.3	**Pulsed: VIR Lens**	N/A	N/A	N/A	N/A

Dr. Sliney concludes "The EYEdeal Scanner fully meets the intent of ISO 15004-2: 2007 to protect the patient for a Group 1 device. There is no risk to the patient undergoing topographic assessment by this instrument under any reasonably foreseeable normal use. Nevertheless, I would recommend that the user manual caution the operator not to scan the same eye more than ten scans per day as a conservative precaution against the potential photochemical retinal hazard."

Sterile Preservative-Free Normal Saline:

Preservative Free Normal Saline (0.9% Sodium Chloride solution) is the standard of care solution recommended for use to fill the reservoir in any commercial scleral lens or PROSE scleral lens. Being preservative-free is vital for use in a scleral lens reservoir as preservatives, such as Benzalkonium chloride (BAK), which are commonly found in many ophthalmic products, could have a significant toxic effect on the ocular surface with constant, sustained contact throughout the day.

Flourescein Sodium Strip (Bio Glo, Contacare Ophthalmics and Diagnostics): An ophthalmic dye used as the gold standard in ophthalmic and optometric practices to evaluate devitalized corneal epithelium. Used in the form of a paper strip impregnated with 1.0 mg. of fluorescein sodium. The impregnated strip is moistened with one to two drops of sterile normal saline and applied to the inferior conjunctival fornix.

13.0 Risks to Subjects

This study overall represents a minimal risk to subjects.

Risk with PROSE devices are those that are already associated with wearing any form of contact lens. All contact lens wearers are at risk for developing an abrasion ('cut' on the eye) during lens application or removal as well as inflammatory and/or infectious complications during lens wear, but there is no added risk of these occurrences by participating in this study.

Adverse events related to ocular surface scanning are not expected due to the safety profile and low scanning energy levels of the EYEdeal Scanning Ophthalmic Instrument. As stipulated above the use of the EYEdeal Scanning Ophthalmic Instrument represents a low risk or "non-significant risk" as stipulated by Dr. David Sliney's evaluation.

Each experimental image-guided design will be verified as reasonable by a BostonSight optometrist or ophthalmologist, who will also inspect the finished PROSE device before it is placed on a patient's eye. All trials of experimental PROSE devices will be conducted at BostonSight, according to current standards for placement of trial devices under the supervision of a study doctor.

If a subject experiences an adverse event during the duration of the study, they will be instructed to call the study coordinator who will communicate with the investigators to determine the best course of action. If the subject needs to be seen due to an adverse event, a study investigator will examine them and the customary procedure for management will be followed.

Any adverse event will be treated and followed in keeping with standard medical and optometric practice. Subjects will be given 24-hour contact information for BostonSight providers and instructions to call if they develop new ocular or visual symptoms while participating in this study. All AEs will be evaluated and managed in an appropriate timeframe at an appropriate facility according to the medical judgment of a BostonSight doctor. All BostonSight patients enrolled in the study will have an ongoing relationship and follow-up with BostonSight for the duration of this study and as long as PROSE devices are being worn.

Any adverse effects or unforeseen events relating to the study will be reported directly to the Principal Investigator and to NEIRB.

Following the conclusion of the study the patient will remain under the care of a BostonSight doctor in the traditional sense, for continued evaluations and management while continuing use of a PROSE device, with financial obligations typical to any BostonSight patient.

14.0 Potential Benefits to Subjects

Subjects may not receive any direct benefit from taking part in this study. If successful, the information obtained from this study could ultimately lead to a reduction in treatment time, and/or an improved design and treatment process. This should potentially decrease cost and increase potential availability to the thousands of patients who can benefit from this new technology.

15.0 Withdrawal of Subjects

Subjects will be withdrawn from the study if they are unable to complete the tasks in the study protocol. In addition, if they experience an adverse event in which the investigator does not feel that the subjects should continue, they will be withdrawn.

16.0 Costs/Payments to Subjects

The only cost that the subjects may be responsible for in this study is the cost of transportation to and from the appointments.

Compensation for completion of the entire study will be given in the form of one copy of the current optimized standard PROSE lens in one eye (eye of subject's choice).

17.0 Compensation for Research-Related Injury

If there is an ocular injury in this study directly related to the conduct of the study , treatment for the injury and any subsequent referrals will be covered by the study. The subject will not receive any direct compensation. If there is an unrelated or non-ocular injury during a subject's enrollment in the study, it will not be covered by the study.

EYEdeal scanning will be responsible for the patient while they are at the EYEdeal Scanning facility. BostonSight will be responsible for the patient while they are at the BostonSight facility. Each company will be required to maintain liability insurance.

18.0 Confidentiality

The subject ID worksheet, informed consent, subject surveys, and examiner worksheets will all be kept in a single binder, locked in the office of the Clinical Research Coordinator. The informed consent forms and the subject ID worksheet will be kept in a separate binder from the study data.

At the start of participation in the study, the subject will be assigned a non-identifiable subject ID that will be used for identification on all other documents used in the study. This

identification document, which will be the only document that decodes the subject, will be kept in a locked filing bin in a locked room within BostonSight, separate from the informed consent and other study documents. Names, email addresses, and telephone numbers will be recorded in this subject ID worksheet, which will be a paper file kept in the locked office of the principal investigator.

All other exam findings will be recorded on the paper forms and stored in a binder. This binder will be kept locked in the Clinical Research Coordinator's office when not being used to add or remove data collection worksheets.

Only the investigators will have access to the paper and electronic records kept in this study.

All study data will be stored for a minimum of 3 years following study completion. The link will be maintained to allow pertinent regulatory or government agencies to inspect the data and ensure that subjects participated in the study. The principal investigator will be responsible for maintaining study data security and subject confidentiality.

19.0 Provisions to Protect the Privacy Interests of Subjects

We will ensure that all data is maintained with confidentiality and will assure subjects of this when they begin the study. If subjects are not comfortable with disclosing any of the information that is asked in the study, they will not be pressured to disclose, but they may not be able to participate if the withholding prevents us from screening or determining eligibility in the study. All PHI (DOB, name, health information) will be stored in the locked office of the Clinical Research Coordinator.

Subjects will only be asked questions that are relevant to the study and their ocular health. The investigators, who are all optometrists or ophthalmologists that regularly see patients and communicate about potentially sensitive information, have been trained to develop proper rapport with patients and study subjects. All investigators will make every effort to avoid seeming intrusive when asking the subjects questions.

20.0 Informed Consent Process

Informed consent will be obtained before any testing is done. The subject will be provided an informed consent document written in non-technical language. The study staff will review the document with the subject and will give the subject adequate time to review the form and ask any questions before deciding whether to participate. After answering any questions, if the study staff believes the subject comprehends the elements of the informed consent document, the study staff will invite the subject to participate in the study and will have the subject sign the consent form. The investigators and key personnel associated with the informed consent

process are trained to not influence the participant in their decision to participate in the research or not. The individual may choose not to sign the consent form without any coercion from the study personnel. Non-participation in the study from patients will not impact future care.

21.0 Process to Document Consent in Writing

Participants will complete the Informed Consent document.

Participants will have opportunity to review an informed consent document and ask questions. They will then sign the form stating their consent to participate in this research study. The subject and the investigator will each retain a copy of the original consent form.

22.0 HIPAA

Study will be performed in compliance with HIPAA regulations. Subjects will be asked to sign a HIPAA authorization to allow access to their private information.

23.0 Data Management

Data will be stored in a study paper file at BostonSight. Electronic data will be stored on a password-protected computer in a locked office. All study data will remain at BostonSight for a minimum of 3 years following study completion. The principal investigator will be responsible for maintaining study data security and subject confidentiality, and the PI and the study coordinator will be responsible for receipt and transmission of the data. The investigative team and inspectors from regulatory agencies such as the US Food and Drug Administration will have access to the data if requested for study monitoring or an audit.

All collected data will be documented on study documents and analyzed for differences between baseline and test data. Hypothesis testing will be performed using statistical analyses including parametric or nonparametric comparisons (i.e., t-tests, signed-rank tests), analysis of variance, general linear models, correlation, or regression techniques.

24.0 Specimen Use and Banking – N/A

25.0 Sharing of Results with Subjects

Study results will not be shared with subjects, unless the investigator feels that the subject should know something about the ocular health of their eye as a result of the study.

26.0 Resources/Support

All investigators in this study are optometrists and ophthalmologists and are qualified to examine subjects and evaluate the performance of the PROSE devices. The investigators all have experience working within BostonSight, and with all the exam rooms, equipment, and data storage rooms. All investigators have completed the necessary training for good clinical practices and are specialists in lens fitting and management. The study coordinator is an experienced coordinator who is also trained on IRB practices and is experienced with informed consent processes and confidentiality.

We do not expect to have difficulty recruiting subjects in this study. All subjects will come from current patients of BostonSight.

Support

BostonSight is the research sponsor and is covering all costs of the study, except EYEdeal is the developer of the "EYEdeal Scanning Ophthalmic Instrument" and has provided access and utilization of the instrument during this study at no charge.

27.0 Citations

[1] Jacobs D, Baran I, Bradley, J et al. PROSE Treatment of corneal ectasia. Contact Lens & Anterior Eye. 35 (2012) 222-227.
[2] Chiu G, Theophanous C, Irvine J et al. Use of Prosthetic Replacement of the Ocular Surface Ecosystem Scleral Lenses in Patients with Ocular Chronic Graft-Versus-Host Disease. Biol Blood Marrow Transplant 21(2015) 2180-2184.
[3] Code of Federal Regulations, Title 21 - Food and Drugs, Subchapter H - Medical Devices, Part 812 - Investigation Device Exemptions, Applicable Sections - 812.2, 812.5, 812.7, 812.46, 812.140, and 812.150.