Alcon®

LADARVISION 4000

Excimer Laser System

PROFESSIONAL USE INFORMATION MANUAL

FOR CustomCornea® LASER ASSISTED IN-SITU KERATOMILEUSIS (LASIK)

PHYSICIAN'S BOOKLET

For hyperopia and hyperopic astigmatism of +0.75D to less than +5.00D sphere with up to -3.00D cylinder (which has a magnitude less than or equal to the sphere in minus cylinder convention) and up to +5.00D cycloplegic spherical equivalent

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed eye care practitioner. U.S. Federal Law restricts the use of this device to practitioners who have been trained in its calibration and operation, and who have experience in the surgical management and treatment of refractive errors.

This document provides information concerning the intended clinical use of the LADARVision®4000 Excimer Laser System. For complete information concerning system components, safety instructions, installation, maintenance, and troubleshooting refer to the LADARVision®4000 Excimer Laser System Operation Manual.

Carefully read all instructions prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient and/or user complications.

Alcon, Inc.
2501 Discovery Drive, Suite 500
Orlando, FL 32826

Tel: (877) 523-2784
Fax: (407) 384-1677
Outside the U.S., contact your local Alcon representative

REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 9638 – original release	05/06
B	DCN 10047 – revise Surgery Planning Software description, pg. 7; remove comparability statement, pg. 11; add "asymmetric" pg. 44; revise pupil dilation drugs, pg. 46	05/06

TABLE OF CONTENTS

This page left blank intentionally.

1. GENERAL SAFETY CONSIDERATIONS

"WARNING:" - Identifies conditions or practices that could result in damage to equipment or other property, personal injury, or loss of life.

WARNING: Specific training from Alcon or an authorized representative of Alcon is required before anyone is qualified to operate the LADARVision®4000 Excimer Laser System. Read and understand this manual and the LADARVision®4000 Excimer Laser System Operation Manual prior to operating the system.

Refer to the LADARVision®4000 Excimer Laser System Operation Manual for additional warnings regarding use of the LADARVision®4000 Excimer Laser System.

2. DEVICE DESCRIPTION

A. WAVEFRONT MEASUREMENT DEVICE (WMD)

The first step in performing CustomCornea® LASIK surgery is to perform a wavefront examination on the patient using a wavefront measurement device (WMD) compatible with the LADARVision®4000 Excimer Laser System. At the present time, the only compatible WMD is the Alcon LADARWave® CustomCornea® Wavefront System.

The LADARWave® CustomCornea® Wavefront System is indicated for measuring, recording, and analyzing visual aberrations (such as myopia, hyperopia, astigmatism, coma and spherical aberration) and for displaying refractive error maps of the eye to assist in prescribing refractive corrections. This device is enabled to export wavefront data and associated anatomical registration information to a compatible treatment laser with an indication for wavefront-guided refractive surgery.

Essential features of the compatible WMD are as follows:

Patient Fixation and Fogging

The WMD includes a fixation optical subsystem that provides the patient with an unambiguous fixation point. In addition, the fixation subsystem includes adjustable optics to compensate for the patient's inherent refractive error. The optics are used to "fog" the eye, first clarifying the fixation target and then it optically adjusts beyond the patient's far point to minimize accommodation.

Centration

Prior to dilation, the WMD is used to record the geometric relationship between the natural daytime pupil center and the limbus of the eye. This information is then used to center the wavefront measurement and subsequent ablative treatment on the natural line of sight.

Wavefront Measurement

The WMD measures the wavefront profile of the eye with a high degree of accuracy and characterizes the profile using Zernike polynomials. The pupil must be large enough so that valid wavefront data can be obtained over a large area. Higher-order aberrations are more significant at night when the pupil is naturally larger. Therefore, when treating these aberrations, measurement over a large pupil provides the greatest utility.

Registration

The WMD uses synchronized video imagery and on-screen software reticules to record the relationship of the wavefront data to the limbus of the eye and to ink marks applied to the sclera just before the wavefront exam. This registration information is used to position the excimer ablation profile at the correct corneal location and cyclotorsional angle.

Data Export

The WMD has the ability to export the wavefront examination data as an electronic file to removable media for transfer to the LADARVision®4000 System. The electronic file is structured in a specific format and contains essential patient information, centration/registration information, and the detailed aberration data. In addition, the electronic file is encrypted in a manner that can only be deciphered by the LADARVision®4000 System.

B. MICROKERATOME

A microkeratome is used to achieve a partial thickness cut of the cornea, which creates a "flap" as part of the LASIK procedure. The microkeratome is a precision instrument used in performing lamellar corneal resections. This instrument cuts a precise corneal disc of pre-selected thickness and diameter. The system generally consists of a head, plates, ring, handle, wrenches, shaft, motor, hand-piece, disposable blades, and power supply with footswitches and power cords. The system is completed with the applanation lens set, tonometer, corneal storage jar, optical zone marker, spatula, stop attachment, and digital thickness gauge.

Microkeratomes Used in the Clinical Trial:

The microkeratomes used in the clinical trial included the BD K-4000[1] (manufactured by Becton-Dickinson), Hansatome[2] (manufactured by Bausch & Lomb), and the Moria[3] CB and LSK (manufactured by Moria).

[1] *BD K-4000* TM of Becton, Dickinson and Company
[2] *Hansatome* Reg. TM of Bausch & Lomb Incorporated
[3] *Moria* Reg. TM of Moria SA

C. CUSTOMCORNEA® SURGERY PLANNING SOFTWARE

The CustomCornea® Surgery Planning Software is a stand-alone computer application linking the diagnostic wavefront data from the WMD with the surgical treatment on the LADARVision®4000 Excimer Laser System. The planning software allows refinement of surgical parameters within the approved wavefront-guided indication for the LADARVision®4000 System, calculates ablation depth, checks for treatment eligibility, and exports all messages and warnings to the excimer laser system.

After completing the surgery planning tasks, the planned treatment file is transferred to the LADARVision®4000 System. The LADARVision®4000 System software imports the treatment file, calculates the excimer treatment pattern, and performs the surgery.

D. LADARVISION®4000 EXCIMER LASER SYSTEM

The LADARVision®4000 System excimer laser beam is of Gaussian profile and small in diameter (<0.90mm). Corneal sculpting is achieved by delivering hundreds to thousands of excimer laser pulses to the eye in a complex pattern of spatially overlapping spots, and precision of this process depends on accurate placement of the laser pulses. The LADARVision®4000 Excimer Laser System incorporates the LADARTracker® closed-loop eye-tracking system to track and compensate for patient eye motion, including saccadic movements, during procedures so that each excimer laser pulse is delivered to the appropriate location on the cornea.

Excimer Laser Characteristics

The ultraviolet laser used in the LADARVision®4000 Excimer Laser System is an argon fluoride excimer laser. This laser produces 10 nanosecond pulses of ultraviolet radiation at a wavelength of 193 nanometers. The laser repetition rate is approximately 60 pulses per second. Characteristics of the laser beam at the corneal treatment plane are shown below:

Treatment Plane Characteristics of the LADARVision®4000 System Excimer Laser Beam

Pulse energy (mJ)	2.4 - 3.0
Beam diameter (mm) [a]	< 0.90
Average fluence (mJ/cm^2) [b]	180-240

Note (a): The Gaussian beam diameter is defined as the mean of the semi-major and semi-minor axes of the elliptical beam cross-section and is the 1/e width in the Gaussian fluence distribution.

Note (b): This is the calculated average value per pulse of the laser fluence over the ablated area.

Additional features of the LADARVision®4000 Excimer Laser System include:

Optical Transmission System

The excimer laser passes through an optical telescope, followed by reflection off a series of mirrors which position the excimer laser pulses in the correct locations at the treatment plane. Tracking mirrors also compensate for patient eye motion, as detected by the LADARTracker® system.

Energy Monitoring/Control

An energy monitor is mounted at the output of the LADARVision®4000 System. Prior to treatment, this energy monitor ensures that the laser pulse energy delivered to the eye will be between 2.4 and 3.0 mJ. During treatment, the detector monitors laser operation.

Gas Handling

The excimer laser enclosure holds the laser, gas bottle, and gas-plumbing manifold. The gas bottle contains the pre-mixed excimer laser gas, which contains neon as the buffer gas, in addition to argon and fluorine. The initial pressure in the gas bottle is 2000 PSI. The outlet nozzle of the gas bottle contains a flow restrictor valve. Gas from the bottle flows to a fluorine-compatible gas regulator, which reduces the line pressure to 55 PSI. Two gas lines exit the regulator. One leads directly to the outlet line of the laser enclosure. In the event of a diaphragm failure, excimer gas will flow from the regulator down this line and out of the enclosure. Outside the laser enclosure, the gas flows through a charcoal-based filter (to remove the F_2) before venting into the room. The second gas line exiting the regulator leads to the excimer laser cavity. At the line connection to the cavity there is a solenoid valve, which responds to commands from the laser control electronics board. A second solenoid valve exists at the gas outlet port of the laser cavity. The outlet gas line also leads out of the laser enclosure and through the charcoal filter.

Eye Tracking System

The LADARVision®4000 System utilizes the LADARTracker® active closed-loop eye tracking system to track and compensate for eye motion during refractive laser surgery. The word "active" here is used to denote two important characteristics of the device. First, the LADARTracker® system actively tracks the position of the eye by irradiating it with pulses of 905 nm infrared "eye-safe" energy and analyzing characteristics of the returning laser radiation. This measurement occurs 4000 times each second in order to detect even rapid eye motion before significant movement of the cornea has occurred.

The LADARTracker® system is also "active" in the sense that it actively compensates for the detected motion, rather than simply disabling the treatment laser when the eye position exceeds some tolerated error range. The LADARTracker® system includes two mirrors that are continually repositioned to keep the eye centered in the field of view of the treatment laser. An independent set of mirrors is used to translate the treatment beam around within this field of view, delivering the ablation pulses to the cornea in a predetermined spatial pattern. The combined system allows for each ablation pulse in the complex pattern to be delivered to the appropriate corneal site, even in the presence of substantial eye movement.

The LADARTracker® system is designed so that precise mirror movements during the course of each surgery are recorded. Because the geometry involved is known, exact eye movements can be calculated from the compensatory movements of the mirrors. It is not possible to perform surgery using the LADARVision®4000 System without the LADARTracker® system engaged, and no patient has ever been treated without concurrent tracking.

Operating Microscope

The stereo viewing operating microscope is located in the optics head. The dual optical paths are independent of the excimer beam path and the LADARTracker® system mirrors. Oblique, omni-directional microscope lighting on either side of the system output window provides visible illumination of the treatment plane. The operating microscope optical system is completely independent from the eye tracking optical system and does not provide "tracked" imagery of the patient eye.

Fixation Target

A visible fixation target is mounted in the system to facilitate the patient looking in the direction of the treatment excimer beam. The fixation target consists of a light emitting diode (LED), a pinhole aperture, an edge-illuminated reticule, and a lens. The lens, in combination with a 300mm focal length achromat in the operating microscope optical path, places the LED at infinity focus from the patient's perspective. The edge-illuminated reticule is a clear, flat etched glass with two sets of horizontal lines. For proper eye alignment, the patient is instructed to shift position until the LED pinhole light is centered within the parallel lines on the reticule and then to maintain that fixation during treatment.

Moveable Bed

A motorized patient bed, which moves on X, Y and Z axes, smoothly and rapidly positions the patient and facilitates bilateral procedures. The bed controls are located on the Control Console and the Control Module. The longitudinal motion range is approximately 15", so that the patient can lie on the bed and then be moved into position under the laser head. The lateral range of motion is 4", allowing surgery to be performed on either eye. The vertical range of motion is 3", allowing adjustment for the proper distance from the laser aperture to the eye for varying head sizes. Each axis has a continually variable speed control for coarse and fine positioning.

Cross Beam Patient Positioning

Cross beam Class I lasers are used to place the cornea at a predetermined height for proper ablation. The cross beam laser sub-system consists of two laser line generators attached to the left and right sides of the upper optical module. The laser diode sources produce 0.9 mwatts each at 633nm. The beam of each red-wavelength laser is transmitted through an absorptive neutral density filter, which attenuates the laser by 97%, and a polarizer. The output of each polarizer is reflected off a stationary fold mirror. The two mirrors are aligned such that the two beams are vertically aligned (one above the other) on the left sclera/limbus boundary and the apex of the cornea is 8 inches below the laser output window. This provides the operator/surgeon with an easy method of setting the height of the patient's eye during centration and surgery.

The maximum laser power at the eye is less than 15 μwatts for each laser. The lasers are separated by 103mm and are 209mm from the eye. With this geometry, the laser spots are separated on the retina by several times their diameter so the energy is not additive. Given the wavelength and power, the maximum permissible Class I exposure duration is 4 minutes and 30 seconds. When the cross beam lasers are turned on, a 2-minute automatic time out is activated to ensure the safe exposure limit is not exceeded. The cross beam lasers comply with Class I accessible emission limits for laser radiation in 21 CFR 1040 as well as ANSI Z136.1-1993.

Plume Removal System

The plume removal system is housed within the calibration stage. During surgery the plume removal system is deployed to a pre-determined height and provides a constant level of plume removal during ablation. The plume is evacuated to a filter cartridge that contained within the system. This filter cartridge is inspected and replaced during preventative maintenance performed by Alcon Technical Service Personnel.

System Software

The LADARVision®4000 System software controlling the proprietary excimer laser runs on an Intel Pentium[4]-based personal computer under a Microsoft Windows[5] operating system. The software enables the user to:

- properly center the treatment;
- make adjustments in the X and Y axes;
- adjust for cyclotorsion and correctly reference astigmatism; and
- place a hinge guard to protect the flap during surgery.

In addition, the software enables the user to properly match the alignment of the wavefront map to the ablation.

Laser Shot Patterns

The LADARVision®4000 System software calculates the "laser shot pattern," i.e., the number of excimer laser pulses to deliver to the eye and the required position of each pulse on the cornea, based on the desired refractive correction and the current laser calibration. The system software also calculates a sequence to fire the pulses in the shot pattern such that no corneal site is revisited by the excimer beam for a finite interval. The laser firing sequence is designed to provide a gradual corneal curvature from the starting surface shape to the corrected final profile.

Rather than the refractive correction being entered manually by the physician based on phoropter refraction, the CustomCornea® treatment requires that the pre-operative aberrations in the eye be measured with a wavefront measurement device. The treatment is based on Zernike data derived from a wavefront measurement device, including treatment of lower-order sphere and astigmatism components and higher-order components, such as coma and spherical aberration.

[4] *Intel* and *Pentium* Reg. TM of Intel Corporation
[5] *Microsoft* and *Windows* Reg. TM of Microsoft Corporation

The electronic file that the LADARVision®4000 System receives from the wavefront measurement device includes the following information:

- Patient information, including name, identification number, and clinical prescription.
- Eye information, including OD/OS and the geometric relationship of the wavefront data to the limbus and to the pupil center.
- Wavefront information, including a Zernike polynomial representation of the wavefront and the physical radius of that description.

The excimer laser beam characteristics (i.e., pulse energy, firing rate, fluence distribution at the treatment plane) are the same for Conventional and CustomCornea® treatment modalities. The Conventional LADARVision®4000 System treatment utilizes sphere, cylinder and axis components entered manually by the operator to generate the ablation profile. The CustomCornea® LASIK shaping algorithm utilizes aberration information unique to a given eye that is obtained from the WMD to guide the ablation of the cornea. The wavefront information is registered to the anatomical geometry of the eye using the WMD while the patient is sitting upright. This registered alignment information is passed to the LADARVision®4000 System, which both permits for the compensation of this alignment information due to the natural cyclotorsion incurred when the patient assumes a prone position and uses the geometry information to accurately position the customized ablation profile on the eye.

CustomCornea® Ablation Zones

For CustomCornea® ablations, the standard optical zone is 6.5mm with a blend zone of 1.25mm for a total ablation zone of 9.0mm.

Safety

The LADARVision®4000 System contains a Class IV laser that conforms to the US FDA 21 CFR 1040 Radiological Health requirements. The laser system was designed to meet the following safety requirements:

- UL 2601-1 (previously UL 544)
- CSA 22.2 No. 601.1-M90
- IEC 60825-1
- EN60601-1-1-2 and EN60601-2-22

NOTE: Additional details regarding operation of this laser can be found in the LADARVision®4000 Excimer Laser System Operation Manual.

3. INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE EVENTS AND COMPLICATIONS

A. *INDICATIONS FOR USE*

The LADARVision®4000 Excimer Laser System is indicated for wavefront-guided Laser Assisted In-Situ Keratomileusis (LASIK):

- for the reduction or elimination of hyperopia and hyperopic astigmatism of +0.75D to less than +5.00D sphere with up to -3.00D cylinder (which has a magnitude less than or equal to the sphere in minus cylinder convention) and up to +5.00D cycloplegic spherical equivalent at the spectacle plane;
- in patients who are 21 years of age or older; and
- in patients with documented stability of refraction for the prior 12 months, as demonstrated by a change in sphere and cylinder of less than or equal to 0.50D.

B. *CONTRAINDICATIONS*

Wavefront-guided LASIK is contraindicated in:

- pregnant or nursing women.
- patients with autoimmune, collagen vascular, or immunodeficiency diseases.
- patients with signs of keratoconus.
- patients who are taking one or both of the following medications: isotretinoin (Accutane[6]) or amiodarone hydrochloride (Cordarone[7]).

C. *WARNINGS*

Wavefront-guided LASIK is not recommended in patients who have:

- diabetes.
- a history of herpes simplex or herpes zoster keratitis.
- significant dry eye that is unresponsive to treatment.
- severe allergies.

A minimum pre-operative pupillary dilation of 7mm and a maximum dilation of 11mm must be achieved and maintained in all patients throughout the refractive procedure to optimize tracking performance.

[6] *Accutane* Reg. TM of Hoffmann-La Roche Inc.
[7] *Cordarone* Reg. TM of Sanofi-Aventis

D. PRECAUTIONS

The safety and effectiveness of the LADARVision®4000 System for wavefront-guided LASIK correction of hyperopia and hyperopic astigmatism have **NOT** been established in patients:

- with unstable hyperopia and hyperopic astigmatism.
- with ocular disease, corneal abnormality, previous corneal or intraocular surgery, or trauma in the ablation zone.
- with a residual posterior stromal corneal thickness less than 250 microns at the completion of ablation.
- with a history of glaucoma.
- who are taking the medication sumatripin succinate (Imitrex[8]).
- under 21 years of age.
- over the long term (more than 9 months after surgery).
- for treatments of hyperopia and hyperopic astigmatism of +5.00D or greater sphere combined with greater than -3.00D cylinder and greater than +5.00D spherical equivalent by cycloplegic refraction.
- for retreatment with wavefront-guided LASIK.

The safety and effectiveness of wavefront-guided CustomCornea® LASIK have only been established for an optical zone of 6.5mm and an ablation zone of 9.0mm.

Pupil size should be evaluated under mesopic illumination conditions. Patients with large mesopic pupils ≥ 6.5mm (optical zone size) should be advised of the potential for negative effects on vision after surgery, such as glare, halos, and nighttime driving difficulty.

Preoperative evaluation for dry eye should be performed. Patients should be advised of the potential for dry eyes post-LASIK surgery.

The physician's adjustment of defocus has not been studied, and its effects on the safety and effectiveness outcomes of this procedure are unknown.

Please be advised that eyes with prior intraocular or corneal surgery of any kind were excluded from clinical trials with the LADARVision®4000 System. Safety and effectiveness, as well as tracking performance, have not been established for such eyes. Although the tracking system may acquire track in surgically altered eyes prior to ablation, the optics of the eye may change in the context of the ablation to potentially interfere with further tracking and compromise the completion of the ablation. Medical judgment should be exercised in the use of the LADARVision®4000 System in pseudophakic patients and others who have had prior intraocular or corneal surgery.

[8] *Imitrex* Reg. TM of Glaxo Group Limited

E. ADVERSE EVENTS AND COMPLICATIONS

Cumulative adverse events and complications reported in a clinical study at any postoperative visit up to 9 months of CustomCornea® LASIK for the correction of hyperopia and hyperopic astigmatism with the LADARVision®4000 System are summarized in Table 1 below.

Table 1. Summary of Adverse Events and Complications At Any Postoperative Visit

ADVERSE EVENTS	n/N	%
Corneal subepithelial infiltrate (related to viral keratoconjunctivitis)	2/346	0.6%
Follicular conjunctivitis with associated loss of > 10 letters of BSCVA	2/346	0.6%
Decrease in BSCVA >10 letters not due to irregular astigmatism as shown by hard contact lens refraction at 6 months or later	1/346	0.3%
Idiopathic choroidal neovascular membrane (unrelated to device)	1/346	0.3%
COMPLICATIONS	**n/N**	**%**
Epithelium in the interface	11/346	3.2%
Diffuse lamellar keratitis (DLK)	5/346	1.4%
Foreign body sensation at one month or later	3/346	0.9%
Filamentary keratitis	2/346	0.6%
Superficial punctate keratitis (SPK) (with medical management)	2/346	0.6%
Pain at one month or later	1/346	0.3%
Peripheral corneal epithelial defect at one month or later across keratectomy or off flap	1/346	0.3%

There were no reports of the following adverse events and complications in the clinical study:

- corneal edema
- corneal epithelial defect involving the keratectomy at one month or later
- double or ghost images
- late onset of corneal haze at six months with a loss of 2 or more lines of best spectacle corrected visual acuity (BSCVA)
- epithelium in the interface with a loss of 2 or more lines of BSCVA
- melting of the flap
- miscreated flap
- misaligned flap
- intraocular pressure (IOP) of more than 25 mmHg
- IOP increase of more than 10 mmHg above baseline
- retinal detachment
- retinal vascular accident

4. CLINICAL STUDY

A. INTRODUCTION

The study in the U.S. using the LADARVision®4000 System began as a prospective, randomized, unmasked, and multi-center trial, where one eye of the patient received CustomCornea® LASIK correction using data from a wavefront measurement system and the fellow eye received a Conventional treatment based on phoropter cycloplegic refraction. For this initial subgroup of subjects, the fellow eye served as a contralateral control.

Upon providing data to support expansion of the number of subjects for enrollment, the U.S. study design was changed to a prospective, non-randomized, unmasked, and multi-center trial where one or both eyes of a subject received wavefront-guided CustomCornea® treatment. The primary control was the preoperative state of the treated eye for comparison to postoperative outcomes. An equivalent study design was also in progress under a Canadian protocol. Data from the U.S. and Canadian studies were pooled since both protocols were equivalent in terms of the inclusion and exclusion criteria, study procedures, subject measurements, and the treatment applied to the eye.

The objective of the multi-center clinical investigation was to establish safety and effectiveness of wavefront-guided CustomCornea® LASIK correction of hyperopia and hyperopic astigmatism. Subjects were followed on Day 1, at 1 week, and at 1, 3, 6, and 9 months postoperatively.

Recruited subjects had the study details and follow-up requirements explained to them and were asked to sign an Informed Consent Document preoperatively. To be eligible for the study, hyperopic subjects must have had a preoperative cycloplegic refraction at the spectacle plane of up to +6.00D sphere with up to -6.00D astigmatism (minus cylinder convention) and up to +6.00D spherical equivalent (SE). Enrollment of hyperopic and hyperopic astigmatic eyes in the study occurred over the preoperative cycloplegic refractive range of +0.75D to +6.00D sphere with up to -5.00D astigmatism and up to +5.75D SE, where the absolute cycloplegic cylinder in minus cylinder convention was less than or equal to the sphere.

Stability of refraction must have been established and documented using previous clinical records or measurement of spectacles. Stability was demonstrated by a change in the manifest sphere and cylinder over the prior 12 months of less than or equal to 0.50D. If a year-old refraction was not available, the change in refraction must have been 0.50D or less per year since the last documented refraction in both the manifest sphere and cylinder to a 1.00D maximum SE change.

The manifest and cycloplegic refraction measured at the preoperative examination must have been within 1.00D of each other in the sphere and cylinder components. In addition, the cycloplegic refraction could not differ by more than 1.00D in sphere or cylinder from the attempted correction determined by the wavefront measurement system.

For the contralateral treatment group, the cycloplegic refraction between the subject's two eyes could not differ by more than 1.00D in sphere or cylinder. In addition, subjects must have been willing to have LASIK correction in both eyes within a 2-week period. These two criteria were not applicable to subjects treated under the bilateral CustomCornea® treatment study design.

Subjects must have been at least 18 years of age and had a best-spectacle corrected visual acuity (BSCVA) of 20/25 or better in the operative eye(s). Subjects must have been willing to return for scheduled follow-up examinations for 9 months after surgery and have their eyes pharmacologically dilated at the required visits.

Subjects who were contact lens wearers were requested to discontinue contact lens wear for a minimum of 2 weeks for soft contact lenses and 3 weeks for hard contact lenses (RGP/PMMA) prior to the preoperative examination. Subjects who had previously worn hard lenses were required to have two examinations conducted 2 to 3 weeks apart to show stability of refraction without lens wear. Prior to surgery, subjects were not to wear their contact lenses in the operative eye(s) for 2 to 3 weeks for soft and hard contact lenses, respectively.

All eyes were required to be treated for a target of emmetropia. All surgeries performed in the study were subject to approval by the Sponsor.

Patients who exhibited any of the following conditions were excluded:

- previous corneal, intraocular, or strabismus surgery in the operative eye(s)
- history of or active clinically significant or vision threatening ocular disease or pathology
- clinically significant corneal scar within the ablation zone or corneal abnormality such as recurrent erosion or severe basement membrane disease
- signs of keratoconus
- irregular corneal astigmatism
- history of herpes keratitis
- autoimmune or connective tissue disease, clinically significant atopic syndrome, or diabetes
- use of chronic systemic corticosteroids or other immunosuppressive therapy
- use of systemic medication with significant ocular side effects
- pregnant or nursing
- use of ophthalmic medications other than artificial tears for treatment of an ocular pathology
- severe dry eye syndrome unresolved by treatment
- known allergy to study medications
- glaucoma or glaucoma filtering surgery
- participation in another ophthalmic clinical trial
- calculated residual posterior stromal thickness of less than 250 microns
- inability to achieve a pupillary dilation of ≥ 7mm
- at risk of angle closure
- an inability to obtain a clear and complete wavefront image

The primary effectiveness parameters for this study were improvement of uncorrected visual acuity (UCVA), predictability and stability of MRSE, reduction of wavefront error, including higher-order aberrations and subject satisfaction. The safety parameters for this study were preservation of BSCVA, absence of significant findings in slit lamp and fundus examination, absence of significant intraocular pressure (IOP) elevation, and incidence of complications and adverse events.

B. RESULTS

1. Demographics

The demographics of the CustomCornea® study shown in Table 2 were typical for a refractive surgery trial performed in the U.S. The mean subject age was 49.8 ± 9.2 years with a range from 19 to 70 years. The majority of subjects were Caucasian (95.4%) and the remaining subjects were Hispanic (2.9%) and Black (1.7%). Slightly more males (54.0%) than females (46.0%) participated in the study. The distribution of right and left eyes that received treatment was approximately equal (51.2% vs. 48.8%). While most subjects (59.5%) did not wear contact lenses prior to surgery, 37.6% wore soft contact lenses and 2.9% wore rigid gas permeable (RGP) lenses.

Table 2. Demographics

346 Eyes of 205 Enrolled Subjects			
Age (In Years)			
Average ± Standard Deviation		49.8 ± 9.2	
Minimum to Maximum		19 to 70	
Race		**N**	**% Eyes**
	Black	6	1.7%
	Caucasian	330	95.4%
	Hispanic	10	2.9%
Gender:	Female	159	46.0%
	Male	187	54.0%
Eye:	Left	169	48.8%
	Right	177	51.2%
Contact Lens History:	None	206	59.5%
	Rigid Gas Permeable (RGP)	10	2.9%
	Soft	130	37.6%

2. Primary Safety and Effectiveness Cohorts

The Primary Safety Cohort consisted of 346 eyes with a preoperative cycloplegic refractive range of +0.75D to +6.00D sphere with up to -5.00D cylinder and up to +5.75D spherical equivalent. The Primary Effectiveness Cohort consisted of 297 eyes with a preoperative cycloplegic refractive range of +0.75D to +6.00D sphere with up to -3.00D cylinder and up to +5.00D spherical equivalent (Table 3). A spherical eye was defined as having less than -0.50D preoperative cycloplegic cylinder and an astigmatic eye was defined as having at least -0.50D preoperative cycloplegic cylinder.

Table 3. Primary Safety and Effectiveness Cohorts

Cohort	N Eyes Enrolled	Preoperative Cycloplegic Refractive Range (D)		
		Sphere	Cylinder	Spherical Equivalent
Safety	**346**	**+0.75 to +6.00**	**0.00 to -5.00**	**+0.50 to +5.75**
Spherical Hyperopia	90	+0.75 to +5.00	0.00 to -0.25	+0.63 to +4.88
Hyperopic Astigmatism	256	+1.00 to +6.00	-0.50 to -5.00	+0.50 to +5.75
Effectiveness	**297**	**+0.75 to +6.00**	**0.00 to -3.00**	**+0.50 to +5.00**
Spherical Hyperopia	85	+0.75 to +5.00	0.00 to -0.25	+0.63 to +4.88
Hyperopic Astigmatism	212	+1.00 to +6.00	-0.50 to -3.00	+0.50 to +5.00

(D) = Diopter

3. Preoperative Cycloplegic Refraction Parameters

For the Primary Safety Cohort, the number of eyes is shown stratified by preoperative cycloplegic sphere and cylinder in Table 4 and by preoperative cycloplegic spherical equivalent and cylinder in Table 5.

Table 4. Preoperative Cycloplegic Refraction Stratified by Sphere and Cylinder: Safety Cohort

SPHERE (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION						
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to -3.00	-3.01 to -4.00	-4.01 to -5.00	TOTAL
+0.75 to +1.99	n/N	35/346	45/346	29/346	0/346	0/346	0/346	109/346
	%	10.1%	13.0%	8.4%	0.0%	0.0%	0.0%	31.5%
+2.00 to +2.99	n/N	33/346	34/346	28/346	7/346	0/346	0/346	102/346
	%	9.5%	9.8%	8.1%	2.0%	0.0%	0.0%	29.5%
+3.00 to +3.99	n/N	10/346	25/346	18/346	6/346	0/346	0/346	59/346
	%	2.9%	7.2%	5.2%	1.7%	0.0%	0.0%	17.1%
+4.00 to +4.99	n/N	11/346	23/346	8/346	6/346	0/346	0/346	48/346
	%	3.2%	6.6%	2.3%	1.7%	0.0%	0.0%	13.9%
+5.00 to +6.00	n/N	1/346	5/346	9/346	8/346	3/346	2/346	28/346
	%	0.3%	1.4%	2.6%	2.3%	0.9%	0.6%	8.1%
TOTAL	n/N	90/346	132/346	92/346	27/346	3/346	2/346	346/346
	%	26.0%	38.2%	26.6%	7.8%	0.9%	0.6%	100.0%

(D) = Diopter

Table 5. Preoperative Cycloplegic Refraction Stratified by Spherical Equivalent and Cylinder: Safety Cohort

SPHERICAL EQUIVALENT (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION						
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to -3.00	-3.01 to -4.00	-4.01 to -5.00	TOTAL
0.00 to +0.99	n/N	6/346	4/346	19/346	0/346	0/346	0/346	29/346
	%	1.7%	1.2%	5.5%	0.0%	0.0%	0.0%	8.4%
+1.00 to +1.99	n/N	30/346	53/346	31/346	9/346	0/346	0/346	123/346
	%	8.7%	15.3%	9.0%	2.6%	0.0%	0.0%	35.5%
+2.00 to +2.99	n/N	33/346	37/346	22/346	6/346	0/346	1/346	99/346
	%	9.5%	10.7%	6.4%	1.7%	0.0%	0.3%	28.6%
+3.00 to +3.99	n/N	9/346	21/346	10/346	5/346	2/346	1/346	48/346
	%	2.6%	6.1%	2.9%	1.4%	0.6%	0.3%	13.9%
+4.00 to +5.00	n/N	12/346	14/346	6/346	7/346	1/346	0/346	40/346
	%	3.5%	4.0%	1.7%	2.0%	0.3%	0.0%	11.6%
+5.01 to +6.00	n/N	0/346	3/346	4/346	0/346	0/346	0/346	7/346
	%	0.0%	0.9%	1.2%	0.0%	0.0%	0.0%	2.0%
TOTAL	n/N	90/346	132/346	92/346	27/346	3/346	2/346	346/346
	%	26.0%	38.2%	26.6%	7.8%	0.9%	0.6%	100.0%

(D) = Diopter

For the Primary Effectiveness Cohort, the number of eyes is shown stratified by preoperative cycloplegic sphere and cylinder in Table 6 and by preoperative cycloplegic spherical equivalent and cylinder in Table 7.

Table 6. Preoperative Cycloplegic Refraction Stratified by Sphere and Cylinder: Effectiveness Cohort

SPHERE (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION				
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to-3.00	TOTAL
+0.75 to +1.99	n/N	35/297	35/297	18/297	0/297	88/297
	%	11.8%	11.8%	6.1%	0.0%	29.6%
+2.00 to +2.99	n/N	29/297	31/297	22/297	7/297	89/297
	%	9.8%	10.4%	7.4%	2.4%	30.0%
+3.00 to +3.99	n/N	9/297	25/297	18/297	5/297	57/297
	%	3.0%	8.4%	6.1%	1.7%	19.2%
+4.00 to +4.99	n/N	11/297	23/297	7/297	6/297	47/297
	%	3.7%	7.7%	2.4%	2.0%	15.8%
+5.00 to +6.00	n/N	1/297	2/297	5/297	8/297	16/297
	%	0.3%	0.7%	1.7%	2.7%	5.4%
TOTAL	n/N	85/297	116/297	70/297	26/297	297/297
	%	28.6%	39.1%	23.6%	8.8%	100.0%

(D) = Diopter

Table 7. Preoperative Cycloplegic Refraction Stratified by Spherical Equivalent and Cylinder: Effectiveness Cohort

SPHERICAL EQUIVALENT (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION				
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to -3.00	TOTAL
0.00 to +0.99	n/N	6/297	0/297	9/297	0/297	15/297
	%	2.0%	0.0%	3.0%	0.0%	5.1%
+1.00 to +1.99	n/N	30/297	46/297	26/297	8/297	110/297
	%	10.1%	15.5%	8.8%	2.7%	37.0%
+2.00 to +2.99	n/N	29/297	35/297	20/297	6/297	90/297
	%	9.8%	11.8%	6.7%	2.0%	30.3%
+3.00 to +3.99	n/N	8/297	21/297	9/297	5/297	43/297
	%	2.7%	7.1%	3.0%	1.7%	14.5%
+4.00 to +5.00	n/N	12/297	14/297	6/297	7/297	39/297
	%	4.0%	4.7%	2.0%	2.4%	13.1%
TOTAL	n/N	85/297	116/297	70/297	26/297	297/297
	%	28.6%	39.1%	23.6%	8.8%	100.0%

(D) = Diopter

4. Accountability

Table 8 and 9 show the accountability of the Primary Safety and Effectiveness Cohorts for this study, which was greater than 99% at all postoperative intervals.

Table 8. Accountability at Each Visit: Safety Cohort

		1 Month	3 Months	6 Months	9 Months
Total Eyes Enrolled: Primary	n	202	202	202	202
Fellow	n	144	144	144	144
Total	N	346	346	346	346
Available for Analysis:	**n**	**346**	**346**	**320**	**161**
	%	**100.0%**	**100.0%**	**92.5%**	**46.5%**
Not Eligible for Interval:	n	0	0	24	185
	%	0.0%	0.0%	6.9%	53.5%
Unavailable: Missed Visit	n	0	0	2	0
	%	0.0%	0.0%	0.6%	0.0%
Lost to Follow-up	n	0	0	0	0
	%	0.0%	0.0%	0.0%	0.0%
% Accountability= [available/(available +unavailable)]	**%**	**100.0%**	**100.0%**	**99.4%**	**100.0%**

Table 9. Accountability at Each Visit: Effectiveness Cohort

		1 Month	3 Months	6 Months	9 Months
Total Eyes Enrolled: Primary	n	175	175	175	175
Fellow	n	122	122	122	122
Total	N	297	297	297	297
Available for Analysis:	**n**	**297**	**297**	**276**	**138**
	%	**100.0%**	**100.0%**	**92.9%**	**46.5%**
Not Eligible for Interval:	n	0	0	19	159
	%	0.0%	0.0%	6.4%	53.5%
Unavailable Missed Visit	n	0	0	2	0
	%	0.0%	0.0%	0.7%	0.0%
Lost to Follow-up	n	0	0	0	0
	%	0.0%	0.0%	0.0%	0.0%
% Accountability= [available/(available + unavailable)]	**%**	**100.0%**	**100.0%**	**99.3%**	**100.0%**

5. Key Effectiveness and Safety Results

The outcomes for uncorrected visual acuity (UCVA) and manifest refraction spherical equivalent (MRSE) are shown for all eyes in the Primary Effectiveness Cohort (Table 10) and by refractive type (Table 11). The effectiveness parameters at 6 months are further stratified by preoperative cycloplegic refraction spherical equivalent (CRSE) (Table 12).

Preoperatively, 33.3% of eyes had a UCVA of 20/40 or better. At 6 months postoperative, the UCVA was 20/20 or better in 59.1% of eyes, 20/25 or better in 80.8% and 20/40 or better in 95.3%. For those eyes with a preoperative best spectacle corrected visual acuity (BSCVA) of 20/20 or better, a UCVA of 20/20 or better was achieved in 62.9% of eyes at 6 months. Accuracy of MRSE was within 0.50D of emmetropia in 70.7% of eyes, within 1.00D in 88.4% and within 2.00D in 98.6% at 6 months. Of the eyes that did not achieve an MRSE within 1.00D of emmetropia at 6 months, 3.3% of eyes were undercorrected by >1.00D of MRSE and 8.3% of eyes were overcorrected.

Whereas the mean MRSE (-0.09D ± 0.69D) was slightly myopic at 6 months, the mean CRSE (+0.13D ± 0.64D) was slightly hyperopic but within 0.25D of the mean MRSE. Accuracy of CRSE at 6 months was within 0.50D of emmetropia in 65.6% of eyes, within 1.00D in 89.1% and within 2.00D in 99.6%. At 6 months, 6.9% of eyes were undercorrected by >1.00D of CRSE and 4.0% of eyes were overcorrected.

The effectiveness data meet the criteria established in the FDA Guidance document for at least 85% of eyes achieving a UCVA of 20/40 or better and accuracy of MRSE within 0.50D in at least 50% of eyes and within 1.00D in 75% of eyes at all postoperative intervals.

Table 10. Summary of Key Effectiveness Parameters Over Time

All Eyes: Effectiveness Cohort		1 Month	3 Months	6 Months	9 Months
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	162/273	167/273	161/256	79/128
	%	59.3%	61.2%	62.9%	61.7%
	CI	(53.3, 65.2)	(55.1, 67.0)	(56.7, 68.8)	(52.7, 70.2)
UCVA 20/20 or better	n/N	162/297	168/297	163/276	81/138
	%	54.5%	56.6%	59.1%	58.7%
	CI	(48.7, 60.3)	(50.7, 62.3)	(53.0, 64.9)	(50.0, 67.0)
UCVA 20/25 or better	n/N	239/297	241/297	223/276	112/138
	%	80.5%	81.1%	80.8%	81.2%
	CI	(75.5, 84.8)	(76.2, 85.4)	(75.6, 85.3)	(73.6, 87.3)
UCVA 20/40 or better	n/N	283/297	282/297	263/276	130/138
	%	95.3%	94.9%	95.3%	94.2%
	CI	(92.2, 97.4)	(91.8, 97.1)	(92.1, 97.5)	(88.9, 97.5)
MRSE ±0.50D of intended	n/N	191/297	193/297	195/276	90/138
	%	64.3%	65.0%	70.7%	65.2%
	CI	(58.6, 69.8)	(59.3, 70.4)	(64.9, 76.0)	(56.6, 73.1)
MRSE ±1.00D of intended	n/N	267/297	264/297	244/276	123/138
	%	89.9%	88.9%	88.4%	89.1%
	CI	(85.9, 93.1)	(84.8, 92.2)	(84.0, 91.9)	(82.7, 93.8)
MRSE ±2.00D of intended	n/N	293/297	294/297	272/276	137/138
	%	98.7%	99.0%	98.6%	99.3%
	CI	(96.6, 99.6)	(97.1, 99.8)	(96.3, 99.6)	(96.0, 100.0)

UCVA = Uncorrected Visual Acuity BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent CI = 95% Confidence Interval D = Diopter

Table 11. Summary of Key Effectiveness Parameters Over Time: Spherical Hyperopia and Hyperopic Astigmatism

Spherical Hyperopia: Effectiveness Cohort		1 Month	3 Months	6 Months	9 Months
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	47/81	50/81	47/73	24/41
	%	58.0%	61.7%	64.4%	58.5%
	CI	(46.5, 68.9)	(50.3, 72.3)	(52.3, 75.3)	(42.1, 73.7)
UCVA 20/20 or better	n/N	47/85	50/85	47/76	25/44
	%	55.3%	58.8%	61.8%	56.8%
	CI	(44.1, 66.1)	(47.6, 69.4)	(50.0, 72.8)	(41.0, 71.7)
UCVA 20/25 or better	n/N	72/85	72/85	65/76	37/44
	%	84.7%	84.7%	85.5%	84.1%
	CI	(75.3, 91.6)	(75.3, 91.6)	(75.6, 92.5)	(69.9, 93.4)
UCVA 20/40 or better	n/N	85/85	83/85	75/76	44/44
	%	100.0%	97.6%	98.7%	100.0%
	CI	(95.8, 100.0)	(91.8, 99.7)	(92.9, 100.0)	(92.0, 100.0)
MRSE ±0.50D of intended	n/N	55/85	56/85	50/76	27/44
	%	64.7%	65.9%	65.8%	61.4%
	CI	(53.6, 74.8)	(54.8, 75.8)	(54.0, 76.3)	(45.5, 75.6)
MRSE ±1.00D of intended	n/N	79/85	79/85	70/76	42/44
	%	92.9%	92.9%	92.1%	95.5%
	CI	(85.3, 97.4)	(85.3, 97.4)	(83.6, 97.0)	(84.5, 99.4)
MRSE ±2.00D of intended	n/N	83/85	84/85	74/76	44/44
	%	97.6%	98.8%	97.4%	100.0%
	CI	(91.8, 99.7)	(93.6, 100.0)	(90.8, 99.7)	(92.0, 100.0)
Hyperopic Astigmatism: Effectiveness Cohort		**1 Month**	**3 Months**	**6 Months**	**9 Months**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	115/192	117/192	114/183	55/87
	%	59.9%	60.9%	62.3%	63.2%
	CI	(52.6, 66.9)	(53.7, 67.9)	(54.8, 69.3)	(52.2, 73.3)
UCVA 20/20 or better	n/N	115/212	118/212	116/200	56/94
	%	54.2%	55.7%	58.0%	59.6%
	CI	(47.3, 61.1)	(48.7, 62.5)	(50.8, 64.9)	(49.0, 69.6)
UCVA 20/25 or better	n/N	167/212	169/212	158/200	75/94
	%	78.8%	79.7%	79.0%	79.8%
	CI	(72.6, 84.1)	(73.7, 84.9)	(72.7, 84.4)	(70.2, 87.4)
UCVA 20/40 or better	n/N	198/212	199/212	188/200	86/94
	%	93.4%	93.9%	94.0%	91.5%
	CI	(89.2, 96.3)	(89.7, 96.7)	(89.8, 96.9)	(83.9, 96.3)
MRSE ± 0.50D of intended	n/N	136/212	137/212	145/200	63/94
	%	64.2%	64.6%	72.5%	67.0%
	CI	(57.3, 70.6)	(57.8, 71.0)	(65.8, 78.6)	(56.6, 76.4)
MRSE ± 1.00D of intended	n/N	188/212	185/212	174/200	81/94
	%	88.7%	87.3%	87.0%	86.2%
	CI	(83.6, 92.6)	(82.0, 91.4)	(81.5, 91.3)	(77.5, 92.4)
MRSE ± 2.00D of intended	n/N	210/212	210/212	198/200	93/94
	%	99.1%	99.1%	99.0%	98.9%
	CI	(96.6, 99.9)	(96.6, 99.9)	(96.4, 99.9)	(94.2, 100.0)

UCVA = Uncorrected Visual Acuity BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent CI = 95% Confidence Interval D = Diopter

Table 12. Summary of Key Effectiveness Parameters at 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

All Eyes: Effectiveness Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	14/15	75/102	49/76	13/34	10/29	161/256
	%	93.3%	73.5%	64.5%	38.2%	34.5%	62.9%
UCVA 20/20 or better	n/N	14/15	76/106	49/80	14/39	10/36	163/276
	%	93.3%	71.7%	61.3%	35.9%	27.8%	59.1%
UCVA 20/25 or better	n/N	15/15	96/106	62/80	28/39	22/36	223/276
	%	100.0%	90.6%	77.5%	71.8%	61.1%	80.8%
UCVA 20/40 or better	n/N	15/15	105/106	76/80	34/39	33/36	263/276
	%	100.0%	99.1%	95.0%	87.2%	91.7%	95.3%
MRSE ± 0.50D of intended	n/N	15/15	89/106	52/80	20/39	19/36	195/276
	%	100.0%	84.0%	65.0%	51.3%	52.8%	70.7%
MRSE ± 1.00D of intended	n/N	15/15	103/106	71/80	29/39	26/36	244/276
	%	100.0%	97.2%	88.8%	74.4%	72.2%	88.4%
MRSE ± 2.00D of intended	n/N	15/15	106/106	79/80	39/39	33/36	272/276
	%	100.0%	100.0%	98.8%	100.0%	91.7%	98.6%
Spherical Hyperopia: Effectiveness Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	6/6	19/27	16/23	1/6	5/11	47/73
	%	100.0%	70.4%	69.6%	16.7%	45.5%	64.4%
UCVA 20/20 or better	n/N	6/6	19/29	16/23	1/6	5/12	47/76
	%	100.0%	65.5%	69.6%	16.7%	41.7%	61.8%
UCVA 20/25 or better	n/N	6/6	26/29	20/23	6/6	7/12	65/76
	%	100.0%	89.7%	87.0%	100.0%	58.3%	85.5%
UCVA 20/40 or better	n/N	6/6	29/29	23/23	6/6	11/12	75/76
	%	100.0%	100.0%	100.0%	100.0%	91.7%	98.7%
MRSE ± 0.50D of intended	n/N	6/6	24/29	15/23	1/6	4/12	50/76
	%	100.0%	82.8%	65.2%	16.7%	33.3%	65.8%
MRSE ± 1.00D of intended	n/N	6/6	29/29	23/23	4/6	8/12	70/76
	%	100.0%	100.0%	100.0%	66.7%	66.7%	92.1%
MRSE ± 2.00D of intended	n/N	6/6	29/29	23/23	6/6	10/12	74/76
	%	100.0%	100.0%	100.0%	100.0%	83.3%	97.4%
Hyperopic Astigmatism: Effectiveness Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	8/9	56/75	33/53	12/28	5/18	114/183
	%	88.9%	74.7%	62.3%	42.9%	27.8%	62.3%
UCVA 20/20 or better	n/N	8/9	57/77	33/57	13/33	5/24	116/200
	%	88.9%	74.0%	57.9%	39.4%	20.8%	58.0%
UCVA 20/25 or better	n/N	9/9	70/77	42/57	22/33	15/24	158/200
	%	100.0%	90.9%	73.7%	66.7%	62.5%	79.0%
UCVA 20/40 or better	n/N	9/9	76/77	53/57	28/33	22/24	188/200
	%	100.0%	98.7%	93.0%	84.8%	91.7%	94.0%
MRSE ± 0.50D of intended	n/N	9/9	65/77	37/57	19/33	15/24	145/200
	%	100.0%	84.4%	64.9%	57.6%	62.5%	72.5%
MRSE ± 1.00D of intended	n/N	9/9	74/77	48/57	25/33	18/24	174/200
	%	100.0%	96.1%	84.2%	75.8%	75.0	87.0%
MRSE ± 2.00D of intended	n/N	9/9	77/77	56/57	33/33	23/24	198/200
	%	100.0%	100.0%	98.2%	100.0%	95.8%	99.0%

UCVA = Uncorrected Visual Acuity
BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent
CI = 95% Confidence Interval
D = Diopter

The key safety outcomes for all 346 eyes in the Primary Safety Cohort are presented for all eyes in Table 13 and by refractive type in Table 14. These same parameters are stratified by preoperative CRSE at 6 months in Table 15.

The safety data meet the criteria established in the FDA guidance document of less than 5% of eyes with a loss of >2 lines of BSCVA, less than 1% having a BSCVA of worse than 20/40, and less than 5% having induced astigmatism >2D.

A trend for early postoperative loss of ≥ 2 lines of BSCVA at 1 month with recovery over time was observed, which is consistent with trends observed previously after Conventional hyperopic LASIK surgery. All eyes except two have shown resolution of the BSCVA to within one line of preoperative BSCVA at a later follow-up examination. Of the two eyes with unresolved loss at 9 months, one eye improved with RGP contact lens refraction to preoperative level and the other eye had idiopathic choroidal neovascularization at 9 months, which was an adverse event unrelated to the device.

Table 13. Summary of Key Safety Parameters Over Time

All Eyes: Safety Cohort		1 Month	3 Months	6 Months	9 Months
Loss of >2 Lines BSCVA	n/N	3/346	1/346	0/320	0/161
	%	0.9%	0.3%	0.0%	0.0%
	CI	(0.2, 2.5)	(0.0, 1.6)	(0.0, 1.1)	(0.0, 2.3)
Loss of 2 Lines BSCVA	n/N	16/346	6/346	3/320	5/161
	%	4.6%	1.7%	0.9%	3.1%
	CI	(2.7, 7.4)	(0.6, 3.7)	(0.2, 2.7)	(1.0, 7.1)
BSCVA worse than 20/40	n/N	1/346	1/346	0/320	0/161
	%	0.3%	0.3%	0.0%	0.0%
	CI	(0.0, 1.6)	(0.0, 1.6)	(0.0, 1.1)	(0.0, 2.3)
Increase >2D cylinder magnitude	n/N	0/346	0/346	0/320	0/161
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 1.1)	(0.0, 1.1)	(0.0, 1.1)	(0.0, 2.3)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	3/315	0/315	1/294	2/148
	%	1.0%	0.0%	0.3%	1.4%
	CI	(0.2, 2.8)	(0.0, 1.2)	(0.0, 1.9)	(0.2, 4.8)

BSCVA = Best Spectacle Corrected Visual Acuity CI = 95% Confidence Interval D = Diopter

Table 14. Summary of Key Safety Parameters Over Time: Spherical Hyperopia and Hyperopic Astigmatism

Spherical Hyperopia: Safety Cohort		1 Month	3 Months	6 Months	9 Months
Loss of >2 Lines BSCVA	n/N	0/90	0/90	0/79	0/46
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.6)	(0.0, 7.7)
Loss of 2 Lines BSCVA	n/N	4/90	3/90	1/79	1/46
	%	4.4%	3.3%	1.3%	2.2%
	CI	(1.2, 11.0)	(0.7, 9.4)	(0.0, 6.9)	(0.1, 11.5)
BSCVA worse than 20/40	n/N	0/90	0/90	0/79	0/46
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.6)	(0.0, 7.7)
Increase >2D cylinder magnitude	n/N	0/90	0/90	0/79	0/46
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.6)	(0.0, 7.7)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	0/85	0/85	0/76	0/43
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.2)	(0.0, 4.2)	(0.0, 4.7)	(0.0, 8.2)
Hyperopic Astigmatism: Safety Cohort		**1 Month**	**3 Months**	**6 Months**	**9 Months**
Loss of >2 Lines BSCVA	n/N	3/256	1/256	0/241	0/115
	%	1.2%	0.4%	0.0%	0.0%
	CI	(0.2, 3.4)	(0.0, 2.2)	(0.0, 1.5)	(0.0, 3.2)
Loss of 2 Lines BSCVA	n/N	12/256	3/256	2/241	4/115
	%	4.7%	1.2%	0.8%	3.5%
	CI	(2.4, 8.0)	(0.2, 3.4)	(0.1, 3.0)	(1.0, 8.7)
BSCVA worse than 20/40	n/N	1/256	1/256	0/241	0/115
	%	0.4%	0.4%	0.0%	0.0%
	CI	(0.0, 2.2)	(0.0, 2.2)	(0.0, 1.5)	(0.0, 3.2)
Increase >2D cylinder magnitude	n/N	0/256	0/256	0/241	0/115
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 1.4)	(0.0, 1.4)	(0.0, 1.5)	(0.0, 3.2)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	3/230	0/230	1/218	2/105
	%	1.3%	0.0%	0.5%	1.9%
	CI	(0.3, 3.8)	(0.0, 1.6)	(0.0, 2.5)	(0.2, 6.7)

BSCVA = Best Spectacle Corrected Visual Acuity CI = 95% Confidence Interval D = Diopter

Table 15. Summary of Key Safety Parameters at 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

All Eyes: Safety Cohort		0.0 to 0.99D	1.0 to 1.99D	2.0 to 2.99D	3.0 to 3.99D	4.0 to 5.0D	>5.0 to 6.0D	Total
Loss of >2 Lines BSCVA	n/N %	0/28 0.0%	0/117 0.0%	0/87 0.0%	0/44 0.0%	0/37 0.0%	0/7 0.0%	0/320 0.0%
Loss of 2 Lines BSCVA	n/N %	0/28 0.0%	1/117 0.9%	0/87 0.0%	1/44 2.3%	0/37 0.0%	1/7 14.3%	3/320 0.9%
BSCVA worse than 20/40	n/N %	0/28 0.0%	0/117 0.0%	0/87 0.0%	0/44 0.0%	0/37 0.0%	0/7 0.0%	0/320 0.0%
Increase >2D cylinder magnitude	n/N %	0/28 0.0%	0/117 0.0%	0/87 0.0%	0/44 0.0%	0/37 0.0%	0/7 0.0%	0/320 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperative	n/N %	0/27 0.0%	0/113 0.0%	0/82 0.0%	0/38 0.0%	0/29 0.0%	1/5 20.0%	1/294 0.3%
Spherical Hyperopia: Safety Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**>5.0 to 6.0D**	**Total**
Loss of >2 Lines BSCVA	n/N %	0/6 0.0%	0/29 0.0%	0/25 0.0%	0/7 0.0%	0/12 0.0%	--	0/79 0.0%
Loss of 2 Lines BSCVA	n/N %	0/6 0.0%	0/29 0.0%	0/25 0.0%	1/7 14.3%	0/12 0.0%	--	1/79 1.3%
BSCVA worse than 20/40	n/N %	0/6 0.0%	0/29 0.0%	0/25 0.0%	0/7 0.0%	0/12 0.0%	--	0/79 0.0%
Increase >2D cylinder magnitude	n/N %	0/6 0.0%	0/29 0.0%	0/25 0.0%	0/7 0.0%	0/12 0.0%	--	0/79 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperative	n/N %	0/6 0.0%	0/27 0.0%	0/25 0.0%	0/7 0.0%	0/11 0.0%	--	0/76 0.0%
Hyperopic Astigmatism: Safety Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**>5.0 to 6.0D**	**Total**
Loss of >2 Lines BSCVA	n/N %	0/22 0.0%	0/88 0.0%	0/62 0.0%	0/37 0.0%	0/25 0.0%	0/7 0.0%	0/241 0.0%
Loss of 2 Lines BSCVA	n/N %	0/22 0.0%	1/88 1.1%	0/62 0.0%	0/37 0.0%	0/25 0.0%	1/7 14.3%	2/241 0.8%
BSCVA worse than 20/40	n/N %	0/22 0.0%	0/88 0.0%	0/62 0.0%	0/37 0.0%	0/25 0.0%	0/7 0.0%	0/241 0.0%
Increase >2D cylinder magnitude	n/N %	0/22 0.0%	0/88 0.0%	0/62 0.0%	0/37 0.0%	0/25 0.0%	0/7 0.0%	0/241 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperative	n/N %	0/21 0.0%	0/86 0.0%	0/57 0.0%	0/31 0.0%	0/18 0.0%	1/5 20.0%	1/218 0.5%

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

6. Comparison of Postoperative Uncorrected Visual Acuity and Preoperative Best Spectacle Corrected Visual Acuity

A comparison of **postoperative** uncorrected visual acuity (UCVA) to **preoperative** best spectacle corrected visual acuity (BSCVA) after CustomCornea® LASIK surgery is presented in Table 16 with differences based on lines of visual acuity. A postoperative UCVA equal to or better than the preoperative BSCVA was achieved in 41.7% of eyes at 6 months.

Table 16. Postoperative Uncorrected Visual Acuity Compared to Preoperative Best Spectacle Corrected Visual Acuity

		1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
UCVA **2 Lines Better** Than Preop BSCVA	n/N %	0/297 0.0%	1/297 0.3%	0/276 0.0%	0/138 0.0%
UCVA **1 Line Better** Than Preop BSCVA	n/N %	18/297 6.1%	28/297 9.4%	24/276 8.7%	13/138 9.4%
UCVA **Equal** to Preop BSCVA	n/N %	93/297 31.3%	86/297 29.0%	91/276 33.0%	49/138 35.5%
UCVA **1 Line Worse** Than Preop BSCVA	n/N %	88/297 29.6%	90/297 30.3%	80/276 29.0%	32/138 23.2%
UCVA **2 Lines Worse** Than Preop BSCVA	n/N %	54/297 18.2%	43/297 14.5%	34/276 12.3%	21/138 15.2%
UCVA **>2 Lines Worse** Than Preop BSCVA	n/N %	44/297 14.8%	49/297 16.5%	47/276 17.0%	23/138 16.7%

UCVA = Uncorrected Visual Acuity BSCVA = Best Spectacle Corrected Visual Acuity

Equal visual acuity is within 2 or 3 letters on the same line of a visual acuity chart

7. Stability of Manifest Refraction

The mean MRSE for the Primary Effectiveness Cohort was stable between 3 and 6 months, as shown in Figure 1 and Table 17.

Figure 1. Manifest Refraction Spherical Equivalent Over Time

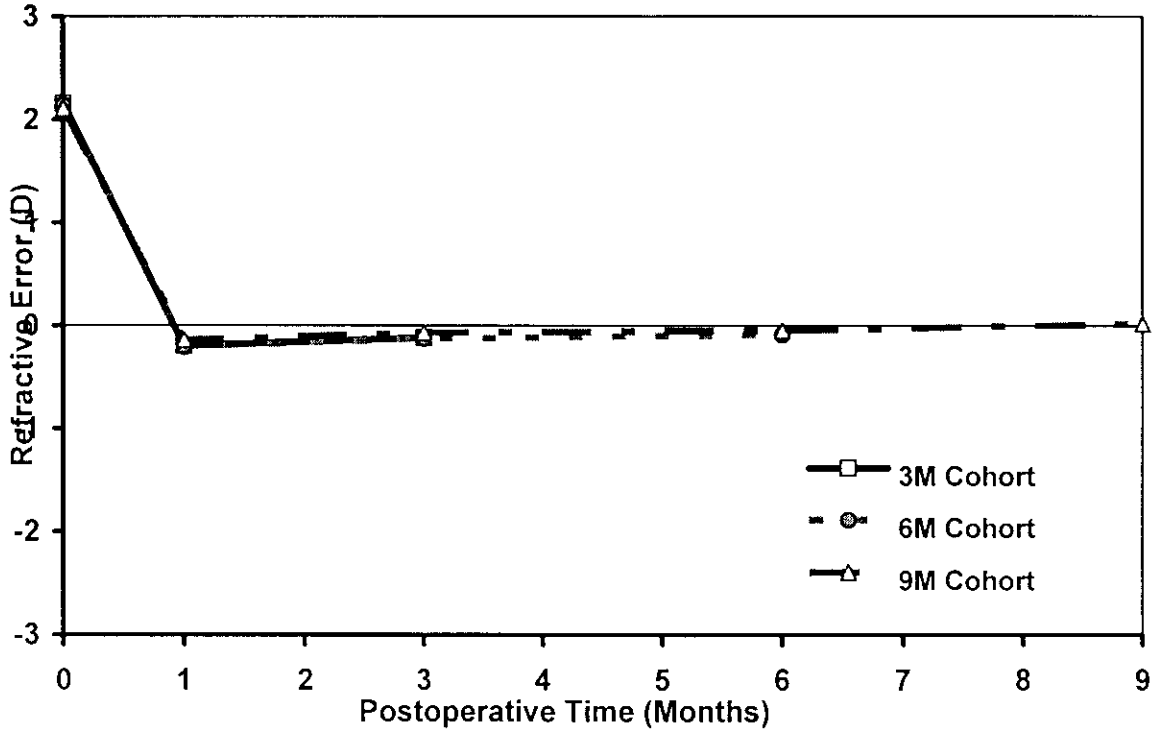


Table 17. Manifest Refraction Spherical Equivalent Over Time

Mean ± SD (95% CI)	n	PREOP	1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
3-Month Cohort	297	2.16 ± 1.07 (2.04, 2.28)	-0.20 ± 0.68 (-0.28, -0.13)	-0.12 ± 0.69 (-0.20, -0.04)	--	--
6-Month Cohort	276	2.14 ± 1.07 (2.01, 2.26)	-0.21 ± 0.69 (-0.30, -0.13)	-0.13 ± 0.71 (-0.21, -0.04)	-0.09 ± 0.69 (-0.17, -0.01)	--
9-Month Cohort	138	2.11 ± 0.99 (1.94, 2.27)	-0.14 ± 0.59 (-0.24, -0.05)	-0.07 ± 0.65 (-0.18, 0.03)	-0.05 ± 0.62 (-0.15, 0.05)	0.02 ± 0.66 (-0.09, 0.13)

SD = Standard Deviation 95% CI = 95% Confidence Interval

Stability of MRSE was analyzed as paired differences in MRSE between 1 and 3 months, between 3 and 6 months, and between 6 and 9 months. Analyses were performed for the entire Primary Effectiveness Cohort with data available at any interval and for consistent cohorts with data available at each interval over time (Table 18).

The data meet the FDA guidance document criterion of at least 95% having a change in MRSE of ≤ 1.00D between all intervals. Refractive stability was reached between 3 and 6 months with 99.6% of the eyes demonstrating a change ≤ 1.00D of MRSE; a mean change in MRSE of 0.04D ± 0.29D between 3 and 6 months with a rate of 0.01D per month; a decrease in the mean change in MRSE from 1 month to 6 months; and a 95% confidence interval (0.00, 0.07) that includes zero for the mean change between 3 and 6 months. Stability was confirmed between 6 and 9 months.

Table 18. Stability of Manifest Refraction Spherical Equivalent

Entire Cohort	**Change in MRSE Between**		**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D	n/N %	294/297 99.0%	275/276 99.6%	137/138 99.3%
	Mean ± SD Change		0.09 ± 0.33	0.04 ± 0.29	0.07 ± 0.32
	95% Confidence Interval		(0.05, 0.13)	(0.00, 0.07)	(0.01, 0.12)
	Mean Change per Month		0.04	0.01	0.02
6-Month Cohort	**Change in MRSE Between**		**1 and 3 Months**	**3 and 6 Months**	
	≤ 1.00D	n/N %	274/276 99.3%	275/276 99.6%	
	Mean ± SD Change		0.09 ± 0.32	0.04 ± 0.29	
	95% Confidence Interval		(0.05, 0.13)	(0.00, 0.07)	
	Mean Change per Month		0.04	0.01	
9-Month Cohort	**Change in MRSE Between**		**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D	n/N %	137/138 99.3%	137/138 99.3%	137/138 99.3%
	Mean ± SD Change		0.07 ± 0.31	0.02 ± 0.29	0.07 ± 0.32
	95% Confidence Interval		(0.02, 0.12)	(-0.02, 0.07)	(0.01, 0.12)
	Mean Change per Month		0.03	0.008	0.02

MRSE = Manifest Refraction Spherical Equivalent SD = Standard Deviation

8. Effectiveness of Astigmatic Correction

Effectiveness of astigmatic correction was evaluated at the 6-month point of stability for hyperopic astigmatic eyes. The mean percentage reduction in absolute manifest cylinder was 53.3% for all eyes with a greater percentage reduction in eyes with higher preoperative cylinder (Table 19). The mean correction ratio based on vector analysis of manifest cylinder was 1.13 for all astigmatic eyes and approximately 1.00 for eyes with -1.00D to -3.00D preoperative manifest cylinder (Table 20). Astigmatic correction by cycloplegic cylinder reflected similar trends to manifest cylinder.

Table 19. Mean Percentage Reduction of Absolute (Non-Vector) Cylinder for Hyperopic Astigmatic Eyes

6 MONTHS				
Preoperative Cylinder	Manifest Cylinder		Cycloplegic Cylinder	
	N	Mean %	N	Mean %
All	198	53.3%	200	53.5%
>0.00 to < 0.50D *	7	0.0%	0	--
0.50 to < 1.00D	106	45.4%	110	41.2%
1.00 to < 2.00D	61	64.7%	67	65.6%
2.00 to 3.00D	24	74.8%	23	77.1%

* By preoperative manifest refraction, two eyes had no cylinder and seven eyes had -0.25D cylinder; by preoperative cycloplegic refraction, these 9 eyes had -0.50D or -0.75D cylinder.

Table 20. Vector Analysis for Hyperopic Astigmatic Eyes

6 MONTHS				
Preoperative Cylinder	Manifest Cylinder		Cycloplegic Cylinder	
	N	Mean ± SD Correction Ratio	N	Mean ± SD Correction Ratio
ALL	198	1.13 ± 0.57	200	1.12 ± 0.47
>0.00 to < 0.50D *	7	2.39 ± 1.44	0	--
0.50 to < 1.00D	106	1.15 ± 0.56	110	1.20 ± 0.57
1.00 to < 2.00D	61	1.00 ± 0.31	67	1.02 ± 0.32
2.00 to 3.00D	24	0.99 ± 0.18	23	1.00 ± 0.14

* By preoperative manifest refraction, two eyes had no cylinder and seven eyes had -0.25D cylinder; by preoperative cycloplegic refraction, these 9 eyes had -0.50D or -0.75D cylinder.

9. Change in Best Spectacle Corrected Visual Acuity

Best spectacle corrected visual acuity (BSCVA) was measured using a standard (high-contrast) visual acuity chart under dim room illumination (10-12 cd/m^2). All eyes had a BSCVA of 20/32 or better at 6 months. At least 73.7% of eyes at all postoperative intervals and 81.6% of eyes at 6 months had no change or a gain in BSCVA from preoperative (Table 21).

Table 21. Change in Best Spectacle Corrected Visual Acuity

		1 Month	3 Months	6 Months	9 Months
Decrease >2 Lines	n/N	3/346	1/346	0/320	0/161
	%	0.9%	0.3%	0.0%	0.0%
Decrease 2 Lines	n/N	16/346	6/346	3/320	5/161
	%	4.6%	1.7%	0.9%	3.1%
Decrease 1 Line	n/N	72/346	63/346	56/320	16/161
	%	20.8%	18.2%	17.5%	9.9%
No change	n/N	185/346	184/346	183/320	88/161
	%	53.5%	53.2%	57.2%	54.7%
Increase 1 Line	n/N	66/346	89/346	77/320	50/161
	%	19.1%	25.7%	24.1%	31.1%
Increase 2 Lines	n/N	4/346	3/346	1/320	2/161
	%	1.2%	0.9%	0.3%	1.2%
Increase >2 Lines	n/N	0/346	0/346	0/320	0/161
	%	0.0%	0.0%	0.0%	0.0%

Low contrast BSCVA was measured using a 10% low contrast visual acuity chart under dim room illumination. While 38.1% of eyes had no change in low contrast BSCVA from preoperative to 6 months, Table 22 shows slightly more eyes had a gain than loss of 1 line (25.6% vs. 22.8%) and of ≥ 2 lines (7.8% vs. 5.6%).

Table 22. Change in Low Contrast Best Spectacle Corrected Visual Acuity

		3 Months	6 Months
Decrease >2 Lines	n/N	13/346	7/320
	%	3.8%	2.2%
Decrease 2 Lines	n/N	19/346	11/320
	%	5.5%	3.4%
Decrease 1 Line	n/N	71/346	73/320
	%	20.5%	22.8%
No change	n/N	136/346	122/320
	%	39.3%	38.1%
Increase 1 Line	n/N	80/346	82/320
	%	23.1%	25.6%
Increase 2 Lines	n/N	25/346	22/320
	%	7.2%	6.9%
Increase >2 Lines	n/N	2/346	3/320
	%	0.6%	0.9%

10. Change in Contrast Sensitivity

Contrast sensitivity was measured under both photopic and mesopic conditions using the CSV-1000 (VectorVision[9]) (Table 23). A clinically significant change from preoperative level was defined as > 2 levels (> 0.3 log) at two or more spatial frequencies.

Under photopic conditions, the majority of eyes (85.3%) did not have a clinically significant change from preoperative to 6 months. The percentage of eyes with a clinically significant gain or loss of photopic contrast sensitivity was approximately equal (7.2% vs. 7.5%). Under mesopic conditions, 67.0% of subjects had no clinically significant change. A clinically significant gain was observed in 20.1% of eyes at 6 months, while a loss was observed in 12.9% of eyes, showing a trend for more gain than loss under mesopic conditions.

In addition, the mean log at each spatial frequency was compared for eyes with data at preop, 3 months and 6 months (consistent 6-month cohort, Table 24). The data reflect a mean gain in all spatial frequencies postoperatively under photopic and mesopic conditions. Statistically significant gains were noted at 6 months for all photopic spatial frequencies and for all mesopic spatial frequencies except 6 cycles per degree (cpd).

Table 23. Change of >2 Levels (> 0.3 Log) at 2 or More Spatial Frequencies

		Photopic		Mesopic*	
		3 MONTHS	6 MONTHS	3 MONTHS	6 MONTHS
Loss	n/N	25/344	24/319	52/327	40/309
	%	7.3%	7.5%	15.9%	12.9%
No Change	n/N	282/344	272/319	198/327	207/309
	%	82.0%	85.3%	60.6%	67.0%
Gain	n/N	37/344	23/319	77/327	62/309
	%	10.8%	7.2%	23.5%	20.1%

*Mesopic illumination with neutral density filters in front of eyes

Table 24. Comparison of Mean Contrast Sensitivity Log by Spatial Frequency: 6-Month Consistent Cohort

Spatial Frequency (cpd)	Preop Mean ± SD	3-Month Mean ± SD	p-value†	6-Month Mean ± SD	p-value†
Photopic	**N=317**	**N=317**		**N=317**	
3	1.70 ± 0.17	1.73 ± 0.18	**0.008**	1.76 ± 0.17	**<0.0001**
6	1.91 ± 0.18	1.94 ± 0.24	**0.042**	1.94 ± 0.21	**0.019**
12	1.53 ± 0.26	1.56 ± 0.29	0.149	1.57 ± 0.29	**0.023**
18	1.04 ± 0.29	1.06 ± 0.31	0.220	1.09 ± 0.29	**0.004**
Mesopic	**N=305**	**N=305**		**N=305**	
3	1.48 ± 0.23	1.54 ± 0.24	**<0.0001**	1.52 ± 0.22	**0.004**
6	1.49 ± 0.28	1.51 ± 0.31	0.372	1.52 ± 0.30	0.211
12	0.89 ± 0.33	0.93 ± 0.38	0.052	0.93 ± 0.37	**0.048**
18	0.34 ± 0.35	0.38 ± 0.40	0.097	0.40 ± 0.36	**0.008**

† p-value from paired t-test of differences between preoperative and postoperative means; p<0.05 is statistically significant, shown in bold

[9] *VectorVision* TM of Brain Lab AG

11. Patient Self-Evaluation

Patients were asked to rate symptoms without glasses or contact lenses after surgery as compared to their recollection of symptoms before surgery, as shown in Table 25.

Table 25. Postoperative Change in Subjective Symptoms without Correction vs. Preoperative

6 MONTHS						
Comfort Symptoms	**N**	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	276	9.4%	6.5%	79.3%	4.7%	0.0%
Dryness	276	9.1%	8.3%	58.0%	23.6%	1.1%
Excessive Tearing	274	4.0%	6.6%	85.8%	3.6%	0.0%
Gritty Feeling	276	6.9%	4.3%	78.3%	9.8%	0.7%
Headache	275	10.2%	10.2%	75.3%	4.4%	0.0%
Light Sensitivity	275	5.5%	16.4%	54.2%	20.0%	4.0%
Pain	276	7.2%	3.6%	85.1%	4.0%	0.0%
Redness	276	7.2%	7.2%	76.4%	8.3%	0.7%
Visual Symptoms						
Blurring of Vision	276	14.1%	16.3%	51.4%	15.2%	2.9%
Double Vision	276	7.2%	3.3%	76.1%	10.5%	2.9%
Fluctuation of Vision	276	6.9%	15.2%	56.2%	17.8%	4.0%
Glare	276	8.3%	12.3%	58.3%	18.5%	2.5%
Halos	275	9.1%	5.1%	70.2%	12.0%	3.6%
Night Driving Difficulty	276	17.0%	23.2%	46.4%	10.5%	2.9%

* Based on the patients' comparison of symptom severity after surgery to their recollection of symptom severity before surgery.

Uncorrected quality of vision at 6 months was unchanged, better or significantly better than preoperative quality of vision in 92.8% of patients, worse in 6.5%, and significantly worse in 0.7% (Table 26). In addition, 79.7% of patients were extremely satisfied or satisfied, 12.0% were not sure, 5.4% were unsatisfied and 2.9% were extremely unsatisfied with surgery results at 6 months (Table 27). At 6 months, 85.5% of patients reported never wearing any distance correction (Table 28).

Table 26. Postoperative Quality of Vision without Correction vs. Preoperative

6 MONTHS N=276	
Significantly Better	56.9%
Better	30.8%
Same	5.1%
Worse	6.5%
Significantly Worse	0.7%

Table 27. Postoperative Satisfaction with Surgery

6 MONTHS N=276	
Extremely Satisfied	47.8%
Satisfied	31.9%
Not Sure	12.0%
Unsatisfied	5.4%
Extremely Unsatisfied	2.9%

Table 28. Postoperative Frequency of Distance Correction

6 MONTHS N=276	
Never	85.5%
Seldom	7.6%
Frequently	2.2%
Constantly	4.7%

A small group of 42 patients received randomized treatment of CustomCornea® LASIK in one eye and Conventional LASIK in the other eye. These patients rated postoperative eye preference **without** glasses or contact lenses for quality of vision during the day and at night, less glare or night driving difficulty and overall eye preference (Table 29).

Table 29. Postoperative Eye Preference Without Glasses or Contact Lens Correction: Contralateral Cohort

Visit		CustomCornea® Eye	Same (No Preference)	Conventional Eye
3 Months (N=42)	Quality of Vision During the Day	40.5%	38.1%	21.4%
	Quality of Vision At Night	33.3%	52.4%	14.3%
	Less Glare or Night Driving Difficulty	14.3%	78.6%	7.1%
	Overall Eye Preference	42.9%	38.1%	19.0%
6 Months (N=41)	Quality of Vision During the Day	31.7%	46.3%	22.0%
	Quality of Vision At Night	31.7%	51.2%	17.1%
	Less Glare or Night Driving Difficulty	14.6%	75.6%	9.8%
	Overall Eye Preference	29.3%	51.2%	19.5%
9 Months (N=41)	Quality of Vision During the Day	29.3%	58.5%	12.2%
	Quality of Vision At Night	26.8%	61.0%	12.2%
	Less Glare or Night Driving Difficulty	12.2%	80.5%	7.3%
	Overall Eye Preference*	22.5%	55.0%	22.5%

* N=40 for Overall Eye Preference at 9 months

12. Retreatment

There are insufficient data for retreatment to establish safety and effectiveness.

13. Wavefront Outcomes

At 6 months, there was an average reduction in total RMS wavefront error by 63.9% and an average increase in higher-order aberrations by 23.6% from preoperative for all eyes in the Primary Effectiveness Cohort with data available at 6 months (N=261). Table 30 displays the preoperative and 6-month total wavefront error and higher-order aberrations through 6th order for eyes with data at preoperative, 1, 3 and 6 months (6-month consistent cohort; N=256). Spherical aberration decreased in magnitude at 6 months from preoperative with a mean directional shift from positive spherical aberration (0.249µm) preoperatively towards negative spherical aberration (-0.147µm) postoperatively, as expected from a hyperopic ablation profile.

Table 30. Mean Aberrations Up to 6th Order: 6-Month Consistent Cohort

Aberration (µm)	PREOP N = 256	6 MONTHS N = 256
Total RMS Error	2.677	1.000
Higher-Order	0.460	0.554
Coma	0.237	0.343
Trefoil	0.203	0.214
Spherical Aberration Magnitude*	0.249	0.219
Spherical Aberration Value**	0.249	-0.147
Secondary Astigmatism	0.072	0.111
Tetrafoil	0.080	0.120
Combined 5th and 6th Order	0.082	0.125

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Average based on the absolute spherical aberration magnitude

** Average based on the signed spherical aberration, reflecting a *positive* or *negative* direction

At 6 months, 99.6% of all eyes had a reduction in total RMS and 49.0% had a reduction in higher-order aberrations from preoperative, as shown in Table 31.

Table 31. Percentage of Eyes with Reduced Aberrations Up to 6th Order From Preoperative

6 MONTHS N = 261	
Aberration	**% Eyes with Reduction in Aberrations**
Total RMS Error	99.6%
Higher-Order	49.0%
Coma	38.7%
Trefoil	47.9%
Spherical Aberration Magnitude*	61.7%
Secondary Astigmatism	29.5%
Tetrafoil	31.0%
Combined 5th and 6th Order	21.8%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Reduction in absolute spherical aberration magnitude

Wavefront-guided CustomCornea® LASIK was compared to the baseline established for Conventional LASIK using preoperative cycloplegic phoropter refraction treated under the same study protocol. Wavefront aberrations at 6 months were analyzed up to 4th-order for comparison.

In a Comparison Cohort, CustomCornea® and Conventional eyes were analyzed over the same preoperative refractive range of +0.75D to +4.25D sphere, up to -3.00D cylinder and up to +4.00D SE. Compared to Conventional eyes, CustomCornea® eyes showed statistically significantly lower mean amplitudes of total root mean square (RMS), higher-order aberrations, coma, and trefoil postoperatively with adjustment of baseline differences (ANCOVA, $p<0.05$). Table 32 shows that on average, CustomCornea® LASIK resulted in a greater mean reduction in total RMS error (62.3% vs. 46.1%) and less induction of higher-order aberrations (8.0% vs. 29.2%) from preoperative compared to Conventional LASIK. On average, both CustomCornea® and Conventional eyes showed a mean directional shift from positive spherical aberration preoperatively towards negative spherical aberration postoperatively, which was not statistically significant between the treatment groups.

Table 32. Mean Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Comparison Cohort

Aberration (µm)	PREOP		6 MONTHS		p-Value†
	CustomCornea® Eyes N = 258	Conventional All Eyes N = 95	CustomCornea® Eyes N = 229	Conventional All Eyes N = 94	
Total RMS Error	2.350	2.424	0.887	1.307	**<0.0001**
Higher-Order	0.451	0.497	0.487	0.642	**<0.0001**
Coma	0.236	0.264	0.307	0.402	**0.0061**
Trefoil	0.204	0.217	0.206	0.322	**<0.0001**
Spherical Aberration Magnitude*	0.251	0.276	0.188	0.201	0.3298
Spherical Aberration Value**	0.250	0.275	-0.108	-0.127	0.1325
Secondary Astigmatism	0.071	0.086	0.106	0.122	0.2566
Tetrafoil	0.081	0.098	0.119	0.159	**0.0045**

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Average based on the absolute spherical aberration magnitude

** Average based on the signed spherical aberration, reflecting a *positive* or *negative* direction

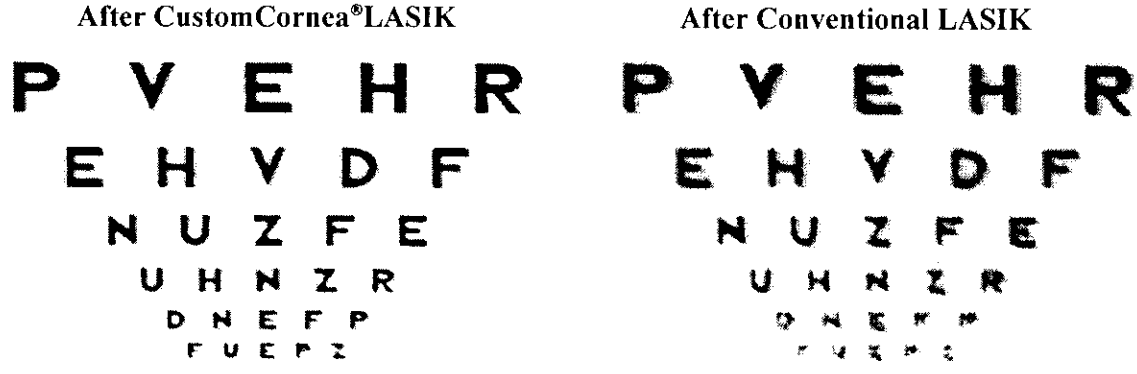
† ANCOVA for postoperative comparison between treatment types, adjusting for preoperative aberration differences; $p<0.05$ is statistically significant, shown in bold

A vision simulation program was used to model the effect of mean higher-order aberration magnitudes at 6 months after CustomCornea® LASIK versus Conventional LASIK in the Comparison Cohort. The difference in image blurring is comparable to a defocus error difference of approximately one tenth of a diopter (i.e., ~0.1D for the CustomCornea® simulation and ~0.2D for the Conventional simulation).

The following charts (Figure 2) provide an illustration of the appearance of the visual acuity chart with glasses or contact lenses after surgery. The charts show the difference in higher-order aberrations present in the eye after CustomCornea® LASIK (left chart) and after Conventional LASIK (right chart).

DO NOT REPRODUCE THE CHARTS BELOW

Figure 2. Simulated chart images for the average higher-order aberrations at 6 months after wavefront-guided surgery compared to after conventional surgery, based on wavefront over a 6 mm diameter pupil.



The percentage of patients with reduced higher-order aberrations was 55.9% for CustomCornea® LASIK compared to 33.0% for Conventional LASIK (Table 33).

Table 33. Percentage of Eyes with Reduced Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Comparison Cohort

6 MONTHS		
Aberration	**CustomCornea® Eyes** N = 229	**All Conventional Eyes** N = 94
Total RMS Error	99.6%	89.4%
Higher-Order	55.9%	33.0%
Coma	42.4%	26.6%
Trefoil	49.8%	27.7%
Spherical Aberration Magnitude*	67.7%	68.1%
Secondary Astigmatism	31.4%	41.5%
Tetrafoil	32.3%	30.9%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Reduction in absolute spherical aberration magnitude

To further evaluate the treatment types, a subgroup of subjects who underwent contralateral treatment of CustomCornea® LASIK in the primary eye and Conventional LASIK in the fellow eye was analyzed. This Contralateral Cohort had a preoperative cycloplegic refractive range of +0.75D to +4.25D sphere, up to -2.25D cylinder and up to +3.88D SE. Compared to Conventional eyes, CustomCornea® eyes in the Contralateral Cohort showed statistically significantly lower mean amplitudes of total RMS, higher-order aberrations, and trefoil postoperatively (ANCOVA, $p<0.05$).

Table 34 shows that on average, CustomCornea® LASIK resulted in a greater mean reduction in total RMS error (62.2% vs. 51.2%) and less induction in higher-order aberrations (5.2% vs. 20.7%) from preoperative compared to Conventional LASIK. On average, both CustomCornea® and Conventional eyes showed a mean directional shift from positive spherical aberration preoperatively towards negative spherical aberration postoperatively, which was not statistically significant between the treatment groups.

Table 34. Mean Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Contralateral Cohort

Aberration (µm)	PREOP		6 MONTHS		p-Value†
	CustomCornea® Eyes N = 42	Conventional Fellow Eyes N = 42	CustomCornea® Eyes N = 41	Conventional Fellow Eyes N = 41	
Total RMS Error	2.127	2.178	0.803	1.062	**0.0012**
Higher-Order	0.420	0.445	0.442	0.537	**0.0089**
Coma	0.210	0.267	0.269	0.318	0.1663
Trefoil	0.201	0.192	0.203	0.249	**0.0389**
Spherical Aberration Magnitude*	0.239	0.226	0.180	0.213	0.3158
Spherical Aberration Value**	0.237	0.223	-0.102	-0.182	0.0590
Secondary Astigmatism	0.056	0.079	0.078	0.084	0.7101
Tetrafoil	0.074	0.081	0.122	0.132	0.6563

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Average based on the absolute spherical aberration magnitude

** Average based on the signed spherical aberration, reflecting a *positive* or *negative* direction

† ANCOVA for postoperative comparison between treatment types, adjusting for preoperative aberration differences. $p<0.05$ is statistically significant, shown in bold

The percentage of subjects in the Contralateral Cohort with reduced higher-order aberrations was 46.3% for CustomCornea® LASIK compared to 36.6% for Conventional LASIK (Table 35).

Table 35. Percentage of Eyes with Reduced Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Contralateral Cohort

	6 MONTHS	
Aberration	CustomCornea® Eyes N = 41	Conventional Fellow Eyes N = 41
Total RMS Error	100.0%	90.2%
Higher-Order	46.3%	36.6%
Coma	43.9%	36.6%
Trefoil	46.3%	36.6%
Spherical Aberration Magnitude*	63.4%	58.5%
Secondary Astigmatism	29.3%	43.9%
Tetrafoil	26.8%	36.6%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Reduction in absolute spherical aberration magnitude

14. Statistical Analysis Outcomes

Statistical analysis was performed to assess for potential associations between demographic and baseline characteristics and clinical outcomes. Demographic and baseline characteristics that were considered to have the most potential for clinical relevance to the procedure included age, gender, race, preoperative cycloplegic sphere, cylinder and CRSE, operative room humidity and temperature. Outcomes evaluated at refractive stability (6 months) included loss of BSCVA, UCVA and accuracy of MRSE.

One-sided exact binomial tests (α=0.05) were used to compare the observed overall rates of safety and effectiveness outcomes to the FDA Guidance document targets. There was no BSCVA loss of > 2 lines at 6 months, thereby meeting the FDA target rate of < 5% of eyes for safety. FDA effectiveness targets were met or exceeded for all effectiveness outcomes, including UCVA 20/40 or better and accuracy of MRSE within 0.50D and within 1.00D of emmetropia at 6 months. For each demographic and baseline subcategory, the observed rate either met the target or the 95% confidence interval contained the FDA target value for effectiveness.

To assess the consistency of outcomes across demographic and baseline subcategories, differences in rates among the subcategories were assessed using the Cochran-Mantel-Haenszel (CMH) test. A p-value of < 0.05 indicates statistically significant differences between demographic and baseline categories. For a loss of 2 or more lines of BSCVA at 6 months, no statistically significant differences among the demographic and baseline categories were found.

Statistically significant differences in the rates of subjects achieving a UCVA of 20/20 or better at 6 months were noted based on room temperature (p=0.0160), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). Eyes treated in a lower room temperature and eyes with lower preoperative cycloplegic sphere or lower preoperative CRSE were more likely to achieve a UCVA of 20/20 or better. No FDA target is established for UCVA 20/20 or better.

For the outcome of UCVA 20/40 or better at 6 months, statistically significant differences in the rates of subjects were observed for preoperative cycloplegic sphere (p=0.0005), cylinder (p=0.0054), and CRSE (p=0.0031). Subjects with lower preoperative cycloplegic sphere, lower preoperative cycloplegic cylinder and lower preoperative CRSE were more likely to achieve a UCVA of 20/40 or better. However, all preoperative sphere, cylinder and CRSE subgroups met or exceeded the FDA target of ≥ 85% of eyes achieving a UCVA 20/40 or better at 6 months.

Baseline categories that showed statistically significant differences in the rates of subjects achieving an accuracy of MRSE within 0.50D of emmetropia were room humidity (p=0.0433), temperature (p=0.0480), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). While there was no consistent trend in MRSE based on room humidity, subjects treated in lower room temperature were more likely to have an MRSE within 0.50D at 6 months. Accuracy of MRSE within 0.50D was more likely in subjects with lower preoperative cycloplegic sphere and lower preoperative CRSE. In addition, all room humidity, temperature, preoperative sphere and preoperative CRSE subgroups met or exceeded the FDA target for MRSE within 0.50D at 6 months.

At 6 months, statistically significant differences were observed for an MRSE outcome within 1.00D based on room humidity (p=0.0113), age (p=0.0061), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). As noted for an MRSE within 0.50D, there was no consistent trend based on room humidity for MRSE within 1.00D and all humidity subgroups met or exceeded the FDA target. A higher percentage of older subjects were within 1.00D MRSE at 6 months compared to younger subjects; however, at least 75% of eyes within each age subgroup had an MRSE within 1.00D, meeting or exceeding the FDA target.

Preoperative latent hyperopia, particularly in younger subjects with greater accommodative reserve, may be a contributing factor to the postoperative MRSE outcome. All eyes enrolled were required to have a difference in preoperative cycloplegic and manifest sphere and cylinder of ≤ 1.00D. However, subjects with a difference between preoperative CRSE and MRSE of ≤ 0.50D were more likely to have an MRSE within 1.00D at 6 months compared to subjects with more than +0.50D of hyperopia by preoperative CRSE (p=0.0158). At 6 months, ≥ 75% of eyes with a difference of ≥ 0.50 or more than +0.50D had an MRSE within 1.00D, meeting or exceeding the FDA target.

Accuracy of MRSE within 1.00D was more likely in subjects with lower preoperative cycloplegic sphere and lower preoperative CRSE. For the +4.00D to +4.99D preoperative sphere range, 69.0% of eyes had an MRSE within 1.00D; however, the 95% confidence interval (52.9%, 82.4%) included the FDA target rate of at least 75% of eyes. All other preoperative sphere subcategories, including the highest sphere range of +5.00D to +6.00D, met or exceeded the FDA targets. For the +3.00D to +3.99D and +4.00D to +5.00D preoperative CRSE ranges, the observed rates for MRSE within 1.00D were 74.4% (57.9%, 87.0% CI) and 72.2% (54.8%, 85.8% CI), respectively, with 95% confidence intervals that included the FDA target. As noted for cycloplegic sphere, all other CRSE subcategories met or exceeded the FDA targets for accuracy of MRSE.

Similar associations were found between overcorrection of the MRSE by >1.00D at 6 months and baseline characteristics such as room humidity (p=0.0057), age (p=0.0001), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). Higher rates of overcorrection by more than 1.00D tended to occur in subjects treated in lower room humidity. Younger subjects, primarily less than 50 years of age, were more likely to be overcorrected than older subjects. Subjects with a difference of more than +0.50D between preoperative CRSE and MRSE were more likely to have MRSE overcorrection by more than 1.00D at 6 months (p=0.0004). Overcorrection was also more likely in subjects with higher preoperative cycloplegic sphere and CRSE.

Considering subjects who were undercorrected by more than 1.00D in MRSE at 6 months, statistically significant differences were noted for preoperative cycloplegic sphere (p=0.0281) and preoperative cycloplegic cylinder (p=0.0033). While undercorrection was more likely to occur in eyes with higher preoperative sphere, a trend for a greater percentage of eyes with overcorrection than undercorrection was observed with higher preoperative sphere. Higher rates of MRSE undercorrection were observed for subjects with more preoperative cylinder.

C. TRACKING EFFECTIVENESS

The LADARVision®4000 System incorporates the LADARTracker® active closed-loop tracking system, which compensates for eye movement during the ablation process. The measurement speed of the LADARTracker® system (4000 measures/second) allows for detection and compensation for saccadic (involuntary) eye movement.

Analysis of eye movement data gathered electronically during the surgical procedures of 554 eyes treated in a study[10] demonstrated that:

- All patients exhibit eye movement during surgery. The average eye motion, defined as the standard deviation in the eye position during the procedure, ranged from 0.04 mm to 1.16 mm, with a mean of 0.35 ± 0.19 mm.
- The LADARTracker® system was able to compensate for the eye movement, resulting in visual and refractive outcomes that were independent of the amplitude of the motion. Patients who had large eye movements during surgery had an equally effective visual acuity outcome as those patients with small eye movements during surgery.
- Computer simulations of surgeries, where the detected movements were not countered by active closed-loop eye tracking, demonstrate that uncompensated eye motion can increase corneal irregularities.
- Measurements of patients' visual acuity indicate that visual acuity tends to decrease with an increase in corneal irregularities.
- Active eye tracking with the LADARTracker® system improves the accuracy of corneal shaping.

[10] LADARVision® System study on PRK Myopia with Astigmatism (P970043)

5. PLANNING AND PROCEDURES

A. PATIENT SELECTION

In addition to the information listed in the indications, contraindications, warnings and precautions sections of this booklet, consideration should be given to the following in determining the appropriate patients for CustomCornea® LASIK:

- To obtain accurate refractive information, patients who are contact lens wearers must be examined after discontinuation of contact lens wear in both eyes for at least 2 to 3 weeks prior to the preoperative examination. Patients who wear RGP or PMMA lenses should have two examinations conducted 2 to 3 weeks apart which show stability of refraction without lens wear. Keratometry mires should be clear and regular on all eyes to exclude eyes with irregular astigmatism or corneal warpage.
- A complete baseline evaluation of patients requesting refractive surgery should be performed within 90 days of the CustomCornea® LASIK surgery.
- A complete preoperative examination should include but is not limited to: UCVA and BSCVA, manifest and cycloplegic refraction, ocular health examination, tonometry, topography, keratometry, pachymetry, wavefront measurement, and mesopic pupil size assessment. Evaluation for dry eye should be performed. Direct and indirect ophthalmoscopy through a dilated pupil are essential.
- Evaluation of the optic nerve and measurement of IOP are necessary. If there are any concerns regarding the appearance of the optic nerve, a threshold test of the visual field should be performed. If elevated pressure and/or incidence of glaucomatous damage are found, topical steroids should only be used with careful medical supervision or the patient should not undergo LASIK surgery.
- Preoperative corneal topography is essential on all patients to exclude topographical abnormalities. This is especially important when asymmetric astigmatism or steep keratometry readings are present, which may indicate keratoconus or other irregularities.
- Central pachymetry must be performed preoperatively to assess corneal thickness. The combination of the planned corneal flap thickness and the ablation depth are subtracted from the pachymetry to ensure a minimum of 250 microns in the posterior stroma remains after surgery.
- A clear and complete wavefront image must be obtained prior to surgery. Presence of media opacity, such as opacification of the crystalline lens, may not allow for a clear and complete wavefront image. The crystalline lens must be evaluated to ensure that nuclear sclerosis or other lens opacity is not present prior to LASIK surgery.
- Agreement between manifest refraction and the wavefront measurement should be within 1D. Differences of >1D should be investigated. It is essential that the refractive information upon which this surgical procedure depends on is accurate and is correctly transmitted to the laser. **It is the sole responsibility of the operating doctor to ensure the information for each individual patient is accurate.**

- The patient should have the ability to tolerate local or topical anesthesia and drops to dilate the pupil. A pupil dilation of at least 7mm to 11mm is required for surgery to proceed. During preoperative procedures that involve dilation of the pupil, it is important to assess that the minimum amount of dilation is achievable.
- The patient should have the ability to lie flat without difficulty.
- The patient should be able to fixate steadily and accurately for the duration of the CustomCornea® LASIK procedure.
- The patient must be able to understand and give an informed consent.
- Patients should be clearly informed of all alternatives for the correction of their hyperopia or hyperopic astigmatism, which include but are not limited to spectacles, contact lenses and other refractive surgeries.

B. OPERATIVE PROCEDURE

NOTE: Before proceeding, please refer to the LADARVision®4000 Excimer Laser System Operation Manual for complete instructions on use of the device.

Prior to surgery, patient details (name and medical record number) are entered into the LADARVision®4000 System and wavefront measurement device. After the wavefront measurement is taken with a compatible wavefront measurement device, such as the LADARWave® System, the surgeon reviews the planned wavefront-guided treatment and ablation depth and refines as indicated with the CustomCornea® Surgery Planning Software prior to the surgery session.

After completing the surgery planning tasks, the planned treatment file is transferred to the LADARVision®4000 System. Data transferred to the LADARVision®4000 System must contain: 1) patient information, including name, medical record number, and manifest refraction; 2) eye information, including right/left eye and the geometric relationship of the wavefront data to limbus and pupil center; and 3) wavefront information, including Zernike polynomial representation of the wavefront and physical radius of that description.

The majority of the surgical procedure is controlled by computer software. The doctor must position and align the patient's head and eye under the laser so that an image of the eye can be easily seen in the computer monitor. The view on the computer screen is the same field of view as through the operating microscope on low power.

The LADARVision®4000 System surgical procedure consists of four basic steps: (1) centration and registration, (2) pupil dilation, (3) laser calibration, and (4) ablation. Each step is summarized below.

1. Centration and Registration

The centration of the ablation zone is determined for the CustomCornea® treatment with the wavefront measurement device. The ablation zone is centered over the undilated pupil using reticules to determine the relative positions of the pupil and limbus. The positioning of the ablation zone is determined prior to pupil dilation (see Step 2) since the pupil center may shift during dilation. Since the position and size of the limbus do not change during pupil dilation, the limbal ring is used as a reference point for centration. The positioning of the pupil and limbal rings are then transferred to the LADARVision®4000 System.

Once the eye is dilated (see Step 2), the conjunctiva is manually marked using a marking pen at the 3 and 9 o'clock positions 1-2mm outside of the limbus. This is performed while the patient is sitting upright behind the slit lamp. These reference marks are used to register the position of the wavefront measurement to ensure the customized ablation pattern is applied in the same orientation as the wavefront measured by the wavefront measurement device and to account for cyclotorsion during ablation.

The wavefront measurements are then taken with the wavefront measurement device prior to proceeding to surgery with the LADARVision®4000 System. The wavefront measurements are aligned to the registration landmarks so that the wavefront information is rebuilt in exactly the desired position accounting for X, Y-axes and cyclotorsional position changes.

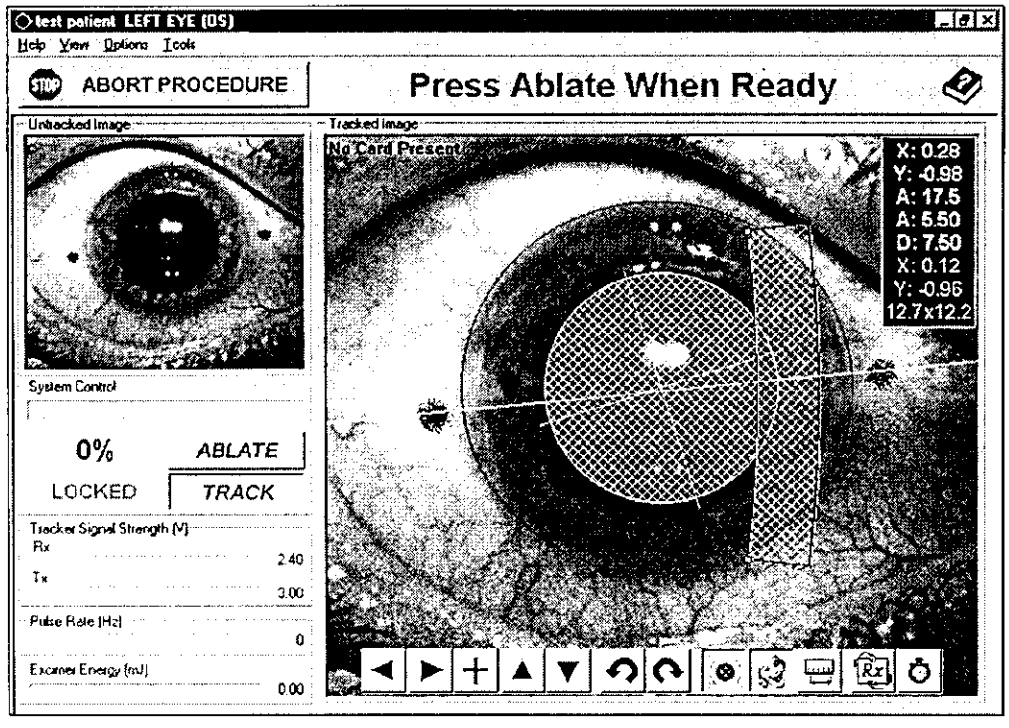
The surgeon reviews the diagnostic wavefront data and plans the wavefront-guided treatment using the CustomCornea® Surgery Planning Software. The planned treatment file is transferred to the LADARVision®4000 System computer by removable media, where the appropriate ablation laser shot pattern is generated. The system software is used at the laser to align to the registration information from the wavefront measurement device. Figure 3 shows the LADARVision®4000 System software display, which provides the ability to position the ablation in the exact location desired, identical to the orientation of the wavefront data. With the patient lying on the treatment bed just prior to surgery, the limbus ring is aligned to provide X and Y-axes information and the horizontal line is rotated to match the marks applied to the eye for cyclotorsion alignment.

2. Pupil Dilation

It is necessary to dilate the pupil to 7mm prior to surgery to engage the tracking system. A combination of 2.5% phenylephrine and 1% cyclopentolate are used. Approximately 45 minutes prior to the procedure, one drop of each mydriatic is instilled followed by a second drop 10 minutes later.

Figure 3. LADARVision®4000 System Software Display

The limbal ring provides for X and Y-axes registration, which is linked to the previously undilated designated pupil center (center of the cross). The horizontal line has been rotated to align with the ink marks to account for cyclotorsion. Also shown is the rectangular hatched area which can be used to protect the hinge from being ablated (Hinge Ablation Mask), and the circular hatched area which designates the ablation zone.



3. Laser Calibration

The laser system must be calibrated immediately before each surgical procedure in order for the treatment to be allowed. Three brief calibration steps are performed by the laser operator: Configure Laser, Geometry Adjust and Volume Per Shot.

Configure Laser is performed to set the laser energy for the procedure. Geometry Adjust ensures that the system is in alignment. Volume Per Shot adjusts the correction algorithm based on the level of laser energy.

These three calibration steps must be completed and within the safe operating parameters before the system will enable the laser to begin a surgery. Once the patient's information is recalled and verified to be correct by the surgeon, the ablation shot pattern is loaded and the laser is ready for activation.

4. Ablation

A sterile instrument tray is prepared for each patient. Starting approximately 15 minutes prior to surgery, one drop of topical anesthetic is administered to the operative eye every 5 minutes. The patient is brought into the laser room, positioned under the laser and a speculum is inserted. Prior to making the LASIK flap, the adequacy of pupil dilation is checked by testing the tracking system. Activation of the tracking system is initiated by engaging the "Track" button. If the tracking system cannot be activated, additional dilation time or stronger dilation agents are used.

The computer monitor displays two images of the patient's eye. A large screen displays the "tracked" image and a smaller screen displays the "untracked" image. The eye seen in the "tracked" image will appear to move normally until the tracking system is engaged, at which time the eye appears still. This image is used to align the registration software. The eye in the "untracked" screen is "live" and the eye will always be seen to move normally. This image is used to aid the doctor in maintaining the position of the patient's head during the procedure.

Once the tracking system is set, it is then disengaged and a LASIK flap is created using a microkeratome. The software allows the surgeon to check position of the ablation zone with respect to the flap by using an ablation zone indicator on the computer screen.

When the LASIK flap is folded back, the tracking system is re-activated and the position of the ablation zone is determined by recalling the geometry of the centration rings stored prior to dilation. The previously stored limbus ring is re-positioned so that the ablation occurs over the center of the undilated pupil. The marks on the eye are aligned with the horizontal reticule in the system software to compensate for cyclotorsion, ensuring that the customized ablation pattern is applied in the exact same orientation as the wavefront measured by the wavefront measurement device. An example of the LADARVision®4000 System software display is shown in Figure 3.

The plume removal system is positioned to remove the ablation effluent. The patient is reminded to fixate on the blinking LED target throughout the procedure. The laser operator then activates the "Ablate" button on the computer screen and the surgeon controls the application of the ablation pulses to the cornea via the footswitch. The laser will not fire without the tracking system being activated. At any time, the surgeon can interrupt the procedure (stop the laser from firing) by releasing the foot pedal. In an emergency situation, the laser operator can also interrupt by activating the appropriate button on the computer screen or on the control panel.

If at any time during the procedure the tracking system disengages, the laser will pause firing. This rarely occurs but is possible if the pupil is not visible to the tracking system such as if the eye becomes out of position, surgical instruments are inadvertently placed between the eye and the laser, or if the pupil constricts significantly during the procedure. In such a case, if the issue causing the pause can be resolved quickly, the tracking system will automatically re-engage and the procedure will continue from where it left off. If the cause for the tracking system interruption cannot be resolved quickly, the procedure can be continued from the last laser pulse fired after tracking and centration have been re-established.

At the end of the ablation, the laser system disengages the tracking system and displays the surgical parameters (including details of any interruption) on the computer screen.

C. POSTOPERATIVE PROCEDURE

Postoperative pharmaceutical treatment consists of one drop of a broad-spectrum antibiotic and one drop of a steroid administered at the end of surgery. The patients are given an antibiotic and steroid to be instilled 4 times a day for the first 7 days.

The subjects may be given oral analgesics as needed for pain control. Artificial tears may be prescribed for instillation of one drop four times a day for two weeks with continued use of artificial tears for several weeks postoperatively as needed. Following cessation of this immediate postoperative drug therapy, no other medications are routinely prescribed unless medically necessary.

A slit lamp examination should be performed on Day 1. Examinations are recommended at a schedule of 1 day, 1 week, 1, 3, 6 and 9 months including UCVA, manifest refraction, BSCVA, ocular health examination including slit lamp and fundus examination, and intraocular pressure.

Alcon®

LADARVISION4000

Excimer Laser System

FACTS YOU NEED TO KNOW ABOUT CustomCornea® LASER ASSISTED IN-SITU KERATOMILEUSIS (LASIK) SURGERY

PATIENT INFORMATION BOOKLET

For farsightedness (hyperopia) and farsightedness with astigmatism of +0.75D to less than +5.00D sphere with up to -3.00D cylinder (which has a magnitude less than or equal to the sphere in minus cylinder convention) and up to +5.00D cycloplegic spherical equivalent

Please read this entire booklet. Discuss its contents with your doctor so that you have all of your questions answered to your satisfaction. Ask any questions you may have before you agree to the surgery.

Alcon, Inc.
2501 Discovery Drive, Suite 500
Orlando, FL 32826 U.S.A.

Tel: (877) 523-2784
Fax: (407) 384-1677
www.ladarvision.com

Outside the U.S., contact your local Alcon office

REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 9638 – original release	05/06
B	DCN 10047 – remove comparability statement, pg. 5	05/06

99

TABLE OF CONTENTS

This page left blank intentionally.

A. Introduction

The purpose of this booklet is to provide you with information on laser eye surgery. Please read this entire booklet carefully. See the "Glossary" (Section K) for an explanation of words shown in *italics*. Discuss your questions with a doctor trained in laser eye surgery. You need to understand the benefits and risks of this surgery before making a decision to have surgery.

Farsightedness, which is also called *hyperopia,* is a condition that can cause blurred distant and near vision. You may have farsightedness if you have more trouble seeing objects clearly when they are near than when they are far away. Farsightedness commonly becomes more noticeable later in life, affecting near vision first and then distant vision. In addition to farsightedness, you may have *astigmatism* if you see that parts of objects appear more blurred than other parts. Glasses, contact lenses, or eye surgery can correct farsightedness and astigmatism to help you see more clearly.

The types of eye surgeries that are available to correct farsightedness and astigmatism are *Conductive Keratoplasty* (CK), *Laser Thermal Keratoplasty* (LTK), *Photorefractive Keratectomy* (PRK), and *Laser Assisted In-Situ Keratomileusis* (LASIK). Other eye surgeries that may be an option to correct vision are *Automated Lamellar Keratoplasty (ALK)* and *Radial Keratotomy (RK)*. These surgeries may not meet the vision requirements for some careers, such as military service.

Eye surgery can help you see more clearly by changing the shape of the *cornea*, the clear front surface of your eye. CK uses *radiofrequency* energy and LTK uses laser energy to heat the tissue and reshape the cornea. PRK and LASIK use an *excimer laser* to remove tissue to reshape the cornea. For LASIK, an instrument called a *microkeratome* first cuts a thin flap of tissue from the front of your cornea. This *corneal flap* is folded back, and the laser removes tissue under the flap to change the shape of the cornea. Then the flap is put back in place for the eye to heal.

Your eyeglass prescription is the usual way to tell how much farsightedness and astigmatism you have. Another way is to measure the shape of the *wavefront* of reflected light coming out of your eye. A wavefront measurement gives more information about your farsightedness and astigmatism than an eyeglass prescription. A wavefront measures all of the *focusing errors* in your eye, including complex errors that eyeglasses cannot correct. These complex focusing errors are called "higher-order *aberrations*".

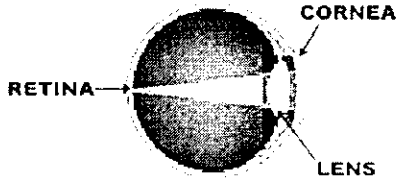
Your doctor can use either your eyeglass prescription or a wavefront measurement to plan LASIK surgery. LASIK surgery based on the eyeglass prescription is called *Conventional LASIK*. LASIK surgery based on the wavefront is called wavefront-guided LASIK. *CustomCornea® LASIK* is wavefront-guided surgery with the LADARVision®4000 Excimer Laser.

LASIK surgery is permanent. You can have LASIK surgery on one eye at a time. The second eye may have surgery on the same day or later, depending upon your choice and your doctor's advice. Discuss with your doctor whether you are a good candidate for CustomCornea® LASIK surgery.

B. How Does CustomCornea® LASIK Correct Farsightedness (Hyperopia) and Astigmatism?

You see objects because your eye focuses light into images. Your eye works like a camera. The camera lens focuses light to form clear images on film. Both the cornea and lens in the eye focus light on the *retina*, the back surface of your eye. Diagram 1 shows that distant vision is clear when light focuses correctly.

DIAGRAM 1: NORMAL EYE

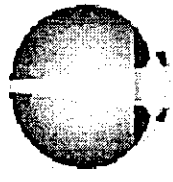


A NORMAL EYE

Light focuses on the retina. Vision is clear.

Farsightedness is a type of focusing error that results in blurred vision that is usually worse at near than at distance. Light from a distant object focuses at a point behind the retina, rather than on the retina. Diagram 2 shows that distant vision is blurry when light focuses incorrectly in a farsighted eye.

DIAGRAM 2: FARSIGHTED EYE

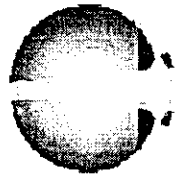


A FARSIGHTED OR HYPEROPIC EYE

Light focuses at a point behind the retina. Vision is blurred.

You may have farsightedness combined with astigmatism, which is another type of focusing error that results in blurred distant and near vision. This condition occurs if the front of your eye is more curved in some directions than others. Light rays from an object focus at different points behind the eye so some parts of objects appear more blurred than other parts. For example, a person with astigmatism might confuse an "R" with a "P" or an "F" on a sign. Diagram 3 shows an example of how light rays focusing at different points behind the retina may cause blurred vision in a farsighted eye with astigmatism.

DIAGRAM 3: FARSIGHTED EYE WITH ASTIGMATISM

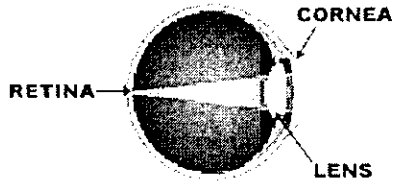


A FARSIGHTED EYE WITH ASTIGMATISM

Light focuses at different points behind the retina. Vision is blurred.

Wearing glasses and contact lenses help your eye focus light properly on the retina. LASIK surgery focuses light properly by reshaping the cornea. LASIK surgery uses an excimer laser to remove a tiny amount of tissue from the cornea. This type of laser does not change any other parts of the eye. Diagram 4 shows that distant vision is clearer after LASIK.

DIAGRAM 4: CORRECTION OF VISION AFTER LASIK



Light focuses on the retina after surgery. Vision is clear.

CustomCornea® LASIK uses a wavefront unique to your eye for treatment. This wavefront is used to guide the laser that reshapes the cornea to correct focusing errors. The doctor measures the wavefront by projecting light into your eye and measuring the reflected light that comes out of your eye.

The LADARVision®4000 System uses a very small laser beam to reshape the cornea. To correct for farsightedness and astigmatism, the cornea receives hundreds to thousands of laser pulses during LASIK surgery. The system must place the laser pulses accurately to precisely reshape the cornea. Precise shaping of the cornea requires tracking and compensating for eye movement during surgery.

Your eyes are constantly making small movements. Some of these movements are involuntary and you do not notice them. You cannot hold your eye perfectly still even if you try. The LADARVision®4000 System tracks and adjusts for eye movement during surgery. A high-speed active eye tracking system, called the LADARTracker® system, measures the eye position 4000 times a second.

In a clinical study[1], eye movement during surgery using the LADARVision® System was evaluated for 554 eyes. This study showed that:

- All eyes moved during surgery.
- The LADARTracker® system adjusted for this eye movement. The results of the surgery were about the same for eyes with large or small eye movements.
- Active eye tracking with the LADARTracker® system improves the accuracy of corneal shaping.

Without a system to track eye movements, any movement of the eye during surgery could move it away from its correct position under the laser beam. Before each laser pulse, the LADARTracker® system calculates where the eye has moved since the last pulse and moves the beam in exactly the same way, so the laser beam hits the cornea in the same place as if the eye had not moved.

[1] LADARVision® System PRK Myopia and Astigmatism study

C. Benefits of CustomCornea® LASIK

CustomCornea® LASIK surgery can correct +0.75D *(diopters)* to less than +5.00D of farsightedness with up to –3.00D of astigmatism and up to +5.00D of spherical equivalent. If you have farsightedness and astigmatism within this range, CustomCornea® LASIK surgery may help you clearly see distant objects without eyeglasses or contact lenses.

Clinical Study to Evaluate Benefits

A clinical study using the LADARVision®4000 system was done to evaluate the benefits and risks of CustomCornea® LASIK. The study included 297 eyes to determine benefits and 346 eyes to determine risks. The study results are shown below and in "Risks of CustomCornea® LASIK" (Section E).

Patient Demographics

Table 1 shows the age, race, gender, and contact lens history of patients in the study.

Table 1. Demographics of 346 Eyes of 205 Study Patients

Age		Race		Gender		Contact Lens History	
Average:	49.8 ± 9.2 years	Black	1.7%	Female	46.0%	None	59.5%
Range:	19 to 70 years	Caucasian	95.4%	Male	54.0%	Hard	2.9%
		Hispanic	2.9%			Soft	37.6%

Visual Acuity Measurement

Visual acuity is a measure of the sharpness of vision using a letter chart. Diagram 5 shows an example of a visual acuity chart consisting of lines of letters. Each line of letters becomes smaller from top to bottom on the chart. Vision is sharper as smaller letters are correctly read from top to bottom. The chart is read at a distance to measure the sharpness of distant vision. Visual acuity is shown by two numbers: the first number is the distance and the second number is the smallest line of letters read correctly. As the second number becomes smaller, the vision is sharper. For example, a smaller line of letters is read correctly for a visual acuity of 20/20 compared to 20/40.

DIAGRAM 5: EXAMPLE OF VISUAL ACUITY CHART

Visual Acuity without Glasses After Surgery

Table 2 shows that at least 94.2% of patients treated for farsightedness and astigmatism saw 20/40 or better **without** glasses after surgery. Most states require that your vision be 20/40 or better if you drive **without** any glasses or contact lenses.

Table 2. Visual Acuity *without* Glasses After Surgery

% of Eyes With:	Preop (N=297)	1 Month (N=297)	3 Months (N=297)	6 Months (N=276)	9 Months (N=138)
20/20 or better*	5.5%	59.3%	61.2%	62.9%	61.7%
20/20 or better	5.1%	54.5%	56.6%	59.1%	58.7%
20/25 or better	13.5%	80.5%	81.1%	80.8%	81.2%
20/40 or better	33.3%	95.3%	94.9%	95.3%	94.2%

N is the number of eyes studied.

* if 20/20 or better with glasses or contact lenses before surgery (preop, 1 month and 3 months: N=273 eyes; 6 months: N=256; 9 months: N=128).

Visual Acuity without Glasses After Surgery and with Glasses Before Surgery

Table 3 shows that 41.7% of patients at 6 months saw as well or better **without** glasses after CustomCornea® surgery as **with** glasses before surgery. Comparison is based on the smallest line of letters on a visual acuity chart read correctly at a distance. Refer to Diagram 4 for an example of a visual acuity chart.

Table 3. Visual Acuity *without* Glasses After Surgery Compared to *with* Glasses Before Surgery

% of Eyes With:	1 Month (N=297)	3 Months (N=297)	6 Months (N=276)	9 Months (N=138)
2 lines better vision *without* glasses after LASIK than vision *with* glasses before surgery	0.0%	0.3%	0.0%	0.0%
1 line better vision *without* glasses after LASIK than vision *with* glasses before surgery	6.1%	9.4%	8.7%	9.4%
same vision* *without* glasses after LASIK than vision *with* glasses before surgery	31.3%	29.0%	33.0%	35.5%
1 line worse vision *without* glasses after LASIK than vision *with* glasses before surgery	29.6%	30.3%	29.0%	23.2%
2 lines worse vision *without* glasses after LASIK than vision *with* glasses before surgery	18.2%	14.5%	12.3%	15.2%
more than 2 lines worse vision *without* glasses after LASIK than vision *with* glasses before surgery	14.8%	16.5%	17.0%	16.7%

N is the number of eyes studied.

* **Same vision** is within 2 or 3 letters on the same line of a visual acuity chart

D. Patient Questionnaire Responses

Patients rated the change in the following symptoms after surgery **without** glasses or contact lenses compared to their recollection of symptoms before surgery (Table 4). Except for the symptom of night driving difficulty, more than half of all patients being treated for farsightedness and astigmatism reported that their symptoms were the same at 6 months after CustomCornea® LASIK surgery **without** glasses as before surgery.

Table 4. Symptoms *without* Glasses After Surgery Compared to Before Surgery*

		6 Months				
Comfort Symptoms	**N**	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	276	9.4%	6.5%	79.3%	4.7%	0.0%
Dryness	276	9.1%	8.3%	58.0%	23.6%	1.1%
Excessive Tearing	274	4.0%	6.6%	85.8%	3.6%	0.0%
Gritty Feeling	276	6.9%	4.3%	78.3%	9.8%	0.7%
Headache	275	10.2%	10.2%	75.3%	4.4%	0.0%
Light Sensitivity	275	5.5%	16.4%	54.2%	20.0%	4.0%
Pain	276	7.2%	3.6%	85.1%	4.0%	0.0%
Redness	276	7.2%	7.2%	76.4%	8.3%	0.7%
Visual Symptoms						
Blurring of Vision	276	14.1%	16.3%	51.4%	15.2%	2.9%
Double Vision	276	7.2%	3.3%	76.1%	10.5%	2.9%
Fluctuation of Vision	276	6.9%	15.2%	56.2%	17.8%	4.0%
Glare	276	8.3%	12.3%	58.3%	18.5%	2.5%
Halos§	275	9.1%	5.1%	70.2%	12.0%	3.6%
Night Driving Difficulty	276	17.0%	23.2%	46.4%	10.5%	2.9%

N is the number of eyes studied.

* Based on the patients' comparison of symptom severity after surgery to their recollection of symptom severity before surgery.

§ *Halos* are circular flares or rings of light that may appear around a headlight or other lighted object.

At 6 months after surgery, patients rated the quality of vision **without** glasses or contact lenses compared to before surgery (Table 5), satisfaction with surgery (Table 6) and frequency of wearing distance correction (Table 7). Quality of vision was rated as unchanged, better, or significantly better than before surgery in 92.8% of patients. Approximately 79.7% of patients reported they were satisfied or extremely satisfied with their results. After treatment for farsightedness and astigmatism, 85.5% of patients in the clinical study reported that they never wore glasses or contact lenses.

Table 5. Quality of Vision *without* Glasses or Contact Lenses After Surgery Compared to Before Surgery

6 MONTHS N=276	
Significantly Better	56.9%
Better	30.8%
Same	5.1%
Worse	6.5%
Significantly Worse	0.7%

N is the number of eyes studied.

Table 6. Satisfaction with Surgery

6 MONTHS N=276	
Extremely Satisfied	47.8%
Satisfied	31.9%
Not Sure	12.0%
Unsatisfied	5.4%
Extremely Unsatisfied	2.9%

N is the number of eyes studied.

Table 7. Frequency of Glasses or Contact Lens Wear For Distance After Surgery

6 MONTHS N=276	
Never	85.5%
Seldom	7.6%
Frequently	2.2%
Constantly	4.7%

N is the number of eyes studied.

A small group of 42 patients received randomized treatment of CustomCornea® LASIK in one eye and Conventional LASIK in the other eye. These patients rated postoperative eye preference **without** glasses or contact lenses for quality of vision during the day and at night, less glare or night driving difficulty and overall eye preference (Table 8).

Table 8. Postoperative Eye Preference Without Glasses or Contact Lens Correction

Visit		CustomCornea® Eye	Same (No Preference)	Conventional Eye
3 Months (N=42)	Quality of Vision During the Day	40.5%	38.1%	21.4%
	Quality of Vision At Night	33.3%	52.4%	14.3%
	Less Glare or Night Driving Difficulty	14.3%	78.6%	7.1%
	Overall Eye Preference	42.9%	38.1%	19.0%
6 Months (N=41)	Quality of Vision During the Day	31.7%	46.3%	22.0%
	Quality of Vision At Night	31.7%	51.2%	17.1%
	Less Glare or Night Driving Difficulty	14.6%	75.6%	9.8%
	Overall Eye Preference	29.3%	51.2%	19.5%
9 Months (N=41)	Quality of Vision During the Day	29.3%	58.5%	12.2%
	Quality of Vision At Night	26.8%	61.0%	12.2%
	Less Glare or Night Driving Difficulty	12.2%	80.5%	7.3%
	Overall Eye Preference*	22.5%	55.0%	22.5%

N is the number of patients studied.

* N=40 for Overall Eye Preference at 9 months

E. Risks of CustomCornea® LASIK

If you are not satisfied with your surgery results, your doctor may suggest another surgery. No data are available for CustomCornea® LASIK retreatments.

IMPORTANT: You may need to wear glasses or contact lenses for some activities after surgery. CustomCornea® LASIK does not take away the need for reading glasses. You may need reading glasses after CustomCornea® LASIK even if you did not need them before.

In some cases, your best vision **with** your glasses or contact lenses may be worse after CustomCornea® LASIK surgery than it was before surgery.

A number of risks from LASIK surgery are related to the corneal flap rather than the laser treatment. Some specific problems include: cutting an incomplete or irregular flap, loss of the flap, misalignment of the flap, and cutting all the way through the cornea with the microkeratome. These problems can lead to other complications, such as infections, *cataracts*, and permanent scarring or deformity of the eye.

Contraindications – When Can't You Have Surgery?

If you have any of the following situations or conditions, the risk of LASIK surgery is greater than the benefit. You should **NOT** have LASIK surgery if you:

- are pregnant or nursing. These conditions may cause temporary and unpredictable changes in your cornea that may interfere with the accuracy of the measurement of your cornea before the LASIK procedure.
- have a *collagen vascular* (e.g., rheumatoid arthritis), *autoimmune* (e.g., lupus), or *immunodeficiency disease* (e.g., AIDS). These conditions affect your body's ability to heal and may result in inflammation or swelling of parts of the body such as muscles, joints, and blood vessels.
- show signs of *keratoconus* or any other condition that causes a thinning of your cornea. This unstable condition of the cornea makes it unsafe to do LASIK procedures on eyes with this condition.
- are taking medications with ocular side effects, such as isotretinoin (Accutane[2]) for acne treatment or amiodarone hydrochloride (Cordarone[3]) for normalizing heart rhythm. These medications may affect the accuracy of the LASIK procedure or the way your cornea heals after surgery. This may result in poor vision after surgery.

[2] *Accutane* Reg. TM of Hoffmann-La Roche Inc.
[3] *Cordarone* Reg. TM of Sanofi-Aventis

What Warnings and Other Information Do You Need to Know About?

Warnings

If you have any of the following conditions, you may have LASIK if your doctor evaluates the seriousness of your condition and believes the benefit of having LASIK is greater than the risk. Discuss with your doctor if you have:

- diabetes. Diabetes may interfere with the healing of the cornea after LASIK.
- a history of *herpes simplex* or *herpes zoster* infection that has affected your eyes. LASIK may be more risky for patients who have an active or previous herpes infection that has affected their eyes.
- significant dry eye that is unresponsive to treatment. LASIK may increase the dry eye condition, which may or may not go away. This dryness may delay healing of the flap or interfere with the surface of the eye after surgery.
- severe allergies. The medications taken for severe allergies may interfere with the ability of the eye to heal after LASIK.

You will need eye drops to enlarge your pupil to at least 7mm to 11mm before surgery so the tracking system can more easily follow your eye during surgery. This effect of eye drops is only temporary.

Precautions

If you have any of the following conditions, you should discuss this with your doctor. The safety and effectiveness for LASIK have **NOT** been established in patients:

- with unstable farsightedness and astigmatism. Eyes with unstable farsightedness and astigmatism are unable to be correctly measured to determine the right amount of the vision correction to provide.
- with conditions that may interfere with the ability to properly measure the eye to determine the right amount of vision correction, and may also affect the healing of the eye after the surgery, such as:
  - disease or corneal condition (for example, scar, infection, etc.).
  - injury to the cornea where LASIK will reshape the cornea.
  - previous surgery on the cornea or inside the eye (for example, cataract surgery).
  - prior history of surgery to correct vision (for example, CK, LTK, PRK, LASIK).
- with a cornea that is too thin for LASIK to be completed safely. A flap needs to be cut into the cornea for the LASIK procedure. A proper flap cannot be created on a thin cornea.
- with a history of *glaucoma* (a condition usually associated with high eye pressure with damage to the nerve in the eye and possible loss of vision). It is unknown whether LASIK is safe for eyes with glaucoma.

- who are taking the medication sumatripin succinate (Imitrex[4]) for migraine headaches. It is unknown whether the use of this medication will interfere with the accuracy of the measurement of your cornea prior to LASIK or the healing of the eye after LASIK.
- under 21 years of age because it is unknown if the eye has reached its adult vision refraction. This may result in measurement of the amount of correction to provide being incorrect.
- over the long term (more than 9 months).
- with farsightedness of +5.00D or greater sphere with greater than –3.00D of astigmatism and greater than +5.00D of spherical equivalent. Corrections falling outside of the approved range have not been studied.
- for retreatment with this laser for LASIK. Retreatments have not been done enough times to allow an understanding of whether it is safe and effective.

Let your doctor know if you are taking any prescription medicines or any medications you bought without a prescription. These medications may interfere with the measurement prior to LASIK or the healing of the eye after LASIK.

The safety and effectiveness of wavefront-guided LASIK have only been established with an optical zone of 6.5mm and a total treatment zone of 9.0mm.

Before surgery, your doctor should evaluate your pupil size under dim lighting conditions. If your pupils in dim light are greater than the optical zone (>6.5mm) proposed by your doctor, consult with your doctor about the risk that the surgery may cause negative effects on your vision, such as glare, halos, and night driving difficulty.

Your doctor should also evaluate you for dry eyes before surgery. You may have dry eyes after LASIK surgery even if you did not have dry eyes before surgery.

During the First Week Following Surgery

- You may feel pain, discomfort, or have a feeling that something is in your eye. It may last up to 7 days after surgery.
- Your vision may be blurry or you may become more sensitive to light as your eye heals.
- You may have temporary swelling of the front surface of your eye.
- The pressure inside your eye may increase, usually due to the use of *anti-inflammatory medication* (eye drops) after surgery. Using another medication or stopping the anti-inflammatory medication can control the abnormal increase in eye pressure.

[4] *Imitrex* Reg TM of Glaxo Group Limited

During One to Six Months Following Surgery

- Your vision should be stable 6 months after surgery. On average in the clinical study, there was 0.21D more correction than the intended amount at 1 month, which lessened to 0.09D at 6 months after surgery. There is often a slow refractive drift as much as 0.25D per year after surgery. Some patients may notice that their vision improves or worsens. These small changes may occur up to 6 months or more after surgery. You should contact your doctor if you notice any change or loss of vision.
- You may become more sensitive to light. You may notice glare or have difficulty in driving at night.
- You may experience some dryness.

Clinical Study to Evaluate Risks

In the clinical study using the LADARVision®4000 System on CustomCornea® LASIK, some people still needed glasses or contact lenses after surgery. At 6 months after surgery, 3.3% of patients had less correction than the intended amount by more than 1D. At 6 months after surgery, 8.3% of patients had more correction than the intended amount by more than 1D and 1.4% of patients had more than 2D of correction from the intended amount.

Visual Acuity with Glasses After Surgery

Table 9 shows that all patients in the study saw 20/32 or better **with** glasses before surgery and at 6 months after surgery.

Table 9. Visual Acuity *with* Glasses (Best Vision)

% of Eyes With:	Preop (N=346)	1 Month (N=346)	3 Months (N=346)	6 Months (N=320)	9 Months (N=161)
20/20 or better	91.0%	87.9%	91.9%	90.9%	90.7%
20/25 or better	99.7%	97.4%	98.8%	98.8%	98.8%
20/32 or better	100.0%	99.7%	99.7%	100.0%	100.0%

N is the number of eyes studied.

Change in Visual Acuity with Glasses After Surgery

Under dim room lighting conditions, the best vision **with** glasses was measured using a standard (high-contrast) visual acuity chart and a 10% *low contrast visual acuity* chart. A standard chart has black letters on a white background. A 10% low contrast visual acuity chart has gray letters on a white background. Black letters are easier to see than gray letters. Low contrast acuity testing is another way to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog. Table 10 compares the change in vision **with** glasses before surgery to 3 and 6 months after surgery.

Table 10. Change in Visual Acuity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Standard Chart		10% Low Contrast Chart	
	3 Months (N=346)	6 Months (N=320)	3 Months (N=346)	6 Months (N=320)
loss of more than 2 lines	0.3%	0.0%	3.8%	2.2%
loss of 2 lines	1.7%	0.9%	5.5%	3.4%
loss of 1 line	18.2%	17.5%	20.5%	22.8%
no change	53.2%	57.2%	39.3%	38.1%
gain of 1 line	25.7%	24.1%	23.1%	25.6%
gain of 2 lines	0.9%	0.3%	7.2%	6.9%
gain of more than 2 lines	0.0%	0.0%	0.6%	0.9%

N is the number of eyes studied.

Contrast Sensitivity

In the clinical study, contrast sensitivity was measured in daylight and in dim light to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog. The majority of subjects reported no change before and after surgery. Table 11 compares the change in contrast sensitivity **with** glasses before surgery to 3 and 6 months after surgery.

Table 11. Change in Contrast Sensitivity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Daylight Conditions		Dim Light Conditions	
	3 Months (N=344)	6 Months (N=319)	3 Months (N=327)	6 Months (N=309)
Loss	7.3%	7.5%	15.9%	12.9%
No change	82.0%	85.3%	60.6%	67.0%
Gain	10.8%	7.2%	23.5%	20.1%

N is the number of eyes studied.

Adverse Events and Complications

Some patients from the clinical study experienced adverse events and complications after CustomCornea® LASIK surgery as shown in Table 12.

Table 12. Adverse Events and Complications	
Greater than or equal to 1% of eyes (N=346) **had:**	
Cells growing under the corneal flap	3.2%
Inflammation of the cornea under the corneal flap	1.4%
Less than 1% of eyes (N=346) **had:**	
Feeling of something in the eye at one month or later	0.9%
Fine strands of cells and mucous attached to the cornea	0.6%
Irritation on the front surface of the cornea that requires medical management	0.6%
Viral infection in the cornea	0.6%
Inflammation of outer lining of the eye (*conjunctivitis)* with a loss of more than 10 letters of visual acuity with glasses	0.6%
Abnormal growth of blood vessels under the retina of unknown cause that is unrelated to the eye surgery procedure	0.3%
Corneal scratch in the peripheral cornea at one month or later	0.3%
Eye pain at one month or later	0.3%
Loss of more than 10 letters of visual acuity with glasses at six months or later	0.3%

N is the number of eyes studied.

There were no reports of the following adverse events and complications in the clinical study:

- breakdown of the flap;
- corneal swelling;
- corneal scratch involving the treated tissue at one month or later;
- corneal cloudiness at six months with a loss of 2 or more lines of visual acuity with glasses;
- cells growing under the corneal flap with a loss of 2 or more lines of visual acuity with glasses;
- double or ghost images;
- problem with creation of the corneal flap;
- poor alignment of the corneal flap;
- eye pressure more than 25 mmHg;
- increase in eye pressure of more than 10 mmHg compared to before surgery;
- separation of the retina from the back of the eye;
- blockage of blood vessels in the retina.

Worse and Significantly Worse Symptoms After Surgery

Patients who were treated for farsightedness and astigmatism rated the change in the following symptoms after surgery **without** glasses or contact lenses as worse or significantly worse compared to their recollection of symptoms before surgery (Table 13).

Table 13. Symptoms *without* Glasses After Surgery Compared to Before Surgery*

	6 Months		
Comfort Symptoms	**N**	**Worse**	**Significantly Worse**
Burning	276	4.7%	0.0%
Dryness	276	23.6%	1.1%
Excessive Tearing	274	3.6%	0.0%
Gritty Feeling	276	9.8%	0.7%
Headache	275	4.4%	0.0%
Light Sensitivity	275	20.0%	4.0%
Pain	276	4.0%	0.0%
Redness	276	8.3%	0.7%
Visual Symptoms			
Blurring of Vision	276	15.2%	2.9%
Double Vision	276	10.5%	2.9%
Fluctuation of Vision	276	17.8%	4.0%
Glare	276	18.5%	2.5%
Halos §	275	12.0%	3.6%
Night Driving Difficulty	276	10.5%	2.9%

N is the number of eyes studied.

* Based on the patients' comparison of symptom severity after surgery to their recollection of symptom severity before surgery.

§ *Halos* are circular flares or rings of light that may appear around a headlight or other lighted object.

F. Are You a Good Candidate For CustomCornea® LASIK?

If you are considering CustomCornea® LASIK, you must:

- be at least 21 years of age.
- have a healthy eye with no eye disease or corneal condition (for example, scar or infection).
- have +0.75D to less than +5.00D sphere of farsightedness with up to -3.00D of astigmatism and up to +5.00D spherical equivalent.
- have stable farsightedness and astigmatism as documented by less than or equal to 0.50D change each year for at least one year before your eye examination before surgery.
- be able to lie flat on your back.
- be able to look at a blinking fixation light during the entire surgery.
- be able to have eye drops that numb your eye and enlarge your pupil.
- understand the risks and benefits of CustomCornea® LASIK compared to other available treatments for farsightedness and astigmatism.
- be willing to sign an Informed Consent Form, if provided by your doctor.

G. What Should You Expect During CustomCornea® LASIK Surgery?

Before the Surgery

Before surgery, your doctor needs to determine your complete medical and eye history and check the health of both your eyes. As part of this exam, your doctor will use a computer program to map the front surface of your eye. This exam will determine if your eyes are healthy and if you are a good candidate for CustomCornea® LASIK.

WARNING: You must stop wearing any contact lenses at least 3 weeks before this eye examination. Failure to do this may affect surgical results.

Tell your doctor if you take any prescription and non-prescription medications or have any allergies. Ask your doctor if you should eat or drink right before the surgery. **You should also arrange for transportation since you must not drive right after the surgery.** Your doctor will let you know when your vision is good enough to drive again.

The Day of Surgery

To prepare for surgery, your doctor will use the wavefront system to take a picture of your eye. This helps to determine where the laser should treat your cornea. Your doctor will put eye drops to dilate (enlarge) the pupil in your eye(s). After 30-40 minutes, your doctor will measure the wavefront unique to your eye to determine the amount of laser treatment you need.

Your doctor will then place numbing eye drops in the eye to be treated. Numbing drops are used to control pain during surgery. The effects of the numbing eye drops will wear off after about 45-60 minutes. Your doctor will ask you to lie on your back on the laser bed. The laser bed is a flat cushioned surface that can be moved to position you for surgery. Your doctor will instruct you to watch a blinking fixation light. Your doctor will place an instrument between your eyelids to hold them open during the surgery. A temporary shield will cover the eye that is not having surgery.

An instrument called the microkeratome creates a flap of tissue in the cornea. Then, your doctor will reposition your head and activate the LADARTracker® system to track your eye movement. Your doctor will ask you to look directly at the blinking light. The laser in the LADARVision®4000 System will remove small amounts of tissue from your cornea. During the laser treatment, you will hear a "clicking" sound of laser pulses. The tracking system will follow eye movements and allow the laser to continue the treatment. You will be under the laser for several minutes. The use of the laser will take about one minute. Overall, the surgery takes about 10 minutes.

IMPORTANT: You must continue looking at the blinking light throughout the treatment, even if your vision begins to become cloudy during the procedure.

After the surgery is complete, your doctor will place some eye drops in your eye. Your doctor may cover your eye with a *bandage contact lens* to help heal the eye. For your eye protection and comfort, your doctor may apply a patch or shield over your eye.

The First Days After Surgery

You may be mildly sensitive to light and have a feeling that something is in your eye. Sunglasses may make you more comfortable. Also, you may experience pain. Your doctor can prescribe pain medication to make you more comfortable during the first few days after the surgery. A plastic shield may be used to protect your eye after LASIK. You will need to use lubricants, *antibiotic*, and *anti-inflammatory medications* in the first few days.

IMPORTANT: Use the lubricants and eye medications as directed by your doctor. Your results depend upon you following your doctor's instructions.

WARNING: Your doctor will monitor you for any side effects if you need to use a topical *steroid medication*. Possible side effects of prolonged topical steroid use are:

- *ocular hypertension* (an increase in the eye pressure);
- *glaucoma* (a condition usually associated with high eye pressure that results in damage to the nerve in the eye and possible loss of vision);
- *cataract formation* (an opacity or clouding of the lens inside the eye that can cause a loss of vision).

DO NOT rub your eyes for the first 3 to 5 days. Rubbing your eye may move the flap. If you notice any sudden decrease in your vision, you should contact your doctor immediately. The flap may have moved and the doctor may need to reposition the flap.

H. Questions to Ask Your Doctor

You may want to ask the following questions to help you decide if CustomCornea® LASIK with the LADARVision®4000 System is right for you:

- What are my other options to correct my farsightedness and astigmatism?
- Will I have to limit my activities after surgery and for how long?
- What are the benefits of CustomCornea® LASIK for my amount of farsightedness and astigmatism?
- What vision can I expect in the first few months after surgery?
- If CustomCornea® LASIK does not correct my vision, what is the possibility that my glasses would need to be stronger than before? Could my need for glasses increase over time?
- Will I be able to wear contact lenses after LASIK if I need them?
- How is LASIK likely to affect my need to wear glasses or contact lenses as I get older?
- Will my cornea heal differently if injured after having LASIK?
- Should I have LASIK surgery in my other eye?
- How long will I have to wait before I can have surgery on my other eye?
- What vision problems might I experience if I have LASIK only on one eye?
- Do I have significant dry eye or large pupils that could produce undesirable side effects after LASIK surgery?

Discuss the cost of surgery and follow-up care needs with your doctor. Most health insurance policies do not cover laser vision correction.

I. Self-Test

Are You An Informed And Educated Patient?

Take the test below to see if you can correctly answer the following questions after reading this booklet.

	TRUE	FALSE
1. LASIK surgery is risk-free.	☐	☐
2. It does not matter if I wear my contact lenses before surgery when my doctor told me not to wear them.	☐	☐
3. Since the LADARVision®4000 System tracks my eye movements, I do not have to fixate on the blinking light.	☐	☐
4. After the surgery, there is a good chance that I will be less dependent on eyeglasses or contact lenses.	☐	☐
5. I may need reading glasses after LASIK surgery, even if I did not need them before.	☐	☐
6. There is a risk that I may lose some vision after LASIK surgery.	☐	☐
7. It does not matter if I am pregnant.	☐	☐
8. If I have an autoimmune disease, I am still a good candidate for LASIK surgery.	☐	☐
9. Significant dry eye or large pupils may produce undesirable side effects after LASIK surgery.	☐	☐

You can find the answers to Self-Test at the bottom of the next page.

J. Summary of Important Information

- CustomCornea® LASIK is a permanent irreversible surgery to the cornea.
- You may need to wear glasses or contact lenses for some activities after surgery. CustomCornea® LASIK does not take away the need for reading glasses, even if you have never worn them before.
- Your vision must be stable before CustomCornea® LASIK surgery. You must provide written evidence that your farsightedness and astigmatism has changed less than or equal to 0.50D each year for at least 1 year.
- Pregnant and nursing women should wait until they are not pregnant and not nursing to have CustomCornea® LASIK surgery.
- You would not be a good candidate if you have *autoimmune or collagen vascular diseases.* If you have a condition that makes wound healing difficult, you would not be a good candidate.
- CustomCornea® LASIK surgery has some risks. Please read and understand this entire booklet, especially the sections on Benefits and Risks before you agree to the surgery.
- Some other options to correct farsightedness and astigmatism include glasses, contact lenses, CK, LTK, PRK, and Conventional LASIK. Other surgical options that may be used to correct vision are ALK and RK.
- ALK, RK, CK, LTK, PRK, Conventional LASIK or CustomCornea® LASIK may not meet the vision requirements of some occupations, such as military service.
- Before considering CustomCornea® LASIK surgery you should:
  a. have a complete eye examination.
  b. talk with at least one eye care professional about CustomCornea® LASIK, especially the potential benefits, risks, and complications. You should discuss the time needed for healing after CustomCornea® LASIK.

Answers to Self-Test Questions:

1. False (see Section E: Risks)
2. False (see Section G: Before the Surgery)
3. False (see Section G: The Day of Surgery)
4. True (see Section C: Benefits)
5. True (see Section E: Risks)
6. True (see Section E: Risks)
7. False (see Section E: Contraindications)
8. False (see Section E: Contraindications)
9. True (see Section E: Precautions)

K. Glossary

This section summarizes important terms used in this information booklet. Please discuss any related questions with your doctor.

Aberration: focusing errors in the eye detectable by wavefront measurements. Examples are farsightedness and astigmatism (lower-order) and complex errors (higher-order).

Antibiotic Medication: a drug used to treat or prevent infection. Your doctor may prescribe this medication after LASIK surgery.

Anti-inflammatory Medication: a drug that reduces inflammation or the body's reaction to injury or disease. Any eye surgery can cause inflammation. Your doctor may prescribe this medication after LASIK surgery.

Astigmatism: a focusing error that results in blurred distant and near vision. The cornea is more curved in some directions than others, and causes light rays to focus at different points from the retina. Parts of objects appear clearer than other parts.

Autoimmune Disease: a condition in which the body attacks itself and results in inflammation or swelling of parts of the body, such as muscles, joints, and blood vessels. An example is lupus. If you have this type of condition, you should not have LASIK surgery.

Automated Lamellar Keratoplasty (ALK): a type of eye surgery that changes the shape of the front surface of the eye using a microkeratome. A flap is created and tissue is removed under the flap with the microkeratome. Then the flap is put back on the eye.

Bandage Contact Lens: a soft contact lens placed on the cornea after surgery to cover the area that was treated with the laser.

Cataract: an opacity, or clouding, of the lens inside the eye that can blur vision.

Collagen Vascular Disease: a condition that may result in inflammation or swelling of parts of the body, such as muscles, joints, and blood vessels. An example is rheumatoid arthritis. If you have this type of condition, you should not have LASIK surgery.

Conductive Keratoplasty (CK): a type of eye surgery that corrects farsightedness by using radiofrequency energy to change the shape of the front surface of the eye by heating the tissue.

Conjunctivitis: inflammation of the conjunctiva, the outer lining of the eye, usually caused by a viral infection, bacterial infection or by allergies.

Contraindications: any special condition that results in the treatment not being recommended.

Contrast Sensitivity: a measure of the ability of the eye to detect small lightness differences between objects and the background in daylight and in dim light. For example, black lines on a gray background are easier to see than gray lines on a gray background. Objects in daylight are also easier to see than in dim light. Contrast sensitivity testing is a way to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog.

Conventional LASIK: LASIK surgery that uses an eyeglass prescription to plan the surgery.

Cornea: the clear front layer of the eye. Surgery such as CK, LTK, PRK, and LASIK reshapes the front surface of the cornea to improve distant vision.

Corneal Flap: a thin slice of tissue on the surface of the cornea made with a microkeratome at the beginning of the LASIK procedure. This flap is folded back before the laser shapes the inner layers of the cornea.

Corneal Swelling: abnormal fluid build-up in the cornea. This condition is usually temporary with no significant effect on vision.

CustomCornea® LASIK: LASIK surgery that uses the wavefront to plan the surgery with the LADARVision®4000 System.

Diopter: a unit of focusing power, used to describe the amount of farsightedness and astigmatism of an eye. Abbreviated as "D".

Excimer Laser: a form of light energy used in Conventional and CustomCornea® LASIK to remove tissue from the cornea.

Farsightedness: a focusing error that results in blurred vision that is usually worse at near than at distance. The cornea and lens in the eye focus light rays at a point behind the retina resulting in blurred images. Farsightedness is also called hyperopia.

Focusing Error: a condition in which your eye forms a blurred image on the retina. Examples are farsightedness, astigmatism, and higher-order aberrations (complex focusing errors).

Glaucoma: an eye disease usually associated with high eye pressure. Glaucoma damages the optic nerve of the eye and usually causes a progressive loss of vision.

Halos: circular flares or rings of light that may appear around a headlight or other lighted object. This symptom may occur before or after surgery.

Herpes Simplex: a type of viral infection that can recur. This virus typically causes cold sores and/or vesicles to appear on the face or other parts of the body. You should discuss any history of this condition with your doctor before having LASIK surgery.

Herpes Zoster: a type of viral infection that can recur. This condition is a reactivation of the chicken pox virus as an adult. Vesicles appear on only one side of the body. You should discuss any history of this condition with your doctor before having LASIK surgery.

Hyperopia: a focusing error that results in blurred vision that is usually worse at near than at distance. The cornea and lens in the eye focus light rays at a point behind the retina resulting in blurred images. Hyperopia is also called farsightedness.

Immunodeficiency Disease: a condition that compromises the body's ability to heal. An example is acquired immunodeficiency syndrome (AIDS). If you have this type of condition, you should not have LASIK surgery.

Inflammation: the body's reaction to injury or disease. Eye surgery, such as PRK and LASIK, can cause inflammation.

Keratoconus: a condition of the cornea that results in a change in the shape of the cornea with thinning. If you have this condition, you should not have LASIK surgery.

Laser Assisted In-Situ Keratomileusis (LASIK): a type of eye surgery that uses a microkeratome and a laser to improve vision. The microkeratome creates a thin, hinged flap of tissue on the cornea that is folded back. The laser shapes the tissue under the flap and the flap is put back on the eye so the tissue heals.

Laser Thermal Keratoplasty (LTK): a type of eye surgery that corrects farsightedness by using laser energy to change the shape of the front surface of the eye by heating the tissue.

Lens: a structure inside the eye that helps to focus light onto the back surface (retina) of the eye.

Low Contrast Visual Acuity: a measure of the sharpness of vision using a 10% low contrast chart with gray letters on a white background. Low contrast acuity testing is another way to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog.

Microkeratome: a surgical instrument used in LASIK to cut a thin flap of tissue from the front surface of the eye before the laser treatment is applied.

Ocular Hypertension: increased eye pressure.

Photorefractive Keratectomy (PRK): a type of eye surgery that uses an excimer laser to reshape the cornea to improve vision. After the epithelium (outermost layer) of the cornea is first scraped away, the laser removes tissue from the exposed surface. After the surgery, the epithelium grows back.

Radial Keratotomy (RK): a type of surgery that changes the shape of the front surface of the eye by creating cuts with a blade.

Radiofrequency: a form of electrical energy (radio waves) used in Conductive Keratoplasty (CK) to reshape the cornea by heating the tissue.

Retina: the layer of nerve tissue at the back of the eye that captures images, similar to film in a camera, and sends information about those images to the brain. Light must be focused correctly on the retina to form clear images.

Steroid Medication: a drug that reduces inflammation or the body's reaction to injury or disease. Your doctor may prescribe this medication after LASIK surgery for a short time to modify the healing of your eye. If you are taking this medication for a disease condition, you should not have LASIK surgery.

Visual Acuity: a measure of the sharpness of vision using a letter chart.

Wavefront: a measure of the total focusing errors (aberrations) including farsightedness, astigmatism, and complex focusing errors (higher-order aberrations). Light is projected into your eye and focused on the retina. Part of this light is reflected back out of your eye to form the wavefront.

L. Patient Assistance Information

To be completed by you or your Primary Eye Care Professional as a reference.

Primary Eye Care Professional

Name: _____

Address: _____

Phone: _____

CustomCornea® LASIK Doctor

Name: _____

Address: _____

Phone: _____

Treatment Location

Name: _____

Address: _____

Phone: _____

Laser Manufacturer

Alcon, Inc.
2501 Discovery Drive, Suite 500
Orlando, FL 32826
Tel: (877) 523-2784 Fax: (407) 384-1677

M. Index

K

L

M

N

O

P

R

T

V

W

Alcon®

LADAR*6000*™
EXCIMER LASER

PROFESSIONAL USE INFORMATION MANUAL

For CustomCornea® Laser Assisted In-Situ Keratomileusis (LASIK)

PHYSICIAN'S BOOKLET

For hyperopia and hyperopic astigmatism of +0.75D to less than +5.00D sphere with up to -3.00D cylinder (which has a magnitude less than or equal to the sphere in minus cylinder convention) and up to +5.00D cycloplegic spherical equivalent

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed eye care practitioner. U.S. Federal Law restricts the use of this device to practitioners who have been trained in its calibration and operation, and who have experience in the surgical management and treatment of refractive errors.

This document provides information concerning the intended clinical use of the LADAR*6000*™ Excimer Laser System. For complete information concerning system components, safety instructions, installation, maintenance, and troubleshooting refer to the LADAR*6000*™ Excimer Laser System Operation Manual.

Carefully read all instructions prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient and/or user complications.

Alcon, Inc.
2501 Discovery Drive, Suite 500
Orlando, FL 32826

Tel: (877) 523-2784
Fax: (407) 384-1677
Outside the U.S., contact your local Alcon representative

REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 9794 – original release	04/06
B	DCN 10046 – revise Surgery Planning Software description, pg. 7; add "pinhole light" pg. 9; add "asymmetric" pg. 44; revise pupil dilation drugs, pg. 46	05/06

TABLE OF CONTENTS

This page left blank intentionally.

1. GENERAL SAFETY CONSIDERATIONS

"WARNING:" - Identifies conditions or practices that could result in damage to equipment or other property, personal injury, or loss of life.

WARNING: Specific training from Alcon or an authorized representative of Alcon is required before anyone is qualified to operate the LADAR*6000*™ System. Read and understand this manual and the LADAR*6000*™ Excimer Laser System Operation Manual prior to operating the system.

Refer to the LADAR*6000*™ Excimer Laser System Operation Manual for additional warnings regarding use of the LADAR*6000*™ System.

2. DEVICE DESCRIPTION

A. WAVEFRONT MEASUREMENT DEVICE (WMD)

The first step in performing CustomCornea® LASIK surgery is to perform a wavefront examination on the patient using a wavefront measurement device (WMD) compatible with the LADAR*6000*™ System. At the present time, the only compatible WMD is the Alcon LADARWave® CustomCornea® Wavefront System.

The LADARWave® CustomCornea® Wavefront System is indicated for measuring, recording, and analyzing visual aberrations (such as myopia, hyperopia, astigmatism, coma and spherical aberration) and for displaying refractive error maps of the eye to assist in prescribing refractive corrections. This device is enabled to export wavefront data and associated anatomical registration information to a compatible treatment laser with an indication for wavefront-guided refractive surgery.

Essential features of the compatible WMD are as follows:

Patient Fixation and Fogging

The WMD includes a fixation optical subsystem that provides the patient with an unambiguous fixation point. In addition, the fixation subsystem includes adjustable optics to compensate for the patient's inherent refractive error. The optics are used to "fog" the eye, first clarifying the fixation target and then it optically adjusts beyond the patient's far point to minimize accommodation.

Centration

Prior to dilation, the WMD is used to record the geometric relationship between the natural daytime pupil center and the limbus of the eye. This information is then used to center the wavefront measurement and subsequent ablative treatment on the natural line of sight.

Wavefront Measurement

The WMD measures the wavefront profile of the eye with a high degree of accuracy and characterizes the profile using Zernike polynomials. The pupil must be large enough so that valid wavefront data can be obtained over a large area. Higher-order aberrations are more significant at night when the pupil is naturally larger. Therefore, when treating these aberrations, measurement over a large pupil provides the greatest utility.

Registration

The WMD uses synchronized video imagery and on-screen software reticules to record the relationship of the wavefront data to the limbus of the eye and to ink marks applied to the sclera just before the wavefront exam. This registration information is used to position the excimer ablation profile at the correct corneal location and cyclotorsional angle.

Data Export

The WMD has the ability to export the wavefront examination data as an electronic file to removable media for transfer to the LADAR*6000*™ System. The electronic file is structured in a specific format and contains essential patient information, centration/registration information, and the detailed aberration data. In addition, the electronic file is encrypted in a manner that can only be deciphered by the LADAR*6000*™ System.

B. MICROKERATOME

A microkeratome is used to achieve a partial thickness cut of the cornea, which creates a "flap" as part of the LASIK procedure. The microkeratome is a precision instrument used in performing lamellar corneal resections. This instrument cuts a precise corneal disc of pre-selected thickness and diameter. The system generally consists of a head, plates, ring, handle, wrenches, shaft, motor, hand-piece, disposable blades, and power supply with footswitches and power cords. The system is completed with the applanation lens set, tonometer, corneal storage jar, optical zone marker, spatula, stop attachment, and digital thickness gauge.

Microkeratomes Used in the Clinical Trial:

The microkeratomes used in the LADARVision®4000 System clinical trial included the BD K-4000[1] (manufactured by Becton-Dickinson), Hansatome[2] (manufactured by Bausch & Lomb), and the Moria[3] CB and LSK (manufactured by Moria).

[1] *BD K-4000* TM of Becton, Dickinson and Company
[2] *Hansatome* Reg. TM of Bausch & Lomb Incorporated
[3] *Moria* Reg. TM of Moria SA

C. CUSTOMCORNEA® SURGERY PLANNING SOFTWARE

The CustomCornea® Surgery Planning Software is a stand-alone computer application linking the diagnostic wavefront data from the WMD with the surgical treatment on the LADAR*6000*™ System. The planning software allows refinement of surgical parameters within the approved wavefront-guided indication for the LADAR*6000*™ System, calculates ablation depth, checks for treatment eligibility, and exports all messages and warnings to the excimer laser system.

After completing the surgery planning tasks, the planned treatment file is transferred to the LADAR*6000*™ System. The LADAR*6000*™ System software imports the treatment file, calculates the excimer treatment pattern, and performs the surgery.

D. LADAR6000™ EXCIMER LASER SYSTEM

The LADAR*6000*™ System excimer laser beam is of Gaussian profile and small in diameter (< 0.90mm). Corneal sculpting is achieved by delivering hundreds to thousands of excimer laser pulses to the eye in a complex pattern of spatially overlapping spots, and precision of this process depends on accurate placement of the laser pulses. The LADAR*6000*™ System incorporates the LADARTracker® closed-loop eye-tracking system to track and compensate for patient eye motion, including saccadic movements, during procedures so that each excimer laser pulse is delivered to the appropriate location on the cornea.

Excimer Laser Characteristics

The ultraviolet laser used in the LADAR*6000*™ System is an argon fluoride excimer laser. This laser produces 12 nanosecond pulses of ultraviolet radiation at a wavelength of 193 nanometers. The laser repetition rate is approximately 92 pulses per second. Characteristics of the laser beam at the corneal treatment plane are shown below:

Treatment Plane Characteristics of the LADAR*6000*™ System Excimer Laser Beam

Pulse energy (mJ)	2.4 - 3.0
Beam diameter (mm) [a]	< 0.90
Average fluence (mJ/cm^2) [b]	180-240

Note (a): The Gaussian beam diameter is defined as the mean of the semi-major and semi-minor axes of the elliptical beam cross-section and is the 1/e width in the Gaussian fluence distribution.

Note (b): This is the calculated average value per pulse of the laser fluence over the ablated area.

Additional features of the LADAR*6000*™ System include:

Optical Transmission System

The excimer laser passes through an optical telescope, followed by reflection off a series of mirrors which position the excimer laser pulses in the correct locations at the treatment plane. Tracking mirrors also compensate for patient eye motion, as detected by the LADARTracker® system.

Energy Monitoring/Control

An energy monitor is mounted at the output of the LADAR*6000*™ System. Prior to treatment, this energy monitor ensures that the laser pulse energy delivered to the eye will be between 2.4 and 3.0 mJ. During treatment, the detector monitors laser operation.

Gas Handling

The excimer laser enclosure holds the laser, gas bottle, and gas-plumbing manifold. The gas bottle contains the pre-mixed excimer laser gas, which contains neon as the buffer gas, in addition to argon and fluorine. The initial pressure in the gas bottle is 2000 PSI. The outlet nozzle of the gas bottle contains a flow restrictor valve. Gas from the bottle flows to a fluorine-compatible gas regulator, which reduces the line pressure to 90 PSI. Two gas lines exit the regulator. One leads directly to the outlet line of the laser enclosure. In the event of a diaphragm failure, excimer gas will flow from the regulator down this line and out of the enclosure. Outside the laser enclosure, the gas flows through a charcoal-based filter (to remove the F_2) before venting into the room. The second gas line exiting the regulator leads to the excimer laser cavity. At the line connection to the cavity there is a solenoid valve, which responds to commands from the laser control electronics board. A second solenoid valve exists at the gas outlet port of the laser cavity. The outlet gas line also leads out of the laser enclosure and through the charcoal filter.

Eye Tracking System

The LADAR*6000*™ System utilizes the LADARTracker® active closed-loop eye tracking system to track and compensate for eye motion during refractive laser surgery. The word "active" here is used to denote two important characteristics of the device. First, the LADARTracker® system actively tracks the position of the eye by irradiating it with pulses of 905 nm infrared "eye-safe" energy and analyzing characteristics of the returning laser radiation. This measurement occurs 4000 times each second in order to detect even rapid eye motion before significant movement of the cornea has occurred.

The LADARTracker® system is also "active" in the sense that it actively compensates for the detected motion, rather than simply disabling the treatment laser when the eye position exceeds some tolerated error range. The LADARTracker® system includes two mirrors that are continually repositioned to keep the eye centered in the field of view of the treatment laser. An independent set of mirrors is used to translate the treatment beam around within this field of view, delivering the ablation pulses to the cornea in a predetermined spatial pattern. The combined system allows for each ablation pulse in the complex pattern to be delivered to the appropriate corneal site, even in the presence of substantial eye movement.

The LADARTracker® system is designed so that precise mirror movements during the course of each surgery are recorded. Because the geometry involved is known, exact eye movements can be calculated from the compensatory movements of the mirrors. It is not possible to perform surgery using the LADAR*6000*™ System without the LADARTracker® system engaged, and no patient has ever been treated without concurrent tracking.

Operating Microscope

The stereo viewing operating microscope is located in the optics head. The dual optical paths are independent of the excimer beam path and the LADARTracker® system mirrors. Oblique, omni-directional microscope lighting on either side of the system output window provides visible illumination of the treatment plane. The operating microscope optical system is completely independent from the eye tracking optical system and does not provide "tracked" imagery of the patient eye.

Fixation Target

A visible fixation target is mounted in the system to facilitate the patient looking in the direction of the treatment excimer beam. The fixation target consists of a light emitting diode (LED), a pinhole aperture, an edge-illuminated reticule, and a lens. The lens, in combination with a 300mm focal length achromat in the operating microscope optical path, places the LED at infinity focus from the patient's perspective. The edge-illuminated reticule is a clear, flat etched glass with two sets of horizontal lines. For proper eye alignment, the patient is instructed to shift position until the LED pinhole light is centered within the ring of white lights and then to maintain that fixation during treatment.

Moveable Bed

A motorized patient bed, which moves on X, Y and Z axes, smoothly and rapidly positions the patient and facilitates bilateral procedures. The bed controls are located on the Control Console and the Control Module. The longitudinal motion range is approximately 15", so that the patient can lie on the bed and then be moved into position under the laser head. The lateral range of motion is 4", allowing surgery to be performed on either eye. The vertical range of motion is 3", allowing adjustment for the proper distance from the laser aperture to the eye for varying head sizes. Each axis has a continually variable speed control for coarse and fine positioning.

Cross Beam Patient Positioning

Cross beam Class I lasers are used to place the cornea at a predetermined height for proper ablation. The cross beam laser sub-system consists of two laser line generators attached to the left and right sides of the upper optical module. The laser diode sources produce 0.9 mwatts each at 633 nm. The beam of each red-wavelength laser is transmitted through an absorptive neutral density filter, which attenuates the laser by 97%, and a polarizer. The output of each polarizer is reflected off a stationary fold mirror. The two mirrors are aligned such that the two beams are vertically aligned (one above the other) on the left sclera/limbus boundary and the apex of the cornea is 8 inches below the laser output window. This provides the operator/surgeon with an easy method of setting the height of the patient's eye during centration and surgery.

The maximum laser power at the eye is less than 15 μwatts for each laser. The lasers are separated by 103mm and are 209mm from the eye. With this geometry, the laser spots are separated on the retina by several times their diameter so the energy is not additive. Given the wavelength and power, the maximum permissible Class I exposure duration is 4 minutes and 30 seconds. When the cross beam lasers are turned on, a 2-minute automatic time out is activated to ensure the safe exposure limit is not exceeded. The cross beam lasers comply with Class I accessible emission limits for laser radiation in 21CFR1040 as well as ANSI Z136.1-1993.

Plume Removal System

The plume removal system is housed within the calibration stage. During surgery the plume removal system is deployed to a pre-determined height and provides a constant level of plume removal during ablation. The plume is evacuated to a filter cartridge contained within the system. This filter cartridge is inspected and replaced during preventive maintenance performed by Alcon Technical Service personnel.

System Software

The LADAR*6000*™ System software controlling the proprietary excimer laser runs on an Intel Pentium[4]-based personal computer under a Microsoft Windows[5] operating system. The software enables the user to:

- properly center the treatment;
- make adjustments in the X and Y axes;
- adjust for cyclotorsion and correctly reference astigmatism; and
- place a hinge guard to protect the flap during surgery.

In addition, the software enables the user to properly match the alignment of the wavefront map to the ablation.

Laser Shot Patterns

The LADAR*6000*™ System software calculates the "laser shot pattern," i.e., the number of excimer laser pulses to deliver to the eye and the required position of each pulse on the cornea, based on the desired refractive correction and the current laser calibration. The system software also calculates a sequence to fire the pulses in the shot pattern such that no corneal site is revisited by the excimer beam for a finite interval. The laser firing sequence is designed to provide a gradual corneal curvature from the starting surface shape to the corrected final profile.

Rather than the refractive correction being entered manually by the physician based on phoropter refraction, the CustomCornea® treatment requires that the pre-operative aberrations in the eye be measured with a wavefront measurement device. The treatment is based on Zernike data derived from a wavefront measurement device, including treatment of lower-order sphere and astigmatism components and higher-order components, such as coma and spherical aberration.

[4] *Intel* and *Pentium* Reg. TM of Intel Corporation
[5] *Microsoft* and *Windows* Reg. TM of Microsoft Corporation

The electronic file that the LADAR*6000*™ System receives from the wavefront measurement device includes the following information:

- Patient information, including name, identification number, and clinical prescription.
- Eye information, including OD/OS and the geometric relationship of the wavefront data to the limbus and to the pupil center.
- Wavefront information, including a Zernike polynomial representation of the wavefront and the physical radius of that description.

The excimer laser beam characteristics (i.e., pulse energy, firing rate, fluence distribution at the treatment plane) are the same for Conventional and CustomCornea® treatment modalities. The Conventional LADAR*6000*™ System treatment utilizes sphere, cylinder and axis components entered manually by the operator to generate the ablation profile. The CustomCornea® LASIK shaping algorithm utilizes aberration information unique to a given eye that is obtained from the WMD to guide the ablation of the cornea. The wavefront information is registered to the anatomical geometry of the eye using the WMD while the patient is sitting upright. This registered alignment information is passed to the LADAR*6000*™ System, which both permits for the compensation of this alignment information due to the natural cyclotorsion incurred when the patient assumes a prone position and uses the geometry information to accurately position the customized ablation profile on the eye.

CustomCornea® Ablation Zones

For CustomCornea® ablations, the standard optical zone is 6.5mm with a blend zone of 1.25mm for a total ablation zone of 9.0mm.

Safety

The LADAR*6000*™ System contains a Class IV laser that conforms to the US FDA 21CFR1040 Radiological Health requirements. The laser system was designed to meet the following safety requirements:

- UL 60601-1
- CSA 601.1
- ANSI/ESNA RP-27.1
- EN 60601-1
- EN 60101-1-2
- EN 60601-1-4
- EN 60101-2-22
- EN 60825-1

NOTE: Additional details regarding operation of this laser can be found in the LADAR*6000*™ Excimer Laser System Operation Manual.

Comparable Devices

The LADAR*6000*™ Excimer Laser System is functionally equivalent to the LADARVision®4000 Excimer Laser System. Clinical studies conducted with the LADARVision®4000 System are applicable to the LADAR*6000*™ System.

3. INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE EVENTS AND COMPLICATIONS

A. *INDICATIONS FOR USE*

The LADAR*6000*™ Excimer Laser System is indicated for wavefront-guided Laser Assisted In-Situ Keratomileusis (LASIK):

- for the reduction or elimination of hyperopia and hyperopic astigmatism of +0.75D to less than +5.00D sphere with up to -3.00D cylinder (which has a magnitude less than or equal to the sphere in minus cylinder convention) and up to +5.00D cycloplegic spherical equivalent at the spectacle plane;
- in patients who are 21 years of age or older; and
- in patients with documented stability of refraction for the prior 12 months, as demonstrated by a change in sphere and cylinder of less than or equal to 0.50D.

B. *CONTRAINDICATIONS*

Wavefront-guided LASIK is contraindicated in:

- pregnant or nursing women.
- patients with autoimmune, collagen vascular, or immunodeficiency diseases.
- patients with signs of keratoconus.
- patients who are taking one or both of the following medications: isotretinoin (Accutane[6]) or amiodarone hydrochloride (Cordarone[7]).

C. *WARNINGS*

Wavefront-guided LASIK is not recommended in patients who have:

- diabetes.
- a history of herpes simplex or herpes zoster keratitis.
- significant dry eye that is unresponsive to treatment.
- severe allergies.

A minimum pre-operative pupillary dilation of 7mm and a maximum dilation of 11mm must be achieved and maintained in all patients throughout the refractive procedure to optimize tracking performance.

[6] *Accutane* Reg. TM of Hoffmann-La Roche Inc.
[7] *Cordarone* Reg. TM of Sanofi-Aventis

D. PRECAUTIONS

The safety and effectiveness of the LADAR*6000*™ System for wavefront-guided LASIK correction of hyperopia and hyperopic astigmatism have **NOT** been established in patients:

- with unstable hyperopia and hyperopic astigmatism.
- with ocular disease, corneal abnormality, previous corneal or intraocular surgery, or trauma in the ablation zone.
- with a residual posterior stromal corneal thickness less than 250 microns at the completion of ablation.
- with a history of glaucoma.
- who are taking the medication sumatripin succinate (Imitrex8).
- under 21 years of age.
- over the long term (more than 9 months after surgery).
- for treatments of hyperopia and hyperopic astigmatism of +5.00D or greater sphere combined with greater than -3.00D cylinder and greater than +5.00D spherical equivalent by cycloplegic refraction.
- for retreatment with wavefront-guided LASIK.

The safety and effectiveness of wavefront-guided CustomCornea® LASIK have only been established for an optical zone of 6.5mm and an ablation zone of 9.0mm.

Pupil size should be evaluated under mesopic illumination conditions. Patients with large mesopic pupils ≥6.5mm (optical zone size) should be advised of the potential for negative effects on vision after surgery, such as glare, halos, and nighttime driving difficulty.

Preoperative evaluation for dry eye should be performed. Patients should be advised of the potential for dry eyes post-LASIK surgery.

The physician's adjustment of defocus has not been studied, and its effects on the safety and effectiveness outcomes of this procedure are unknown.

Please be advised that eyes with prior intraocular or corneal surgery of any kind were excluded from clinical trials with the LADARVision®4000 System. Safety and effectiveness, as well as tracking performance, have not been established for such eyes. Although the tracking system may acquire track in surgically altered eyes prior to ablation, the optics of the eye may change in the context of the ablation to potentially interfere with further tracking and compromise the completion of the ablation. Medical judgment should be exercised in the use of the LADAR*6000*™ System in pseudophakic patients and others who have had prior intraocular or corneal surgery.

[8] *Imitrex* Reg. TM of Glaxo Group Limited

E. ADVERSE EVENTS AND COMPLICATIONS

Cumulative adverse events and complications reported in a clinical study at any postoperative visit up to 9 months of CustomCornea® LASIK for the correction of hyperopia and hyperopic astigmatism with the LADARVision®4000 System are summarized in Table 1 below.

Table 1. Summary of Adverse Events and Complications At Any Postoperative Visit

ADVERSE EVENTS	n/N	%
Corneal subepithelial infiltrate (related to viral keratoconjunctivitis)	2/346	0.6%
Follicular conjunctivitis with associated loss of > 10 letters of BSCVA	2/346	0.6%
Decrease in BSCVA >10 letters not due to irregular astigmatism as shown by hard contact lens refraction at 6 months or later	1/346	0.3%
Idiopathic choroidal neovascular membrane (unrelated to device)	1/346	0.3%
COMPLICATIONS	**n/N**	**%**
Epithelium in the interface	11/346	3.2%
Diffuse lamellar keratitis (DLK)	5/346	1.4%
Foreign body sensation at one month or later	3/346	0.9%
Filamentary keratitis	2/346	0.6%
Superficial punctate keratitis (SPK) (with medical management)	2/346	0.6%
Pain at one month or later	1/346	0.3%
Peripheral corneal epithelial defect at one month or later across keratectomy or off flap	1/346	0.3%

There were no reports of the following adverse events and complications in the clinical study:

- corneal edema
- corneal epithelial defect involving the keratectomy at one month or later
- double or ghost images
- late onset of corneal haze at six months with a loss of 2 or more lines of best spectacle corrected visual acuity (BSCVA)
- epithelium in the interface with a loss of 2 or more lines of BSCVA
- melting of the flap
- miscreated flap
- misaligned flap
- intraocular pressure (IOP) of more than 25 mmHg
- IOP increase of more than 10 mmHg above baseline
- retinal detachment
- retinal vascular accident

4. CLINICAL STUDY

A. INTRODUCTION

The study in the U.S. using the LADARVision®4000 System began as a prospective, randomized, unmasked, and multi-center trial, where one eye of the patient received CustomCornea® LASIK correction using data from a wavefront measurement system and the fellow eye received a Conventional treatment based on phoropter cycloplegic refraction. For this initial subgroup of subjects, the fellow eye served as a contralateral control.

Upon providing data to support expansion of the number of subjects for enrollment, the U.S. study design was changed to a prospective, non-randomized, unmasked, and multi-center trial where one or both eyes of a subject received wavefront-guided CustomCornea® treatment. The primary control was the preoperative state of the treated eye for comparison to postoperative outcomes. An equivalent study design was also in progress under a Canadian protocol. Data from the U.S. and Canadian studies were pooled since both protocols were equivalent in terms of the inclusion and exclusion criteria, study procedures, subject measurements, and the treatment applied to the eye.

The objective of the multi-center clinical investigation was to establish safety and effectiveness of wavefront-guided CustomCornea® LASIK correction of hyperopia and hyperopic astigmatism. Subjects were followed on Day 1, at 1 week, and at 1, 3, 6, and 9 months postoperatively.

Recruited subjects had the study details and follow-up requirements explained to them and were asked to sign an Informed Consent Document preoperatively. To be eligible for the study, hyperopic subjects must have had a preoperative cycloplegic refraction at the spectacle plane of up to +6.00D sphere with up to -6.00D astigmatism (minus cylinder convention) and up to +6.00D spherical equivalent (SE). Enrollment of hyperopic and hyperopic astigmatic eyes in the study occurred over the preoperative cycloplegic refractive range of +0.75D to +6.00D sphere with up to -5.00D astigmatism and up to +5.75D SE, where the absolute cycloplegic cylinder in minus cylinder convention was less than or equal to the sphere.

Stability of refraction must have been established and documented using previous clinical records or measurement of spectacles. Stability was demonstrated by a change in the manifest sphere and cylinder over the prior 12 months of less than or equal to 0.50D. If a year-old refraction was not available, the change in refraction must have been 0.50D or less per year since the last documented refraction in both the manifest sphere and cylinder to a 1.00D maximum SE change.

The manifest and cycloplegic refraction measured at the preoperative examination must have been within 1.00D of each other in the sphere and cylinder components. In addition, the cycloplegic refraction could not differ by more than 1.00D in sphere or cylinder from the attempted correction determined by the wavefront measurement system.

For the contralateral treatment group, the cycloplegic refraction between the subject's two eyes could not differ by more than 1.00D in sphere or cylinder. In addition, subjects must have been willing to have LASIK correction in both eyes within a 2-week period. These two criteria were not applicable to subjects treated under the bilateral CustomCornea® treatment study design.

Subjects must have been at least 18 years of age and had a best-spectacle corrected visual acuity (BSCVA) of 20/25 or better in the operative eye(s). Subjects must have been willing to return for scheduled follow-up examinations for 9 months after surgery and have their eyes pharmacologically dilated at the required visits.

Subjects who were contact lens wearers were requested to discontinue contact lens wear for a minimum of 2 weeks for soft contact lenses and 3 weeks for hard contact lenses (RGP/PMMA) prior to the preoperative examination. Subjects who had previously worn hard lenses were required to have two examinations conducted 2 to 3 weeks apart to show stability of refraction without lens wear. Prior to surgery, subjects were not to wear their contact lenses in the operative eye(s) for 2 to 3 weeks for soft and hard contact lenses, respectively.

All eyes were required to be treated for a target of emmetropia. All surgeries performed in the study were subject to approval by the Sponsor.

Patients who exhibited any of the following conditions were excluded:

- previous corneal, intraocular, or strabismus surgery in the operative eye(s)
- history of or active clinically significant or vision threatening ocular disease or pathology
- clinically significant corneal scar within the ablation zone or corneal abnormality such as recurrent erosion or severe basement membrane disease
- signs of keratoconus
- irregular corneal astigmatism
- history of herpes keratitis
- autoimmune or connective tissue disease, clinically significant atopic syndrome, or diabetes
- use of chronic systemic corticosteroids or other immunosuppressive therapy
- use of systemic medication with significant ocular side effects
- pregnant or nursing
- use of ophthalmic medications other than artificial tears for treatment of an ocular pathology
- severe dry eye syndrome unresolved by treatment
- known allergy to study medications
- glaucoma or glaucoma filtering surgery
- participation in another ophthalmic clinical trial
- calculated residual posterior stromal thickness of less than 250 microns
- inability to achieve a pupillary dilation of ≥ 7mm
- at risk of angle closure
- an inability to obtain a clear and complete wavefront image

The primary effectiveness parameters for this study were improvement of uncorrected visual acuity (UCVA), predictability and stability of MRSE, reduction of wavefront error, including higher-order aberrations and subject satisfaction. The safety parameters for this study were preservation of BSCVA, absence of significant findings in slit lamp and fundus examination, absence of significant intraocular pressure (IOP) elevation, and incidence of complications and adverse events.

B. RESULTS

1. Demographics

The demographics of the CustomCornea® study shown in Table 2 were typical for a refractive surgery trial performed in the U.S. The mean subject age was 49.8 ± 9.2 years with a range from 19 to 70 years. The majority of subjects were Caucasian (95.4%) and the remaining subjects were Hispanic (2.9%) and Black (1.7%). Slightly more males (54.0%) than females (46.0%) participated in the study. The distribution of right and left eyes that received treatment was approximately equal (51.2% vs. 48.8%). While most subjects (59.5%) did not wear contact lenses prior to surgery, 37.6% wore soft contact lenses and 2.9% wore rigid gas permeable (RGP) lenses.

Table 2. Demographics

346 Eyes of 205 Enrolled Subjects			
Age (In Years)			
Average ± Standard Deviation		49.8 ± 9.2	
Minimum to Maximum		19 to 70	
Race		**N**	**% Eyes**
	Black	6	1.7%
	Caucasian	330	95.4%
	Hispanic	10	2.9%
Gender:	Female	159	46.0%
	Male	187	54.0%
Eye:	Left	169	48.8%
	Right	177	51.2%
Contact Lens History:	None	206	59.5%
	Rigid Gas Permeable (RGP)	10	2.9%
	Soft	130	37.6%

2. Primary Safety and Effectiveness Cohorts

The Primary Safety Cohort consisted of 346 eyes with a preoperative cycloplegic refractive range of +0.75D to +6.00D sphere with up to -5.00D cylinder and up to +5.75D spherical equivalent. The Primary Effectiveness Cohort consisted of 297 eyes with a preoperative cycloplegic refractive range of +0.75D to +6.00D sphere with up to –3.00D cylinder and up to +5.00D spherical equivalent (Table 3). A spherical eye was defined as having less than -0.50D preoperative cycloplegic cylinder and an astigmatic eye was defined as having at least -0.50D preoperative cycloplegic cylinder.

Table 3. Primary Safety and Effectiveness Cohorts

Cohort	N Eyes Enrolled	Preoperative Cycloplegic Refractive Range (D)		
		Sphere	Cylinder	Spherical Equivalent
Safety	**346**	**+0.75 to +6.00**	**0.00 to -5.00**	**+0.50 to +5.75**
Spherical Hyperopia	90	+0.75 to +5.00	0.00 to -0.25	+0.63 to +4.88
Hyperopic Astigmatism	256	+1.00 to +6.00	-0.50 to -5.00	+0.50 to +5.75
Effectiveness	**297**	**+0.75 to +6.00**	**0.00 to -3.00**	**+0.50 to +5.00**
Spherical Hyperopia	85	+0.75 to +5.00	0.00 to -0.25	+0.63 to +4.88
Hyperopic Astigmatism	212	+1.00 to +6.00	-0.50 to -3.00	+0.50 to +5.00

(D) = Diopter

3. Preoperative Cycloplegic Refraction Parameters

For the Primary Safety Cohort, the number of eyes is shown stratified by preoperative cycloplegic sphere and cylinder in Table 4 and by preoperative cycloplegic spherical equivalent and cylinder in Table 5.

Table 4. Preoperative Cycloplegic Refraction Stratified by Sphere and Cylinder: Safety Cohort

SPHERE (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION						
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to -3.00	-3.01 to -4.00	-4.01 to -5.00	TOTAL
+0.75 to +1.99	n/N	35/346	45/346	29/346	0/346	0/346	0/346	109/346
	%	10.1%	13.0%	8.4%	0.0%	0.0%	0.0%	31.5%
+2.00 to +2.99	n/N	33/346	34/346	28/346	7/346	0/346	0/346	102/346
	%	9.5%	9.8%	8.1%	2.0%	0.0%	0.0%	29.5%
+3.00 to +3.99	n/N	10/346	25/346	18/346	6/346	0/346	0/346	59/346
	%	2.9%	7.2%	5.2%	1.7%	0.0%	0.0%	17.1%
+4.00 to +4.99	n/N	11/346	23/346	8/346	6/346	0/346	0/346	48/346
	%	3.2%	6.6%	2.3%	1.7%	0.0%	0.0%	13.9%
+5.00 to +6.00	n/N	1/346	5/346	9/346	8/346	3/346	2/346	28/346
	%	0.3%	1.4%	2.6%	2.3%	0.9%	0.6%	8.1%
TOTAL	n/N	90/346	132/346	92/346	27/346	3/346	2/346	346/346
	%	26.0%	38.2%	26.6%	7.8%	0.9%	0.6%	100.0%

(D) = Diopter

Table 5. Preoperative Cycloplegic Refraction Stratified by Spherical Equivalent and Cylinder: Safety Cohort

SPHERICAL EQUIVALENT (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION						
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to -3.00	-3.01 to -4.00	-4.01 to -5.00	TOTAL
0.00 to +0.99	n/N	6/346	4/346	19/346	0/346	0/346	0/346	29/346
	%	1.7%	1.2%	5.5%	0.0%	0.0%	0.0%	8.4%
+1.00 to +1.99	n/N	30/346	53/346	31/346	9/346	0/346	0/346	123/346
	%	8.7%	15.3%	9.0%	2.6%	0.0%	0.0%	35.5%
+2.00 to +2.99	n/N	33/346	37/346	22/346	6/346	0/346	1/346	99/346
	%	9.5%	10.7%	6.4%	1.7%	0.0%	0.3%	28.6%
+3.00 to +3.99	n/N	9/346	21/346	10/346	5/346	2/346	1/346	48/346
	%	2.6%	6.1%	2.9%	1.4%	0.6%	0.3%	13.9%
+4.00 to +5.00	n/N	12/346	14/346	6/346	7/346	1/346	0/346	40/346
	%	3.5%	4.0%	1.7%	2.0%	0.3%	0.0%	11.6%
+5.01 to +6.00	n/N	0/346	3/346	4/346	0/346	0/346	0/346	7/346
	%	0.0%	0.9%	1.2%	0.0%	0.0%	0.0%	2.0%
TOTAL	n/N	90/346	132/346	92/346	27/346	3/346	2/346	346/346
	%	26.0%	38.2%	26.6%	7.8%	0.9%	0.6%	100.0%

(D) = Diopter

For the Primary Effectiveness Cohort, the number of eyes is shown stratified by preoperative cycloplegic sphere and cylinder in Table 6 and by preoperative cycloplegic spherical equivalent and cylinder in Table 7.

Table 6. Preoperative Cycloplegic Refraction Stratified by Sphere and Cylinder: Effectiveness Cohort

SPHERE (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION				
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to-3.00	TOTAL
+0.75 to +1.99	n/N	35/297	35/297	18/297	0/297	88/297
	%	11.8%	11.8%	6.1%	0.0%	29.6%
+2.00 to +2.99	n/N	29/297	31/297	22/297	7/297	89/297
	%	9.8%	10.4%	7.4%	2.4%	30.0%
+3.00 to +3.99	n/N	9/297	25/297	18/297	5/297	57/297
	%	3.0%	8.4%	6.1%	1.7%	19.2%
+4.00 to +4.99	n/N	11/297	23/297	7/297	6/297	47/297
	%	3.7%	7.7%	2.4%	2.0%	15.8%
+5.00 to +6.00	n/N	1/297	2/297	5/297	8/297	16/297
	%	0.3%	0.7%	1.7%	2.7%	5.4%
TOTAL	n/N	85/297	116/297	70/297	26/297	297/297
	%	28.6%	39.1%	23.6%	8.8%	100.0%

(D) = Diopter

Table 7. Preoperative Cycloplegic Refraction Stratified by Spherical Equivalent and Cylinder: Effectiveness Cohort

SPHERICAL EQUIVALENT (D)		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION				
		0.00 to -0.49	-0.50 to -0.99	-1.00 to -1.99	-2.00 to -3.00	TOTAL
0.00 to +0.99	n/N	6/297	0/297	9/297	0/297	15/297
	%	2.0%	0.0%	3.0%	0.0%	5.1%
+1.00 to +1.99	n/N	30/297	46/297	26/297	8/297	110/297
	%	10.1%	15.5%	8.8%	2.7%	37.0%
+2.00 to +2.99	n/N	29/297	35/297	20/297	6/297	90/297
	%	9.8%	11.8%	6.7%	2.0%	30.3%
+3.00 to +3.99	n/N	8/297	21/297	9/297	5/297	43/297
	%	2.7%	7.1%	3.0%	1.7%	14.5%
+4.00 to +5.00	n/N	12/297	14/297	6/297	7/297	39/297
	%	4.0%	4.7%	2.0%	2.4%	13.1%
TOTAL	n/N	85/297	116/297	70/297	26/297	297/297
	%	28.6%	39.1%	23.6%	8.8%	100.0%

(D) = Diopter

4. Accountability

Table 8 and 9 show the accountability of the Primary Safety and Effectiveness Cohorts for this study, which was greater than 99% at all postoperative intervals.

Table 8. Accountability at Each Visit: Safety Cohort

		1 Month	3 Months	6 Months	9 Months
Total Eyes Enrolled: Primary	n	202	202	202	202
Fellow	n	144	144	144	144
Total	N	346	346	346	346
Available for Analysis:	**n**	**346**	**346**	**320**	**161**
	%	**100.0%**	**100.0%**	**92.5%**	**46.5%**
Not Eligible for Interval:	n	0	0	24	185
	%	0.0%	0.0%	6.9%	53.5%
Unavailable: Missed Visit	n	0	0	2	0
	%	0.0%	0.0%	0.6%	0.0%
Lost to Follow-up	n	0	0	0	0
	%	0.0%	0.0%	0.0%	0.0%
% Accountability= [available/(available +unavailable)]	**%**	**100.0%**	**100.0%**	**99.4%**	**100.0%**

Table 9. Accountability at Each Visit: Effectiveness Cohort

		1 Month	3 Months	6 Months	9 Months
Total Eyes Enrolled: Primary	n	175	175	175	175
Fellow	n	122	122	122	122
Total	N	297	297	297	297
Available for Analysis:	**n**	**297**	**297**	**276**	**138**
	%	**100.0%**	**100.0%**	**92.9%**	**46.5%**
Not Eligible for Interval:	n	0	0	19	159
	%	0.0%	0.0%	6.4%	53.5%
Unavailable: Missed Visit	n	0	0	2	0
	%	0.0%	0.0%	0.7%	0.0%
Lost to Follow-up	n	0	0	0	0
	%	0.0%	0.0%	0.0%	0.0%
% Accountability= [available/(available + unavailable)]	**%**	**100.0%**	**100.0%**	**99.3%**	**100.0%**

5. Key Effectiveness and Safety Results

The outcomes for uncorrected visual acuity (UCVA) and manifest refraction spherical equivalent (MRSE) are shown for all eyes in the Primary Effectiveness Cohort (Table 10) and by refractive type (Table 11). The effectiveness parameters at 6 months are further stratified by preoperative cycloplegic refraction spherical equivalent (CRSE) (Table 12).

Preoperatively, 33.3% of eyes had a UCVA of 20/40 or better. At 6 months postoperative, the UCVA was 20/20 or better in 59.1% of eyes, 20/25 or better in 80.8% and 20/40 or better in 95.3%. For those eyes with a preoperative best spectacle corrected visual acuity (BSCVA) of 20/20 or better, a UCVA of 20/20 or better was achieved in 62.9% of eyes at 6 months. Accuracy of MRSE was within 0.50D of emmetropia in 70.7% of eyes, within 1.00D in 88.4% and within 2.00D in 98.6% at 6 months. Of the eyes that did not achieve an MRSE within 1.00D of emmetropia at 6 months, 3.3% of eyes were undercorrected by >1.00D of MRSE and 8.3% of eyes were overcorrected.

Whereas the mean MRSE (-0.09D ± 0.69D) was slightly myopic at 6 months, the mean CRSE (+0.13D ± 0.64D) was slightly hyperopic but within 0.25D of the mean MRSE. Accuracy of CRSE at 6 months was within 0.50D of emmetropia in 65.6% of eyes, within 1.00D in 89.1% and within 2.00D in 99.6%. At 6 months, 6.9% of eyes were undercorrected by >1.00D of CRSE and 4.0% of eyes were overcorrected.

The effectiveness data meet the criteria established in the FDA Guidance document for at least 85% of eyes achieving a UCVA of 20/40 or better and accuracy of MRSE within 0.50D in at least 50% of eyes and within 1.00D in 75% of eyes at all postoperative intervals.

Table 10. Summary of Key Effectiveness Parameters Over Time

All Eyes: Effectiveness Cohort		1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	162/273	167/273	161/256	79/128
	%	59.3%	61.2%	62.9%	61.7%
	CI	(53.3, 65.2)	(55.1, 67.0)	(56.7, 68.8)	(52.7, 70.2)
UCVA 20/20 or better	n/N	162/297	168/297	163/276	81/138
	%	54.5%	56.6%	59.1%	58.7%
	CI	(48.7, 60.3)	(50.7, 62.3)	(53.0, 64.9)	(50.0, 67.0)
UCVA 20/25 or better	n/N	239/297	241/297	223/276	112/138
	%	80.5%	81.1%	80.8%	81.2%
	CI	(75.5, 84.8)	(76.2, 85.4)	(75.6, 85.3)	(73.6, 87.3)
UCVA 20/40 or better	n/N	283/297	282/297	263/276	130/138
	%	95.3%	94.9%	95.3%	94.2%
	CI	(92.2, 97.4)	(91.8, 97.1)	(92.1, 97.5)	(88.9, 97.5)
MRSE ±0.50D of intended	n/N	191/297	193/297	195/276	90/138
	%	64.3%	65.0%	70.7%	65.2%
	CI	(58.6, 69.8)	(59.3, 70.4)	(64.9, 76.0)	(56.6, 73.1)
MRSE ±1.00D of intended	n/N	267/297	264/297	244/276	123/138
	%	89.9%	88.9%	88.4%	89.1%
	CI	(85.9, 93.1)	(84.8, 92.2)	(84.0, 91.9)	(82.7, 93.8)
MRSE ±2.00D of intended	n/N	293/297	294/297	272/276	137/138
	%	98.7%	99.0%	98.6%	99.3%
	CI	(96.6, 99.6)	(97.1, 99.8)	(96.3, 99.6)	(96.0, 100.0)

UCVA = Uncorrected Visual Acuity
BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent
CI = 95% Confidence Interval
D = Diopter

Table 11. Summary of Key Effectiveness Parameters Over Time: Spherical Hyperopia and Hyperopic Astigmatism

Spherical Hyperopia: Effectiveness Cohort		1 Month	3 Months	6 Months	9 Months
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	47/81	50/81	47/73	24/41
	%	58.0%	61.7%	64.4%	58.5%
	CI	(46.5, 68.9)	(50.3, 72.3)	(52.3, 75.3)	(42.1, 73.7)
UCVA 20/20 or better	n/N	47/85	50/85	47/76	25/44
	%	55.3%	58.8%	61.8%	56.8%
	CI	(44.1, 66.1)	(47.6, 69.4)	(50.0, 72.8)	(41.0, 71.7)
UCVA 20/25 or better	n/N	72/85	72/85	65/76	37/44
	%	84.7%	84.7%	85.5%	84.1%
	CI	(75.3, 91.6)	(75.3, 91.6)	(75.6, 92.5)	(69.9, 93.4)
UCVA 20/40 or better	n/N	85/85	83/85	75/76	44/44
	%	100.0%	97.6%	98.7%	100.0%
	CI	(95.8, 100.0)	(91.8, 99.7)	(92.9, 100.0)	(92.0, 100.0)
MRSE ±0.50D of intended	n/N	55/85	56/85	50/76	27/44
	%	64.7%	65.9%	65.8%	61.4%
	CI	(53.6, 74.8)	(54.8, 75.8)	(54.0, 76.3)	(45.5, 75.6)
MRSE ±1.00D of intended	n/N	79/85	79/85	70/76	42/44
	%	92.9%	92.9%	92.1%	95.5%
	CI	(85.3, 97.4)	(85.3, 97.4)	(83.6, 97.0)	(84.5, 99.4)
MRSE ±2.00D of intended	n/N	83/85	84/85	74/76	44/44
	%	97.6%	98.8%	97.4%	100.0%
	CI	(91.8, 99.7)	(93.6, 100.0)	(90.8, 99.7)	(92.0, 100.0)
Hyperopic Astigmatism: Effectiveness Cohort		**1 Month**	**3 Months**	**6 Months**	**9 Months**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	115/192	117/192	114/183	55/87
	%	59.9%	60.9%	62.3%	63.2%
	CI	(52.6, 66.9)	(53.7, 67.9)	(54.8, 69.3)	(52.2, 73.3)
UCVA 20/20 or better	n/N	115/212	118/212	116/200	56/94
	%	54.2%	55.7%	58.0%	59.6%
	CI	(47.3, 61.1)	(48.7, 62.5)	(50.8, 64.9)	(49.0, 69.6)
UCVA 20/25 or better	n/N	167/212	169/212	158/200	75/94
	%	78.8%	79.7%	79.0%	79.8%
	CI	(72.6, 84.1)	(73.7, 84.9)	(72.7, 84.4)	(70.2, 87.4)
UCVA 20/40 or better	n/N	198/212	199/212	188/200	86/94
	%	93.4%	93.9%	94.0%	91.5%
	CI	(89.2, 96.3)	(89.7, 96.7)	(89.8, 96.9)	(83.9, 96.3)
MRSE ± 0.50D of intended	n/N	136/212	137/212	145/200	63/94
	%	64.2%	64.6%	72.5%	67.0%
	CI	(57.3, 70.6)	(57.8, 71.0)	(65.8, 78.6)	(56.6, 76.4)
MRSE ± 1.00D of intended	n/N	188/212	185/212	174/200	81/94
	%	88.7%	87.3%	87.0%	86.2%
	CI	(83.6, 92.6)	(82.0, 91.4)	(81.5, 91.3)	(77.5, 92.4)
MRSE ± 2.00D of intended	n/N	210/212	210/212	198/200	93/94
	%	99.1%	99.1%	99.0%	98.9%
	CI	(96.6, 99.9)	(96.6, 99.9)	(96.4, 99.9)	(94.2, 100.0)

UCVA = Uncorrected Visual Acuity BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent CI = 95% Confidence Interval D = Diopter

Table 12. Summary of Key Effectiveness Parameters at 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

All Eyes: Effectiveness Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	14/15 93.3%	75/102 73.5%	49/76 64.5%	13/34 38.2%	10/29 34.5%	161/256 62.9%
UCVA 20/20 or better	n/N %	14/15 93.3%	76/106 71.7%	49/80 61.3%	14/39 35.9%	10/36 27.8%	163/276 59.1%
UCVA 20/25 or better	n/N %	15/15 100.0%	96/106 90.6%	62/80 77.5%	28/39 71.8%	22/36 61.1%	223/276 80.8%
UCVA 20/40 or better	n/N %	15/15 100.0%	105/106 99.1%	76/80 95.0%	34/39 87.2%	33/36 91.7%	263/276 95.3%
MRSE ± 0.50D of intended	n/N %	15/15 100.0%	89/106 84.0%	52/80 65.0%	20/39 51.3%	19/36 52.8%	195/276 70.7%
MRSE ± 1.00D of intended	n/N %	15/15 100.0%	103/106 97.2%	71/80 88.8%	29/39 74.4%	26/36 72.2%	244/276 88.4%
MRSE ± 2.00D of intended	n/N %	15/15 100.0%	106/106 100.0%	79/80 98.8%	39/39 100.0%	33/36 91.7%	272/276 98.6%
Spherical Hyperopia: Effectiveness Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	6/6 100.0%	19/27 70.4%	16/23 69.6%	1/6 16.7%	5/11 45.5%	47/73 64.4%
UCVA 20/20 or better	n/N %	6/6 100.0%	19/29 65.5%	16/23 69.6%	1/6 16.7%	5/12 41.7%	47/76 61.8%
UCVA 20/25 or better	n/N %	6/6 100.0%	26/29 89.7%	20/23 87.0%	6/6 100.0%	7/12 58.3%	65/76 85.5%
UCVA 20/40 or better	n/N %	6/6 100.0%	29/29 100.0%	23/23 100.0%	6/6 100.0%	11/12 91.7%	75/76 98.7%
MRSE ± 0.50D of intended	n/N %	6/6 100.0%	24/29 82.8%	15/23 65.2%	1/6 16.7%	4/12 33.3%	50/76 65.8%
MRSE ± 1.00D of intended	n/N %	6/6 100.0%	29/29 100.0%	23/23 100.0%	4/6 66.7%	8/12 66.7%	70/76 92.1%
MRSE ± 2.00D of intended	n/N %	6/6 100.0%	29/29 100.0%	23/23 100.0%	6/6 100.0%	10/12 83.3%	74/76 97.4%
Hyperopic Astigmatism: Effectiveness Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	8/9 88.9%	56/75 74.7%	33/53 62.3%	12/28 42.9%	5/18 27.8%	114/183 62.3%
UCVA 20/20 or better	n/N %	8/9 88.9%	57/77 74.0%	33/57 57.9%	13/33 39.4%	5/24 20.8%	116/200 58.0%
UCVA 20/25 or better	n/N %	9/9 100.0%	70/77 90.9%	42/57 73.7%	22/33 66.7%	15/24 62.5%	158/200 79.0%
UCVA 20/40 or better	n/N %	9/9 100.0%	76/77 98.7%	53/57 93.0%	28/33 84.8%	22/24 91.7%	188/200 94.0%
MRSE ± 0.50D of intended	n/N %	9/9 100.0%	65/77 84.4%	37/57 64.9%	19/33 57.6%	15/24 62.5%	145/200 72.5%
MRSE ± 1.00D of intended	n/N %	9/9 100.0%	74/77 96.1%	48/57 84.2%	25/33 75.8%	18/24 75.0%	174/200 87.0%
MRSE ± 2.00D of intended	n/N %	9/9 100.0%	77/77 100.0%	56/57 98.2%	33/33 100.0%	23/24 95.8%	198/200 99.0%

UCVA = Uncorrected Visual Acuity BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent CI = 95% Confidence Interval D = Diopter

The key safety outcomes for all 346 eyes in the Primary Safety Cohort are presented for all eyes in Table 13 and by refractive type in Table 14. These same parameters are stratified by preoperative CRSE at 6 months in Table 15.

The safety data meet the criteria established in the FDA guidance document of less than 5% of eyes with a loss of >2 lines of BSCVA, less than 1% having a BSCVA of worse than 20/40, and less than 5% having induced astigmatism >2D.

A trend for early postoperative loss of ≥ 2 lines of BSCVA at 1 month with recovery over time was observed, which is consistent with trends observed previously after Conventional hyperopic LASIK surgery. All eyes except two have shown resolution of the BSCVA to within one line of preoperative BSCVA at a later follow-up examination. Of the two eyes with unresolved loss at 9 months, one eye improved with RGP contact lens refraction to preoperative level and the other eye had idiopathic choroidal neovascularization at 9 months, which was an adverse event unrelated to the device.

Table 13. Summary of Key Safety Parameters Over Time

All Eyes: Safety Cohort		1 Month	3 Months	6 Months	9 Months
Loss of >2 Lines BSCVA	n/N	3/346	1/346	0/320	0/161
	%	0.9%	0.3%	0.0%	0.0%
	CI	(0.2, 2.5)	(0.0, 1.6)	(0.0, 1.1)	(0.0, 2.3)
Loss of 2 Lines BSCVA	n/N	16/346	6/346	3/320	5/161
	%	4.6%	1.7%	0.9%	3.1%
	CI	(2.7, 7.4)	(0.6, 3.7)	(0.2, 2.7)	(1.0, 7.1)
BSCVA worse than 20/40	n/N	1/346	1/346	0/320	0/161
	%	0.3%	0.3%	0.0%	0.0%
	CI	(0.0, 1.6)	(0.0, 1.6)	(0.0, 1.1)	(0.0, 2.3)
Increase >2D cylinder magnitude	n/N	0/346	0/346	0/320	0/161
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 1.1)	(0.0, 1.1)	(0.0, 1.1)	(0.0, 2.3)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	3/315	0/315	1/294	2/148
	%	1.0%	0.0%	0.3%	1.4%
	CI	(0.2, 2.8)	(0.0, 1.2)	(0.0, 1.9)	(0.2, 4.8)

BSCVA = Best Spectacle Corrected Visual Acuity CI = 95% Confidence Interval D = Diopter

Table 14. Summary of Key Safety Parameters Over Time: Spherical Hyperopia and Hyperopic Astigmatism

Spherical Hyperopia: Safety Cohort		1 Month	3 Months	6 Months	9 Months
Loss of >2 Lines BSCVA	n/N	0/90	0/90	0/79	0/46
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.6)	(0.0, 7.7)
Loss of 2 Lines BSCVA	n/N	4/90	3/90	1/79	1/46
	%	4.4%	3.3%	1.3%	2.2%
	CI	(1.2, 11.0)	(0.7, 9.4)	(0.0, 6.9)	(0.1, 11.5)
BSCVA worse than 20/40	n/N	0/90	0/90	0/79	0/46
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.6)	(0.0, 7.7)
Increase >2D cylinder magnitude	n/N	0/90	0/90	0/79	0/46
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.6)	(0.0, 7.7)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	0/85	0/85	0/76	0/43
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 4.2)	(0.0, 4.2)	(0.0, 4.7)	(0.0, 8.2)
Hyperopic Astigmatism: Safety Cohort		**1 Month**	**3 Months**	**6 Months**	**9 Months**
Loss of >2 Lines BSCVA	n/N	3/256	1/256	0/241	0/115
	%	1.2%	0.4%	0.0%	0.0%
	CI	(0.2, 3.4)	(0.0, 2.2)	(0.0, 1.5)	(0.0, 3.2)
Loss of 2 Lines BSCVA	n/N	12/256	3/256	2/241	4/115
	%	4.7%	1.2%	0.8%	3.5%
	CI	(2.4, 8.0)	(0.2, 3.4)	(0.1, 3.0)	(1.0, 8.7)
BSCVA worse than 20/40	n/N	1/256	1/256	0/241	0/115
	%	0.4%	0.4%	0.0%	0.0%
	CI	(0.0, 2.2)	(0.0, 2.2)	(0.0, 1.5)	(0.0, 3.2)
Increase >2D cylinder magnitude	n/N	0/256	0/256	0/241	0/115
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 1.4)	(0.0, 1.4)	(0.0, 1.5)	(0.0, 3.2)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	3/230	0/230	1/218	2/105
	%	1.3%	0.0%	0.5%	1.9%
	CI	(0.3, 3.8)	(0.0, 1.6)	(0.0, 2.5)	(0.2, 6.7)

BSCVA = Best Spectacle Corrected Visual Acuity CI = 95% Confidence Interval D = Diopter

Table 15. Summary of Key Safety Parameters at 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

All Eyes: Safety Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**>5.0 to 6.0D**	**Total**
Loss of >2 Lines BSCVA	n/N	0/28	0/117	0/87	0/44	0/37	0/7	0/320
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Loss of 2 Lines BSCVA	n/N	0/28	1/117	0/87	1/44	0/37	1/7	3/320
	%	0.0%	0.9%	0.0%	2.3%	0.0%	14.3%	0.9%
BSCVA worse than 20/40	n/N	0/28	0/117	0/87	0/44	0/37	0/7	0/320
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Increase >2D cylinder magnitude	n/N	0/28	0/117	0/87	0/44	0/37	0/7	0/320
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
BSCVA worse than 20/25 if 20/20 or better preoperative	n/N	0/27	0/113	0/82	0/38	0/29	1/5	1/294
	%	0.0%	0.0%	0.0%	0.0%	0.0%	20.0%	0.3%
Spherical Hyperopia: Safety Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**>5.0 to 6.0D**	**Total**
Loss of >2 Lines BSCVA	n/N	0/6	0/29	0/25	0/7	0/12	--	0/79
	%	0.0%	0.0%	0.0%	0.0%	0.0%		0.0%
Loss of 2 Lines BSCVA	n/N	0/6	0/29	0/25	1/7	0/12	--	1/79
	%	0.0%	0.0%	0.0%	14.3%	0.0%		1.3%
BSCVA worse than 20/40	n/N	0/6	0/29	0/25	0/7	0/12	--	0/79
	%	0.0%	0.0%	0.0%	0.0%	0.0%		0.0%
Increase >2D cylinder magnitude	n/N	0/6	0/29	0/25	0/7	0/12	--	0/79
	%	0.0%	0.0%	0.0%	0.0%	0.0%		0.0%
BSCVA worse than 20/25 if 20/20 or better preoperative	n/N	0/6	0/27	0/25	0/7	0/11	--	0/76
	%	0.0%	0.0%	0.0%	0.0%	0.0%		0.0%
Hyperopic Astigmatism: Safety Cohort		**0.0 to 0.99D**	**1.0 to 1.99D**	**2.0 to 2.99D**	**3.0 to 3.99D**	**4.0 to 5.0D**	**>5.0 to 6.0D**	**Total**
Loss of >2 Lines BSCVA	n/N	0/22	0/88	0/62	0/37	0/25	0/7	0/241
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Loss of 2 Lines BSCVA	n/N	0/22	1/88	0/62	0/37	0/25	1/7	2/241
	%	0.0%	1.1%	0.0%	0.0%	0.0%	14.3%	0.8%
BSCVA worse than 20/40	n/N	0/22	0/88	0/62	0/37	0/25	0/7	0/241
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Increase >2D cylinder magnitude	n/N	0/22	0/88	0/62	0/37	0/25	0/7	0/241
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
BSCVA worse than 20/25 if 20/20 or better preoperative	n/N	0/21	0/86	0/57	0/31	0/18	1/5	1/218
	%	0.0%	0.0%	0.0%	0.0%	0.0%	20.0%	0.5%

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

6. Comparison of Postoperative Uncorrected Visual Acuity and Preoperative Best Spectacle Corrected Visual Acuity

A comparison of **postoperative** uncorrected visual acuity (UCVA) to **preoperative** best spectacle corrected visual acuity (BSCVA) after CustomCornea® LASIK surgery is presented in Table 16 with differences based on lines of visual acuity. A postoperative UCVA equal to or better than the preoperative BSCVA was achieved in 41.7% of eyes at 6 months.

Table 16. Postoperative Uncorrected Visual Acuity Compared to Preoperative Best Spectacle Corrected Visual Acuity

		1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
UCVA **2 Lines Better** Than Preop BSCVA	n/N	0/297	1/297	0/276	0/138
	%	0.0%	0.3%	0.0%	0.0%
UCVA **1 Line Better** Than Preop BSCVA	n/N	18/297	28/297	24/276	13/138
	%	6.1%	9.4%	8.7%	9.4%
UCVA **Equal** to Preop BSCVA	n/N	93/297	86/297	91/276	49/138
	%	31.3%	29.0%	33.0%	35.5%
UCVA **1 Line Worse** Than Preop BSCVA	n/N	88/297	90/297	80/276	32/138
	%	29.6%	30.3%	29.0%	23.2%
UCVA **2 Lines Worse** Than Preop BSCVA	n/N	54/297	43/297	34/276	21/138
	%	18.2%	14.5%	12.3%	15.2%
UCVA **>2 Lines Worse** Than Preop BSCVA	n/N	44/297	49/297	47/276	23/138
	%	14.8%	16.5%	17.0%	16.7%

UCVA = Uncorrected Visual Acuity BSCVA = Best Spectacle Corrected Visual Acuity

Equal visual acuity is within 2 or 3 letters on the same line of a visual acuity chart

7. Stability of Manifest Refraction

The mean MRSE for the Primary Effectiveness Cohort was stable between 3 and 6 months, as shown in Figure 1 and Table 17.

Figure 1. Manifest Refraction Spherical Equivalent Over Time

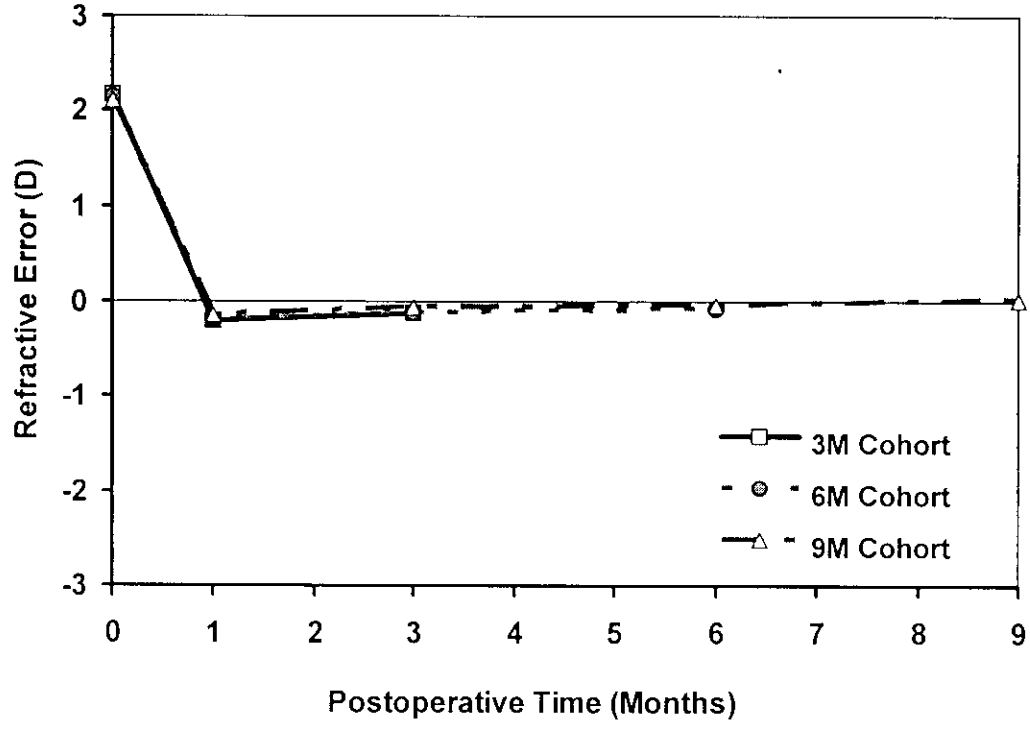


Table 17. Manifest Refraction Spherical Equivalent Over Time

Mean ± SD (95% CI)	n	PREOP	1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
3-Month Cohort	297	2.16 ± 1.07 (2.04, 2.28)	-0.20 ± 0.68 (-0.28, -0.13)	-0.12 ± 0.69 (-0.20, -0.04)	--	--
6-Month Cohort	276	2.14 ± 1.07 (2.01, 2.26)	-0.21 ± 0.69 (-0.30, -0.13)	-0.13 ± 0.71 (-0.21, -0.04)	-0.09 ± 0.69 (-0.17, -0.01)	--
9-Month Cohort	138	2.11 ± 0.99 (1.94, 2.27)	-0.14 ± 0.59 (-0.24, -0.05)	-0.07 ± 0.65 (-0.18, 0.03)	-0.05 ± 0.62 (-0.15, 0.05)	0.02 ± 0.66 (-0.09, 0.13)

SD = Standard Deviation 95% CI = 95% Confidence Interval

Stability of MRSE was analyzed as paired differences in MRSE between 1 and 3 months, between 3 and 6 months, and between 6 and 9 months. Analyses were performed for the entire Primary Effectiveness Cohort with data available at any interval and for consistent cohorts with data available at each interval over time (Table 18).

The data meet the FDA guidance document criterion of at least 95% having a change in MRSE of ≤ 1.00D between all intervals. Refractive stability was reached between 3 and 6 months with 99.6% of the eyes demonstrating a change ≤ 1.00D of MRSE; a mean change in MRSE of 0.04D ± 0.29D between 3 and 6 months with a rate of 0.01D per month; a decrease in the mean change in MRSE from 1 month to 6 months; and a 95% confidence interval (0.00, 0.07) that includes zero for the mean change between 3 and 6 months. Stability was confirmed between 6 and 9 months.

Table 18. Stability of Manifest Refraction Spherical Equivalent

Entire Cohort	**Change in MRSE Between**		**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D	n/N %	294/297 99.0%	275/276 99.6%	137/138 99.3%
	Mean ± SD Change		0.09 ± 0.33	0.04 ± 0.29	0.07 ± 0.32
	95% Confidence Interval		(0.05, 0.13)	(0.00, 0.07)	(0.01, 0.12)
	Mean Change per Month		0.04	0.01	0.02
6-Month Cohort	**Change in MRSE Between**		**1 and 3 Months**	**3 and 6 Months**	
	≤ 1.00D	n/N %	274/276 99.3%	275/276 99.6%	
	Mean ± SD Change		0.09 ± 0.32	0.04 ± 0.29	
	95% Confidence Interval		(0.05, 0.13)	(0.00, 0.07)	
	Mean Change per Month		0.04	0.01	
9-Month Cohort	**Change in MRSE Between**		**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D	n/N %	137/138 99.3%	137/138 99.3%	137/138 99.3%
	Mean ± SD Change		0.07 ± 0.31	0.02 ± 0.29	0.07 ± 0.32
	95% Confidence Interval		(0.02, 0.12)	(-0.02, 0.07)	(0.01, 0.12)
	Mean Change per Month		0.03	0.008	0.02

MRSE = Manifest Refraction Spherical Equivalent SD = Standard Deviation

8. Effectiveness of Astigmatic Correction

Effectiveness of astigmatic correction was evaluated at the 6-month point of stability for hyperopic astigmatic eyes. The mean percentage reduction in absolute manifest cylinder was 53.3% for all eyes with a greater percentage reduction in eyes with higher preoperative cylinder (Table 19). The mean correction ratio based on vector analysis of manifest cylinder was 1.13 for all astigmatic eyes and approximately 1.00 for eyes with -1.00D to -3.00D preoperative manifest cylinder (Table 20). Astigmatic correction by cycloplegic cylinder reflected similar trends to manifest cylinder.

Table 19. Mean Percentage Reduction of Absolute (Non-Vector) Cylinder for Hyperopic Astigmatic Eyes

6 MONTHS				
Preoperative Cylinder	Manifest Cylinder		Cycloplegic Cylinder	
	N	Mean %	N	Mean %
All	198	53.3%	200	53.5%
>0.00 to < 0.50D *	7	0.0%	0	--
0.50 to < 1.00D	106	45.4%	110	41.2%
1.00 to < 2.00D	61	64.7%	67	65.6%
2.00 to 3.00D	24	74.8%	23	77.1%

* By preoperative manifest refraction, two eyes had no cylinder and seven eyes had -0.25D cylinder; by preoperative cycloplegic refraction, these 9 eyes had -0.50D or -0.75D cylinder.

Table 20. Vector Analysis for Hyperopic Astigmatic Eyes

6 MONTHS				
Preoperative Cylinder	Manifest Cylinder		Cycloplegic Cylinder	
	N	Mean ± SD Correction Ratio	N	Mean ± SD Correction Ratio
ALL	198	1.13 ± 0.57	200	1.12 ± 0.47
>0.00 to < 0.50D *	7	2.39 ± 1.44	0	--
0.50 to < 1.00D	106	1.15 ± 0.56	110	1.20 ± 0.57
1.00 to < 2.00D	61	1.00 ± 0.31	67	1.02 ± 0.32
2.00 to 3.00D	24	0.99 ± 0.18	23	1.00 ± 0.14

* By preoperative manifest refraction, two eyes had no cylinder and seven eyes had -0.25D cylinder; by preoperative cycloplegic refraction, these 9 eyes had -0.50D or -0.75D cylinder.

9. Change in Best Spectacle Corrected Visual Acuity

Best spectacle corrected visual acuity (BSCVA) was measured using a standard (high-contrast) visual acuity chart under dim room illumination (10-12 cd/m^2). All eyes had a BSCVA of 20/32 or better at 6 months. At least 73.7% of eyes at all postoperative intervals and 81.6% of eyes at 6 months had no change or a gain in BSCVA from preoperative (Table 21).

Table 21. Change in Best Spectacle Corrected Visual Acuity

		1 Month	3 Months	6 Months	9 Months
Decrease >2 Lines	n/N	3/346	1/346	0/320	0/161
	%	0.9%	0.3%	0.0%	0.0%
Decrease 2 Lines	n/N	16/346	6/346	3/320	5/161
	%	4.6%	1.7%	0.9%	3.1%
Decrease 1 Line	n/N	72/346	63/346	56/320	16/161
	%	20.8%	18.2%	17.5%	9.9%
No change	n/N	185/346	184/346	183/320	88/161
	%	53.5%	53.2%	57.2%	54.7%
Increase 1 Line	n/N	66/346	89/346	77/320	50/161
	%	19.1%	25.7%	24.1%	31.1%
Increase 2 Lines	n/N	4/346	3/346	1/320	2/161
	%	1.2%	0.9%	0.3%	1.2%
Increase >2 Lines	n/N	0/346	0/346	0/320	0/161
	%	0.0%	0.0%	0.0%	0.0%

Low contrast BSCVA was measured using a 10% low contrast visual acuity chart under dim room illumination. While 38.1% of eyes had no change in low contrast BSCVA from preoperative to 6 months, Table 22 shows slightly more eyes had a gain than loss of 1 line (25.6% vs. 22.8%) and of ≥ 2 lines (7.8% vs. 5.6%).

Table 22. Change in Low Contrast Best Spectacle Corrected Visual Acuity

		3 Months	6 Months
Decrease >2 Lines	n/N	13/346	7/320
	%	3.8%	2.2%
Decrease 2 Lines	n/N	19/346	11/320
	%	5.5%	3.4%
Decrease 1 Line	n/N	71/346	73/320
	%	20.5%	22.8%
No change	n/N	136/346	122/320
	%	39.3%	38.1%
Increase 1 Line	n/N	80/346	82/320
	%	23.1%	25.6%
Increase 2 Lines	n/N	25/346	22/320
	%	7.2%	6.9%
Increase >2 Lines	n/N	2/346	3/320
	%	0.6%	0.9%

10. Change in Contrast Sensitivity

Contrast sensitivity was measured under both photopic and mesopic conditions using the CSV-1000 (VectorVision[9]) (Table 23). A clinically significant change from preoperative level was defined as > 2 levels (> 0.3 log) at two or more spatial frequencies.

Under photopic conditions, the majority of eyes (85.3%) did not have a clinically significant change from preoperative to 6 months. The percentage of eyes with a clinically significant gain or loss of photopic contrast sensitivity was approximately equal (7.2% vs. 7.5%). Under mesopic conditions, 67.0% of subjects had no clinically significant change. A clinically significant gain was observed in 20.1% of eyes at 6 months, while a loss was observed in 12.9% of eyes, showing a trend for more gain than loss under mesopic conditions.

In addition, the mean log at each spatial frequency was compared for eyes with data at preop, 3 months and 6 months (consistent 6-month cohort, Table 24). The data reflect a mean gain in all spatial frequencies postoperatively under photopic and mesopic conditions. Statistically significant gains were noted at 6 months for all photopic spatial frequencies and for all mesopic spatial frequencies except 6 cycles per degree (cpd).

Table 23. Change of >2 Levels (> 0.3 Log) at 2 or More Spatial Frequencies

		Photopic		Mesopic*	
		3 MONTHS	6 MONTHS	3 MONTHS	6 MONTHS
Loss	n/N	25/344	24/319	52/327	40/309
	%	7.3%	7.5%	15.9%	12.9%
No Change	n/N	282/344	272/319	198/327	207/309
	%	82.0%	85.3%	60.6%	67.0%
Gain	n/N	37/344	23/319	77/327	62/309
	%	10.8%	7.2%	23.5%	20.1%

*Mesopic illumination with neutral density filters in front of eyes

Table 24. Comparison of Mean Contrast Sensitivity Log by Spatial Frequency: 6-Month Consistent Cohort

Spatial Frequency (cpd)	Preop Mean ± SD	3-Month Mean ± SD	p-value†	6-Month Mean ± SD	p-value†
Photopic	**N=317**	**N=317**		**N=317**	
3	1.70 ± 0.17	1.73 ± 0.18	**0.008**	1.76 ± 0.17	**<0.0001**
6	1.91 ± 0.18	1.94 ± 0.24	**0.042**	1.94 ± 0.21	**0.019**
12	1.53 ± 0.26	1.56 ± 0.29	0.149	1.57 ± 0.29	**0.023**
18	1.04 ± 0.29	1.06 ± 0.31	0.220	1.09 ± 0.29	**0.004**
Mesopic	**N=305**	**N=305**		**N=305**	
3	1.48 ± 0.23	1.54 ± 0.24	**<0.0001**	1.52 ± 0.22	**0.004**
6	1.49 ± 0.28	1.51 ± 0.31	0.372	1.52 ± 0.30	0.211
12	0.89 ± 0.33	0.93 ± 0.38	0.052	0.93 ± 0.37	**0.048**
18	0.34 ± 0.35	0.38 ± 0.40	0.097	0.40 ± 0.36	**0.008**

† p-value from paired t-test of differences between preoperative and postoperative means; p<0.05 is statistically significant shown in bold

[9] *VectorVision* TM of Brain Lab AG

11. Patient Self-Evaluation

Patients were asked to rate symptoms without glasses or contact lenses after surgery as compared to their recollection of symptoms before surgery, as shown in Table 25.

Table 25. Postoperative Change in Subjective Symptoms without Correction vs. Preoperative*

6 MONTHS						
Comfort Symptoms	**N**	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	276	9.4%	6.5%	79.3%	4.7%	0.0%
Dryness	276	9.1%	8.3%	58.0%	23.6%	1.1%
Excessive Tearing	274	4.0%	6.6%	85.8%	3.6%	0.0%
Gritty Feeling	276	6.9%	4.3%	78.3%	9.8%	0.7%
Headache	275	10.2%	10.2%	75.3%	4.4%	0.0%
Light Sensitivity	275	5.5%	16.4%	54.2%	20.0%	4.0%
Pain	276	7.2%	3.6%	85.1%	4.0%	0.0%
Redness	276	7.2%	7.2%	76.4%	8.3%	0.7%
Visual Symptoms						
Blurring of Vision	276	14.1%	16.3%	51.4%	15.2%	2.9%
Double Vision	276	7.2%	3.3%	76.1%	10.5%	2.9%
Fluctuation of Vision	276	6.9%	15.2%	56.2%	17.8%	4.0%
Glare	276	8.3%	12.3%	58.3%	18.5%	2.5%
Halos	275	9.1%	5.1%	70.2%	12.0%	3.6%
Night Driving Difficulty	276	17.0%	23.2%	46.4%	10.5%	2.9%

* Based on the patients' comparison of symptom severity after surgery to their recollection of symptom severity before surgery.

Uncorrected quality of vision at 6 months was unchanged, better or significantly better than preoperative quality of vision in 92.8% of patients, worse in 6.5%, and significantly worse in 0.7% (Table 26). In addition, 79.7% of patients were extremely satisfied or satisfied, 12.0% were not sure, 5.4% were unsatisfied and 2.9% were extremely unsatisfied with surgery results at 6 months (Table 27). At 6 months, 85.5% of patients reported never wearing any distance correction (Table 28).

Table 26. Postoperative Quality of Vision without Correction vs. Preoperative

6 MONTHS N=276	
Significantly Better	56.9%
Better	30.8%
Same	5.1%
Worse	6.5%
Significantly Worse	0.7%

Table 27. Postoperative Satisfaction with Surgery

6 MONTHS N=276	
Extremely Satisfied	47.8%
Satisfied	31.9%
Not Sure	12.0%
Unsatisfied	5.4%
Extremely Unsatisfied	2.9%

Table 28. Postoperative Frequency of Distance Correction

6 MONTHS N=276	
Never	85.5%
Seldom	7.6%
Frequently	2.2%
Constantly	4.7%

A small group of 42 patients received randomized treatment of CustomCornea® LASIK in one eye and Conventional LASIK in the other eye. These patients rated postoperative eye preference **without** glasses or contact lenses for quality of vision during the day and at night, less glare or night driving difficulty and overall eye preference (Table 29).

Table 29. Postoperative Eye Preference Without Glasses or Contact Lens Correction: Contralateral Cohort

Visit		CustomCornea® Eye	Same (No Preference)	Conventional Eye
3 Months (N=42)	Quality of Vision During the Day	40.5%	38.1%	21.4%
	Quality of Vision At Night	33.3%	52.4%	14.3%
	Less Glare or Night Driving Difficulty	14.3%	78.6%	7.1%
	Overall Eye Preference	42.9%	38.1%	19.0%
6 Months (N=41)	Quality of Vision During the Day	31.7%	46.3%	22.0%
	Quality of Vision At Night	31.7%	51.2%	17.1%
	Less Glare or Night Driving Difficulty	14.6%	75.6%	9.8%
	Overall Eye Preference	29.3%	51.2%	19.5%
9 Months (N=41)	Quality of Vision During the Day	29.3%	58.5%	12.2%
	Quality of Vision At Night	26.8%	61.0%	12.2%
	Less Glare or Night Driving Difficulty	12.2%	80.5%	7.3%
	Overall Eye Preference*	22.5%	55.0%	22.5%

* N=40 for Overall Eye Preference at 9 months

12. Retreatment

There are insufficient data for retreatment to establish safety and effectiveness.

13. Wavefront Outcomes

At 6 months, there was an average reduction in total RMS wavefront error by 63.9% and an average increase in higher-order aberrations by 23.6% from preoperative for all eyes in the Primary Effectiveness Cohort with data available at 6 months (N=261). Table 30 displays the preoperative and 6-month total wavefront error and higher-order aberrations through 6th order for eyes with data at preoperative, 1, 3 and 6 months (6-month consistent cohort; N=256). Spherical aberration decreased in magnitude at 6 months from preoperative with a mean directional shift from positive spherical aberration (0.249μm) preoperatively towards negative spherical aberration (-0.147μm) postoperatively, as expected from a hyperopic ablation profile.

Table 30. Mean Aberrations Up to 6th Order: 6-Month Consistent Cohort

Aberration (μm)	PREOP N = 256	6 MONTHS N = 256
Total RMS Error	2.677	1.000
Higher-Order	0.460	0.554
Coma	0.237	0.343
Trefoil	0.203	0.214
Spherical Aberration Magnitude*	0.249	0.219
Spherical Aberration Value**	0.249	-0.147
Secondary Astigmatism	0.072	0.111
Tetrafoil	0.080	0.120
Combined 5th and 6th Order	0.082	0.125

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Average based on the absolute spherical aberration magnitude

** Average based on the signed spherical aberration, reflecting a *positive* or *negative* direction

At 6 months, 99.6% of all eyes had a reduction in total RMS and 49.0% had a reduction in higher-order aberrations from preoperative, as shown in Table 31.

Table 31. Percentage of Eyes with Reduced Aberrations Up to 6th Order From Preoperative

6 MONTHS N = 261	
Aberration	**% Eyes with Reduction in Aberrations**
Total RMS Error	99.6%
Higher-Order	49.0%
Coma	38.7%
Trefoil	47.9%
Spherical Aberration Magnitude*	61.7%
Secondary Astigmatism	29.5%
Tetrafoil	31.0%
Combined 5th and 6th Order	21.8%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Reduction in absolute spherical aberration magnitude

Wavefront-guided CustomCornea® LASIK was compared to the baseline established for Conventional LASIK using preoperative cycloplegic phoropter refraction treated under the same study protocol. Wavefront aberrations at 6 months were analyzed up to 4th order for comparison.

In a Comparison Cohort, CustomCornea® and Conventional eyes were analyzed over the same preoperative refractive range of +0.75D to +4.25D sphere, up to -3.00D cylinder and up to +4.00D SE. Compared to Conventional eyes, CustomCornea® eyes showed statistically significantly lower mean amplitudes of total root mean square (RMS), higher-order aberrations, coma, and trefoil postoperatively with adjustment of baseline differences (ANCOVA, $p<0.05$). Table 32 shows that on average, CustomCornea® LASIK resulted in a greater mean reduction in total RMS error (62.3% vs. 46.1%) and less induction of higher-order aberrations (8.0% vs. 29.2%) from preoperative compared to Conventional LASIK. On average, both CustomCornea® and Conventional eyes showed a mean directional shift from positive spherical aberration preoperatively towards negative spherical aberration postoperatively, which was not statistically significant between the treatment groups.

Table 32. Mean Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Comparison Cohort

Aberration (µm)	PREOP		6 MONTHS		p-Value†
	CustomCornea® Eyes N = 258	Conventional All Eyes N = 95	CustomCornea® Eyes N = 229	Conventional All Eyes N = 94	
Total RMS Error	2.350	2.424	0.887	1.307	**<0.0001**
Higher-Order	0.451	0.497	0.487	0.642	**<0.0001**
Coma	0.236	0.264	0.307	0.402	**0.0061**
Trefoil	0.204	0.217	0.206	0.322	**<0.0001**
Spherical Aberration Magnitude*	0.251	0.276	0.188	0.201	0.3298
Spherical Aberration Value**	0.250	0.275	-0.108	-0.127	0.1325
Secondary Astigmatism	0.071	0.086	0.106	0.122	0.2566
Tetrafoil	0.081	0.098	0.119	0.159	**0.0045**

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Average based on the absolute spherical aberration magnitude

** Average based on the signed spherical aberration, reflecting a *positive* or *negative* direction

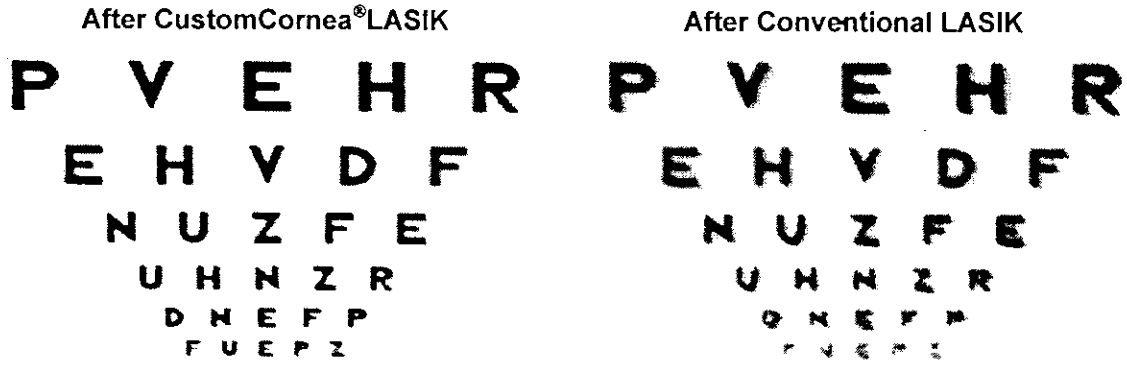
† ANCOVA for postoperative comparison between treatment types, adjusting for preoperative aberration differences; $p<0.05$ is statistically significant, shown in bold

A vision simulation program was used to model the effect of mean higher-order aberration magnitudes at 6 months after CustomCornea® LASIK versus Conventional LASIK in the Comparison Cohort. The difference in image blurring is comparable to a defocus error difference of approximately one tenth of a diopter (i.e., ~0.1D for the CustomCornea® simulation and ~0.2D for the Conventional simulation).

The following charts (Figure 2) provide an illustration of the appearance of the visual acuity chart with glasses or contact lenses after surgery. The charts show the difference in higher-order aberrations present in the eye after CustomCornea® LASIK (left chart) and after Conventional LASIK (right chart).

DO NOT REPRODUCE THE CHARTS BELOW

Figure 2. Simulated chart images for the average higher-order aberrations at 6 months after wavefront-guided surgery compared to after conventional surgery, based on wavefront over a 6 mm diameter pupil.



The percentage of patients with reduced higher-order aberrations was 55.9% for CustomCornea® LASIK compared to 33.0% for Conventional LASIK (Table 33).

Table 33. Percentage of Eyes with Reduced Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Comparison Cohort

6 MONTHS		
Aberration	**CustomCornea® Eyes** N = 229	**All Conventional Eyes** N = 94
Total RMS Error	99.6%	89.4%
Higher-Order	55.9%	33.0%
Coma	42.4%	26.6%
Trefoil	49.8%	27.7%
Spherical Aberration Magnitude*	67.7%	68.1%
Secondary Astigmatism	31.4%	41.5%
Tetrafoil	32.3%	30.9%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Reduction in absolute spherical aberration magnitude

To further evaluate the treatment types, a subgroup of subjects who underwent contralateral treatment of CustomCornea® LASIK in the primary eye and Conventional LASIK in the fellow eye was analyzed. This Contralateral Cohort had a preoperative cycloplegic refractive range of +0.75D to +4.25D sphere, up to –2.25D cylinder and up to +3.88D SE. Compared to Conventional eyes, CustomCornea® eyes in the Contralateral Cohort showed statistically significantly lower mean amplitudes of total RMS, higher-order aberrations, and trefoil postoperatively (ANCOVA, $p<0.05$).

Table 34 shows that on average, CustomCornea® LASIK resulted in a greater mean reduction in total RMS error (62.2% vs. 51.2%) and less induction in higher-order aberrations (5.2% vs. 20.7%) from preoperative compared to Conventional LASIK. On average, both CustomCornea® and Conventional eyes showed a mean directional shift from positive spherical aberration preoperatively towards negative spherical aberration postoperatively, which was not statistically significant between the treatment groups.

Table 34. Mean Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Contralateral Cohort

Aberration (µm)	PREOP		6 MONTHS		p-Value†
	CustomCornea® Eyes N = 42	Conventional Fellow Eyes N = 42	CustomCornea® Eyes N = 41	Conventional Fellow Eyes N = 41	
Total RMS Error	2.127	2.178	0.803	1.062	**0.0012**
Higher-Order	0.420	0.445	0.442	0.537	**0.0089**
Coma	0.210	0.267	0.269	0.318	0.1663
Trefoil	0.201	0.192	0.203	0.249	**0.0389**
Spherical Aberration Magnitude*	0.239	0.226	0.180	0.213	0.3158
Spherical Aberration Value**	0.237	0.223	-0.102	-0.182	0.0590
Secondary Astigmatism	0.056	0.079	0.078	0.084	0.7101
Tetrafoil	0.074	0.081	0.122	0.132	0.6563

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Average based on the absolute spherical aberration magnitude

** Average based on the signed spherical aberration, reflecting a *positive* or *negative* direction

† ANCOVA for postoperative comparison between treatment types, adjusting for preoperative aberration differences; $p<0.05$ is statistically significant, shown in bold

The percentage of subjects in the Contralateral Cohort with reduced higher-order aberrations was 46.3% for CustomCornea® LASIK compared to 36.6% for Conventional LASIK (Table 35).

Table 35. Percentage of Eyes with Reduced Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Contralateral Cohort

	6 MONTHS	
Aberration	CustomCornea® Eyes N = 41	Conventional Fellow Eyes N = 41
Total RMS Error	100.0%	90.2%
Higher-Order	46.3%	36.6%
Coma	43.9%	36.6%
Trefoil	46.3%	36.6%
Spherical Aberration Magnitude*	63.4%	58.5%
Secondary Astigmatism	29.3%	43.9%
Tetrafoil	26.8%	36.6%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Reduction in absolute spherical aberration magnitude

14. Statistical Analysis Outcomes

Statistical analysis was performed to assess for potential associations between demographic and baseline characteristics and clinical outcomes. Demographic and baseline characteristics that were considered to have the most potential for clinical relevance to the procedure included age, gender, race, preoperative cycloplegic sphere, cylinder and CRSE, operative room humidity and temperature. Outcomes evaluated at refractive stability (6 months) included loss of BSCVA, UCVA and accuracy of MRSE.

One-sided exact binomial tests (α=0.05) were used to compare the observed overall rates of safety and effectiveness outcomes to the FDA Guidance document targets. There was no BSCVA loss of > 2 lines at 6 months, thereby meeting the FDA target rate of < 5% of eyes for safety. FDA effectiveness targets were met or exceeded for all effectiveness outcomes, including UCVA 20/40 or better and accuracy of MRSE within 0.50D and within 1.00D of emmetropia at 6 months. For each demographic and baseline subcategory, the observed rate either met the target or the 95% confidence interval contained the FDA target value for effectiveness.

To assess the consistency of outcomes across demographic and baseline subcategories, differences in rates among the subcategories were assessed using the Cochran-Mantel-Haenszel (CMH) test. A p-value of < 0.05 indicates statistically significant differences between demographic and baseline categories. For a loss of 2 or more lines of BSCVA at 6 months, no statistically significant differences among the demographic and baseline categories were found.

Statistically significant differences in the rates of subjects achieving a UCVA of 20/20 or better at 6 months were noted based on room temperature (p=0.0160), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). Eyes treated in a lower room temperature and eyes with lower preoperative cycloplegic sphere or lower preoperative CRSE were more likely to achieve a UCVA of 20/20 or better. No FDA target is established for UCVA 20/20 or better.

For the outcome of UCVA 20/40 or better at 6 months, statistically significant differences in the rates of subjects were observed for preoperative cycloplegic sphere (p=0.0005), cylinder (p=0.0054), and CRSE (p=0.0031). Subjects with lower preoperative cycloplegic sphere, lower preoperative cycloplegic cylinder and lower preoperative CRSE were more likely to achieve a UCVA of 20/40 or better. However, all preoperative sphere, cylinder and CRSE subgroups met or exceeded the FDA target of ≥85% of eyes achieving a UCVA 20/40 or better at 6 months.

Baseline categories that showed statistically significant differences in the rates of subjects achieving an accuracy of MRSE within 0.50D of emmetropia were room humidity (p=0.0433), temperature (p=0.0480), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). While there was no consistent trend in MRSE based on room humidity, subjects treated in lower room temperature were more likely to have an MRSE within 0.50D at 6 months. Accuracy of MRSE within 0.50D was more likely in subjects with lower preoperative cycloplegic sphere and lower preoperative CRSE. In addition, all room humidity, temperature, preoperative sphere and preoperative CRSE subgroups met or exceeded the FDA target for MRSE within 0.50D at 6 months.

At 6 months, statistically significant differences were observed for an MRSE outcome within 1.00D based on room humidity (p=0.0113), age (p=0.0061), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). As noted for an MRSE within 0.50D, there was no consistent trend based on room humidity for MRSE within 1.00D and all humidity subgroups met or exceeded the FDA target. A higher percentage of older subjects were within 1.00D MRSE at 6 months compared to younger subjects; however, at least 75% of eyes within each age subgroup had an MRSE within 1.00D, meeting or exceeding the FDA target.

Preoperative latent hyperopia, particularly in younger subjects with greater accommodative reserve, may be a contributing factor to the postoperative MRSE outcome. All eyes enrolled were required to have a difference in preoperative cycloplegic and manifest sphere and cylinder of ≤1.00D. However, subjects with a difference between preoperative CRSE and MRSE of ≤0.50D were more likely to have an MRSE within 1.00D at 6 months compared to subjects with more than +0.50D of hyperopia by preoperative CRSE (p=0.0158). At 6 months, ≥75% of eyes with a difference of ≥0.50 or more than +0.50D had an MRSE within 1.00D, meeting or exceeding the FDA target.

Accuracy of MRSE within 1.00D was more likely in subjects with lower preoperative cycloplegic sphere and lower preoperative CRSE. For the +4.00D to +4.99D preoperative sphere range, 69.0% of eyes had an MRSE within 1.00D; however, the 95% confidence interval (52.9%, 82.4%) included the FDA target rate of at least 75% of eyes. All other preoperative sphere subcategories, including the highest sphere range of +5.00D to +6.00D, met or exceeded the FDA targets. For the +3.00D to +3.99D and +4.00D to +5.00D preoperative CRSE ranges, the observed rates for MRSE within 1.00D were 74.4% (57.9%, 87.0% CI) and 72.2% (54.8%, 85.8% CI), respectively, with 95% confidence intervals that included the FDA target. As noted for cycloplegic sphere, all other CRSE subcategories met or exceeded the FDA targets for accuracy of MRSE.

Similar associations were found between overcorrection of the MRSE by >1.00D at 6 months and baseline characteristics such as room humidity (p=0.0057), age (p=0.0001), preoperative cycloplegic sphere (p<0.0001) and preoperative CRSE (p<0.0001). Higher rates of overcorrection by more than 1.00D tended to occur in subjects treated in lower room humidity. Younger subjects, primarily less than 50 years of age, were more likely to be overcorrected than older subjects. Subjects with a difference of more than +0.50D between preoperative CRSE and MRSE were more likely to have MRSE overcorrection by more than 1.00D at 6 months (p=0.0004). Overcorrection was also more likely in subjects with higher preoperative cycloplegic sphere and CRSE.

Considering subjects who were undercorrected by more than 1.00D in MRSE at 6 months, statistically significant differences were noted for preoperative cycloplegic sphere (p=0.0281) and preoperative cycloplegic cylinder (p=0.0033). While undercorrection was more likely to occur in eyes with higher preoperative sphere, a trend for a greater percentage of eyes with overcorrection than undercorrection was observed with higher preoperative sphere. Higher rates of MRSE undercorrection were observed for subjects with more preoperative cylinder.