

Alcon®

LADARVISION®4000

Excimer Laser System

PROFESSIONAL USE INFORMATION MANUAL FOR CustomCornea® LASER ASSISTED IN-SITU KERATOMILEUSIS (LASIK)

PHYSICIAN'S BOOKLET

For Myopia: up to -7D with less than -0.50D of Astigmatism

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

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

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

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

Tel: (877) 523-2784

Fax: (407) 384-1677

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

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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.

“NOTE:” - Identifies conditions or practices warranting special attention.

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. 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 relation 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 up to the 4th order.

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 right corneal location and cyclotorsional angle.

Data Export

The WMD has the ability to export the wavefront examination data as an electronic file to floppy disk 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.

Wavefront Measurement Devices Used in the Clinical Trial

There were two versions of the WMD used in the clinical trial, the CustomCornea® Measurement Device (Alcon) and the LADARWave™ CustomCornea® Wavefront System (Alcon). Both versions are accurately characterized by the description provided above.

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. The flap thickness created by the microkeratome should be at least 160µm.

Microkeratomes Used in the Clinical Trial:

The microkeratomes used in the clinical trial were the Hansatome¹ (manufactured by Bausch & Lomb), the Innovatome² (manufactured by Paradigm but previously owned by Innovative Optics) and the SKBM® microkeratome (manufactured by Alcon).

¹ Hansatome Reg. TM of Hansa Research & Development, Inc.

² Innovatome Reg. TM of Innovative Optics, Inc.

C. **LADARVision®4000 EXCIMER LASER SYSTEM**

The LADARVision®4000 excimer laser beam is of Gaussian profile and small in diameter (0.8mm) and corneal sculpting is achieved by delivering hundreds to thousands of excimer laser pulses to the eye in a complex pattern of spatially overlapping spots. Precise shaping of the cornea depends on accurate placement of the laser pulses. The LADARVision®4000 Excimer Laser System incorporates the LADARTracker® closed-loop laser radar eye-tracking system to track and compensate for patient eye motion, including saccadic movements, during procedures so that each excimer laser pulse is delivered to the appropriate location on the cornea.

Excimer Laser Characteristics

The ultraviolet laser used in the LADARVision®4000 Excimer Laser System is an argon fluoride excimer laser. This laser produces 10 nanosecond pulses of ultraviolet radiation at a wavelength of 193 nanometers. The laser repetition rate is between 50 and 60 pulses per second. The characteristics of the laser beam at the corneal treatment plane are shown below.

Treatment Plane Characteristics of the LADARVision®4000 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 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 LADARVision®4000 eye tracking system.

Energy monitoring/control

An energy monitor ensures that the laser pulse energy delivered to the eye will be calibrated and will be monitored during 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.

Eye tracking system

The LADARVision®4000 system utilizes the LADARTracker® active closed-loop laser radar 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 adjustable magnification is independent of the excimer beam path and the tracking system mirrors. Omni-directional illumination provides visible illumination of the treatment plane.

Fixation target

A visible fixation target at infinity focus from the patient’s perspective consists of a red light emitting diode (LED), a pinhole aperture, an edge-illuminated reticule, and a lens. 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. 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. This provides the operator/surgeon with an easy method of setting the height of the patient's eye during centration and surgery.

System Software

The LADARVision®4000 system software controlling the proprietary excimer laser runs on an Intel Pentium³-based personal computer under a Microsoft Windows⁴ 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.

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 LADARVision®4000 system Conventional 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 (aligned) to the anatomical geometry of the patient's eye while in an up-right position using the WMD. 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, an optical zone of 6.5mm is used with a blend zone of 1.25mm for a total ablation zone of 9mm.

³ Intel and Pentium are Reg TM of Intel Corporation

⁴ Microsoft and Windows are Reg TM of Microsoft Corporation
7260-0034 Rev B

Safety

The LADARVision®4000 Excimer System contains a Class IV laser that conforms with 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
- EN601-1-1-2
- EN601-2-22

NOTE: Additional details regarding operation of this laser can be found in the LADARVision®4000 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 myopia up to $-7.00D$ sphere with less than $-0.50D$ of astigmatism at the spectacle plane;
- in patients who are 21 years of age or older; and
- in patients with documented stability of refraction for the prior 12 months, as demonstrated by a change of less than or equal to $0.50D$.

B. CONTRAINDICATIONS

Wavefront-guided LASIK is contraindicated in:

- pregnant or nursing women.
- patients with signs of keratoconus.
- patients who are taking one or both of the following medications: isotretinoin (Accutane⁵); amiodarone hydrochloride (Cordarone⁶).
- patients with autoimmune, collagen vascular, or immunodeficiency diseases.

⁵ Accutane Reg TM of Hoffman-La Roche Inc.

⁶ Cordarone Reg TM of Sanofi

C. WARNINGS

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

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

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.

D. PRECAUTIONS

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

- with progressive myopia, ocular disease, corneal abnormality, previous corneal or intraocular surgery, or trauma in the ablation zone.
- with prior history of refractive surgery (for example, RK, PRK, LASIK).
- with a residual corneal thickness less than 250 microns at the completion of ablation (see the section on Operative Procedure).
- with a history of glaucoma.
- who are taking the medication Sumatriptin (Imitrex⁷).
- under 21 or over 65 years of age.
- over the long term (more than 6 months after surgery).
- for treatments greater than 7D of myopia combined with greater than or equal to -0.50D of astigmatism.
- for retreatment with wavefront-guided LASIK.

Pupil size should be evaluated under mesopic illumination conditions. Patients with large mesopic pupils ≥ 6.5 mm (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.

⁷ Imitrex Reg TM of Glaxo Group Limited

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.

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

There were not sufficient numbers of patients with a MRSE above $-6D$ to determine the level of effectiveness or the complication rates of CustomCornea® LASIK for this refractive error range with the same reliability as for eyes with lower refractive errors.

E. ADVERSE EVENTS AND COMPLICATIONS

Adverse events and complications reported in a clinical study of CustomCornea® LASIK for the correction of myopia and astigmatism with the LADARVision®4000 System are summarized in Table 1 below.

Table 1. Summary Of Adverse Events and Complications At Any Postoperative Visit		
ADVERSE EVENTS		
	%	(n/N)
Miscreated flap (related to microkeratome)	0.2%	(1/427)†
Recalcitrant Diffuse Lamellar Keratitis (DLK) with Blepharitis	0.5%	(2/426)*
Retinal horseshoe tear (unrelated to device)	0.2%	(1/426)
COMPLICATIONS		
Conjunctivitis	0.2%	(1/426)
Corneal edema 1 week to <1 month	1.9%	(8/426)
Diffuse Lamellar Keratitis (includes rule out DLK vs. debris)	3.5%	(15/426)
Double/ghost images	2.1%	(9/426)
Epithelial defect by microkeratome	0.2%	(1/426)
Epithelium in the interface	3.3%	(14/426)
Focal inflammatory reaction in interface	0.2%	(1/426)
Foreign body sensation at 1 month or later	0.5%	(2/426)
Pain at 1 month or later	0.2%	(1/426)
Striae	0.5%	(2/426)

* Includes both eyes of one patient

† One eye received conventional laser ablation three months after miscreated flap and was not included in primary cohort analysis.

In addition, there were two systemic adverse events that were unrelated to the device reported after the 3-month study visit including death of one patient due to colon cancer and the diagnosis of multiple sclerosis in another patient.

In the clinical study of CustomCornea® LASIK, patients were asked to rate the following symptoms at 3 and 6 months compared to before surgery for the correction of spherical myopia. Symptoms rated as worse or significantly worse than preoperative are shown in Table 2. The entire patient symptoms table showing all ratings from significantly better to significantly worse are displayed in Table 15 of Results (Section 4B7).

Table 2. Change in Subjective Symptoms From Preoperative				
3 MONTHS				
Symptom	Worse		Significantly Worse	
	%	n/N	%	n/N
Blurring of Vision	21.2%	(29/137)	1.5%	(2/137)
Burning	5.8%	(8/137)	0.7%	(1/137)
Double Vision	7.3%	(10/137)	0.7%	(1/137)
Dryness	21.5%	(29/135)	7.4%	(10/135)
Excessive Tearing	0.0%	(0/137)	0.0%	(0/137)
Fluctuation of Vision	24.1%	(33/137)	1.5%	(2/137)
Glare	16.8%	(23/137)	0.0%	(0/137)
Gritty Feeling	10.9%	(15/137)	0.7%	(1/137)
Halos	19.0%	(26/137)	0.7%	(1/137)
Headache	5.1%	(7/137)	0.0%	(0/137)
Light Sensitivity	7.3%	(10/137)	0.7%	(1/137)
Night Driving Difficulty	13.9%	(19/137)	3.6%	(5/137)
Pain	5.1%	(7/137)	0.0%	(0/137)
Redness	8.0%	(11/137)	0.0%	(0/137)
6 MONTHS				
Blurring of Vision	16.2%	(22/136)	2.9%	(4/136)
Burning	5.9%	(8/136)	1.5%	(2/136)
Double Vision	5.9%	(8/136)	0.7%	(1/136)
Dryness	20.6%	(28/136)	2.2%	(3/136)
Excessive Tearing	0.0%	(0/135)	0.0%	(0/135)
Fluctuation of Vision	16.9%	(23/136)	0.7%	(1/136)
Glare	14.7%	(20/136)	0.0%	(0/136)
Gritty Feeling	8.8%	(12/136)	1.5%	(2/136)
Halos	13.2%	(18/136)	0.0%	(0/136)
Headache	1.5%	(2/136)	0.0%	(0/136)
Light Sensitivity	4.4%	(6/136)	0.0%	(0/136)
Night Driving Difficulty	18.4%	(25/136)	0.7%	(1/136)
Pain	0.7%	(1/136)	0.0%	(0/136)
Redness	5.9%	(8/136)	0.0%	(0/136)

4. CLINICAL STUDY

A. INTRODUCTION

The study in the U.S. began as a prospective, randomized, unmasked, and multi-center trial, where one eye of the patient received CustomCornea® LASIK correction using data from a wavefront measurement system and the fellow eye received a Conventional treatment based on phoropter manifest refraction.

Upon providing data to support expansion of the number of patients for enrollment, the study design was changed to a prospective, non-randomized, unmasked, and multi-center trial with bilateral wavefront-guided CustomCornea® LASIK correction. Data from the U.S. study was pooled with data from a Canadian protocol, which was the same as the U.S. protocol in terms of the 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® myopic LASIK correction with the LADARVision®4000 Excimer Laser System.

Eligibility criteria for patients included: being at least 18 years of age; eyes with up to -15D myopia at the spectacle plane with astigmatism up to -6D; best spectacle corrected visual acuity (BSCVA) of 20/25 or better; and a stable manifest refraction as documented by a 0.50D change or less per year. The manifest refraction could not differ by more than 1.00D in sphere or cylinder from the attempted correction determined by the wavefront measurement system. In addition, the manifest and cycloplegic refraction measured at the preoperative examination must have been within 0.50D of each other in the sphere and cylinder components. All eyes were required to be treated for emmetropia (no monovision). Contact lens wearers had to abstain from contact lens use prior to baseline examination for 2 to 3 weeks.

Patients who exhibited any of the following conditions were excluded: previous intraocular, corneal or strabismus surgery; history of or active ocular disease; significant corneal scar within the ablation zone; corneal abnormality; progressive myopia; keratoconus; irregular corneal astigmatism; history of herpes keratitis; autoimmune or connective tissue disease; significant atopy; diabetes; use of immunosuppressive therapy; pregnant or nursing; use of ophthalmic medications; use of systemic medication with significant ocular side effects; severe dry eye syndrome unresolved by treatment; allergy to study medications; residual stromal thickness of less than 250 microns; glaucoma or glaucoma filtering surgery; inability to achieve a pupillary dilation of ≥ 7 mm risk of angle closure; or an inability to obtain a clear and complete wavefront image.

Patients were followed on Day 1, at 1 week, and at 1, 3, and 6 months postoperatively. The primary efficacy parameters for this study were improvement of uncorrected visual acuity (UCVA), predictability and stability of manifest refraction spherical equivalent (MRSE), and reduction of wavefront error, including higher-order aberrations. The primary safety parameters were preservation of BSCVA and incidence of complications and adverse events.

B. RESULTS

1. Demographics

The demographics of this study shown in Table 3 were very typical for a contemporary refractive surgery trial performed in the U.S. The study population was primarily Caucasians and no patients were over 65 years old.

Table 3. Demographics			
426 Eyes of 264 Enrolled Patients			
Age (In Years)		38.1 ± 8.4	
Average ± Standard Deviation		20 to 64	
Minimum to Maximum			
Race		Number	Percentage
	Asian	10	2.3%
	Black	1	0.2%
	Caucasian	411	96.5%
	Other*	4	0.9%
Gender			
	Female	184	43.2%
	Male	242	56.8%
Contact Lens History			
	None	97	22.8%
	PMMA	2	0.5%
	RGP	18	4.2%
	Soft	309	72.5%

*2 eyes (1 patient) Philippino; 2 eyes (1 patient) Guyanese.
 PMMA = Polymethyl methacrylate RGP = Rigid gas permeable

2. Preoperative Manifest Refraction Parameters

Table 4 contains the number of eyes stratified by the preoperative manifest refraction.

Table 4. Preoperative Manifest Refraction Stratified By Sphere & Cylinder						
SPHERE	CYLINDER					TOTAL
	0 to -0.49	-0.50 to -0.99	-1.0 to -1.99	-2.0 to -2.99	-3.0 to -4.0	
0.0 to -0.99	1/426 0.2%	2/426 0.5%	7/426 1.6%	4/426 0.9%	5/426 1.2%	19/426 4.5%
-1.0 to -1.99	23/426 5.4%	23/426 5.4%	24/426 5.6%	2/426 0.5%	4/426 0.9%	76/426 17.8%
-2.0 to -2.99	40/426 9.4%	22/426 5.2%	20/426 4.7%	2/426 0.5%	2/426 0.5%	86/426 20.2%
-3.0 to -3.99	31/426 7.3%	55/426 12.9%	24/426 5.6%	7/426 1.6%	0/426 0.0%	117/426 27.5%
-4.0 to -4.99	27/426 6.3%	34/426 8.0%	18/426 4.2%	5/426 1.2%	0/426 0.0%	84/426 19.7%
-5.0 to -5.99	13/426 3.1%	17/426 4.0%	5/426 1.2%	0/426 0.0%	0/426 0.0%	35/426 8.2%
-6.0 to -7.0	4/426 0.9%	2/426 0.5%	3/426 0.7%	0/426 0.0%	0/426 0.0%	9/426 2.1%
TOTAL	139/426 32.6%	155/426 36.4%	101/426 23.7%	20/426 4.7%	11/426 2.6%	426/426 100.0%

3. Safety and Efficacy Results

The primary cohort consisted of 426 eyes including 139 eyes with less than -0.50D of astigmatism and 287 eyes with -0.50D to -4D of astigmatism based on manifest refraction. The safety cohort consisted of all 426 eyes treated for myopia with up to -4D of astigmatism and the effectiveness cohort consisted of the 139 eyes treated for spherical myopia (less than -0.50D of astigmatism).

Preoperatively, 95.7% of eyes had an uncorrected visual acuity (UCVA) worse than 20/40. A postoperative UCVA of 20/40 or better was reported in $\geq 97.8\%$ of eyes at all visits (Table 5). The key safety and efficacy results at 3 and 6 months after surgery are stratified by diopter in Tables 6 and 7.

Table 5. Summary of Key Efficacy Variables Over Time				
Efficacy Variables (Efficacy Cohort: 139 Spherical Myopic Eyes)		1 MONTH	3 MONTHS	6 MONTHS
UCVA 20/20 or better	% (n/N) CI	86.3% (120/139) (79.5, 91.6)	80.6% (112/139) (73.0, 86.8)	79.9% (111/139) (72.2, 86.2)
UCVA 20/25 or better	% (n/N) CI	94.2% (131/139) (89.0, 97.5)	94.2% (131/139) (89.0, 97.5)	91.4% (127/139) (85.4, 95.5)
UCVA 20/40 or better	% (n/N) CI	99.3% (138/139) (96.1, 100.0)	97.8% (136/139) (93.8, 99.6)	98.6% (137/139) (94.9, 99.8)
MRSE ± 0.50 D of intended	% (n/N) CI	83.5% (116/139) (76.2, 89.2)	78.4% (109/139) (70.6, 84.9)	74.8% (104/139) (66.8, 81.8)
MRSE ± 1.00 D of intended	% (n/N) CI	97.1% (135/139) (92.8, 99.2)	95.0% (132/139) (89.9, 98.0)	95.7% (133/139) (90.8, 98.4)
Safety Variables (Safety Cohort: 426 Eyes)		1 MONTH	3 MONTHS	6 MONTHS
Loss of >2 Lines BSCVA	% (n/N) CI	0.5% (2/426) (0.1, 1.7)	0.2% (1/426) (0.0, 1.3)	0.0% (0/424) (0.0, 0.9)
Loss of 2 Lines BSCVA	% (n/N) CI	1.4% (6/426) (0.5, 3.0)	0.5% (2/426) (0.1, 1.7)	0.7% (3/424) (0.1, 2.1)
BSCVA worse than 20/40	% (n/N) CI	0.0% (0/426) (0.0, 0.9)	0.0% (0/426) (0.0, 0.9)	0.0% (0/424) (0.0, 0.9)
Increase >2D cylinder magnitude	% (n/N) CI	0.0% (0/426) (0.0, 0.9)	0.0% (0/426) (0.0, 0.9)	0/424 (0.0%) (0.0, 1.6)
BSCVA worse than 20/25 if 20/20 or better preoperatively	% (n/N) CI	0.2% (1/423) (0.0, 1.3)	0.0% (0/423) (0.0, 0.9)	0.2% (1/421) (0.0, 1.3)

BSCVA = Best spectacle corrected visual acuity
MRSE = Manifest refraction spherical equivalent

CI = 95% Confidence interval
UCVA = Uncorrected visual acuity

Table 6. Summary of Key Efficacy Variables at 3 Months Stratified by Diopter of Preoperative Manifest Refraction Spherical Equivalent

		0 to -0.99	-1 to -1.99	-2 to -2.99	-3 to -3.99	-4 to -4.99	-5 to -5.99	-6 to -7.00	Total
Efficacy Variables (Efficacy Cohort: 139 Spherical Myopic Eyes)									
UCVA 20/20 or better	n	1/1	21/23	32/40	23/31	24/27	8/13	3/4	112/139
	%	100.0%	91.3%	80.0%	74.2%	88.9%	61.5%	75.0%	80.6%
UCVA 20/25 or better	n	1/1	23/23	38/40	30/31	26/27	10/13	3/4	131/139
	%	100.0%	100.0%	95.0%	96.8%	96.3%	76.9%	75.0%	94.2%
UCVA 20/40 or better	n	1/1	23/23	40/40	31/31	27/27	11/13	3/4	136/139
	%	100.0%	100.0%	100.0%	100.0%	100.0%	84.6%	75.0%	97.8%
MRSE \pm 0.50D of intended	n	1/1	22/23	30/40	24/31	19/27	10/13	3/4	109/139
	%	100.0%	95.7%	75.0%	77.4%	70.4%	76.9%	75.0%	78.4%
MRSE \pm 1.00D of intended	n	1/1	23/23	38/40	30/31	26/27	11/13	3/4	132/139
	%	100.0%	100.0%	95.0%	96.8%	96.3%	84.6%	75.0%	95.0%
Safety Variables (Safety Cohort: 426 Eyes)									
Loss of >2 Lines BSCVA	n	0/2	0/60	0/95	1/103	0/97	0/58	0/11	1/426
	%	0.0%	0.0%	0.0%	1.0%	0.0%	0.0%	0.0%	0.2%
Loss of 2 Lines BSCVA	n	0/2	0/60	1/95	0/103	1/97	0/58	0/11	2/426
	%	0.0%	0.0%	1.1%	0.0%	1.0%	0.0%	0.0%	0.5%
BSCVA worse than 20/40	n	0/2	0/60	0/95	0/103	0/97	0/58	0/11	0/426
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Increase >2D cylinder magnitude	n	0/2	0/60	0/95	0/103	0/97	0/58	0/11	0/426
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n	0/2	0/60	0/95	0/102	0/97	0/56	0/11	0/423
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

BSCVA = Best Spectacle Corrected Visual Acuity
 MRSE = Manifest Refraction Spherical Equivalent

D = Diopter
 UCVA = Uncorrected Visual Acuity

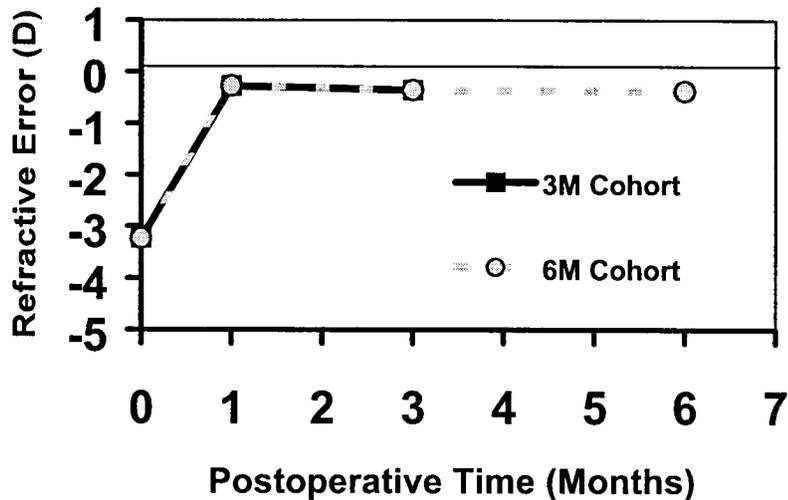
Table 7. Summary of Key Efficacy Variables at 6 Months Stratified by Diopter of Preoperative Manifest Refraction Spherical Equivalent

		0 to -0.99	-1 to -1.99	-2 to -2.99	-3 to -3.99	-4 to -4.99	-5 to -5.99	-6 to -7.00	Total
Efficacy Variables (Efficacy Cohort: 139 Spherical Myopic Eyes)									
UCVA 20/20 or better	n	1/1	19/23	30/40	28/31	22/27	9/13	2/4	111/139
	%	100.0%	82.6%	75.0%	90.3%	81.5%	69.2%	50.0%	79.9%
UCVA 20/25 or better	n	1/1	22/23	35/40	29/31	25/27	12/13	3/4	127/139
	%	100.0%	95.7%	87.5%	93.5%	92.6%	92.3%	75.0%	91.4%
UCVA 20/40 or better	n	1/1	23/23	40/40	31/31	27/27	12/13	3/4	137/139
	%	100.0%	100.0%	100.0%	100.0%	100.0%	92.3%	75.0%	98.6%
MRSE \pm 0.50D of intended	n	1/1	20/23	29/40	22/31	18/27	11/13	3/4	104/139
	%	100.0%	87.0%	72.5%	71.0%	66.7%	84.6%	75.0%	74.8%
MRSE \pm 1.00D of intended	n	1/1	23/23	39/40	30/31	26/27	11/13	3/4	133/139
	%	100.0%	100.0%	97.5%	96.8%	96.3%	84.6%	75.0%	95.7%
Safety Variables (Safety Cohort: 424 Eyes)									
Loss of >2 Lines BSCVA	n	0/1	0/59	0/95	0/103	0/97	0/58	0/11	0/424
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Loss of 2 Lines BSCVA	n	0/1	1/59	0/95	1/103	0/97	1/58	0/11	3/424
	%	0.0%	1.7%	0.0%	1.0%	0.0%	1.7%	0.0%	0.7%
BSCVA worse than 20/40	n	0/1	0/59	0/95	0/103	0/97	0/58	0/11	0/424
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Increase >2D cylinder magnitude	n	0/1	0/59	0/95	0/103	0/97	0/58	0/11	0/424
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	n	0/1	0/59	0/95	0/102	0/97	1/56	0/11	1/421
	%	0.0%	0.0%	0.0%	0.0%	0.0%	1.8%	0.0%	0.2%

BSCVA = Best Spectacle Corrected Visual Acuity
 MRSE = Manifest Refraction Spherical Equivalent

D = Diopter
 UCVA = Uncorrected Visual Acuity

Slight undercorrection was observed postoperatively (Table 8). Stability of MRSE, defined as ≥95% of eyes with a change of ≤1.00D, was achieved by 3 months (Tables 9 and 10).



Mean ± Standard Deviation	PREOP	1 MONTH	3 MONTHS	6 MONTHS
3 Month Cohort (Diopter)	-3.23 ± 1.31	-0.27 ± 0.34	-0.35 ± 0.42	--
6 Month Cohort (Diopter)	-3.23 ± 1.31	-0.27 ± 0.34	-0.35 ± 0.42	-0.37 ± 0.39

Change in Spherical Equivalent Between	1 AND 3 MONTHS
≤1.00 Diopter [% (n/N)]	100.0% (139/139)
Mean Difference ± Standard Deviation	-0.07 ± 0.27
95% Confidence Interval	(-0.12, -0.03)

Change in Spherical Equivalent Between	1 AND 3 MONTHS	3 AND 6 MONTHS
≤1.00 Diopter [% (n/N)]	100.0% (139/139)	100.0% (139/139)
Mean Difference ± Standard Deviation	-0.07 ± 0.27	-0.03 ± 0.26
95% Confidence Interval	(-0.12, -0.03)	(-0.07, 0.02)

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

A comparison of **postoperative** uncorrected visual acuity (UCVA) to **preoperative** best spectacle corrected visual acuity (BSCVA) after CustomCornea® LASIK surgery is presented in Table 11.

Table 11. Postoperative Uncorrected Visual Acuity Compared to Preoperative Best Spectacle Corrected Visual Acuity						
	1 MONTH		3 MONTHS		6 MONTHS	
	%	(n/N)	%	(n/N)	%	(n/N)
2 Lines Better	2.2%	(3/139)	1.4%	(2/139)	2.2%	(3/139)
1 Line Better	12.2%	(17/139)	13.7%	(19/139)	15.1%	(21/139)
Equal	44.6%	(62/139)	40.3%	(56/139)	35.3%	(49/139)
1 Line Worse	26.6%	(37/139)	23.7%	(33/139)	23.7%	(33/139)
2 Lines Worse	8.6%	(12/139)	11.5%	(16/139)	14.4%	(20/139)
>2 Lines Worse	5.8%	(8/139)	9.4%	(13/139)	9.4%	(13/139)

5. Change in Best Spectacle Corrected Visual Acuity

Best spectacle corrected visual acuity (BSCVA) was measured using a standard (high-contrast) visual acuity chart under dim room illumination (10-12 cd/m²). Low contrast best spectacle corrected visual acuity was measured using a 10% low contrast visual acuity chart under dim room illumination.

Tables 12 and 13 show the change in BSCVA and low contrast BSCVA after surgery as compared to before surgery.

Table 12. Change in Best Spectacle Corrected Visual Acuity for Spherical Myopic Eyes						
	1 MONTH		3 MONTHS		6 MONTHS	
	%	(n/N)	%	(n/N)	%	(n/N)
Decrease >2 Lines	0.0%	(0/139)	0.0%	(0/139)	0.0%	(0/139)
Decrease 2 Lines	2.2%	(3/139)	1.4%	(2/139)	0.0%	(0/139)
Decrease 1 Line	10.1%	(14/139)	15.1%	(21/139)	8.6%	(12/139)
No change	58.3%	(81/139)	52.5%	(73/139)	53.2%	(74/139)
Increase 1 Line	26.6%	(37/139)	28.8%	(40/139)	35.3%	(49/139)
Increase 2 Lines	2.2%	(3/139)	2.2%	(3/139)	2.9%	(4/139)
Increase >2 Lines	0.7%	(1/139)	0.0%	(0/139)	0.0%	(0/139)

Table 13. Change in Low Contrast Best Spectacle Corrected Visual Acuity for Spherical Myopic Eyes				
	3 MONTHS		6 MONTHS	
	%	(n/N)	%	(n/N)
Decrease >2 Lines	0.0%	(0/139)	0.0%	(0/139)
Decrease 2 Lines	7.2%	(10/139)	2.2%	(3/139)
Decrease 1 Line	15.1%	(21/139)	18.7%	(26/139)
No change	42.4%	(59/139)	40.3%	(56/139)
Increase 1 Line	30.2%	(42/139)	30.2%	(42/139)
Increase 2 Lines	4.3%	(6/139)	6.5%	(9/139)
Increase >2 Lines	0.7%	(1/139)	2.2%	(3/139)

6. Change in Contrast Sensitivity after Surgery

A contrast sensitivity study was conducted to assess the effects of CustomCornea® myopic LASIK surgery on how well patients can see in conditions such as very dim light, rain, snow, and fog. Table 14 shows the change in contrast sensitivity measured under photopic and mesopic lighting conditions after CustomCornea® surgery compared to preoperative levels.

Table 14. Change of >2 Levels (> 0.3 Log) on CSV-1000 at 2 or More Spatial Frequencies for Spherical Myopic Eyes				
Photopic Conditions				
Change > 0.3 (log unit)	Decrease		Increase	
Post-op Time	3 MONTHS	6 MONTHS	3 MONTHS	6 MONTHS
% (n/N)	2.2% (3/138)	0.7% (1/138)	4.3% (6/138)	2.2% (3/138)
Mesopic Conditions*				
Change > 0.3 (log unit)	Decrease		Increase	
Post-op Time	3 MONTHS	6 MONTHS	3 MONTHS	6 MONTHS
% (n/N)	5.8% (8/138)	5.8% (8/138)	10.1% (14/138)	15.2% (21/138)

*Mesopic illumination with neutral density filters in front of eyes

7. Patient Symptoms and Satisfaction

Patients were asked to rate the following symptoms at 3 and 6 months compared to before CustomCornea® LASIK surgery for the correction of spherical myopia. As shown in Table 15, patients rated symptoms as significantly better, better, no change, worse, or significantly worse than preoperative.

Table 15. Change in Subjective Symptoms From Preoperative					
3 MONTHS (N=137)					
Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
Blurring of Vision	6.6%	12.4%	58.4%	21.2%	1.5%
Burning	2.2%	6.6%	84.7%	5.8%	0.7%
Double Vision	0.7%	0.0%	91.2%	7.3%	0.7%
Dryness*	5.9%	17.0%	48.1%	21.5%	7.4%
Excessive Tearing	0.7%	8.0%	91.2%	0.0%	0.0%
Fluctuation of Vision	2.2%	11.7%	60.6%	24.1%	1.5%
Glare	1.5%	13.1%	68.6%	16.8%	0.0%
Gritty Feeling	5.1%	9.5%	73.7%	10.9%	0.7%
Halos	2.9%	12.4%	65.0%	19.0%	0.7%
Headache	2.9%	5.8%	86.1%	5.1%	0.0%
Light Sensitivity	0.0%	13.9%	78.1%	7.3%	0.7%
Night Driving Difficulty	5.1%	12.4%	65.0%	13.9%	3.6%
Pain	2.9%	3.6%	88.3%	5.1%	0.0%
Redness	3.6%	13.1%	75.2%	8.0%	0.0%
6 MONTHS (N=136)					
Blurring of Vision	7.4%	11.0%	62.5%	16.2%	2.9%
Burning	2.9%	10.3%	79.4%	5.9%	1.5%
Double Vision	1.5%	3.7%	88.2%	5.9%	0.7%
Dryness	8.1%	12.5%	56.6%	20.6%	2.2%
Excessive Tearing*	1.5%	5.2%	93.3%	0.0%	0.0%
Fluctuation of Vision	3.7%	7.4%	71.3%	16.9%	0.7%
Glare	2.9%	12.5%	69.9%	14.7%	0.0%
Gritty Feeling	8.1%	8.8%	72.8%	8.8%	1.5%
Halos	5.1%	6.6%	75.0%	13.2%	0.0%
Headache	2.9%	5.9%	89.7%	1.5%	0.0%
Light Sensitivity	3.7%	10.3%	81.6%	4.4%	0.0%
Night Driving Difficulty	6.6%	12.5%	61.8%	18.4%	0.7%
Pain	4.4%	5.9%	89.0%	0.7%	0.0%
Redness	4.4%	16.2%	73.5%	5.9%	0.0%

*N=135 eyes

Quality of vision was rated as unchanged, better, or significantly better in 89.8% of patients at 3 months and 88.3% at 6 months. Eighty-five percent of patients at 3 months and 79.4% at 6 months reported they were satisfied or extremely satisfied with their results. Distance correction was never worn by 95.6% of patients at 3 months and 94.1% at 6 months.

8. Retreatment

No data are available for CustomCornea® LASIK retreatments using the LADARVision®4000 system.

9. Comparison to Conventional LASIK (Based on Manifest Phoropter Refraction)

Wavefront-guided CustomCornea® LASIK using the LADARVision®4000 system has demonstrated slightly superior optical quality (reduced monochromatic aberrations) compared to Conventional LASIK with the LADARVision®4000 system. Minor improvements with CustomCornea® LASIK were noted in visual acuity and contrast sensitivity relative to Conventional LASIK with the LADARVision®4000 system.

The amount of postoperative higher-order aberrations was less for CustomCornea® LASIK eyes than for the Conventional LASIK eyes. The average increase in higher-order aberrations after surgery was:

- 27% at 3 months and 20% at 6 months for CustomCornea® LASIK eyes.
- 77% at 3 months and 82% at 6 months for Conventional LASIK eyes.

For most patients, CustomCornea® LASIK did not reduce higher-order aberrations from baseline levels prior to surgery. However, the percentage of patients with reduced higher-order aberrations after surgery compared to before surgery was:

- 35% at 3 months and 38% at 6 months for CustomCornea® LASIK eyes.
- 11% at 3 months and 14% at 6 months for Conventional LASIK eyes.

Regardless of the treatment of the other higher-order aberrations, the accuracy of the correction for myopia is still the primary determinant of uncorrected image quality and visual acuity. There are no data to support improved functional performance (activities of daily living such as reading and driving) or satisfaction rates in patients with wavefront-guided CustomCornea® LASIK using the LADARVision®4000 system as compared to Conventional LASIK with the LADARVision®4000 system.

The accuracy of the myopic correction is the primary determinant in patient satisfaction and subjective symptoms. In the clinical study, the CustomCornea® LASIK eyes showed slight myopic undercorrection on average relative to the Conventional LASIK eyes. For the 20 patients in the study who received CustomCornea® LASIK in one eye and Conventional LASIK in the other eye, there was no significant difference in subjective symptoms between the two treatments.

A vision simulation program (CTView⁸ by Sarver and Associates) was used to model the effect of various wavefront errors on the retinal point-spread function (i.e., the effective blur pattern) and a simulated eye chart image for CustomCornea® and Conventional LASIK eyes. Visual comparisons of letter charts blurred by defocus or higher-order aberrations suggest that the benefit of smaller amounts of higher-order aberrations after wavefront-guided surgery compared to Conventional LASIK corresponds to approximately 0.2D of defocus on average.

The following charts are 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

Difference in Higher-Order Aberrations using the LADARVision®4000 System

After CustomCornea® LASIK

After Conventional LASIK

P V E H R
E H V D F
N U Z F E
U H N Z R
D N E F P
F V E P Z

P V E H R
E H V D F
N U Z F E
U H N Z R
D N E F P
F V E P Z

⁸ CTView TM of Sarver and Associates, Inc.

C. TRACKING EFFECTIVENESS

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

Analysis of eye movement data gathered electronically during the surgical procedures of 554 eyes treated in a study⁹ demonstrated that:

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

⁹ LADARVision® System study on PRK Myopia with Astigmatism (P970043)

5. PLANNING AND PROCEDURES

A. PATIENT SELECTION

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

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

- Agreement between manifest refraction and the wavefront measurement should be within 1D. Differences of >1D should be investigated. It is essential that the refractive information upon which this surgical procedure depends on is accurate and is correctly transmitted to the laser. **It is the sole responsibility of the operating doctor to ensure the information for each individual patient is accurate.**
- The patient should have the ability to tolerate local or topical anesthesia and drops to dilate the pupil. A pupil dilation of at least 7mm to 11mm is required for surgery to proceed. During preoperative procedures that involve dilation of the pupil, it is important to assess that the minimum amount of dilation is achievable.
- The patient should have the ability to lie flat without difficulty.
- The patient should be able to fixate steadily and accurately for the duration of the CustomCornea® LASIK procedure.
- The patient must be able to understand and give an informed consent.
- Patients should be clearly informed of all alternatives for the correction of their myopia and astigmatism, which include but are not limited to spectacles, contact lenses and other refractive surgeries such as radial keratotomy.

B. OPERATIVE PROCEDURE

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

Prior to surgery, patient details (name and medical record number) are entered into the LADARVision®4000 and wavefront measurement device systems. The wavefront data used for treatment is transported to the LADARVision®4000 system from a compatible wavefront measurement device. Data transferred from the wavefront measurement device must contain: 1) patient information, including name, medical record number, and manifest refraction; 2) eye information, including right/left eye and the geometric relationship of the wavefront data to limbus and pupil center; and 3) wavefront information, including Zernike polynomial representation of the wavefront and physical radius of that description. Once the wavefront data is loaded into the LADARVision®4000 system, the attempted corneal plane correction is displayed to the surgeon, along with the optic zone, blend zone and peak depth of ablation.

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

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

1. Centration and Registration

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

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

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

The wavefront data is transferred to the LADARVision®4000 system computer by disk, where the appropriate ablation laser shot pattern is generated. The system software is used at the laser to align to the registration information from the wavefront measurement device. Figure 1 shows the LADARVision®4000 system software display, which provides the ability to position the ablation in the exact location desired, identical to the orientation of the wavefront data. With the patient lying on the treatment bed just prior to surgery, the limbus ring is aligned to provide X and Y axes information and the horizontal line is rotated to match the marks applied to the eye for cyclotorsion alignment.

2. Pupil Dilation

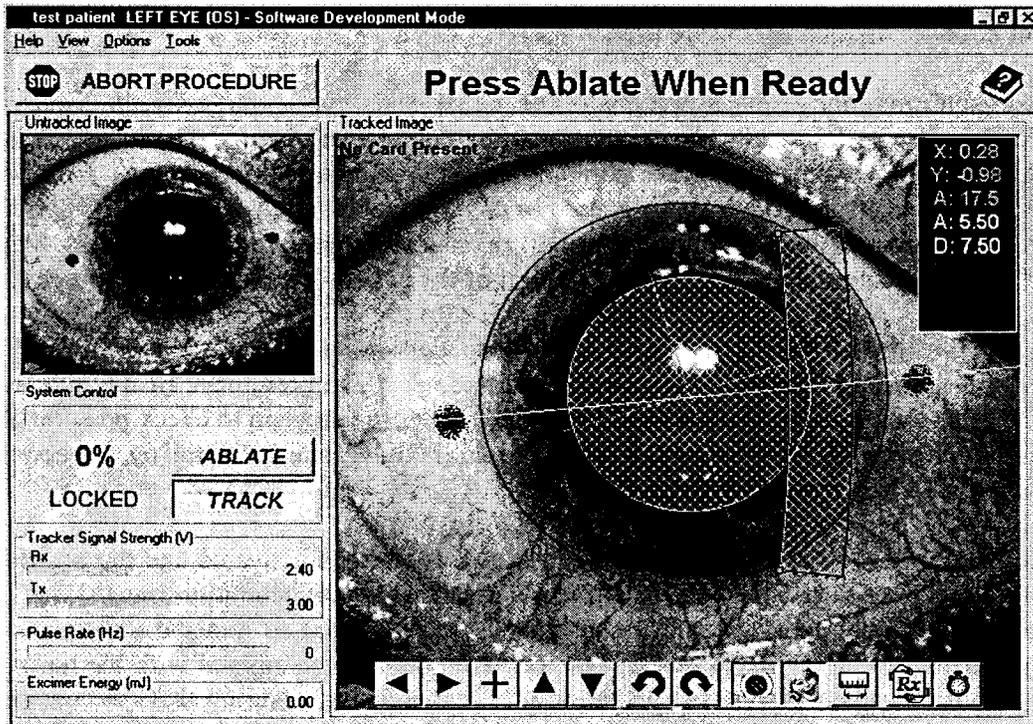
It is necessary to dilate the pupil to 7mm prior to surgery to engage the tracking system. A combination of 2.5% phenylephrine (MYDFRIN™¹⁰ solution) and 1% tropicamide (MYDRIACYL™¹¹ solution) are used. Approximately 45 minutes prior to the procedure, one drop of each mydriatic is instilled followed by a second drop 10 minutes later.

¹⁰ MYDFRIN Reg US Pat & TM Off.

¹¹ MYDRIACYL Reg US Pat & TM Off.

Figure 1. LADARVision®4000 system software display:

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



3. Laser Calibration

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

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

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

4. Ablation

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

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

Once the tracking system is set, it is then disengaged and a LASIK flap of at least 160 microns in thickness is created using a microkeratome. (The preference of microkeratome brand used is the surgeon's choice.) The software allows the surgeon to check position of the ablation zone with respect to the flap by using an ablation zone indicator on the computer screen.

When the LASIK flap is folded back, the tracking system is re-activated and the position of the ablation zone is determined by recalling the geometry of the centration rings stored prior to dilation. The previously stored limbus ring is re-positioned so that the ablation occurs over the center of the undilated pupil. The marks on the eye are aligned with the horizontal reticule in the system software to compensate for cyclotorsion, ensuring that the customized ablation pattern is applied in the exact same orientation as the wavefront measured by the wavefront measurement device. An example of the LADARVision®4000 system software display is shown in Figure 1.

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

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

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

C. POSTOPERATIVE PROCEDURE

Postoperative pharmaceutical treatment consists of one drop of a broad-spectrum antibiotic and, if desired, a steroid and non-steroidal anti-inflammatory drug (NSAID). The patients are given an antibiotic/steroid combination to be instilled for the first 7 days on a tapering dosage from 4 to 2 times a day. Following cessation of this immediate postoperative drug therapy, no other medications are routinely prescribed unless medically necessary.

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

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