Tonometry Precision and Accuracy During PROSE Scleral Lens Wear: A Pilot Study

SPONSOR:

N/A

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1.0 Objectives

The goal of this pilot study is to determine the precision and accuracy of measurements of intraocular pressure (IOP) when a PROSE (Prosthetic Replacement of the Ocular Surface Ecosystem) scleral lens is on the eye.

The PROSE device (PD) is a specialized scleral lens that is filled with preservative-free saline and then applied to the eye in order to treat a variety of ocular conditions. The PROSE device vaults the cornea without touch and lands gently on the conjunctival tissue overlying the sclera. Because scleral lenses vault and therefore cover the cornea, measuring IOP during lens wear is challenging as traditional techniques rely on corneal contact. Measuring IOP before insertion and after removal of the PROSE device likely does not correspond to the IOP when the lens is actively on the eye.

This is a prospective study of the precision and accuracy of tonometry measurements with scleral lens wear. Three non-traditional means of IOP measurements will be used: scleral TonoPen, scleral pneumatonometry, and transpalpebral Diaton tonometer. Data on precision and accuracy of these instruments in this pilot study aims to guide decision making in a full study on the effects of scleral lenses on IOP.

2.0 Background

The PROSE device is a refractive treatment for individuals with pathologies that require a rigid lens to mask irregularities on the front refracting surface of their eye (the cornea). PROSE is also used in cases of ocular surface disease to protect and support the ocular surface in an effort to reduce dryness, prevent ocular surface breakdown, ulceration, and perforation. The PROSE device is similar to a scleral lens in theory though it allows for unique customizations that are unavailable in currently marketed scleral lens designs, including fenestrations and channels (air and fluid ventilation, respectively).

Recent literature has suggested that intraocular pressure may rise during scleral lens wear, although variability exists in methods and results within the literature.[1-3] Possible causes include negative pressure and suction created underneath the lens during settling or due to the pressure applied by the lens on the structures involved in aqueous outflow, namely the trabecular meshwork and the episcleral veins.[1-3] The challenge in elucidating this concept is that the scleral lens and its relationship to the cornea is a closed environment that is difficult to study.

Traditional measurements of intraocular pressure rely on corneal contact. Methods of IOP measurement that do not rely on corneal contact instead use either scleral contact (i.e. scleral pneumatonometry and scleral TonoPen) or contact with the eye through the eyelid (transpalpebral Diaton). This study will use these three methods due to the fact that they are the only options currently available to measure IOP without corneal contact, which is a requirement for IOP measurement during scleral lens wear.

An important consideration when using these instruments is that measurements taken over the extraocular muscles may give inaccurate results. Literature suggests that superotemporal and inferotemporal measurements using the pneumatonometer provide the most accurate and

comparable results to a direct corneal measurement perhaps due to the avoidance of measurement over the extraocular muscles.[4] Scleral pneumatonometry IOP measurements can potentially be used to estimate corneal IOP using a published equation posited by Kuo et al.[5]

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. Written documentation has been obtained in accordance with the relevant county and local privacy requirements, where applicable
3. Male or female, 18 years of age and older prior to the initial visit
4. Has a current diagnosis of corneal ectasia, i.e. keratoconus, pellucid margin degeneration
5. Is an established wearer of PROSE in both eyes; without fenestrations or channels; with diameter equal to or greater than 18.0 mm
6. Upon examination by the investigator, there is adequate exposure of the sclera as required for IOP measurements with the planned device
7. In the opinion of the investigator, the subject has the ability to follow study instructions
8. 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 aphakic (i.e., missing their natural lens inside the eye)
2. Is currently participating in any other type of eye-related clinical or research study
3. Is pregnant or nursing as reported by the subject
4. Less than 18 years of age
5. 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
6. Has had previous ocular surgery within the past 12 weeks
7. Has a diagnosis of glaucoma, glaucoma suspect, ocular hypertension or prior glaucoma surgery

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

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 30 subjects will be enrolled in this study with 10 subjects in each of the three cohorts. This is a low risk study. We can expect an approximate 10% drop-out rate, so we will expect to recruit approximately 33 subjects; and the first 30 to be eligible and complete the study will be used for data analysis.

The first 10 subjects that are eligible to proceed and consented will be consecutively enrolled in the first cohort (scleral TonoPen). The second 10 subjects that are eligible to proceed and consented will be consecutively enrolled in the second cohort (scleral pneumatonometry). The third 10 subjects that are eligible to proceed and consented will be consecutively enrolled in the third cohort (Diaton). Sequential assignment allows for focus on one instrument and one technique at a time by one investigator.

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 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. A partial HIPAA waiver is requested to permit the investigators to use the database to identify prospective patients.

7.0 Multi-Site Research Communication – N/A

8.0 Study Timelines

The total duration of the subjects' participation in the study will be approximately 1 visit.
It is anticipated that to enroll all study subjects, it will take approximately 6 months.

The estimated date for completion of this study is 12 months after the start of recruitment.

The study visit will contain:

a. Completion of informed consent
b. Collection of baseline data of the eye
    i. Corneal and conjunctival staining, Oxford grading
    ii. Corneal IOP measurement via TonoPen
c. Collection of baseline data on the PROSE device fit
d. IOP measurement with lenses in place via one of three methods:
    i. Scleral TonoPen
    ii. Scleral pneumatonometry
    iii. Diaton

The study visit will take approximately 65 minutes in total. All assessment performed will be for research purposes and not part of the subjects standard clinical care.

9.0 Study Endpoints

The study design allows for the subjects to serve as their own control. The subjects' baseline IOP will be measured with the standard clinical approach via corneal TonoPen. Corneal TonoPen was chosen as the control method for intraocular pressure measurements as it is a standard of care method and process used every day in clinical practice by ophthalmologists and optometrists. This will be compared to the IOP measurement obtained in the same subject with lenses in place.

The primary endpoints in this study are as follows:

1. Intraocular pressure
    a. TonoPen, corneal without lens
        i. Baseline, one measurement
    b. TonoPen, scleral with lens
        i. IOP and confidence level will be recorded
        ii. Attempt **5 measurements maximum**
            - Goal of achieving 3 measurements in total with confidence level of 90% of higher
        iii. One measurement defined as a completed result or attempting to measure until the machine times out
    c. Pneumatonometer, scleral with lens
        i. Measurement in "manual IOP mode"
        ii. IOP and standard deviation (SD) will be recorded for each measurement
        iii. Attempt **10 measurements maximum**
            - Goal of achieving 3 measurements in total with a SD of 2 mmHg or less
        iv. One measurement defined as a completed result or attempting to measure until the machines times out
    d. Diaton, transpalpebral with lens

i. Up to 6 individual attempts are included in each complete measurement, with the instrument averaging the measurements for a result
ii. Reliable average is confirmed:
    - When the instrument shows symbol <<A>> and the mean IOP value is non-flickering
    - When the instrument shows symbol <<A>> and the mean IOP value is flickering with a result of equal or less than 19 mmHg
iii. Attempt **5 complete measurements maximum**
    - Goal of achieving 3 reliable measurements
    - Reliability defined (per manufacturer Diaton, Ryazan State Instrument-Making Enterprise, www.diaton-tonometer.com) as:
        a. +/- 2mmHg error in range 5-20mmHg
        b. +/- 10% error in range 20-60mmHg

Correct calibration of each instrument will be ensured prior to the study per individual manufacturer's standards. The first measurement of every subject will not be included but will serve as one practice measurement to familiarize the subject with the measurement process.

10.0 Procedures Involved

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

During the visit:

1. Informed consent will be completed
2. Record the patient's general medical history and habitual contact lens information, including lens design, power, and diameter.
3. An investigator will conduct visual acuity assessments of both eyes (Snellen).
4. Assess the fit of the PROSE device via slit lamp assessment of both eyes.
5. Assess the cornea and conjunctiva of both eyes with the PROSE device on and off.
6. Measure corneal intraocular pressure of both eyes after PROSE device removal
7. The investigator will instill one drop of topical anesthetic in both eyes followed by a lubricating preservative-free artificial tear drop, such as Refresh Plus, prior to IOP measurements.
8. Measure intraocular pressure of both eyes with the PD on via (method depends on which cohort the subject is in):
    a. Scleral TonoPen
    b. Scleral pneumatonometry
    c. Transpalpebral Diaton
9. Reassess the ocular surface of both eyes after intraocular pressure measurement at the slit lamp biomicroscope with and without fluorescein staining in order to rule out adverse events, such as conjunctival abrasion or erosion or other irritations.

Procedure	Length of Time Required for	Frequency of Repetition

Informed consent & HIPAA	20 minutes	Once
General History and Medications	10 minutes	Once
Visual Acuity	2 minutes	Once
Slit-lamp Examination (with PD)	4 minutes	Once
Corneal IOP Measurement (TonoPen)	5 minutes	Once
IOP Measurement (One of the below will be completed)		
COHORT 1: Scleral TonoPen	20 minutes	5 (maximum)
COHORT 2: Scleral Pneumatonometer		10 (maximum)
COHORT 3: Transpalpebral Diaton		5 (maximum)
Slit-lamp Examination after measurement	4 minutes	Once
TOTAL TIME	**65 minutes**	

The testing descriptions are summarized in the table below:

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 4 minutes per eye. Photographs will be taken at the discretion of the investigator.

Sodium Fluorescein	Sodium fluorescein staining will be used to evaluate ocular surface damage indicated by cell damage or death. Corneal and conjunctival staining will be scored using the Oxford grading scale.
Diaton tonometry	The Diaton device will be placed on the superior lid as the participant looks down to measure the intraocular pressure transpalpebrally.
Pneumatonometry	One drop of topical anesthetic (Proparacaine) will be instilled into each eye. The pneumatonometer will be placed on the superotemporal sclera and overlying conjunctival tissue as the participant looks down and in to measure the intraocular pressure.
Scleral TonoPen	One drop of topical anesthetic (Proparacaine) will be instilled into each eye. The participant will look down and in as the TonoPen probe lightly contacts the superior temporal sclera and overlying conjunctival tissue.
Corneal TonoPen	One drop of topical anesthetic (Proparacaine) will be instilled into each eye. The participant will look straight ahead and a probe will lightly contact the cornea to measure the intraocular pressure.

Table 3. Descriptions of tests

The following data will be collected in this study:

- Intraocular pressure via several different methods
    - Corneal TonoPen
    - Scleral TonoPen
    - Scleral pneumatonometry
    - Transpalpebral Diaton

11.0 Setting

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

12.0 Drugs or Devices

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.

All devices included in the study are standard of care, are intended to be used to measure intraocular pressure in clinical practice, and are FDA approved to do so. The Diaton was created to allow IOP measurement without contact with the ocular structures as the instrument touches only the outer part of the upper eyelid. The TonoPen and the pneumatonometer are typically used on the cornea but include an option of scleral measurement when corneal pathology or post-surgical conditions contraindicate corneal contact. There is literature supporting use of the pneumatonometer on the sclera for IOP measurement.[4-8] Literature supporting use of the TonoPen on the sclera for IOP measurement is also available.[4,9]

13.0 Risks to Subjects

This study presents 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 by participating in this study. Measurement of IOP via conjunctival/scleral contact does introduce the risk of conjunctival abrasions, irritation, redness, or discomfort.

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. Additionally the subjects are encouraged to call immediately if experiencing any pain or other discomfort after the exam, which may be an indicator of irritation following intraocular pressure measurements.

In a review of current literature, no reported adverse events or serious adverse events were found ifor each specific manner of IOP measurement with the instruments to be used in this study (scleral TonoPen, scleral pneumatonometry, Diaton). No documented adverse events for these instruments were found in literature at the time of submission.

If, in the unlikely event, during the study a patient experiences any serious adverse event, they will be removed from the study and the IRB will be notified.

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 be given in $20 gift card.

17.0 Compensation for Research-Related Injury

If there is an ocular injury in this study directly related to the use of the lenses or during IOP measurement, 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 principal investigator'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 20 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. A partial waiver is requested for study recruitment. 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

All investigators in this study are optometrists 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.

27.0 Citations

1. McMonnies CW. *A hypothesis that scleral contact lenses could elevate intraocular pressure*. Clin Exp Optom 2016; 99: 594-596.

2. Michaud L, et al. *Intra-ocular pressure variation associated with the wear of scleral lenses of different diameters*. Contact Lens and Anterior Eye 2019; 42: 104-110.

3. Nau, et al. *Intraocular Pressure After 2 Hours of Small-Diameter Scleral Lens Wear.* Eye Contact Lens 2016; 42(6): 350-353.

4. Tai et al. *Correlation of Tono-Pen and Pneumatonometer Measurements from Four Scleral Quadrants with Intraocular Pressure Measurements from the Cornea*. J Clin Exp Ophthalmol 2015; 6(6): 504.

5. Kuo et al. *Correlation of Serial Scleral and Corneal Pneumatonometry*. Ophthalmology 2015; 122: 1771-1776.

6. Lee JH, Sanchez LR, Porco T, et al. *Correlation of corneal and scleral pneumatonometry in pediatric patients*. Ophthalmology 2018; 125 :1209-1214.

7. Kapamajian M, et al. *Correlation of corneal and scleral pneumatonometry: An Alternative Method for Intraocular Pressure Measurement.* American Journal of Ophthalmology Nov 2013; 156(5) : 902-906.

8. Magalhaes OA, Aldave AJ. *Scleral Pneumatonometry in Penetrating Keratoplasty: A Clinic Study.* Cornea Oct 2017; 36(10): 1200-1205.

9. Kolin T, Wedemeyer LL, Kolin E, Braun Y. *Comparison of scleral and corneal Tono-Pen readings.* Journal of AAPOS Aug 2003; 7(4): 291-292.