Alcon®

LADARVISION®4000

Excimer Laser System

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

PATIENT INFORMATION BOOKLET

For Nearsightedness (Myopia) up to -8.00D Sphere with -0.50D to -4.00D of Astigmatism

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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A. Introduction

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

You may have nearsightedness if you have trouble seeing objects clearly when they are far away. *Nearsightedness,* which is also called *myopia,* is a type of condition that causes blurred vision. In addition to nearsightedness, you may have *astigmatism* if you see that parts of objects appear more blurred than other parts. Glasses, contact lenses, or eye surgery can correct nearsightedness with astigmatism to help you see distant objects more clearly.

The types of eye surgeries that are available to correct nearsightedness with astigmatism are *Radial Keratotomy* (RK), *Photorefractive Keratectomy* (PRK), and *Laser Assisted In-Situ Keratomileusis* (LASIK). These surgeries may not meet the vision requirements for some careers, such as military service.

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

Your eyeglass prescription is the usual way to tell how much nearsightedness with 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 nearsightedness with 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*".

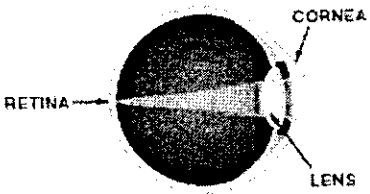
Your doctor can use either your eyeglass prescription or a wavefront measurement to plan LASIK surgery. LASIK surgery based on the eyeglass prescription is called *Conventional LASIK.* LASIK surgery based on the wavefront is called wavefront-guided LASIK. *CustomCornea® LASIK* is wavefront-guided surgery 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 Nearsightedness (Myopia) with 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 onto film. Both the cornea and lens in the eye focus light onto the back surface of the eye, called the *retina*. Diagram 1 shows that distant vision is clear when light focuses correctly.

DIAGRAM 1: NORMAL EYE

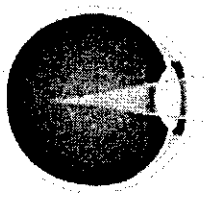


A NORMAL EYE

Light focuses on the retina. Vision is clear.

Nearsightedness is a type of focusing error that results in blurred distant vision. Light from a distant object focuses in front of the retina, rather than on the retina. Diagram 2 shows that distant vision is blurry when light focuses incorrectly in a nearsighted eye.

DIAGRAM 2: NEARSIGHTED EYE

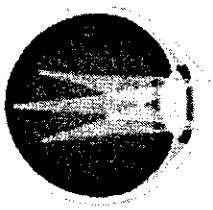


A NEARSIGHTED or MYOPIC EYE

Light focuses in front of the retina. Vision is blurred.

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

DIAGRAM 3: ASTIGMATIC EYE

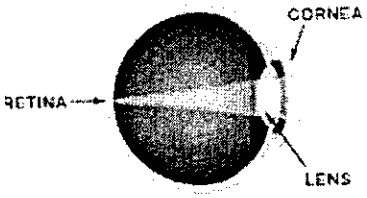


AN ASTIGMATIC EYE

Light focuses at different points in front of the retina. Vision is blurred.

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

DIAGRAM 4: CORRECTION OF VISION AFTER LASIK



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

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

The LADARVision®4000 system uses a very small laser beam to reshape the cornea. To correct for nearsightedness with 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®4000 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 up to -8.00 *diopters* (D) of nearsightedness with -0.50D to -4.00D of astigmatism. If you have nearsightedness with 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 was done to evaluate the benefits and risks of CustomCornea® LASIK. The study included 232 eyes to determine benefits and 331 eyes to determine 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 331 Eyes of 167 Study Patients

Age		Race		Gender		Contact Lens History	
Average:	37 ± 9 years	Asian	2.4%	Female	40.8%	None	24.2%
Range:	19 to 57 years	Black	0.6%	Male	59.2%	Hard	10.6%
		Caucasian	94.6%			Soft	65.3%
		East Indian	0.6%				
		Hispanic	1.8%				

Visual Acuity *without* Glasses After Surgery

Visual acuity measures the sharpness of vision using a letter chart. Table 2 shows that at least 97% of patients treated for nearsightedness with astigmatism saw 20/40 or better **without** glasses after surgery. Most states require that your vision be 20/40 or better if you drive **without** any glasses or contact lenses.

Table 2. Visual Acuity *without* Glasses After Surgery

% of Eyes With:	3 Months (N=232)	6 Months (N=232)
20/20 or better*	81%	86%
20/20 or better	79%	84%
20/25 or better	96%	94%
20/40 or better	99%	97%

N is the number of eyes studied.

* if 20/20 or better with glasses or contact lenses before surgery (N= 225 eyes).

Visual Acuity *without* Glasses After Surgery and *with* Glasses Before Surgery

Table 3 shows that 60.3% of the patients at 3 months and 67.2% 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:	3 Months (N=232)	6 Months (N=232)
2 lines better vision than with glasses	0.9%	1.3%
1 line better vision than with glasses	15.9%	21.6%
the same vision as with glasses	43.5%	44.4%
1 line worse vision than with glasses	26.3%	23.7%
2 lines worse vision than with glasses	11.2%	4.3%
more than 2 lines worse vision than with glasses	2.2%	4.7%

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** your glasses or contact lenses may be worse after CustomCornea® LASIK surgery than it was before surgery.

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

Contraindications – When Can't You Have Surgery?

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

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

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.

[2] *Accutane* is a registered trademark of Hoffmann-La Roche Inc.
[3] *Cordarone* is a registered trademark of Sanofi-Synthelabo

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 or worsening nearsightedness with astigmatism. Eyes with unstable nearsightedness with astigmatism are unable to be correctly measured to determine the right amount of the vision correction to provide.
- with conditions that may interfere with the ability to properly measure the eye to determine the right amount of vision correction, and may also affect the healing of the eye after the surgery, such as:
  - disease or corneal condition (for example, scar, infection, etc.).
  - injury to the center of 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, RK, PRK, LASIK).
- with a cornea that is too thin for LASIK to be completed safely. A flap needs to be cut into the cornea for the LASIK procedure. A proper flap cannot be created on a thin cornea.
- with a history of *glaucoma* (a condition usually associated with high eye pressure with damage to the nerve in the eye and possible loss of vision). It is unknown whether LASIK is safe for eyes with glaucoma.
- who are taking the medication sumatripin (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 6 months).
- with greater than -8.00D sphere of nearsightedness with less than –0.50D of astigmatism or greater than -4.00D of astigmatism. 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 9mm.

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.

[4] Imitrex Reg TM of Glaxo Group Limited

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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.

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 results are shown below:

Under daylight testing conditions, contrast sensitivity after CustomCornea® LASIK surgery as compared to before surgery showed a:

- gain in 6.0% of patients at 3 months and 6.5% at 6 months.
- loss in 6.5% of patients at 3 months and 1.7% at 6 months.

Under dim light testing conditions, contrast sensitivity after CustomCornea® LASIK surgery as compared to before surgery showed a:

- gain in 18.5% of patients at 3 months and 22.4% at 6 months.
- loss in 8.6% of patients at 3 months and 7.3% at 6 months.

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.

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 3 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 on CustomCornea® LASIK, vision **without** glasses improved for all eyes. Some people still needed glasses or contact lenses after surgery. At 3 months after surgery, 7% of patients had greater than 1D and 0.4% of patients had greater than 2D of correction over the intended amount. Under testing conditions using eyedrops to reduce focusing ability, 18% of patients had greater than 1D and 2% of patients had greater than 2D of correction over the intended amount at 3 months.

Visual Acuity *with* Glasses After Surgery

Table 4 shows that all patients from the study saw 20/32 or better **with** glasses at 3 and 6 months after surgery. Of those patients who saw 20/20 or better **with** glasses or contact lenses before surgery, 98.8% of patients at 3 months and 99.4% of patients at 6 months saw 20/20 or better **with** glasses or contact lenses after surgery.

Table 4. Visual Acuity *with* Glasses (Best Vision)

% of Eyes With:	3 Months (N=331)	6 Months (N=331)
20/20 or better*	98.8%	99.4%
20/20 or better	97.6%	98.8%
20/25 or better	100%	99.7%
20/32 or better	100%	100%

N is the number of eyes studied.
* if 20/20 or better with glasses or contact lenses before surgery (N=323 eyes).

Change in Visual Acuity *with* Glasses After Surgery

Under dim room lighting conditions, the best vision **with** glasses was measured using a standard (high-contrast) visual acuity chart and a 10% *low contrast visual acuity* chart. A standard chart has black letters on a white background. A 10% low contrast visual acuity chart has gray letters on a white background. Black letters are easier to see than gray letters. Low contrast acuity testing is another way to determine how well patients can see in poor contrast conditions such as very dim light, rain, snow, and fog. Table 5 compares the change in vision **with** glasses at 3 and 6 months before and after surgery.

Table 5. Change in Visual Acuity *with* Glasses After Surgery Compared to Before Surgery

% of Eyes With:	Standard Chart		10% Low Contrast Chart	
	3 Months (N= 331)	6 Months (N= 331)	3 Months (N= 331)	6 Months (N= 331)
loss of more than 2 lines	0.0%	0.0%	0.9%	0.6%
loss of 2 lines	0.0%	0.0%	4.2%	3.0%
loss of 1 line	7.3%	8.5%	14.8%	8.8%
no change	55.9%	47.7%	37.2%	38.7%
gain of 1 line	35.0%	41.4%	36.6%	38.1%
gain of 2 lines	1.8%	2.4%	6.0%	8.8%
gain of more than 2 lines	0.0%	0.0%	0.3%	2.1%

N is the number of eyes studied.

Adverse Events and Complications

Some patients from the clinical study experienced adverse events and complications after CustomCornea® LASIK surgery as shown in Table 6.

Table 6. Adverse Events and Complications	
Greater than or equal to 1% of eyes (N=331) **had:**	
Corneal swelling between one week and less than one month	1.5%
Less than 1% of eyes (N=331) **had:**	
Cells growing under the flap	0.9%
Inflammation of the cornea under the flap	0.9%
Corneal swelling of the flap at one month or later	0.6%
Double or ghost images	0.6%
Feeling of something in the eye at one month or later	0.6%
Corneal wrinkle in the flap	0.3%
Flap creation without a hinge with the microkeratome	0.3%
Irregular flap creation with the microkeratome	0.3%

N is the number of eyes studied.

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

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

Worse and Significantly Worse Symptoms After Surgery

Patients who were treated for nearsightedness with astigmatism rated the change in the following symptoms after surgery **without** glasses or contact lenses as worse or significantly worse compared to before surgery **with** glasses or contact lenses (Table 7).

Table 7. Symptoms *without* Glasses After Surgery Compared to *with* Glasses Before Surgery

	3 Months (N=232)		6 Months (N=232)	
Symptom	**Worse**	**Significantly Worse**	**Worse**	**Significantly Worse**
Blurring of Vision	12.1%	1.3%	15.9%	0.4%
Burning	5.2%*	0.0%*	3.5%**	0.9%**
Double Vision	5.2%**	2.6%**	6.9%	0.4%
Dryness	23.3%	2.2%	17.7%	1.7%
Excessive Tearing	0.0%*	0.0%*	0.0%*	0.0%*
Fluctuation of Vision	22.4%	2.2%	16.4%	1.7%
Glare	20.8%**	1.7%**	13.4%	0.0%
Gritty Feeling	9.5%	0.9%	4.3%	0.0%
Halos §	19.8%	1.3%	16.4%	0.9%
Headache	5.2%	0.0%	2.6%	0.9%
Light Sensitivity	21.6%	0.9%	15.9%	0.4%
Night Driving Difficulty	9.5%	1.7%	10.3%	0.0%
Pain	3.4%	0.0%	2.6%*	0.0%*
Redness	5.6%	0.4%	1.3%	0.0%

N is the number of eyes studied.

For the symptoms noted with asterisks, *230 patients responded and **231 responded.

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

E. Patient Questionnaire Responses

After treatment for nearsightedness with astigmatism, 94% of patients reported at 3 months and 95% reported at 6 months that they never wore glasses or contact lenses. Quality of vision **without** glasses or contact lenses after surgery was compared to **with** glasses or contact lenses before surgery. Quality of vision was rated as unchanged, better, or significantly better than before surgery in 93% of patients at 3 months and 94% at 6 months. Approximately 88% of patients at 3 and 6 months reported they were satisfied or extremely satisfied with their results.

Patients rated the change in the following symptoms after surgery **without** glasses or contact lenses compared to before surgery **with** glasses or contact lenses. Table 8 shows that more than half of all patients being treated for nearsightedness with astigmatism reported that their symptoms were the same at 3 and 6 months after CustomCornea® LASIK surgery **without** glasses as before surgery **with** glasses.

Table 8. Symptoms *without* Glasses After Surgery Compared to *with* Glasses Before Surgery

Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
3 Months (N=232)					
Blurring of Vision	9.1%	10.3%	67.2%	12.1%	1.3%
Burning*	6.1%	11.7%	77.0%	5.2%	0.0%
Double Vision**	7.4%	3.0%	81.8%	5.2%	2.6%
Dryness	7.8%	14.7%	52.2%	23.3%	2.2%
Excessive Tearing*	5.2%	6.1%	88.7%	0.0%	0.0%
Fluctuation of Vision	9.1%	10.8%	55.6%	22.4%	2.2%
Glare**	6.1%	14.3%	57.1%	20.8%	1.7%
Gritty Feeling	7.8%	9.9%	72.0%	9.5%	0.9%
Halos §	6.5%	14.2%	58.2%	19.8%	1.3%
Headache	6.0%	9.9%	78.9%	5.2%	0.0%
Light Sensitivity	4.3%	14.7%	58.6%	21.6%	0.9%
Night Driving Difficulty	7.3%	21.6%	59.9%	9.5%	1.7%
Pain	6.0%	8.6%	81.9%	3.4%	0.0%
Redness	6.5%	10.3%	77.2%	5.6%	0.4%
6 Months (N=232)					
Blurring of Vision	10.8%	10.3%	62.5%	15.9%	0.4%
Burning**	7.4%	11.3%	77.1%	3.5%	0.9%
Double Vision	9.5%	4.3%	78.9%	6.9%	0.4%
Dryness	11.2%	14.2%	55.2%	17.7%	1.7%
Excessive Tearing*	6.5%	4.3%	89.1%	0.0%	0.0%
Fluctuation of Vision	11.6%	9.9%	60.3%	16.4%	1.7%
Glare	9.9%	18.5%	58.2%	13.4%	0.0%
Gritty Feeling	12.1%	10.3%	73.3%	4.3%	0.0%
Halos §	10.8%	17.7%	54.3%	16.4%	0.9%
Headache	9.9%	12.1%	74.6%	2.6%	0.9%
Light Sensitivity	7.8%	18.5%	57.3%	15.9%	0.4%
Night Driving Difficulty	15.9%	20.3%	53.4%	10.3%	0.0%
Pain*	8.3%	9.6%	79.6%	2.6%	0.0%
Redness	9.1%	16.8%	72.8%	1.3%	0.0%

N is the number of eyes studied.

For the symptoms noted with asterisks, *230 patients responded and **231 responded.

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

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

If you are considering CustomCornea® LASIK, you must:

- be at least 21 years of age.
- have a healthy eye with no eye disease or corneal condition (for example, scar, infection, etc.).
- have up to -8.00D sphere of nearsightedness combined with -0.50D to -4.00D of astigmatism.
- have stable nearsightedness with 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 nearsightedness with astigmatism.
- be willing to sign an Informed Consent Form, if provided by your doctor.

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

Before The Surgery

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

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

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

The Day Of Surgery

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

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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.

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H. Questions To Ask Your Doctor

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

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

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

I. Self-Test

Are You An Informed And Educated Patient?

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

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

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

J. Summary Of Important Information

- CustomCornea® LASIK is a permanent irreversible surgery to the cornea.
- You may need to wear glasses or contact lenses for some activities after surgery. CustomCornea® LASIK does not take away the need for reading glasses, even if you have never worn them before.
- Your vision must be stable before CustomCornea® LASIK surgery. You must provide written evidence that your nearsightedness with 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 nearsightedness with astigmatism include glasses, contact lenses, RK, PRK, and Conventional LASIK.
- RK, PRK, Conventional LASIK or CustomCornea® LASIK may not meet the vision requirements of some occupations, such as military service.
- Before considering CustomCornea® LASIK surgery you should:
  a. have a complete eye examination.
  b. talk with at least one eye care professional about CustomCornea® LASIK, especially the potential benefits, risks, and complications. You should discuss the time needed for healing after CustomCornea® LASIK.

Answers to Self-Test Questions:

1. False (see Section D: Risks)
2. False (see Section G: Before the Surgery)
3. False (see Section G: The Day of Surgery)
4. True (see Section C: Benefits)
5. True (see Section 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)

K. Glossary

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

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

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

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

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

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

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. Surgery such as PRK, LASIK and RK 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.

Corneal Wrinkle: temporary appearance of fine white lines in the cornea due to swelling.

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 nearsightedness and astigmatism of an eye. Abbreviated as "D".

Excimer Laser: a type of laser used in Conventional and CustomCornea® LASIK to remove tissue from the cornea.

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

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

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

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

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

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

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

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

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

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.

Myopia: a focusing error that results in blurrier vision at distance than near. Myopia is also called nearsightedness.

Nearsightedness: a focusing error that results in blurrier vision at distance than near. Nearsightedness is also called myopia.

Ocular Hypertension: increased eye pressure.

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

Radial Keratotomy (RK): a type of eye surgery that changes the shape of the front surface of the eye by making a special pattern of cuts in the cornea to correct nearsightedness.

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

L. Patient Assistance Information

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

Primary Eye Care Professional

Name: _____

Address: _____

Phone: _____

CustomCornea® LASIK Doctor

Name: _____

Address: _____

Phone: _____

Treatment Location

Name: _____

Address: _____

Phone: _____

Laser Manufacturer

Alcon, Inc.
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Orlando, FL 32826 U.S.A.
Tel: (877) 523-2784 Fax: (407) 384-1677

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Alcon®

LADARVISION®4000

Excimer Laser System

PROFESSIONAL USE INFORMATION MANUAL

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

PHYSICIAN'S BOOKLET

For Myopic Astigmatism up to -8.00D Sphere with -0.50D to -4.00D Cylinder and up to -8.00D of Spherical Equivalent

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

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

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

Alcon, Inc.
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Orlando, FL 32826

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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.

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 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. 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 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.

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 Amadeus[1] (manufactured by Surgical Instruments Systems, Ltd. and owned by Advanced Medical Optics), BD K-4000[2] (manufactured by Becton-Dickinson), Hansatome[3] (manufactured by Bausch & Lomb), and the Moria[4] M2 (manufactured by Moria).

[1] *Amadeus* Reg. TM of SIS AG, Surgical Instrument Systems
[2] *BD K-4000* TM of Becton, Dickinson and Company
[3] *Hansatome* Reg. TM of Hansa Research & Development, Inc.
[4] *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 and calculation of ablation depth.

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, enforces the eligibility, calculates the excimer treatment pattern, and performs the surgery.

D. LADARVision®4000 EXCIMER LASER SYSTEM

The LADARVision®4000 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 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 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 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 is located in the optics head. The dual optical paths are independent of the excimer beam path and the LADARTracker® 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 red 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 place the LED at infinity focus from the patient's perspective. The edge-illuminated reticule is a clear glass flat etched with two sets of horizontal lines. These lines are also visible to the patient at an effective focal length of approximately 18 inches. 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 633 nm. The beam of each red-wavelength laser is transmitted through an absorptive neutral density filter, which attenuates the laser by 97%, and a polarizer. The output of each polarizer is reflected off a stationary fold mirror. The two mirrors are aligned such that the two beams are vertically aligned (one above the other) on the left sclera/limbus boundary and the apex of the cornea is 8 inches below the laser output window. This provides the operator/surgeon with an easy method of setting the height of the patient's eye during centration and surgery.

The maximum laser power at the eye is less than 15 μwatts for each laser. The lasers are separated by 103 mm and are 209 mm 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.

System Software

The LADARVision®4000 system software controlling the proprietary excimer laser runs on an Intel Pentium[5]-based personal computer under a Microsoft Windows[6] 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 manually entered 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. 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.

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

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 9mm.

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 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 myopic astigmatism up to -8.00D sphere with -0.50D to -4.00D cylinder and up to -8.00D spherical equivalent at the spectacle plane;
- in patients who are 21 years of age or older; and
- in patients with documented stability of refraction for the prior 12 months, as demonstrated by a change in sphere and cylinder of less than or equal to 0.50D for a spherical equivalent up to -6.00D and less than or equal to 0.75D for a spherical equivalent greater than -6.00D.

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[7]) or amiodarone hydrochloride (Cordarone[8]).

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.

D. PRECAUTIONS

The safety and effectiveness of the LADARVision®4000 system for wavefront-guided LASIK correction of myopic astigmatism 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 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[9]).
- under 21 years of age.
- over the long term (more than 6 months after surgery).
- for treatments of myopic astigmatism greater than -8.00D sphere combined with less than -0.50D cylinder or with greater than -4.00D cylinder and greater than -8.00D spherical equivalent.
- for retreatment with wavefront-guided LASIK.

[7] Accutane Reg. TM of Hoffmann-La Roche Inc.
[8] Cordarone Reg. TM of Sanofi-Synthelabo
[9] Imitrex Reg. TM of Glaxo Group Limited

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 9mm.

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.

A contrast sensitivity study was conducted to assess the effects of myopic astigmatic LASIK surgery on how well patients can see in conditions such as very dim light, rain, snow, and fog. The results are presented below.

Under daylight testing conditions, contrast sensitivity after CustomCornea® LASIK surgery as compared to before surgery showed a:

- gain in 6.0% of patients at 3 months and 6.5% at 6 months.
- loss in 6.5% of patients at 3 months and 1.7% at 6 months.

Under dim light testing conditions, contrast sensitivity after CustomCornea® LASIK surgery as compared to before surgery showed a:

- gain in 18.5% of patients at 3 months and 22.4% at 6 months.
- loss in 8.6% of patients at 3 months and 7.3% at 6 months.

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 judgement should be exercised in the use of the LADARVision®4000 system in pseudophakic patients and others who have had prior intraocular or corneal 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.

E. ADVERSE EVENTS AND COMPLICATIONS

Cumulative adverse events and complications reported in a clinical study at any postoperative visit up to 6 months 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	%
Corneal cap edema at one month or later (related to microkeratome)	2/331	0.6%
Free Cap (related to microkeratome)	1/331	0.3%
Miscreated flap (related to microkeratome)	1/332 §	0.3%
COMPLICATIONS		
Corneal edema at one week to less than one month	5/331	1.5%
Diffuse lamellar keratitis	3/331	0.9%
Double/ghost images	2/331	0.6%
Epithelium in the interface	3/331	0.9%
Foreign body sensation at one month or later	2/331	0.6%
Striae	1/331	0.3%

§ One eye did not receive laser ablation after the miscreated flap and was not included in the primary cohort analysis.

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

- pain at one month or later;
- corneal epithelial defect at one month or later;
- corneal infiltrate or ulcer;
- late onset of corneal haze at six months with a loss of 2 or more lines of best spectacle corrected visual acuity (BSCVA);
- loss of more than 10 letters (more than 2 lines) of BSCVA at six months;
- epithelium in the interface with a loss of 2 or more lines of BSCVA;
- melting of the flap;
- misaligned flap;
- intraocular pressure (IOP) of more than 25 mmHg;
- IOP increase of more than 10 mmHg above baseline;
- retinal detachment;
- retinal vascular accident.

4. CLINICAL STUDY

A. *INTRODUCTION*

The study in the U.S. 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 inclusion and exclusion criteria, study procedures, subject measurements, and the treatment applied to the eye. The objective of the multi-center clinical investigation was to establish safety and effectiveness of wavefront-guided CustomCornea® LASIK correction of myopia and astigmatism. Patients were followed on Day 1, at 1 week, and at 1, 3, and 6 months postoperatively.

To be eligible for the study, patients had to have the following criteria: at least 18 years of age; up to -15.00D sphere with up to -6.00D of astigmatism and up to -15.00D MRSE at the spectacle plane; best spectacle corrected visual acuity (BSCVA) of 20/25 or better; and a stable manifest refraction, as documented by a change in sphere and cylinder of up to 0.50D per year for an MRSE up to 6.00D of myopia, or up to 0.75D for an MRSE greater than 6.00D of myopia. 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. The preoperative manifest and cycloplegic refraction must have been within 0.50D of each other in the sphere and cylinder components for an MRSE of less than 7.00D of myopia, or within 0.75D for an MRSE greater than or equal to 7.00D of myopia. All eyes were required to be treated for emmetropia. Contact lens wearers had to abstain from contact lens use prior to baseline examination for 2 to 3 weeks. Subjects who had worn RGP and PMMA lenses were required to show stability of refraction without lens wear.

Patients who exhibited any of the following conditions were excluded: previous intraocular, corneal or strabismus surgery; history of or active ocular disease; glaucoma or glaucoma filtering surgery; clinically significant corneal scar within the ablation zone or corneal abnormality such as recurrent erosion or severe basement membrane disease; progressive or unstable myopia; keratoconus; irregular corneal astigmatism; history of herpes keratitis; autoimmune or connective tissue disease; clinically significant atopic syndrome; 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; known allergy to study medications; residual posterior stromal thickness of less than 250 microns; inability to achieve a pupillary dilation of ≥ 7mm; at risk of angle closure; or an inability to obtain a clear and complete wavefront image.

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

B. RESULTS

1. Demographics

The demographics of the CustomCornea® study shown in Table 2 were typical for a refractive surgery trial performed in the U.S. The mean subject age was 37 years with a range from 19 to 57 years. The gender distribution was 59.2% males and 40.8% females. The racial distribution consisted of 94.6% Caucasian, 2.4% Asian, 1.8% Hispanic, 0.6% Black and 0.6% East Indian. The treatment of right and left eyes was approximately equal. The majority (65.3%) of subjects had a history of soft contact lens wear, 24.2% had no history of contact lens wear, and 10.6% had a history of RGP or PMMA lens wear.

Table 2. Demographics

331 Eyes of 167 Enrolled Subjects			
Age (In Years)			
Average ± Standard Deviation		37.0 ± 9.0	
Minimum to Maximum		19 to 57	
Race		**Number**	**% Eyes**
	Asian	8	2.4%
	Black	2	0.6%
	Caucasian	313	94.6%
	East Indian	2	0.6%
	Hispanic	6	1.8%
Gender:	Female	135	40.8%
	Male	196	59.2%
Eye:	Left	166	50.2%
	Right	165	49.8%
Contact Lens History:	None	80	24.2%
	PMMA	4	1.2%
	RGP	31	9.4%
	Soft	216	65.3%

PMMA = Polymethyl methacrylate; RGP = Rigid gas permeable

2. Preoperative Manifest Refraction Parameters

Table 3 displays the number of eyes stratified by preoperative manifest sphere and cylinder.

Table 3. Preoperative Manifest Refraction Stratified By Sphere & Cylinder

SPHERE (D)		CYLINDER (D) 0 to -0.49	-0.50 to -0.99	-1.0 to -1.99	-2.0 to -2.99	-3.0 to -3.99	-4.0 to -5.0	TOTAL
0.0 to -0.99	n/N	0/331	3/331	11/331	8/331	2/331	1/331	25/331
	%	0.0%	0.9%	3.3%	2.4%	0.6%	0.3%	7.6%
-1.0 to -1.99	n/N	16/331	14/331	20/331	7/331	3/331	2/331	62/331
	%	4.8%	4.2%	6.0%	2.1%	0.9%	0.6%	18.7%
-2.0 to -2.99	n/N	8/331	16/331	20/331	8/331	4/331	0/331	56/331
	%	2.4%	4.8%	6.0%	2.4%	1.2%	0.0%	16.9%
-3.0 to -3.99	n/N	18/331	16/331	21/331	1/331	1/331	1/331	58/331
	%	5.4%	4.8%	6.3%	0.3%	0.3%	0.3%	17.5%
-4.0 to -4.99	n/N	7/331	18/331	19/331	2/331	0/331	0/331	46/331
	%	2.1%	5.4%	5.7%	0.6%	0.0%	0.0%	13.9%
-5.0 to –5.99	n/N	11/331	8/331	12/331	2/331	1/331	0/331	34/331
	%	3.3%	2.4%	3.6%	0.6%	0.3%	0.0%	10.3%
-6.0 to –6.99	n/N	6/331	5/331	9/331	0/331	0/331	0/331	20/331
	%	1.8%	1.5%	2.7%	0.0%	0.0%	0.0%	6.0%
-7.0 to –7.99	n/N	4/331	12/331	2/331	1/331	0/331	0/331	19/331
	%	1.2%	3.6%	0.6%	0.3%	0.0%	0.0%	5.7%
-8.0 to –8.99	n/N	3/331	2/331	2/331	0/331	0/331	0/331	7/331
	%	0.9%	0.6%	0.6%	0.0%	0.0%	0.0%	2.1%
-9.0 to –9.75	n/N	1/331	0/331	3/331	0/331	0/331	0/331	4/331
	%	0.3%	0.0%	0.9%	0.0%	0.0%	0.0%	1.2%
TOTAL	n/N	74/331	94/331	119/331	29/331	11/331	4/331	331/331
	%	22.4%	28.4%	36.0%	8.8%	3.3%	1.2%	100.0%

(D) = Diopter

3. Accountability

Table 4 shows the accountability for this study, which was 100% at 1, 3 and 6 months. All 331 eyes were available at 1, 3 and 6 months.

Table 4. Accountability at Each Visit

			1 MONTH	3 MONTHS	6 MONTHS
Total Enrolled:	Primary	n	167	167	167
	Fellow	n	164	164	164
	Total	N	331	331	331
Available for Analysis		n	331	331	331
		%	100.0%	100.0%	100.0%
Not Eligible for Interval / In Process:		n	0	0	0
		%	0.0%	0.0%	0.0%
Unavailable Missed Visit / Lost to Follow-up		n	0	0	0
		%	0.0%	0.0%	0.0%
% Accountability= [available/(available + unavailable)]			100.0%	100.0%	100.0%

4. Key Efficacy and Safety Results

The primary cohort consisted of 331 eyes including 74 spherical myopic eyes with less than -0.50D cylinder and 257 myopic astigmatic eyes with -0.50D to -5.00D cylinder based on manifest refraction. The effectiveness cohort consisted of 232 myopic astigmatic eyes with -0.50D to -5.00D cylinder, and the safety cohort consisted of all 331 eyes.

Preoperatively, only 3.0% of myopic astigmatic eyes had a UCVA of 20/40 or better. A postoperative UCVA of 20/40 or better was reported in 99.1% of myopic astigmatic eyes at 3 months and 97.4% at 6 months. The MRSE was within 0.50D of emmetropia in 78.0% of myopic astigmatic eyes and within 1.0D in 92.2% at 3 months. Similarly at 6 months, the MRSE was within 0.50D of emmetropia in 80.2% of myopic astigmatic eyes and within 1.0D in 91.8%. Of the myopic astigmatic eyes that did not achieve an MRSE within 1D of emmetropia, all were overcorrected except one eye was undercorrected at 3 months and three eyes were undercorrected at 6 months. Overcorrection greater than 1D of MRSE was seen in 7% of the cohort, with 0.4% overcorrected by greater than 2D MRSE at 3 months. Cycloplegic refraction SE overcorrection of greater than 1D was seen in 18% of the eyes, with 2% being overcorrected by greater than 2D at 3 months.

No eyes lost > 2 lines of BSCVA from preoperative or had a BSCVA of worse than 20/40 at any interval. At 1 month, 2.4% of eyes lost 2 lines of BSCVA. At 3 and 6 months, there was no loss of more than 1 line of BSCVA. No eyes had an induced cylinder magnitude of greater than 1.25D at any postoperative interval.

The key safety and efficacy results are shown over time in Table 5. The key safety and efficacy results at 3 and 6 months after surgery are stratified by diopter of MRSE in Tables 6 and 7, respectively.

Table 5. Summary of Key Efficacy and Safety Variables Over Time

Efficacy Variables (Efficacy Cohort: 232 Myopic Astigmatic Eyes)		**1 Month**	**3 Months**	**6 Months**
UCVA 20/20 or better for eyes with preop BSCVA of 20/20 or better	n/N % CI	176/225 78.2% (72.3, 83.4)	182/225 80.9% (75.1, 85.8)	193/225 85.8% (80.5, 90.1)
UCVA 20/20 or better	n/N % CI	177/232 76.3% (70.3, 81.6)	184/232 79.3% (73.5, 84.3)	195/232 84.1% (78.7, 88.5)
UCVA 20/25 or better	n/N % CI	217/232 93.5% (89.6, 96.3)	223/232 96.1% (92.8, 98.2)	219/232 94.4% (90.6, 97.0)
UCVA 20/40 or better	n/N % CI	229/232 98.7% (96.3, 99.7)	230/232 99.1% (96.9, 99.9)	226/232 97.4% (94.5, 99.0)
MRSE ±0.50D of intended	n/N % CI	186/232 80.2% (74.5, 85.1)	181/232 78.0% (72.1, 83.2)	186/232 80.2% (74.5, 85.1)
MRSE ±1.00D of intended	n/N % CI	213/232 91.8% (87.5, 95.0)	214/232 92.2% (88.0, 95.3)	213/232 91.8% (87.5, 95.0)
MRSE ±2.00D of intended	n/N % CI	231/232 99.6% (97.6, 100.0)	231/232 99.6% (97.6, 100.0)	231/232 99.6% (97.6, 100.0)
Safety Variables (Safety Cohort: 331 Eyes)		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	n/N % CI	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)
Loss of 2 Lines BSCVA	n/N % CI	8/331 2.4% (1.0, 4.7)	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)
BSCVA worse than 20/40	n/N % CI	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)
Increase >2D cylinder magnitude	n/N % CI	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)	0/331 0.0% (0.0, 1.1)
BSCVA worse than 20/25 if 20/20 or better preoperatively	n/N % CI	0/323 0.0% (0.0, 1.1)	0/323 0.0% (0.0, 1.1)	0/323 0.0% (0.0, 1.1)

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

Table 6. Summary of Key Safety and Efficacy Variables at 3 Months Stratified by Diopter of Preop MRSE

		0 to -0.99D	-1 to -1.99D	-2 to -2.99D	-3 to -3.99D	-4 to -4.99D	-5 to -5.99D	-6 to -6.99D	-7 to -7.99D	-8 to -8.99D	-9 to -9.99D	-10 to -10.63D	Total
Efficacy Variables (Efficacy Cohort: 232 Myopic Astigmatic Eyes)													
UCVA 20/20 or better for eyes preop BSCVA 20/20 or better	n/N	2/2	27/31	39/46	29/36	32/38	23/32	10/13	14/18	3/4	2/2	1/3	182/225
	%	100.0%	87.1%	84.8%	80.6%	84.2%	71.9%	76.9%	77.8%	75.0%	100.0%	33.3%	80.9%
UCVA 20/20 or better	n/N	2/2	27/32	39/47	30/38	32/39	24/33	10/13	14/19	3/4	2/2	1/3	184/232
	%	100.0%	84.4%	83.0%	78.9%	82.1%	72.7%	76.9%	73.7%	75.0%	100.0%	33.3%	79.3%
UCVA 20/25 or better	n/N	2/2	32/32	44/47	38/38	37/39	31/33	12/13	18/19	4/4	2/2	3/3	223/232
	%	100.0%	100.0%	93.6%	100.0%	94.9%	93.9%	92.3%	94.7%	100.0%	100.0%	100.0%	96.1%
UCVA 20/40 or better	n/N	2/2	32/32	46/47	38/38	39/39	33/33	12/13	19/19	4/4	2/2	3/3	230/232
	%	100.0%	100.0%	97.9%	100.0%	100.0%	100.0%	92.3%	100.0%	100.0%	100.0%	100.0%	99.1%
MRSE ±0.50D of intended	n/N	2/2	32/32	39/47	28/38	34/39	21/33	9/13	12/19	1/4	1/2	2/3	181/232
	%	100.0%	100.0%	83.0%	73.7%	87.2%	63.6%	69.2%	63.2%	25.0%	50.0%	66.7%	78.0%
MRSE ±1.00D of intended	n/N	2/2	32/32	45/47	36/38	36/39	30/33	11/13	15/19	3/4	2/2	2/3	214/232
	%	100.0%	100.0%	95.7%	94.7%	92.3%	90.9%	84.6%	78.9%	75.0%	100.0%	66.7%	92.2%
MRSE ±2.00D of intended	n/N	2/2	32/32	47/47	38/38	39/39	33/33	13/13	18/19	4/4	2/2	3/3	231/232
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	94.7%	100.0%	100.0%	100.0%	99.6%
Safety Variables (Safety Cohort: 331 Eyes)													
Loss of >2 Lines BSCVA	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Loss of 2 Lines BSCVA	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
BSCVA worse than 20/40	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Increase >2D cylinder magnitude	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	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/N	0/2	0/55	0/55	0/57	0/51	0/44	0/21	0/24	0/7	0/4	0/3	0/323
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

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

Table 7. Summary of Key Safety and Efficacy Variables at 6 Months Stratified by Diopter of Preop MRSE

		0 to -0.99D	-1 to -1.99D	-2 to -2.99D	-3 to -3.99D	-4 to -4.99D	-5 to -5.99D	-6 to -6.99D	-7 to -7.99D	-8 to -8.99D	-9 to -9.99D	-10 to -10.63D	Total
Efficacy Variables (Efficacy Cohort: 232 Myopic Astigmatic Eyes)													
UCVA 20/20 or better for eyes preop BSCVA 20/20 or better	n/N	2/2	30/31	40/46	33/36	32/38	23/32	11/13	15/18	3/4	2/2	2/3	193/225
	%	100.0%	96.8%	87.0%	91.7%	84.2%	71.9%	84.6%	83.3%	75.0%	100.0%	66.7%	85.8%
UCVA 20/20 or better	n/N	2/2	30/32	40/47	33/38	32/39	24/33	11/13	16/19	3/4	2/2	2/3	195/232
	%	100.0%	93.8%	85.1%	86.8%	82.1%	72.7%	84.6%	84.2%	75.0%	100.0%	66.7%	84.1%
UCVA 20/25 or better	n/N	2/2	32/32	42/47	37/38	35/39	32/33	12/13	18/19	4/4	2/2	3/3	219/232
	%	100.0%	100.0%	89.4%	97.4%	89.7%	97.0%	92.3%	94.7%	100.0%	100.0%	100.0%	94.4%
UCVA 20/40 or better	n/N	2/2	32/32	45/47	38/38	36/39	33/33	12/13	19/19	4/4	2/2	3/3	226/232
	%	100.0%	100.0%	95.7%	100.0%	92.3%	100.0%	92.3%	100.0%	100.0%	100.0%	100.0%	97.4%
MRSE ±0.50D of intended	n/N	2/2	30/32	38/47	30/38	33/39	25/33	10/13	13/19	2/4	1/2	2/3	186/232
	%	100.0%	93.8%	80.9%	78.9%	84.6%	75.8%	76.9%	68.4%	50.0%	50.0%	66.7%	80.2%
MRSE ±1.00D of intended	n/N	2/2	32/32	45/47	34/38	35/39	31/33	11/13	15/19	3/4	2/2	3/3	213/232
	%	100.0%	100.0%	95.7%	89.5%	89.7%	93.9%	84.6%	78.9%	75.0%	100.0%	100.0%	91.8%
MRSE ±2.00D of intended	n/N	2/2	32/32	47/47	38/38	39/39	33/33	13/13	18/19	4/4	2/2	3/3	231/232
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	94.7%	100.0%	100.0%	100.0%	99.6%
Safety Variables (Safety Cohort: 331 Eyes)													
Loss of >2 Lines BSCVA	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Loss of 2 Lines BSCVA	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
BSCVA worse than 20/40	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Increase >2D cylinder magnitude	n/N	0/2	0/56	0/56	0/60	0/52	0/45	0/21	0/25	0/7	0/4	0/3	0/331
	%	0.0%	0.0%	0.0%	0.0%	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/N	0/2	0/55	0/55	0/57	0/51	0/44	0/21	0/24	0/7	0/4	0/3	0/323
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

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

5. 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 for myopic astigmatism is presented in Table 8. A postoperative UCVA was equal to or better than the preoperative BSCVA in 60.3% of eyes at 3 months and 67.2% at 6 months.

Table 8. Postoperative Uncorrected Visual Acuity Compared to Preoperative Best Spectacle Corrected Visual Acuity for Myopic Astigmatic Eyes

		3 MONTHS	6 MONTHS
UCVA **2 Lines Better** Than Preop BSCVA	n/N %	2/232 0.9%	3/232 1.3%
UCVA **1 Line Better** Than Preop BSCVA	n/N %	37/232 15.9%	50/232 21.6%
UCVA **Equal to** Preop BSCVA	n/N %	101/232 43.5%	103/232 44.4%
UCVA **1 Line Worse** Than Preop BSCVA	n/N %	61/232 26.3%	55/232 23.7%
UCVA **2 Lines Worse** Than Preop BSCVA	n/N %	26/232 11.2%	10/232 4.3%
UCVA **>2 Lines Worse** Than Preop BSCVA	n/N %	5/232 2.2%	11/232 4.7%

6. Stability of Manifest Refraction

The mean MRSE for myopic astigmatic eyes was stable between 1 and 3 months, as shown in Figure 1 and Table 9. A trend for slight overcorrection in spherical equivalent was observed. Stability of MRSE, defined as ≥ 95% of eyes with a change of ≤ 1.0D, was achieved by 3 months, as shown in Table 10 for the entire cohort of myopic astigmatic eyes.

Figure 1. Manifest Refraction Spherical Equivalent Over Time

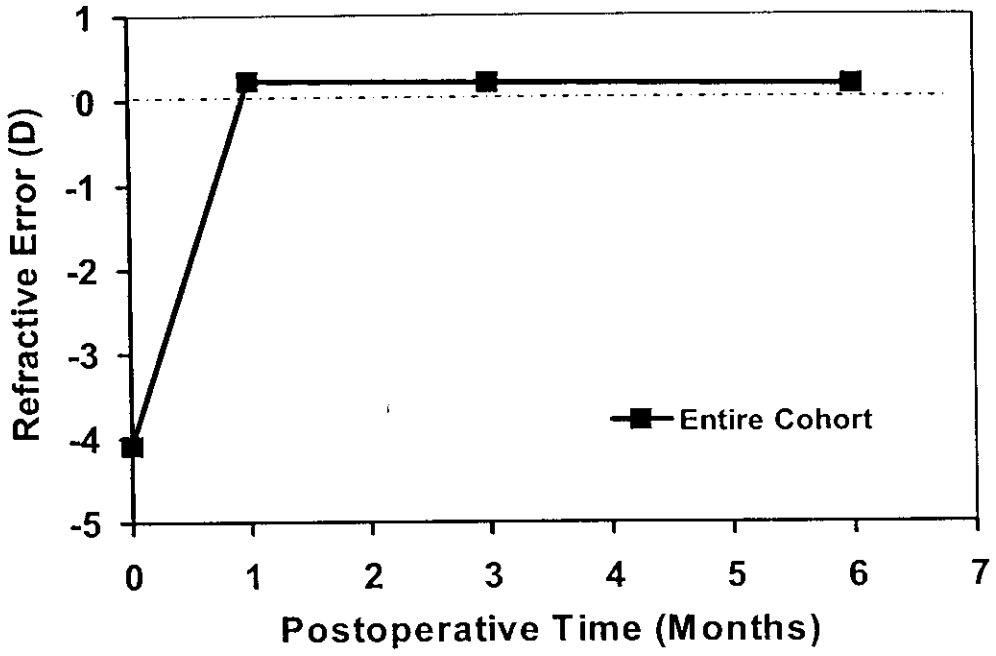


Table 9. Manifest Refraction Spherical Equivalent Over Time for Entire Cohort of Myopic Astigmatic Eyes				
Mean ± Standard Deviation (Diopter)	PREOP	1 MONTH	3 MONTHS	6 MONTHS
Entire Cohort (N=232)	-4.10 ± 2.04	+0.22 ± 0.52	+0.20 ± 0.52	+0.19 ± 0.54

Table 10. Stability of Manifest Refraction Spherical Equivalent for Entire Cohort of Myopic Astigmatic Eyes		
Change in Spherical Equivalent Between	1 AND 3 MONTHS (N=232)	3 AND 6 MONTHS (N=232)
≤1.00 Diopter [% (n/N)]	99.1% (230/232)	100.0% (232/232)
Mean Difference ± Standard Deviation	-0.02 ± 0.32	-0.01 ± 0.28
95% Confidence Interval	(-0.06, 0.02)	(-0.05, 0.02)

7. Efficacy of Astigmatic Correction

Efficacy of astigmatic correction was evaluated at the 3-month point of stability and additionally at 6 months for myopic astigmatic eyes with ≥ 0.50D of preoperative manifest cylinder. The mean percentage reduction in absolute cylinder was 65.7% at 3 months and 66.8% at 6 months for all astigmatic eyes (Table 11). A greater percentage reduction was observed in eyes with higher preoperative cylinder. The correction ratio for all astigmatic eyes was 1.04 at 3 months and 1.03 at 6 months, approaching the ideal value of 1.0 (Table 12).

Table 11. Mean Percentage Reduction of Absolute (Non-Vector) Cylinder for Myopic Astigmatic Eyes

		3 MONTHS	6 MONTHS
Preoperative Cylinder	**N**	**Mean %**	**Mean %**
All	232	65.7%	66.8%
0 to 0.50D	45	53.3%	60.0%
>0.50 to 1.00D	71	58.0%	58.5%
>1.00 to 2.00D	84	71.6%	70.9%
>2.00 to 3.00D	22	84.1%	83.6%
>3.00 to 4.00D	8	85.9%	86.9%
>4.00 to 5.00D	2	81.9%	85.0%

Table 12. Vector Analysis for Myopic Astigmatic Eyes

		3 MONTHS	6 MONTHS
Preoperative Cylinder	**N**	**Mean ± SD Correction Ratio**	**Mean ± SD Correction Ratio**
All	232	1.04 ± 0.37	1.03 ± 0.37
0 to 0.50D	45	1.08 ± 0.60	1.11 ± 0.56
>0.50 to 1.00D	71	1.04 ± 0.38	0.99 ± 0.43
>1.00 to 2.00D	84	1.01 ± 0.23	1.01 ± 0.23
>2.00 to 3.00D	22	1.04 ± 0.14	1.03 ± 0.13
>3.00 to 4.00D	8	1.04 ± 0.14	1.05 ± 0.13
>4.00 to 5.00D	2	1.12 ± 0.01	1.03 ± 0.05

8. Change in Best Spectacle Corrected Visual Acuity

Best spectacle corrected visual acuity (BSCVA) was measured using a standard (high-contrast) visual acuity chart under dim room illumination (10-12 cd/m^2). At 3 and 6 months, respectively, 92.7% and 91.5% of eyes had no change or a gain in BSCVA from preoperative (Table 13).

Table 13. Change in Best Spectacle Corrected Visual Acuity for All Eyes

		1 Month	3 Months	6 Months
Decrease >2 Lines	n/N	0/331	0/331	0/331
	%	0.0%	0.0%	0.0%
Decrease 2 Lines	n/N	8/331	0/331	0/331
	%	2.4%	0.0%	0.0%
Decrease 1 Line	n/N	35/331	24/331	28/331
	%	10.6%	7.3%	8.5%
No change	n/N	179/331	185/331	158/331
	%	54.1%	55.9%	47.7%
Increase 1 Line	n/N	107/331	116/331	137/331
	%	32.3%	35.0%	41.4%
Increase 2 Lines	n/N	2/331	6/331	8/331
	%	0.6%	1.8%	2.4%
Increase >2 Lines	n/N	0/331	0/331	0/331
	%	0.0%	0.0%	0.0%

Low contrast BSCVA was measured using a 10% low contrast visual acuity chart under dim room illumination. Change in low contrast BSCVA from preoperative is shown in Table 14. A trend for improvement in low contrast BSCVA was also observed following treatment with more eyes demonstrating a gain of ≥1 line as compared to a loss of ≥1 line at 3 and 6 months.

Table 14. Change in Low Contrast Best Spectacle Corrected Visual Acuity for All Eyes

		3 Months	6 Months
Decrease >2 Lines	n/N	3/331	2/331
	%	0.9%	0.6%
Decrease 2 Lines	n/N	14/331	10/331
	%	4.2%	3.0%
Decrease 1 Line	n/N	49/331	29/331
	%	14.8%	8.8%
No change	n/N	123/331	128/331
	%	37.2%	38.7%
Increase 1 Line	n/N	121/331	126/331
	%	36.6%	38.1%
Increase 2 Lines	n/N	20/331	29/331
	%	6.0%	8.8%
Increase >2 Lines	n/N	1/331	7/331
	%	0.3%	2.1%

9. Change in Contrast Sensitivity

A contrast sensitivity study was conducted to assess the effects of CustomCornea® LASIK surgery for myopic astigmatism on how well patients can see in conditions such as very dim light, rain, snow, and fog. Contrast sensitivity was measured under both photopic and mesopic conditions using CSV-1000 (VectorVision) (Table 15). A clinically significant change from preoperative level was defined as > 2 levels (> 0.3 log) at two or more spatial frequencies.

Under photopic conditions, the percentage of eyes with a gain or loss in contrast sensitivity was approximately equal at 3 months, but more eyes had a gain compared to loss at 6 months. Photopic contrast sensitivity gain was observed in 6.0% of eyes at 3 months and 6.5% at 6 months, whereas loss was observed in 6.5% and 1.7% of eyes at these respective visits. Under mesopic conditions, a higher percentage of eyes had a postoperative gain as compared to loss. Mesopic contrast sensitivity gain was observed in 18.5% of eyes at 3 months and 22.4% at 6 months, whereas loss was observed in 8.6% and 7.3% of eyes at these respective visits. At 6 months, 98.3% of eyes had no change or improvement under photopic conditions and 92.7% had no change or improvement under mesopic conditions.

Table 15. Change of >2 Levels (> 0.3 Log) on CSV-1000 at 2 or More Spatial Frequencies for Myopic Astigmatic Eyes

	Photopic Conditions			
	Decrease		Increase	
	3 Months	6 Months	3 Months	6 Months
n/N	15/232	4/232	14/232	15/232
%	6.5%	1.7%	6.0%	6.5%
	Mesopic Conditions*			
	Decrease		Increase	
	3 Months	6 Months	3 Months	6 Months
n/N	20/232	17/232	43/232	52/232
%	8.6%	7.3%	18.5%	22.4%

*Mesopic illumination with neutral density filters in front of eyes

10. Patient Symptoms and Satisfaction

Patients were asked to rate symptoms at 3 and 6 months after CustomCornea® LASIK surgery *without* glasses or contact lenses compared to before surgery *with* glasses or contact lenses (Table 16). Postoperatively, patients rated symptoms *without* correction as significantly better, better, no change, worse, or significantly worse than preoperative *with* correction.

Table 16. Postoperative Change in Subjective Symptoms without Correction vs. Preoperative with Correction for Myopic Astigmatic Eyes

Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
3 MONTHS (N=232)					
Blurring of Vision	9.1%	10.3%	67.2%	12.1%	1.3%
Burning*	6.1%	11.7%	77.0%	5.2%	0.0%
Double Vision†	7.4%	3.0%	81.8%	5.2%	2.6%
Dryness	7.8%	14.7%	52.2%	23.3%	2.2%
Excessive Tearing*	5.2%	6.1%	88.7%	0.0%	0.0%
Fluctuation of Vision	9.1%	10.8%	55.6%	22.4%	2.2%
Glare†	6.1%	14.3%	57.1%	20.8%	1.7%
Gritty Feeling	7.8%	9.9%	72.0%	9.5%	0.9%
Halos	6.5%	14.2%	58.2%	19.8%	1.3%
Headache	6.0%	9.9%	78.9%	5.2%	0.0%
Light Sensitivity	4.3%	14.7%	58.6%	21.6%	0.9%
Night Driving Difficulty	7.3%	21.6%	59.9%	9.5%	1.7%
Pain	6.0%	8.6%	81.9%	3.4%	0.0%
Redness	6.5%	10.3%	77.2%	5.6%	0.4%
6 MONTHS (N=232)					
Blurring of Vision	10.8%	10.3%	62.5%	15.9%	0.4%
Burning†	7.4%	11.3%	77.1%	3.5%	0.9%
Double Vision	9.5%	4.3%	78.9%	6.9%	0.4%
Dryness	11.2%	14.2%	55.2%	17.7%	1.7%
Excessive Tearing*	6.5%	4.3%	89.1%	0.0%	0.0%
Fluctuation of Vision	11.6%	9.9%	60.3%	16.4%	1.7%
Glare	9.9%	18.5%	58.2%	13.4%	0.0%
Gritty Feeling	12.1%	10.3%	73.3%	4.3%	0.0%
Halos	10.8%	17.7%	54.3%	16.4%	0.9%
Headache	9.9%	12.1%	74.6%	2.6%	0.9%
Light Sensitivity	7.8%	18.5%	57.3%	15.9%	0.4%
Night Driving Difficulty	15.9%	20.3%	53.4%	10.3%	0.0%
Pain*	8.3%	9.6%	79.6%	2.6%	0.0%
Redness	9.1%	16.8%	72.8%	1.3%	0.0%

*N=230 †N=231

Postoperative quality of vision *without* correction as compared to preoperative quality of vision *with* correction was rated as unchanged, better, or significantly better in 93.1% of patients at 3 months and 94.4% at 6 months (Table 17). There were 88.3% of patients at 3 months and 87.9% at 6 months who reported they were satisfied or extremely satisfied with their results (Table 18). Distance correction was never worn by 93.9% of the patients at 3 months and 94.8% at 6 months (Table 19).

Table 17. Postoperative Quality of Vision without Correction vs. Preoperative with Correction for Myopic Astigmatic Eyes

	3 MONTHS N=231	6 MONTHS N=232
Significantly Better	55.8%	63.8%
Better	28.1%	21.1%
Same	9.1%	9.5%
Worse	5.2%	5.2%
Significantly Worse	1.7%	0.4%

Table 18. Postoperative Satisfaction with Surgery for Myopic Astigmatic Eyes

	3 MONTHS N=230	6 MONTHS N=232
Extremely Satisfied	57.8%	67.7%
Satisfied	30.4%	20.3%
Not Sure	8.7%	6.9%
Unsatisfied	1.3%	5.2%
Extremely Unsatisfied	1.7%	0.0%

Table 19. Postoperative Frequency of Distance Correction for Myopic Astigmatic Eyes

	3 MONTHS N=231	6 MONTHS N=230
Never	93.9%	94.8%
Seldom	3.5%	0.0%
Frequently	0.9%	3.5%
Constantly	1.7%	1.7%

11. Retreatment

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

12. Change in Higher-Order Aberrations

Wavefront aberrations were analyzed through 6th-order for CustomCornea® myopic astigmatic eyes. At 3 months, there was an average reduction in total RMS wavefront error by 84.5% and an average increase in higher-order aberrations by 19.4% from preoperative (Table 20). Six-month data showed similar trends with an average reduction in total RMS wavefront error by 85.0% and an average increase in higher-order aberrations by 20.6% from preoperative.

Table 20. Mean Percentage Change in Aberrations Up to 6th-Order From Preoperative for Myopic Astigmatic Eyes

Aberration	3 MONTHS N = 232	6 MONTHS N = 232
Total RMS	-84.5%	-85.0%
Higher-Order	19.4%	20.6%
Coma	10,1%	9.1%
Trefoil	17.7%	18.5%
Spherical Aberration	-6.8%	0.1%
Secondary Astigmatism	64.2%	70.6%
Tetrafoil	67.9%	67.5%
Combined 5th and 6th Order	103.3%	100.3%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

All eyes had a postoperative reduction in total wavefront RMS error and 42.2% had a reduction in higher-order aberrations at 3 and 6 months (Table 21).

Table 21. Percentage of Eyes with Reduced Aberrations Up to 6th-Order From Preoperative for Myopic Astigmatic Eyes

Aberration	3 MONTHS N = 232	6 MONTHS N = 232
Total RMS	100.0%	100.0%
Higher-Order	42.2%	42.2%
Coma	47.4%	50.0%
Trefoil	47.0%	44.8%
Spherical Aberration	53.9%	51.7%
Secondary Astigmatism	30.2%	31.0%
Tetrafoil	28.9%	30.2%
Combined 5th and 6th Order	7.8%	8.2%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

In addition, CustomCornea® LASIK eyes were compared to Conventional LASIK eyes based on manifest phoropter refraction treated in the study over the same preoperative refractive range of up to -7.00D sphere with -0.50D to -2.50D cylinder. Wavefront aberrations were analyzed up to 4th-order for comparison.

The amount of postoperative higher-order aberrations was significantly less for the CustomCornea® LASIK eyes than for the Conventional LASIK eyes (Table 22). The average increase in higher-order aberrations after surgery was:

- 6.9% at 3 months and 8.1% at 6 months following CustomCornea® LASIK.
- 55.4% at 3 months and 56.9% at 6 months following Conventional LASIK.

Table 22. Mean Percentage Change in Aberrations Up to 4th-Order From Preoperative for Myopic Astigmatic Eyes

	3 Months		6 Months	
Aberration	**CustomCornea®** N = 197	**Conventional** N = 84	**CustomCornea®** N = 197	**Conventional** N = 88
Total RMS	-84.7	-75.1	-85.3	-74.8
Higher-Order	6.9	55.4	8.1	56.9
Coma	1.5	51.6	-1.5	40.0
Trefoil	4.4	2.3	6.9	9.3
Spherical Aberration	-8.6	139.5	-2.3	154.3
Secondary Astigmatism	52.9	38.1	55.9	47.6
Tetrafoil	49.3	57.5	50.7	41.1

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

For approximately one-half of patients, CustomCornea® LASIK reduced higher-order aberrations from baseline levels prior to surgery. The percentage of patients with reduced higher-order aberrations (Table 23) after surgery compared to before surgery was:

- 47.7% at 3 months and 49.2% at 6 months for CustomCornea® LASIK.
- 17.9% at 3 months and 19.3% at 6 months for Conventional LASIK.

Table 23. Percentage of Eyes with Reduced Aberrations Up to 4th-Order From Preoperative for Myopic Astigmatic Eyes

	3 Months		6 Months	
	CustomCornea® N = 197	**Conventional** N = 84	**CustomCornea®** N = 197	**Conventional** N = 88
Total RMS	100.0%	96.4%	100.0%	97.7%
Higher Order	47.7%	17.9%	49.2%	19.3%
Coma	50.8%	34.5%	53.8%	38.6%
Trefoil	49.2%	52.4%	47.2%	47.7%
Spherical Aberration	55.3%	16.7%	54.3%	13.6%
Secondary Astigmatism	32.0%	40.5%	33.0%	25.0%
Tetrafoil	31.0%	25.0%	32.0%	37.5%

RMS = Root Mean Square Wavefront Analysis Diameter = 6.0mm

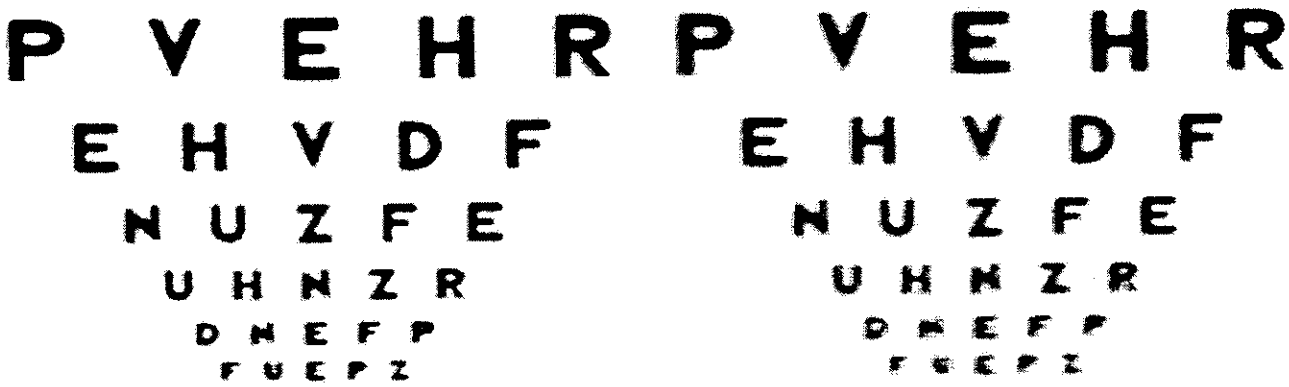
A vision simulation program was used to model the effect of various wavefront errors on a simulated eye chart image for CustomCornea® and Conventional LASIK eyes with myopic astigmatism. Visual comparisons of letter charts blurred by higher-order aberrations suggest that the benefit of smaller amounts of higher-order aberrations after wavefront-guided CustomCornea® LASIK surgery compared to Conventional LASIK corresponds to approximately 0.2D of defocus on average.

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

DO NOT REPRODUCE THE CHARTS BELOW

Figure 2. Difference in Higher-Order Aberrations using the LADARVision®4000 System for Correction of Myopic Astigmatism

After CustomCornea® | **LASIK After Conventional LASIK**



13. Statistical Analysis Outcomes

Logistic regression analysis was performed to investigate the association between various baseline and demographic characteristics and outcomes related to CustomCornea® LASIK for correction of myopic astigmatism. This approach provided the ability to assess the effect of one variable while controlling for other factors that influence outcome. Outcomes assessed included uncorrected visual acuity (UCVA), accuracy of manifest refraction spherical equivalent (MRSE), and loss of best spectacle corrected visual acuity (BSCVA). Since there was no loss of 2 or more lines of BSCVA at 3 or 6 months, statistical analysis could not be performed on this outcome.

Statistical analysis showed that age, preoperative cylinder, and room temperature were found to be associated with achieving a UCVA of 20/20 or better at 6 months. Age was also associated with a UCVA of 20/40 or better at 6 months. While the FDA guidance document does not specify performance requirements for a UCVA of 20/20 or better, the results for all subgroups, met or exceeded the FDA guidance standard that requires at least 85% of eyes to achieve a UCVA of 20/40 or better.

At 6 months, a UCVA of 20/20 or better and a UCVA of 20/40 or better were more likely to be achieved in subjects less than 50 years of age, although all ages stratified by decade met the FDA guidance standard for UCVA of 20/40 or better. A UCVA of 20/20 or better was more likely to be achieved in eyes with less than -4D preoperative cylinder; however, all cylinder subgroups by diopter exceeded the FDA guidance standard for a UCVA of 20/40 or better. The mean room temperature during surgery for eyes with a UCVA of 20/20 or better was slightly higher than for eyes that did not achieve 20/20, although the mean difference between the two groups was < 1°F.

Statistical analysis showed that age, preoperative sphere, temperature and humidity were significantly associated with an accuracy of MRSE within 0.50D of emmetropia. At 6 months, the results for all subgroups, except for one sphere subgroup with 3 eyes, met or exceeded the FDA guidance standard of ≥ 50% of eyes with an MRSE within 0.50D.

While subjects less than 50 years of age were more likely to have an MRSE within 0.50D, all ages stratified by decade met the FDA guidance standard. Eyes with less than -8D preoperative sphere were more likely to achieve an MRSE within 0.50D, although eyes in all other sphere subgroups including eyes with a sphere between -9.0 and -9.75D were within the FDA guidance standard. The mean room temperature during surgery was slightly lower for eyes that had an MRSE within 0.50D than for eyes that did not, but the difference between the groups was < 1°F. Similarly, while the difference between the groups was < 1%, the room humidity during surgery was slightly higher for eyes that had an MRSE within 0.50D than for eyes that did not.

Age, preoperative sphere, gender and humidity were associated with an accuracy of MRSE within 1.0D of emmetropia. At 6 months, the results for all subgroups, except for one sphere subgroup, met or exceeded the FDA guidance standard of ≥ 75% of eyes with an MRSE within 1.0D.

Subjects less than 50 years of age were more likely to have an MRSE within 1.0D; however, all ages stratified by decade met the FDA guidance standard. Eyes in all sphere subgroups up to -9.75D met the FDA guidance standard, except for the range between -7 to -7.99D preoperative sphere. Slightly more males than females achieved an MRSE within 1.0D; however, the mean preoperative MRSE was higher for females who did not achieve an MRSE within 1.0D. An MRSE within 1.0D was more likely to be achieved at lower room humidity during surgery than for eyes that were not within 1.0D, although the mean difference between the two groups was < 3%.

The same factors, age, preoperative sphere, gender and humidity, were also associated with overcorrection of the MRSE by more than 1.0D at 6 months. Higher room humidity was associated with undercorrection of the MRSE by more than 1.0D; however, only three eyes had undercorrection more than 1.0D at 6 months.

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 study[10] demonstrated that:

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

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

5. PLANNING AND PROCEDURES

A. *PATIENT SELECTION*

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

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

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

B. OPERATIVE PROCEDURE

Note: Before proceeding, please refer to the LADARVision®4000 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. After the wavefront measurement is taken with a compatible wavefront measurement device, such as the LADARWave® system, the surgeon reviews the planned wavefront-guided treatment and ablation depth and refines as indicated with the CustomCornea® Surgery Planning Software prior to the surgery session.

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

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

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

1. Centration and Registration

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

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

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

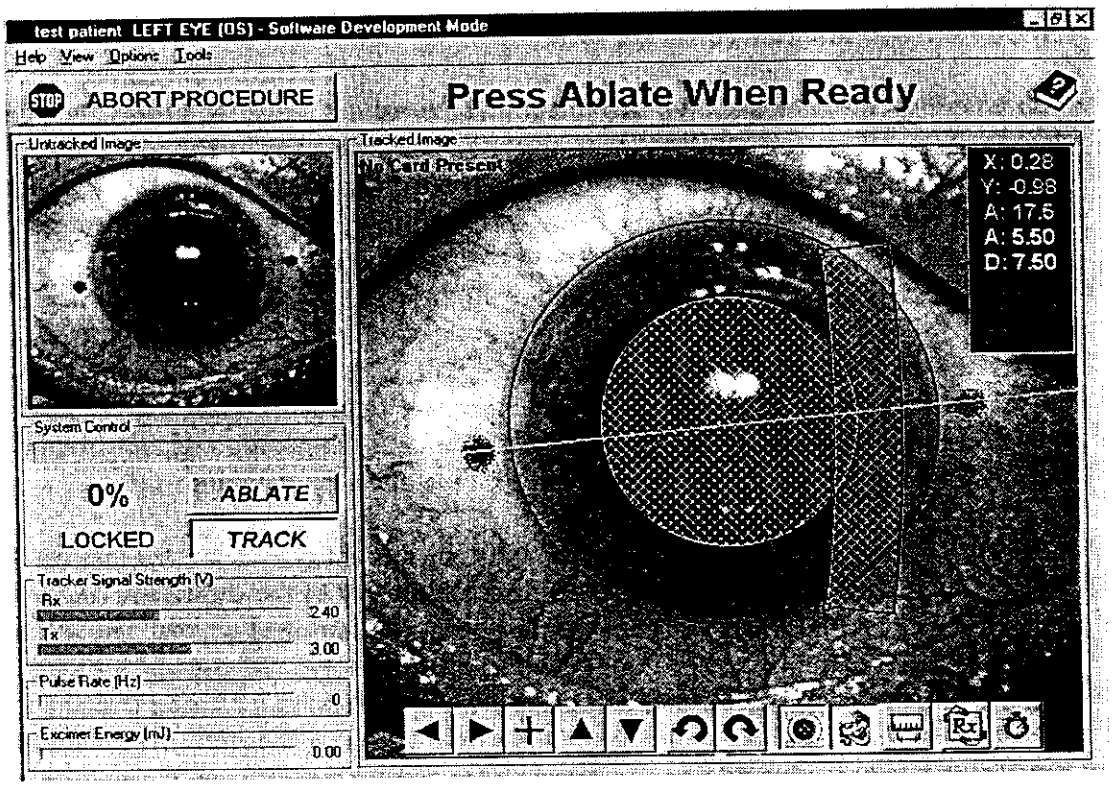
The surgeon reviews the diagnostic wavefront data and plans the wavefront-guided treatment using the CustomCornea® Surgery Planning Software. The planned treatment file is transferred to the LADARVision®4000 system computer by disk, where the appropriate ablation laser shot pattern is generated. The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

2. Pupil Dilation

It is necessary to dilate the pupil to 7mm prior to surgery to engage the tracking system. A combination of 2.5% phenylephrine (MYDFRIN® solution) and 1% tropicamide (MYDRIACYL® 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.

Figure 3. 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 is created using a microkeratome. The software allows the surgeon to check position of the ablation zone with respect to the flap by using an ablation zone indicator on the computer screen.

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

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

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

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

C. POSTOPERATIVE PROCEDURE

Postoperative pharmaceutical treatment consists of one drop of a broad-spectrum antibiotic and, 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 on Day 1. 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.

Alcon®

CustomCornea® Surgery Planning Software

System Operation Manual*

For Use With the

LADARVISION 4000
Excimer Laser System

* A FULL COPY OF THIS MANUAL IS LOCATED IN AMMENDMENT 3

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