Novel Use of Cyclosporine Ophthalmic Emulsion 0.05% in a PROSE Device

NCT#: NCT04918823

Version: 8/27/2024

Novel use of Restasis (Cyclosporine Ophthalmic Emulsion 0.05%) on application of PROSE devices for Management of Patients with Ocular Surface Disease: A Pilot Study

SPONSOR:

Self-funded: BostonSight, Needham MA

ADDITIONAL SUPPORT:

AbbVie Inc. (Investigational Product: Restasis 0.05% ophthalmic emulsion)

LifeStyle Inc. (Purilens: Buffered Normal Saline)

PRINCIPAL INVESTIGATOR:

Daniel Brocks, MD

464 Hillside Avenue, Suite 205

Needham, MA 02494

(781) 726-7337

dbrocks@bostonsight.org

1.0 Objectives

The goal of this prospective observational pilot study is to evaluate the tolerability and safety of RESTASIS (cyclosporine ophthalmic solution 0.05%) when added to the PROSE (Prosthetic Replacement of the Ocular Surface Ecosystem) lens reservoir in patients with ocular surface disease (OSD). Secondary endpoints include early (1-month) efficacy data for ocular signs and symptoms.

2.0 Background

PROSE treatment is for individuals with irregular ocular surfaces that require a rigid lens to mask irregularities on the front refracting surface of their eye, the cornea. As well, and more relevant to this study, PROSE treatment is used for cases of ocular surface disease to protect and support the ocular surface to reduce dryness and prevent ocular surface breakdown, which can lead to ulceration and perforation. The PROSE device is like a scleral lens in theory though it allows for unique customizations of the fit that are unavailable in currently marketed scleral lens designs. Traditional commercial scleral lenses as well as PROSE serve a therapeutic purpose by bathing the ocular surface with normal saline, also known as 0.9% sodium chloride solution, which provides constant lubrication and protection. Because this liquid is maintaining contact with the cornea and ocular surface for long periods of time as the lens is on the eye, the concept of using the device for drug delivery via addition of a preservative-free topical medication to the scleral lens bowl along with saline has been explored in various publications.[1,2,3]

Per the TFOS DEWS II published in 2017[4], dry eye syndrome (also known as ocular surface disease) is defined as a "multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular inflammation and damage, and neurosensory abnormalities play etiological roles." Dry eye is often categorized as aqueous deficient (stemming from issues with the lacrimal gland itself, usually categorized as Sjogren's and Non-Sjogren's) or evaporative (stemming from issues with the meibomian glands that produce the lipid layer of the tear film) or mixed mechanism involving both aqueous and evaporative components.

For many patients with ocular surface disease, numerous therapies are typically attempted with limited or no success. Often, the most successful treatment regimen is multiple therapies targeting several different mechanisms. This is because ocular surface disease and dry eye syndrome itself is a complex and multifactorial disease, benefiting from several concurrent therapies. PROSE itself does not directly address the compromised production of the aqueous component of tears nor the dysfunction of the meibomian glands, however it acts as a physical barrier and provides constant lubrication to the ocular surface. Despite the benefits of PROSE, many patients require additional treatment to obtain complete relief of symptoms.

One category of ocular surface disease treatments that is being studied more in recent years is immunomodulating agents. Restasis (Cyclosporine ophthalmic emulsion 0.05%) is one such topical immunomodulating agent. Restasis is FDA approved "to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivits sicca". [5]

Generally speaking, over the last 20 years, topical ocular cyclosporine treatment has become a frequently used modality in ophthalmology and optometry limbal stem cell deficiency. The "novel use" in this study refers to the method by which the Restasis product is being delivered to the eye (in the PROSE reservoir) and the sustained contact with the ocular surface which this drug delivery method provides. No anticipated effect on structure, safety or efficacy of the PROSE device would be anticipated with this novel use.

For this study, all subjects will receive Restasis (Cyclosporine ophthalmic emulsion 0.05%). One drop of the dispensed study drop will be instilled in the PROSE lens reservoir twice a day and the remainder of the reservoir will be filled with normal saline (0.9% sodium chloride solution). In order to standardize solutions used in the PROSE reservoir, all patients recruited will be either currently using or will be switched to buffered preservative-free normal saline (Purilens, Lifestyle Inc., pH 7.4[6]) to better match the reported pH of RESTASIS (pH 6.5-8.0[5]).

Outcomes will include subjective responses regarding the subject's symptoms and visual function in addition to the objective assessments of the health of the ocular surface seen on clinical examination. Results will be measured at baseline, after 1 week, and after 1 month of the study.

3.0 Inclusion and Exclusion Criteria

The participant will be eligible to participate if the following criteria apply:

1. Written Informed Consent has been obtained prior to any study-related procedures taking place
2. Subject is Male or Female, 18 years of age or older prior to the initial visit
3. Is an established wearer of PROSE devices for > 6 months in both eyes

4. Has a finalized PROSE lens design in both eyes, in the opinion of the clinician
5. The PROSE design does NOT include fenestrations
6. Subject requires PROSE devices to treat symptoms and/or signs from underlying dry eye disease, GVHD, Sjogren's syndrome, limbal stem cell deficiency, keratoconjunctivitis sicca, or ocular surface disease
7. Baseline Corneal staining grade of 2 or higher in total, both eyes combined (NEI Grading System)[7]
8. Baseline Ocular Surface Disease Index 13 or greater
9. In the opinion of the investigator, the subject can follow study instructions
10. In the opinion of the investigator, the subject can complete all study procedures and visits
11. Able to wear PROSE device continuously for at least 6 hours at a time without removal, in each eye
12. Able to wear PROSE device for at least 10 total hours a day, in each eye
13. Able to wear PROSE device in subsequent continuous sessions of 6 hours, followed by a break to re-instill Restasis in device bowl, followed by another period of continuous wear of at least 4 hours
14. Currently using buffered preservative free normal saline (Purilens) in the device bowl or willing to transition to buffered preservative free normal saline (Purilens) use in the device bowl during the study

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. Currently uses or has a prior history of using Restasis in the last 3 months
6. Currently uses or has a prior history of using Cequa in the last 3 months
7. Is currently using Xiidra **and** has been using Xiidra for less than 3 months
8. Has a history of an allergic reaction or hypersensitivity to any active or inactive ingredient found in Restasis or Cequa or Purilens.
9. Is wearing a PROSE device with Tangible HydraPEG coating
10. The subject is not wearing their PROSE devices daily
11. The subject is only wearing a device for one eye.
12. The participant is monocular
13. The subject wears a PROSE lens with fenestrations
14. The participant carries a diagnosis of glaucoma or ocular hypertension or glaucoma suspect AND is currently using glaucoma medications

15. The participant is NOT able to wear PROSE devices for 6 hours continuously, followed by a break to re-instill Restasis, followed by an additional period of at least 4 hours of continuous wear
16. Allergy to sodium fluorescein
17. Allergy to lissamine green
18. Allergy or intolerance to Purilens solution.

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

This study will enroll a minimum of 10 subjects. We expect an approximate 10% drop-out rate, so we will expect to recruit approximately 12 subjects; and the first 10 to be eligible and complete the study will be used for data analysis. All subjects will receive the study drug, Restasis (cyclosporine ophthalmic solution 0.05%).

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. 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 details.
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 and by the use of sending patient/doctor information letters and/or e-mails regarding the study.

7.0 Multi-Site Research Communication – N/A

8.0 Study Timelines

The total duration of the subjects' participation in the study will be between 4-6 weeks. It is anticipated that to enroll all study subjects, it will take approximately 8 months. The estimated date for completion of this study is 12 months after the start of recruitment.

The study will enroll 2 groups of subjects:

- Group A: Those subjects already using preservative free buffered normal saline (Purilens) at the time of enrollment to the study

- Group B: Those subjects NOT currently using preservative free buffered normal saline (Purilens) at the time of enrollment but who are willing to be switched to preservative free buffered normal saline (Purilens) as part of the study protocol

Visit 1A:

a. Completion of informed consent
b. Collect past medical history, past ocular history, allergies, medications as well as habitual contact lens information, including lens design, power, and diameter.
c. Subject's evaluation of symptoms via a baseline tolerability questionnaire and baseline Ocular Surface Disease Index (OSDI)
d. Visual acuity assessments of both eyes (logMAR)
e. Baseline assessment of PROSE device:
    a. Confirm acceptable fit
f. Baseline Oculus Keratograph 5M R-Scan with lens (automatic classification of redness)
g. Remove lens
h. Baseline Oculus Keratograph 5M R-Scan without lens (automatic classification of redness)
i. Baseline slit lamp examination (without lens) including:
    a. anterior segment and ocular surface
    b. conjunctival redness (Efron Grading Scale, Modified Efron Grading Scale)
    c. corneal staining with sodium flourescein (NEI Grading System)
    d. conjunctival staining with lissamine green (NEI Grading System)
j. Initiation of study, with either:
    a. Group A (subjects currently using Purilens): Dispense Restasis for initiation of usage in device bowl
        i. Instructions for use: 1 drop of RESTASIS in the lens bowl followed by filling the remainder of the lens bowl with Purilens qAM. After 6 consecutive hours of wear, remove and reapply lens with 1 drop of RESTASIS in the lens bowl followed by filling the remainder of the lens bowl with Purilens. Wear lens without removal for at least 4 more consecutive hours.
    b. Group B (subjects NOT currently using Purilens): the subject will be provided Purilens for use over the next two weeks and return for Visit 1B
k. Reapply lens and wait 15 minutes
    a. Document closed vs open PROSE device system: apply lens and wait 15 minutes. Then assess whether flourescein seeps under haptic within 5 minutes .

Visit 1B: (Group B only – 2 weeks after dispensing Purilens)

a. Update past medical history, past ocular history, allergies, medication
b. Subject's evaluation of symptoms via a baseline tolerability questionnaire and baseline Ocular Surface Disease Index (OSDI)
c. Visual acuity assessments of both eyes (logMAR)
d. Baseline Oculus Keratograph 5M R-Scan with lens (automatic classification of redness)

e. Remove lens
f. Baseline Oculus Keratograph 5M R-Scan without lens (automatic classification of redness)
g. Baseline slit lamp examination (without lens) including:
    a. anterior segment and ocular surface
    b. conjunctival redness (Efron Grading Scale, Modified Efron Grading Scale)
    c. corneal staining with sodium flourescein (NEI Grading System)
    d. conjunctival staining with lissamine green (NEI Grading System)
h. Initiation of study for Group B:
    a. Group B (subjects changed to Purilens at visit 1A): Dispense Restasis for initiation of usage in device bowl
        i. Instructions for use: 1 drop of RESTASIS in the lens bowl followed by filling the remainder of the lens bowl with Purilens qAM. After 6 consecutive hours of wear, remove and reapply lens with 1 drop of RESTASIS in the lens bowl followed by filling the remainder of the lens bowl with Purilens. Wear lens without removal for at least 4 more consecutive hours.

Visit 2: (1 Week post Restasis dispensing)
a. Update past medical history, past ocular history, allergies, medications
b. Visual acuity assessments of both eyes (logMAR)
c. Subject's evaluation of symptoms via OSDI
d. Tolerability questionnaire
e. Oculus Keratograph 5M R-Scan with lens (automatic classification of redness)
f. Remove lens
g. Oculus Keratograph 5M R-Scan without lens (automatic classification of redness)
h. Slit lamp examination (without lens) including:
    a. anterior segment and ocular surface
    b. conjunctival redness (Efron Grading Scale, Modified Efron Grading Scale)
    c. corneal staining with sodium flourescein (NEI Grading System)
    d. conjunctival staining with lissamine green (NEI Grading System)

Visit 3: (4 Weeks post Restasis dispensing)
a. Update past medical history, past ocular history, allergies, medication
b. Visual acuity assessments of both eyes (logMAR)
c. Subject's evaluation of symptoms via OSDI
d. Tolerability questionnaire
e. Oculus Keratograph 5M R-Scan with lens (automatic classification of redness)
f. Remove lens
g. Oculus Keratograph 5M R-Scan without lens (automatic classification of redness)
h. Slit lamp examination (without lens) including:
    a. anterior segment and ocular surface
    b. conjunctival redness (Efron Grading Scale, Modified Efron Grading Scale)
    c. corneal staining with sodium flourescein (NEI Grading System)

d. conjunctival staining with lissamine green (NEI Grading System)

9.0 Study Endpoints

The study endpoints to analyze safety, tolerability and efficacy are as follows:

a) Visual Acuity (logMAR)
b) Tolerability questionnaire
c) Ocular Surface Disease Index (OSDI)
d) Corneal staining with sodium flourescein (NEI Grading System)
e) Conjunctival staining with lissamine green (NEI Grading System)
f) Conjunctival redness, Efron and modified Efron scale
g) Oculus Keratograph 5M R-Scan value

10.0 Procedures Involved

The following table outlines each of the study visits and tells what procedures will be done at each visit:

Procedure	**Length of Time Required for Participants**
VISIT 1A: Initial Evaluation	
Informed consent & HIPAA	30 minutes
General History and medications	3 minutes
Visual Acuity	2 minutes
Tolerability Survey & OSDI	10 minutes
Slit-lamp Examination with assessment of PROSE devices	5 minutes
R-scan (pre and post PROSE removal)	10 minutes
Slit-lamp examination (after lens removal)	5 minutes
Instructions and dispensing product	10 minutes
TOTAL TIME	**75 minutes**

Procedure	**Length of Time Required for Participants**
VISIT 1B: Evaluation after 2 weeks with buffered saline	
General History and medications	3 minutes

Visual Acuity	2 minutes
Tolerability Survey & OSDI	10 minutes
Slit-lamp examination (after lens removal)	5 minutes
R-scan (pre and post PROSE remova)l	10 minutes
Instructions and dispensing product	10 minutes
TOTAL TIME	**40 minutes**

Procedure	**Length of Time Required for Participants**
VISIT 2: Week 1 after dispense Restasis	
General History and medications	3 minutes
Visual Acuity	2 minutes
Tolerability Survey & OSDI	10 minutes
R-scan (pre and post PROSE removal)	10 minutes
Slit-lamp Examination (after lens removal)	10 minutes
TOTAL TIME	**35 minutes**

Procedure	**Length of Time Required for Participants**
VISIT 3: Week 4 after dispense Restasis	
General History and medications	3 minutes
Visual Acuity	2 minutes
Tolerability Survey & OSDI	10 minutes
R-scan (pre and post PROSE removal)	10 minutes
Slit-lamp Examination (after lens removal)	10 minutes
TOTAL TIME	**35 minutes**

Figure 1. Table including organization of examinations done at each study visit

Test	Description
General History and Medications	Participants will be asked questions about their general, ocular and medication use histories along with contact lens use history if applicable.
Lens Evaluation	The PROSE device fit and vision will be evaluated.
Visual Acuity	The participant's vision in each eye while wearing lenses 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 contact lenses 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 2-3 minutes per eye.
Sodium Fluorescein/Lissamine Green	Sodium fluorescein/Lissmaine Green staining will be used to evaluate ocular surface damage indicated by cell damage or death and for assessing an open vs closed PROSE device system. Corneal and conjunctival staining will be scored using the NEI Grading System.
R-Scan	Non-invasive imaging modality with automated classification of ocular redness level. Instrument used: OCULUS Keratograph 5M. 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 investigator will perform a scan of the eye to obtain an image of the front surface of the eye. The computer will then use an embedded software algorithm to quantify the level of redness on a scale from 0 to 4 in 0.1 increments.
Questionnaires	Subjects will be asked to fill out the following questionnaires: • Ocular Surface Disease Index (OSDI) • Restasis Tolerability Questionnaire

Figure 2. Table including descriptions of tests

Statistical Analysis:

Subject data will be compared to their baseline status prior to initiating usage of the study drug. Subjects will be reevaluated at 1 week and 1 month visits and the data will be evaluated and compared to baseline. This is a small preliminary pilot study to evaluate tolerability of this treatment model utilizing Restasis. Given the small number of subjects and given our question of initial tolerability, the predominant nature of the results are observational and meant to provide an early means of addressing the question of tolerability.

The following data will be collected. They are all minimal to no risk.

- Visual acuity
    - Visual acuity will be measured on a Snellen chart and converted to logMAR values
- Tolerability survey
    - The Tolerability Questionnaire involves the subject answer a series of questions to assess their symptoms.
- Ocular Surface Disease Index (OSDI)
    - The Ocular Surface Disease Index is a validated questionnaire consisting of a group of 12 questions designed to assess symptoms of ocular surface disease. The questionnaire is administered by a trained medical staff member. All questions are answered on a scale of 0 to 4 (or the subject has an option to not answer a question). The end score is then mathematically converted to a 0-100 scale, with 0 being no symptoms and 100 being the most severe symptom score.
- Corneal staining (NEI Grading System)
    - Corneal staining is a routine ophthalmic and optometric test which utilizes Sodium Fluorescein stain on the eye to evaluate the health of the ocular surface. The amount of stain adherent to the ocular surface is then recorded utilizing standardized scales. It is minimal risk, including risk of irritation, redness, burning and stinging.
    - The NEI Grading System is a standardized method for quantifying the level of ocular surface signs noted on slit lamp examination. The scale ranges, in whole numbers, from 0 to 3, in 5 distinct sections on the cornea, with 0 indicating that the particular sign is not present and 3 being the most severe version of that specific sign (ie corneal staining, conjunctival staining, conjunctival redness) being measured. The overall score for one eye's cornea (5 sections on each cornea) ranges from 0 to 15.
- Conjunctival staining (NEI Grading System)
    - Conjunctival staining is a routine ophthalmic and optometric test which utilizes Lissamine Green stain on the eye to evaluate the health of the ocular surface. The amount of stain adherent to the ocular surface is then recorded utilizing standardized scales. It is minimal risk, including risk of irritation, redness, burning and stinging.
    - The NEI Grading System is a standardized method for quantifying the level of ocular surface signs noted on slit lamp examination. The scale ranges, in whole numbers, from 0 to 3, in 6 distinct sections on the cornea, with 0 indicating that the particular sign is not present and 3 being the most severe version of that

specific sign (ie corneal staining, conjunctival staining, conjunctival redness) being measured. The overall score for one eye's conjunctiva (6 sections on each eye's conjunctiva) ranges from 0 to 18.

- Conjunctival Redness (Efron and modified Efron scale)
    - Conjunctival redness involves the visual inspection of the ocular surface by the investigator and grading of the amount of redness on a standardized scale.
    - The Efron Grading Scales for Contact Lens Complications is a standardized method for quantifying the level of ocular surface signs noted on slit lamp examination. The scale ranges, in whole numbers, from 0 to 4, with 0 indicating that the particular sign is not present and 4 being the most severe version of that specific sign (ie corneal staining, conjunctival staining, conjunctival redness) being measured.
- Oculus Keratograph 5M R-Scan value
    - This device is a non-invasive imaging modality which takes an image of the front surface of the eye and through the use of a computerized algorithm categorizes the level of redness automatically on a continuous scale that increases in increments of 0.1 starting from 0 up to 4.
    - The investigator will image the ocular surface utilizing the Oculus Keratograph 5M device. The computer will then use an embedded software algorithm to quantify the level of redness on a scale from 0 to 4 in 0.1 increments, with 0 being no redness and 4 being the most severe redness level.

Findings for all endpoints will evaluated to measure subjective and objective differences in clinical signs and symptoms.

11.0 Setting

Subjects will be asked to complete the study visits, which will be conducted in clinical facilities at BostonSight, Needham, MA.

12.0 Drugs or Devices

PROSE (Prosthetic Replacement of Ocular Surface Ecosystem):

The PROSE device is considered a class II medical device by the FDA. All rigid lens materials are FDA approved for use in a rigid contact lens, and they are not investigative devices.

RESTASIS (cyclosporine ophthalmic solution 0.05%) (AbbVie Inc.)

RESTASIS (cyclosporine ophthalmic solution 0.05%) is a topical immunomodulator indicated to increase tear production in patients with ocular surface inflammation associated with keratoconjunctivitis sicca. RESTASIS appears as a translucent homogenous emulsion. The osmolarity is 230 to 320 mOsmol/kg and the pH of the solution is 6.5-8.0.
RESTASIS is a FDA approved drug for the increase of tear production in patients with keratoconjunctivitis sicca (dry eye syndrome). FDA approval initially occurred in 1983 and was most recently approved as of October 2003.[5]

The ingredients for RESTASIS are listed below:[5]

- Active Ingredients: Cyclosporine 0.05%
- Inactive Ingredients: Glycerin, castor oil, polysorbate 80, carbomer copolymer type A, purified water, and sodium hydroxide to adjust pH.

"In clinical trials the most common adverse reaction following the use of RESTASIS® was ocular burning (17%). Other reactions reported in 1% to 5% of patients included conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging, and visual disturbance (most often blurring)".[5]

Purilens (Lifestyle Inc)

Purilens is an FDA approved sterile buffered saline solution for cleaning, disinfecting, and storing of contact lenses.[8] It is formulated with sodium chloride and boric acid. Although it is not specifically approved for filling scleral lenses, it is commonly used as off-label for filling scleral lenses and generally accepted as standard of care.[9,10,11] Purilens is a pH balanced buffered saline with pH of 7.4, to match the pH of natural human tears.[11]

In our study buffered preservative-free Normal Saline (Purilens) will be used routinely to fill the PROSE reservoir. If a patient is not currently using Purilens to fill the PROSE reservoir they will initiate doing so for two weeks prior to being dispensed the study drug.

Lissamine Green Ophthalmic Strip (Green Glo, Contacare Ophthalmics and Diagnostics): An ophthalmic dye used as the gold standard in ophthalmic and optometric practices to evaluate devitalized conjunctival epithelium. Used in the form of a paper strip impregnated with 1.5 mg. of Lissamine Green. The impregnated strip is moistened with one to two drops of sterile normal saline and applied to the inferior conjunctival fornix.

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.

Oculus Keratograph 5M (Oculus, Inc)

The Ocular Keratograph 5M is an FDA cleared ophthalmic device which is exempt from premarket notification requirements. It is an FDA exempt medical device. It is an ophthalmic device used to image the ocular surface. Embedded software algorithms analyze the obtained image to quantify a variety of ocular surface findings. For this study, we will utilize the R-scan function, an automatic classification of redness which quantifies the ocular surface injection (redness). This finding is a surrogate for ocular surface inflammation and the ability to objectively quantify this finding (as opposed to a clinician grading based on their subjective examination) provides standardization for research. The following technical data is provided by Oculus, Inc.

Technical Data

OCULUS Keratograph® 5M

General information		
Measuring range	3 - 38 mm 9 - 99 D	
Accuracy	± 0.1 D	
Reproducibility	± 0.1 D	
Number of rings	22	
Working distance	78 - 100 mm	
Number of evaluated data points	22 000	
Camera	Digital CCD camera	
Illumination source	Placido illumination: Placido illumination: Imaging illumination: Meibography: Tear film dynamics: Pupillometry illumination:	white diodes infrared diodes (880 nm) blue diodes (465 nm) infrared diodes (840 nm) white diodes infrared diodes (880 nm)
Technical specifications		
Dimensions (W x D x H)	280 x 480 - 505 x 485 - 515 mm (11 x 18.9 - 19.9 x 19.1 - 20.3 in)	
Weight	Measuring equipment: 3.2 kg (7.1 lbs) With base and sliding plate: 8 kg (17.6 lbs)	
Max. power consumption	18 W	
Voltage	90 - 264 V AC	
Frequency	47 - 63 Hz	
Recommended computer specifications	CPU Intel® Core™ i5-6600, 500 GB HDD, 8 GB memory, Windows® 7 - Windows® 10	

CE in accordance with Medical Device Directive 93/42/EEC

13.0 Risks to Subjects / Evaluating, Monitoring and Reporting Adverse Events / Quality Assurance

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 hypothesized added risk of these occurrences by participating in this study.

Use of RESTASIS does introduce the risk of a hypersensitivity or toxic reaction to an active or inactive ingredient in RESTASIS which could result in corneal or conjunctival irritation, redness, and/or discomfort.

"In clinical trials the most common adverse reaction following the use of RESTASIS® was ocular burning (17%). Other reactions reported in 1% to 5% of patients included conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging, and visual disturbance (most often blurring)".[5]

As with any study there may be unanticipated adverse reactions or outcomes.

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.

If an adverse event such as an abrasion occurs during a study visit, the condition will be treated as it is customarily, and the fees associated with treatment will be covered by the study.

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.

Overview of Monitoring and Reporting:

Monitoring of source data

The clinical research coordinator will provide oversight to ensure all primary data are collected and entered into a database accurately.

Safety monitoring

A 24-hour dedicated telephone line to the clinical research coordinator and/or physician will be provided for the subjects to call. Sponsor will adhere to commitments made to the Institutional Review Board.

Adverse event reporting guidelines:

All adverse events must be reported in the subject's source documents, and recorded on an Adverse Event Case Report Form regardless of whether or not they are considered to be related to the test article. The recording should be within 24 hours of the time that the AE came to the attention of the Investigator. For non-serious AE it is sufficient to enter the AE information into the CRF. The Clinical Research Coordinator will review the database on a regular basis.

Reporting will include the actions taken, as follows:

- None
- Subject discontinued from study
- Required concomitant medication
- Required procedure
- Other

Any action, including a decision that no action is required, must be documented by the Investigator on the source and CRF.

In the event of any SAE reported or observed during the trial, whether or not attributable to the trial product, the Investigator, or designee, shall report the event to the Sponsor within 24 hours being made aware of the event. An initial report should be made with the understanding that it may be lacking in detail. Serious adverse events must be reported within 24 hours of knowledge of the event to the Principle Investigator via telephone or email. All SAEs shall be entered into the CRF as soon as possible regardless of the method by which it was first reported. A Serious Adverse Event Form must be completed for all serious adverse events and submitted to the Sponsor within 24 hours of the Investigator's knowledge of the event, and to the Institutional Review Board/Independent Ethics Committee/FDA according to their reporting requirements. When new significant information is obtained as well as when the outcome of an event is known, the Investigator must provide this information as soon as it becomes available. Copies of the subject's de-identified medical records as well as results of any relevant laboratory tests performed should be submitted as soon as available. If the subject was hospitalized, a copy of the de-identified discharge summary should be forwarded as soon as it becomes available. In

certain cases, a letter from the Investigator that summarizes the events related to the case may be required.

The Investigator shall promptly notify the IRB and FDA of any SAEs, or any other information that may affect the safe use of the study product during the course of the study in accordance with applicable IRB policies and procedures.

BostonSight shall implement and maintain quality control and quality assurance procedures to ensure that the study is conducted and data are generated, documented, and reported in compliance with the protocol, GCP, and applicable regulatory requirements. Specifically, this study shall be conducted in accordance with the provisions of the Declaration of Helsinki, FDA regulations 21 CFR 50, 54, 56, and 312.50, and the ICH guidelines on GCP (ICH E6).

The clinical research coordinator will regularly inspect all CRFs, study documents, and research facilities associated with this study during and after completion of the study.

The study site may also be subject to inspection by the FDA, IRB, or other regulatory agencies. The Sponsor should be promptly notified of any audit scheduled with any regulatory agency.

A protocol deviation is any noncompliance with the clinical trial protocol or ICH GCP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations. The Investigator may not deviate from the protocol without a formal protocol amendment having been established and approved by the IRB, except when necessary to eliminate imminent hazards to the subject or when the change(s) involve only logistical or administrative aspects of the trial. Deviations should be reported promptly to the Sponsor and may also require reporting to the IRB.

In the event of serious or repeated deviations, corrective and preventative actions are to be developed by the site and implemented promptly. A deviation may result in the subject having to be withdrawn from the trial, potentially rendering that subject non-evaluable.

14.0 Potential Benefits to Subjects

There may be no benefit to the subject for participation in this study.

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.

The data from a subject that withdraws or is terminated from the study will not be included in the analysis.

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 will not be provided, however, RESTASIS will be provided at no charge to the subject by AbbVie, Inc and the PURILENS will be provided at no charge by Lifestyle, Inc.

17.0 Compensation for Research-Related Injury

If there is an ocular injury in this study directly related to 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

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 principal investigator. 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 Principal Investigator.

Subjects will only be asked questions that are relevant to the study and their ocular health. The investigators, who are all optometrists 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. Informed consent is estimated to take approximately 30 minutes for this study.

21.0 Process to Document Consent in Writing

Participants will complete the Informed Consent document.

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, study sponsor 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

All investigators in this study are optometrists or 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.

BostonSight is the research sponsor and is covering all costs of the study, AbbVie, Inc is providing the study drug (Restasis) no charge. Additionally, Lifestyle, Inc is providing Purilens at no charge.

Citations:

---

[1] Yin J, Jacobs DB. "Long term outcome of using Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) as a drug delivery system for bevacizumab in the treatment of corneal neovascularization." Ocular Surface. 2019 Jan; 17(1): 134-141.

[2] Laballe E, et al. "Preclinical assessment of scleral lens as a reservoir-based ocular therapeutic system." Cont Lens Ant Eye. 2016 Oct; 39(5): 394-396.

[3] Kalwerisky K, et al. "Use of the Boston Ocular Surface Prosthesis in the management of severe periorbital thermal injuries: a case series of 10 patients." Ophthalmology. 2012 Mar; 119(3): 516-521.

[4] TFOS DEWS II Report Executive Summary
https://www.tearfilm.org/public/TFOSDEWSII-Executive.pdf

[5] Restasis (Cyclosporine ophthalmic emulsion 0.05%) Package Insert
https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/050790s020lbl.pdf

[6] https://www.clspectrum.com/issues/2019/may-2019/contact-lens-case-reports

[7] https://www.aao.org/image/neiindustry-grading-system
[8] *510(K) SUMMARY SEP 10 2010 FOR (PURILENS)- Food and Drug*
www.accessdata.fda.gov/cdrh_docs/pdf9/K093367.pdf

[9] Sterling, Jeffrey. "Getting Started with Scleral Lenses." *Review of Cornea and Contact Lenses*, 15 Sept. 2019, reviewofcontactlenses.com/article/getting-started-with-scleral-lenses.

[10] Caroline, Patrick J., et al. "Contact Lens Case Reports: The Effect of PH When Filling Scleral Lenses for Dry Eye." *Contact Lens Spectrum*, 1 May 2019, www.clspectrum.com/issues/2019/may-2019/contact-lens-case-reports.

[11] *PuriLens Plus Saline*, www.purilens.com/purilens_faqs.html.