Study Protocol

A PROSPECTIVE, MULTI-CENTER EVALUATION OF CORNEAL FLAP CREATION USING CHEETAH FEMTOSECOND LASER SYSTEM AND CHEETAH PATIENT INTERFACE

PROTOCOL NUMBER: CHTA-103-FLAP

NCT Number: NCT03789669

Document Date: May 5th, 2023

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Clinical Investigation of the
A PROSPECTIVE, MULTI-CENTER EVALUATION OF CORNEAL FLAP CREATION USING CHEETAH FEMTOSECOND LASER SYSTEM AND CHEETAH PATIENT INTERFACE

PROTOCOL NUMBER: CHTA-103-FLAP

SPONSOR: Johnson & Johnson Surgical Vision, Inc.
31 Technology Drive
Irvine, CA 92618

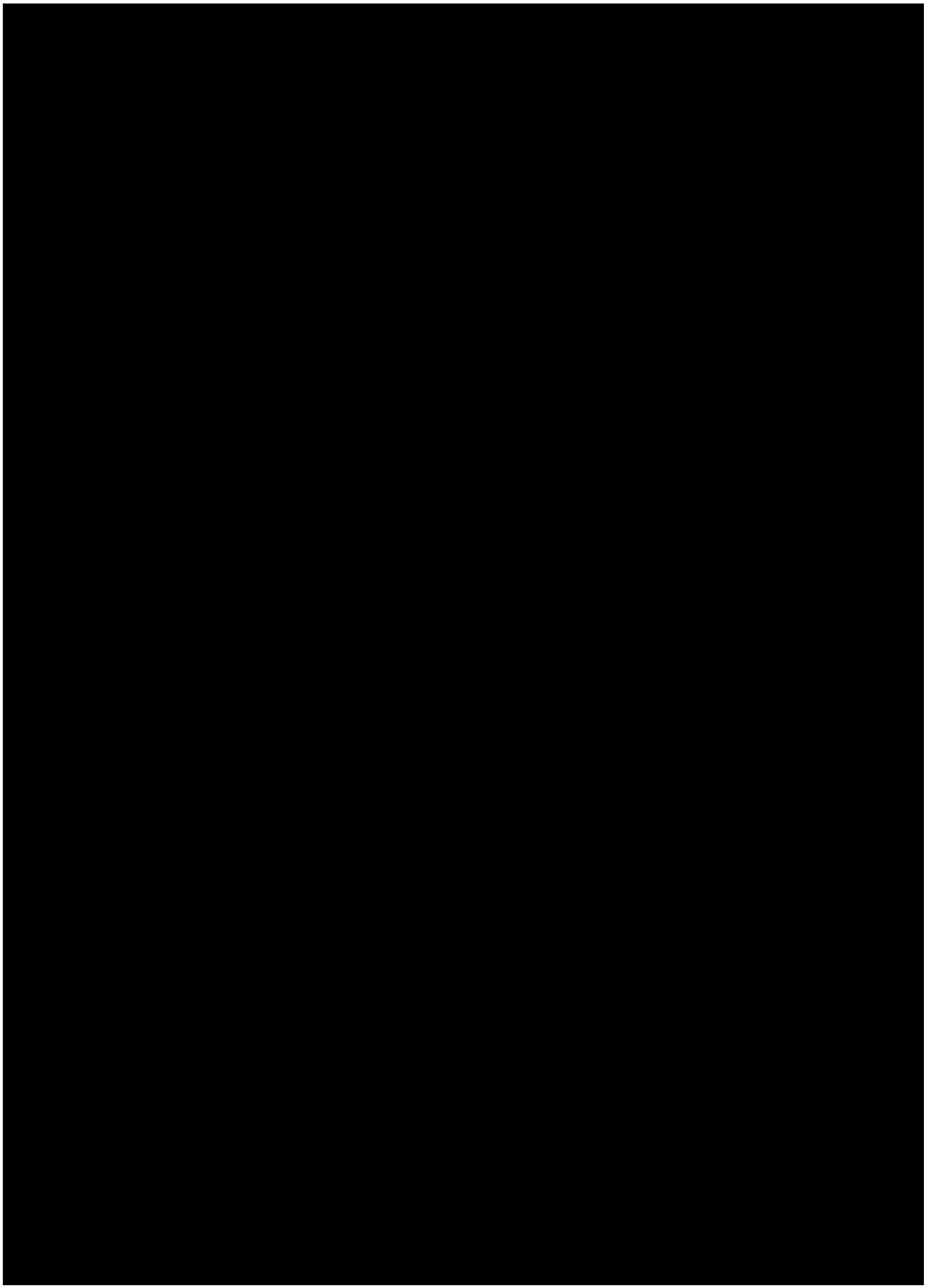
Investigator Agreement

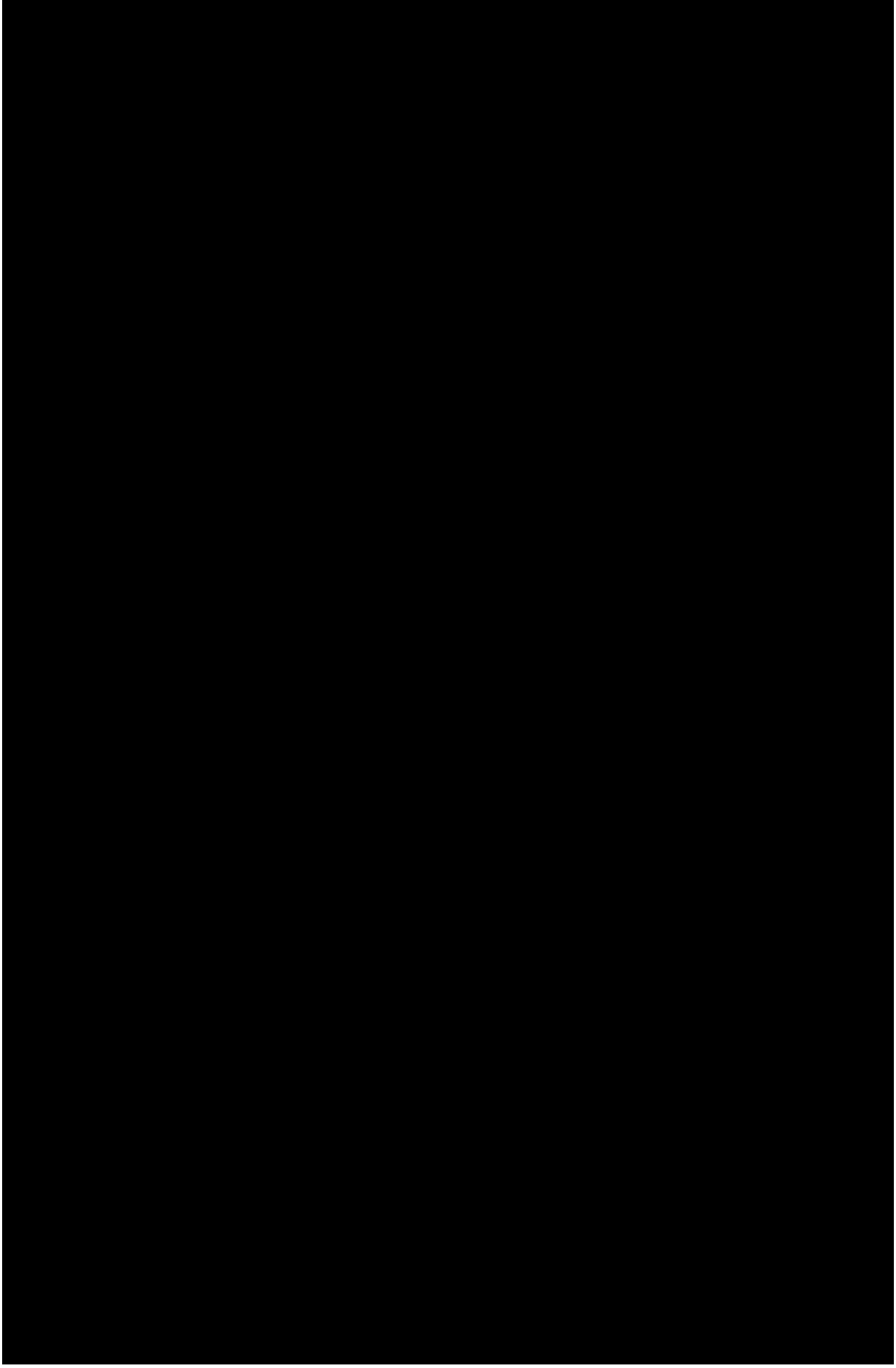
As an Investigator, I agree to:

- Implement and conduct this study diligently and in strict compliance with this agreement; the protocol; Good Clinical Practices; 21CFR812, ISO 14155 and all other applicable FDA regulations; conditions of approval imposed by the reviewing Institutional Review Board (IRB), FDA or other regulatory authorities; and all other applicable laws and regulations.
- Supervise all testing of the device where human subjects are involved.
- Ensure that the requirements for obtaining informed consent are met.
- Obtain authorization for use/disclosure of health information (e.g., HIPAA authorization or equivalent).
- Maintain all information supplied by Johnson & Johnson in confidence and, when this information is submitted to an independent IRB or any other group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Investigator Printed Name	Signature	Date
Subinvestigator Printed Name	Signature	Date





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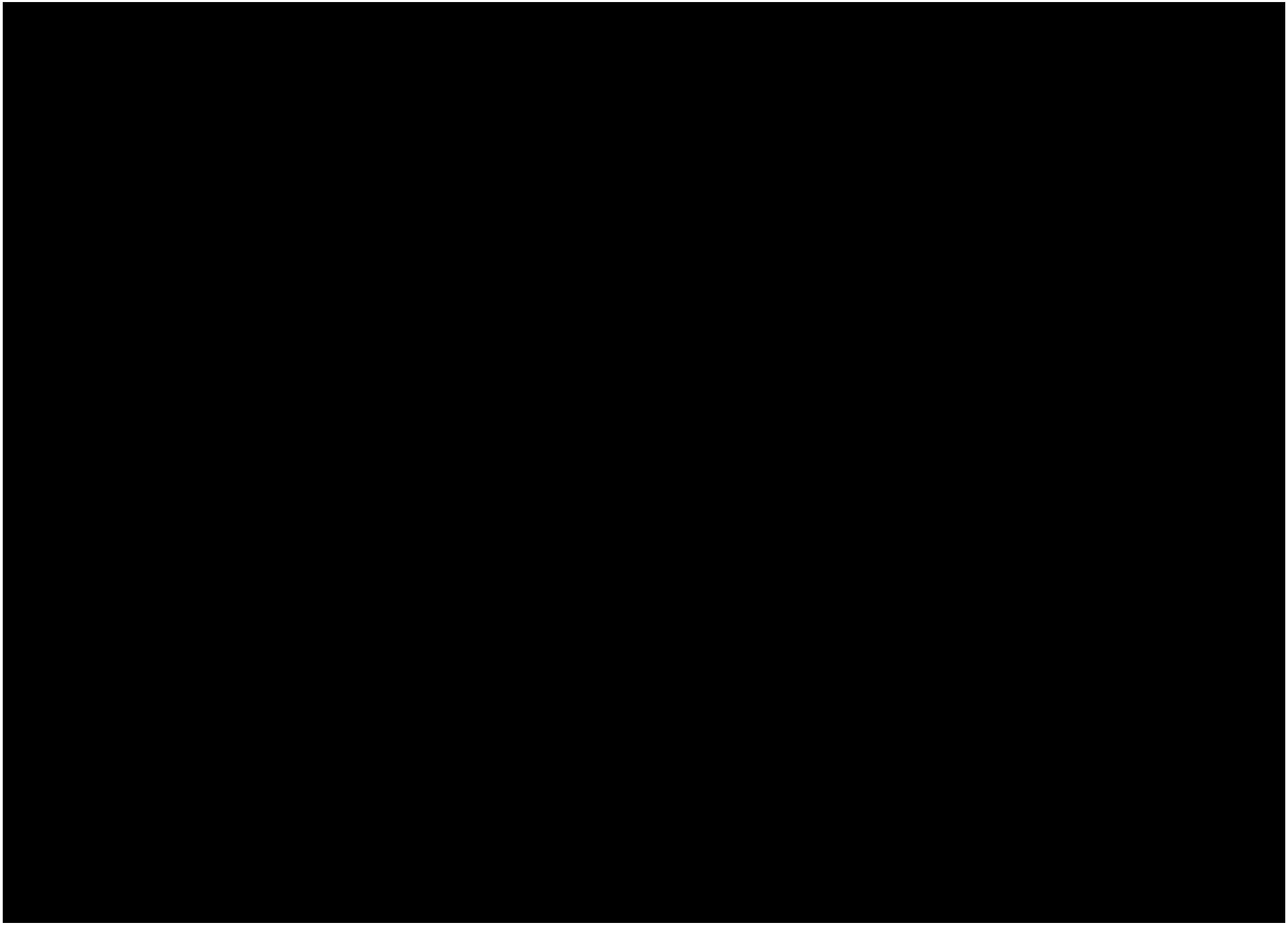


SYNOPSIS

PROTOCOL: A Prospective, Multi-Center Evaluation of Corneal Flap Creation Using Cheetah Femtosecond Laser System and Cheetah Patient Interface.

Protocol Number: CHTA-103-FLAP

STUDY TREATMENTS: Investigational Product:

1) Cheetah system

2) Cheetah Patient Interface (one or two piece)

Control Product:

1) IntraLase FS

2) Cheetah system with [redacted] PI

STUDY OBJECTIVE: This is a [redacted] prospective clinical trial to clinically optimize the Cheetah femtosecond laser settings for flap creation [redacted] and evaluate the flap quality of the Cheetah system [redacted]

[redacted]

OVERALL STUDY DESIGN:

Structure: Prospective, randomized (ratio of 1:1 for right eye and left eye, [redacted] multicenter, interventional study.

Number of sites: Up to 5 sites

[redacted]

[redacted]

[redacted]

STUDY POPULATION CHARACTERISTICS:

[redacted]

Number of Subjects: Up to 30 treated subjects in phase I.
In Phase II, a minimum of 40 eyes treated with optimized Cheetah settings are needed. Up to 300 subjects may be treated in both eyes (one study eye, and one control) to achieve the minimum 40 eyes with optimized settings and additional eye data for further device experience.

[redacted]

[redacted]

Inclusion Criteria [redacted] (all criteria apply to both eyes):

- Age ≥18 years old.
- Subjects with myopia or hyperopia with or without astigmatism (including mixed astigmatism) eligible for commercial LASIK treatment.
- A residual anticipated stromal bed thickness of at least 250 microns based on preoperative central corneal pachymetry minus the maximum treatment depth to be ablated plus the intended flap thickness.
- Distance Best Spectacle Corrected Visual Acuity (BSCVA) of 20/20 or better
- Distance Uncorrected Visual Acuity (UCVA) of 20/32 or worse
- Signed informed consent and HIPAA authorization or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment.
- Willing and capable of complying with follow-up examinations for the duration of the study

Exclusion Criteria [redacted] (all criteria apply to both eyes):

- Concurrent use of systemic (including inhaled) medications that may impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.
    - **NOTE: The use of inhaled or systemic corticosteroids, whether chronic or acute, is deemed to adversely affect healing and subjects using such medications are specifically excluded from eligibility.**
- History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease,

immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

  - **NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity, or control, will specifically exclude subjects from eligibility.**

- Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.
- History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic blepharitis/conjunctivitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.
  - **NOTE: Subjects with open angle glaucoma, regardless of medication regimen or control, or an IOP greater than 21 mmHg at screening, are specifically excluded from eligibility**.
- Evidence of keratoconus, corneal dystrophy or irregularity, corneal edema, corneal lesion, hypotony, or abnormal topography.
- Known sensitivity or inappropriate responsiveness to any of the medications used in the postoperative course.
- A fellow eye that does not meet all inclusion criteria and does not fall within approved indications for treatment using excimer Laser.
- Desire for monovision correction
- Women who are pregnant, breast-feeding, or intend to become pregnant during the study.
- Participation in any other clinical study, with the exception of a fellow eye treated in this protocol.

[redacted]

DATA ANALYSIS:

[redacted]

[redacted] the key evaluation [redacted] stromal bed surface quality, [redacted] using the investigational vs control product. The analysis population will include both eyes of all treated [redacted] subjects and will be used for all end points. An interim database lock may be performed after approximately 40 subjects have been treated with optimized settings and reached the 1-month postoperative follow-up.

[redacted]

1. BACKGROUND/INTRODUCTION

JJSV's current femtosecond laser platform is the IntraLase iFS. It creates flaps through precise individual microphotodisruptions of corneal tissue created by tightly focused ultrashort pulses which are delivered through a disposable applanation lens while fixating the eye under vacuum.

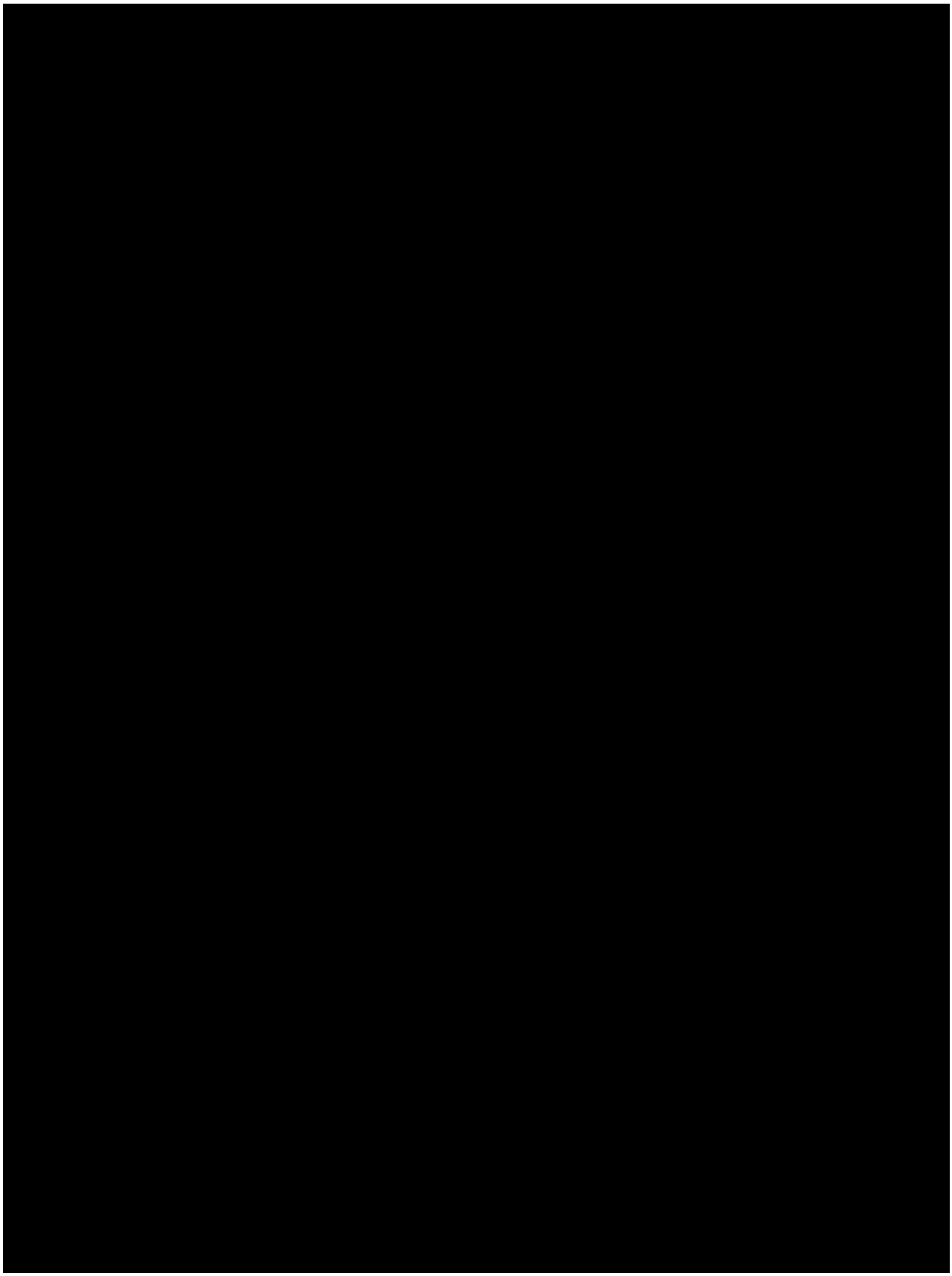
The Cheetah system is a new femtosecond laser developed by JJSV for the same clinical purpose as the IntraLase iFS system. Similar to the IntraLase iFS, it is used in conjunction with a sterile disposable patient interface (PI), that serves as a physical connection between a patient's eye and the system to facilitate accurate laser incisions to the patient's cornea.

[redacted]

The design objective was to develop a flap maker that will be equivalent or better compared to the commercial products. In this study the flap quality and workflow of the study eye will be compared to the control product.

2. CLINICAL HYPOTHESIS

The hypothesis is that the flap quality of the study eye will be equivalent or better than the control eye.



4. ACRONYMS

The following acronyms are used throughout the document:

- D: Diopters
- BSCVA: Best Spectacle Corrected Visual Acuity
- UCVA: Uncorrected Visual Acuity
- MRSE: Manifest Refractive Spherical Equivalent
- OBL: Opaque Bubble Layer
- PI: Patient Interface
- OCT: Optical Coherence Tomography
- QID: 4 times a day (in Latin – quarter in die)

5. STUDY OBJECTIVES AND ENDPOINTS

The purpose of this prospective clinical trial is to [redacted] evaluate the flap quality of the Cheetah femtosecond laser [redacted]

[redacted]

5.1 PRIMARY STUDY ENDPOINTS

[redacted] stromal bed surface quality, [redacted] of the study eye will be graded on a scale of 1-5 relative to the control eye. A score of 3 means that the study eye is similar to the control eye; a score of 4 or 5 means that the study eye is superior to the control eye; and a score of 1 or 2 means that the control eye is superior to the study eye. 90% of all subjects are expected to have a score equal to or greater than 3 [redacted].

5.2 OTHER ENDPOINTS

[redacted]

- Optical Coherence Tomography (OCT) measurements – Anterior OCT scans will be taken pre- and post-surgery and measurements of the cornea and flap thickness will be recorded.
- BSCVA – Percent of eyes with a loss of >2 lines of best spectacle corrected visual acuity relative to preoperative acuity will be compared between the 2 eyes.
- UCVA – Percent of eyes with uncorrected visual acuity of 20/40, 20/32, 20/25, 20/20, and 20/16 or better will be compared between the 2 eyes.

[redacted]

6. STUDY PRODUCTS

6.1 CHEETAH SYSTEM

The Cheetah system (Models Beta 2a,Figure 1; or Production Equivalent (ELITA), Figure 2 is an ophthalmic laser surgical system that is developed for use in the creation of a corneal flap in patients undergoing LASIK surgery or other treatment requiring initial resection of the cornea. Either model can be used in this study.

Figure 1. Cheetah Beta2a Femtosecond Laser system

Figure 2. Production Equivalent (ELITA) Femtosecond Laser System

The Cheetah System is an investigational device. It is approved in the EU and UK, but is not yet approved in the U.S.A. The Principal Investigator is responsible for ensuring that the Cheetah system is only used to treat subjects enrolled in this study.

6.2 CHEETAH PATIENT INTERFACE

The Patient Interface (PI) is an accessory to the Cheetah System. The PI serves as a physical connection between a patient's eye and the system to facilitate accurate laser incisions to the patient's cornea.

[redacted]

[redacted] The two piece patient Interface consists of the PI cone that contains the applanation lens and attaches to the system and the PI suction ring which has vacuum line to the system [redacted] The PI cone has a protective cap to assist in connecting it to the system while keeping the applanation lens free from fingerprints and contaminants. During docking, the PI cone is attached to the PI mount of the Cheetah system and the PI suction ring is attached to the patient's eye. The PI cone is lowered toward the patient's eye and mechanically attaches to the PI suction ring. [redacted]

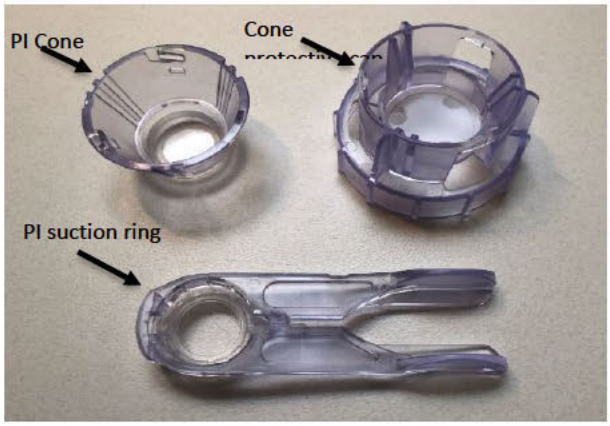


Figure 3. Cheetah Patient Interface components

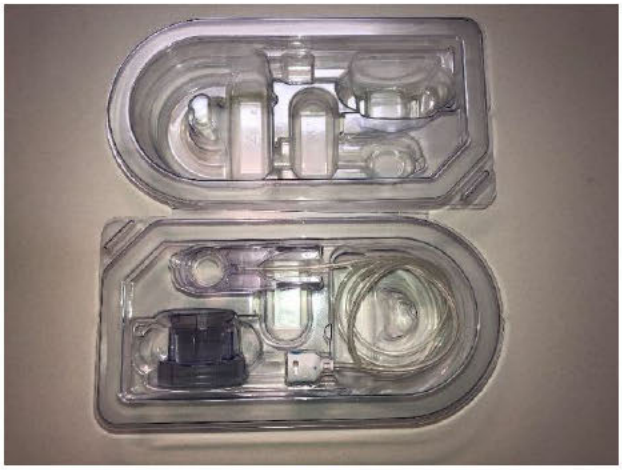


Figure 4. Cheetah Patient Interface in packaging tray with vacuum line system. The PI cone is packed inside its protective cap

[redacted]

The two piece Cheetah patient interface is approved in the EU, UK, and U.S.A. The Principal Investigator is responsible for ensuring that the Patient Interface is only used to dock subjects enrolled in this study.

7. STUDY POPULATION

This study will include only subjects who meet all the study inclusion and none of the exclusion criteria All subjects who qualify will be

offered enrollment in the study. Any questions regarding patient eligibility are to be discussed with JJSV prior to subject enrollment.

7.1 INCLUSION CRITERIA

[redacted]

Inclusion Criteria [redacted] (all criteria apply to both eyes):

1) Age ≥18 years old.
2) Subjects with myopia or hyperopia with or without astigmatism (including mixed astigmatism) eligible for commercial LASIK treatment.
3) A residual anticipated stromal bed thickness of at least 250 microns based on preoperative central corneal pachymetry minus the maximum treatment depth to be ablated plus the intended flap thickness.
4) Distance Best Spectacle Corrected Visual Acuity (BSCVA) of 20/20 or better
5) Distance Uncorrected Visual Acuity (UCVA) of 20/32 or worse
6) Signed informed consent and HIPAA authorization or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment.
7) Willing and capable of complying with follow-up examinations for the duration of the study

7.2 EXCLUSION CRITERIA

[redacted]

Exclusion Criteria [redacted] (all criteria apply to both eyes):

1) Concurrent use of systemic (including inhaled) medications that may impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

   NOTE: The use of inhaled or systemic corticosteroids, whether chronic or acute, is deemed to adversely affect healing and subjects using such medications are specifically excluded from eligibility.

2) History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

   NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity, or control, will specifically exclude subjects from eligibility.

3) Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.
4) History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic blepharitis/conjunctivitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.

   NOTE: Subjects with open angle glaucoma, regardless of medication regimen or control, or an IOP greater than 21 mmHg at screening, are specifically excluded from eligibility.
5) Evidence of keratoconus, corneal dystrophy or irregularity, corneal edema, corneal lesion, hypotony, or abnormal topography.
6) Known sensitivity or inappropriate responsiveness to any of the medications used in the postoperative course.
7) A fellow eye that does not meet all inclusion criteria and does not fall within approved indications for treatment using excimer Laser.
8) Desire for monovision correction
9) Women who are pregnant, breast-feeding, or intend to become pregnant during the study.
10) Participation in any other clinical study, with the exception of a fellow eye treated in this protocol.

8. INVESTIGATOR SELECTION

8.1 INVESTIGATOR QUALIFICATIONS

JJSV will select ophthalmic surgeons who have completed a residency in ophthalmology (or its documented equivalent), are licensed to practice medicine and perform LASIK at his or her investigative site.

Investigators will be selected from surgeons who are experienced in using the IntraLase® keratome. All sites are required to have adequate staff support for reporting and subject follow-up, as well as the necessary instrumentation to conduct study testing. Each site will have one designated principal investigator; some sites may have additional surgical sub-investigators.

8.2 INVESTIGATOR OBLIGATIONS

Investigators are required to fulfill the following obligations:

- Conduct the study in accordance with the relevant and current protocol. Investigator will only make changes to a protocol after notifying and obtaining approval from JJSV and the Investigational Review Board (IRB) or Independent Ethics Committee (IEC), except when necessary to protect the safety, rights or welfare of subjects
- Personally conduct and supervise the study
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
- Be responsible for protecting the rights, safety and welfare of subjects under the investigator's care and be responsible for the control and documentation of the devices under investigation
- Inform patients that the device(s) are being used for investigational purposes and that requirements relating to obtaining informed consent and IRB/IEC approval are met according to 21CFR50, 21CFR56, 21CFR812 and all other applicable laws and regulations
- Maintain confidentiality as required by HIPAA or similar laws and regulations
- Shall not obtain written informed consent from any subject to participate or allow any subject to participate before obtaining IRB/IEC approval and approval from the regulatory agency of the country in which the study is being conducted by the investigator
- Document in each subject's case history that informed consent was obtained prior to participation in the study as required by 21CFR812
- Report to JJSV and the reviewing IRB/IEC any adverse experiences that occur during the course of the study in accordance with applicable laws and regulations
- Maintain adequate and accurate records in accordance with applicable laws and regulations and make available all study documents and subject medical records for inspection by either JJSV, duly authorized regulatory agencies (e.g., FDA) and/or the IRB/IEC
- Submit progress reports on the investigation to JJSV and the reviewing IRB/IEC at regular intervals, but no less often than yearly as required by 21CFR812.150
- Report all changes in research activity and all unanticipated problems involving risks to patients to the IRB/IEC and JJSV
- Supervise and permit investigational device use and disposition in accordance with applicable regulations and protocol requirements. Upon completion of enrollment or termination of the study or the investigator's part of the study, or at JJSV's request, return to JJSV any remaining supply of the investigational device
- Provide sufficient accurate financial information to JJSV to allow JJSV to submit complete and accurate certification or disclosure statements as required by 21CFR54. Promptly update this information if any relevant changes occur during the course of the investigation or for up to one year following completion of the study
- Comply with all other obligations of clinical investigators and requirements according to all applicable FDA regulations (e.g., 21CFR812), all other applicable laws and regulations, and all conditions of approval imposed by the reviewing IRB/IEC, and the regulatory agency of the country in which the study is being conducted

- Ensure that all associates, colleagues and employees assisting in the conduct of the study are adequately informed about the protocol, the investigational device, their study-related duties and functions and agree to fulfill their obligations in meeting the above commitments.

Investigators shall provide adequate time and resources to conduct and report on the study. The Investigator, or delegate, shall notify JJSV of any change in the conduct of the study including changes in study personnel assigned to the study project, location of the investigational device(s), or maintenance of study records, etc.

8.3 INVESTIGATOR APPROVAL

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB/IEC as appropriate. All correspondence with the IRB/IEC should be retained in the Investigator Study Files/Notebook. Copies of IRB/IEC submissions and approvals should be forwarded to JJSV. Study sites will obtain IRB/IEC approvals and fulfill any other site-specific and/or region-specific regulatory requirements. The investigator is required to report to JJSV within five working days any withdrawal of approval by the reviewing IRB/IEC for his/her participation in the investigation.

Prior to the start of subject enrollment, the following documents must be signed and returned to JJSV:

- Confidentiality Agreement
- Clinical Trial Agreement
- Investigator Agreement/Protocol Signature page
- Clinical Investigator Brochure Signature page
- Financial Disclosure form
- Signed and dated copy of investigator's current curriculum vitae
- Copy of the investigator's current medical license (as available per country)
- Hospital/Ambulatory Surgery Center Clinical Study Acknowledgement, if required

By signing the study documents, the investigator agrees to conduct this study according to the obligations above and all other applicable regulatory and legal requirements.

9. EXPERIMENTAL PLAN

9.1 OVERVIEW

This study will be conducted in accordance with U.S. Code of Federal Regulations, the Declaration of Helsinki, ISO 14155 and all other applicable laws and regulations. The study will not begin until regulatory and IRB/IEC approvals have been obtained.

[redacted]

After signing the informed consent, subjects meeting all inclusion and none of the exclusion criteria [redacted] may be scheduled for surgery.

[redacted]

Although the study is not masked, to maintain consistency, it is recommended that a single individual (study technician or coordinator designated by the investigator) conduct all study-related vision testing, although a back-up person should also be designated and trained.

[redacted]

[redacted]

9.3 PREOPERATIVE PROCEDURES

All subjects enrolled in the study must sign the current IRB/IEC-approved informed consent document and meet the inclusion/exclusion criteria [redacted] The informed consent must be signed before any study-specific examinations are performed, and this must be documented in the source documents. Any additional required documents, based on country/state specific requirements, such as an Authorization for Use/Disclosure of Health Information Form (HIPAA authorization) or similar medical treatment privacy law documentation must also be signed.

All preoperative testing for the study must be completed within 120 days prior to surgery. The informed consent must be signed prior to any study-specific examinations being performed. Following the informed consent process, completion of the preoperative study exam and determination that the subject's eye/s meet all of the required entrance criteria, the eye/s may be treated in the study.

As the Informed Consent Form is signed at the beginning of the preoperative study exam, some subjects may not qualify after study-specific testing is performed. Subjects will be considered screen-failures if they do not qualify or if they qualify but decide not to proceed with surgery. These subjects will be exited from the study.

[redacted]

9.4 RANDOMIZATION

A randomization list will be created by an internal independent JJSV biostatistician for each investigative site. Subjects' eyes [redacted] will be randomized on a 1:1 basis between the study eye eye and the control eye. Randomization will take place after the subject has signed the informed consent document and has met all inclusion and exclusion criteria.

As part of the informed consent process, the investigator or delegate will explain to the subject the requirements of a randomized study and the differences expected between the study eye and the control eye.

9.5 STUDY PATIENT INTERFACE (PI) SUPPLY

For each subject, one investigational Cheetah PI [redacted] and one commercial IntraLase iFS PI (when needed) shall be available. Investigational Cheetah PIs will be obtained from the site investigational PI consignment, supplied by JJSV prior to study initiation and as needed during the study. Commercial IntraLase iFS PIs will be obtained from the site's own inventory. Two PIs [redacted] should be available for each case: a primary and a back-up PI. Unused back-up investigational PIs are to be returned to the site consignment. At the completion of study enrollment, any remaining

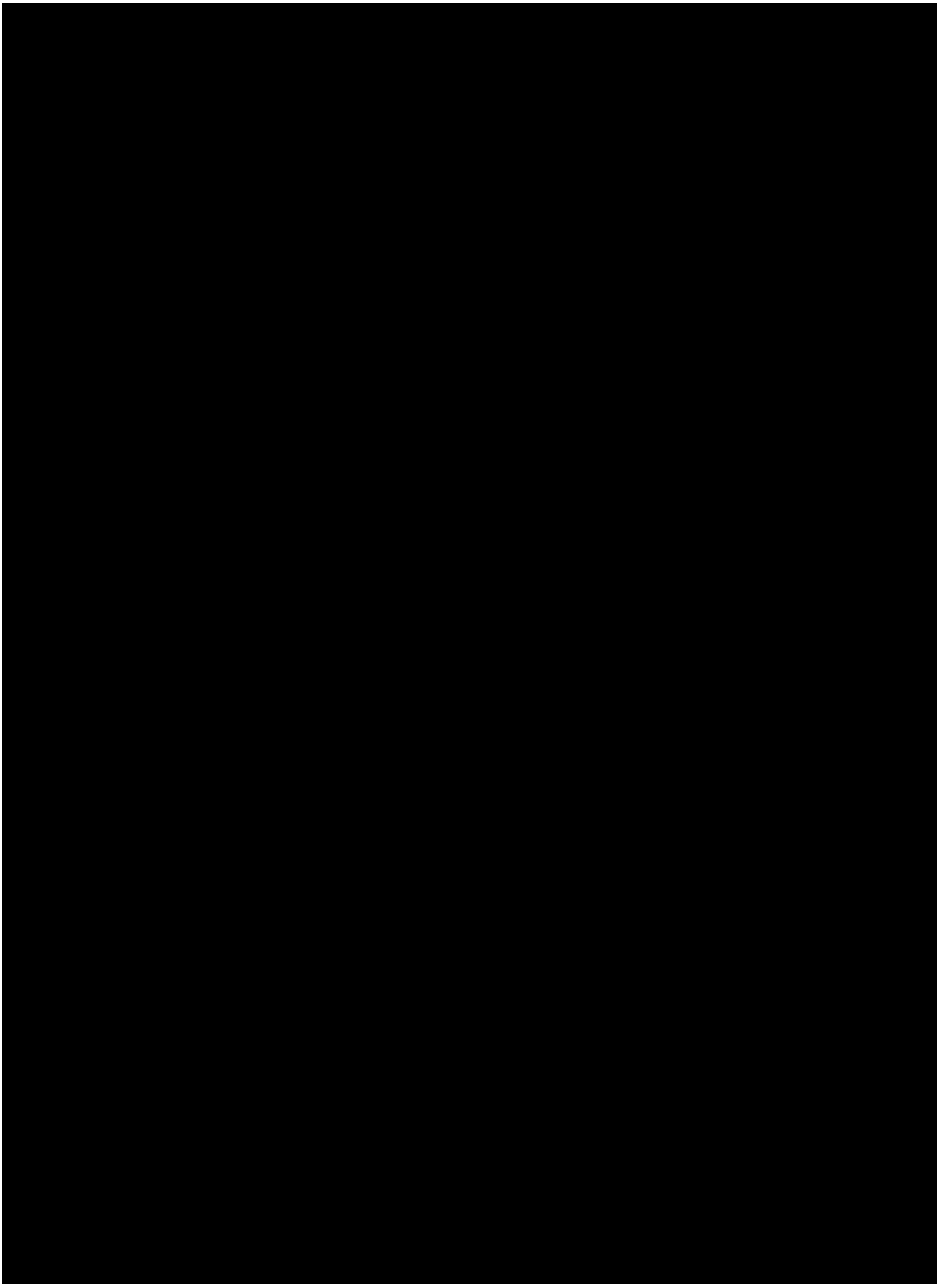
investigational PIs will be shipped back to JJSV. At all times, the storage, access and use of all investigational PIs must be controlled and complete PI accountability maintained (See Section 15.2 PI Accountability).

[redacted]

[redacted]

- Evaluation of flap quality - [redacted] bed surface, [redacted] through investigator questionnaire
- [redacted]
- [redacted]
- Adverse event/complications
- [redacted]
- [redacted]

[redacted]



9.8 RETREATMENT PROCEDURES

NON-REFRACTIVE RETREATMENTS

Non-refractive retreatments or procedures without further laser treatment (e.g., flap lifts, adjustments, realignments, replacement, treatment of complications, removal of epithelial ingrowth, etc.) may be performed at any time with the advance notification of the Sponsor. All flap adjustment procedures will be noted and reported to the Sponsor.

REFRACTIVE RETREATMENTS

Refractive retreatments may be performed after completion of the [redacted] postoperative exam and after the subject has exited from the study.

9.9 EXIT OF SUBJECTS

An Exit Case Report Form will be completed for all subjects, either when they complete the study or if they exit early.

It is the responsibility of the investigator to provide complete follow-up data to JJSV for each subject, and every attempt should be made to gather that complete follow-up data for all subjects enrolled as missing data can have a negative effect on the study results. Patients who would be traveling, relocating or otherwise unavailable for postoperative follow-up visits should not be chosen for this clinical study.

Subjects will be considered “lost-to-follow-up” from the study only if irretrievably lost for unavoidable reasons such as: subject moved/unable to locate, subject uncooperative/refuses further study participation, subject ill/unable to travel. In the event of subject relocation, efforts must be made by the investigator to secure follow-up information (i.e., slit-lamp findings and general visual acuity, etc.) from the subject’s new physician.

A subject [redacted] will be considered a non-randomized screen failure if he/she does not meet the inclusion/exclusion criteria or if consent is withdrawn prior to randomization.

A subject will be considered a randomized screen failure if the subject is randomized but does not undergo surgery for various reasons including: the subject withdrawing consent prior to treatment or the subject died prior to treatment.

[redacted]

If a subject is exited early from the study, the investigator will complete an Exit Case Report Form indicating the reason for study exit. In the event of a serious adverse event, the subject may be exited from the study; however, efforts must be made by the investigator to follow the subject until resolution of the adverse event.

All study subjects are to be instructed to undergo regular eye examinations at least yearly and also to return to their doctor if any eye complications are experienced in the interim.

9.10 UNSCHEDULED VISITS

During the study period, if a non-protocol-required visit is done for the purpose of medically-indicated follow-up for a study eye, data from this visit should be reported using the Unscheduled Visit CRF. The need for unscheduled visits is at the investigator's discretion. Specific examinations to be performed at unscheduled visits are also at the discretion of the investigator (based on the reason for the unscheduled visit) and data are to be recorded in the appropriate section of the case report form.

Data to be collected may include:

- manifest refraction
- Uncorrected and best corrected distance visual acuity using a LogMAR chart
- Intraocular pressure
- Slit-lamp examination for medical and/or lens findings
- Dilated fundus exam
- Ocular symptoms
- Adverse events
- Medications

9.11 PROTOCOL DEVIATIONS

Any departure from the protocol procedures represents a protocol deviation. Protocol deviations may be subject-based (e.g., inclusion/exclusion criteria, informed consent deviation, etc.) or procedural-based (e.g., out-of-interval visits, non-compliance with testing procedures, etc.). All protocol deviations will be documented using protocol

deviation case report forms. Any deviation made to protect the life or physical well-being of a subject in an emergency as well as any use of the investigational device without obtaining informed consent must be reported to JJSV and local ethics committee within 5 working days. Protocol deviations will be monitored by JJSV, and if the non-compliance is persistent or egregious, JJSV may take action, including but not limited to termination of the investigator's participation in the study. The investigator is also responsible for informing the reviewing IRB/IEC of instances of protocol non-compliance in accordance with the IRB/IEC requirements.

10. ADVERSE EVENTS AND PRODUCT COMPLAINTS

10.1 ADVERSE EVENT DEFINITIONS

Adverse Event (AE)

An adverse event is defined (following ISO 14155) as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the study device.

Serious Adverse Event (SAE)

An adverse event is considered serious (following ISO 14155) if it is an untoward occurrence which may or may not be related to use of the study device that

- is sight- or life-threatening,
- results in death,
- requires inpatient hospitalization or prolongation of hospitalization (a planned hospitalization for a pre-existing condition without a serious deterioration in health is not considered a serious adverse event),
- results in permanent impairment of a body structure or body function,
- necessitates medical or surgical intervention to prevent permanent impairment to a body structure or function, or
- results in fetal distress, fetal death or a congenital abnormality or birth defect

Device-Related Adverse Event/Adverse Device Effect (ADE)

A device-related adverse event is defined as any adverse even that is believed to be definitely, probably or possibly related to the study device (following the guidelines in Section 11.4, Causal Relationship). A device-related event is also considered an adverse device effect (ADE; following ISO 14155) resulting from the use of the study device that may result from user error, insufficiencies or inadequacies in the instructions for use, deployment, implantation, installation, operation of any malfunction of the device.

Study-Specific Anticipated Adverse Events

The following is a list including, but not limited to, ocular adverse events that are anticipated and must be reported to JJSV for this study. Any events that are unlikely but anticipated (i.e., endophthalmitis) will be reported to the FDA and other appropriate regulatory agencies.

- Diffuse lamellar keratitis (DLK) (Grade 3 or above)
- Pressure Induced Stromal Keratitis (PISK)
- Corneal infiltrate or ulcer
- Corneal epithelial defects upon flap creation
- Any persistent corneal epithelial defect at 1 month or later
- Corneal edema at 1 month or later
- Epithelium in the interface with loss of 2 or more lines of BSCVA (≥10 ETDRS letters)
- Miscreated flap (decentered, lost, incomplete, too thin or other)
- Melting of the flap
- IOP with increase > 10 mmHg above baseline on two consecutive examinations or an IOP greater than 30 mmHg on two consecutive examinations
- Haze at 3 months or later with loss of 2 or more lines of BSCVA (≥10 ETDRS letters)
- Interface haze
- Decrease in BSCVA of 2 or more lines (≥10 ETRDS letters) not due to irregular astigmatism as shown by hard contact lens refraction (or pin hole acuity if hard contact lens refraction is not medically advisable) at 3 months or later
- Retinal detachment
- Retinal vascular accidents
- Any other vision-threatening event
- Ocular penetration
- Rainbow glare
- Severe glare, severe dry eye, or severe halos at 3 months or later

[redacted]

Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE)

Any UADE (USA 21CFR 812.3(s)) or USADE (ISO 14155) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan (i.e., this protocol), application (including a supplementary plan or application), or risk assessment, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

10.2 PRODUCT COMPLAINT/DEVICE DEFICIENCY DEFINITION

A product complaint/device deficiency is defined (21 CFR 820.3(b) and ISO 14155) as any alleged deficiency related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device. This may include malfunctions, use error and inadequacies in labeling. Product complaints can pertain to any marketed JJSV device being used in the study as well as the investigational device. The investigator is to assess whether the deficiency could have led to a serious adverse event without suitable action or intervention or under less fortunate circumstances.

10.3 ADVERSE EVENT AND COMPLAINT REPORTING REQUIREMENTS

All adverse events and any complaint encountered using any JJSV product, regardless of severity and whether or not attributed to the study device(s), are to be reported to JJSV and recorded on the case report form corresponding to the visit during which awareness of the event occurred. Adverse events are also to be reported to the reviewing IRB/IEC as per the IRB/IEC's reporting requirements. If required, adverse events will be reported to the appropriate regulatory agencies (e.g., FDA) according to all applicable laws and regulations. Specific instructions on notification procedures to JJSV are included in **Appendix K**, Adverse Event Reporting.

Reporting of adverse events shall follow the USA Code of Federal Regulations (21CFR812) for sites in the USA. For sites located outside the USA, reporting of adverse events shall follow ISO 14155 and country-specific guidelines, of which the

shortest/strictest timeline requirement for reporting adverse events will be followed. General guidelines are provided below:

Adverse Event Reporting

An adverse event that is not serious or device-related is to be reported to JJSV in a timely manner. Notification of non-serious and non-device related adverse events will occur by recording events on the CRF when noted. Such adverse events are also to be reported to the reviewing IRB/IEC per their reporting requirements.

Complaints/Device Deficiency Reporting

A general product complaint or device deficiency is to be reported to JJSV in a timely manner. Notification of complaints/device deficiencies will occur by either recording complaints on the CRF when the complaint occurred (e.g. operative form) or by a phone call to the Sponsor. Any device deficiency that could have led to a serious adverse event without suitable action or intervention, or under less fortunate circumstances, must be reported to the sponsor immediately (no later than 48 hours after detection). Device deficiencies that could have led to a serious adverse event should also be reported to the investigator's IRB/IEC per their reporting requirements.

Serious and/or Device-Related Adverse Event Reporting

Serious and/or device related events (ADEs) are to be documented using the Detailed Adverse Event CRF. In the event of a serious adverse event (SAE), which may or may not be related to use of the study device, JJSV must be notified immediately (no later than 48 hours after detection). Any SAE is to be reported by phone (and/or email) and by submitting the completed Detailed Adverse Event CRF. Any SAE or device-related AE should also be reported to the investigator's IRB/IEC per their reporting requirements.

Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE) Reporting

If during the study, a serious adverse event occurs that may reasonably be regarded as device-related and was not previously expected in nature, severity, or degree of incidence, the investigator is to report the UADE/USADE to JJSV within 48 hours, and to the investigator's IRB/IEC as soon as possible (no later than 10 working days after learning of the event for sites in the USA as required by 21CFR812, and per country requirements, otherwise).

10.4 CAUSAL RELATIONSHIP

The investigator should always be alert to adverse events that may be related to the study device or the use of the study device (i.e., the procedure specific to the initial application of the device). An attempt should be made in every case to determine the

causality of the event. The following definitions are to be used as guidelines in determining the relationship between the event and the study device and/or use of the device.

Definitely related:	If the event is associated with the device and/or the use of the device beyond a reasonable doubt, a causal relationship exists between the adverse event and the device and/or the use of the study device.
Probably related:	There is a reasonable possibility of a causal relationship between the adverse event and the device and/or the use of the study device and/or the adverse event cannot be reasonably explained by another cause.
Possibly related:	The adverse event has not been determined to be related to the device or the use of the device, but no other cause has been identified and the device and/or the use of the study device cannot be ruled out as a possible cause.
Unlikely to be related:	The possibility of a potential causal relationship between adverse event and the device and/or the use of the device could exist, but the adverse event can be reasonably explained by another cause.
Not related:	There is no possibility of a causal relationship between the adverse event and the device and/or the use of the study device and/or the adverse event can be attributed to another cause.

If an adverse event is believed to be definitely, probably or possibly related to the study device and/or the use of the device, the event will be considered related to the study device and/or the use of the device.

10.5 ADVERSE EVENT FOLLOW-UP

For every adverse event, appropriate measures should be undertaken to treat and/or monitor the subject until resolution or stabilization occurs. Obtain and maintain in the subject's files all pertinent medical data relating to the event including the subject's medical records and medical reports and/or judgments from colleagues or outside specialists who assisted in the treatment and follow-up of the subject. The investigator should keep JJSV closely informed as to the outcome of serious and/or device-related adverse events, thereby allowing JJSV to comply with the appropriate regulatory reporting requirements. A Detailed Adverse Event Update CRF should be completed each time the subject returns to the investigator or other specialist(s) for follow-up of serious and/or device-related adverse event until resolution of the event. Any subject who is exited from the study due to a serious and/or device-related adverse event will be followed until the outcome is determined.

11. PROTOCOL CHANGES/AMENDMENTS

If the investigator desires to modify any procedure and/or the design of the study, he or she must contact and obtain consent from JJSV regarding the proposed changes prior to implementation. Any modifications (including additional data collection) require approval by the FDA and/or all other appropriate regulatory agencies, as well as approval of the governing IRB/IECs prior to implementation.

12. ETHICS REVIEW AND PATIENT WELFARE

12.1 INSTITUTIONAL REVIEW BOARD (IRB)/ INDEPENDENT ETHICS COMMITTEE (IEC)

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator Notebook. Copies of IRB/IEC submissions and approvals should be forwarded to JJSV.

The investigator is responsible for notifying the IRB/IEC of reportable adverse events as well as any other circumstance in which additional procedures outside the protocol were conducted to eliminate apparent hazards to subjects.

12.2 INFORMED CONSENT

The current version of the IRB/IEC-approved study informed consent must be signed by each study subject prior to any study-specific examinations being performed. The IRB/IEC-approved informed consent is to be signed and dated by the subject as well as by the person who conducted the informed consent discussion. The signed informed consent will be maintained by the investigator as a permanent part of the subject's medical records. A copy of the signed and dated form is to be provided to the subject. The investigator will provide JJSV written acknowledgement on the preoperative case report form that a signed agreement of informed consent has been obtained and is in the investigator's possession for each subject. As required by 21CFR812 Part G, the site shall document in the source documents that informed consent was obtained prior to participation in the study for each subject enrolled.

NOTE: The informed consent process also includes obtaining the subject's signature on an Authorization for Use/Disclosure of Health Information for Research Form or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries.

NOTE: The sponsor will secure appropriate insurance for study subjects prior to study start.

13. DOCUMENTATION

13.1 SOURCE DOCUMENTS

Source documents must be kept for all study subjects. Source documents may include a subject's medical records, hospital charts, clinic charts, the investigator's subject study files, as well as results of any diagnostic tests or procedures such as topographies or laboratory tests with photographs or instrument printouts.

Each site is expected to adhere to the clinic's own standard documentation requirements for medical charts/clinic notes. However, for the purposes of this clinical study, the medical charts/clinic notes must also include, at a minimum, the following data that will be considered source data and will be reviewed by JJSV:

- Subject's name and study identification number
- Subject's contact information
- Study protocol number and the Sponsor name (JJSV)
- A statement that informed consent was obtained prior to participation in the study (including the date)
- Dates of all subject visits and surgeries throughout the duration of the study
- Concurrent medications
- Corrected and uncorrected distance visual acuity (NOTE: ETDRS visual acuity score cards are considered source documentation and are to be retained by the site in the subject CRF notebooks)
- Manifest refraction
- Occurrence and status of any operative complications, postoperative medical findings and adverse events
- Occurrence and status of any subject complaints, e.g., ocular/visual symptoms
- The date the subject exited the study, and a notation as to whether the subject completed the study or reason for early exit.

13.2 SUBJECT CONFIDENTIALITY

Subjects will be assigned a site/subject number to maintain subject confidentiality. Subject names may possibly be disclosed to the JJSV or regulatory agencies during inspection of medical records related to the study, but reasonable precautions will be taken to maintain confidentiality of personal information to the extent permitted by applicable laws and regulations.

13.3 CASE REPORT FORM COMPLETION

This study will use an electronic data capture (EDC) management system. The investigator is responsible for ensuring that data are properly recorded on each subject's case report forms and related documents. Prior to database lock, the investigator will verify completeness and accuracy of data submitted to JJSV.

[redacted]

14. MONITORING

JJSV will perform three types of monitoring to ensure compliance with regulations: data monitoring, administrative monitoring, and safety monitoring.

14.1 DATA MONITORING

In order to ensure a well-controlled clinical trial, JJSV will follow specific data monitoring procedures.

To minimize data omissions and inconsistencies on clinical reports and to ensure that data are accurately transcribed to computer data files, JJSV will follow internal data processing procedures that include automated and manual quality control checks to identify any data discrepancies. Any such items will be resolved and documented as needed on the case report forms at the investigative site and in the data management system at JJSV.

Prevention of Missing Data

Methods used to safeguard against missing data that can have deleterious effects on the study integrity and reliability of its outcomes will include training study staff with centralized and on-site programs. In addition, subjects will be encouraged at the time of informed consent to avoid missing study visits, as missing data may affect the study reliability and diminish the scientific value of their contribution to the study.

14.2 ADMINISTRATIVE MONITORING

Administrative monitoring procedures will ensure that study devices, subjects, and forms can be traced and will allow monitoring of investigator progress and compliance. Accountability and traceability of study devices will be monitored by JJSV.

Device Accountability

Complete patient interface (PIs) accountability will be maintained at the investigative site by maintaining records of all investigational PIs received from and returned to JJSV. A site log will be used to track PIs for date of receipt, serial number, use and disposition/return to JJSV. This site log and any other investigational PI information will be maintained in the study binder and monitored by JJSV personnel. During periodic investigative site monitoring visits, JJSV personnel will review investigative site PI inventory records and logs to ensure PI accountability compliance and complete investigational PI traceability.

Since the Patient Interface of the IntraLase iFS are commercially available, supply records for the IntraLase iFS PIs will solely be the responsibility of the site and managed by their customary methods.

Site Monitoring Plan

Prior to performing any study LASIK flaps, the requirements of the study and reporting mechanisms will be explained to each investigator either personally at the investigative site or at a formal study investigator meeting. When necessary, a pre-study site qualification visit may be performed to assess the adequacy of the site to perform the study for sites that have not previously worked with JJSV or have undergone significant changes, or have not been visited in the past year. A study initiation visit will be conducted for all sites prior to or at the time of the first LASIK flap treatment.

Throughout the duration of the study, site visits to monitor compliance to this protocol will be made at each investigative site. During a routine site monitoring visit, JJSV will review informed consent documents and subject eligibility, and the data on study case report forms will be verified against subject charts and other source documents to ensure complete and accurate reporting. The subject files will also be reviewed to assure that all adverse events and any issues encountered with JJSV products have been reported in a timely fashion.

JJSV will also review source documents to verify that all required items have been documented in the subject medical charts. Refer to Section 14.1, Source Documents, for a list of items that are required for source documentation. In addition to subject files, study logs will be checked and conformance to lighting levels for visual acuity tests will be verified.

Training on study-specific procedures may also be conducted during monitoring visits.

Upon study completion, a final close-out site visit to each site will be made to monitor the last of the subject data records and finalize any outstanding study issues.

A separate Study Monitoring Plan will be established prior to study start that will define the type and frequency of monitoring visits and frequency of record monitoring.

<u>MONITORING SCHEDULE (EXAMPLE IF NO SEPARTE STUDY MONITORING PLAN)</u>

JJSV will visit each study site for site initiation visit to set up equipment and train all site staff on the study. JJSV will attend the first 1-month examinations at each study site. Interim monitoring visits will be conducted at least once a year or more often as needed according to subject exam compliance, clarity and consistency of data received by JJSV, resolution of data queries within the data management system, etc. JJSV will perform close out visits, and collect the equipment provided to the site to conduct the study.

14.3 SAFETY MONITORING

This study will utilize a Medical Monitor for safety monitoring. The medical monitor will review results throughout the clinical trial as necessary to ensure the continued safety of the device and to ensure that no subjects are exposed to unreasonable risk. The medical monitor will be available to answer all questions from investigators. The medical monitor will review and assess any reports of serious and/or device-related adverse events as well as device deficiencies that could have led to a serious adverse event, and discuss these with the reporting investigator(s) as necessary. The medical monitor, as well as any other qualified personnel designated by JJSV, shall also review any interim progress reports, as applicable.

15. PUBLICATIONS

Refer to the Clinical Trial Agreement for information regarding JJSV publication policies.

16. RISK ANALYSIS

POTENTIAL RISKS AND RISK MANAGEMENT

As part of the risk assessment and analysis, all risks were eliminated or reduced to as low as possible (or ALAP) through identified control measures. After all available control measures have been implemented; any residual risk was addressed via a Risk Benefits Analysis (RBA).

RISKS OF THE CHEETAH FEMTOSECOND LASER AND CHEETAH PI

The Cheetah femtosecond laser and Cheetah patient interface (PIs) are designed for the creation of corneal flaps for LASIK treatments. The potential risks and complications to subjects when using the Cheetah laser system in the study, include similar risks to routine use of femtosecond laser for refractive surgery with a market-approved procedure. The central wavelength [redacted], which is different than the IntraLase wavelength (1053nm), is commonly used in other commercial systems (VisuMax, Victus, WaveLight FS 200, Femto LDV). The Cheetah femtosecond laser and Cheetah patient interfaces are not expected to introduce new risks for flap creation.

GENERAL RISKS OF FLAP CREATION WITH A FEMTOSECOND LASER

General risks of flap creation for LASIK include a number of potential complications which may require medical treatment and/or secondary surgical intervention. These risks can include: corneal abrasion, corneal edema, corneal pain, epithelial ingrowth, epithelial defect, infection, flap de-centration, incomplete flap creation, flap tearing or incomplete lift-off, free cap, photophobia, corneal inflammation such as diffuse lamellar keratitis (DLK), corneal infiltrates and iritis, thin or thick flaps, flap striae, delayed healing, retinal

detachment, increased intraocular pressure, and hemorrhage. Complications can result in poor vision, loss of vision or loss of the eye.

RISK MANAGEMENT

Subjects will be closely monitored thought the trial duration. The occurrence of adverse events and complaints will be assessed at each study visit and reported to JJSV according to Section 11.0, Adverse Events and Product Complaints. Additionally, JJSV will monitor incoming data following the procedures outlined in Section 15.0, Monitoring. The Medical Monitor will ensure subjects are not exposed to additional risks by monitoring serious adverse events, device-related adverse events, and device-deficiencies that could have led to serious adverse events (Section 15.3, Safety Monitoring).

POTENTIAL BENEFITS

The primary benefits of laser refractive surgery with the investigational Cheetah system are the correction of myopic and hyperopic with or without astigmatic refractive errors which may reduce or eliminate the need for glasses or contact lenses for distance vision.

CONCLUSION

The hazards/risks associated with the Cheetah femtosecond laser and PIs, are acceptable and similar to those of IntraLase FS and iFS. The potential clinical benefits of the Cheetah femtosecond laser and Cheetah PIs, outweigh the residual risks when the device is used as intended.

17. RECORDS RETENTION

All study-related correspondence, subject records, consent forms, Authorization for Use/Disclosure of Health Information Forms or similar medical treatment privacy law documentation, records of the distribution and use of all study products, and original case report forms should be maintained by the investigator.

The investigator must maintain and have access to the following essential documents until notified by the Sponsor. Note: This may be for a minimum of 25 years after completion of the study unless country-specific requirements are longer. JJSV requires notification if the investigator wishes to relinquish ownership of the data so that mutually agreed-upon arrangements can be made for transfer of ownership to a suitably qualified, responsible person.

- All case report forms
- All adverse event information (detailed adverse event forms, follow-up letters, etc.)
- Investigational supply records/inventory
- IRB/IEC and regulatory approval documentation

- Study correspondence
- Study agreements
- Site visit documentation
- Protocol(s) and the reason for any deviations from the protocol
- Subject log(s)
- Clinical Investigator's Brochure
- Completed subject informed consent forms and medical privacy forms (e.g., Authorization for Use/Disclosure of Health information or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries)
- Subject medical chart/clinic notes

18. TERMINATION OF THE INVESTIGATION

The clinical investigation will be suspended in the event of high levels of complications and/or adverse events that are unexpected in nature and/or severity and evaluated as to causality relative to the study device. The clinical investigation may be suspended if the Medical Monitor or IRB/IEC, upon review and evaluation of the clinical data, finds unacceptable clinical performance or the level of single or total complications and/or adverse events unacceptable for continuation of the investigation.

If causality is shown not to be related to the study device, the study may be resumed in accordance with the IRB/IEC and regulations of the FDA and governing countries. The study will be terminated if causality is shown to be related to the study device.

Additionally, the investigator, or JJSV, may stop a subject's participation at any time. JJSV may also stop the study at any time for reasons it determines appropriate. However, no suspension of the study would be made to disadvantage the study subjects. Following suspension of the study for any reason, all study subjects who have already received treatment would continue to be followed through completion of the study visit schedule.

19. STATISTICAL METHODS

This section highlights the analyses for the primary study endpoints as well as other study endpoints. [redacted]

19.1 ANALYSIS POPULATION

[redacted]

The analysis population will be both eyes of treated subjects and will be used for all endpoints.

19.2 PRIMARY STUDY ENDPOINTS

surface quality, of the study eye will be evaluated relative to the control eye on a scale of 1 to 5 A score of 3 means that the study eye is similar to the control eye; a score of 4 means that the study eye is superior to the control eye; a score of 5 means that the study eye is much better than the control eye; a score of 1 means that the control eye is much better than the study eye and a score of 2 means the control eye is superior to the study eye.

At least 90% of subjects are expected to have a score equal to or greater than 3 for

19.3 ADDITIONAL ENDPOINTS

Summary statistics (mean, standard deviation, minimum and maximum) will be reported for flap thickness (from OCT) .

[redacted]

[redacted]

[redacted]

[redacted]

The incidence of adverse events will be summarized by AE type.

19.4 [redacted] GENERAL STATISTICS

Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min.), and maximum (Max.) as appropriate for continuous variables. For categorical data, the frequency counts and proportions will be computed.

[redacted]

[redacted]