VAULT EVALUATION AFTER IMPLANTATION OF AN IMPLANTABLE COLLAMER LENS

Sponsor:

Carolina Eyecare Physicians, LLC
1101 Clarity Rd., Suite 100
Mt. Pleasant, SC 29464
(843) 881 3937
Kerry D. Solomon, MD, Principal Investigator
Helga P. Sandoval, MD, MSCR, Director of Research

Study Product:

The EVO/EVO+ Visian and EVO/EVO+ Visian TORIC Implantable Collamer Lenses (ICL)

Protocol Number:

CEP-23-003
Initial version date: 01DEC2023
Final version date: 19DEC2023

Investigator Agreement:

I have read the clinical study described herein, recognize its confidentiality and agree to conduct the described trial in compliance with Good Clinical Practices (GCP), the Declaration of Helsinki, this protocol and all applicable regulatory requirements. Study will not start until IRB approval has been granted. Additionally, I will comply with all procedures for obtaining informed consent, data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the sponsor.

Name of the Investigator: _____

Name of the Institution: _____

Address: _____

_____

Investigator: _____
Signature Date

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INTRODUCTION

The implantable collamer lens (ICL) is a lens designed to correct mid to high degrees of refractive error that is implanted in the posterior chamber of a phakic eye. ICLs are a better alternative than older lenses designed to be placed in the anterior chamber because they pose a lower risk of endothelial cell loss and are also more cosmetically appealing, since they are less visible externally.

Collamer lenses are made off a blend of a polymer and collagen making it highly permeable to oxygen and nutrients to prevent the lens from interfering with the exchanges of nutrients between the crystalline lens and the aqueous and therefore prevent the cataract formation after implantation. Over the years, it became clear that the permeability of the lenses was not enough to prevent potential complications such as pigment dispersion, peripheral anterior synechia, pupillary block, glaucoma and the cataract formation[1], which would also occur as the result of the contact between the ICL and the crystalline lens. In order to further avoid the cataract formation, specially the ASCC[1] – considered to be typical of this type of lenses[2] - the lenses went through design modifications and the latest model had the posterior face concavity increased aiming to completely vault the anterior crystalline lens capsule, resting only on the anterior zonular fibers.[3]

To succeed when performing surgery with the implantation of these lenses it is crucial to be able to accurately predict not only the postoperative refraction but also the correct lens size and specially the ICL lens vault, to preclude the afore mentioned possible complications. Although nowadays we can predict the vault size more objectively, with the use of devices such as anterior segment optical coherence tomography (AS-OCT), Pentacam or ultrasound biomicroscopy (UBM), still there is no gold standard to do so, and studies have already shown that indeed the measurements can differ among different techniques.[4,5]

The purpose of this study is to evaluate the vault after implantation of an implantable collamer lens (ICL) with the use of anterior segment optical coherence tomography (AS-OCT), Pentacam and ultrasound biomicroscopy (UBM) to assess the following measurements: anterior chamber depth (ACD), horizontal white to white (WTW), sulcus to sulcus (STS), and angle to angle (ATA).

1. **OBJECTIVE:**
   To evaluate the vault after implantation of an implantable collamer lens (ICL).

2. **STUDY DESIGN AND METHODS:**

   A. Test article: EVO/EVO+ Visian and EVO/EVO+ Visian TORIC Implantable Collamer Lenses.

   B. Study Design: Prospective, single site, non-randomized study.

   C. **Subjects:** A total of 33 subjects who met the Inclusion/Exclusion criteria will be enrolled.
      1. **Inclusion Criteria:**

Subjects **MUST** fulfill the following conditions to qualify for enrollment into the trial

1. Gender: Males and Females.
2. Age: 21 to 45 years of age
3. Willing and able to provide written informed consent for participation in the study
4. Willing and able to comply with scheduled visits and other study procedures.
5. Scheduled to undergo ICL implantation in both eyes within 1 to 30 days between surgeries.
6. Subjects who require an ICL power in the range of -3.00 to -15.00 D.

2. Exclusion Criteria:

Subjects with **ANY** of the following conditions on the eligibility exam may **NOT** be enrolled into the trial.

1. Patients who do not qualify for an ICL according to the Direction For Use (DFU)
2. Unstable or worsening myopia
3. Use of any systemic or topical drug known to interfere with visual performance.
4. Irregular astigmatism.
5. History of retinal detachment.
6. Pseudoexfoliation syndrome or any other condition that has the potential to weaken the zonules.
7. Pigment dispersion
8. Previous intraocular surgery.
9. Previous refractive surgery.
10. Previous keratoplasty
11. Pupil abnormalities
12. Any clinically significant, serious or severe medical or psychiatric condition that may increase the risk associated with study participation or may interfere with the interpretation of study results.
13. Participation in (or current participation) any ophthalmic investigational drug or ophthalmic device trial within the previous 30 days prior to the start date of this trial.

The principal investigator reserves the right to declare a patient ineligible or non-evaluable based on medical evidence that indicates the patient is unsuitable for the trial.

3. Exclusion Criteria during surgery

If any of the following exclusion criteria are applicable to the study eye, the subject should not continue in the study.

1. Significant vitreous loss.
2. Significant anterior chamber hyphema.
3. Uncontrollable intraocular pressure.

Note: Any subject in which surgery has been aborted for either eye should immediately be discontinued from the study and an exit form completed for that subject. These subjects will be followed up as per the clinic standard of care, monitored for safety, and their data will be

excluded from the study efficacy analysis (obtained from FDA Database Research Results Feb, 05, 2009). All adverse events will be appropriately documented and reported.

Additionally, participants who are considered to be a vulnerable subject population are not to be enrolled into the study without prior written authorization from both the Sponsor and the IRB to ensure that a description of additional safeguards are in place during the consenting and enrollment processes. Vulnerable populations include, but are not limited to, the following:

1. Prisoners
2. Nursing home residents /institutionalized individuals
3. Mentally disabled /cognitively impaired individuals
4. Sponsor employees and their family members
5. Site employees and their family members that are directly and indirectly involved with the study
6. Students of the principal investigator participating in the study
7. Economically and/or educationally disadvantaged individuals
8. Comatose individuals / traumatized individuals
9. Adults who do not read and/or write
10. Hearing impaired individuals
11. Terminally ill individuals / individuals with life-threatening conditions

3. STUDY PROCEDURES

A. Informed Consent / Subject enrollment

Potential subjects will be identified from the patients presenting at the clinic. Additionally, an ad will be placed in social media and in the practice website, if deemed necessary. Once identified as a study candidate, the patient will be asked if he/she would like to participate. The sub-investigator, study coordinator or an appropriately trained staff member will answer any and all questions and will obtain informed consent. A copy of the signed informed consent document will be given to the subject. The principal investigator will be available if the subject wants to discuss further details with him. Any testing that is part of the investigative site's standard preoperative ICL evaluation may be performed prior to the informed consent being signed, provided these tests are conducted within 6 months of surgery. The patient will understand that participation in the study, or declining to participate, will not affect his/her quality of care.

No subject will be enrolled into the study that does not meet the inclusion/exclusion criteria and does not sign the current approved informed consent document. Informed consent will be obtained prior to collecting any data for the study. The original signed documents will be maintained by the investigator as a permanent part of the subject's research records.

B. Surgery Procedures:

Surgeries would be completed following the surgeon's standard of care.

C. Study Visit Schedule and Assessments (Table 1).

1. Visit Schedule: Subjects will be examined at the following intervals:

1. Visit 0: Screening and enrollment: Preoperative evaluation completed not more than eight weeks before surgery
2. Visit 1: Day of Surgery
3. Visit 2: Day 1: (12 to 48 hours) after surgery
4. Visit 3: Week 1: 7 ±2 days after surgery
4. Visit 3: Month 1: 30 ±7 days postoperative after second eye surgery

D. Measurements and evaluations

1. Visit 0 - Screening: Informed consent process will be conducted at this visit. Assessments include uncorrected and best-corrected distance visual acuity (UCDVA and BCDVA, ETDRS chart), manifest refraction, slit lamp examination including dilated fundus exam, gonioscopy, endothelial cell count, biometry (lenstar and/or IOL Master 700), anterior segment optical coherence tomography (AS-OCT), ultrasound biomicroscopy (UBM) and Pentacam. Any testing that is part of the site's standard of care preoperative ICL surgery evaluation may be performed prior to the informed consent being signed provided these tests are conducted within 6 months of the surgery date and notation of the date performed is entered onto the CRF. The surgeon's standard pre ICL surgery treatment will be used in all his patients.

2. Visit 1 - Day of surgery each eye: The surgeon may use his preferred surgical technique. The lens will be implanted in the sulcus. The following information will be captured on the day of surgery: lens implanted and power, target refraction for ICL power implanted, additional surgical procedures, intraoperative complications, and any device deficiencies. The surgeon's standard post-surgery treatment will be used in all his patients.

3. Visit 2 – Day 1 each eye: Monocular UCVA (ETDRS), slit lamp examination, and any adverse events.

4. Visit 3 – Week 1 each eye: Monocular UCVA and BCVA (ETDRS), manifest refraction, slit lamp examination, and any adverse events.

5. Visit 4 – Month 1 both eyes: Slit lamp examination, manifest refraction, monocular UCDVA and BCDVA using ETDRS, dilated fundus exam (as deemed necessary by the investigator), anterior segment optical coherence tomography (AS-OCT), ultrasound biomicroscopy (UBM), and any adverse events.

All adverse events and complaints will be monitored and recorded at all study visits.

Table 1. Visits and Study Assessments

	Visit 0 Screening	Visit 1/1A Day of Surgery	Visit 2/2A Day 1	Visit 3/3A Week 1	Visit 4 Month 1
Informed Consent	X				
Inclusion/Exclusion	X				
Demographics/	X				
PMH/Ocular history	X				
Concomitant medications	X				
UCVA ETDRS (4m)	X		X	X	X
Manifest refraction	X			X	X
BCVA ETDRS (4m)	X			X	X
SLE	X		X	X	X
Dilated fundus exam	X				X‡
Gonioscopy	X				
Endothelial cell count	X				
Pentacam	X				
AS- OCT	X				X
UBM	X				X
Intraoperative data		X			
Adverse events		X	X	X	X

X To be performed as scheduled
‡ To be performed as deemed necessary by the investigator.

4. STUDY ENDPOINT CRITERIA

A. Patient Completion of Study: If a study patient has completed the final visit (Visit 4) of the study, he/she is considered to have completed the study.

B. Patient Discontinuation: Each study patient may voluntarily discontinue the study at any time they choose. Study patients who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study. Study patients discontinued during the enrollment phase (prior to surgery) of the study will be replaced.

C. Patient Termination: A study patient will be terminated if the study patient develops any severe adverse event that may be related to the study. A study patient will receive appropriate treatment at the discretion of the investigator. Notification of termination will be clearly

documented. These study patients are considered to have completed the study and will not be replaced.

D. Study Termination: The investigator with appropriate notification may terminate the study. If, after clinical observations, the investigator feels that it may be unwise to continue the study, he may stop the study.

E. Study Completion: The study will be complete when all enrolled patients have completed Visit 4 or have been terminated from the study.

5. STATISTICAL CONSIDERATIONS

A. Sample size

In order to calculate the sample size, we need to know an accurate estimate of the standard deviation of the outcome measure which we do not know; therefore, we consider this study a pilot trial. When estimating the sample size for a pilot study, the simplest method is to apply a sample size rule of thumb. Browne[6] suggests a general flat rule to 'use at least 30 subjects or greater to estimate a parameter'. Allowing 10 % for an assumed dropout rate, a total of 33 subjects will be enrolled.

B. Statistical Analysis

All data will be collected by the site and entered into a database. Subjects will be assigned an ID number. Data analysis will be performed without patient identification. Statistical analysis will be performed using standard descriptive statistics and other tests as deemed appropriate based on the characteristics of the data to be analyzed. All statistical tests will be two-sided and interpreted at a 5% significance level. Data analysis will be conducted by a third-party consultant.

C. Study Endpoints:

1. Primary Endpoints:

- Mean difference between predicted and actual central vault at 1-month after ICL implantation

2. Secondary Endpoints:

- Mean predicted central vault
- Mean predicted peripheral vault
- Mean preoperative angle measurement
- Mean difference between predicted and actual peripheral vault at 1-month visit
- Percentage of eyes within ±100 µm of predicted vault at 1-month visit

Central vault is defined as the perpendicular distance between the posterior surface of the ICL and anterior surface of the crystalline lens while peripheral vault is defined as the distance measured perpendicularly to the surface of the crystalline lens at the level

of the edge of the optical zone of the phakic lens**.** Predicted vault will be assessed using different diagnostic tools.

D. Safety Analyses

The type, severity, duration and frequency of reported ocular adverse events will be tabulated for each group. Adverse events will also be summarized for events that were considered treatment related.

6. DATA HANDLING AND RECORD KEEPING

A. Confidentiality

To ensure confidentiality in this study, records of the participants will be examined only by the principal investigator and research staff involved in the study. Study records will be kept on file at the site. Any statistical analysis and publication will not include any subject identifiers. Medical records will be made available only for review by the investigators, the IRB, and other State or Federal Regulatory Agencies, if necessary. All information in these records will be kept confidential.

B. Records Retention

The PI is accountable for the integrity, retention and security of all study related data. The investigator must maintain accurate, complete and current records relating to the clinical study. The investigator must maintain the required records during the investigation and for a period of 3 years after the date on which the investigation is terminated or completed.

7. STUDY MONITORING, AUDITING, AND INSPECTING

The nature and location of all source documents will be identified to ensure that original data required to complete the case report forms (CRFs) exist and are accessible for verification by the project manager. If electronic source records are maintained, these records must be 21 CFR Part 11 compliant and will be printed and certified.

The required examination must be recorded on the CRFs. Provided CRFs can be used as source document. All data reported must have corresponding entries in the source documents. The principal investigator or sub-investigator must review the reported data and certify that the CRFs are accurate and complete. No subject identifiers should be recorded on the CRFs beyond subject number, subject initials and study specific identifiers.

Designated study personnel will enter collected data from CRFs into a database created for the purpose of this study. Additionally, monitoring be made by the study manager or her designee throughout the study.

Upon completion of the CRFs, the data will be reviewed by study manager and statistician for accuracy and completeness. If corrections and/or any additions to the data are deemed necessary, queries will be generated. Designated research staff are expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data in the

database are reflected in the subjects' source documentation. Any changes will need to be initialed and dated by the authorized personnel making such changes.
Data will not be sold to or shared with third parties but could be used for future research.
Electronic data may be stored and accessed on a portable device. The laptop is password protected and only the study manager has access to it.

8. INVESTIGATIONAL PRODUCT

A. Description

The already FDA approved EVO ICL and EVO TICL lenses (Implantable Collamer® Lens) are intraocular implants manufactured from Collamer®, a proprietary hydroxyethyl methacrylate (HEMA)/porcine collagen containing biocompatible polymer material. The EVO ICL lens contains a UV absorber made from a UV absorbing material. The lens features a plate-haptic design with a central convex/concave optical zone and a 0.36 mm diameter central port; the lens incorporates a forward vault to minimize contact of the ICL with the central anterior capsule. While the parent devices (non-EVO/non-central port Visian MICL lens and Visian TICL lens) require preoperative peripheral iridotomies (PIs) to facilitate aqueous flow, the EVO/EVO+ ICL lenses include a central port that allows the flow of aqueous humor through the lens, thus eliminating the need for PIs prior to implantation.

The EVO ICL lens features an optic diameter that varies with the dioptric power; the smallest optic diameter being 4.9mm and the largest 6.1mm. The EVO ICL lens is capable of being folded and inserted into the posterior chamber through an incision of 3.5mm or less. The EVO ICL lens is intended to be placed entirely within the posterior chamber directly behind the iris and in front of the anterior capsule of the human crystalline lens. When correctly positioned, the EVO ICL lens functions as a refractive element to optically reduce moderate to high myopia with or without astigmatism.

B. Treatment/Dosing Regimen

The EVO non-toric ICL is indicated to correct myopia with spherical equivalent (SE) ranging from -3.0 D to ≤ -15.0 D with less than or equal to 2.5 D of astigmatism at the spectacle plane, and for the reduction of myopia with SE ranging from greater than -15.0 D to -20.0 D with less than or equal to 2.5 D of astigmatism at the spectacle plane. Additionally, the EVO toric ICL (TICL) is indicated for the correction of myopic astigmatism with SE ranging from -3.0 D to ≤-15.0 D (in the spectacle plane) with cylinder (spectacle plane) of 1.0 D to 4.0 D. 2. for the reduction of myopic astigmatism with SE ranging from greater than -15.0 D to -20.0 D (in the spectacle plane) with cylinder (spectacle plane)1.0 D to 4.0 D. 3.

Both lenses are intended to be used in patients (between 21 and 45 years of age) with an anterior chamber depth (ACD) of 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens and a stable refractive history (within 0.5 D for both spherical equivalent and cylinder for 1 year prior to implantation). The lenses are intended to be placed in the posterior chamber (ciliary sulcus) of the phakic eye.

C. Method for Assigning Subjects to Treatment/Dosing Groups

N/A

D. Subject Compliance Monitoring

Since the ICL is implanted at the time of surgery, subject compliance will not be an issue in this particular study.

E. Packaging, Receiving, Storage, Dispensing and Return

ICLs will be ordered, received, stored and dispensed following the current ASC standard procedures and the manufacturer's recommendations.

9. ETHICAL CONSIDERATION

This clinical trial will be conducted in accordance with the principles of the Declaration of Helsinki, and Good clinical practice. The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that all personnel involved in the conduct of the clinical trial are qualified to perform their assigned duties through relevant education, training, and experience. Deviations from the clinical protocol must be documented in each subject's study records including the dates and reasons for each deviation. The PI must ensure that all aspects of the trial are in compliance with the applicable regulatory laws and conditions of approval imposed by the IRB.

10. RISKS AND BENEFITS

The risk of being in the study is not greater than the risk of undergoing routine ICL surgery. However, there is always the risk that uncommon or previously unknown side effects may occur. The study includes additional postoperative examinations at no cost.

11. IN CASE OF AN INJURY RELATED TO THIS RESEARCH STUDY

Every effort to prevent study-related injury will be taken by the study doctor and staff. In the event a patient is injured as a direct result of the study while following the study instructions and requirements, the patient will be instructed to immediately contact the principal investigator and/or study staff. Treatment will be provided as needed for those injuries caused directly by this research study. In the event of injury or illness caused by or occurring during the participation in this study, all charges for medical care provided will be billed to the patient's insurance company. The medical care costs for injuries or illnesses that are not caused directly by the research study will not be covered.

12. CONFIDENTIALITY/PUBLICATION OF THE STUDY

The existence of this Study is confidential and should not be discussed with persons outside of the Study. A description of this clinical trial will be available on http://www.ClinicalTrials.gov. Results will be submitted for publication and presentation at national and/or international meetings. A manuscript will be submitted to peer-review journals for publication but there is no guarantee of acceptance.

13. REFERENCES

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6. Browne RH. On the use of a pilot sample for sample size determination. Stat Med 1995; 14: 1933–1940.