Alcon®

LADARVISION 4000

Excimer Laser System

PROFESSIONAL USE INFORMATION MANUAL

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

PHYSICIAN'S BOOKLET

For Mixed Astigmatism of 1.00D to less than 5.00D cycloplegic cylinder magnitude

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.

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REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 10065 – original release	

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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.

a) 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 when 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 that is 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 mixed astigmatism of 1.00D to less than 5.00D cycloplegic cylinder magnitude at the spectacle plane, which is greater than the sphere magnitude, and the cylinder and sphere have opposite signs;
- 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 mixed astigmatism have **NOT** been established in patients:

- with unstable mixed 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 mixed astigmatism of less than 1.00D cycloplegic cylinder magnitude or for 5.00D or greater cycloplegic cylinder magnitude.
- 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 at any postoperative visit up to 9 months in the clinical study for CustomCornea® LASIK correction of mixed astigmatism are summarized in Table 1. The data meet the safety criteria established in the FDA Guidance Document of less than 1% occurrence of each type of adverse event and less than 5% overall.

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

ADVERSE EVENTS	n/N	%
Miscreated flap (related to microkeratome)	2/111†	1.8%
Corneal infiltrate (related to viral epidemic keratoconjunctivitis)	1/110	0.9%
COMPLICATIONS		
Grade ≥ 1 Superficial Punctate Keratitis (SPK) at one month or later	11/110	10.0%
Epithelium in the interface	6/111†	5.4%
Diffuse lamellar keratitis (DLK)	5/110	4.5%
Pain at one month or later	2/110	1.8%
Foreign body sensation at one month or later	1/110	0.9%

† One eye did not receive laser ablation after the miscreated flap and was not included in the analysis of eyes receiving laser treatment (N=111).

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

- corneal edema at one week or later;
- corneal epithelial defect (central or peripheral) at one month or later;
- decrease in best spectacle corrected visual acuity (BSCVA) of more than 10 letters (> 2 lines) not due to irregular astigmatism, as shown by hard contact lens refraction at six months or later;
- epithelium in the interface with a loss of BSCVA of 2 or more lines;
- intraocular pressure increase of more than 10 mmHg above baseline;
- intraocular pressure of more than 25 mmHg;
- late onset of corneal haze at six months or later with a loss of BSCVA of 2 or more lines;
- melting of the flap;
- misaligned flap;
- retinal detachment; and
- 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 system and the fellow eye received a Conventional treatment based on phoropter cycloplegic refraction. For this initial subgroup of patients, the fellow eye served as a contralateral control.

Upon providing data to support expansion of the number of patients 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 patient 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, patient 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 mixed astigmatism. Patients were followed at 1 day, 1 week, and 1, 3, 6, and 9 months postoperatively. 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.

Recruited patients 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, mixed astigmatic patients must have had a preoperative cycloplegic refraction at the spectacle plane of > 0.00D to +6.00D sphere with < 0.00D to -6.00D astigmatism (minus cylinder convention) with an absolute cylinder magnitude greater than the sphere magnitude. Enrollment of mixed astigmatic eyes in the study occurred over the preoperative cycloplegic refractive range of +0.25D to +4.25D sphere with -1.00D to -6.00D astigmatism and -1.38D to +1.63D spherical equivalent (SE).

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 system.

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

Patients must have been at least 18 years of age and had a BSCVA of 20/25 or better in the operative eye(s). Patients 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.

Patients 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. Patients 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, patients were not to wear their contact lenses in the operative eye(s) for 2 to 3 weeks for soft and hard contact lenses, respectively.

Patients who exhibited any of the following conditions were excluded from the study:

- previous corneal, intraocular, or strabismus surgery in the operative eye(s)
- history of 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 manifest refraction spherical equivalent (MRSE) and manifest cylinder; reduction of wavefront error, including higher-order aberrations; and patient 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

A total of 110 eyes of 63 patients were enrolled in the Primary Cohort. The demographics of the study population (Table 2) were typical for a refractive surgery trial performed in the U.S. The mean ± standard deviation patient age was 40.6 ± 10.7 years with a range from 20 to 60 years. The majority of patients were Caucasian (94.5%) and the remaining patients were Hispanic (3.6%) and Indian (1.8%). Slightly more females (53.6%) than males (46.4%) participated in the study. The distribution of right and left eyes that received treatment was approximately equal (49.1% vs. 50.9%). While most patients (64.5%) did not wear contact lenses prior to surgery, 32.7% wore soft contact lenses and 2.7% wore rigid gas permeable (RGP) lenses.

Table 2. Demographics

110 Eyes of 63 Enrolled Patients			
Age (In Years)			
Average ± Standard Deviation		40.6 ± 10.7	
Minimum to Maximum		20 to 60	
Race		**N**	**% Eyes**
	Caucasian	104	94.5%
	Hispanic	4	3.6%
	Indian	2	1.8%
Gender	Female	59	53.6%
	Male	51	46.4%
Eye	Left	56	50.9%
	Right	54	49.1%
Contact Lens History	None	71	64.5%
	Soft	36	32.7%
	Rigid Gas Permeable (RGP)	3	2.7%

2. Accountability

The accountability for this study was ≥ 98.2% at all postoperative intervals (Table 3). Postoperative data were available for 110 eyes (100%) up to 6 months and for 108 eyes (98.2%) at 9 months. One patient (2 eyes) missed the 9-month visit because the patient moved out of the country prior to the opening of the 9-month visit window.

Table 3. Accountability at Each Visit

		1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
Total Eyes Enrolled	n	110	110	110	110
Available for Analysis	**n** **%**	**110** **100.0%**	**110** **100.0%**	**110** **100.0%**	**108** **98.2%**
Unavailable Missed Visit	n %	0 0.0%	0 0.0%	0 0.0%	2 1.8%
% Accountability= [available/(available + unavailable)]	%	**100.0%**	**100.0%**	**100.0%**	**98.2%**

3. Preoperative Cycloplegic Refraction Parameters

The study population of mixed astigmatic eyes had a preoperative cycloplegic cylinder magnitude greater than the sphere in minus cylinder convention. Preoperative cycloplegic refractive range was +0.25D to +4.25D sphere with -1.00D to -6.00D cylinder and -1.38D to +1.63D spherical equivalent. The mean ± standard deviation for the preoperative cycloplegic refraction was +1.50D ± 0.94D sphere, -2.90D ± 1.20D cylinder and +0.06D ± 0.65D spherical equivalent. Table 4 displays the number of eyes stratified by preoperative cycloplegic sphere and cylinder. Table 5 displays the number of eyes stratified by preoperative cycloplegic spherical equivalent and cylinder.

Table 4. Preoperative Cycloplegic Refraction Stratified by Sphere and Cylinder

		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION					
SPHERE (D)		-1.00 to -1.99	-2.00 to -2.99	-3.00 to -3.99	-4.00 to -4.99	-5.00 to -6.00	TOTAL
> 0.00 to +0.99	n/N	15/110	14/110	7/110	0/110	0/110	36/110
	%	13.6%	12.7%	6.4%	0.0%	0.0%	32.7%
+1.00 to +1.99	n/N	9/110	19/110	10/110	3/110	0/110	41/110
	%	8.2%	17.3%	9.1%	2.7%	0.0%	37.3%
+2.00 to +2.99	n/N	0/110	4/110	6/110	9/110	4/110	23/110
	%	0.0%	3.6%	5.5%	8.2%	3.6%	20.9%
+3.00 to +3.99	n/N	0/110	0/110	2/110	5/110	2/110	9/110
	%	0.0%	0.0%	1.8%	4.5%	1.8%	8.2%
+4.00 to +5.00	n/N	0/110	0/110	0/110	0/110	1/110	1/110
	%	0.0%	0.0%	0.0%	0.0%	0.9%	0.9%
TOTAL	n/N	24/110	37/110	25/110	17/110	7/110	110/110
	%	21.8%	33.6%	22.7%	15.5%	6.4%	100.0%

D= Diopter

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

		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION					
SPHERICAL EQUIVALENT (D)		-1.00 to -1.99	-2.00 to -2.99	-3.00 to -3.99	-4.00 to -4.99	-5.00 to -6.00	TOTAL
-1.00 to -2.00	n/N	0/110	1/110	5/110	2/110	0/110	8/110
	%	0.0%	0.9%	4.5%	1.8%	0.0%	7.3%
0.00 to -0.99	n/N	9/110	19/110	11/110	3/110	3/110	45/110
	%	8.2%	17.3%	10.0%	2.7%	2.7%	40.9%
+0.01 to +0.99	n/N	15/110	15/110	4/110	9/110	2/110	45/110
	%	13.6%	13.6%	3.6%	8.2%	1.8%	40.9%
+1.00 to +2.00	n/N	0/110	2/110	5/110	3/110	2/110	12/110
	%	0.0%	1.8%	4.5%	2.7%	1.8%	10.9%
TOTAL	n/N	24/110	37/110	25/110	17/110	7/110	110/110
	%	21.8%	33.6%	22.7%	15.5%	6.4%	100.0%

D= Diopter

4. Key Effectiveness Outcomes

a) Summary Stratified by Visit and by Diopter

The key effectiveness outcomes for UCVA and accuracy of MRSE and manifest cylinder are shown by visit in Table 6. These parameters at 3 and 6 months are also shown stratified by preoperative cycloplegic cylinder in Table 7 and by preoperative cycloplegic refraction spherical equivalent (CRSE) in Table 8.

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 of intended in at least 50% of eyes and within 1.00D in 75% of eyes at all postoperative intervals.

Table 6. Summary of Key Effectiveness Parameters Over Time

Effectiveness Parameters		1 Month	3 Months	6 Months	9 Months
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	68/94	60/94	67/94	64/92
	%	72.3%	63.8%	71.3%	69.6%
	CI	(62.2, 81.1)	(53.3, 73.5)	(61.0, 80.1)	(59.1, 78.7)
UCVA 20/20 or better	n/N	70/110	62/110	70/110	66/108
	%	63.6%	56.4%	63.6%	61.1%
	CI	(53.9, 72.6)	(46.6, 65.8)	(53.9, 72.6)	(51.3, 70.3)
UCVA 20/25 or better	n/N	95/110	89/110	96/110	91/108
	%	86.4%	80.9%	87.3%	84.3%
	CI	(78.5, 92.2)	(72.3, 87.8)	(79.6, 92.9)	(76.0, 90.6)
UCVA 20/40 or better	n/N	106/110	105/110	108/110	101/108
	%	96.4%	95.5%	98.2%	93.5%
	CI	(91.0, 99.0)	(89.7, 98.5)	(93.6, 99.8)	(87.1, 97.4)
MRSE ± 0.50D of intended	n/N	79/110	78/110	84/110	81/108
	%	71.8%	70.9%	76.4%	75.0%
	CI	(62.4, 80.0)	(61.5, 79.2)	(67.3, 83.9)	(65.7, 82.8)
MRSE ± 1.00D of intended	n/N	104/110	102/110	100/110	96/108
	%	94.5%	92.7%	90.9%	88.9%
	CI	(88.5, 98.0)	(86.2, 96.8)	(83.9, 95.6)	(81.4, 94.1)
MRSE ± 2.00D of intended	n/N	109/110	109/110	110/110	108/108
	%	99.1%	99.1%	100.0%	100.0%
	CI	(95.0, 100.0)	(95.0, 100.0)	(96.7, 100.0)	(96.6, 100.0)
Cylinder magnitude ≤ 0.50D of intended	n/N	71/110	73/110	71/110	66/108
	%	64.5%	66.4%	64.5%	61.1%
	CI	(54.9, 73.4)	(56.7, 75.1)	(54.9, 73.4)	(51.3, 70.3)
Cylinder magnitude ≤ 1.00D of intended	n/N	96/110	100/110	98/110	95/108
	%	87.3%	90.9%	89.1%	88.0%
	CI	(79.6, 92.9)	(83.9, 95.6)	(81.7, 94.2)	(80.3, 93.4)
Cylinder magnitude ≤ 2.00D of intended	n/N	108/110	109/110	109/110	107/108
	%	98.2%	99.1%	99.1%	99.1%
	CI	(93.6, 99.8)	(95.0, 100.0)	(95.0, 100.0)	(94.9, 100.0)

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

Table 7. Summary of Key Effectiveness Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Cylinder

3 MONTHS							
Effectiveness Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	16/22 72.7%	20/36 55.6%	18/23 78.3%	5/9 55.6%	1/4 25.0%	60/94 63.8%
UCVA 20/20 or better	n/N %	16/24 66.7%	21/37 56.8%	18/25 72.0%	6/17 35.3%	1/7 14.3%	62/110 56.4%
UCVA 20/25 or better	n/N %	24/24 100.0%	28/37 75.7%	23/25 92.0%	12/17 70.6%	2/7 28.6%	89/110 80.9%
UCVA 20/40 or better	n/N %	24/24 100.0%	33/37 89.2%	25/25 100.0%	17/17 100.0%	6/7 85.7%	105/110 95.5%
MRSE ± 0.50D of intended	n/N %	23/24 95.8%	25/37 67.6%	17/25 68.0%	9/17 52.9%	4/7 57.1%	78/110 70.9%
MRSE ± 1.00D of intended	n/N %	24/24 100.0%	35/37 94.6%	23/25 92.0%	14/17 82.4%	6/7 85.7%	102/110 92.7%
MRSE ± 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	16/17 94.1%	7/7 100.0%	109/110 99.1%
Cylinder magnitude ≤ 0.50D of intended	n/N %	20/24 83.3%	25/37 67.6%	14/25 56.0%	13/17 76.5%	1/7 14.3%	73/110 66.4%
Cylinder magnitude ≤ 1.00D of intended	n/N %	24/24 100.0%	36/37 97.3%	23/25 92.0%	14/17 82.4%	3/7 42.9%	100/110 90.9%
Cylinder magnitude ≤ 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	17/17 100.0%	6/7 85.7%	109/110 99.1%
6 MONTHS							
Effectiveness Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	21/22 95.5%	19/36 52.8%	20/23 87.0%	7/9 77.8%	0/4 0.0%	67/94 71.3%
UCVA 20/20 or better	n/N %	21/24 87.5%	20/37 54.1%	20/25 80.0%	9/17 52.9%	0/7 0.0%	70/110 63.6%
UCVA 20/25 or better	n/N %	24/24 100.0%	29/37 78.4%	25/25 100.0%	14/17 82.4%	4/7 57.1%	96/110 87.3%
UCVA 20/40 or better	n/N %	24/24 100.0%	35/37 94.6%	25/25 100.0%	17/17 100.0%	7/7 100.0%	108/110 98.2%
MRSE ± 0.50D of intended	n/N %	24/24 100.0%	28/37 75.7%	18/25 72.0%	10/17 58.8%	4/7 57.1%	84/110 76.4%
MRSE ± 1.00D of intended	n/N %	24/24 100.0%	34/37 91.9%	22/25 88.0%	14/17 82.4%	6/7 85.7%	100/110 90.9%
MRSE ± 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	17/17 100.0%	7/7 100.0%	110/110 100.0%
Cylinder magnitude ≤ 0.50D of intended	n/N %	19/24 79.2%	24/37 64.9%	15/25 60.0%	11/17 64.7%	2/7 28.6%	71/110 64.5%
Cylinder magnitude ≤ 1.00D of intended	n/N %	23/24 95.8%	35/37 94.6%	24/25 96.0%	14/17 82.4%	2/7 28.6%	98/110 89.1%
Cylinder magnitude ≤ 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	17/17 100.0%	6/7 85.7%	109/110 99.1%

UCVA = Uncorrected Visual Acuity
BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent
D = Diopter

Table 8. Summary of Key Effectiveness Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

3 MONTHS						
Effectiveness Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	5/6 83.3%	24/41 58.5%	24/36 66.7%	7/11 63.6%	60/94 63.8%
UCVA 20/20 or better	n/N %	5/8 62.5%	24/45 53.3%	26/45 57.8%	7/12 58.3%	62/110 56.4%
UCVA 20/25 or better	n/N %	7/8 87.5%	39/45 86.7%	34/45 75.6%	9/12 75.0%	89/110 80.9%
UCVA 20/40 or better	n/N %	8/8 100.0%	43/45 95.6%	43/45 95.6%	11/12 91.7%	105/110 95.5%
MRSE ± 0.50D of intended	n/N %	7/8 87.5%	35/45 77.8%	27/45 60.0%	9/12 75.0%	78/110 70.9%
MRSE ± 1.00D of intended	n/N %	8/8 100.0%	42/45 93.3%	41/45 91.1%	11/12 91.7%	102/110 92.7%
MRSE ± 2.00D of intended	n/N %	8/8 100.0%	45/45 100.0%	44/45 97.8%	12/12 100.0%	109/110 99.1%
Cylinder magnitude ≤ 0.50D of intended	n/N %	4/8 50.0%	30/45 66.7%	32/45 71.1%	7/12 58.3%	73/110 66.4%
Cylinder magnitude ≤ 1.00D of intended	n/N %	8/8 100.0%	40/45 88.9%	42/45 93.3%	10/12 83.3%	100/110 90.9%
Cylinder magnitude ≤ 2.00D of intended	n/N %	8/8 100.0%	44/45 97.8%	45/45 100.0%	12/12 100.0%	109/110 99.1%
6 MONTHS						
Effectiveness Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	5/6 83.3%	29/41 70.7%	27/36 75.0%	6/11 54.5%	67/94 71.3%
UCVA 20/20 or better	n/N %	6/8 75.0%	29/45 64.4%	29/45 64.4%	6/12 50.0%	70/110 63.6%
UCVA 20/25 or better	n/N %	8/8 100.0%	41/45 91.1%	36/45 80.0%	11/12 91.7%	96/110 87.3%
UCVA 20/40 or better	n/N %	8/8 100.0%	44/45 97.8%	45/45 100.0%	11/12 91.7%	108/110 98.2%
MRSE ± 0.50D of intended	n/N %	7/8 87.5%	34/45 75.6%	34/45 75.6%	9/12 75.0%	84/110 76.4%
MRSE ± 1.00D of intended	n/N %	8/8 100.0%	42/45 93.3%	39/45 86.7%	11/12 91.7%	100/110 90.9%
MRSE ± 2.00D of intended	n/N %	8/8 100.0%	45/45 100.0%	45/45 100.0%	12/12 100.0%	110/110 100.0%
Cylinder magnitude ≤ 0.50D of intended	n/N %	4/8 50.0%	27/45 60.0%	33/45 73.3%	7/12 58.3%	71/110 64.5%
Cylinder magnitude ≤ 1.00D of intended	n/N %	8/8 100.0%	39/45 86.7%	42/45 93.3%	9/12 75.0%	98/110 89.1%
Cylinder magnitude ≤ 2.00D of intended	n/N %	8/8 100.0%	44/45 97.8%	45/45 100.0%	12/12 100.0%	109/110 99.1%

UCVA = Uncorrected Visual Acuity
BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent
D = Diopter

b) Uncorrected Visual Acuity

Uncorrected visual acuity is displayed in Table 9. Preoperatively, 35.5% of eyes had a UCVA of 20/40 or better. At 3 months, the UCVA was 20/20 or better in 56.4% of eyes, 20/25 or better in 80.9% and 20/40 or better in 95.5%. At 6 months, the UCVA was 20/20 or better in 63.6% of eyes, 20/25 or better in 87.3% and 20/40 or better in 98.2%. For those eyes with a preoperative BSCVA of 20/20 or better, a UCVA of 20/20 or better was achieved in 63.8% and 71.3% of eyes at 3 and 6 months, respectively.

Table 9. Cumulative Uncorrected Visual Acuity at Distance

		PREOP	1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
20/10	n/N	0/110	1/110	2/110	3/110	3/108
	%	0.0%	0.9%	1.8%	2.7%	2.8%
20/12.5 or better	n/N	0/110	8/110	11/110	11/110	9/108
	%	0.0%	7.3%	10.0%	10.0%	8.3%
20/16 or better	n/N	0/110	33/110	33/110	39/110	40/108
	%	0.0%	30.0%	30.0%	35.5%	37.0%
20/20 or better	n/N	1/110	70/110	62/110	70/110	66/108
	%	0.9%	63.6%	56.4%	63.6%	61.1%
20/25 or better	n/N	4/110	95/110	89/110	96/110	91/108
	%	3.6%	86.4%	80.9%	87.3%	84.3%
20/32 or better	n/N	17/110	104/110	98/110	104/110	99/108
	%	15.5%	94.5%	89.1%	94.5%	91.7%
20/40 or better	n/N	39/110	106/110	105/110	108/110	101/108
	%	35.5%	96.4%	95.5%	98.2%	93.5%
20/50 or better	n/N	53/110	109/110	110/110	109/110	107/108
	%	48.2%	99.1%	100.0%	99.1%	99.1%
20/63 or better	n/N	68/110	110/110	110/110	110/110	107/108
	%	61.8%	100.0%	100.0%	100.0%	99.1%
20/80 or better	n/N	84/110	110/110	110/110	110/110	108/108
	%	76.4%	100.0%	100.0%	100.0%	100.0%
20/100 or better	n/N	98/110	110/110	110/110	110/110	108/108
	%	89.1%	100.0%	100.0%	100.0%	100.0%
Worse than 20/100	n/N	12/110	0/110	0/110	0/110	0/108
	%	10.9%	0.0%	0.0%	0.0%	0.0%

c) Comparison of Postoperative Uncorrected Visual Acuity and Preoperative Best Spectacle Corrected Visual Acuity

A comparison of **postoperative** UCVA to **preoperative** BSCVA after CustomCornea® LASIK surgery is presented in Table 10 with differences based on lines of visual acuity. A postoperative UCVA equal to or better than the preoperative BSCVA was achieved in 56.4% and 60.0% of eyes at 3 and 6 months, respectively.

Table 10. 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 %	0/110 0.0%	0/110 0.0%	2/110 1.8%	2/108 1.9%
UCVA **1 Line Better** Than Preop BSCVA	n/N %	13/110 11.8%	18/110 16.4%	19/110 17.3%	20/108 18.5%
UCVA **Equal*** to Preop BSCVA	n/N %	53/110 48.2%	44/110 40.0%	45/110 40.9%	43/108 39.8%
UCVA **1 Line Worse** Than Preop BSCVA	n/N %	26/110 23.6%	21/110 19.1%	29/110 26.4%	21/108 19.4%
UCVA **2 Lines Worse** Than Preop BSCVA	n/N %	9/110 8.2%	13/110 11.8%	7/110 6.4%	11/108 10.2%
UCVA **>2 Lines Worse** Than Preop BSCVA	n/N %	9/110 8.2%	14/110 12.7%	8/110 7.3%	11/108 10.2%

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

d) Accuracy of Manifest Refraction Spherical Equivalent

As shown in Table 11, accuracy of MRSE was within 0.50D of emmetropia in 70.9% of eyes, within 1.00D in 92.7% and within 2.00D in 99.1% at 3 months. At 6 months, the MRSE was within 0.50D of emmetropia in 76.4% of eyes, within 1.00D in 90.9% and within 2.00D in 100%. Of the eyes that did not achieve an MRSE within 1.00D of emmetropia, 5.5% at 3 months and 7.3% at 6 months had more than +1.00D of hyperopia, whereas 1.8% at 3 and 6 months had more than -1.00D of myopia. One eye (0.9%) had more than +2.00D of hyperopia by MRSE at 3 months.

Table 11. Accuracy of Manifest Refraction Spherical Equivalent

		1 Month	3 Months	6 Months	9 Months
± 0.50D	n/N %	79/110 71.8%	78/110 70.9%	84/110 76.4%	81/108 75.0%
± 1.00D	n/N %	104/110 94.5%	102/110 92.7%	100/110 90.9%	96/108 88.9%
± 2.00D	n/N %	109/110 99.1%	109/110 99.1%	110/110 100.0%	108/108 100.0%
> ± 2.00D	n/N %	1/110 0.9%	1/110 0.9%	0/110 0.0%	0/108 0.0%
Postop Hyperopic MRSE > +1.00D	n/N %	5/110 4.5%	6/110 5.5%	8/110 7.3%	9/108 8.3%
Postop Hyperopic MRSE > +2.00D	n/N %	1/110 0.9%	1/110 0.9%	0/110 0.0%	0/108 0.0%
Postop Myopic MRSE < -1.00D	n/N %	1/110 0.9%	2/110 1.8%	2/110 1.8%	3/108 2.8%
Postop Myopic MRSE < -2.00D	n/N %	0/110 0.0%	0/110 0.0%	0/110 0.0%	0/108 0.0%

MRSE = Manifest Refraction Spherical Equivalent D = Diopter

e) Accuracy of Manifest Refraction by Meridian

Accuracy of manifest refraction is displayed for the preoperative hyperopic meridian in Table 12 and for the preoperative myopic meridian in Table 13. Slight undercorrection along the preoperative hyperopic meridian was observed based on a mean correction error of +0.15D ± 0.69D at 3 months and +0.20D ± 0.63D at 6 months. Along the preoperative myopic meridian, slight undercorrection was observed based on a mean correction error of -0.09D ± 0.67D at 3 months and -0.07D ± 0.61D at 6 months.

Table 12. Accuracy of Manifest Refraction in Preoperative *Hyperopic* Meridian

Correction Error		1 Month	3 Months	6 Months	9 Months
Mean ± SD (D)		+0.07 ± 0.68	+0.15 ± 0.69	+0.20 ± 0.63	+0.17 ± 0.63
0.00 ± 0.50D	n/N	79/110	74/110	77/110	73/108
	%	71.8%	67.3%	70.0%	67.6%
Undercorrected (Postoperative Hyperopia)					
> 0.50 to 1.00D	n/N	10/110	18/110	16/110	15/108
	%	9.1%	16.4%	14.5%	13.9%
> 1.00 to 2.00D	n/N	4/110	7/110	8/110	7/108
	%	3.6%	6.4%	7.3%	6.5%
> 2.00D	n/N	2/110	2/110	2/110	2/108
	%	1.8%	1.8%	1.8%	1.9%
Overcorrected (Postoperative Myopia)					
> 0.50 to 1.00D	n/N	10/110	5/110	5/110	10/108
	%	9.1%	4.5%	4.5%	9.3%
> 1.00 to 2.00D	n/N	5/110	4/110	2/110	1/108
	%	4.5%	3.6%	1.8%	0.9%
> 2.00D	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%

Table 13. Accuracy of Manifest Refraction in Preoperative *Myopic* Meridian

Correction Error		1 Month	3 Months	6 Months	9 Months
Mean ± SD (D)		-0.12 ± 0.64	-0.09 ± 0.67	-0.07 ± 0.61	-0.13 ± 0.66
0.00 ± 0.50D	n/N	73/110	67/110	71/110	66/108
	%	66.4%	60.9%	64.5%	61.1%
Undercorrected (Postoperative Myopia)					
> 0.50 to 1.00D	n/N	17/110	20/110	17/110	19/108
	%	15.5%	18.2%	15.5%	17.6%
> 1.00 to 2.00D	n/N	6/110	5/110	5/110	6/108
	%	5.5%	4.5%	4.5%	5.6%
> 2.00D	n/N	1/110	0/110	0/110	0/108
	%	0.9%	0.0%	0.0%	0.0%
Overcorrected (Postoperative Hyperopia)					
> 0.50 to 1.00D	n/N	9/110	11/110	8/110	10/108
	%	8.2%	10.0%	7.3%	9.3%
> 1.00 to 2.00D	n/N	4/110	7/110	9/110	7/108
	%	3.6%	6.4%	8.2%	6.5%
> 2.00D	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%

SD = Standard Deviation D = Diopter

f) Accuracy of Manifest Refraction Sphere and Cylinder Magnitude

Table 14 displays the accuracy of manifest sphere and cylinder magnitude. Postoperative manifest sphere was within 0.50D of emmetropia in 71.3% of eyes, within 1.00D in 87.0% and within 2.00D in 98.1% at 3 months. Manifest sphere was within 0.50D of emmetropia in 70.4% of eyes, within 1.00D in 88.0% and within 2.00D in 98.1% at 6 months.

Postoperative manifest cylinder magnitude was ≤ 0.50D of emmetropia in 66.4% of eyes, ≤ 1.00D in 90.9% and ≤ 2.00D in 99.1% at 3 months. Cylinder magnitude was ≤ 0.50D in 64.5% of eyes, ≤ 1.00D in 89.1% and ≤ 2.00D in 99.1% at 6 months.

Table 14. Accuracy of Manifest Sphere and Cylinder Magnitude

Sphere*		**1 MONTH (N=108)**	**3 MONTHS (N=108)**	**6 MONTHS (N=108)**	**9 MONTHS (N=106)**
Postop Mean ± SD (D)		+0.27 ± 0.65	+0.31 ± 0.68	+0.35 ± 0.62	+0.33 ± 0.64
Attempted Mean ± SD (D)		+1.20 ± 0.88	+1.20 ± 0.88	+1.20 ± 0.88	+1.19 ± 0.89
Achieved Mean ± SD (D)		+0.92 ± 0.98	+0.89 ± 1.03	+0.85 ± 1.00	+0.87 ± 1.04
% Achieved		69 ± 85	64 ± 79	61 ± 85	60 ± 91
± 0.50D	n/N	81/108	77/108	76/108	77/106
	%	75.0%	71.3%	70.4%	72.6%
± 1.00D	n/N	99/108	94/108	95/108	94/106
	%	91.7%	87.0%	88.0%	88.7%
± 2.00D	n/N	106/108	106/108	106/108	104/106
	%	98.1%	98.1%	98.1%	98.1%
Cylinder		**1 MONTH (N=110)**	**3 MONTHS (N=110)**	**6 MONTHS (N=110)**	**9 MONTHS (N=108)**
Postop Mean ± SD (D)		-0.58 ± 0.55	-0.53 ± 0.53	-0.55 ± 0.47	-0.59 ± 0.46
Attempted Mean ± SD (D)		-2.89 ± 1.21	-2.89 ± 1.21	-2.89 ± 1.21	-2.90 ± 1.21
Achieved Mean ± SD (D)		-2.30 ± 1.12	-2.36 ± 1.12	-2.34 ± 1.15	-2.31 ± 1.17
% Achieved		78 ± 20	81 ± 18	79 ± 18	77 ± 20
≤ 0.50D	n/N	71/110	73/110	71/110	66/108
	%	64.5%	66.4%	64.5%	61.1%
≤ 1.00D	n/N	96/110	100/110	98/110	95/108
	%	87.3%	90.9%	89.1%	88.0%
≤ 2.00D	n/N	108/110	109/110	109/110	107/108
	%	98.2%	99.1%	99.1%	99.1%

* Excludes two eyes with a preoperative manifest sphere of 0D.

g) Effectiveness of Astigmatism Correction

Effectiveness of astigmatism correction at 3 and 6 months was evaluated based on the percentage reduction in cylinder magnitude and by vector analysis (Table 15). The mean percentage reduction in absolute manifest cylinder was 80.6% at 3 months and 79.1% at 6 months with an overall trend for a greater percentage reduction in eyes with higher preoperative cylinder. The mean correction ratio based on vector analysis of manifest cylinder was 0.92 at 3 months and 0.91 at 6 months.

Table 15. Effectiveness of Astigmatic Correction By Manifest Cylinder

3 MONTHS			
Preoperative Cylinder	**N**	**Mean Percentage Reduction in Cylinder Magnitude**	**Vector Analysis Mean ± SD Correction Ratio**
All	110	80.6%	0.92 ± 0.18
1.00 to < 2.00D	26	75.9%	0.86 ± 0.21
2.00 to < 3.00D	34	79.9%	0.94 ± 0.17
3.00 to < 4.00D	26	84.1%	0.93 ± 0.14
4.00 to < 5.00D	16	87.1%	1.01 ± 0.12
5.00 to 6.00D	8	74.4%	0.83 ± 0.24
6 MONTHS			
Preoperative Cylinder	**N**	**Mean Percentage Reduction in Cylinder Magnitude**	**Vector Analysis Mean ± SD Correction Ratio**
All	110	79.1%	0.91 ± 0.17
1.00 to < 2.00D	26	72.3%	0.84 ± 0.20
2.00 to < 3.00D	34	77.3%	0.92 ± 0.17
3.00 to < 4.00D	26	83.9%	0.93 ± 0.16
4.00 to < 5.00D	16	87.0%	0.98 ± 0.12
5.00 to 6.00D	8	78.0%	0.86 ± 0.20

SD = Standard Deviation D = Diopter

Correction Ratio is the ratio of achieved vs. intended vector magnitude

h) Refraction Over Time

Table 16 presents the manifest and cycloplegic phoropter refraction over time and the wavefront refraction from the wavefront measurement under cycloplegic conditions.

The mean manifest spherical equivalent was +0.03D ± 0.62D at 3 months and +0.06D ± 0.57D at 6 months. The mean cycloplegic and wavefront spherical equivalents were similar over time. As expected under cycloplegic conditions, the cycloplegic and wavefront spherical equivalents reflected more hyperopia that was within 0.50D of the manifest spherical equivalent preoperatively and postoperatively.

The mean manifest cylinder was -0.53D ± 0.53D at 3 months and -0.55D ± 0.47D at 6 months. The mean cycloplegic cylinder was similar to the manifest cylinder over time. The mean wavefront cylinder was within 0.25D of the manifest and cycloplegic refractions postoperatively.

Table 16. Mean Refraction Over Time

Mean ± Standard Deviation	PREOP	1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
Manifest Refraction (D)	N=110	N=110	N=110	N=110	N=108
Spherical Equivalent	-0.27 ± 0.67	-0.03 ± 0.59	0.03 ± 0.62	0.06 ± 0.57	0.02 ± 0.59
Cylinder	-2.89 ± 1.21	-0.58 ± 0.55	-0.53 ± 0.53	-0.55 ± 0.47	-0.59 ± 0.46
Cycloplegic Refraction (D)*	N=110	--	N=110	N=108	--
Spherical Equivalent	0.06 ± 0.65	--	0.49 ± 0.56	0.44 ± 0.56	--
Cylinder	-2.90 ± 1.20	--	-0.49 ± 0.51	-0.52 ± 0.49	--
Wavefront Refraction (D)**	N=110	N=103	N=100	N=103	N=100
Spherical Equivalent	0.04 ± 0.71	0.35 ± 0.45	0.44 ± 0.46	0.31 ± 0.46	0.39 ± 0.52
Cylinder	-2.91 ± 1.25	-0.71 ± 0.49	-0.69 ± 0.47	-0.65 ± 0.35	-0.74 ± 0.52

Refractions at the spectacle plane D = Diopter

* Cycloplegic refraction not required at 1 month and 9 months

** Wavefront measurement under cycloplegic conditions with refraction analyzed over 3.5mm diameter

5. Stability of Manifest Refraction

Refractive stability was analyzed as paired differences in the non-vector manifest cylinder magnitude between consecutive visits (Table 17). Eyes with data available at each postoperative interval were evaluated in a 6-month consistent cohort of 110 eyes and a 9-month cohort of 108 eyes.

Cylinder stability was achieved between 1 and 3 months with 100% of eyes demonstrating ≤ 1.00D magnitude change and a mean change of -0.05D ± 0.29D at a rate of -0.03D change per month for the 6-month consistent cohort. Cylinder stability was confirmed between 3 and 6 months with 100% of eyes demonstrating ≤ 1.00D magnitude change and a decrease in the mean change over time to 0.02D ± 0.24D at a rate of 0.01D change per month. The 95% confidence interval of the mean change in cylinder magnitude overlapped between postoperative intervals with a narrow range (≤ 0.11D) between the upper and lower limits.

The 9-month consistent cohort supported the overall trends in cylinder stability observed among the 6-month cohort. Between all consecutive postoperative intervals, at least 99.1% of eyes showed ≤ 1.00D of cylinder magnitude change. The mean change in cylinder magnitude was 0.05D ± 0.25D between 6 and 9 months at a rate of 0.02D change per month.

Table 17. Stability of Manifest Cylinder Magnitude

6-Month Cohort (N=110)	**Change in Cylinder Magnitude Between**	**1 and 3 Months**	**3 and 6 Months**	
	≤ 1.00D n/N	110/110	110/110	
	≤ 1.00D %	100.0%	100.0%	
	Mean Change* ± Standard Deviation	-0.05 ± 0.29	0.02 ± 0.24	
	95% Confidence Interval of Mean Change	(-0.11, 0.00)	(-0.03, 0.06)	
	Mean Change* per Month	-0.03	0.01	
9-Month Cohort (N=108)	**Change in Cylinder Magnitude Between**	**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D n/N	108/108	108/108	107/108
	≤ 1.00D %	100.0%	100.0%	99.1%
	Mean Change* ± Standard Deviation	-0.05 ± 0.29	0.01 ± 0.23	0.05 ± 0.25
	95% Confidence Interval of Mean Change	(-0.11, 0.00)	(-0.03, 0.05)	(0.00, 0.10)
	Mean Change* per Month	-0.03	0.003	0.02

D = Diopter

* Positive value reflects an increase in magnitude and a negative value reflects a decrease in magnitude between visits.

Similarly, refractive stability was analyzed as paired differences in MRSE between consecutive visits for the 6-month and 9-month consistent cohorts of eyes with data available at each postoperative interval (Table 18).

Stability of MRSE was achieved between 1 and 3 months with 100% of eyes demonstrating a change in MRSE ≤ 1.00D and a mean change of 0.06D ± 0.29D at a rate of 0.03D change per month for the 6-month consistent cohort. Stability was confirmed between 3 and 6 months with 100% of eyes demonstrating a change in MRSE ≤ 1.00D and a decrease in the mean change over time to 0.03D ± 0.25D at a rate of 0.01D change per month. The 95% confidence interval of the mean change in MRSE overlapped between postoperative intervals with a narrow range (≤ 0.11D) between the upper and lower limits.

The 9-month consistent cohort showed similar MRSE stability trends to the 6-month cohort. All eyes demonstrated a change in MRSE ≤ 1.00D between postoperative visits. Between 6 and 9 months, the mean MRSE change was -0.04D ± 0.26D at a rate of -0.01D change per month.

Table 18. Stability of Manifest Refraction Spherical Equivalent

	Change in MRSE Between		**1 and 3 Months**	**3 and 6 Months**	
6-Month Cohort (N=110)	≤ 1.00D	n/N %	110/110 100.0%	110/110 100.0%	
	Mean Change ± Standard Deviation		0.06 ± 0.29	0.03 ± 0.25	
	95% Confidence Interval of Mean Change		(0.00, 0.11)	(-0.01, 0.08)	
	Mean Change per Month		0.03	0.01	
	Change in MRSE Between		**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
9-Month Cohort (N=108)	≤ 1.00D	n/N %	108/108 100.0%	108/108 100.0%	108/108 100.0%
	Mean Change ± Standard Deviation		0.06 ± 0.29	0.03 ± 0.25	-0.04 ± 0.26
	95% Confidence Interval of Mean Change		(0.00, 0.11)	(-0.02, 0.07)	(-0.09, 0.01)
	Mean Change per Month		0.03	0.01	-0.01

D = Diopter

6. Wavefront Outcomes

Table 19 displays the mean change from preoperative in total root mean square (RMS) wavefront error and in higher-order aberrations through 6th order. The mean change in total RMS wavefront error decreased by 64.1% at 3 months and 67.2% at 6 months from preoperative. Higher-order aberrations were not significantly changed from preoperative on average with an increase of 2.3% at 3 months and 2.2% at 6 months. Spherical aberration decreased in magnitude at 3 and 6 months from preoperative with a mean directional shift from positive spherical aberration preoperatively (0.233μm) towards slightly negative spherical aberration at 3 months (-0.003μm) and 6 months (-0.007μm).

Table 19. Mean Change in Aberrations Up to 6th Order From Preoperative*

	3 MONTHS (N=100)		6 MONTHS (N=103)	
Aberration	**Mean Change (μm)**	**Mean Change (%)**	**Mean Change (μm)**	**Mean Change (%)**
Total RMS Error	-1.905	-64.1	-1.998	-67.2
Higher-Order	0.010	2.3	0.010	2.2
Coma	0.030	12.5	0.034	13.9
Trefoil	0.008	4.0	0.005	2.7
Spherical Aberration Magnitude †	-0.114	-48.4	-0.101	-42.8
Spherical Aberration Value ‡	-0.236	-101.2	-0.240	-102.9
Secondary Astigmatism	0.073	92.8	0.066	84.3
Tetrafoil	0.023	30.4	0.027	35.3
Combined 5th and 6th Order	0.037	49.5	0.035	46.6

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Positive change represents increase from preop; Negative change represents decrease from preop

† Based on absolute spherical aberration magnitude ‡ Based on signed spherical aberration value

At 3 and 6 months, 100% of eyes had a reduction in total RMS error from preoperative. A reduction in higher-order aberrations from preoperative was observed in 55.0% of eyes at 3 months and 54.4% at 6 months (Table 20).

Table 20. Percentage of Eyes with Reduced Aberrations Up to 6th Order From Preoperative

	3 MONTHS (N=100)	6 MONTHS (N=103)
Aberration	**% Eyes with Reduction in Aberrations**	
Total RMS Error	100.0%	100.0%
Higher-Order	55.0%	54.4%
Coma	48.0%	49.5%
Trefoil	49.0%	45.6%
Spherical Aberration Magnitude †	80.0%	78.6%
Secondary Astigmatism	18.0%	17.5%
Tetrafoil	32.0%	32.0%
Combined 5th and 6th Order	18.0%	17.5%

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 correction of mixed astigmatism using phoropter refraction for eyes treated under the same study protocol over the same preoperative cycloplegic refractive range of -1.00D to -3.50D cylinder. Wavefront aberrations at 3 and 6 months were analyzed up to 4th order for the Comparison Cohort (Table 21).

Compared to Conventional eyes, CustomCornea® eyes showed:

- statistically significantly lower mean amplitudes of total RMS error, higher-order aberrations, trefoil, spherical aberration magnitude, secondary astigmatism and tetrafoil at 3 and 6 months postoperatively (t-test with unequal variance; $p<0.05$).
- greater mean decrease in total RMS error from preoperative at 3 and 6 months.
- a mean decrease in higher-order aberrations from preoperative compared to a mean increase for Conventional eyes at 3 and 6 months.

Spherical aberration value for the CustomCornea® eyes was positive preoperatively (0.235µm) and at 3 months (0.041µm) and 6 months (0.029µm). Similarly for the Conventional eyes, spherical aberration value was positive preoperatively (0.176µm) and at 3 months (0.099µm) and 6 months (0.112µm).

Table 21. Mean Change in Aberrations Up to 4th Order from Preoperative*: CustomCornea® vs. Conventional Comparison Cohort

3 MONTHS					
Aberration	**CustomCornea® (N=74)**		**Conventional (N=26)**		**p-Value §**
	µm	**%**	**µm**	**%**	
Total RMS Error	-1.509	-62.2	-0.990	-39.8	**<0.0001**
Higher-Order	-0.060	-13.7	0.199	51.3	**<0.0001**
Coma	-0.008	-3.3	0.108	55.7	0.1542
Trefoil	-0.021	-11.1	0.167	91.6	**<0.0001**
Spherical Aberration Magnitude †	-0.132	-56.0	-0.016	-8.9	**0.0167**
Spherical Aberration Value ‡	-0.195	-82.8	-0.076	-43.4	0.1332
Secondary Astigmatism	0.046	62.3	0.086	98.8	**0.0142**
Tetrafoil	0.021	30.3	0.048	51.9	**0.0029**
6 MONTHS					
Aberration	**CustomCornea® (N=81)**		**Conventional (N=25)**		**p-Value §**
	µm	**%**	**µm**	**%**	
Total RMS Error	-1.534	-63.2	-0.985	-39.6	**<0.0001**
Higher-Order	-0.053	-12.0	0.232	59.8	**<0.0001**
Coma	-0.010	-3.9	0.135	69.5	0.0905
Trefoil	-0.014	-7.7	0.160	88.1	**0.0001**
Spherical Aberration Magnitude †	-0.120	-51.1	-0.008	-4.6	**0.0224**
Spherical Aberration Value ‡	-0.206	-87.5	-0.064	-36.4	**0.0421**
Secondary Astigmatism	0.047	63.4	0.091	104.3	**0.0272**
Tetrafoil	0.027	38.3	0.066	72.3	**0.0004**

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Positive change represents increase from preop; Negative change represents decrease from preop

† Based on absolute spherical aberration magnitude ‡ Based on signed spherical aberration value

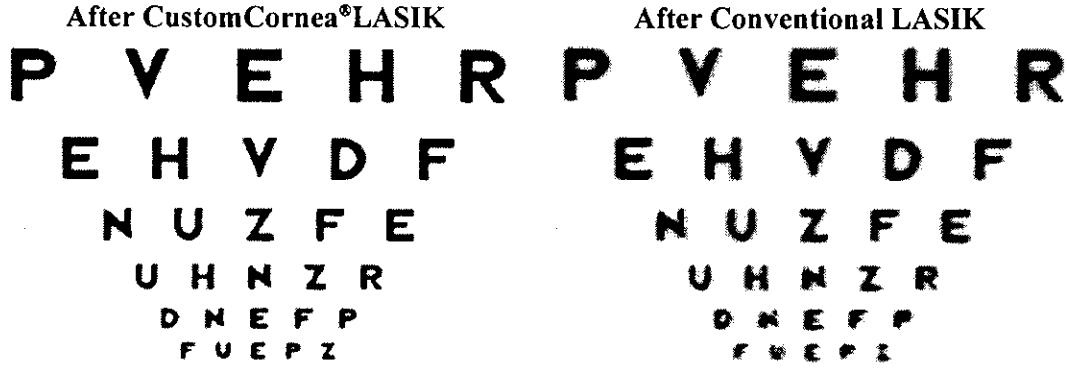
§ t-test with unequal variance for postoperative comparison between treatment types; $p<0.05$ statistically significant, shown in bold

A vision simulation program was used to model the effect of mean higher-order aberration magnitudes at 3 months after wavefront-guided CustomCornea® LASIK versus Conventional LASIK. The CustomCornea® cohort is restricted to those eyes over a comparable preoperative cylinder range to all Conventional mixed astigmatic eyes treated in the study (-1.00D to -3.50D). The difference in image blurring is comparable to a defocus error difference of approximately 0.11D (i.e., 0.10D for the CustomCornea® simulation and 0.21D for the Conventional simulation).

The following charts (Figure 1) 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 1. Simulated chart images for the average higher-order aberrations at 3 months after wavefront-guided surgery compared to after conventional surgery, based on wavefront over a 6 mm diameter pupil.



As shown in Table 22, more eyes had a reduction in higher-order aberrations after CustomCornea® LASIK compared to after Conventional LASIK at 3 months (66.2% vs. 7.7%) and 6 months (61.7% vs. 8.0%).

Table 22. Percentage of Eyes with Reduced Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Comparison Cohort

	3 MONTHS		6 MONTHS	
Aberration	CustomCornea® (N = 74)	Conventional (N = 26)	CustomCornea® (N = 81)	Conventional (N = 25)
Total RMS Error	100.0%	92.3%	100.0%	96.0%
Higher-Order	66.2%	7.7%	61.7%	8.0%
Coma	55.4%	19.2%	55.6%	28.0%
Trefoil	55.4%	7.7%	51.9%	20.0%
Spherical Aberration Magnitude†	86.5%	57.7%	85.2%	52.0%
Secondary Astigmatism	21.6%	19.2%	19.8%	16.0%
Tetrafoil	32.4%	23.1%	30.9%	20.0%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

† Reduction in absolute spherical aberration magnitude

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7. Key Safety Outcomes

a) Summary Stratified by Visit and by Diopter

The key safety outcomes are presented by visit in Table 23. These parameters at 3 and 6 months are also shown stratified by preoperative cycloplegic cylinder in Table 24 and by preoperative CRSE in Table 25.

No eyes had a loss of more than 2 lines of BSCVA and one eye (0.9%) had a loss of 2 lines at 1 month. All eyes had a BSCVA within 1 line of preoperative BSCVA at 3 months or later. Preoperative BSCVA was 20/25 or better for all eyes. Postoperative BSCVA was 20/32 or better at all postoperative intervals and 20/25 or better at 3 months or later.

The safety data meet the criteria established in the FDA Guidance Document of less than 5% of eyes with a loss of more than 2 lines of BSCVA, less than 1% having a BSCVA of worse than 20/40, and less than 5% having an increase in cylinder magnitude of more than 2D at all postoperative intervals.

Table 23. Summary of Key Safety Parameters Over Time

Safety Parameters		1 Month	3 Months	6 Months	9 Months
Loss of > 2 Lines BSCVA	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
Loss of 2 Lines BSCVA	n/N	1/110	0/110	0/110	0/108
	%	0.9%	0.0%	0.0%	0.0%
	CI	(0.0, 5.0)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
BSCVA worse than 20/40	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
Increase > 2D cylinder magnitude	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	1/94	0/94	0/94	0/92
	%	1.1%	0.0%	0.0%	0.0%
	CI	(0.0, 5.8)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 3.9)

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

Table 24. Summary of Key Safety Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Cylinder

3 MONTHS							
Safety Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/22 0.0%	0/36 0.0%	0/23 0.0%	0/9 0.0%	0/4 0.0%	0/94 0.0%
6 MONTHS							
Safety Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/22 0.0%	0/36 0.0%	0/23 0.0%	0/9 0.0%	0/4 0.0%	0/94 0.0%

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

Table 25. Summary of Key Safety Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

3 MONTHS						
Safety Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/6 0.0%	0/41 0.0%	0/36 0.0%	0/11 0.0%	0/94 0.0%
6 MONTHS						
Safety Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/6 0.0%	0/41 0.0%	0/36 0.0%	0/11 0.0%	0/94 0.0%

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

b) Change in Best Spectacle Corrected Visual Acuity

Using a standard (high-contrast) visual acuity chart, BSCVA was measured under dim room illumination (10-12 cd/m^2). At least 90.9% of eyes had a gain or no change in BSCVA from preoperative at all postoperative intervals (Table 26). A trend for postoperative BSCVA gain of 1 line was observed compared to a loss of 1 line at 3 months (39.1% vs. 6.4%) and at 6 months (38.2% vs. 3.6%). While a small percentage of eyes had a BSCVA gain of 2 lines at 3 months (0.9%) and at 6 months (3.6%), no eyes had a BSCVA loss of 2 lines at 3 months or later.

Table 26. Change in Best Spectacle Corrected Visual Acuity

		1 Month	3 Months	6 Months	9 Months
Decrease > 2 Lines	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
Decrease 2 Lines	n/N	1/110	0/110	0/110	0/108
	%	0.9%	0.0%	0.0%	0.0%
Decrease 1 Line	n/N	9/110	7/110	4/110	6/108
	%	8.2%	6.4%	3.6%	5.6%
No change	n/N	68/110	59/110	60/110	51/108
	%	61.8%	53.6%	54.5%	47.2%
Increase 1 Line	n/N	29/110	43/110	42/110	48/108
	%	26.4%	39.1%	38.2%	44.4%
Increase 2 Lines	n/N	3/110	1/110	4/110	3/108
	%	2.7%	0.9%	3.6%	2.8%
Increase > 2 Lines	n/N	0/110	0/110	0/110	0/108
	%	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 (Table 27). Slightly more eyes had a gain than loss of 1 line of low contrast BSCVA at 3 months (30.6% vs. 17.6%) and at 6 months (33.6% vs. 19.1%). In addition, more eyes had a gain than loss of $\geq$ 2 lines of low contrast BSCVA at 3 months (7.4% vs. 4.6%) and 6 months (8.2% vs. 2.7%).

Table 27. Change in Low Contrast Best Spectacle Corrected Visual Acuity

		3 Months	6 Months
Decrease > 2 Lines	n/N	1/108	0/110
	%	0.9%	0.0%
Decrease 2 Lines	n/N	4/108	3/110
	%	3.7%	2.7%
Decrease 1 Line	n/N	19/108	21/110
	%	17.6%	19.1%
No change	n/N	43/108	40/110
	%	39.8%	36.4%
Increase 1 Line	n/N	33/108	37/110
	%	30.6%	33.6%
Increase 2 Lines	n/N	7/108	8/110
	%	6.5%	7.3%
Increase > 2 Lines	n/N	1/108	1/110
	%	0.9%	0.9%

8. Change in Contrast Sensitivity

Contrast sensitivity was measured under both photopic and mesopic conditions using the CSV-1000 (VectorVision[9]). A clinically significant change from preoperative level was defined as > 2 levels (> 0.3 log units) at two or more spatial frequencies (Table 28).

The majority of eyes did not have a clinically significant change in contrast sensitivity from preoperative to postoperative. Of the eyes with a change in photopic contrast sensitivity, slightly fewer eyes showed a gain than loss at 3 months (2.7% vs. 6.4%) and an equal percentage of eyes (5.5%) had a gain or loss at 6 months. Under mesopic conditions, a trend for more eyes with a gain than loss of contrast sensitivity was observed at 3 months (22.4% vs. 11.2%) and at 6 months (26.2% vs. 10.3%).

In addition, a gain from preoperative was observed in the mean contrast sensitivity log at each spatial frequency under photopic and mesopic conditions at 3 and 6 months (Table 29). While no statistically significant change was observed at 3 months, statistically significant ($p<0.05$) gains were noted at 6 cycles per degree (cpd) under photopic conditions and for all spatial frequencies under mesopic conditions at 6 months.

Table 28. 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	7/110	6/110	12/107	11/107
	%	6.4%	5.5%	11.2%	10.3%
No Change	n/N	100/110	98/110	71/107	68/107
	%	90.9%	89.1%	66.4%	63.6%
Gain	n/N	3/110	6/110	24/107	28/107
	%	2.7%	5.5%	22.4%	26.2%

Table 29. Comparison of Mean Contrast Sensitivity Log by Spatial Frequency

Spatial Frequency (cpd)	Preop Mean ± SD	3-Month Mean ± SD	p-value†	6-Month Mean ± SD	p-value†
Photopic	(N=110)	(N=110)		(N=110)	
3	1.73 ± 0.15	1.75 ± 0.19	0.156	1.75 ± 0.17	0.115
6	1.92 ± 0.19	1.94 ± 0.25	0.204	1.96 ± 0.22	***0.018***
12	1.56 ± 0.25	1.56 ± 0.28	0.986	1.57 ± 0.31	0.748
18	1.09 ± 0.26	1.08 ± 0.31	0.764	1.08 ± 0.32	0.892
Mesopic*	(N=107)	(N=107)		(N=107)	
3	1.51 ± 0.23	1.55 ± 0.26	0.134	1.56 ± 0.24	***0.036***
6	1.48 ± 0.25	1.52 ± 0.28	0.238	1.56 ± 0.27	***0.009***
12	0.91 ± 0.32	0.98 ± 0.31	0.086	1.00 ± 0.33	***0.048***
18	0.41 ± 0.34	0.42 ± 0.36	0.749	0.50 ± 0.36	***0.016***

*Mesopic illumination with neutral density filters in front of eyes

† 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

9. Patient Questionnaire

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 30. The symptoms reported as "worse" or "significantly worse" in >10% of eyes at 6 months were dryness, light sensitivity, blurring of vision, fluctuation of vision, glare, halos, and night driving difficulty.

Table 30. Postoperative Change in Subjective Symptoms without Correction vs. Preoperative*

3 MONTHS (N=110)					
Comfort Symptoms	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	0.0%	10.0%	86.4%	2.7%	0.9%
Dryness	3.6%	7.3%	47.3%	40.0%	1.8%
Excessive Tearing	1.8%	2.7%	95.5%	0.0%	0.0%
Gritty Feeling	3.6%	5.5%	83.6%	6.4%	0.9%
Headache	7.3%	17.3%	70.9%	4.5%	0.0%
Light Sensitivity	10.9%	7.3%	54.5%	27.3%	0.0%
Pain	4.5%	5.5%	81.8%	6.4%	1.8%
Redness	0.0%	11.8%	81.8%	4.5%	1.8%
Visual Symptoms					
Blurring of Vision	14.5%	17.3%	46.4%	20.0%	1.8%
Double Vision	11.8%	8.2%	71.8%	8.2%	0.0%
Fluctuation of Vision	5.5%	8.2%	62.7%	20.0%	3.6%
Glare	10.9%	10.0%	52.7%	26.4%	0.0%
Halos	8.2%	5.5%	59.1%	27.3%	0.0%
Night Driving Difficulty	21.8%	10.0%	48.2%	20.0%	0.0%
6 MONTHS (N=110)					
Comfort Symptoms	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	4.5%	9.1%	79.1%	6.4%	0.9%
Dryness	5.5%	6.4%	49.1%	36.4%	2.7%
Excessive Tearing	2.7%	4.5%	90.0%	2.7%	0.0%
Gritty Feeling	2.7%	5.5%	84.5%	6.4%	0.9%
Headache	9.1%	10.0%	76.4%	4.5%	0.0%
Light Sensitivity	10.9%	11.8%	54.5%	20.9%	1.8%
Pain	6.4%	4.5%	84.5%	4.5%	0.0%
Redness	3.6%	7.3%	81.8%	7.3%	0.0%
Visual Symptoms					
Blurring of Vision	13.6%	15.5%	49.1%	13.6%	8.2%
Double Vision	7.3%	12.7%	73.6%	4.5%	1.8%
Fluctuation of Vision	8.2%	10.0%	55.5%	21.8%	4.5%
Glare	10.0%	8.2%	68.2%	13.6%	0.0%
Halos	10.0%	3.6%	63.6%	19.1%	3.6%
Night Driving Difficulty	19.1%	19.1%	47.3%	10.9%	3.6%

* Based on the patients' comparison of symptom severity after surgery as better or worse compared to their recollection of symptom severity before surgery.

Compared to preoperative, uncorrected quality of vision at 6 months was reported as better or significantly better in 86.3% of eyes, same in 4.5% and worse or significantly worse in 9.1% (Table 31). Satisfaction with surgery at 6 months was reported as satisfied or extremely satisfied in 73.7% of eyes, unsure in 10.9%, and unsatisfied or extremely unsatisfied in 15.4% (Table 32). Frequency of wearing distance correction at 6 months was reported as never in 81.8% of eyes and at least some of the time in 18.2% with frequent or constant use in 11.8% (Table 33).

Table 31. Postoperative Quality of Vision without Correction vs. Preoperative*

	3 MONTHS (N=108)	6 MONTHS (N=110)
Significantly Better	54.6%	52.7%
Better	28.7%	33.6%
Same	7.4%	4.5%
Worse	7.4%	5.5%
Significantly Worse	1.9%	3.6%

* Based on the patients' comparison of quality of vision after surgery as better or worse compared to their recollection of quality of vision before surgery.

Table 32. Postoperative Satisfaction with Surgery

	3 MONTHS (N=108)	6 MONTHS (N=110)
Extremely Satisfied	47.2%	48.2%
Satisfied	26.9%	25.5%
Not Sure	15.7%	10.9%
Unsatisfied	6.5%	11.8%
Extremely Unsatisfied	3.7%	3.6%

Table 33. Postoperative Frequency of Distance Correction

	3 MONTHS (N=108)	6 MONTHS (N=110)
Never	85.2%	81.8%
Seldom	3.7%	6.4%
Frequently	1.9%	1.8%
Constantly	9.3%	10.0%

10. Retreatment

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

11. Statistical Analysis Outcomes

Statistical analysis was performed to assess for potential associations between demographic and baseline characteristics and clinical outcomes. Age, gender, race, preoperative cycloplegic cylinder, preoperative CRSE, operative room humidity and temperature were the characteristics considered to have the most potential for clinical relevance to the procedure. Outcomes evaluated at refractive stability (3 months) and at 6 months included: BSCVA loss of ≥ 2 lines; UCVA of 20/20 or better and 20/40 or better; and accuracy of MRSE, manifest sphere and manifest cylinder magnitude within 0.50D and 1.00D of emmetropia.

One-sided exact binomial tests (α=0.05) were used to support the observed overall rates of safety and effectiveness outcomes to the FDA Guidance Document targets. There was no BSCVA loss of ≥ 2 lines at 3 and 6 months, thereby meeting the FDA target rate of < 5% of eyes with BSCVA loss of > 2 lines for safety. FDA targets were met or exceeded for effectiveness outcomes overall, including UCVA 20/40 or better and accuracy of MRSE within 0.50D and within 1.00D of emmetropia. For each baseline subgroup, the observed rate either met the target or the 95% confidence interval (CI) contained the FDA target.

To assess the consistency of outcomes across characteristics, differences in rates among subgroups were assessed using the Cochran-Mantel-Haenszel (CMH) test. No statistical significance was observed among subgroups of preoperative CRSE for any outcome. Statistically significant ($p<0.05$) trends among subgroups are listed below by characteristic.

Among age subgroups by decade over a range of 20 to 60 years, higher rates were observed in younger patients as compared to older patients for the following outcomes:

- UCVA 20/20 or better at 3 months (p=0.0129). The observed rate was ≥ 60.0% for subgroups between 20 to 49 years vs. 33.3% for 50 to 60 years. At 6 months, no statistical significance remained among age subgroups for UCVA 20/20 or better.
- UCVA of 20/40 or better at 3 months (p=0.0020). The observed rate was 100% for subgroups between 20 to 49 years vs. 81.5% for 50 to 60 years, although the 95% CI contained the FDA target of 85%. At 6 months, no statistical significance by age remained and all age subgroups exceeded the FDA target for UCVA of 20/40 or better.
- MRSE within 0.50D at 3 and 6 months (p=0.0114 and p=0.0056). The observed rate was ≥ 76.2% at 3 and 6 months for subgroups between 20 to 49 years vs. 40.7% at 3 months and 51.9% at 6 months for 50 to 60 years with the FDA target of 50% included in the 95% CI. All age subgroups met or exceeded the FDA target for MRSE within 0.50D at 6 months.
- No statistical significance by age was observed for accuracy of MRSE within 1.00D and all age subgroups met or exceeded the FDA target for MRSE within 1.00D at 3 and 6 months. However, older patients, primarily between 40 and 60 years, were more likely to have a hyperopic MRSE of more than +1.00D at 3 and 6 months (p=0.0108 and p=0.0013). Younger patients were more likely to have a myopic MRSE of more than -1.00D at 3 and 6 months (p=0.0391), which was observed in two eyes of a 20 year-old patient.
- Manifest sphere within 0.50D at 3 and 6 months (p=0.0005 and p=0.0027). The observed rate was ≥ 71.4% for subgroups between 20 to 49 years vs. 37.0% for 50 to 60 years.
- Manifest sphere within 1.00D at 6 months (p=0.0005). The observed rate was ≥ 91.4% for subgroups between 20 to 49 years vs. 66.7% for 50 to 60 years. Older patients, primarily between 40 and 60 years, were more likely to have a hyperopic manifest sphere of more than +1.00D at 3 and 6 months (p=0.0042 and p=0.0005). Younger patients were more likely to have a myopic manifest sphere of more than -1.00D at 3 months (p=0.0391), which was observed in two eyes of a 20 year-old patient.

Preoperative astigmatism measured in subgroups by diopter of cycloplegic cylinder over a range from -1.00D to -6.00D. Eyes with lower preoperative astigmatism showed higher rates as compared to eyes with higher preoperative astigmatism for the following outcomes (observed rates at 3 and 6 months by preoperative cycloplegic cylinder are shown in Table 6):

- UCVA 20/20 or better at 3 and 6 months (p=0.0404 and p=0.0060). All preoperative cylinder subgroups met or exceeded the FDA target for UCVA of 20/40 or better at 3 and 6 months.
- MRSE within 0.50D at 3 and 6 months (p=0.0038 and p=0.0011). All preoperative cylinder subgroups met or exceeded the FDA target for MRSE within 0.50D,at 3 and 6 months.
- MRSE within 1.00D at 3 and 6 months (p=0.0304 and p=0.0433). All preoperative cylinder subgroups met or exceeded the FDA target for MRSE within 1.00D at 3 and 6 months.
- Manifest sphere within 1.00D at 3 months (p=0.0082). No statistical significance based on preoperative cylinder remained for manifest sphere at 6 months. In addition, eyes with higher preoperative astigmatism were more likely to have a hyperopic manifest sphere of more than +1.00D at 3 months compared to eyes with lower preoperative astigmatism (p=0.0412).
- Manifest cylinder magnitude ≤ 0.50D at 3 months (p=0.0227).
- Manifest cylinder magnitude ≤ 1.00D at 3 and 6 months (p=0.0002 and p=0.0012).

Race was analyzed in two subgroups, 94.5% Caucasians and 5.5% other races, including Hispanic (3.6%) and Indian (1.8%). Note that apparent associations by race should be interpreted with caution because of the small sample size of six eyes in the other races subgroup. Caucasians had higher rates than other races for the following outcomes:

- MRSE within 0.50D at 3 months (p=0.0380). The observed rate was 73.1% for Caucasians vs. two of six eyes (33.3%) in the other races subgroup, although the 95% CI contained the FDA target of 50%. At 6 months, no statistically significant difference remained by race for MRSE within 0.50D. Both subgroups met or exceeded the FDA target for MRSE within 0.50D at 6 months and for MRSE within 1.00D at 3 and 6 months.
- Manifest sphere within 0.50D at 6 months (p=0.0380). The observed rate was 73.1% for Caucasians vs. two of six eyes (33.3%) in the other races subgroup.
- Manifest cylinder magnitude ≤ 1.00D at 3 months (p=0.0345). The observed rate was 92.3% for Caucasians vs. four of six eyes (66.7%) in the other races subgroup. At 6 months, no statistically significant difference based on race remained for manifest cylinder outcomes.

Room temperature, room humidity and gender each had one statistically significant association with postoperative manifest sphere or manifest cylinder magnitude, as follows:

- Eyes treated in a room with a lower temperature between 65.0°F and 69.9°F showed higher rates than eyes treated in a room between 70.0°F and 74.9°F for manifest sphere within 1.00D at 3 months (97.0% vs. 83.1%; p=0.0467).
- Eyes treated in a lower room humidity showed higher rates as compared to eyes treated in higher room humidity for manifest cylinder magnitude ≤ 1.00D at 6 months (p=0.0450). The observed rate was ≥ 81.3% for room humidity subgroups between 18% to 59% vs. 0.0% for the two eyes of one patient treated in a room humidity of 63%.
- Females showed higher rates as compared to males for manifest cylinder magnitude ≤ 1.00D at 3 months (96.6% vs. 84.3%; p=0.0260) and at 6 months (96.6% vs. 80.4%; p=0.0068).

12. Comparative Analysis by Defocus Type

To optimize the CustomCornea® wavefront-guided LASIK treatment of mixed astigmatism, eyes were categorized as myopic or hyperopic based on the preoperative wavefront defocus error. Myopic or hyperopic components of the algorithm were used as determined by the preoperative wavefront defocus. The study included 85 eyes with a myopic defocus and 25 eyes with a hyperopic defocus based on the preoperative wavefront.

Clinical outcomes at 3 and 6 months for each preoperative wavefront defocus type were compared to established target rates for refractive surgery. In addition, outcomes were compared between myopic and hyperopic defocus types. Outcomes evaluated at refractive stability (3 months) and at 6 months included: BSCVA loss of $\geq$ 2 lines; UCVA of 20/20 or better and 20/40 or better; and accuracy of MRSE, manifest sphere and manifest cylinder magnitude within 0.50D and 1.00D of emmetropia. Postoperative outcomes of myopia or hyperopia of more than 1.00D by MRSE and manifest sphere were also evaluated.

One-sided exact binomial tests (α=0.05) were used to compare the observed overall rates of eyes meeting safety and effectiveness criteria to the FDA Guidance Document target rates. There was no BSCVA loss of $\geq$ 2 lines at 3 and 6 months for both subgroups, thereby meeting the FDA target rate of < 5% of eyes with BSCVA loss of > 2 lines for safety. Both defocus types of mixed astigmatic eyes exceeded FDA targets overall for effectiveness including for UCVA of 20/40 or better and accuracy of MRSE within 0.50D and 1.00D of emmetropia at 3 and 6 months.

To compare clinical outcomes of mixed astigmatic eyes by preoperative defocus type, the Cochran-Mantel-Haenszel (CMH) test was used to assess for differences. A p-value < 0.05 would indicate a statistically significant difference in outcomes between defocus types. Myopic and hyperopic defocus groups had outcomes that were not significantly different. Tables 34 and 35 display the comparative analysis by defocus type at 3 and 6 months.

Table 34. Comparative Analysis of Mixed Astigmatic Eyes by Defocus Type at 3 Months

Criteria	CMH P-Value*		Myopic Defocus	Hyperopic Defocus	Total	FDA Target P-Value**
Key Effectiveness Parameters						
UCVA 20/20 or better	0.6183	n/N % CI	49/85 57.6% (46.4, 68.3)	13/25 52.0% (31.3, 72.2)	62/110 56.4% (46.6, 65.8)	--
UCVA 20/40 or better	0.2166	n/N % CI	80/85 94.1% (86.8, 98.1)	25/25 100.0% (86.3, 100.0)	105/110 95.5% (89.7, 98.5)	≥ 85% 0.9999
MRSE ± 0.50D	0.7169	n/N % CI	61/85 71.8% (61.0, 81.0)	17/25 68.0% (46.5, 85.1)	78/110 70.9% (61.5, 79.2)	≥ 50% 1.0000
MRSE ± 1.00D	0.8740	n/N % CI	79/85 92.9% (85.3, 97.4)	23/25 92.0% (74.0, 99.0)	102/110 92.7% (86.2, 96.8)	≥ 75% 1.0000
Accuracy of Manifest Sphere and Cylinder						
Manifest Sphere ± 0.50D	0.0417	n/N % CI	57/85 67.1% (56.0, 76.9)	22/25 88.0% (68.8, 97.5)	79/110 71.8% (62.4, 80.0)	--
Manifest Sphere ± 1.00D	0.9017	n/N % CI	74/85 87.1% (78.0, 93.4)	22/25 88.0% (68.8, 97.5)	96/110 87.3% (79.6, 92.9)	--
Manifest Cylinder Magnitude ≤ 0.50D	0.4994	n/N % CI	55/85 64.7% (53.6, 74.8)	18/25 72.0% (50.6, 87.9)	73/110 66.4% (56.7, 75.1)	--
Manifest Cylinder Magnitude ≤ 1.00D	0.1736	n/N % CI	79/85 92.9% (85.3, 97.4)	21/25 84.0% (63.9, 95.5)	100/110 90.9% (83.9, 95.6)	--
Postoperative Manifest Spherical Equivalent and Manifest Sphere						
Postoperative MRSE > +1.00D (Hyperopic)	0.1738	n/N % CI	6/85 7.1% (2.6, 14.7)	0/25 0.0% (0.0, 13.7)	6/110 5.5% (2.0, 11.5)	--
Postoperative MRSE < -1.00D (Myopic)	0.0088	n/N % CI	0/85 0.0% (0.0, 4.2)	2/25 8.0% (1.0, 26.0)	2/110 1.8% (0.2, 6.4)	--
Postoperative Manifest Sphere > +1.00D (Hyperopic)	0.2095	n/N % CI	11/85 12.9% (6.6, 22.0)	1/25 4.0% (0.1, 20.4)	12/110 10.9% (5.8, 18.3)	--
Postoperative Manifest Sphere < -1.00D (Myopic)	0.0088	n/N % CI	0/85 0.0% (0.0, 4.2)	2/25 8.0% (1.0, 26.0)	2/110 1.8% (0.2, 6.4)	--

* Cochran-Mantel-Haenszel (CMH) Test with rank scores

** One-sided exact binomial test comparison to the FDA target

CI = 95% Confidence Interval

$p < 0.05$ is statistically significant

UCVA = Uncorrected Visual Acuity

MRSE = Manifest Refraction Spherical Equivalent

D = Diopter

BSCVA = Best Spectacle Corrected Visual Acuity

Table 35. Comparative Analysis of Mixed Astigmatic Eyes by Defocus Type at 6 Months

Criteria	CMH P-Value*		Myopic Defocus	Hyperopic Defocus	Total	FDA Target P-Value**
Key Effectiveness Parameters						
UCVA 20/20 or better	0.3687	n/N % CI	56/85 65.9% (54.8, 75.8)	14/25 56.0% (34.9, 75.6)	70/110 63.6% (53.9, 72.6)	--
UCVA 20/40 or better	0.4410	n/N % CI	83/85 97.6% (91.8, 99.7)	25/25 100.0% (86.3, 100.0)	108/110 98.2% (93.6, 99.8)	≥ 85% 1.0000
MRSE ± 0.50D	0.6279	n/N % CI	64/85 75.3% (64.7, 84.0)	20/25 80.0% (59.3, 93.2)	84/110 76.4% (67.3, 83.9)	≥ 50% 1.0000
MRSE ± 1.00D	0.8299	n/N % CI	77/85 90.6% (82.3, 95.8)	23/25 92.0% (74.0, 99.0)	100/110 90.9% (83.9, 95.6)	≥ 75% 1.0000
Accuracy of Manifest Sphere and Cylinder						
Manifest Sphere ± 0.50D	0.5257	n/N % CI	59/85 69.4% (58.5, 79.0)	19/25 76.0% (54.9, 90.6)	78/110 70.9% (61.5, 79.2)	--
Manifest Sphere ± 1.00D	0.1703	n/N % CI	73/85 85.9% (76.6, 92.5)	24/25 96.0% (79.6, 99.9)	97/110 88.2% (80.6, 93.6)	--
Manifest Cylinder Magnitude ≤ 0.50D	0.9485	n/N % CI	55/85 64.7% (53.6, 74.8)	16/25 64.0% (42.5, 82.0)	71/110 64.5% (54.9, 73.4)	--
Manifest Cylinder Magnitude ≤ 1.00D	0.0987	n/N % CI	78/85 91.8% (83.8, 96.6)	20/25 80.0% (59.3, 93.2)	98/110 89.1% (81.7, 94.2)	--
Postoperative Manifest Spherical Equivalent and Manifest Sphere						
Postoperative MRSE > +1.00D (Hyperopic)	0.1128	n/N % CI	8/85 9.4% (4.2, 17.7)	0/25 0.0% (0.0, 13.7)	8/110 7.3% (3.2, 13.8)	--
Postoperative MRSE < -1.00D (Myopic)	0.0088	n/N % CI	0/85 0.0% (0.0, 4.2)	2/25 8.0% (1.0, 26.0)	2/110 1.8% (0.2, 6.4)	--
Postoperative Manifest Sphere > +1.00D (Hyperopic)	0.1703	n/N % CI	12/85 14.1% (7.5 , 23.4)	1/25 4.0% (0.1, 20.4)	13/110 11.8% (6.4, 19.4)	--
Postoperative Manifest Sphere < -1.00D (Myopic)	NA	n/N % CI	0/85 0.0% (0.0, 4.2)	0/25 0.0% (0.0, 13.7)	0/110 0.0% (0.0, 3.3)	--

* Cochran-Mantel-Haenszel (CMH) Test with rank scores NA = Not Applicable

** One-sided exact binomial test comparison to the FDA target

CI = 95% Confidence Interval $p < 0.05$ is statistically significant

UCVA = Uncorrected Visual Acuity MRSE = Manifest Refraction Spherical Equivalent

D = Diopter BSCVA = Best Spectacle Corrected Visual Acuity

Alcon®

LADARVISION 4000

Excimer Laser System

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

PATIENT INFORMATION BOOKLET

For Mixed Astigmatism of 1.00D to less than 5.00D cycloplegic cylinder magnitude

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.

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REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 10065 – original release	

TABLE OF CONTENTS

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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 J) 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.

Mixed astigmatism is a condition that causes blurred distant and near vision because the eye is both *nearsighted* and *farsighted*. If you have mixed astigmatism, you may have difficulty seeing clearly at distance and near. Glasses, contact lenses, or eye surgery can correct mixed astigmatism to help you see more clearly.

Laser Assisted In-Situ Keratomileusis (LASIK) is a type of eye surgery available to correct mixed astigmatism. 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.

LASIK surgery can help you see more clearly by changing the shape of the *cornea*, the clear front surface of your eye. LASIK surgery uses an *excimer laser* to remove tissue to reshape the cornea. 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 mixed 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 mixed 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*".

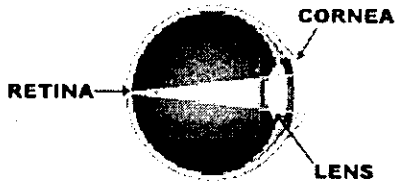
Your doctor can use either your eyeglass prescription or a wavefront measurement to plan LASIK surgery. LASIK surgery based on the eyeglass prescription is called *Conventional LASIK*. LASIK surgery based on the wavefront is called wavefront-guided LASIK. *CustomCornea® LASIK* is wavefront-guided surgery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

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 Mixed 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

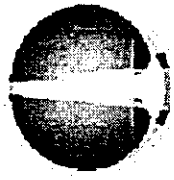


A NORMAL EYE

Light focuses on the retina.
Vision is clear.

Astigmatism is a focusing error that results in blurred distant and near vision. The cornea is more curved in some directions than others causing light to focus at different points from the retina. Vision is blurred because light does not focus correctly on the retina. When light focuses at a point in front of the retina, the eye is nearsighted. When light focuses at a point behind the retina, the eye is farsighted. An eye with mixed astigmatism is both nearsighted and farsighted. Diagram 2 shows how light focusing at different points from the retina causes blurred vision in an eye with mixed astigmatism.

DIAGRAM 2: EYE WITH MIXED ASTIGMATISM

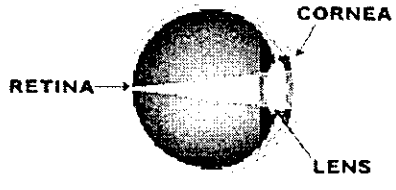


A MIXED ASTIGMATIC EYE

Light focuses in front of and 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 3 shows that distant vision is clearer after LASIK.

DIAGRAM 3: 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 mixed 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 between 1.00 to less than 5.00 *diopters (D)* of mixed astigmatism. If you have mixed 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 110 eyes to determine benefits and risks. The study results are shown below and in "Risks of CustomCornea® LASIK" (Section D).

Patient Demographics

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

Table 1. Demographics of 110 Eyes of 63 Study Patients

Age		Race		Gender		Contact Lens History	
Average: 40.6 ± 10.7 years		Caucasian	94.5%	Female	53.6%	None	64.5%
Range: 20 to 60 years		Hispanic	3.6%	Male	46.4%	Hard	2.7%
		Indian	1.8%			Soft	32.7%

Visual Acuity Measurement

Visual acuity is a measure of the sharpness of vision using a letter chart. Diagram 4 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 4: EXAMPLE OF VISUAL ACUITY CHART

Visual Acuity without Glasses

The clinical study evaluated visual acuity **without** glasses at a distance using a letter chart. Table 2 shows that at least 93.5% of patients treated for mixed 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

% of Eyes With:	Before Surgery (N=110)	1 Month (N=110)	3 Months (N=110)	6 Months (N=110)	9 Months (N=108)
20/20 or better*	1.1%	72.3%	63.8%	71.3%	69.6%
20/20 or better	0.9%	63.6%	56.4%	63.6%	61.1%
20/25 or better	3.6%	86.4%	80.9%	87.3%	84.3%
20/40 or better	35.5%	96.4%	95.5%	98.2%	93.5%

* if visual acuity was 20/20 or better with glasses or contact lenses before surgery (N=94 eyes at all visits up to 6 months; N=92 at 9 months). N is the number of eyes studied.

Visual Acuity without Glasses After Surgery and with Glasses Before Surgery

The clinical study compared visual acuity **without** glasses at a distance after surgery to visual acuity **with** glasses before surgery using a letter chart. Table 3 shows that 56.4% of patients at 3 months and 60.0% at 6 months, saw as well or better **without** glasses after CustomCornea® surgery as **with** glasses before surgery.

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

% of Eyes With:	1 Month (N=110)	3 Months (N=110)	6 Months (N=110)	9 Months (N=108)
2 lines better vision *without* glasses after LASIK than vision *with* glasses before surgery	0.0%	0.0%	1.8%	1.9%
1 line better vision *without* glasses after LASIK than vision *with* glasses before surgery	11.8%	16.4%	17.3%	18.5%
same vision* *without* glasses after LASIK as vision *with* glasses before surgery	48.2%	40.0%	40.9%	39.8%
1 line worse vision *without* glasses after LASIK than vision *with* glasses before surgery	23.6%	19.1%	26.4%	19.4%
2 lines worse vision *without* glasses after LASIK than vision *with* glasses before surgery	8.2%	11.8%	6.4%	10.2%
more than 2 lines worse vision *without* glasses after LASIK than vision *with* glasses before surgery	8.2%	12.7%	7.3%	10.2%

* **Same vision** is within 2 or 3 letters on the same line of a visual acuity chart. N is the number of eyes studied.

Patient Demographics and Surgery Outcomes

Patient demographics were related to the following surgery outcomes in the clinical study at **3 months after surgery**.

- A visual acuity of 20/20 or better without glasses or contact lenses after surgery was more likely in younger patients and patients with lower amounts of astigmatism before surgery. A visual acuity of 20/40 or better without glasses or contact lenses after surgery was more likely in younger patients.

- Reduction of farsightedness or nearsightedness to 0.50D or less after surgery was more likely in younger patients, Caucasian patients* and patients with lower amounts of astigmatism before surgery. Reduction of farsightedness or nearsightedness to 1.00D or less after surgery was more likely in patients with lower amounts of astigmatism before surgery.

- Reduction of astigmatism to 0.50D or less after surgery was more likely in patients with lower amounts of astigmatism before surgery. Reduction of astigmatism to 1.00D or less after surgery was more likely in females, Caucasian patients* and patients with lower amounts of astigmatism before surgery.

Patient demographics were related to the following surgery outcomes in the clinical study at **6 months after surgery**.

- A visual acuity of 20/20 or better without glasses or contact lenses after surgery was more likely in patients with lower amounts of astigmatism before surgery.

- Reduction of farsightedness or nearsightedness to 0.50D or less after surgery was more likely in younger patients, Caucasian patients* and patients with lower amounts of astigmatism before surgery. Reduction of farsightedness or nearsightedness to 1.00D or less after surgery was more likely in younger patients and patients with lower amounts of astigmatism before surgery.

- Reduction of astigmatism to 1.00D or less after surgery was more likely in females and patients with lower amounts of astigmatism before surgery.

* Note that the clinical study included only 5.5% of patients of races other than Caucasian.

Patient Questionnaire

Patients in the clinical study were asked to rate the quality of vision after surgery compared to their recollection of quality of vision before surgery. Table 4 shows that compared to before surgery, quality of vision without glasses or contact lenses at 6 months after surgery was reported as better or significantly better in 86.3% of eyes, same in 4.5% and worse or significantly worse in 9.1%.

Table 4. Quality of Vision *without* Glasses or Contact Lenses After Surgery Compared to Before Surgery*		
	3 MONTHS N=108	6 MONTHS N=110
Significantly Better	54.6%	52.7%
Better	28.7%	33.6%
Same	7.4%	4.5%
Worse	7.4%	5.5%
Significantly Worse	1.9%	3.6%

N is the number of eyes studied.

* Based on the patients' comparison of quality of vision after surgery as better or worse compared to their recollection of quality of vision before surgery.

Table 5 shows that satisfaction with surgery at 6 months was reported as satisfied or extremely satisfied in 73.7% of eyes, unsure in 10.9%, and unsatisfied or extremely unsatisfied in 15.4%.

Table 5. Satisfaction with Surgery		
	3 MONTHS N=108	6 MONTHS N=110
Extremely Satisfied	47.2%	48.2%
Satisfied	26.9%	25.5%
Not Sure	15.7%	10.9%
Unsatisfied	6.5%	11.8%
Extremely Unsatisfied	3.7%	3.6%

N is the number of eyes studied.

Table 6 shows that frequency of wearing glasses or contact lenses for distance vision at 6 months was reported as never in 81.8% of eyes and at least some of the time in 18.2% with frequent or constant use in 11.8%.

Table 6. Frequency of Glasses or Contact Lens Wear for Distance After Surgery		
	3 MONTHS N=108	6 MONTHS N=110
Never	85.2%	81.8%
Seldom	3.7%	6.4%
Frequently	1.9%	1.8%
Constantly	9.3%	10.0%

N is the number of eyes studied.

D. 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** 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 mixed astigmatism. Eyes with unstable mixed astigmatism are unable to be measured correctly 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, LASIK surgery).
- 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 mixed astigmatism less than 1.00D or for 5.00D or greater. 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 3 months 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 for CustomCornea® LASIK, some people still needed glasses or contact lenses after surgery.

Astigmatism remained after surgery for some patients. After surgery, 9.1% of patients at 3 months and 10.9% of patients at 6 months had astigmatism of more than 1D and 0.9% of patients at 3 and 6 months had astigmatism of more than 2D.

Farsightedness remained after surgery for some patients. After surgery, 5.5% of patients at 3 months and 7.3% of patients at 6 months had more than 1D of farsightedness and 0.9% of patients at 3 months had more than 2D of farsightedness. Older patients, primarily between 40 and 60 years, were more likely to have more than 1D of farsightedness at 3 and 6 months. Patients with higher amounts of astigmatism before surgery were more likely to have 1D of farsightedness at 3 months after surgery.

Nearsightedness remained after surgery for some patients. At 3 and 6 months, 1.8% of patients had more than 1D of nearsightedness. Younger patients were more likely to have more than 1D of nearsightedness at 3 and 6 months, which was observed in both eyes of a 20 year-old patient.

Visual Acuity with Glasses

The clinical study evaluated visual acuity **with** glasses at a distance using a letter chart. Table 7 shows that all patients in the study saw 20/25 or better **with** glasses before surgery and at 3 months or later after surgery.

Table 7. Visual Acuity *with* Glasses (Best Vision)

% of Eyes With:	Before Surgery (N=110)	1 Month (N=110)	3 Months (N=110)	6 Months (N=110)	9 Months (N=108)
20/20 or better	85.5%	89.1%	89.1%	92.7%	93.5%
20/25 or better	100.0%	99.1%	100.0%	100.0%	100.0%
20/32 or better	100.0%	100.0%	100.0%	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 change in best vision **with** glasses after surgery was compared to vision **with** glasses before surgery 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 visual acuity testing is a way to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog. Table 8 compares the change in vision **with** glasses before surgery to 3 and 6 months after surgery.

Table 8. Change in Visual Acuity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Standard Chart		10% Low Contrast Chart	
	3 Months (N=110)	6 Months (N=110)	3 Months (N=108)	6 Months (N=110)
loss of more than 2 lines	0.0%	0.0%	0.9%	0.0%
loss of 2 lines	0.0%	0.0%	3.7%	2.7%
loss of 1 line	6.4%	3.6%	17.6%	19.1%
no change	53.6%	54.5%	39.8%	36.4%
gain of 1 line	39.1%	38.2%	30.6%	33.6%
gain of 2 lines	0.9%	3.6%	6.5%	7.3%
gain of more than 2 lines	0.0%	0.0%	0.9%	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 9 compares the change in contrast sensitivity **with** glasses before surgery to 3 and 6 months after surgery.

Table 9. Change in Contrast Sensitivity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Daylight Conditions		Dim Light Conditions	
	3 Months (N=110)	6 Months (N=110)	3 Months (N=107)	6 Months (N=107)
Loss	6.4%	5.5%	11.2%	10.3%
No change	90.9%	89.1%	66.4%	63.6%
Gain	2.7%	5.5%	22.4%	26.2%

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 10.

Table 10. Adverse Events and Complications	
Greater than or equal to 1% of eyes (N=110) **had:**	
Irritation on the front surface of the cornea at one month or later	10.0%
Cells growing under the corneal flap *	5.4%
Inflammation of the cornea under the corneal flap	4.5%
Problem with creation of the corneal flap *	1.8%
Pain at one month or later	1.8%
Less than 1% of eyes (N=110) **had:**	
Feeling of something in the eye at one month or later	0.9%
Viral infection in the cornea	0.9%

N is the number of eyes studied.

* One eye did not receive laser ablation after a problem with the creation of the corneal flap and was not included in the analysis of eyes receiving laser surgery (N=111).

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

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

Worse and Significantly Worse Symptoms After Surgery

Patients who were treated for mixed astigmatism in the clinical study rated the change in the following symptoms shown in Table 11 as worse or significantly worse after surgery without glasses or contact lenses compared to their recollection of symptoms before surgery. The symptoms reported as "worse" or "significantly worse" in >10% of eyes at 6 months were dryness, light sensitivity, blurring of vision, fluctuation of vision, glare, halos, and night driving difficulty.

Table 11. Worse or Significantly Worse Symptoms *without* Glasses After Surgery Compared to Before Surgery*

	3 Months (N=110)		**6 Months** (N=110)	
Comfort Symptoms	**Worse**	**Significantly Worse**	**Worse**	**Significantly Worse**
Burning	2.7%	0.9%	6.4%	0.9%
Dryness	40.0%	1.8%	36.4%	2.7%
Excessive Tearing	0.0%	0.0%	2.7%	0.0%
Gritty Feeling	6.4%	0.9%	6.4%	0.9%
Headache	4.5%	0.0%	4.5%	0.0%
Light Sensitivity	27.3%	0.0%	20.9%	1.8%
Pain	6.4%	1.8%	4.5%	0.0%
Redness	4.5%	1.8%	7.3%	0.0%
Visual Symptoms				
Blurring of Vision	20.0%	1.8%	13.6%	8.2%
Double Vision	8.2%	0.0%	4.5%	1.8%
Fluctuation of Vision	20.0%	3.6%	21.8%	4.5%
Glare	26.4%	0.0%	13.6%	0.0%
Halos §	27.3%	0.0%	19.1%	3.6%
Night Driving Difficulty	20.0%	0.0%	10.9%	3.6%

N is the number of eyes studied.

* Based on the patients' comparison of symptom severity after surgery as worse compared 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.

E. 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 mixed astigmatism of 1.00D to less than 5.00D.
- have stable mixed 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 mixed astigmatism.
- be willing to sign an Informed Consent Form, if provided by your doctor.

F. 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.

G. 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 mixed 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 mixed 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.

H. 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.

I. 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 mixed 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 mixed astigmatism include glasses, contact lenses, and Conventional LASIK. Other surgical options that may be used to correct vision are ALK and RK.
- ALK, RK and LASIK surgery 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 D: Risks)
2. False (see Section F: Before the Surgery)
3. False (see Section F: The Day of Surgery)
4. True (see Section C: Benefits)
5. True (see Section D: Risks)
6. True (see Section D: Risks)
7. False (see Section D: Contraindications)
8. False (see Section D: Contraindications)
9. True (see Section D: Precautions)

J. 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 mixed 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 causing light to focus at different points from the retina. Vision is blurred because light does not focus correctly on the retina. Types of astigmatism include nearsighted, farsighted and mixed.

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.

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. LASIK surgery 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 mixed astigmatism, farsightedness or nearsightedness in 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 focus light at a point behind the retina resulting in blurred images. Farsightedness is also called hyperopia.

Focusing Error: a condition in which the eye forms a blurred image on the retina. Examples are mixed astigmatism, farsightedness, nearsightedness 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.

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 can also 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.

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.

Mixed Astigmatism: a focusing error that results in blurred distant and near vision. An eye with mixed astigmatism is both nearsighted and farsighted. The cornea is more curved in some directions than others causing light to focus at different points in front of and behind the retina. Vision is blurred because light does not focus correctly on the retina.

Nearsightedness: a focusing error that results in blurred vision that is usually worse at distance than at near. The cornea and lens focus light at a point in front of the retina resulting in blurred images. Nearsightedness is also called myopia.

Ocular Hypertension: increased eye pressure.

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

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 mixed 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.

K. 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

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Alcon®

LADAR*6000*™

EXCIMER LASER

PROFESSIONAL USE INFORMATION MANUAL

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

PHYSICIAN'S BOOKLET

For Mixed Astigmatism of 1.00D to less than 5.00D cycloplegic cylinder magnitude

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.

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

REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 10064 – original release	

TABLE OF CONTENTS

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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*™ 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 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*™ 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 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 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 when 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 is contained within the system. This filter cartridge is inspected and replaced during preventative 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 21 CFR 1040 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 mixed astigmatism of 1.00D to less than 5.00D cycloplegic cylinder magnitude at the spectacle plane, which is greater than the sphere magnitude, and the cylinder and sphere have opposite signs;
- 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 mixed astigmatism have **NOT** been established in patients:

- with unstable mixed 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 mixed astigmatism of less than 1.00D cycloplegic cylinder magnitude or for 5.00D or greater cycloplegic cylinder magnitude.
- 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 at any postoperative visit up to 9 months in the clinical study for CustomCornea® LASIK correction of mixed astigmatism are summarized in Table 1. The data meet the safety criteria established in the FDA Guidance Document of less than 1% occurrence of each type of adverse event and less than 5% overall.

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

ADVERSE EVENTS	n/N	%
Miscreated flap (related to microkeratome)	2/111†	1.8%
Corneal infiltrate (related to viral epidemic keratoconjunctivitis)	1/110	0.9%
COMPLICATIONS		
Grade ≥ 1 Superficial Punctate Keratitis (SPK) at one month or later	11/110	10.0%
Epithelium in the interface	6/111†	5.4%
Diffuse lamellar keratitis (DLK)	5/110	4.5%
Pain at one month or later	2/110	1.8%
Foreign body sensation at one month or later	1/110	0.9%

† One eye did not receive laser ablation after the miscreated flap and was not included in the analysis of eyes receiving laser treatment (N=111).

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

- corneal edema at one week or later;
- corneal epithelial defect (central or peripheral) at one month or later;
- decrease in best spectacle corrected visual acuity (BSCVA) of more than 10 letters (> 2 lines) not due to irregular astigmatism, as shown by hard contact lens refraction at six months or later;
- epithelium in the interface with a loss of BSCVA of 2 or more lines;
- intraocular pressure increase of more than 10 mmHg above baseline;
- intraocular pressure of more than 25 mmHg;
- late onset of corneal haze at six months or later with a loss of BSCVA of 2 or more lines;
- melting of the flap;
- misaligned flap;
- retinal detachment; and
- 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 system and the fellow eye received a Conventional treatment based on phoropter cycloplegic refraction. For this initial subgroup of patients, the fellow eye served as a contralateral control.

Upon providing data to support expansion of the number of patients 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 patient 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, patient 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 mixed astigmatism. Patients were followed at 1 day, 1 week, and 1, 3, 6, and 9 months postoperatively. 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.

Recruited patients 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, mixed astigmatic patients must have had a preoperative cycloplegic refraction at the spectacle plane of > 0.00D to +6.00D sphere with < 0.00D to -6.00D astigmatism (minus cylinder convention) with an absolute cylinder magnitude greater than the sphere magnitude. Enrollment of mixed astigmatic eyes in the study occurred over the preoperative cycloplegic refractive range of +0.25D to +4.25D sphere with -1.00D to -6.00D astigmatism and -1.38D to +1.63D spherical equivalent (SE).

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 system.

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

Patients must have been at least 18 years of age and had a BSCVA of 20/25 or better in the operative eye(s). Patients 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.

Patients 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. Patients 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, patients were not to wear their contact lenses in the operative eye(s) for 2 to 3 weeks for soft and hard contact lenses, respectively.

Patients who exhibited any of the following conditions were excluded from the study:

- 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 $\geq$ 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 manifest refraction spherical equivalent (MRSE) and manifest cylinder; reduction of wavefront error, including higher-order aberrations; and patient 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

A total of 110 eyes of 63 patients were enrolled in the Primary Cohort. The demographics of the study population (Table 2) were typical for a refractive surgery trial performed in the U.S. The mean ± standard deviation patient age was 40.6 ± 10.7 years with a range from 20 to 60 years. The majority of patients were Caucasian (94.5%) and the remaining patients were Hispanic (3.6%) and Indian (1.8%). Slightly more females (53.6%) than males (46.4%) participated in the study. The distribution of right and left eyes that received treatment was approximately equal (49.1% vs. 50.9%). While most patients (64.5%) did not wear contact lenses prior to surgery, 32.7% wore soft contact lenses and 2.7% wore rigid gas permeable (RGP) lenses.

Table 2. Demographics

110 Eyes of 63 Enrolled Patients			
Age (In Years) Average ± Standard Deviation Minimum to Maximum		40.6 ± 10.7 20 to 60	
Race		**N**	**% Eyes**
	Caucasian	104	94.5%
	Hispanic	4	3.6%
	Indian	2	1.8%
Gender	Female	59	53.6%
	Male	51	46.4%
Eye	Left	56	50.9%
	Right	54	49.1%
Contact Lens History	None	71	64.5%
	Soft	36	32.7%
	Rigid Gas Permeable (RGP)	3	2.7%

2. Accountability

The accountability for this study was ≥ 98.2% at all postoperative intervals (Table 3). Postoperative data were available for 110 eyes (100%) up to 6 months and for 108 eyes (98.2%) at 9 months. One patient (2 eyes) missed the 9-month visit because the patient moved out of the country prior to the opening of the 9-month visit window.

Table 3. Accountability at Each Visit

		1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
Total Eyes Enrolled	n	110	110	110	110
Available for Analysis	**n** **%**	**110** **100.0%**	**110** **100.0%**	**110** **100.0%**	**108** **98.2%**
Unavailable Missed Visit	n %	0 0.0%	0 0.0%	0 0.0%	2 1.8%
% Accountability= [available/(available + unavailable)]	%	**100.0%**	**100.0%**	**100.0%**	**98.2%**

3. Preoperative Cycloplegic Refraction Parameters

The study population of mixed astigmatic eyes had a preoperative cycloplegic cylinder magnitude greater than the sphere in minus cylinder convention. Preoperative cycloplegic refractive range was +0.25D to +4.25D sphere with -1.00D to -6.00D cylinder and -1.38D to +1.63D spherical equivalent. The mean ± standard deviation for the preoperative cycloplegic refraction was +1.50D ± 0.94D sphere, -2.90D ± 1.20D cylinder and +0.06D ± 0.65D spherical equivalent. Table 4 displays the number of eyes stratified by preoperative cycloplegic sphere and cylinder. Table 5 displays the number of eyes stratified by preoperative cycloplegic spherical equivalent and cylinder.

Table 4. Preoperative Cycloplegic Refraction Stratified by Sphere and Cylinder

		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION					
SPHERE (D)		-1.00 to -1.99	-2.00 to -2.99	-3.00 to -3.99	-4.00 to -4.99	-5.00 to -6.00	TOTAL
> 0.00 to +0.99	n/N	15/110	14/110	7/110	0/110	0/110	36/110
	%	13.6%	12.7%	6.4%	0.0%	0.0%	32.7%
+1.00 to +1.99	n/N	9/110	19/110	10/110	3/110	0/110	41/110
	%	8.2%	17.3%	9.1%	2.7%	0.0%	37.3%
+2.00 to +2.99	n/N	0/110	4/110	6/110	9/110	4/110	23/110
	%	0.0%	3.6%	5.5%	8.2%	3.6%	20.9%
+3.00 to +3.99	n/N	0/110	0/110	2/110	5/110	2/110	9/110
	%	0.0%	0.0%	1.8%	4.5%	1.8%	8.2%
+4.00 to +5.00	n/N	0/110	0/110	0/110	0/110	1/110	1/110
	%	0.0%	0.0%	0.0%	0.0%	0.9%	0.9%
TOTAL	n/N	24/110	37/110	25/110	17/110	7/110	110/110
	%	21.8%	33.6%	22.7%	15.5%	6.4%	100.0%

D= Diopter

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

		CYLINDER MAGNITUDE (D) IN MINUS CYLINDER CONVENTION					
SPHERICAL EQUIVALENT (D)		-1.00 to -1.99	-2.00 to -2.99	-3.00 to -3.99	-4.00 to -4.99	-5.00 to -6.00	TOTAL
-1.00 to -2.00	n/N	0/110	1/110	5/110	2/110	0/110	8/110
	%	0.0%	0.9%	4.5%	1.8%	0.0%	7.3%
0.00 to -0.99	n/N	9/110	19/110	11/110	3/110	3/110	45/110
	%	8.2%	17.3%	10.0%	2.7%	2.7%	40.9%
+0.01 to +0.99	n/N	15/110	15/110	4/110	9/110	2/110	45/110
	%	13.6%	13.6%	3.6%	8.2%	1.8%	40.9%
+1.00 to +2.00	n/N	0/110	2/110	5/110	3/110	2/110	12/110
	%	0.0%	1.8%	4.5%	2.7%	1.8%	10.9%
TOTAL	n/N	24/110	37/110	25/110	17/110	7/110	110/110
	%	21.8%	33.6%	22.7%	15.5%	6.4%	100.0%

D= Diopter

4. Key Effectiveness Outcomes

a) Summary Stratified by Visit and by Diopter

The key effectiveness outcomes for UCVA and accuracy of MRSE and manifest cylinder are shown by visit in Table 6. These parameters at 3 and 6 months are also shown stratified by preoperative cycloplegic cylinder in Table 7 and by preoperative cycloplegic refraction spherical equivalent (CRSE) in Table 8.

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 of intended in at least 50% of eyes and within 1.00D in 75% of eyes at all postoperative intervals.

Table 6. Summary of Key Effectiveness Parameters Over Time

Effectiveness Parameters		1 Month	3 Months	6 Months	9 Months
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N	68/94	60/94	67/94	64/92
	%	72.3%	63.8%	71.3%	69.6%
	CI	(62.2, 81.1)	(53.3, 73.5)	(61.0, 80.1)	(59.1, 78.7)
UCVA 20/20 or better	n/N	70/110	62/110	70/110	66/108
	%	63.6%	56.4%	63.6%	61.1%
	CI	(53.9, 72.6)	(46.6, 65.8)	(53.9, 72.6)	(51.3, 70.3)
UCVA 20/25 or better	n/N	95/110	89/110	96/110	91/108
	%	86.4%	80.9%	87.3%	84.3%
	CI	(78.5, 92.2)	(72.3, 87.8)	(79.6, 92.9)	(76.0, 90.6)
UCVA 20/40 or better	n/N	106/110	105/110	108/110	101/108
	%	96.4%	95.5%	98.2%	93.5%
	CI	(91.0, 99.0)	(89.7, 98.5)	(93.6, 99.8)	(87.1, 97.4)
MRSE ± 0.50D of intended	n/N	79/110	78/110	84/110	81/108
	%	71.8%	70.9%	76.4%	75.0%
	CI	(62.4, 80.0)	(61.5, 79.2)	(67.3, 83.9)	(65.7, 82.8)
MRSE ± 1.00D of intended	n/N	104/110	102/110	100/110	96/108
	%	94.5%	92.7%	90.9%	88.9%
	CI	(88.5, 98.0)	(86.2, 96.8)	(83.9, 95.6)	(81.4, 94.1)
MRSE ± 2.00D of intended	n/N	109/110	109/110	110/110	108/108
	%	99.1%	99.1%	100.0%	100.0%
	CI	(95.0, 100.0)	(95.0, 100.0)	(96.7, 100.0)	(96.6, 100.0)
Cylinder magnitude ≤ 0.50D of intended	n/N	71/110	73/110	71/110	66/108
	%	64.5%	66.4%	64.5%	61.1%
	CI	(54.9, 73.4)	(56.7, 75.1)	(54.9, 73.4)	(51.3, 70.3)
Cylinder magnitude ≤ 1.00D of intended	n/N	96/110	100/110	98/110	95/108
	%	87.3%	90.9%	89.1%	88.0%
	CI	(79.6, 92.9)	(83.9, 95.6)	(81.7, 94.2)	(80.3, 93.4)
Cylinder magnitude ≤ 2.00D of intended	n/N	108/110	109/110	109/110	107/108
	%	98.2%	99.1%	99.1%	99.1%
	CI	(93.6, 99.8)	(95.0, 100.0)	(95.0, 100.0)	(94.9, 100.0)

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

Table 7. Summary of Key Effectiveness Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Cylinder

3 MONTHS							
Effectiveness Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	16/22 72.7%	20/36 55.6%	18/23 78.3%	5/9 55.6%	1/4 25.0%	60/94 63.8%
UCVA 20/20 or better	n/N %	16/24 66.7%	21/37 56.8%	18/25 72.0%	6/17 35.3%	1/7 14.3%	62/110 56.4%
UCVA 20/25 or better	n/N %	24/24 100.0%	28/37 75.7%	23/25 92.0%	12/17 70.6%	2/7 28.6%	89/110 80.9%
UCVA 20/40 or better	n/N %	24/24 100.0%	33/37 89.2%	25/25 100.0%	17/17 100.0%	6/7 85.7%	105/110 95.5%
MRSE ± 0.50D of intended	n/N %	23/24 95.8%	25/37 67.6%	17/25 68.0%	9/17 52.9%	4/7 57.1%	78/110 70.9%
MRSE ± 1.00D of intended	n/N %	24/24 100.0%	35/37 94.6%	23/25 92.0%	14/17 82.4%	6/7 85.7%	102/110 92.7%
MRSE ± 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	16/17 94.1%	7/7 100.0%	109/110 99.1%
Cylinder magnitude ≤ 0.50D of intended	n/N %	20/24 83.3%	25/37 67.6%	14/25 56.0%	13/17 76.5%	1/7 14.3%	73/110 66.4%
Cylinder magnitude ≤ 1.00D of intended	n/N %	24/24 100.0%	36/37 97.3%	23/25 92.0%	14/17 82.4%	3/7 42.9%	100/110 90.9%
Cylinder magnitude ≤ 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	17/17 100.0%	6/7 85.7%	109/110 99.1%
6 MONTHS							
Effectiveness Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	21/22 95.5%	19/36 52.8%	20/23 87.0%	7/9 77.8%	0/4 0.0%	67/94 71.3%
UCVA 20/20 or better	n/N %	21/24 87.5%	20/37 54.1%	20/25 80.0%	9/17 52.9%	0/7 0.0%	70/110 63.6%
UCVA 20/25 or better	n/N %	24/24 100.0%	29/37 78.4%	25/25 100.0%	14/17 82.4%	4/7 57.1%	96/110 87.3%
UCVA 20/40 or better	n/N %	24/24 100.0%	35/37 94.6%	25/25 100.0%	17/17 100.0%	7/7 100.0%	108/110 98.2%
MRSE ± 0.50D of intended	n/N %	24/24 100.0%	28/37 75.7%	18/25 72.0%	10/17 58.8%	4/7 57.1%	84/110 76.4%
MRSE ± 1.00D of intended	n/N %	24/24 100.0%	34/37 91.9%	22/25 88.0%	14/17 82.4%	6/7 85.7%	100/110 90.9%
MRSE ± 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	17/17 100.0%	7/7 100.0%	110/110 100.0%
Cylinder magnitude ≤ 0.50D of intended	n/N %	19/24 79.2%	24/37 64.9%	15/25 60.0%	11/17 64.7%	2/7 28.6%	71/110 64.5%
Cylinder magnitude ≤ 1.00D of intended	n/N %	23/24 95.8%	35/37 94.6%	24/25 96.0%	14/17 82.4%	2/7 28.6%	98/110 89.1%
Cylinder magnitude ≤ 2.00D of intended	n/N %	24/24 100.0%	37/37 100.0%	25/25 100.0%	17/17 100.0%	6/7 85.7%	109/110 99.1%

UCVA = Uncorrected Visual Acuity
BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent
D = Diopter

Table 8. Summary of Key Effectiveness Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

3 MONTHS						
Effectiveness Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	5/6 83.3%	24/41 58.5%	24/36 66.7%	7/11 63.6%	60/94 63.8%
UCVA 20/20 or better	n/N %	5/8 62.5%	24/45 53.3%	26/45 57.8%	7/12 58.3%	62/110 56.4%
UCVA 20/25 or better	n/N %	7/8 87.5%	39/45 86.7%	34/45 75.6%	9/12 75.0%	89/110 80.9%
UCVA 20/40 or better	n/N %	8/8 100.0%	43/45 95.6%	43/45 95.6%	11/12 91.7%	105/110 95.5%
MRSE ± 0.50D of intended	n/N %	7/8 87.5%	35/45 77.8%	27/45 60.0%	9/12 75.0%	78/110 70.9%
MRSE ± 1.00D of intended	n/N %	8/8 100.0%	42/45 93.3%	41/45 91.1%	11/12 91.7%	102/110 92.7%
MRSE ± 2.00D of intended	n/N %	8/8 100.0%	45/45 100.0%	44/45 97.8%	12/12 100.0%	109/110 99.1%
Cylinder magnitude ≤ 0.50D of intended	n/N %	4/8 50.0%	30/45 66.7%	32/45 71.1%	7/12 58.3%	73/110 66.4%
Cylinder magnitude ≤ 1.00D of intended	n/N %	8/8 100.0%	40/45 88.9%	42/45 93.3%	10/12 83.3%	100/110 90.9%
Cylinder magnitude ≤ 2.00D of intended	n/N %	8/8 100.0%	44/45 97.8%	45/45 100.0%	12/12 100.0%	109/110 99.1%
6 MONTHS						
Effectiveness Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
UCVA 20/20 or better if Preop BSCVA 20/20 or better	n/N %	5/6 83.3%	29/41 70.7%	27/36 75.0%	6/11 54.5%	67/94 71.3%
UCVA 20/20 or better	n/N %	6/8 75.0%	29/45 64.4%	29/45 64.4%	6/12 50.0%	70/110 63.6%
UCVA 20/25 or better	n/N %	8/8 100.0%	41/45 91.1%	36/45 80.0%	11/12 91.7%	96/110 87.3%
UCVA 20/40 or better	n/N %	8/8 100.0%	44/45 97.8%	45/45 100.0%	11/12 91.7%	108/110 98.2%
MRSE ± 0.50D of intended	n/N %	7/8 87.5%	34/45 75.6%	34/45 75.6%	9/12 75.0%	84/110 76.4%
MRSE ± 1.00D of intended	n/N %	8/8 100.0%	42/45 93.3%	39/45 86.7%	11/12 91.7%	100/110 90.9%
MRSE ± 2.00D of intended	n/N %	8/8 100.0%	45/45 100.0%	45/45 100.0%	12/12 100.0%	110/110 100.0%
Cylinder magnitude ≤ 0.50D of intended	n/N %	4/8 50.0%	27/45 60.0%	33/45 73.3%	7/12 58.3%	71/110 64.5%
Cylinder magnitude ≤ 1.00D of intended	n/N %	8/8 100.0%	39/45 86.7%	42/45 93.3%	9/12 75.0%	98/110 89.1%
Cylinder magnitude ≤ 2.00D of intended	n/N %	8/8 100.0%	44/45 97.8%	45/45 100.0%	12/12 100.0%	109/110 99.1%

UCVA = Uncorrected Visual Acuity
BSCVA = Best Spectacle Corrected Visual Acuity
MRSE = Manifest Refraction Spherical Equivalent
D = Diopter

b) Uncorrected Visual Acuity

Uncorrected visual acuity is displayed in Table 9. Preoperatively, 35.5% of eyes had a UCVA of 20/40 or better. At 3 months, the UCVA was 20/20 or better in 56.4% of eyes, 20/25 or better in 80.9% and 20/40 or better in 95.5%. At 6 months, the UCVA was 20/20 or better in 63.6% of eyes, 20/25 or better in 87.3% and 20/40 or better in 98.2%. For those eyes with a preoperative BSCVA of 20/20 or better, a UCVA of 20/20 or better was achieved in 63.8% and 71.3% of eyes at 3 and 6 months, respectively.

Table 9. Cumulative Uncorrected Visual Acuity at Distance

		PREOP	1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
20/10	n/N	0/110	1/110	2/110	3/110	3/108
	%	0.0%	0.9%	1.8%	2.7%	2.8%
20/12.5 or better	n/N	0/110	8/110	11/110	11/110	9/108
	%	0.0%	7.3%	10.0%	10.0%	8.3%
20/16 or better	n/N	0/110	33/110	33/110	39/110	40/108
	%	0.0%	30.0%	30.0%	35.5%	37.0%
20/20 or better	n/N	1/110	70/110	62/110	70/110	66/108
	%	0.9%	63.6%	56.4%	63.6%	61.1%
20/25 or better	n/N	4/110	95/110	89/110	96/110	91/108
	%	3.6%	86.4%	80.9%	87.3%	84.3%
20/32 or better	n/N	17/110	104/110	98/110	104/110	99/108
	%	15.5%	94.5%	89.1%	94.5%	91.7%
20/40 or better	n/N	39/110	106/110	105/110	108/110	101/108
	%	35.5%	96.4%	95.5%	98.2%	93.5%
20/50 or better	n/N	53/110	109/110	110/110	109/110	107/108
	%	48.2%	99.1%	100.0%	99.1%	99.1%
20/63 or better	n/N	68/110	110/110	110/110	110/110	107/108
	%	61.8%	100.0%	100.0%	100.0%	99.1%
20/80 or better	n/N	84/110	110/110	110/110	110/110	108/108
	%	76.4%	100.0%	100.0%	100.0%	100.0%
20/100 or better	n/N	98/110	110/110	110/110	110/110	108/108
	%	89.1%	100.0%	100.0%	100.0%	100.0%
Worse than 20/100	n/N	12/110	0/110	0/110	0/110	0/108
	%	10.9%	0.0%	0.0%	0.0%	0.0%

c) Comparison of Postoperative Uncorrected Visual Acuity and Preoperative Best Spectacle Corrected Visual Acuity

A comparison of **postoperative** UCVA to **preoperative** BSCVA after CustomCornea® LASIK surgery is presented in Table 10 with differences based on lines of visual acuity. A postoperative UCVA equal to or better than the preoperative BSCVA was achieved in 56.4% and 60.0% of eyes at 3 and 6 months, respectively.

Table 10. 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	0/110	0/110	2/110	2/108
	%	0.0%	0.0%	1.8%	1.9%
UCVA **1 Line Better** Than Preop BSCVA	n/N	13/110	18/110	19/110	20/108
	%	11.8%	16.4%	17.3%	18.5%
UCVA **Equal*** to Preop BSCVA	n/N	53/110	44/110	45/110	43/108
	%	48.2%	40.0%	40.9%	39.8%
UCVA **1 Line Worse** Than Preop BSCVA	n/N	26/110	21/110	29/110	21/108
	%	23.6%	19.1%	26.4%	19.4%
UCVA **2 Lines Worse** Than Preop BSCVA	n/N	9/110	13/110	7/110	11/108
	%	8.2%	11.8%	6.4%	10.2%
UCVA **>2 Lines Worse** Than Preop BSCVA	n/N	9/110	14/110	8/110	11/108
	%	8.2%	12.7%	7.3%	10.2%

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

d) Accuracy of Manifest Refraction Spherical Equivalent

As shown in Table 11, accuracy of MRSE was within 0.50D of emmetropia in 70.9% of eyes, within 1.00D in 92.7% and within 2.00D in 99.1% at 3 months. At 6 months, the MRSE was within 0.50D of emmetropia in 76.4% of eyes, within 1.00D in 90.9% and within 2.00D in 100%. Of the eyes that did not achieve an MRSE within 1.00D of emmetropia, 5.5% at 3 months and 7.3% at 6 months had more than +1.00D of hyperopia, whereas 1.8% at 3 and 6 months had more than -1.00D of myopia. One eye (0.9%) had more than +2.00D of hyperopia by MRSE at 3 months.

Table 11. Accuracy of Manifest Refraction Spherical Equivalent

		1 Month	3 Months	6 Months	9 Months
± 0.50D	n/N %	79/110 71.8%	78/110 70.9%	84/110 76.4%	81/108 75.0%
± 1.00D	n/N %	104/110 94.5%	102/110 92.7%	100/110 90.9%	96/108 88.9%
± 2.00D	n/N %	109/110 99.1%	109/110 99.1%	110/110 100.0%	108/108 100.0%
> ± 2.00D	n/N %	1/110 0.9%	1/110 0.9%	0/110 0.0%	0/108 0.0%
Postop Hyperopic MRSE > +1.00D	n/N %	5/110 4.5%	6/110 5.5%	8/110 7.3%	9/108 8.3%
Postop Hyperopic MRSE > +2.00D	n/N %	1/110 0.9%	1/110 0.9%	0/110 0.0%	0/108 0.0%
Postop Myopic MRSE < -1.00D	n/N %	1/110 0.9%	2/110 1.8%	2/110 1.8%	3/108 2.8%
Postop Myopic MRSE < -2.00D	n/N %	0/110 0.0%	0/110 0.0%	0/110 0.0%	0/108 0.0%

MRSE = Manifest Refraction Spherical Equivalent D = Diopter

e) Accuracy of Manifest Refraction by Meridian

Accuracy of manifest refraction is displayed for the preoperative hyperopic meridian in Table 12 and for the preoperative myopic meridian in Table 13. Slight undercorrection along the preoperative hyperopic meridian was observed based on a mean correction error of +0.15D ± 0.69D at 3 months and +0.20D ± 0.63D at 6 months. Along the preoperative myopic meridian, slight undercorrection was observed based on a mean correction error of -0.09D ± 0.67D at 3 months and -0.07D ± 0.61D at 6 months.

Table 12. Accuracy of Manifest Refraction in Preoperative *Hyperopic* Meridian

Correction Error		1 Month	3 Months	6 Months	9 Months
Mean ± SD (D)		+0.07 ± 0.68	+0.15 ± 0.69	+0.20 ± 0.63	+0.17 ± 0.63
0.00 ± 0.50D	n/N	79/110	74/110	77/110	73/108
	%	71.8%	67.3%	70.0%	67.6%
Undercorrected (Postoperative Hyperopia)					
> 0.50 to 1.00D	n/N	10/110	18/110	16/110	15/108
	%	9.1%	16.4%	14.5%	13.9%
> 1.00 to 2.00D	n/N	4/110	7/110	8/110	7/108
	%	3.6%	6.4%	7.3%	6.5%
> 2.00D	n/N	2/110	2/110	2/110	2/108
	%	1.8%	1.8%	1.8%	1.9%
Overcorrected (Postoperative Myopia)					
> 0.50 to 1.00D	n/N	10/110	5/110	5/110	10/108
	%	9.1%	4.5%	4.5%	9.3%
> 1.00 to 2.00D	n/N	5/110	4/110	2/110	1/108
	%	4.5%	3.6%	1.8%	0.9%
> 2.00D	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%

Table 13. Accuracy of Manifest Refraction in Preoperative *Myopic* Meridian

Correction Error		1 Month	3 Months	6 Months	9 Months
Mean ± SD (D)		-0.12 ± 0.64	-0.09 ± 0.67	-0.07 ± 0.61	-0.13 ± 0.66
0.00 ± 0.50D	n/N	73/110	67/110	71/110	66/108
	%	66.4%	60.9%	64.5%	61.1%
Undercorrected (Postoperative Myopia)					
> 0.50 to 1.00D	n/N	17/110	20/110	17/110	19/108
	%	15.5%	18.2%	15.5%	17.6%
> 1.00 to 2.00D	n/N	6/110	5/110	5/110	6/108
	%	5.5%	4.5%	4.5%	5.6%
> 2.00D	n/N	1/110	0/110	0/110	0/108
	%	0.9%	0.0%	0.0%	0.0%
Overcorrected (Postoperative Hyperopia)					
> 0.50 to 1.00D	n/N	9/110	11/110	8/110	10/108
	%	8.2%	10.0%	7.3%	9.3%
> 1.00 to 2.00D	n/N	4/110	7/110	9/110	7/108
	%	3.6%	6.4%	8.2%	6.5%
> 2.00D	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%

SD = Standard Deviation D = Diopter

f) Accuracy of Manifest Refraction Sphere and Cylinder Magnitude

Table 14 displays the accuracy of manifest sphere and cylinder magnitude. Postoperative manifest sphere was within 0.50D of emmetropia in 71.3% of eyes, within 1.00D in 87.0% and within 2.00D in 98.1% at 3 months. Manifest sphere was within 0.50D of emmetropia in 70.4% of eyes, within 1.00D in 88.0% and within 2.00D in 98.1% at 6 months.

Postoperative manifest cylinder magnitude was ≤ 0.50D of emmetropia in 66.4% of eyes, ≤ 1.00D in 90.9% and ≤ 2.00D in 99.1% at 3 months. Cylinder magnitude was ≤ 0.50D in 64.5% of eyes, ≤ 1.00D in 89.1% and ≤ 2.00D in 99.1% at 6 months.

Table 14. Accuracy of Manifest Sphere and Cylinder Magnitude

Sphere*		1 Month (N=108)	3 Months (N=108)	6 Months (N=108)	9 Months (N=106)
Postop Mean ± SD (D)		+0.27 ± 0.65	+0.31 ± 0.68	+0.35 ± 0.62	+0.33 ± 0.64
Attempted Mean ± SD (D)		+1.20 ± 0.88	+1.20 ± 0.88	+1.20 ± 0.88	+1.19 ± 0.89
Achieved Mean ± SD (D)		+0.92 ± 0.98	+0.89 ± 1.03	+0.85 ± 1.00	+0.87 ± 1.04
% Achieved		69 ± 85	64 ± 79	61 ± 85	60 ± 91
± 0.50D	n/N	81/108	77/108	76/108	77/106
	%	75.0%	71.3%	70.4%	72.6%
± 1.00D	n/N	99/108	94/108	95/108	94/106
	%	91.7%	87.0%	88.0%	88.7%
± 2.00D	n/N	106/108	106/108	106/108	104/106
	%	98.1%	98.1%	98.1%	98.1%
Cylinder		**1 Month (N=110)**	**3 Months (N=110)**	**6 Months (N=110)**	**9 Months (N=108)**
Postop Mean ± SD (D)		-0.58 ± 0.55	-0.53 ± 0.53	-0.55 ± 0.47	-0.59 ± 0.46
Attempted Mean ± SD (D)		-2.89 ± 1.21	-2.89 ± 1.21	-2.89 ± 1.21	-2.90 ± 1.21
Achieved Mean ± SD (D)		-2.30 ± 1.12	-2.36 ± 1.12	-2.34 ± 1.15	-2.31 ± 1.17
% Achieved		78 ± 20	81 ± 18	79 ± 18	77 ± 20
≤ 0.50D	n/N	71/110	73/110	71/110	66/108
	%	64.5%	66.4%	64.5%	61.1%
≤ 1.00D	n/N	96/110	100/110	98/110	95/108
	%	87.3%	90.9%	89.1%	88.0%
≤ 2.00D	n/N	108/110	109/110	109/110	107/108
	%	98.2%	99.1%	99.1%	99.1%

* Excludes two eyes with a preoperative manifest sphere of 0D.

g) Effectiveness of Astigmatism Correction

Effectiveness of astigmatism correction at 3 and 6 months was evaluated based on the percentage reduction in cylinder magnitude and by vector analysis (Table 15). The mean percentage reduction in absolute manifest cylinder was 80.6% at 3 months and 79.1% at 6 months with an overall trend for a greater percentage reduction in eyes with higher preoperative cylinder. The mean correction ratio based on vector analysis of manifest cylinder was 0.92 at 3 months and 0.91 at 6 months.

Table 15. Effectiveness of Astigmatic Correction By Manifest Cylinder

3 MONTHS			
Preoperative Cylinder	**N**	**Mean Percentage Reduction in Cylinder Magnitude**	**Vector Analysis Mean ± SD Correction Ratio**
All	110	80.6%	0.92 ± 0.18
1.00 to < 2.00D	26	75.9%	0.86 ± 0.21
2.00 to < 3.00D	34	79.9%	0.94 ± 0.17
3.00 to < 4.00D	26	84.1%	0.93 ± 0.14
4.00 to < 5.00D	16	87.1%	1.01 ± 0.12
5.00 to 6.00D	8	74.4%	0.83 ± 0.24
6 MONTHS			
Preoperative Cylinder	**N**	**Mean Percentage Reduction in Cylinder Magnitude**	**Vector Analysis Mean ± SD Correction Ratio**
All	110	79.1%	0.91 ± 0.17
1.00 to < 2.00D	26	72.3%	0.84 ± 0.20
2.00 to < 3.00D	34	77.3%	0.92 ± 0.17
3.00 to < 4.00D	26	83.9%	0.93 ± 0.16
4.00 to < 5.00D	16	87.0%	0.98 ± 0.12
5.00 to 6.00D	8	78.0%	0.86 ± 0.20

SD = Standard Deviation D = Diopter

Correction Ratio is the ratio of achieved vs. intended vector magnitude

h) Refraction Over Time

Table 16 presents the manifest and cycloplegic phoropter refraction over time and the wavefront refraction from the wavefront measurement under cycloplegic conditions.

The mean manifest spherical equivalent was +0.03D ± 0.62D at 3 months and +0.06D ± 0.57D at 6 months. The mean cycloplegic and wavefront spherical equivalents were similar over time. As expected under cycloplegic conditions, the cycloplegic and wavefront spherical equivalents reflected more hyperopia that was within 0.50D of the manifest spherical equivalent preoperatively and postoperatively.

The mean manifest cylinder was -0.53D ± 0.53D at 3 months and -0.55D ± 0.47D at 6 months. The mean cycloplegic cylinder was similar to the manifest cylinder over time. The mean wavefront cylinder was within 0.25D of the manifest and cycloplegic refractions postoperatively.

Table 16. Mean Refraction Over Time

Mean ± Standard Deviation	PREOP	1 MONTH	3 MONTHS	6 MONTHS	9 MONTHS
Manifest Refraction (D)	N=110	N=110	N=110	N=110	N=108
Spherical Equivalent	-0.27 ± 0.67	-0.03 ± 0.59	0.03 ± 0.62	0.06 ± 0.57	0.02 ± 0.59
Cylinder	-2.89 ± 1.21	-0.58 ± 0.55	-0.53 ± 0.53	-0.55 ± 0.47	-0.59 ± 0.46
Cycloplegic Refraction (D)*	N=110	--	N=110	N=108	--
Spherical Equivalent	0.06 ± 0.65	--	0.49 ± 0.56	0.44 ± 0.56	--
Cylinder	-2.90 ± 1.20	--	-0.49 ± 0.51	-0.52 ± 0.49	--
Wavefront Refraction (D)**	N=110	N=103	N=100	N=103	N=100
Spherical Equivalent	0.04 ± 0.71	0.35 ± 0.45	0.44 ± 0.46	0.31 ± 0.46	0.39 ± 0.52
Cylinder	-2.91 ± 1.25	-0.71 ± 0.49	-0.69 ± 0.47	-0.65 ± 0.35	-0.74 ± 0.52

Refractions at the spectacle plane D = Diopter

* Cycloplegic refraction not required at 1 month and 9 months

** Wavefront measurement under cycloplegic conditions with refraction analyzed over 3.5mm diameter

5. Stability of Manifest Refraction

Refractive stability was analyzed as paired differences in the non-vector manifest cylinder magnitude between consecutive visits (Table 17). Eyes with data available at each postoperative interval were evaluated in a 6-month consistent cohort of 110 eyes and a 9-month cohort of 108 eyes.

Cylinder stability was achieved between 1 and 3 months with 100% of eyes demonstrating ≤ 1.00D magnitude change and a mean change of -0.05D ± 0.29D at a rate of -0.03D change per month for the 6-month consistent cohort. Cylinder stability was confirmed between 3 and 6 months with 100% of eyes demonstrating ≤ 1.00D magnitude change and a decrease in the mean change over time to 0.02D ± 0.24D at a rate of 0.01D change per month. The 95% confidence interval of the mean change in cylinder magnitude overlapped between postoperative intervals with a narrow range (≤ 0.11D) between the upper and lower limits.

The 9-month consistent cohort supported the overall trends in cylinder stability observed among the 6-month cohort. Between all consecutive postoperative intervals, at least 99.1% of eyes showed ≤ 1.00D of cylinder magnitude change. The mean change in cylinder magnitude was 0.05D ± 0.25D between 6 and 9 months at a rate of 0.02D change per month.

Table 17. Stability of Manifest Cylinder Magnitude

6-Month Cohort (N=110)	**Change in Cylinder Magnitude Between**	**1 and 3 Months**	**3 and 6 Months**	
	≤ 1.00D n/N	110/110	110/110	
	≤ 1.00D %	100.0%	100.0%	
	Mean Change* ± Standard Deviation	-0.05 ± 0.29	0.02 ± 0.24	
	95% Confidence Interval of Mean Change	(-0.11, 0.00)	(-0.03, 0.06)	
	Mean Change* per Month	-0.03	0.01	
9-Month Cohort (N=108)	**Change in Cylinder Magnitude Between**	**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D n/N	108/108	108/108	107/108
	≤ 1.00D %	100.0%	100.0%	99.1%
	Mean Change* ± Standard Deviation	-0.05 ± 0.29	0.01 ± 0.23	0.05 ± 0.25
	95% Confidence Interval of Mean Change	(-0.11, 0.00)	(-0.03, 0.05)	(0.00, 0.10)
	Mean Change* per Month	-0.03	0.003	0.02

D = Diopter

* Positive value reflects an increase in magnitude and a negative value reflects a decrease in magnitude between visits.

Similarly, refractive stability was analyzed as paired differences in MRSE between consecutive visits for the 6-month and 9-month consistent cohorts of eyes with data available at each postoperative interval (Table 18).

Stability of MRSE was achieved between 1 and 3 months with 100% of eyes demonstrating a change in MRSE ≤ 1.00D and a mean change of 0.06D ± 0.29D at a rate of 0.03D change per month for the 6-month consistent cohort. Stability was confirmed between 3 and 6 months with 100% of eyes demonstrating a change in MRSE ≤ 1.00D and a decrease in the mean change over time to 0.03D ± 0.25D at a rate of 0.01D change per month. The 95% confidence interval of the mean change in MRSE overlapped between postoperative intervals with a narrow range (≤ 0.11D) between the upper and lower limits.

The 9-month consistent cohort showed similar MRSE stability trends to the 6-month cohort. All eyes demonstrated a change in MRSE ≤ 1.00D between postoperative visits. Between 6 and 9 months, the mean MRSE change was -0.04D ± 0.26D at a rate of -0.01D change per month.

Table 18. Stability of Manifest Refraction Spherical Equivalent

6-Month Cohort (N=110)	**Change in MRSE Between**	**1 and 3 Months**	**3 and 6 Months**	
	≤ 1.00D n/N	110/110	110/110	
	≤ 1.00D %	100.0%	100.0%	
	Mean Change ± Standard Deviation	0.06 ± 0.29	0.03 ± 0.25	
	95% Confidence Interval of Mean Change	(0.00, 0.11)	(-0.01, 0.08)	
	Mean Change per Month	0.03	0.01	
9-Month Cohort (N=108)	**Change in MRSE Between**	**1 and 3 Months**	**3 and 6 Months**	**6 and 9 Months**
	≤ 1.00D n/N	108/108	108/108	108/108
	≤ 1.00D %	100.0%	100.0%	100.0%
	Mean Change ± Standard Deviation	0.06 ± 0.29	0.03 ± 0.25	-0.04 ± 0.26
	95% Confidence Interval of Mean Change	(0.00, 0.11)	(-0.02, 0.07)	(-0.09, 0.01)
	Mean Change per Month	0.03	0.01	-0.01

D = Diopter

6. Wavefront Outcomes

Table 19 displays the mean change from preoperative in total root mean square (RMS) wavefront error and in higher-order aberrations through 6th-order. The mean change in total RMS wavefront error decreased by 64.1% at 3 months and 67.2% at 6 months from preoperative. Higher-order aberrations were not significantly changed from preoperative on average with an increase of 2.3% at 3 months and 2.2% at 6 months. Spherical aberration decreased in magnitude at 3 and 6 months from preoperative with a mean directional shift from positive spherical aberration preoperatively (0.233μm) towards slightly negative spherical aberration at 3 months (- 0.003μm) and 6 months (-0.007μm).

Table 19. Mean Change in Aberrations Up to 6th-Order From Preoperative*

	3 MONTHS (N=100)		6 MONTHS (N=103)	
Aberration	**Mean Change (μm)**	**Mean Change (%)**	**Mean Change (μm)**	**Mean Change (%)**
Total RMS Error	-1.905	-64.1	-1.998	-67.2
Higher-Order	0.010	2.3	0.010	2.2
Coma	0.030	12.5	0.034	13.9
Trefoil	0.008	4.0	0.005	2.7
Spherical Aberration Magnitude †	-0.114	-48.4	-0.101	-42.8
Spherical Aberration Value ‡	-0.236	-101.2	-0.240	-102.9
Secondary Astigmatism	0.073	92.8	0.066	84.3
Tetrafoil	0.023	30.4	0.027	35.3
Combined 5th and 6th Order	0.037	49.5	0.035	46.6

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Positive change represents increase from preop; Negative change represents decrease from preop

† Based on absolute spherical aberration magnitude ‡ Based on signed spherical aberration value

At 3 and 6 months, 100% of eyes had a reduction in total RMS error from preoperative. A reduction in higher-order aberrations from preoperative was observed in 55.0% of eyes at 3 months and 54.4% at 6 months (Table 20).

Table 20. Percentage of Eyes with Reduced Aberrations Up to 6th-Order From Preoperative

	3 MONTHS (N=100)	6 MONTHS (N=103)
Aberration	**% Eyes with Reduction in Aberrations**	
Total RMS Error	100.0%	100.0%
Higher-Order	55.0%	54.4%
Coma	48.0%	49.5%
Trefoil	49.0%	45.6%
Spherical Aberration Magnitude †	80.0%	78.6%
Secondary Astigmatism	18.0%	17.5%
Tetrafoil	32.0%	32.0%
Combined 5th and 6th Order	18.0%	17.5%

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 correction of mixed astigmatism using phoropter refraction for eyes treated under the same study protocol over the same preoperative cycloplegic refractive range of -1.00D to -3.50D cylinder. Wavefront aberrations at 3 and 6 months were analyzed up to 4th-order for the Comparison Cohort (Table 21).

Compared to Conventional eyes, CustomCornea® eyes showed:

- statistically significantly lower mean amplitudes of total RMS error, higher-order aberrations, trefoil, spherical aberration magnitude, secondary astigmatism and tetrafoil at 3 and 6 months postoperatively (t-test with unequal variance; $p<0.05$).
- greater mean decrease in total RMS error from preoperative at 3 and 6 months.
- a mean decrease in higher-order aberrations from preoperative compared to a mean increase for Conventional eyes at 3 and 6 months.

Spherical aberration value for the CustomCornea® eyes was positive preoperatively (0.235µm) and at 3 months (0.041µm) and 6 months (0.029µm). Similarly for the Conventional eyes, spherical aberration value was positive preoperatively (0.176µm) and at 3 months (0.099µm) and 6 months (0.112µm).

Table 21. Mean Change in Aberrations Up to 4th-Order from Preoperative*: CustomCornea® vs. Conventional Comparison Cohort

3 MONTHS					
Aberration	**CustomCornea® (N=74)**		**Conventional (N=26)**		**p-Value §**
	µm	**%**	**µm**	**%**	
Total RMS Error	-1.509	-62.2	-0.990	-39.8	**<0.0001**
Higher-Order	-0.060	-13.7	0.199	51.3	**<0.0001**
Coma	-0.008	-3.3	0.108	55.7	0.1542
Trefoil	-0.021	-11.1	0.167	91.6	**<0.0001**
Spherical Aberration Magnitude †	-0.132	-56.0	-0.016	-8.9	**0.0167**
Spherical Aberration Value ‡	-0.195	-82.8	-0.076	-43.4	0.1332
Secondary Astigmatism	0.046	62.3	0.086	98.8	**0.0142**
Tetrafoil	0.021	30.3	0.048	51.9	**0.0029**
6 MONTHS					
Aberration	**CustomCornea® (N=81)**		**Conventional (N=25)**		**p-Value §**
	µm	**%**	**µm**	**%**	
Total RMS Error	-1.534	-63.2	-0.985	-39.6	**<0.0001**
Higher-Order	-0.053	-12.0	0.232	59.8	**<0.0001**
Coma	-0.010	-3.9	0.135	69.5	0.0905
Trefoil	-0.014	-7.7	0.160	88.1	**0.0001**
Spherical Aberration Magnitude †	-0.120	-51.1	-0.008	-4.6	**0.0224**
Spherical Aberration Value ‡	-0.206	-87.5	-0.064	-36.4	**0.0421**
Secondary Astigmatism	0.047	63.4	0.091	104.3	**0.0272**
Tetrafoil	0.027	38.3	0.066	72.3	**0.0004**

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

* Positive change represents increase from preop; Negative change represents decrease from preop

† Based on absolute spherical aberration magnitude ‡ Based on signed spherical aberration value

§ t-test with unequal variance for postoperative comparison between treatment types; $p<0.05$ statistically significant, shown in bold

A vision simulation program was used to model the effect of mean higher-order aberration magnitudes at 3 months after wavefront-guided CustomCornea® LASIK versus Conventional LASIK. The CustomCornea® cohort is restricted to those eyes over a comparable preoperative cylinder range to all Conventional mixed astigmatic eyes treated in the study (-1.00D to -3.50D). The difference in image blurring is comparable to a defocus error difference of approximately 0.11D (i.e., 0.10D for the CustomCornea® simulation and 0.21D for the Conventional simulation).

The following charts (Figure 1) 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 1. Simulated chart images for the average higher-order aberrations at 3 months after wavefront-guided surgery compared to after conventional surgery, based on wavefront over a 6 mm diameter pupil.

After CustomCornea®LASIK **After Conventional LASIK**

As shown in Table 22, more eyes had a reduction in higher-order aberrations after CustomCornea® LASIK compared to after Conventional LASIK at 3 months (66.2% vs. 7.7%) and 6 months (61.7% vs. 8.0%).

Table 22. Percentage of Eyes with Reduced Aberrations Up to 4th Order from Preoperative: CustomCornea® vs. Conventional Comparison Cohort

	3 MONTHS		6 MONTHS	
Aberration	**CustomCornea®** (N = 74)	**Conventional** (N = 26)	**CustomCornea®** (N = 81)	**Conventional** (N = 25)
Total RMS Error	100.0%	92.3%	100.0%	96.0%
Higher-Order	66.2%	7.7%	61.7%	8.0%
Coma	55.4%	19.2%	55.6%	28.0%
Trefoil	55.4%	7.7%	51.9%	20.0%
Spherical Aberration Magnitude †	86.5%	57.7%	85.2%	52.0%
Secondary Astigmatism	21.6%	19.2%	19.8%	16.0%
Tetrafoil	32.4%	23.1%	30.9%	20.0%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

† Reduction in absolute spherical aberration magnitude

7. Key Safety Outcomes

a) Summary Stratified by Visit and by Diopter

The key safety outcomes are presented by visit in Table 23. These parameters at 3 and 6 months are also shown stratified by preoperative cycloplegic cylinder in Table 24 and by preoperative CRSE in Table 25.

No eyes had a loss of more than 2 lines of BSCVA and one eye (0.9%) had a loss of 2 lines at 1 month. All eyes had a BSCVA within 1 line of preoperative BSCVA at 3 months or later. Preoperative BSCVA was 20/25 or better for all eyes. Postoperative BSCVA was 20/32 or better at all postoperative intervals and 20/25 or better at 3 months or later.

The safety data meet the criteria established in the FDA Guidance Document of less than 5% of eyes with a loss of more than 2 lines of BSCVA, less than 1% having a BSCVA of worse than 20/40, and less than 5% having an increase in cylinder magnitude of more than 2D at all postoperative intervals.

Table 23. Summary of Key Safety Parameters Over Time

Safety Parameters		1 Month	3 Months	6 Months	9 Months
Loss of > 2 Lines BSCVA	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
Loss of 2 Lines BSCVA	n/N	1/110	0/110	0/110	0/108
	%	0.9%	0.0%	0.0%	0.0%
	CI	(0.0, 5.0)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
BSCVA worse than 20/40	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
Increase > 2D cylinder magnitude	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
	CI	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.3)	(0.0, 3.4)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N	1/94	0/94	0/94	0/92
	%	1.1%	0.0%	0.0%	0.0%
	CI	(0.0, 5.8)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 3.9)

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

Table 24. Summary of Key Safety Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Cylinder

3 MONTHS							
Safety Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/22 0.0%	0/36 0.0%	0/23 0.0%	0/9 0.0%	0/4 0.0%	0/94 0.0%
6 MONTHS							
Safety Parameters		**-1.00 to -1.99**	**-2.00 to -2.99**	**-3.00 to -3.99**	**-4.00 to -4.99**	**-5.00 to -6.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/24 0.0%	0/37 0.0%	0/25 0.0%	0/17 0.0%	0/7 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/22 0.0%	0/36 0.0%	0/23 0.0%	0/9 0.0%	0/4 0.0%	0/94 0.0%

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

Table 25. Summary of Key Safety Parameters at 3 and 6 Months Stratified by Diopter (D) of Preoperative Cycloplegic Refraction Spherical Equivalent

3 MONTHS						
Safety Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/6 0.0%	0/41 0.0%	0/36 0.0%	0/11 0.0%	0/94 0.0%
6 MONTHS						
Safety Parameters		**-1.00 to -2.00**	**0.00 to -0.99**	**+0.01 to +0.99**	**+1.00 to +2.00**	**Total**
Loss of > 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Loss of 2 Lines BSCVA	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/40	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
Increase > 2D cylinder magnitude	n/N %	0/8 0.0%	0/45 0.0%	0/45 0.0%	0/12 0.0%	0/110 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N %	0/6 0.0%	0/41 0.0%	0/36 0.0%	0/11 0.0%	0/94 0.0%

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

b) Change in Best Spectacle Corrected Visual Acuity

Using a standard (high-contrast) visual acuity chart, BSCVA was measured under dim room illumination (10-12 cd/m^2). At least 90.9% of eyes had a gain or no change in BSCVA from preoperative at all postoperative intervals (Table 26). A trend for postoperative BSCVA gain of 1 line was observed compared to a loss of 1 line at 3 months (39.1% vs. 6.4%) and at 6 months (38.2% vs. 3.6%). While a small percentage of eyes had a BSCVA gain of 2 lines at 3 months (0.9%) and at 6 months (3.6%), no eyes had a BSCVA loss of 2 lines at 3 months or later.

Table 26. Change in Best Spectacle Corrected Visual Acuity

		1 Month	3 Months	6 Months	9 Months
Decrease > 2 Lines	n/N	0/110	0/110	0/110	0/108
	%	0.0%	0.0%	0.0%	0.0%
Decrease 2 Lines	n/N	1/110	0/110	0/110	0/108
	%	0.9%	0.0%	0.0%	0.0%
Decrease 1 Line	n/N	9/110	7/110	4/110	6/108
	%	8.2%	6.4%	3.6%	5.6%
No change	n/N	68/110	59/110	60/110	51/108
	%	61.8%	53.6%	54.5%	47.2%
Increase 1 Line	n/N	29/110	43/110	42/110	48/108
	%	26.4%	39.1%	38.2%	44.4%
Increase 2 Lines	n/N	3/110	1/110	4/110	3/108
	%	2.7%	0.9%	3.6%	2.8%
Increase > 2 Lines	n/N	0/110	0/110	0/110	0/108
	%	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 (Table 27). Slightly more eyes had a gain than loss of 1 line of low contrast BSCVA at 3 months (30.6% vs. 17.6%) and at 6 months (33.6% vs. 19.1%). In addition, more eyes had a gain than loss of ≥ 2 lines of low contrast BSCVA at 3 months (7.4% vs. 4.6%) and 6 months (8.2% vs. 2.7%).

Table 27. Change in Low Contrast Best Spectacle Corrected Visual Acuity

		3 Months	6 Months
Decrease > 2 Lines	n/N	1/108	0/110
	%	0.9%	0.0%
Decrease 2 Lines	n/N	4/108	3/110
	%	3.7%	2.7%
Decrease 1 Line	n/N	19/108	21/110
	%	17.6%	19.1%
No change	n/N	43/108	40/110
	%	39.8%	36.4%
Increase 1 Line	n/N	33/108	37/110
	%	30.6%	33.6%
Increase 2 Lines	n/N	7/108	8/110
	%	6.5%	7.3%
Increase > 2 Lines	n/N	1/108	1/110
	%	0.9%	0.9%

8. Change in Contrast Sensitivity

Contrast sensitivity was measured under both photopic and mesopic conditions using the CSV-1000 (VectorVision[9]). A clinically significant change from preoperative level was defined as > 2 levels (> 0.3 log units) at two or more spatial frequencies (Table 28).

The majority of eyes did not have a clinically significant change in contrast sensitivity from preoperative to postoperative. Of the eyes with a change in photopic contrast sensitivity, slightly fewer eyes showed a gain than loss at 3 months (2.7% vs. 6.4%) and an equal percentage of eyes (5.5%) had a gain or loss at 6 months. Under mesopic conditions, a trend for more eyes with a gain than loss of contrast sensitivity was observed at 3 months (22.4% vs. 11.2%) and at 6 months (26.2% vs. 10.3%).

In addition, a gain from preoperative was observed in the mean contrast sensitivity log at each spatial frequency under photopic and mesopic conditions at 3 and 6 months (Table 29). While no statistically significant change was observed at 3 months, statistically significant gains ($p<0.05$) were noted at 6 cycles per degree (cpd) under photopic conditions and for all spatial frequencies under mesopic conditions at 6 months.

Table 28. 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	7/110	6/110	12/107	11/107
	%	6.4%	5.5%	11.2%	10.3%
No Change	n/N	100/110	98/110	71/107	68/107
	%	90.9%	89.1%	66.4%	63.6%
Gain	n/N	3/110	6/110	24/107	28/107
	%	2.7%	5.5%	22.4%	26.2%

Table 29. Comparison of Mean Contrast Sensitivity Log by Spatial Frequency

Spatial Frequency (cpd)	Preop Mean ± SD	3-Month Mean ± SD	p-value†	6-Month Mean ± SD	p-value†
Photopic	(N=110)	(N=110)		(N=110)	
3	1.73 ± 0.15	1.75 ± 0.19	0.156	1.75 ± 0.17	0.115
6	1.92 ± 0.19	1.94 ± 0.25	0.204	1.96 ± 0.22	***0.018***
12	1.56 ± 0.25	1.56 ± 0.28	0.986	1.57 ± 0.31	0.748
18	1.09 ± 0.26	1.08 ± 0.31	0.764	1.08 ± 0.32	0.892
Mesopic*	(N=107)	(N=107)		(N=107)	
3	1.51 ± 0.23	1.55 ± 0.26	0.134	1.56 ± 0.24	***0.036***
6	1.48 ± 0.25	1.52 ± 0.28	0.238	1.56 ± 0.27	***0.009***
12	0.91 ± 0.32	0.98 ± 0.31	0.086	1.00 ± 0.33	***0.048***
18	0.41 ± 0.34	0.42 ± 0.36	0.749	0.50 ± 0.36	***0.016***

*Mesopic illumination with neutral density filters in front of eyes

† 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

9. Patient Questionnaire

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 30. The symptoms reported as "worse" or "significantly worse" in >10% of eyes at 6 months were dryness, light sensitivity, blurring of vision, fluctuation of vision, glare, halos, and night driving difficulty.

Table 30. Postoperative Change in Subjective Symptoms without Correction vs. Preoperative*

3 MONTHS (N=110)					
Comfort Symptoms	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	0.0%	10.0%	86.4%	2.7%	0.9%
Dryness	3.6%	7.3%	47.3%	40.0%	1.8%
Excessive Tearing	1.8%	2.7%	95.5%	0.0%	0.0%
Gritty Feeling	3.6%	5.5%	83.6%	6.4%	0.9%
Headache	7.3%	17.3%	70.9%	4.5%	0.0%
Light Sensitivity	10.9%	7.3%	54.5%	27.3%	0.0%
Pain	4.5%	5.5%	81.8%	6.4%	1.8%
Redness	0.0%	11.8%	81.8%	4.5%	1.8%
Visual Symptoms					
Blurring of Vision	14.5%	17.3%	46.4%	20.0%	1.8%
Double Vision	11.8%	8.2%	71.8%	8.2%	0.0%
Fluctuation of Vision	5.5%	8.2%	62.7%	20.0%	3.6%
Glare	10.9%	10.0%	52.7%	26.4%	0.0%
Halos	8.2%	5.5%	59.1%	27.3%	0.0%
Night Driving Difficulty	21.8%	10.0%	48.2%	20.0%	0.0%
6 MONTHS (N=110)					
Comfort Symptoms	**Significantly Better**	**Better**	**No Change**	**Worse**	**Significantly Worse**
Burning	4.5%	9.1%	79.1%	6.4%	0.9%
Dryness	5.5%	6.4%	49.1%	36.4%	2.7%
Excessive Tearing	2.7%	4.5%	90.0%	2.7%	0.0%
Gritty Feeling	2.7%	5.5%	84.5%	6.4%	0.9%
Headache	9.1%	10.0%	76.4%	4.5%	0.0%
Light Sensitivity	10.9%	11.8%	54.5%	20.9%	1.8%
Pain	6.4%	4.5%	84.5%	4.5%	0.0%
Redness	3.6%	7.3%	81.8%	7.3%	0.0%
Visual Symptoms					
Blurring of Vision	13.6%	15.5%	49.1%	13.6%	8.2%
Double Vision	7.3%	12.7%	73.6%	4.5%	1.8%
Fluctuation of Vision	8.2%	10.0%	55.5%	21.8%	4.5%
Glare	10.0%	8.2%	68.2%	13.6%	0.0%
Halos	10.0%	3.6%	63.6%	19.1%	3.6%
Night Driving Difficulty	19.1%	19.1%	47.3%	10.9%	3.6%

* Based on the patients' comparison of symptom severity after surgery as better or worse compared to their recollection of symptom severity before surgery.

Compared to preoperative, uncorrected quality of vision at 6 months was reported as better or significantly better in 86.3% of eyes, same in 4.5% and worse or significantly worse in 9.1% (Table 31). Satisfaction with surgery at 6 months was reported as satisfied or extremely satisfied in 73.7% of eyes, unsure in 10.9%, and unsatisfied or extremely unsatisfied in 15.4% (Table 32). Frequency of wearing distance correction at 6 months was reported as never in 81.8% of eyes and at least some of the time in 18.2% with frequent or constant use in 11.8% (Table 33).

Table 31. Postoperative Quality of Vision without Correction vs. Preoperative*

	3 MONTHS (N=108)	6 MONTHS (N=110)
Significantly Better	54.6%	52.7%
Better	28.7%	33.6%
Same	7.4%	4.5%
Worse	7.4%	5.5%
Significantly Worse	1.9%	3.6%

* Based on the patients' comparison of quality of vision after surgery as better or worse compared to their recollection of quality of vision before surgery.

Table 32. Postoperative Satisfaction with Surgery

	3 MONTHS (N=108)	6 MONTHS (N=110)
Extremely Satisfied	47.2%	48.2%
Satisfied	26.9%	25.5%
Not Sure	15.7%	10.9%
Unsatisfied	6.5%	11.8%
Extremely Unsatisfied	3.7%	3.6%

Table 33. Postoperative Frequency of Distance Correction

	3 MONTHS (N=108)	6 MONTHS (N=110)
Never	85.2%	81.8%
Seldom	3.7%	6.4%
Frequently	1.9%	1.8%
Constantly	9.3%	10.0%

10. Retreatment

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

11. Statistical Analysis Outcomes

Statistical analysis was performed to assess for potential associations between demographic and baseline characteristics and clinical outcomes. Age, gender, race, preoperative cycloplegic cylinder, preoperative CRSE, operative room humidity and temperature were the characteristics considered to have the most potential for clinical relevance to the procedure. Outcomes evaluated at refractive stability (3 months) and at 6 months included: BSCVA loss of ≥ 2 lines; UCVA of 20/20 or better and 20/40 or better; and accuracy of MRSE, manifest sphere and manifest cylinder magnitude within 0.50D and 1.00D of emmetropia.

One-sided exact binomial tests (α=0.05) were used to support the observed overall rates of safety and effectiveness outcomes to the FDA Guidance Document targets. There was no BSCVA loss of ≥ 2 lines at 3 and 6 months, thereby meeting the FDA target rate of < 5% of eyes with BSCVA loss of > 2 lines for safety. FDA targets were met or exceeded for effectiveness outcomes overall, including UCVA 20/40 or better and accuracy of MRSE within 0.50D and within 1.00D of emmetropia. For each baseline subgroup, the observed rate either met the target or the 95% confidence interval (CI) contained the FDA target.

To assess the consistency of outcomes across characteristics, differences in rates among subgroups were assessed using the Cochran-Mantel-Haenszel (CMH) test. No statistical significance was observed among subgroups of preoperative CRSE for any outcome. Statistically significant ($p<0.05$) trends among subgroups are listed below by characteristic.

Among age subgroups by decade over a range of 20 to 60 years, higher rates were observed in younger patients as compared to older patients for the following outcomes:

- UCVA 20/20 or better at 3 months (p=0.0129). The observed rate was ≥ 60.0% for subgroups between 20 to 49 years vs. 33.3% for 50 to 60 years. At 6 months, no statistical significance remained among age subgroups for UCVA 20/20 or better.
- UCVA of 20/40 or better at 3 months (p=0.0020). The observed rate was 100% for subgroups between 20 to 49 years vs. 81.5% for 50 to 60 years, although the 95% CI contained the FDA target of 85%. At 6 months, no statistical significance by age remained and all age subgroups exceeded the FDA target for UCVA of 20/40 or better.
- MRSE within 0.50D at 3 and 6 months (p=0.0114 and p=0.0056). The observed rate was ≥ 76.2% at 3 and 6 months for subgroups between 20 to 49 years vs. 40.7% at 3 months and 51.9% at 6 months for 50 to 60 years with the FDA target of 50% included in the 95% CI. All age subgroups met or exceeded the FDA target for MRSE within 0.50D at 6 months.
- No statistical significance by age was observed for accuracy of MRSE within 1.00D and all age subgroups met or exceeded the FDA target for MRSE within 1.00D at 3 and 6 months. However, older patients, primarily between 40 and 60 years, were more likely to have a hyperopic MRSE of more than +1.00D at 3 and 6 months (p=0.0108 and p=0.0013). Younger patients were more likely to have a myopic MRSE of more than -1.00D at 3 and 6 months (p=0.0391), which was observed in two eyes of a 20 year-old patient.
- Manifest sphere within 0.50D at 3 and 6 months (p=0.0005 and p=0.0027). The observed rate was ≥ 71.4% for subgroups between 20 to 49 years vs. 37.0% for 50 to 60 years.
- Manifest sphere within 1.00D at 6 months (p=0.0005). The observed rate was ≥ 91.4% for subgroups between 20 to 49 years vs. 66.7% for 50 to 60 years. Older patients, primarily between 40 and 60 years, were more likely to have a hyperopic manifest sphere of more than +1.00D at 3 and 6 months (p=0.0042 and p=0.0005). Younger patients were more likely to have a myopic manifest sphere of more than -1.00D at 3 months (p=0.0391), which was observed in two eyes of a 20 year-old patient.

Preoperative astigmatism measured in subgroups by diopter of cycloplegic cylinder over a range from -1.00D to -6.00D. Eyes with lower preoperative astigmatism showed higher rates as compared to eyes with higher preoperative astigmatism for the following outcomes (observed rates at 3 and 6 months by preoperative cycloplegic cylinder are shown in Table 6):

- UCVA 20/20 or better at 3 and 6 months (p=0.0404 and p=0.0060). All preoperative cylinder subgroups met or exceeded the FDA target for UCVA of 20/40 or better at 3 and 6 months.
- MRSE within 0.50D at 3 and 6 months (p=0.0038 and p=0.0011). All preoperative cylinder subgroups met or exceeded the FDA target for MRSE within 0.50D at 3 and 6 months.
- MRSE within 1.00D at 3 and 6 months (p=0.0304 and p=0.0433). All preoperative cylinder subgroups met or exceeded the FDA target for MRSE within 1.00D at 3 and 6 months.
- Manifest sphere within 1.00D at 3 months (p=0.0082). No statistical significance based on preoperative cylinder remained for manifest sphere at 6 months. In addition, eyes with higher preoperative astigmatism were more likely to have a hyperopic manifest sphere of more than +1.00D at 3 months compared to eyes with lower preoperative astigmatism (p=0.0412).
- Manifest cylinder magnitude ≤ 0.50D at 3 months (p=0.0227).
- Manifest cylinder magnitude ≤ 1.00D at 3 and 6 months (p=0.0002 and p=0.0012).

Race was analyzed in two subgroups, 94.5% Caucasians and 5.5% other races, including Hispanic (3.6%) and Indian (1.8%). Note that apparent associations by race should be interpreted with caution because of the small sample size of six eyes in the other races subgroup. Caucasians had higher rates than other races for the following outcomes:

- MRSE within 0.50D at 3 months (p=0.0380). The observed rate was 73.1% for Caucasians vs. two of six eyes (33.3%) in the other races subgroup, although the 95% CI contained the FDA target of 50%. At 6 months, no statistically significant difference remained by race for MRSE within 0.50D. Both subgroups met or exceeded the FDA target for MRSE within 0.50D at 6 months and for MRSE within 1.00D at 3 and 6 months.
- Manifest sphere within 0.50D at 6 months (p=0.0380). The observed rate was 73.1% for Caucasians vs. two of six eyes (33.3%) in the other races subgroup.
- Manifest cylinder magnitude ≤ 1.00D at 3 months (p=0.0345). The observed rate was 92.3% for Caucasians vs. four of six eyes (66.7%) in the other races subgroup. At 6 months, no statistically significant difference based on race remained for manifest cylinder outcomes.

Room temperature, room humidity and gender each had one statistically significant association with postoperative manifest sphere or manifest cylinder magnitude, as follows:

- Eyes treated in a room with a lower temperature between 65.0°F and 69.9°F showed higher rates than eyes treated in a room between 70.0°F and 74.9°F for manifest sphere within 1.00D at 3 months (97.0% vs. 83.1%; p=0.0467).
- Eyes treated in a lower room humidity showed higher rates as compared to eyes treated in higher room humidity for manifest cylinder magnitude ≤ 1.00D at 6 months (p=0.0450). The observed rate was ≥ 81.3% for room humidity subgroups between 18% to 59% vs. 0.0% for the two eyes of one patient treated in a room humidity of 63%.
- Females showed higher rates as compared to males for manifest cylinder magnitude ≤1.00D at 3 months (96.6% vs. 84.3%; p=0.0260) and at 6 months (96.6% vs. 80.4%; p=0.0068).

12. Comparative Analysis by Defocus Type

To optimize the CustomCornea® wavefront-guided LASIK treatment of mixed astigmatism, eyes were categorized as myopic or hyperopic based on the preoperative wavefront defocus error. Myopic or hyperopic components of the algorithm were used as determined by the preoperative wavefront defocus. The study included 85 eyes with a myopic defocus and 25 eyes with a hyperopic defocus based on the preoperative wavefront.

Clinical outcomes at 3 and 6 months for each preoperative wavefront defocus type were compared to established target rates for refractive surgery. In addition, outcomes were compared between myopic and hyperopic defocus types. Outcomes evaluated at refractive stability (3 months) and at 6 months included: BSCVA loss of $\geq$ 2 lines; UCVA of 20/20 or better and 20/40 or better; and accuracy of MRSE, manifest sphere and manifest cylinder magnitude within 0.50D and 1.00D of emmetropia. Postoperative outcomes of myopia or hyperopia of more than 1.00D by MRSE and manifest sphere were also evaluated.

One-sided exact binomial tests (α=0.05) were used to compare the observed overall rates of eyes meeting safety and effectiveness criteria to the FDA Guidance Document target rates. There was no BSCVA loss of $\geq$ 2 lines at 3 and 6 months for both subgroups, thereby meeting the FDA target rate of < 5% of eyes with BSCVA loss of > 2 lines for safety. Both defocus types of mixed astigmatic eyes exceeded FDA targets overall for effectiveness including for UCVA of 20/40 or better and accuracy of MRSE within 0.50D and 1.00D of emmetropia at 3 and 6 months.

To compare clinical outcomes of mixed astigmatic eyes by preoperative defocus type, the Cochran-Mantel-Haenszel (CMH) test was used to assess for differences. A p-value < 0.05 would indicate a statistically significant difference in outcomes between defocus types. Myopic and hyperopic defocus groups had outcomes that were not significantly different. Tables 34 and 35 display the comparative analysis by defocus type at 3 and 6 months.

Table 34. Comparative Analysis of Mixed Astigmatic Eyes by Defocus Type at 3 Months

Criteria	CMH P-Value*		Myopic Defocus	Hyperopic Defocus	Total	FDA Target P-Value**
Key Effectiveness Parameters						
UCVA 20/20 or better	0.6183	n/N % CI	49/85 57.6% (46.4, 68.3)	13/25 52.0% (31.3, 72.2)	62/110 56.4% (46.6, 65.8)	--
UCVA 20/40 or better	0.2166	n/N % CI	80/85 94.1% (86.8, 98.1)	25/25 100.0% (86.3, 100.0)	105/110 95.5% (89.7, 98.5)	≥ 85% 0.9999
MRSE ± 0.50D	0.7169	n/N % CI	61/85 71.8% (61.0, 81.0)	17/25 68.0% (46.5, 85.1)	78/110 70.9% (61.5, 79.2)	≥ 50% 1.0000
MRSE ± 1.00D	0.8740	n/N % CI	79/85 92.9% (85.3, 97.4)	23/25 92.0% (74.0, 99.0)	102/110 92.7% (86.2, 96.8)	≥ 75% 1.0000
Accuracy of Manifest Sphere and Cylinder						
Manifest Sphere ± 0.50D	0.0417	n/N % CI	57/85 67.1% (56.0, 76.9)	22/25 88.0% (68.8, 97.5)	79/110 71.8% (62.4, 80.0)	--
Manifest Sphere ± 1.00D	0.9017	n/N % CI	74/85 87.1% (78.0, 93.4)	22/25 88.0% (68.8, 97.5)	96/110 87.3% (79.6, 92.9)	--
Manifest Cylinder Magnitude ≤ 0.50D	0.4994	n/N % CI	55/85 64.7% (53.6, 74.8)	18/25 72.0% (50.6, 87.9)	73/110 66.4% (56.7, 75.1)	--
Manifest Cylinder Magnitude ≤ 1.00D	0.1736	n/N % CI	79/85 92.9% (85.3, 97.4)	21/25 84.0% (63.9, 95.5)	100/110 90.9% (83.9, 95.6)	--
Postoperative Manifest Spherical Equivalent and Manifest Sphere						
Postoperative MRSE > +1.00D (Hyperopic)	0.1738	n/N % CI	6/85 7.1% (2.6, 14.7)	0/25 0.0% (0.0, 13.7)	6/110 5.5% (2.0, 11.5)	--
Postoperative MRSE < -1.00D (Myopic)	0.0088	n/N % CI	0/85 0.0% (0.0, 4.2)	2/25 8.0% (1.0, 26.0)	2/110 1.8% (0.2, 6.4)	--
Postoperative Manifest Sphere > +1.00D (Hyperopic)	0.2095	n/N % CI	11/85 12.9% (6.6, 22.0)	1/25 4.0% (0.1, 20.4)	12/110 10.9% (5.8, 18.3)	--
Postoperative Manifest Sphere < -1.00D (Myopic)	0.0088	n/N % CI	0/85 0.0% (0.0, 4.2)	2/25 8.0% (1.0, 26.0)	2/110 1.8% (0.2, 6.4)	--

* Cochran-Mantel-Haenszel (CMH) Test with rank scores

** One-sided exact binomial test comparison to the FDA target

CI = 95% Confidence Interval

p < 0.05 is statistically significant

UCVA = Uncorrected Visual Acuity

MRSE = Manifest Refraction Spherical Equivalent

D = Diopter

BSCVA = Best Spectacle Corrected Visual Acuity

Table 35. Comparative Analysis of Mixed Astigmatic Eyes by Defocus Type at 6 Months

Criteria	CMH P-Value*		Myopic Defocus	Hyperopic Defocus	Total	FDA Target P-Value**
Key Effectiveness Parameters						
UCVA 20/20 or better	0.3687	n/N % CI	56/85 65.9% (54.8, 75.8)	14/25 56.0% (34.9, 75.6)	70/110 63.6% (53.9, 72.6)	--
UCVA 20/40 or better	0.4410	n/N % CI	83/85 97.6% (91.8, 99.7)	25/25 100.0% (86.3, 100.0)	108/110 98.2% (93.6, 99.8)	≥ 85% 1.0000
MRSE ± 0.50D	0.6279	n/N % CI	64/85 75.3% (64.7, 84.0)	20/25 80.0% (59.3, 93.2)	84/110 76.4% (67.3, 83.9)	≥ 50% 1.0000
MRSE ± 1.00D	0.8299	n/N % CI	77/85 90.6% (82.3, 95.8)	23/25 92.0% (74.0, 99.0)	100/110 90.9% (83.9, 95.6)	≥ 75% 1.0000
Accuracy of Manifest Sphere and Cylinder						
Manifest Sphere ± 0.50D	0.5257	n/N % CI	59/85 69.4% (58.5, 79.0)	19/25 76.0% (54.9, 90.6)	78/110 70.9% (61.5, 79.2)	--
Manifest Sphere ± 1.00D	0.1703	n/N % CI	73/85 85.9% (76.6, 92.5)	24/25 96.0% (79.6, 99.9)	97/110 88.2% (80.6, 93.6)	--
Manifest Cylinder Magnitude ≤ 0.50D	0.9485	n/N % CI	55/85 64.7% (53.6, 74.8)	16/25 64.0% (42.5, 82.0)	71/110 64.5% (54.9, 73.4)	--
Manifest Cylinder Magnitude ≤ 1.00D	0.0987	n/N % CI	78/85 91.8% (83.8, 96.6)	20/25 80.0% (59.3, 93.2)	98/110 89.1% (81.7, 94.2)	--
Postoperative Manifest Spherical Equivalent and Manifest Sphere						
Postoperative MRSE > +1.00D (Hyperopic)	0.1128	n/N % CI	8/85 9.4% (4.2, 17.7)	0/25 0.0% (0.0, 13.7)	8/110 7.3% (3.2, 13.8)	--
Postoperative MRSE < -1.00D (Myopic)	0.0088	n/N % CI	0/85 0.0% (0.0, 4.2)	2/25 8.0% (1.0, 26.0)	2/110 1.8% (0.2, 6.4)	--
Postoperative Manifest Sphere > +1.00D (Hyperopic)	0.1703	n/N % CI	12/85 14.1% (7.5 , 23.4)	1/25 4.0% (0.1, 20.4)	13/110 11.8% (6.4, 19.4)	--
Postoperative Manifest Sphere < -1.00D (Myopic)	NA	n/N % CI	0/85 0.0% (0.0, 4.2)	0/25 0.0% (0.0, 13.7)	0/110 0.0% (0.0, 3.3)	--

* Cochran-Mantel-Haenszel (CMH) Test with rank scores NA = Not Applicable

** One-sided exact binomial test comparison to the FDA target

CI = 95% Confidence Interval $p < 0.05$ is statistically significant

UCVA = Uncorrected Visual Acuity MRSE = Manifest Refraction Spherical Equivalent

D = Diopter BSCVA = Best Spectacle Corrected Visual Acuity

Alcon®

LADAR6000™
EXCIMER LASER

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

PATIENT INFORMATION BOOKLET

For Mixed Astigmatism of 1.00D to less than 5.00D cycloplegic cylinder magnitude

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.

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REVISION CONTROL SHEET

Revision	Description	Date
A	DCN 10064 – original release	

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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 J) 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.

Mixed astigmatism is a condition that causes blurred distant and near vision because the eye is both *nearsighted* and *farsighted*. If you have mixed astigmatism, you may have difficulty seeing clearly at distance and near. Glasses, contact lenses, or eye surgery can correct mixed astigmatism to help you see more clearly.

Laser Assisted In-Situ Keratomileusis (LASIK) is a type of eye surgery available to correct mixed astigmatism. 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.

LASIK surgery can help you see more clearly by changing the shape of the *cornea*, the clear front surface of your eye. LASIK surgery uses an *excimer laser* to remove tissue to reshape the cornea. 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 mixed 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 mixed 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*".

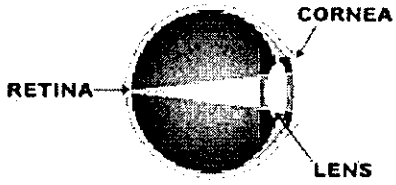
Your doctor can use either your eyeglass prescription or a wavefront measurement to plan LASIK surgery. LASIK surgery based on the eyeglass prescription is called *Conventional LASIK*. LASIK surgery based on the wavefront is called wavefront-guided LASIK. *CustomCornea® LASIK* is wavefront-guided surgery with the LADAR*6000*™ Excimer Laser System or the LADARVision®4000 System. The LADARVision®4000 System and LADAR*6000*™ System have comparable functions. Clinical studies done with the LADARVision®4000 System are applicable to the LADAR*6000*™ System.

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 Mixed 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

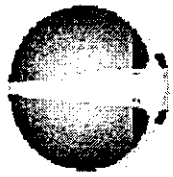


A NORMAL EYE

Light focuses on the retina.
Vision is clear.

Astigmatism is a focusing error that results in blurred distant and near vision. The cornea is more curved in some directions than others causing light to focus at different points from the retina. Vision is blurred because light does not focus correctly on the retina. When light focuses at a point in front of the retina, the eye is nearsighted. When light focuses at a point behind the retina, the eye is farsighted. An eye with mixed astigmatism is both nearsighted and farsighted. Diagram 2 shows how light focusing at different points from the retina causes blurred vision in an eye with mixed astigmatism.

DIAGRAM 2: EYE WITH MIXED ASTIGMATISM

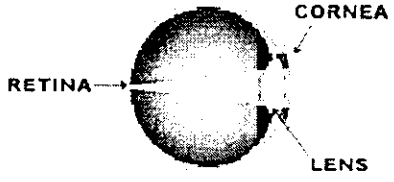


A MIXED ASTIGMATIC EYE

Light focuses in front of and 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 3 shows that distant vision is clearer after LASIK.

DIAGRAM 3: 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 LADAR*6000*™ System uses a very small laser beam to reshape the cornea. To correct for mixed 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 LADAR*6000*™ 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 between 1.00 to less than 5.00 *diopters (D)* of mixed astigmatism. If you have mixed 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 110 eyes to determine benefits and risks. The study results are shown below and in "Risks of CustomCornea® LASIK" (Section D).

Patient Demographics

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

Table 1. Demographics of 110 Eyes of 63 Study Patients

Age		Race		Gender		Contact Lens History	
Average: 40.6 ± 10.7 years		Caucasian	94.5%	Female	53.6%	None	64.5%
Range:	20 to 60 years	Hispanic	3.6%	Male	46.4%	Hard	2.7%
		Indian	1.8%			Soft	32.7%

Visual Acuity Measurement

Visual acuity is a measure of the sharpness of vision using a letter chart. Diagram 4 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 4: EXAMPLE OF VISUAL ACUITY CHART

Visual Acuity without Glasses

The clinical study evaluated visual acuity **without** glasses at a distance using a letter chart. Table 2 shows that at least 93.5% of patients treated for mixed 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

% of Eyes With:	Before Surgery (N=110)	1 Month (N=110)	3 Months (N=110)	6 Months (N=110)	9 Months (N=108)
20/20 or better*	1.1%	72.3%	63.8%	71.3%	69.6%
20/20 or better	0.9%	63.6%	56.4%	63.6%	61.1%
20/25 or better	3.6%	86.4%	80.9%	87.3%	84.3%
20/40 or better	35.5%	96.4%	95.5%	98.2%	93.5%

* if visual acuity was 20/20 or better with glasses or contact lenses before surgery (N=94 eyes at all visits up to 6 months; N=92 at 9 months). N is the number of eyes studied.

Visual Acuity without Glasses After Surgery and with Glasses Before Surgery

The clinical study compared visual acuity **without** glasses at a distance after surgery to visual acuity **with** glasses before surgery using a letter chart. Table 3 shows that 56.4% of patients at 3 months and 60.0% at 6 months, saw as well or better **without** glasses after CustomCornea® surgery as **with** glasses before surgery.

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

% of Eyes With:	1 Month (N=110)	3 Months (N=110)	6 Months (N=110)	9 Months (N=108)
2 lines better vision *without* glasses after LASIK than vision *with* glasses before surgery	0.0%	0.0%	1.8%	1.9%
1 line better vision *without* glasses after LASIK than vision *with* glasses before surgery	11.8%	16.4%	17.3%	18.5%
same vision* *without* glasses after LASIK as vision *with* glasses before surgery	48.2%	40.0%	40.9%	39.8%
1 line worse vision *without* glasses after LASIK than vision *with* glasses before surgery	23.6%	19.1%	26.4%	19.4%
2 lines worse vision *without* glasses after LASIK than vision *with* glasses before surgery	8.2%	11.8%	6.4%	10.2%
more than 2 lines worse vision *without* glasses after LASIK than vision *with* glasses before surgery	8.2%	12.7%	7.3%	10.2%

* **Same vision** is within 2 or 3 letters on the same line of a visual acuity chart. N is the number of eyes studied.

Patient Demographics and Surgery Outcomes

Patient demographics were related to the following surgery outcomes in the clinical study at **3 months after surgery**.

- A visual acuity of 20/20 or better without glasses or contact lenses after surgery was more likely in younger patients and patients with lower amounts of astigmatism before surgery. A visual acuity of 20/40 or better without glasses or contact lenses after surgery was more likely in younger patients.

- Reduction of farsightedness or nearsightedness to 0.50D or less after surgery was more likely in younger patients, Caucasian patients* and patients with lower amounts of astigmatism before surgery. Reduction of farsightedness or nearsightedness to 1.00D or less after surgery was more likely in patients with lower amounts of astigmatism before surgery.

- Reduction of astigmatism to 0.50D or less after surgery was more likely in patients with lower amounts of astigmatism before surgery. Reduction of astigmatism to 1.00D or less after surgery was more likely in females, Caucasian patients* and patients with lower amounts of astigmatism before surgery.

Patient demographics were related to the following surgery outcomes in the clinical study at **6 months after surgery**.

- A visual acuity of 20/20 or better without glasses or contact lenses after surgery was more likely in patients with lower amounts of astigmatism before surgery.

- Reduction of farsightedness or nearsightedness to 0.50D or less after surgery was more likely in younger patients, Caucasian patients* and patients with lower amounts of astigmatism before surgery. Reduction of farsightedness or nearsightedness to 1.00D or less after surgery was more likely in younger patients and patients with lower amounts of astigmatism before surgery.

- Reduction of astigmatism to 1.00D or less after surgery was more likely in females and patients with lower amounts of astigmatism before surgery.

Note that the clinical study included only 5.5% of patients of races other than Caucasian.

Patient Questionnaire

Patients in the clinical study were asked to rate the quality of vision after surgery compared to their recollection of quality of vision before surgery. Table 4 shows that compared to before surgery, quality of vision without glasses or contact lenses at 6 months after surgery was reported as better or significantly better in 86.3% of eyes, same in 4.5% and worse or significantly worse in 9.1%.

Table 4. Quality of Vision *without* Glasses or Contact Lenses After Surgery Compared to Before Surgery*		
	3 MONTHS N=108	6 MONTHS N=110
Significantly Better	54.6%	52.7%
Better	28.7%	33.6%
Same	7.4%	4.5%
Worse	7.4%	5.5%
Significantly Worse	1.9%	3.6%

N is the number of eyes studied.

* Based on the patients' comparison of quality of vision after surgery as better or worse compared to their recollection of quality of vision before surgery.

Table 5 shows that satisfaction with surgery at 6 months was reported as satisfied or extremely satisfied in 73.7% of eyes, unsure in 10.9%, and unsatisfied or extremely unsatisfied in 15.4%.

Table 5. Satisfaction with Surgery		
	3 MONTHS N=108	6 MONTHS N=110
Extremely Satisfied	47.2%	48.2%
Satisfied	26.9%	25.5%
Not Sure	15.7%	10.9%
Unsatisfied	6.5%	11.8%
Extremely Unsatisfied	3.7%	3.6%

N is the number of eyes studied.

Table 6 shows that frequency of wearing glasses or contact lenses for distance vision at 6 months was reported as never in 81.8% of eyes and at least some of the time in 18.2% with frequent or constant use in 11.8%.

Table 6. Frequency of Glasses or Contact Lens Wear for Distance After Surgery		
	3 MONTHS N=108	6 MONTHS N=110
Never	85.2%	81.8%
Seldom	3.7%	6.4%
Frequently	1.9%	1.8%
Constantly	9.3%	10.0%

N is the number of eyes studied.

D. 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** 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 mixed astigmatism. Eyes with unstable mixed astigmatism are unable to be measured correctly 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, LASIK surgery).
- 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 mixed astigmatism less than 1.00D or for 5.00D or greater. 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 3 months 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 for CustomCornea® LASIK, some people still needed glasses or contact lenses after surgery.

Astigmatism remained after surgery for some patients. After surgery, 9.1% of patients at 3 months and 10.9% of patients at 6 months had astigmatism of more than 1D and 0.9% of patients at 3 and 6 months had astigmatism of more than 2D.

Farsightedness remained after surgery for some patients. After surgery, 5.5% of patients at 3 months and 7.3% of patients at 6 months had more than 1D of farsightedness and 0.9% of patients at 3 months had more than 2D of farsightedness. Older patients, primarily between 40 and 60 years, were more likely to have more than 1D of farsightedness at 3 and 6 months. Patients with higher amounts of astigmatism before surgery were more likely to have 1D of farsightedness at 3 months after surgery.

Nearsightedness remained after surgery for some patients. At 3 and 6 months, 1.8% of patients had more than 1D of nearsightedness. Younger patients were more likely to have more than 1D of nearsightedness at 3 and 6 months, which was observed in both eyes of a 20 year-old patient.

Visual Acuity with Glasses

The clinical study evaluated visual acuity **with** glasses at a distance using a letter chart. Table 7 shows that all patients in the study saw 20/25 or better **with** glasses before surgery and at 3 months or later after surgery.

Table 7. Visual Acuity *with* Glasses (Best Vision)

% of Eyes With:	Before Surgery (N=110)	1 Month (N=110)	3 Months (N=110)	6 Months (N=110)	9 Months (N=108)
20/20 or better	85.5%	89.1%	89.1%	92.7%	93.5%
20/25 or better	100.0%	99.1%	100.0%	100.0%	100.0%
20/32 or better	100.0%	100.0%	100.0%	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 change in best vision **with** glasses after surgery was compared to vision **with** glasses before surgery 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 visual acuity testing is a way to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog. Table 8 compares the change in vision **with** glasses before surgery to 3 and 6 months after surgery.

Table 8. Change in Visual Acuity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Standard Chart		10% Low Contrast Chart	
	3 Months (N=110)	6 Months (N=110)	3 Months (N=108)	6 Months (N=110)
loss of more than 2 lines	0.0%	0.0%	0.9%	0.0%
loss of 2 lines	0.0%	0.0%	3.7%	2.7%
loss of 1 line	6.4%	3.6%	17.6%	19.1%
no change	53.6%	54.5%	39.8%	36.4%
gain of 1 line	39.1%	38.2%	30.6%	33.6%
gain of 2 lines	0.9%	3.6%	6.5%	7.3%
gain of more than 2 lines	0.0%	0.0%	0.9%	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 9 compares the change in contrast sensitivity **with** glasses before surgery to 3 and 6 months after surgery.

Table 9. Change in Contrast Sensitivity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Daylight Conditions		Dim Light Conditions	
	3 Months (N=110)	6 Months (N=110)	3 Months (N=107)	6 Months (N=107)
Loss	6.4%	5.5%	11.2%	10.3%
No change	90.9%	89.1%	66.4%	63.6%
Gain	2.7%	5.5%	22.4%	26.2%

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 10.

Table 10. Adverse Events and Complications	
Greater than or equal to 1% of eyes (N=110) **had:**	
Irritation on the front surface of the cornea at one month or later	10.0%
Cells growing under the corneal flap *	5.4%
Inflammation of the cornea under the corneal flap	4.5%
Problem with creation of the corneal flap *	1.8%
Pain at one month or later	1.8%
Less than 1% of eyes (N=110) **had:**	
Feeling of something in the eye at one month or later	0.9%
Viral infection in the cornea	0.9%

N is the number of eyes studied.

* One eye did not receive laser ablation after a problem with the creation of the corneal flap and was not included in the analysis of eyes receiving laser surgery (N=111).

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

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

Worse and Significantly Worse Symptoms After Surgery

Patients who were treated for mixed astigmatism in the clinical study rated the change in the following symptoms shown in Table 11 as worse or significantly worse after surgery **without** glasses or contact lenses compared to their recollection of symptoms before surgery. The symptoms reported as "worse" or "significantly worse" in >10% of eyes at 6 months were dryness, light sensitivity, blurring of vision, fluctuation of vision, glare, halos, and night driving difficulty.

Table 11. Worse or Significantly Worse Symptoms *without* Glasses After Surgery Compared to Before Surgery*

	3 Months (N=110)		**6 Months** (N=110)	
Comfort Symptoms	**Worse**	**Significantly Worse**	**Worse**	**Significantly Worse**
Burning	2.7%	0.9%	6.4%	0.9%
Dryness	40.0%	1.8%	36.4%	2.7%
Excessive Tearing	0.0%	0.0%	2.7%	0.0%
Gritty Feeling	6.4%	0.9%	6.4%	0.9%
Headache	4.5%	0.0%	4.5%	0.0%
Light Sensitivity	27.3%	0.0%	20.9%	1.8%
Pain	6.4%	1.8%	4.5%	0.0%
Redness	4.5%	1.8%	7.3%	0.0%
Visual Symptoms				
Blurring of Vision	20.0%	1.8%	13.6%	8.2%
Double Vision	8.2%	0.0%	4.5%	1.8%
Fluctuation of Vision	20.0%	3.6%	21.8%	4.5%
Glare	26.4%	0.0%	13.6%	0.0%
Halos §	27.3%	0.0%	19.1%	3.6%
Night Driving Difficulty	20.0%	0.0%	10.9%	3.6%

N is the number of eyes studied.

* Based on the patients' comparison of symptom severity after surgery as worse compared 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.

E. 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 mixed astigmatism of 1.00D to less than 5.00D.
- have stable mixed 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 mixed astigmatism.
- be willing to sign an Informed Consent Form, if provided by your doctor.

F. 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 LADAR*6000*™ 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.

G. Questions to Ask Your Doctor

You may want to ask the following questions to help you decide if CustomCornea® LASIK with the LADAR*6000*™ System is right for you:

- What are my other options to correct my mixed 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 mixed 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.

H. 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 LADAR*6000*™ 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.

I. 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 mixed 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 mixed astigmatism include glasses, contact lenses, and Conventional LASIK. Other surgical options that may be used to correct vision are ALK and RK.
- ALK, RK and LASIK surgery 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 D: Risks)
2. False (see Section F: Before the Surgery)
3. False (see Section F: The Day of Surgery)
4. True (see Section C: Benefits)
5. True (see Section D: Risks)
6. True (see Section D: Risks)
7. False (see Section D: Contraindications)
8. False (see Section D: Contraindications)
9. True (see Section D: Precautions)

J. 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 mixed 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 causing light to focus at different points from the retina. Vision is blurred because light does not focus correctly on the retina. Types of astigmatism include nearsighted, farsighted and mixed.

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.

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. LASIK surgery 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 LADAR*6000*™ System.

Diopter: a unit of focusing power, used to describe the amount of mixed astigmatism, farsightedness or nearsightedness in 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 focus light at a point behind the retina resulting in blurred images. Farsightedness is also called hyperopia.

Focusing Error: a condition in which the eye forms a blurred image on the retina. Examples are mixed astigmatism, farsightedness, nearsightedness 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.

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 can also 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.

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.

Mixed Astigmatism: a focusing error that results in blurred distant and near vision. An eye with mixed astigmatism is both nearsighted and farsighted. The cornea is more curved in some directions than others causing light to focus at different points in front of and behind the retina. Vision is blurred because light does not focus correctly on the retina.

Nearsightedness: a focusing error that results in blurred vision that is usually worse at distance than at near. The cornea and lens focus light at a point in front of the retina resulting in blurred images. Nearsightedness is also called myopia.

Ocular Hypertension: increased eye pressure.

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

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 mixed 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.

K. 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

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Orlando, FL 32826
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