CARL ZEISS MEDITEC INC.
MEL 80 Excimer Laser System

LASER IN SITU KERATOMILEUSIS (LASIK) PROFESSIONAL USE INFORMATION

The MEL 80 Excimer Laser is indicated for use in primary Laser Assisted *in situ* Keratomileusis (LASIK) treatments for the reduction or elimination of naturally occurring hyperopia of less than or equal to +5.0 D with or without refractive astigmatism of > +0.5 D and ≤ +3.0 D, with a maximum MRSE of +5.0 D, in patients who are 21 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by change in sphere and cylinder of ≤ 0.5 D.

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 practitioner. U.S. Federal Law restricts 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 Carl Zeiss Meditec MEL 80 Excimer Laser System. For complete information concerning system components, safety instructions, installation, maintenance, and troubleshooting, refer to the Carl Zeiss Meditec MEL 80 Excimer Laser System User Manual.

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

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CARL ZEISS MEDITEC INC.
MEL 80 EXCIMER LASER SYSTEM
PROFESSIONAL USE INFORMATION

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SECTION 1

SAFETY CONSIDERATIONS & GENERAL WARNINGS

Restricted Device: Federal (U.S.) law restricts these devices to sale by, or on the order of, a physician.

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

Warning: Specific training from Carl Zeiss Meditec or an authorized representative of Carl Zeiss Meditec is required before anyone is qualified to operate the MEL 80 Excimer Laser. Read and understand the MEL 80 Excimer Laser User Manual before operating this system.

Refer to the MEL 80 Excimer Laser System User Manual for additional warnings regarding the use of this system.

High Pressure Gas Cylinders
In the MEL 80 Excimer Laser, pressure vessels are used. Observe the relevant national and international regulations. If you notice a pungent smell (fluorine gas), open the windows, leave the room, and call the Carl Zeiss Meditec Service Department.

Warning of High-Energy Radiation
The MEL 80 Excimer Laser is a medical laser device that emits high-intensity ultraviolet radiation with energy levels of up to 2 mJ. These energy levels and short pulse durations result in extreme pulse powers and, if applied in an uncontrolled manner, may cause severe injury.

Warning for Reflective Material
Consider that reflective material may deflect the laser beam in an uncontrollable manner.

SECTION 2
DEVICE DESCRIPTION

2.1 LASER SYSTEM

The specifications for the Carl Zeiss Meditec MEL 80 Excimer Laser System are provided below. This laser is locked out for treatments exceeding +5.0 D sphere and +5.0 D MRSE. The laser is also locked out for cylinder ≤ +0.50 D and > +3.0 D. Optical zones below 6.0 mm and above 6.5 mm are also locked out.

Laser Type:	Argon Fluoride
Laser Wavelength:	193 nanometers
Laser Pulse Duration:	4 to 7 nanoseconds
Laser Head Repetition Rate:	250 Hz
Effective Corneal Repetition Rate:	12.5 Hz
Fluence (at the treatment area):	> 150 mJ/cm^2 (peak)
Laser Spot Size (FWHM diameter)	0.7 mm ± 0.1 mm
Range of Ablation Diameter:	For naturally occurring hyperopia, up to 10.0 mm (optical zone of 6.0 to 6.5 mm, with a transition zone of 2.0 to 4.0 mm. Note: the laser does not apply shots outside of the 10.0 mm diameter)
Eyetracker - Tracking frequency	250 Hz

2.1.1 Features and Components of the MEL 80 Excimer Laser System:

Laser Arm	The Laser Arm contains the operating microscope, the debris removal system (called CCA+), the galvanometric scanners, the eye tracking camera, a portion of the optical system, the control panel and the laser arm interface.
Laser Unit	The excimer laser unit consists of the laser head with high voltage power supply, the trigger unit and the laser interface. The communication with the central control unit PC104 is done fiber-optically via the laser interface, which also optically controls the trigger unit. The laser head is provided with premix gas by the gas handling system.

Optics	The optics form the excimer raw beam and guide it to the treatment plane by means of a beam shaper, two lenses, and different mirrors, so that a well-defined beam of Gaussian shape emerges. A vacuum pump is used to evacuate air present in the beam path; this function is initiated automatically when the laser is started.
PC104	The central control unit PC104 with laser control software (called POLO) provides the control of the whole laser system. It performs the following tasks: execution of the treatment (i.e. triggering of the laser head), monitoring and setting of the scanner position, control of the blower and plume suction (debris removal), communication with user interface software (called OPASS), execution of the gas management system functions, and energy control via high voltage setting and energy measuring.
Control Panel	The control panel provides control of the distance lasers (which are used for correct height adjustment of the patient's eye), the white light illumination, and the eyetracker parameters. The control panel displays messages in the event of a lost connection between OPASS and POLO via a mini display.
Eyetracker	A fast eyetracker unit ensures alignment of the laser beam to the eye of the patient. It is comprised of a 250 Hz infrared CCD camera, an infrared LED illumination system (810 nm) and a separate control computer (EyePAC).
Operating Microscope	An operating stereomicroscope (OPMI) allows the surgeon to observe the patient's eye during the treatment. An array of light emitting diodes (LEDs) provides the illumination for the OPMI.
Gas Handling System	The gas handling system consists of a flushing gas (helium) and a laser gas (premix) bottle, pipes, valves, pressure sensors, vacuum pump, filters (halogen), and pressure reducers. The central control unit performs an automatic gas change on user request. The bottles are placed inside the device.
CCA+ Debris Removal	A blower and suction unit called the cone for controlled atmosphere (CCA+) debris removal provides a controlled environment at the patient's eye by removing the debris. It is mounted on a swivel arm (the entire component is referred to as the CCA+ unit), and also carries the infrared illumination. The CCA+ unit can be moved away when not in use.
Patient Bed	A motor-driven patient bed is movable in all 3 dimensions (X-, Y- and Z-directions). In addition, the patient headrest can be moved in the Z-direction and can be tilted in a dorsal and ventral direction. The bed can be swung out manually for easy exit of the patient.
Slit Lamp (optional)	The slit lamp produces an evenly illuminated field approximately 8 cm in front of a reflecting prism, the geometry and color of which can be varied by the use of apertures and filters. The slit lamp has a 6V (10W) halogen bulb, a slit width of 0.15 mm to 0.75 mm, and a slit height and illumination field size of 2 mm to 12 mm (continuous).

SECTION 3

INDICATIONS, CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

3.1 INDICATIONS FOR USE

The MEL 80 Excimer Laser is indicated for use in primary Laser Assisted *in situ* Keratomileusis (LASIK) treatments for the reduction or elimination of naturally occurring hyperopia of less than or equal to +5.0 D with or without refractive astigmatism of > +0.5 D and ≤ +3.0 D, with a maximum MRSE of +5.0 D, in patients who are 21 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by change in sphere and cylinder of ≤ 0.5 D.

3.2 CONTRAINDICATIONS

Conditions under which risk of use outweighs possible benefit. LASIK surgery is contraindicated in:

- Patients with severe dry eye;
- Patients with active corneal infection or inflammation;
- Patients with glaucoma with marked optic nerve cupping, advanced visual field loss or visual acuity loss, because of the risk of further loss of visual function related to microkeratome-induced pressure spikes;
- Patients with projected residual corneal stromal bed thickness after ablation of less than 250 microns, because this may lead to ectasia;
- Patients with active connective tissue diseases or autoimmune diseases which have been associated with corneal melting, such as rheumatoid arthritis, Wegener's granulomatosis, relapsing polychondritis, and polyarteritis nodosa;
- Pregnant or nursing women;
- Patients with signs of ectatic disorders such as keratoconus or pellucid marginal degeneration;
- Patients with active, uncontrolled diabetes mellitus or visually significant diabetic complications;
- Patients with recent herpes keratitis (simplex or zoster) or significant corneal damage (poor sensation, scarring, neovascularization) from prior herpes infection; and
- Patients with immunodeficiency diseases, such as AIDS.

3.3 WARNINGS

Warnings are conditions for which there is reasonable evidence of serious risk with use of this device. There is reason to believe that there is increased risk for serious adverse consequences if LASIK surgery is performed in the following patients:

- Patients who are taking isotretinoin (Accutane®). This increases risk of dry eye and may cause increased complications after LASIK.
- Patients with significant dry eye. LASIK may increase dryness with accompanying discomfort and visual problems. (See Contraindications for related information.)
- Patients with severe allergies. Patients who rub their eyes a lot may be at risk for dislodging the corneal flap, since the strength of the flap attachment to underlying corneal layers is significantly and permanently reduced after surgery. Additionally, LASIK may increase the dryness often associated with anti-allergy medication.
- Patients with well-controlled diabetes mellitus. Diabetes may be related to poorer healing and a higher complication rate. (See Contraindications for related information.)
- Patients with well-controlled glaucoma, ocular hypertension, or are being followed for suspicion of glaucoma, because of the risk of steroid response causing disease progression, and the post-LASIK difficulty in accurately monitoring intraocular pressure due to changes in corneal thickness. (See Contraindications for related information.)
- Patients with a prior history of herpes simplex or herpes zoster keratitis, because it is possible that LASIK may lead to reactivation of the virus. (See Contraindications for related information.)
- Patients with stable and well-controlled connective tissue diseases or autoimmune diseases, because they may be slower healing and have less predictable outcomes. Additionally, the stability and control of the disease (and risk, if any, of corneal melt) may be difficult to quantify. Because of this difficulty, increased caution should be used if LASIK is considered in patients with well controlled, stable disease. The surgeon should consider consulting with the doctor who is treating the underlying disease. The surgeon should consider unilateral surgery. The surgeon should thoroughly discuss the potential risks with the patient. (See Contraindications for related information)
- Patients with inactive and controlled immunocompromised conditions, because they may be at increased risk of infection. (See Contraindications for related information.)
- Patients whose refractive error is not stable, because the correct refractive treatment is difficult to determine.
- Patients with a history of blepharitis.
- Patients with a history of eye rubbing. The LASIK flap never completely heals, and it can be dislodged by eye rubbing. Patients who are not sure they can refrain from rubbing their eyes after LASIK may not be good LASIK candidates.

3.4 PRECAUTIONS

The safety and effectiveness of LASIK with the MEL 80 Excimer Laser System has **NOT** been established in the following patients:

- Patients taking amiodarone hydrochloride (e.g., Cordarone®). Use can cause keratopathy and might affect epithelial healing after LASIK.
- Patients taking the medication sumatriptan succinate (Imitrex®).
- Patients with a family history of keratoconus, pellucid marginal degeneration or other ectatic disorders. Such patients should be carefully checked for an undiagnosed mild condition that may lead to post-LASIK ectasia.
- Patients with progressive hyperopia and/or astigmatism or ocular disease.
- Patients with corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage.
- Patients with a history of uveitis.
- Patients with previous corneal or intraocular surgery, or trauma.
- Patients who have had prior LASIK treatment.
- Patients under 21 years of age.
- Patients needing treatments of > +5.0 D of hyperopia, > +5.0 D MRSE, or with ≤ +0.5 D or > +3.0 D of astigmatism.
- Patients with large mesopic pupils, greater than optical zone size, as evaluated under mesopic illumination conditions. Such patients should be advised of the potential for negative effects on vision after LASIK, such as glare, halos, and night time driving difficulty.
- Patients with a history of strabismus who are being treated for hyperopia may have an increased risk of manifest exotropia after surgery.
- Patients with 0.75 D or more of latent hyperopia as determined by the difference between the preoperative MRSE and CRSE.
- Patients with media problems (corneal, lens, and/or vitreous opacities including, but not limited to, cataract).
- Patients with iris problems including, but not limited to, coloboma and previous iris surgery compromising proper eyetracking.
- Patients taking medications likely to affect wound healing including, but not limited to, antimetabolites.
- Patients with a history of keloid formation.
- Patients taking hormone replacement therapy or antihistamines who may experience delayed re-epithelialization of the cornea following surgery.
- Patients undergoing retreatment with the MEL 80 Excimer Laser System. The risk and accuracy of LASIK retreatment, or LASIK after another surgery to correct vision, has not been evaluated.
- Over the long term (more than 24 months after surgery).

A LASIK flap diameter that is minimally larger (i.e., larger by < 2.2 mm) than the optical zone size may result in decreased success rate.

Pupil size should be evaluated under mesopic illumination conditions. Effects of treatment on vision under poor illumination cannot be predicted prior to surgery. Some patients may find it more difficult than usual to see in conditions such as very dim light, rain, snow, fog, and glare from bright lights at night. These symptoms could be worsened in patients with large pupil sizes.

The optical zone should be (a) at least as large as the mesopic pupil and (b) small enough to leave at least 250 microns of residual stromal thickness. Prospective patients who cannot satisfy both of these criteria should be disqualified for treatment.

Preoperative evaluation for dry eye should be performed. This may be particularly important for patients who have been contact lens intolerant because of symptoms of dryness. Patients should be advised of potential for worsening of symptoms associated with dry eye syndrome post-LASIK surgery.

The effects of LASIK on visual performance under poor lighting conditions have not been fully characterized. It is possible that following LASIK treatment, patients will find it more difficult to see in conditions such as very dim light, rain, snow, fog, or glare from bright lights at night. Visual performance possibly could be worsened in patients with large pupil sizes.

Intraocular pressure is more difficult to interpret after LASIK because of the resulting corneal thinning. Patients should be informed that they should tell future eye care professionals that they have had LASIK.

Future intraocular lens calculations for cataract surgery may be affected by LASIK. The surgeon should give the patient a patient information card that has eye measurements from before the LASIK surgery. Patients should be advised to keep this card and give it to their future cataract surgeon.

The risk/benefit ratio of the LASIK procedure may be significantly increased in patients who have significantly reduced visual function in one eye (e.g., amblyopia).

Prior to surgery, prospective patients should be provided with a copy of the Patient Information Brochure for this product and informed of the possible risks and benefits associated with its use.

SECTION 4
CLINICAL RESULTS

4.1 STUDY OBJECTIVES

A prospective, non-randomized, multicenter clinical study of 369 eyes was conducted at six (6) clinical sites. Patients with spherical hyperopia and astigmatic hyperopia were treated with the MEL 80™ Excimer Laser, and followed for a 24-month period. The safety and effectiveness of the MEL 80™ Excimer Laser was determined by evaluation of the UCVA outcomes (at least 85% of laser treated eyes with UCVA of 20/40 or better), predictability (at least 50% of treated eyes with MRSE within ± 0.50 D deviation from attempted correction, and at least 75% of treated eyes with MRSE within ± 1.00 D deviation from attempted correction), stability of the postoperative MRSE, subject satisfaction, preservation of BSCVA, induced astigmatism, incidence of adverse events/complications, and patient symptoms.

Patients were screened for eligibility, and informed consent was obtained from those who met screening criteria and were interested in participating in the study. Eligible patients were examined preoperatively to obtain a medical history and to establish a baseline for ocular condition. Baseline and postoperative measurements (taken at 1 day, 7 days, 1 month, 3 months, 6 months, 9 months, 12 months, 18 months, and 24 months post-surgery) included manifest refraction, cycloplegic refraction, distance visual acuity (best corrected and uncorrected), slit-lamp examination, corneal topography (central keratometry via simulated K readings), pachymetry (baseline only), fundus examination, and intraocular pressure (IOP).

4.2 DATA ANALYSIS AND RESULTS

The safety summaries presented in this section were based on the entire PMA cohort while the effectiveness analyses were based on available data of treated eyes at each visit or available data for the treated subgroups. Due to aborted laser treatment, missing visits or examinations, and different subgroups, the safety cohort and effectiveness cohorts for the data analyses were different.

4.2.1 Demographics and Baseline Parameters

Demographic characteristics of the study population are presented in Table 1. The baseline refraction parameters stratified by MRSE and cylinder components are presented in Table 2.A for eyes treated for spherical hyperopia only and in Table 2.B for eyes treated for astigmatic hyperopia. The shaded columns indicate treatments outside of the approved range, and are not part of the effectiveness cohort. For eyes treated for spherical hyperopia only (Table 2.A), the mean MRSE with algorithm adjustment for the approved range was +2.468 D (SD 1.115).

For eyes treated for astigmatic hyperopia, the mean MRSE in the approved range was +2.965 D (SD 1.222) and the mean MRCYL was 0.970 D (SD 0.609); see Table 2.B. The intended correction was the full manifest refraction, with the goal of achieving a plano refraction after the surgery.

TABLE 1
DEMOGRAPHICS
ALL TREATED EYES

Demographics	Percentage	Number
NUMBER OF EYES & SUBJECTS[1]	369 Eyes of 189 Enrolled Subjects	
GENDER[2]		
Male	54.5%	103
Female	45.5%	86
RACE[2]		
White	94.7%	179
Black	3.2%	6
Asian	1.1%	2
Other	1.1%	2
SURGICAL EYE[2]		
Right	50.1%	185
Left	49.9%	184
AGE (in years)[2]		
Mean (SD)	46.6 (9.3)	
Minimum, Maximum	22.0, 69.0	

1 Two eyes had aborted procedures and were not included in the effectiveness analyses.
2 Gender, Race, and Age were based on subjects, but Surgical Eye is based on eyes.

TABLE 2.A
PREOPERATIVE REFRACTION PARAMETERS
STRATIFIED BY MRSE AND CYLINDER COMPONENTS
EYES TREATED FOR SPHERICAL HYPEROPIA ONLY

MRSE	Manifest Cylinder				Total	
	0.00 D		0.25 D			
	%	n/N	%	n/N	%	n/N
Without Algorithm Adjustment **MRSE: Mean: 2.468, SD: 1.270, Range: 1.25 to 5.88** **MRCYL:Mean: 0.065, SD: 0.112, Range: 0.00 to 0.25**						
0.00 to 1.00 D	0.0%	(0/27)	0.0%	(0/27)	0.0%	(0/27)
1.01 to 2.00 D	44.4%	(12/27)	14.8%	(4/27)	59.3%	(16/27)
2.01 to 3.00 D	11.1%	(3/27)	0.0%	(0/27)	11.1%	(3/27)
3.01 to 4.00 D	18.5%	(5/27)	0.0%	(0/27)	18.5%	(5/27)
4.01 to 5.00 D	0.0%	(0/27)	3.7%	(1/27)	3.7%	(1/27)
5.01 to 6.00 D	0.0%	(0/27)	7.4%	(2/27)	7.4%	(2/27)
Total	74.1%	(20/27)	25.9%	(7/27)	100.0%	(27/27)
With Algorithm Adjustment **MRSE: Mean: 2.468, SD: 1.115, Range: 1.00 to 5.25** **MRCYL:Mean: 0.033, SD: 0.086, Range: 0.00 to 0.25**						
0.00 to 1.00 D	3.3%	(2/60)	0.0%	(0/60)	3.3%	(2/60)
1.01 to 2.00 D	28.3%	(17/60)	6.7%	(4/60)	35.0%	(21/60)
2.01 to 3.00 D	31.7%	(19/60)	3.3%	(2/60)	35.0%	(21/60)
3.01 to 4.00 D	8.3%	(5/60)	1.7%	(1/60)	10.0%	(6/60)
4.01 to 5.00 D	11.7%	(7/60)	1.7%	(1/60)	13.3%	(8/60)
5.01 to 6.00 D	3.3%	(2/60)	0.0%	(0/60)	3.3%	(2/60)
Total	86.7%	(52/60)	13.3%	(8/60)	100.0%	(60/60)

The shaded cells were not included in the effectiveness cohort.

TABLE 2.B
PREOPERATIVE REFRACTION PARAMETERS
STRATIFIED BY MRSE AND CYLINDER COMPONENTS
EYES TREATED FOR ASTIGMATIC HYPEROPIA

MRSE	Manifest Cylinder								Total	
	0.25 to 0.50 D		0.51 to 1.00 D		1.01 to 2.00 D		2.01 to 3.00 D			
	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N
Without Algorithm Adjustment **MRSE: Mean: 2.965, SD: 1.253, Range: 1.00 to 6.38** **MRCYL:Mean: 0.943, SD: 0.583, Range: 0.25 to 2.75**										
0.00 to 1.00 D	1.2%	(1/83)	1.2%	(1/83)	0.0%	(0/83)	0.0%	(0/83)	2.4%	(2/83)
1.01 to 2.00 D	13.3%	(11/83)	9.6%	(8/83)	3.6%	(3/83)	2.4%	(2/83)	28.9%	(24/83)
2.01 to 3.00 D	6.0%	(5/83)	4.8%	(4/83)	3.6%	(3/83)	1.2%	(1/83)	15.7%	(13/83)
3.01 to 4.00 D	7.2%	(6/83)	16.9%	(14/83)	8.4%	(7/83)	0.0%	(0/83)	32.5%	(27/83)
4.01 to 5.00 D	6.0%	(5/83)	3.6%	(3/83)	3.6%	(3/83)	1.2%	(1/83)	14.5%	(12/83)
5.01 to 6.00 D	2.4%	(2/83)	1.2%	(1/83)	1.2%	(1/83)	0.0%	(0/83)	4.8%	(4/83)
6.01 to 7.00 D	0.0%	(0/83)	0.0%	(0/83)	1.2%	(1/83)	0.0%	(0/83)	1.2%	(1/83)
Total	36.1%	(30/83)	37.3%	(31/83)	21.7%	(18/83)	4.8%	(4/83)	100.0%	(83/83)
With Algorithm Adjustment **MRSE: Mean: 2.965, SD: 1.222, Range: 0.88 to 6.38** **MRCYL:Mean: 0.970, SD: 0.609, Range: 0.50 to 3.00**										
0.00 to 1.00 D	2.5%	(5/199)	0.0%	(0/199)	1.5%	(3/199)	0.0%	(0/199)	4.0%	(8/199)
1.01 to 2.00 D	10.6%	(21/199)	7.5%	(15/199)	4.0%	(8/199)	2.0%	(4/199)	24.1%	(48/199)
2.01 to 3.00 D	14.1%	(28/199)	8.5%	(17/199)	6.0%	(12/199)	0.5%	(1/199)	29.1%	(58/199)
3.01 to 4.00 D	11.6%	(23/199)	5.5%	(11/199)	4.5%	(9/199)	3.5%	(7/199)	25.1%	(50/199)
4.01 to 5.00 D	5.0%	(10/199)	2.0%	(4/199)	5.5%	(11/199)	0.5%	(1/199)	13.1%	(26/199)
5.01 to 6.00 D	1.5%	(3/199)	1.0%	(2/199)	1.0%	(2/199)	0.0%	(0/199)	3.5%	(7/199)
6.01 to 7.00 D	0.0%	(0/199)	0.0%	(0/199)	1.0%	(2/199)	0.0%	(0/199)	1.0%	(2/199)
Total	45.2%	(90/199)	24.6%	(49/199)	23.6%	(47/199)	6.5%	(13/199)	100.0%	(199/199)

Two eyes (with refraction of 3.50+1.00x176, 3.00+1.25x20) were reported with an aborted procedure and were not treated later. These eyes were excluded from the effectiveness analyses.
The shaded cells were not included in the effectiveness cohort. Additionally, 1 eye in the non-shaded cells was not included in the effectiveness cohort due to an aborted procedure.

4.2.2 Accountability

A total of 369 eyes were enrolled in the study. Accountability at 9 months was very high with only 8 eyes lost to follow-up. A total of 16 eyes missed the 9-month visit, and 2 eyes were discontinued due to aborted treatment (because of problems with the microkeratome). Accountability for all treated eyes through 12 months is presented in Table 3.A.

TABLE 3.A
ACCOUNTABILITY
ALL TREATED EYES

Total Subjects (N) = 369		Day 1	Day 7	1 Month	3 Months	6 Months	9 Months	12 Months
Available for Analysis	%, n/N	99.7% 368/369	99.7% 368/369	99.7% 368/369	97.8% 361/369	97.3% 359/369	93.0% 343/369	94.6% 349/369
Discontinued*	%, n/N	0.3% 1/369	0.3% 1/369	0.3% 1/369	0.5% 2/369	0.5% 2/369	0.5% 2/369	0.5% 2/369
Deceased	%, n/N	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369
Retreatment	%, n/N	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369
Aborted	%, n/N	0.3% 1/369	0.3% 1/369	0.3% 1/369	0.5% 2/369	0.5% 2/369	0.5% 2/369	0.5% 2/369
Active (Not yet eligible for the interval)	%, n/N	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369
Lost to Follow-up†	%, n/N	0.0% 0/369	0.0% 0/369	0.0% 0/369	0.0% 0/369	1.1% 4/369	2.2% 8/369	2.2% 8/369
Missed Visit‡	%, n/N	0.0% 0/369	0.0% 0/369	0.0% 0/369	1.6% 6/369	1.1% 4/369	4.3% 16/369	2.7% 10/369
% Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible)		100.0% 368/368	100.0% 368/368	100.0% 368/368	98.4% 361/367	97.8% 359/367	93.5% 343/367	95.1% 349/367

160 eyes were in the effectiveness cohort: treated with algorithm adjustment, treated for MRSE and MRSPH of 5.0 D or less, and treated for sphere or astigmatic eyes treated for MRCYL of > 0.50 D.
N = Total number of eyes enrolled.

* Discontinued = due to retreatment, aborted procedure, or death. The eyes with aborted procedures and without successful treatments later were not included in the effectiveness analyses.

† Lost to follow-up: Eyes were not examined at the 24-month visit, and were not considered active or discontinued.

‡ Missed visit: Eyes were not examined at the scheduled visit, however, were examined or may have been examined at a subsequent visit.

Accountability at 9 months for the effectiveness cohort eyes was very high with only 4 eyes lost to follow-up and no eyes were discontinued. Accountability for the effectiveness cohort of eyes through 12 months is presented in Table 3.B.

TABLE 3.B
ACCOUNTABILITY
EFFECTIVENESS COHORT EYES

Total Subjects (N) = 160		Day 1	Day 7	1 Month	3 Months	6 Months	9 Months	12 Months
Available for Analysis	%, n/N	100.0% 160/160	100.0% 160/160	100.0% 160/160	98.8% 158/160	100.0% 160/160	93.1% 149/160	95.6% 153/160
Discontinued*	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160
Deceased	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160
Retreatment	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160
Aborted	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160
Active (Not yet eligible for the interval)	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160
Lost to Follow-up†	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	0.0% 0/160	2.5% 4/160	2.5% 4/160
Missed Visit‡	%, n/N	0.0% 0/160	0.0% 0/160	0.0% 0/160	1.3% 2/160	0.0% 0/160	4.4% 7/160	1.9% 3/160
% Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible)		100.0% 160/160	100.0% 160/160	100.0% 160/160	98.8% 158/160	100.0% 160/160	93.1% 149/160	95.6% 153/160

N = Total number of eyes enrolled.

* Discontinued = due to retreatment, aborted procedure, or death.

† Lost to follow-up: Eyes were not examined at the 24-month visit, and were not considered active or discontinued.

‡ Missed visit: Eyes were not examined at the scheduled visit, however, were examined or may have been examined at a subsequent visit.

4.2.3 Safety Outcomes: Change in BSCVA, Complications, Adverse Events, and Subjective Symptoms

Table 4.A shows the cumulative key safety variables at the last available visit. The shaded columns indicate treatments outside of the approved range, and are not part of the effectiveness cohort.

TABLE 4.A
SUMMARY OF KEY SAFETY VARIABLES AT LAST AVAILABLE VISIT
ALL TREATED EYES STRATIFIED BY ALGORITHM AND TREATMENT

Key Safety Variables	Without Algorithm Adjustment			With Algorithm Adjustment			Total
	Sphere % (n/N)	Sphere + 0.5 D Cylinder % (n/N)	Sphere + >0.5 D Cylinder % (n/N)	Sphere % (n/N)	Sphere + 0.5 D Cylinder % (n/N)	Sphere + >0.5 D Cylinder % (n/N)	% (n/N)
Loss of ≥ 2 lines BSCVA	0.0% (0/27)	0.0% (0/30)	1.9% (1/52)	0.0% (0/60)	0.0% (0/90)	0.0% (0/108)	0.3% (1/367)
Loss of > 2 lines BSCVA	0.0% (0/27)	0.0% (0/30)	0.0% (0/52)	0.0% (0/60)	0.0% (0/90)	0.0% (0/108)	0.0% (0/367)
BSCVA worse than 20/40	0.0% (0/27)	0.0% (0/30)	0.0% (0/52)	0.0% (0/60)	0.0% (0/90)	0.0% (0/108)	0.0% (0/367)
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0% (0/27)	0.0% (0/28)	0.0% (0/52)	0.0% (0/59)	0.0% (0/87)	0.0% (0/98)	0.0% (0/351)
Haze ≥ trace with loss of BSCVA > 2 lines	0.0% (0/27)	0.0% (0/30)	0.0% (0/52)	0.0% (0/60)	0.0% (0/90)	0.0% (0/108)	0.0% (0/367)
Increased manifest refractive astigmatism > 2.0D*	0.0% (0/27)	3.3% (1/30)	0.0% (0/52)	0.0% (0/60)	0.0% (0/90)	0.0% (0/108)	0.3% (1/367)

Data collected through July 15, 2008. **2 eyes with aborted procedures were excluded.**
The shaded columns were not included in the effectiveness cohort. Additionally, 8 eyes in the non-shaded columns were not included in the effectiveness cohort due to MRSE or MRSPH > 5.0 D.
* For eyes treated with spherical hyperopia only.

Change in BSCVA stratified by visit and by diopter of preoperative MRSE for all treated eyes is presented in Tables 4.B and Table 4.C. At the 9 month visit, 5 eyes lost more than 2 lines, and 11 eyes lost 2 lines of BSCVA. As shown in Table 4.D, 4 eyes in the sphere only group and 5 eyes in the sphere + >0.50 D cylinder group lost 2 lines of BSCVA. These subjects were asked to return for an additional examination, and at this visit, only one eye had a loss of 2 lines of BSCVA. No eyes lost > 2 lines BSCVA (Table 4.A).

TABLE 4.B
CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA)
ALL TREATED EYES

Change in BSCVA from Preop	1 Month % (n/N)	3 Months % (n/N)	6 Months % (n/N)	9 Months % (n/N)	12 Months % (n/N)
Decrease > 2 lines (Decrease >10 letters)	1.4% (5/368)	0.8% (3/361)	1.9% (7/359)	1.5% (5/341)	1.1% (4/349)
Decrease 2 lines (Decrease 8 to 10 letters)	2.7% (10/368)	1.7% (6/361)	2.5% (9/359)	3.2% (11/341)	2.3% (8/349)
Decrease 1 line (Decrease 3 to 7 letters)	22.6% (83/368)	18.3% (66/361)	19.2% (69/359)	16.4% (56/341)	17.8% (62/349)
No change (Change within 2 letters)	56.5% (208/368)	58.2% (210/361)	51.0% (183/359)	54.0% (184/341)	50.4% (176/349)
Increase 1 line (Increase 3 to 7 letters)	15.5% (57/368)	18.3% (66/361)	22.6% (81/359)	22.3% (76/341)	24.4% (85/349)
Increase 2 lines (Increase 8 to 10 letters)	1.4% (5/368)	2.8% (10/361)	2.8% (10/359)	2.6% (9/341)	4.0% (14/349)
Increase > 2 lines (Increase >10 letters)	0.0% (0/368)	0.0% (0/361)	0.0% (0/359)	0.0% (0/341)	0.0% (0/349)
No Data on CRFs*	0	0	0	2	0
Total CRFs†	368	361	359	343	349
Missed Visit‡	1	8	10	26	20

N = Number of available CRFs received with non-missing values at preop and each postoperative visit. BSCVA measurement was not required at Day-1 visit.

* Number of available CRFs received with missing values at preop or the corresponding postoperative visit.

† Number of available CRFs received at each visit.

‡ Number of eyes missed visit.

TABLE 4.C
CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA) STRATIFIED BY PREOPERATIVE MRSE
ALL TREATED EYES

Change in BSCVA from Preop	Preoperative MRSE							Total
	0.00 to 1.00 D % (n/N)	1.01 to 2.00 D % (n/N)	2.01 to 3.00 D % (n/N)	3.01 to 4.00 D % (n/N)	4.01 to 5.00 D % (n/N)	5.01 to 6.00 D % (n/N)	6.01 to 7.00 D % (n/N)	% (n/N)
9 Months								
Decrease > 2 lines (Decrease >10 letters)	0.0% (0/10)	1.0% (1/97)	0.0% (0/87)	3.7% (3/82)	0.0% (0/47)	6.7% (1/15)	0.0% (0/3)	1.5% (5/341)
Decrease 2 lines (Decrease 8 to 10 letters)	0.0% (0/10)	2.1% (2/97)	1.1% (1/87)	6.1% (5/82)	6.4% (3/47)	0.0% (0/15)	0.0% (0/3)	3.2% (11/341)
Decrease 1 line (Decrease 3 to 7 letters)	20.0% (2/10)	11.3% (11/97)	16.1% (14/87)	15.9% (13/82)	23.4% (11/47)	26.7% (4/15)	33.3% (1/3)	16.4% (56/341)
No change (Change within 2 letters)	40.0% (4/10)	56.7% (55/97)	52.9% (46/87)	51.2% (42/82)	57.4% (27/47)	53.3% (8/15)	66.7% (2/3)	54.0% (184/341)
Increase 1 line (Increase 3 to 7 letters)	40.0% (4/10)	25.8% (25/97)	24.1% (21/87)	23.2% (19/82)	10.6% (5/47)	13.3% (2/15)	0.0% (0/3)	22.3% (76/341)
Increase 2 lines (Increase 8 to 10 letters)	0.0% (0/10)	3.1% (3/97)	5.7% (5/87)	0.0% (0/82)	2.1% (1/47)	0.0% (0/15)	0.0% (0/3)	2.6% (9/341)
Increase > 2 lines (Increase >10 letters)	0.0% (0/10)	0.0% (0/97)	0.0% (0/87)	0.0% (0/82)	0.0% (0/47)	0.0% (0/15)	0.0% (0/3)	0.0% (0/341)
Not Data on CRFs*	0	2	0	0	0	0	0	2
Total CRFs†	10	99	87	82	47	15	3	343
Missed Visit‡	2	10	8	6	NA	NA	NA	26
12 Months								
Decrease > 2 lines (Decrease >10 letters)	0.0% (0/12)	1.0% (1/102)	0.0% (0/92)	3.8% (3/80)	0.0% (0/46)	0.0% (0/14)	0.0% (0/3)	1.1% (4/349)
Decrease 2 lines (Decrease 8 to 10 letters)	0.0% (0/12)	0.0% (0/102)	1.1% (1/92)	6.3% (5/80)	4.3% (2/46)	0.0% (0/14)	0.0% (0/3)	2.3% (8/349)
Decrease 1 line (Decrease 3 to 7 letters)	8.3% (1/12)	18.6% (19/102)	9.8% (9/92)	18.8% (15/80)	34.8% (16/46)	7.1% (1/14)	33.3% (1/3)	17.8% (62/349)
No change (Change within 2 letters)	33.3% (4/12)	53.9% (55/102)	48.9% (45/92)	45.0% (36/80)	50.0% (23/46)	85.7% (12/14)	33.3% (1/3)	50.4% (176/349)
Increase 1 line (Increase 3 to 7 letters)	50.0% (6/12)	22.5% (23/102)	33.7% (31/92)	25.0% (20/80)	6.5% (3/46)	7.1% (1/14)	33.3% (1/3)	24.4% (85/349)
Increase 2 lines (Increase 8 to 10 letters)	8.3% (1/12)	3.9% (4/102)	6.5% (6/92)	1.3% (1/80)	4.3% (2/46)	0.0% (0/14)	0.0% (0/3)	4.0% (14/349)
Increase > 2 lines (Increase >10 letters)	0.0% (0/12)	0.0% (0/102)	0.0% (0/92)	0.0% (0/80)	0.0% (0/46)	0.0% (0/14)	0.0% (0/3)	0.0% (0/349)
Not Data on CRFs*	0	0	0	0	0	0	0	0
Total CRFs†	12	102	92	80	46	14	3	349
Missed Visit‡	NA	7	3	8	1	1	NA	20

Eyes in the shaded cells were not included in the effectiveness cohort. Some eyes in the non-shaded cells were not included in the effectiveness cohort due to no algorithm adjustment, MRSE or MRSPH treatment of > 5.0 D, or MRCYL treatment of 0.50 D.

N = Number of CRFs received with non-missing values for each subgroup.

* Number of available CRFs received with missing BSCVA at the corresponding visit.

† Number of available CRFs received at the corresponding visit.

‡ Number of eyes missed visit.

TABLE 4.D
CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA) STRATIFIED BY TREATMENT ALL TREATED EYES

Change in BSCVA from Preop	Treatment			Total
	Sphere % (n/N)	Sphere + 0.5 D Cylinder % (n/N)	Sphere + >0.5 D Cylinder % (n/N)	% (n/N)
9 Months				
Decrease > 2 lines (Decrease >10 letters)	0.0% (0/85)	4.5% (5/112)	0.0% (0/144)	1.5% (5/341)
Decrease 2 lines (Decrease 8 to 10 letters)	4.7% (4/85)	1.8% (2/112)	3.5% (5/144)	3.2% (11/341)
Decrease 1 line (Decrease 3 to 7 letters)	14.1% (12/85)	19.6% (22/112)	15.3% (22/144)	16.4% (56/341)
No change (Change within 2 letters)	60.0% (51/85)	47.3% (53/112)	55.6% (80/144)	54.0% (184/341)
Increase 1 line (Increase 3 to 7 letters)	20.0% (17/85)	23.2% (26/112)	22.9% (33/144)	22.3% (76/341)
Increase 2 lines (Increase 8 to 10 letters)	1.2% (1/85)	3.6% (4/112)	2.8% (4/144)	2.6% (9/341)
Increase > 2 lines (Increase >10 letters)	0.0% (0/85)	0.0% (0/112)	0.0% (0/144)	0.0% (0/341)
Not Data on CRFs*	0	2	0	2
Total CRFs†	85	114	144	343
Missed Visit‡	2	6	18	26
12 Months				
Decrease > 2 lines (Decrease >10 letters)	0.0% (0/87)	3.4% (4/116)	0.0% (0/146)	1.1% (4/349)
Decrease 2 lines (Decrease 8 to 10 letters)	2.3% (2/87)	2.6% (3/116)	2.1% (3/146)	2.3% (8/349)
Decrease 1 line (Decrease 3 to 7 letters)	14.9% (13/87)	18.1% (21/116)	19.2% (28/146)	17.8% (62/349)
No change (Change within 2 letters)	55.2% (48/87)	50.0% (58/116)	47.9% (70/146)	50.4% (176/349)
Increase 1 line (Increase 3 to 7 letters)	24.1% (21/87)	23.3% (27/116)	25.3% (37/146)	24.4% (85/349)
Increase 2 lines (Increase 8 to 10 letters)	3.4% (3/87)	2.6% (3/116)	5.5% (8/146)	4.0% (14/349)
Increase > 2 lines (Increase >10 letters)	0.0% (0/87)	0.0% (0/116)	0.0% (0/146)	0.0% (0/349)
Not Data on CRFs*	0	0	0	0
Total CRFs†	87	116	146	349
Missed Visit‡	NA	4	16	20

Eyes in the shaded cells were not included in the effectiveness cohort. Some eyes in the non-shaded cells were not included in the effectiveness cohort due to no algorithm adjustment, MRSE or MRSPH treatment of > 5.0 D, or MRCYL treatment of 0.50 D.

N = Number of CRFs received with non-missing values for each subgroup.

* Number of available CRFs received with missing BSCVA at the corresponding visit.

† Number of available CRFs received at the corresponding visit.

‡ Number of eyes missed visit.

Table 5 presents a summary of all complications reported for all treated eyes. At the 9-month visit, the complications included dry eye (0.3%), epithelium in the interface (0.3%), pain at 1 month or later (0.6%), punctal plug insertion (0.9%), superficial punctate keratitis (SPK) (0.6%), and vitreous floaters (0.6%). Cumulative events reported through the course of the study at a frequency of >1% included conjunctivitis (1.1%), corneal edema between 1 week to less than 1 month after the procedure (1.1%), diffuse lamellar keratitis (DLK) (4.6%), ghost/double images (2.4%), dry eye (4.1%), epithelium at flap edge (1.9%), epithelium in the interface (7.9%), foreign body sensation (2.4%), punctal plug insertion (13.3%), superficial punctuate keratitis (SPK) (6.8%), steroid-induced IOP increase (2.2%), and transient light sensitivity syndrome, or TLSS (3.3%).

TABLE 5
COMPLICATIONS
ALL TREATED EYES

Complications	D 1 N=368 % (n)	D 7 N=368 % (n)	1 M N=368 % (n)	3 M N=361 % (n)	6 M N=359 % (n)	9 M N=343 % (n)	12 M N=349 % (n)	Cum* N=369 % (n)
Allergic conjunctivitis	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.8% (3)
Blepharitis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.5% (2)
Conjunctivitis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)	0.0% (0)	0.0% (0)	1.1% (4)
Corneal abrasion	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.5% (2)
Corneal edema between 1 week to less than 1 month after the procedure	0.0% (0)	0.8% (3)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.1% (4)
Corneal haze	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Corneal scar	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Debris in the interface	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Diffuse lamellar keratitis[1]	3.8% (14)	0.5% (2)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	4.6% (17)
Double/ghost images in the operative eye	0.0% (0)	0.3% (1)	0.0% (0)	1.4% (5)	0.8% (3)	0.0% (0)	0.0% (0)	2.4% (9)
Dry eye	0.0% (0)	0.8% (3)	1.1% (4)	0.6% (2)	1.1% (4)	0.3% (1)	0.3% (1)	4.1% (15)
Enhancement not done due to flap fibrosis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Epithelium at flap edge	0.0% (0)	0.8% (3)	1.1% (4)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	1.9% (7)
Epithelium in the interface	0.3% (1)	1.1% (4)	3.0% (11)	3.6% (13)	1.7% (6)	0.3% (1)	0.3% (1)	7.9% (29)
Foreign body sensation at 1 month or later	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	1.4% (5)	2.4% (9)
Iritis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Loose epithelium	0.0% (0)	0.5% (2)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.5% (2)
Meibomian gland dysfunction	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.5% (2)
Mucus under edge of flap	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.3% (1)
Pain at 1 month or later	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)	0.6% (2)	0.6% (2)	0.5% (2)
Possible allergic reaction to plugs or eyedrops	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.5% (2)
Post-operative flap complications: (flap is not the size and shape initially intended, the microkeratome stopped in mid-cut, or the resultant flap is misaligned)	0.3% (1)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Punctal plug inserted	0.0% (0)	5.2% (19)	5.2% (19)	0.6% (2)	0.8% (3)	0.9% (3)	0.0% (0)	13.3% (49)
Punctal plug replaced	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.3% (1)
Rough epithelium	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
SPK	0.0% (0)	2.4% (9)	3.0% (11)	0.0% (0)	0.0% (0)	0.6% (2)	0.3% (1)	6.8% (25)
Steroid induced IOP increase	0.0% (0)	0.5% (2)	1.6% (6)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.2% (8)
Subconjunctival hemorrhage	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
TLSS	0.0% (0)	0.0% (0)	1.6% (6)	0.6% (2)	0.0% (0)	0.0% (0)	0.0% (0)	3.3% (12)
Trace Microstriae	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Trace corneal haze	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)	0.6% (2)	0.0% (0)	0.0% (0)	0.5% (2)
Vitreous floaters	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)	0.6% (2)	0.6% (2)	0.6% (2)	0.8% (3)

N = number of eyes returned for the visits. n = number of eyes reported with the corresponding event. % = n ÷N ×100.

* Unsch = Unscheduled visits. Cumulative = during the course of the study. Eyes without any follow-up visits were excluded.

1 12 of 17 reports of diffuse lamellar keratitis (DLK) were associated with use of the Intralase Laser Keratome and 5 of 17 reports of DLK were associated with the Hansatome Microkeratome.

Table 6 shows the cumulative adverse event rate for all reported events was ≤ 0.5% on a cumulative basis for all categories except diabetes (1.1%).

TABLE 6
ADVERSE EVENTS REPORTED AT ANY POSTOPERATIVE VISIT
ALL TREATED EYES STRATIFIED BY ALGORITHM AND TREATMENT

	Without Algorithm Adjustment			With Algorithm Adjustment			
Adverse Event	Sphere % (n/N)	Sphere + 0.5 D Cylinder % (n/N)	Sphere + >0.5 D Cylinder % (n/N)	Sphere % (n/N)	Sphere + 0.5 D Cylinder % (n/N)	Sphere + >0.5 D Cylinder % (n/N)	Total % (n/N)
Corneal epithelial defect involving the keratectomy at one month or later	0.0% (0/27)	0.0% (0/30)	1.9% (1/53)	0.0% (0/60)	0.0% (0/90)	0.0% (0/109)	0.3% (1/369)
Decrease in BSCVA ≥ 2 lines at the most recent evaluation	0.0% (0/27)	0.0% (0/30)	1.9% (1/53)	0.0% (0/60)	0.0% (0/90)	0.0% (0/109)	0.3% (1/369)
Diabetes	0.0% (0/27)	3.3% (1/30)	1.9% (1/53)	0.0% (0/60)	2.2% (2/90)	0.0% (0/109)	1.1% (4/369)
Melting of the flap	0.0% (0/27)	0.0% (0/30)	1.9% (1/53)	0.0% (0/60)	0.0% (0/90)	0.0% (0/109)	0.3% (1/369)
Miscreated flap (lost, incomplete, too thin)	0.0% (0/27)	3.3% (1/30)	1.9% (1/53)	0.0% (0/60)	0.0% (0/90)	0.0% (0/109)	0.5% (2/369)
Ocular migraine	0.0% (0/27)	0.0% (0/30)	3.8% (2/53)	0.0% (0/60)	0.0% (0/90)	0.0% (0/109)	0.5% (2/369)
Vitreous floaters	0.0% (0/27)	0.0% (0/30)	1.9% (1/53)	0.0% (0/60)	0.0% (0/90)	0.0% (0/109)	0.3% (1/369)

N = number of treated eyes. n = number of eyes reported with the corresponding event. % = n ÷ N ×100%.
Data collected through July 15, 2008.
The shaded columns were not included in the effectiveness cohort. Additionally, 9 eyes in the non-shaded columns were not included in the effectiveness cohort due to MRSE or MRSPH > 5.0 D.

Table 7.A presents a summary of the clinically significant patient symptoms (those rated moderate to severe) with at least a 3% change from baseline to month 9. These include dryness (increased from 5% at baseline to 11%), excessive tearing (decreased 3% to 0%), gritty/scratchy feeling (increased from 1% at baseline to 5%), fluctuation of vision (increased 5% to 8%), variation of vision in normal light (increased from 1% at baseline to 6%), and variation of vision in dim light (increased from 7% at baseline to 11%).

Clinically significant symptoms (those rated moderate to severe) with at least a 3% change from baseline to month 12 were light sensitivity (decreased from 10% at baseline to 5%), dryness (increased from 5% at baseline to 10%), gritty/scratchy feeling (increased from 1% at baseline to 4%), variation of vision in normal light (increased from 1% at baseline to 7%), and variation of vision in dim light (increased from 7% at baseline to 14%).

TABLE 7.A
CLINICALLY SIGNIFICANT PATIENT SYMPTOMS*
ALL TREATED EYES

Symptom	Preop		6 Months		9 Months		12 Months	
	%	n/N	%	n/N	%	n/N	%	n/N
Light sensitivity	10.2%	37/361	7.8%	28/357	8.2%	28/341	4.6%	16/347
Headaches	2.5%	9/361	2.2%	8/357	2.3%	8/341	0.6%	2/347
Pain/burning	0.8%	3/361	2.5%	9/356	2.3%	8/341	0.3%	1/347
Dryness	5.3%	19/361	13.4%	48/357	11.4%	39/341	10.4%	36/346
Excessive tearing	3.0%	11/361	0.8%	3/357	0.0%	0/340	1.2%	4/347
Gritty, scratchy	1.1%	4/361	5.0%	18/357	5.0%	17/341	4.3%	15/347
Glare	5.3%	19/361	5.9%	21/357	3.8%	13/341	3.8%	13/346
Halos	2.2%	8/361	5.0%	18/357	3.5%	12/341	4.0%	14/347
Blurred vision	8.6%	31/361	10.1%	36/357	9.7%	33/341	10.4%	36/347
Double vision	0.6%	2/361	4.5%	16/357	2.6%	9/341	2.3%	8/346
Fluctuation of vision	5.0%	18/361	10.6%	38/357	7.9%	27/341	7.5%	26/347
Variation - bright light	5.5%	20/361	6.4%	23/357	3.2%	11/341	7.2%	25/347
Variation - normal light	1.1%	4/361	4.2%	15/356	5.9%	20/339	6.6%	23/347
Variation - dim light	6.9%	25/361	13.4%	48/357	11.4%	39/341	14.4%	50/347
Night driving vision	9.4%	34/361	12.4%	44/356	7.6%	26/341	9.5%	33/347
Other	1.4%	5/361	1.4%	5/356	2.1%	7/341	2.0%	7/347

* A level of moderate, marked, or severe is clinically significant. N = Number of eyes with non-missing responses. % = n ÷ N × 100%.

Table 7.B shows the symptoms that were worse 9 months after LASIK. Any symptom for which there is a one grade increase from baseline is considered "worse" and at least a two grade increase is considered "significantly worse". Symptoms that had the highest percentage of "significantly worse" grading were dryness (8.1%), gritty/scratchy (4.8%), blurred vision (7.2%), fluctuation of vision (5.7%), variation in normal light (4.5%), variation in dim light (9.9%), and night driving (4.2%).

TABLE 7.B
COMPARISON OF SYMPTOMS BEFORE AND AFTER SURGERY AT 9 MONTHS
ALL TREATED EYES

Symptom	Worse % (n/N)	Significantly Worse % (n/N)
Light sensitivity	17.9% (60/335)	3.3% (11/335)
Headaches	7.5% (25/335)	1.5% (5/335)
Pain/burning	6.9% (23/335)	1.8% (6/335)
Dryness	26.0% (87/335)	8.1% (27/335)
Excessive tearing	3.0% (10/334)	0.0% (0/334)
Gritty, scratchy	9.0% (30/335)	4.8% (16/335)
Glare	18.5% (62/335)	2.1% (7/335)
Halos	14.6% (49/335)	3.0% (10/335)
Blurred vision	15.2% (51/335)	7.2% (24/335)
Double vision	6.3% (21/335)	2.1% (7/335)
Fluctuation of vision	19.4% (65/335)	5.7% (19/335)
Variation - bright light	11.6% (39/335)	1.2% (4/335)
Variation - normal light	7.2% (24/333)	4.5% (15/333)
Variation - dim light	13.1% (44/335)	9.9% (33/335)
Night driving vision	14.6% (49/335)	4.2% (14/335)
Other	1.2% (4/335)	2.1% (7/335)

4.2.4 Key Effectiveness Parameters

A total of 369 eyes (189 subjects) were enrolled in the study. After treating the first 110 eyes (76 subjects), an analysis was performed on the data. The analysis showed these eyes were being undercorrected. It was determined that an algorithm adjustment of +0.75 D would improve the effectiveness of the treatment. The remaining 259 eyes (113 subjects) were treated with an algorithm adjustment of +0.75 D added to the sphere component. Since the algorithm adjustment was determined to be beneficial, only the eyes treated with the ablation algorithm adjustment (259 eyes) would be included in the effectiveness analysis. Through analysis of these 259 eyes, it was found that insufficient effectiveness data existed to approve the following range of treatment: sphere > +5.0 D, cylinder ≤ +0.50 D and > +3.00 D, and MRSE > +5.0 D. Excluding the eyes treated outside of these parameters, the Effectiveness Cohort consists of 160 eyes, with 149 eyes available at the 9 month point of refractive stability.

Presented in Tables 8.A and 8.B are the summary of key effectiveness variables for eyes in the effectiveness cohort stratified by visit. The summary of key

effectiveness variables at 9 months for eyes in the effectiveness cohort stratified by treatment is also shown.

As shown in Table 8.A for the effectiveness cohort of eyes, the three primary outcomes for percent of eyes with 20/40 or better uncorrected visual acuity and percent of eyes within ± 0.50 D and ± 1.00 D of attempted correction exceed target values established in the study protocol consistent with FDA guidance. At 9 months, 66.4% of eyes had UCVA 20/20 or better, and 96.6% of eyes had UCVA 20/40 or better. At 12 months, 66.7% of eyes had UCVA 20/20 or better, and 96.7% of eyes had UCVA 20/40 or better. In Table 8.B, the sphere only and the sphere + > 0.5 D cylinder treatment groups showed similar results to the eyes in Table 7.A. That is, at 9 months, for the sphere only treated eyes, 77.2% of eyes had UCVA 20/20 or better, and 96.5% of eyes had UCVA 20/40 or better. At 9 months, for the sphere + >0.5 D cylinder eyes, 59.8% of eyes had UCVA 20/20 or better, and 96.7% of eyes had UCVA 20/40 or better.

TABLE 8.A
SUMMARY OF KEY EFFECTIVENESS VARIABLES
EFFECTIVENESS COHORT

Key Effectiveness Variables	1 Month % (n/N) 95% CI*	3 Months % (n/N) 95% CI*	6 Months % (n/N) 95% CI*	9 Months % (n/N) 95% CI*	12 Months % (n/N) 95% CI*
UCVA 20/20 or better	46.3% (74/160) (38.3%, 54.3%)	58.9% (93/158) (50.8%, 66.6%)	61.9% (99/160) (53.9%, 69.4%)	66.4% (99/149) (58.3%, 74.0%)	66.7% (102/153) (58.6%, 74.1%)
UCVA 20/40 or better	95.6% (153/160) (91.2%, 98.2%)	96.8% (153/158) (92.8%, 99.0%)	97.5% (156/160) (93.7%, 99.3%)	96.6% (144/149) (92.3%, 98.9%)	96.7% (148/153) (92.5%, 98.9%)
MRSE†, Attempted vs. Achieved, ±0.50D	71.3% (114/160) (63.6%, 78.1%)	76.6% (121/158) (69.2%, 82.9%)	73.8% (118/160) (66.2%, 80.4%)	74.5% (111/149) (66.7%, 81.3%)	78.4% (120/153) (71.1%, 84.7%)
MRSE†, Attempted vs. Achieved, ±1.00D	90.0% (144/160) (84.3%, 94.2%)	94.9% (150/158) (90.3%, 97.8%)	92.5% (148/160) (87.3%, 96.1%)	90.6% (135/149) (84.7%, 94.8%)	92.2% (141/153) (86.7%, 95.9%)
MRSE†, Attempted vs. Achieved, ±2.00D	100.0% (160/160) (97.7%, 100.0%)	100.0% (158/158) (97.7%, 100.0%)	100.0% (160/160) (97.7%, 100.0%)	100.0% (149/149) (97.6%, 100.0%)	100.0% (153/153) (97.6%, 100.0%)

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values at each visit.
* The exact confidence interval was calculated based on Clopper-Pearson exact method.
† MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

TABLE 8.B
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY)
EFFECTIVENESS COHORT STRATIFIED BY TREATMENT

Key Effectiveness Variables	Sphere % (n/N) 95% CI*	Sphere + >0.5 D Cylinder % (n/N) 95% CI*
UCVA 20/20 or better	77.2% (44/57) (64.2%, 87.3%)	59.8% (55/92) (49.0%, 69.9%)
UCVA 20/40 or better	96.5% (55/57) (87.9%, 99.6%)	96.7% (89/92) (90.8%, 99.3%)
MRSE†, Attempted vs. Achieved, ±0.50D	77.2% (44/57) (64.2%, 87.3%)	72.8% (67/92) (62.6%, 81.6%)
MRSE†, Attempted vs. Achieved, ±1.00D	93.0% (53/57) (83.0%, 98.1%)	89.1% (82/92) (80.9%, 94.7%)
MRSE†, Attempted vs. Achieved, ±2.00D	100.0% (57/57) (93.7%, 100.0%)	100.0% (92/92) (96.1%, 100.0%)

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values in each group.
* The exact confidence interval was calculated based on Clopper-Pearson exact method.
† MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

4.2.4.1 Key Effectiveness Parameters by Preoperative MRSE

Key effectiveness outcomes at 9 months stratified by each diopter of preoperative MRSE are presented in Tables 9.A, 9.B, and 9.C for the entire effectiveness cohort, for the effectiveness cohort of eyes treated for spherical hyperopia only with the algorithm adjustment, and for the effectiveness cohort of eyes treated for astigmatic hyperopia with the algorithm adjustment, respectively. As shown in Table 9.A, at 9 months postoperatively, over 91% of eyes across all preoperative MRSE subgroups had uncorrected visual acuity of 20/40 or better.

The accuracy of the intended correction decreased somewhat with increasing preoperative MRSE. As can be seen in Table 9.A, efficacy data for the overall effectiveness cohort stratified in one diopter increments of preoperative MRSE meet the protocol target values. Similar results were also shown for both the effectiveness cohort of eyes treated for spherical hyperopia treated with the algorithm adjustment and for the effectiveness cohort of eyes treated for astigmatic hyperopia with the algorithm adjustment (Tables 9.B and 9.C, respectively).

TABLE 9.A
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY PREOPERATIVE MRSE
EFFECTIVENESS COHORT

Key Effectiveness Variables	Preoperative MRSE					Total
	0.00 to 1.00 D % (n/N)	1.01 to 2.00 D % (n/N)	2.01 to 3.00 D % (n/N)	3.01 to 4.00 D % (n/N)	4.01 to 5.00 D % (n/N)	% (n/N)
UCVA 20/20 or better	66.7% (2/3)	80.5% (33/41)	57.1% (28/49)	75.0% (24/32)	50.0% (12/24)	66.4% (99/149)
UCVA 20/40 or better	100.0% (3/3)	97.6% (40/41)	91.8% (45/49)	100.0% (32/32)	100.0% (24/24)	96.6% (144/149)
MRSE*, Attempted vs. Achieved, ± 0.50D	66.7% (2/3)	82.9% (34/41)	69.4% (34/49)	78.1% (25/32)	66.7% (16/24)	74.5% (111/149)
MRSE*, Attempted vs. Achieved, ± 1.00D	100.0% (3/3)	92.7% (38/41)	85.7% (42/49)	96.9% (31/32)	87.5% (21/24)	90.6% (135/149)
MRSE*, Attempted vs. Achieved, ± 2.00D	100.0% (3/3)	100.0% (41/41)	100.0% (49/49)	100.0% (32/32)	100.0% (24/24)	100.0% (149/149)

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

TABLE 9.B
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY PREOPERATIVE MRSE
EFFECTIVENESS COHORT TREATED FOR SPHERICAL HYPEROPIA ONLY AND WITH ALGORITHM ADJUSTMENT

Key Effectiveness Variables	Preoperative MRSE					Total
	0.00 to 1.00 D % (n/N)	1.01 to 2.00 D % (n/N)	2.01 to 3.00 D % (n/N)	3.01 to 4.00 D % (n/N)	4.01 to 5.00 D % (n/N)	% (n/N)
UCVA 20/20 or better	100.0% (2/2)	90.0% (18/20)	57.1% (12/21)	83.3% (5/6)	87.5% (7/8)	77.2% (44/57)
UCVA 20/40 or better	100.0% (2/2)	100.0% (20/20)	90.5% (19/21)	100.0% (6/6)	100.0% (8/8)	96.5% (55/57)
MRSE*, Attempted vs. Achieved, ± 0.50D	100.0% (2/2)	85.0% (17/20)	66.7% (14/21)	66.7% (4/6)	87.5% (7/8)	77.2% (44/57)
MRSE*, Attempted vs. Achieved, ± 1.00D	100.0% (2/2)	100.0% (20/20)	81.0% (17/21)	100.0% (6/6)	100.0% (8/8)	93.0% (53/57)
MRSE*, Attempted vs. Achieved, ± 2.00D	100.0% (2/2)	100.0% (20/20)	100.0% (21/21)	100.0% (6/6)	100.0% (8/8)	100.0% (57/57)

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

TABLE 9.C
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY PREOPERATIVE MRSE
EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D AND WITH ALGORITHM ADJUSTMENT

Key Effectiveness Variables	Preoperative MRSE					Total
	0.00 to 1.00 D % (n/N)	1.01 to 2.00 D % (n/N)	2.01 to 3.00 D % (n/N)	3.01 to 4.00 D % (n/N)	4.01 to 5.00 D % (n/N)	% (n/N)
UCVA 20/20 or better	0.0% (0/1)	71.4% (15/21)	57.1% (16/28)	73.1% (19/26)	31.3% (5/16)	59.8% (55/92)
UCVA 20/40 or better	100.0% (1/1)	95.2% (20/21)	92.9% (26/28)	100.0% (26/26)	100.0% (16/16)	96.7% (89/92)
MRSE*, Attempted vs. Achieved, ± 0.50D	0.0% (0/1)	81.0% (17/21)	71.4% (20/28)	80.8% (21/26)	56.3% (9/16)	72.8% (67/92)
MRSE*, Attempted vs. Achieved, ± 1.00D	100.0% (1/1)	85.7% (18/21)	89.3% (25/28)	96.2% (25/26)	81.3% (13/16)	89.1% (82/92)
MRSE*, Attempted vs. Achieved, ± 2.00D	100.0% (1/1)	100.0% (21/21)	100.0% (28/28)	100.0% (26/26)	100.0% (16/16)	100.0% (92/92)

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

4.2.4.2 Stratification of Key Efficacy Parameters by Optical Zone

The effect of the optical zone on the efficacy parameters of uncorrected visual acuity and accuracy of the postoperative refraction is shown in Table 10. The analyses revealed that the optical zone size did not play a significant role in efficacy outcomes with regard to the proportion of eyes with UCVA of 20/40 or better postoperatively. However, a greater number of eyes treated with a 6.5 mm optic zone were within ± 0.50 D and within ± 1.00 D of attempted versus achieved MRSE at 9 months.

TABLE 10
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY OPTICAL ZONE
SPHERICAL EYES AND ASTIGMATIC EYES WITH CYLINDER OF > 0.50 D WITH ALGORITHM ADJUSTMENT

Key Effectiveness Variables	Optical Zone 6.0 mm % (n/N)	Optical Zone 6.5 mm % (n/N)	Total % (n/N)
UCVA 20/20 or better	50.0% (3/6)	67.1% (96/143)	66.4% (99/149)
UCVA 20/40 or better	100.0% (6/6)	96.5% (138/143)	96.6% (144/149)
MRSE*, Attempted vs. Achieved, ± 0.50D	50.0% (3/6)	75.5% (108/143)	74.5% (111/149)
MRSE*, Attempted vs. Achieved, ± 1.00D	66.7% (4/6)	91.6% (131/143)	90.6% (135/149)
MRSE*, Attempted vs. Achieved, ± 2.00D	100.0% (6/6)	100.0% (143/143)	100.0% (149/149)

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

4.2.4.3 Mean Manifest Refractive Spherical Equivalent

Mean manifest refractive spherical equivalent (MRSE) results for the effectiveness cohort of eyes through the 12 month postoperative visit is shown in Table 11. From 9 months to 12 months there was very little change in mean MRSE (-0.062 D and -0.023 D, respectively).

TABLE 11
MEAN MANIFEST REFRACTION SPHERICAL EQUIVALENT
EFFECTIVENESS COHORT

	Preop	1 Month	3 Months	6 Months	9 Months	12 Months
N	160	160	158	160	149	153
Mean	2.699	-0.336	-0.210	-0.148	-0.062	-0.023
95% Confidence Interval	2.533, 2.866	-0.418, -0.254	-0.291, -0.130	-0.230, -0.067	-0.155, 0.031	-0.109, 0.064
Standard Deviation	1.067	0.526	0.512	0.522	0.575	0.541

Refraction measurement was not required at Day-1 Visit.
Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available CRFs received with non-missing values at each visit.

4.2.4.4 Stability of the Manifest Refraction

Stability of the MRSE is presented in Table 12.A for the effectiveness cohort of eyes, in Table 12.B for the effectiveness cohort of eyes treated for spherical hyperopia only, and in Table 12.C for the effectiveness cohort of eyes treated for astigmatic hyperopia. Stability of the manifest refraction cylinder (MRCYL) for the effectiveness cohort of eyes is presented in Table 12.D.

As shown in Table 12.A for the consistent cohort of eyes, the mean change in MRSE between 6 and 9 months was 0.071 D (SD 0.328 D), and between 9 and 12 months, the mean change was 0.059 D, (SD 0.287 D). Between 6 and 9 months and 9 and 12 months, the change in MRSE per month was 0.024 D and 0.020 D, respectively, well below the target value of 0.04 D. In addition, >99% of eyes had a change in MRSE of ≤ 1.00 D at both intervals. Thus, stability of MRSE was demonstrated at 9 months postoperatively.

TABLE 12.A
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE)
EFFECTIVENESS COHORT

MRSE[1]	1 and 3 Months	3 and 6 Months	6 and 9 Months	9 and 12 Months
Pairwise Sequential Visits*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	96.8% (153/158) (92.8%, 99.0%)	98.7% (156/158) (95.5%, 99.8%)	99.3% (148/149) (96.3%, 100.0%)	100.0% (148/148) (97.5%, 100.0%)
Mean change between visits SD 95% CI	0.122 0.421 (0.056, 0.188)	0.063 0.303 (0.016, 0.111)	0.073 0.328 (0.020, 0.126)	0.059 0.287 (0.012, 0.106)
Mean change per month	0.061	0.021	0.024	0.020
Mean change per year (change per month × 12)	0.731	0.253	0.292	0.236
Consistent Cohort*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	96.6% (143/148) (92.3%, 98.9%)	98.6% (146/148) (95.2%, 99.8%)	99.3% (147/148) (96.3%, 100.0%)	100.0% (148/148) (97.5%, 100.0%)
Mean change between visits SD 95% CI	0.127 0.426 (0.057, 0.196)	0.058 0.307 (0.008, 0.108)	0.071 0.328 (0.018, 0.124)	0.059 0.287 (0.012, 0.106)
Mean change per month	0.063	0.019	0.024	0.020
Mean change per year (change per month × 12)	0.760	0.233	0.284	0.236

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRSE.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

Tables 12.B and 12.C show the stability of MRSE for the effectiveness cohort of eyes treated for spherical hyperopia only with algorithm adjustment and astigmatic hyperopia with algorithm adjustment, respectively.

TABLE 12.B
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE) EFFECTIVENESS COHORT TREATED FOR SPHERICAL HYPEROPIA ONLY AND WITH ALGORITHM ADJUSTMENT

MRSE[1]	1 and 3 Months	3 and 6 Months	6 and 9 Months	9 and 12 Months
Pairwise Sequential Visits*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	98.2% (56/57) (90.6%, 100.0%)	96.5% (55/57) (87.9%, 99.6%)	98.2% (56/57) (90.6%, 100.0%)	100.0% (57/57) (93.7%, 100.0%)
Mean change between visits SD 95% CI	0.081 0.401 (-0.025, 0.187)	0.072 0.361 (-0.023, 0.168)	0.039 0.402 (-0.067, 0.146)	0.094 0.324 (0.008, 0.180)
Mean change per month	0.041	0.024	0.013	0.031
Mean change per year (change per month × 12)	0.487	0.289	0.158	0.377
Consistent Cohort*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	98.2% (56/57) (90.6%, 100.0%)	96.5% (55/57) (87.9%, 99.6%)	98.2% (56/57) (90.6%, 100.0%)	100.0% (57/57) (93.7%, 100.0%)
Mean change between visits SD 95% CI	0.081 0.401 (-0.025, 0.187)	0.072 0.361 (-0.023, 0.168)	0.039 0.402 (-0.067, 0.146)	0.094 0.324 (0.008, 0.180)
Mean change per month	0.041	0.024	0.013	0.031
Mean change per year (change per month × 12)	0.487	0.289	0.158	0.377

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRSE.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

TABLE 12.C
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE) EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D AND WITH ALGORITHM ADJUSTMENT

MRSE[1]	1 and 3 Months	3 and 6 Months	6 and 9 Months	9 and 12 Months
Pairwise Sequential Visits*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	96.0% (97/101) (90.2%, 98.9%)	100.0% (101/101) (96.4%, 100.0%)	100.0% (92/92) (96.1%, 100.0%)	100.0% (91/91) (96.0%, 100.0%)
Mean change between visits SD 95% CI	0.145 0.433 (0.059, 0.230)	0.058 0.267 (0.005, 0.111)	0.094 0.271 (0.038, 0.150)	0.037 0.261 (-0.017, 0.091)
Mean change per month	0.072	0.019	0.031	0.012
Mean change per year (change per month × 12)	0.869	0.233	0.375	0.148
Consistent Cohort*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	95.6% (87/91) (89.1%, 98.8%)	100.0% (91/91) (96.0%, 100.0%)	100.0% (91/91) (96.0%, 100.0%)	100.0% (91/91) (96.0%, 100.0%)
Mean change between visits SD 95% CI	0.155 0.441 (0.063, 0.247)	0.049 0.269 (-0.007, 0.106)	0.091 0.271 (0.034, 0.147)	0.037 0.261 (-0.017, 0.091)
Mean change per month	0.078	0.016	0.030	0.012
Mean change per year (change per month × 12)	0.931	0.198	0.363	0.148

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRSE.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

As shown in Table 12.D for the consistent cohort of eyes, the mean change in manifest refraction cylinder (MRCYL) between 6 and 9 months and 9 and 12 months was -0.071 D (SD 0.350 D) and 0.014 D (SD 0.342), respectively, for the effectiveness cohort eyes. Between 6 and 9 months and 9 and 12 months, the mean change in MRCYL per month was -0.024 D and 0.005 D, respectively, well below the target value of 0.04 D. In addition, > 97% of eyes had a change of MRCYL by ≤ 1.00 D at both intervals. Thus, stability was demonstrated at 9 months postoperatively.

TABLE 12.D
STABILITY OF MANIFEST REFRACTION CYLINDER (MRCYL)
EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D AND WITH ALGORITHM ADJUSTMENT

MRCYL[1]	1 and 3 Months	3 and 6 Months	6 and 9 Months	9 and 12 Months
Pairwise Sequential Visits*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	99.0% (100/101) (94.6%, 100.0%)	99.0% (100/101) (94.6%, 100.0%)	97.8% (90/92) (92.4%, 99.7%)	98.9% (90/91) (94.0%, 100.0%)
Mean change between visits SD 95% CI	0.037 0.305 (-0.023, 0.097)	0.072 0.294 (0.014, 0.130)	-0.073 0.349 (-0.146, -0.001)	0.014 0.342 (-0.058, 0.085)
Mean change per month	0.019	0.024	-0.024	0.005
Mean change per year (change per month × 12)	0.223	0.287	-0.293	0.055
Consistent Cohort*				
Eyes with ≤ 1.00 D change (n/N, %, [% CI])[2]	98.9% (90/91) (94.0%, 100.0%)	98.9% (90/91) (94.0%, 100.0%)	97.8% (89/91) (92.3%, 99.7%)	98.9% (90/91) (94.0%, 100.0%)
Mean change between visits SD 95% CI	0.047 0.309 (-0.018, 0.111)	0.077 0.297 (0.015, 0.139)	-0.071 0.350 (-0.144, 0.001)	0.014 0.342 (-0.058, 0.085)
Mean change per month	0.023	0.026	-0.024	0.005
Mean change per year (change per month × 12)	0.280	0.308	-0.286	0.055

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRCYL.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

4.2.4.5 Cylinder Correction/Vector Analysis

Vector magnitude analyses for the effectiveness cohort of eyes with cylinder correction of > 0.50 D are presented in Table 13 at 6, 9, and 12 months. IRC, SIRC, and SIRC/IRC ratio data at each postoperative exam are provided in Table 14.

Vector magnitude analyses are shown for the effectiveness cohort of eyes treated for astigmatic hyperopia with cylinder > 0.50 D and with the algorithm adjustment at 6, 9, and 12 months in Table 13. The achieved versus intended vector magnitude ratio, or Correction Ratio CR (SIRC/IRC), at 9 months was 0.95, which is very close to the target value of 1.0. The 6 month and 12 month CR values were similar to the 9 month CR value (i.e., 0.99 and 0.97, respectively).

TABLE 13
VECTOR MAGNITUDE ANALYSIS SUMMARY
EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D & WITH COMPLETE PREOPERATIVE AND POSTOPERATIVE REFRACTION WITH ABLATION ALGORITHM ADJUSTMENT

Statistics	Preoperative[1]	Postoperative[1]	|IRC|[2]	|SIRC|[2]	CR[2]
6 Months					
N	102	102	102	102	102
Mean	1.355	0.426	1.458	1.403	0.99
Standard Deviation	0.599	0.511	0.651	0.651	0.30
Minimum	0.750	0.000	0.772	0.131	0.09
Maximum	3.000	2.500	3.282	3.183	2.24
9 Months					
N	92	92	92	92	92
Mean	1.356	0.364	1.465	1.348	0.95
Standard Deviation	0.616	0.466	0.672	0.626	0.31
Minimum	0.750	0.000	0.776	0.056	0.07
Maximum	3.000	1.750	3.282	2.940	2.19
12 Months					
N	95	95	95	95	95
Mean	1.350	0.376	1.456	1.388	0.97
Standard Deviation	0.612	0.522	0.667	0.654	0.28
Minimum	0.750	0.000	0.776	0.027	0.03
Maximum	3.000	2.000	3.282	3.055	1.81

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available CRFs received with non-missing values at each visit.
1 Manifest refraction on spectacle plane.
2 Refraction was converted from the spectacle to the corneal plane and cylinder axis of left eye was flipped around the vertical axis. Then IRC, SIRC and CR were calculated. CR = |SIRC|/|IRC|.

A vector analysis summary is presented below in Table 14 for the effectiveness cohort of eyes treated for astigmatic hyperopia with cylinder of > 0.50 D and with the ablation algorithm adjustment at 9 months postoperatively. At 9 months, the mean Correction Ratio (CR) was 1.038 for eyes with a preoperative cylinder between +0.51 to +1.00 D, 0.869 for eyes with a preoperative cylinder between +1.01 to +2.00 D, and 0.877 for astigmatic hyperopia eyes with a preoperative cylinder between +2.01 to +3.00 D.

TABLE 14
VECTOR ANALYSIS SUMMARY AT 9 MONTHS (POINT OF STABILITY)
EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D WITH ALGORITHM ADJUSTMENT

Preoperative Cylinder	n	|IRC| Mean ± SD	|SIRC| Mean ± SD	|EV|[1] Mean ± SD	CR[2] Mean ± SD	ER[3] Mean ± SD
9 Months						
All	92	1.465 ± 0.672	1.348 ± 0.626	0.420 ± 0.460	0.951 ± 0.306	0.303 ± 0.355
0.51 to 1.00 D	44	0.925 ± 0.136	0.974 ± 0.422	0.317 ± 0.422	1.038 ± 0.361	0.335 ± 0.439
1.01 to 2.00 D	35	1.664 ± 0.301	1.432 ± 0.429	0.507 ± 0.467	0.869 ± 0.242	0.309 ± 0.278
2.01 to 3.00 D	13	2.755 ± 0.326	2.384 ± 0.332	0.532 ± 0.525	0.877 ± 0.155	0.181 ± 0.169

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
Refraction was converted from the spectacle to the corneal plane and cylinder axis of left eye was flipped around the vertical axis. Then IRC, SIRC, CR and ER were calculated.
1 EV = IRC - SIRC.
2 CR = |SIRC|/|IRC|.
3 ER = |EV|/|IRC|.

4.2.4.6 POSTOPERATIVE UNCORRECTED VISUAL ACUITY COMPARED TO PREOPERATIVE BEST CORRECTED VISUAL ACUITY

Table 15 shows that at 9 and 12 months after surgery, 49.7% (74/149) and 51.0% (78/153) of the study patients saw as well *without* glasses after surgery as *with* glasses before surgery, respectively.

TABLE 15
POSTOPERATIVE UNCORRECTED VISUAL ACUITY (UCVA) COMPARED TO PREOPERATIVE BEST SPECTACLE CORRECTED VISUAL ACUITY (BSCVA) EFFECTIVENESS COHORT

Uncorrected Visual Acuity	1 Month % (n/N)	3 Months % (n/N)	6 Months % (n/N)	9 Months % (n/N)	12 Months % (n/N)
UCVA >2 Lines Better than Preop BSCVA	0.0% (0/160)	0.0% (0/158)	0.0% (0/160)	0.0% (0/149)	0.0% (0/153)
UCVA 2 Lines Better than Preop BSCVA	0.6% (1/160)	2.5% (4/158)	1.9% (3/160)	2.0% (3/149)	5.2% (8/153)
UCVA 1 Line Better than Preop BSCVA	7.5% (12/160)	11.4% (18/158)	11.9% (19/160)	8.1% (12/149)	11.8% (18/153)
UCVA Equal to Preop BSCVA	22.5% (36/160)	29.1% (46/158)	31.9% (51/160)	39.6% (59/149)	34.0% (52/153)
UCVA 1 Line Worse than Preop BSCVA	31.9% (51/160)	29.1% (46/158)	27.5% (44/160)	26.8% (40/149)	26.8% (41/153)
UCVA 2 Lines Worse than Preop BSCVA	16.9% (27/160)	12.0% (19/158)	15.6% (25/160)	11.4% (17/149)	13.1% (20/153)
UCVA >2 Lines Worse than Preop BSCVA	20.6% (33/160)	15.8% (25/158)	11.3% (18/160)	12.1% (18/149)	9.2% (14/153)
UCVA Better than or Equal to Preop BSCVA	30.6% (49/160)	43.0% (68/158)	45.6% (73/160)	49.7% (74/149)	51.0% (78/153)
Not reported*	0	0	0	0	0
Total†	160	158	160	149	153

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available CRFs received with non-missing values at each visit.
* Number of available CRFs received with missing values at each visit.
† Number of available CRFs received at each visit.

4.2.4.7 Patient Symptoms and Satisfaction

Subjects filled out a subject questionnaire at the preoperative visit and at all follow-up visits starting at 3 months. They graded their symptoms according to severity as either none, mild, moderate, marked, or severe (see Table 16.A). Table 16.B presents the patient symptoms change from baseline to 9 months postoperatively. Any symptom for which there is at least a one grade increase from baseline is considered "worse" and at least a one grade decrease is considered "better".

Table 16.A provides all patient symptoms for all treated eyes both preoperatively and at 6, 9, and 12 months. Symptoms are grouped by severity level into absent, mild, moderate, marked, and severe. Symptoms in the mild category are not considered to be clinically significant. It can be seen that those symptoms reported at 9 and 12 months fall predominantly into the "mild" category. Symptoms (those rated moderate to severe) reported with an incidence of at least 5% occurrence at month 9 include light sensitivity (moderate, 7.0%), dryness (moderate, 8.5%), blurred vision (moderate, 7.9%), fluctuation of vision (moderate, 5.6%), variation of vision in normal light (moderate, 5.6%), and variation of vision in dim light (moderate, 7.0%). At 9 months, no symptom was reported as marked or severe with an incidence of 5% or greater.

TABLE 16.A
PATIENT SYMPTOMS
ALL TREATED EYES
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Symptom	Visit	N	Absent % (n)	Mild % (n)	Moderate % (n)	Marked % (n)	Severe % (n)
Light sensitivity	**Preop**	361	74.8% (270)	15.0% (54)	9.1% (33)	0.6% (2)	0.6% (2)
	6 Months	357	66.1% (236)	26.1% (93)	4.5% (16)	3.4% (12)	0.0% (0)
	9 Months	341	70.4% (240)	21.4% (73)	7.0% (24)	1.2% (4)	0.0% (0)
	12 Months	347	67.7% (235)	27.7% (96)	2.3% (8)	2.3% (8)	0.0% (0)
Headaches	**Preop**	361	90.9% (328)	6.6% (24)	1.7% (6)	0.8% (3)	0.0% (0)
	6 Months	357	89.6% (320)	8.1% (29)	2.2% (8)	0.0% (0)	0.0% (0)
	9 Months	341	89.4% (305)	8.2% (28)	2.3% (8)	0.0% (0)	0.0% (0)
	12 Months	347	92.5% (321)	6.9% (24)	0.6% (2)	0.0% (0)	0.0% (0)
Pain/burning	**Preop**	361	94.7% (342)	4.4% (16)	0.6% (2)	0.3% (1)	0.0% (0)
	6 Months	356	87.1% (310)	10.4% (37)	2.5% (9)	0.0% (0)	0.0% (0)
	9 Months	341	90.9% (310)	6.7% (23)	2.3% (8)	0.0% (0)	0.0% (0)
	12 Months	347	92.5% (321)	7.2% (25)	0.3% (1)	0.0% (0)	0.0% (0)
Dryness	**Preop**	361	75.6% (273)	19.1% (69)	5.0% (18)	0.3% (1)	0.0% (0)
	6 Months	357	52.9% (189)	33.6% (120)	9.8% (35)	3.4% (12)	0.3% (1)
	9 Months	341	55.1% (188)	33.4% (114)	8.5% (29)	2.3% (8)	0.6% (2)
	12 Months	346	54.0% (187)	35.5% (123)	7.8% (27)	2.6% (9)	0.0% (0)
Excessive tearing	**Preop**	361	92.8% (335)	4.2% (15)	1.7% (6)	0.8% (3)	0.6% (2)
	6 Months	357	96.9% (346)	2.2% (8)	0.8% (3)	0.0% (0)	0.0% (0)
	9 Months	340	95.3% (324)	4.7% (16)	0.0% (0)	0.0% (0)	0.0% (0)
	12 Months	347	93.4% (324)	5.5% (19)	0.9% (3)	0.3% (1)	0.0% (0)
Gritty, scratchy	**Preop**	361	87.8% (317)	11.1% (40)	0.6% (2)	0.3% (1)	0.3% (1)
	6 Months	357	80.7% (288)	14.3% (51)	4.2% (15)	0.8% (3)	0.0% (0)
	9 Months	341	80.1% (273)	15.0% (51)	3.8% (13)	1.2% (4)	0.0% (0)
	12 Months	347	78.7% (273)	17.0% (59)	3.5% (12)	0.9% (3)	0.0% (0)
Glare	**Preop**	361	82.5% (298)	12.2% (44)	4.7% (17)	0.0% (0)	0.6% (2)
	6 Months	357	72.0% (257)	22.1% (79)	3.6% (13)	2.2% (8)	0.0% (0)
	9 Months	341	73.3% (250)	22.9% (78)	2.6% (9)	1.2% (4)	0.0% (0)
	12 Months	346	75.7% (262)	20.5% (71)	3.2% (11)	0.6% (2)	0.0% (0)
Halos	**Preop**	361	92.5% (334)	5.3% (19)	2.2% (8)	0.0% (0)	0.0% (0)
	6 Months	357	79.0% (282)	16.0% (57)	2.8% (10)	2.0% (7)	0.3% (1)
	9 Months	341	80.1% (273)	16.4% (56)	2.1% (7)	1.5% (5)	0.0% (0)
	12 Months	347	83.3% (289)	12.7% (44)	3.5% (12)	0.6% (2)	0.0% (0)

N = Number of Self-evaluation Forms received with non-missing response for the corresponding symptom at each visit.
% = n ÷ N × 100%.

TABLE 16.A *(CONTINUED)*
PATIENT SYMPTOMS
ALL TREATED EYES

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Symptom	Visit	N	Absent % (n)	Mild % (n)	Moderate % (n)	Marked % (n)	Severe % (n)
Blurred vision	**Preop**	361	85.3% (308)	6.1% (22)	4.7% (17)	3.0% (11)	0.8% (3)
	6 Months	357	71.7% (256)	18.2% (65)	7.3% (26)	2.0% (7)	0.8% (3)
	9 Months	341	71.6% (244)	18.8% (64)	7.9% (27)	1.8% (6)	0.0% (0)
	12 Months	347	72.9% (253)	16.7% (58)	8.9% (31)	1.4% (5)	0.0% (0)
Double vision	**Preop**	361	96.7% (349)	2.8% (10)	0.6% (2)	0.0% (0)	0.0% (0)
	6 Months	357	87.4% (312)	8.1% (29)	3.4% (12)	1.1% (4)	0.0% (0)
	9 Months	341	90.6% (309)	6.7% (23)	2.6% (9)	0.0% (0)	0.0% (0)
	12 Months	346	91.3% (316)	6.4% (22)	2.3% (8)	0.0% (0)	0.0% (0)
Fluctuation of vision	**Preop**	361	88.1% (318)	6.9% (25)	5.0% (18)	0.0% (0)	0.0% (0)
	6 Months	357	65.3% (233)	24.1% (86)	7.0% (25)	3.6% (13)	0.0% (0)
	9 Months	341	68.9% (235)	23.2% (79)	5.6% (19)	1.8% (6)	0.6% (2)
	12 Months	347	70.6% (245)	21.9% (76)	5.5% (19)	2.0% (7)	0.0% (0)
Variation - bright light	**Preop**	361	87.0% (314)	7.5% (27)	3.9% (14)	1.1% (4)	0.6% (2)
	6 Months	357	73.9% (264)	19.6% (70)	5.3% (19)	0.6% (2)	0.6% (2)
	9 Months	341	83.6% (285)	13.2% (45)	1.5% (5)	1.8% (6)	0.0% (0)
	12 Months	347	80.7% (280)	12.1% (42)	4.3% (15)	2.9% (10)	0.0% (0)
Variation - normal light	**Preop**	361	90.6% (327)	8.3% (30)	0.6% (2)	0.6% (2)	0.0% (0)
	6 Months	356	80.6% (287)	15.2% (54)	3.7% (13)	0.6% (2)	0.0% (0)
	9 Months	339	86.4% (293)	7.7% (26)	5.6% (19)	0.3% (1)	0.0% (0)
	12 Months	347	86.5% (300)	6.9% (24)	6.1% (21)	0.6% (2)	0.0% (0)
Variation - dim light	**Preop**	361	82.0% (296)	11.1% (40)	5.3% (19)	1.7% (6)	0.0% (0)
	6 Months	357	62.7% (224)	23.8% (85)	10.6% (38)	2.8% (10)	0.0% (0)
	9 Months	341	69.8% (238)	18.8% (64)	7.0% (24)	4.4% (15)	0.0% (0)
	12 Months	347	68.6% (238)	17.0% (59)	11.5% (40)	2.9% (10)	0.0% (0)
Night driving vision	**Preop**	361	70.9% (256)	19.7% (71)	6.6% (24)	2.2% (8)	0.6% (2)
	6 Months	356	68.5% (244)	19.1% (68)	7.9% (28)	3.4% (12)	1.1% (4)
	9 Months	341	70.1% (239)	22.3% (76)	4.7% (16)	2.9% (10)	0.0% (0)
	12 Months	347	70.9% (246)	19.6% (68)	7.8% (27)	1.7% (6)	0.0% (0)
Other	**Preop**	361	98.1% (354)	0.6% (2)	0.8% (3)	0.0% (0)	0.6% (2)
	6 Months	356	96.6% (344)	2.0% (7)	1.1% (4)	0.0% (0)	0.3% (1)
	9 Months	341	96.8% (330)	1.2% (4)	1.5% (5)	0.6% (2)	0.0% (0)
	12 Months	347	95.1% (330)	2.9% (10)	1.2% (4)	0.6% (2)	0.3% (1)

N = Number of Self-evaluation Forms received with non-missing response for the corresponding symptom at each visit.
% = n ÷ N × 100%.

Table 16.B presents the change in patient symptoms from baseline to 9 months for all treated eyes. A greater proportion of subjects experienced a worsening rather than an improvement from baseline to 9 months in light sensitivity, dryness, glare, halos, blurred vision, double vision, fluctuation of vision, and variation of vision in bright, normal, and dim light.

TABLE 16.B
PATIENT SYMPTOMS CHANGE FROM BASELINE AT 9 MONTHS
ALL TREATED EYES

Symptom	N	Significantly Better % (n)	Better % (n)	No Change % (n)	Worse % (n)	Significantly Worse % (n)
Light sensitivity	335	5.7% (19)	7.5% (25)	65.7% (220)	17.9% (60)	3.3% (11)
Headaches	335	1.8% (6)	6.0% (20)	83.3% (279)	7.5% (25)	1.5% (5)
Pain/burning	335	0.0% (0)	5.1% (17)	86.3% (289)	6.9% (23)	1.8% (6)
Dryness	335	1.8% (6)	9.6% (32)	54.6% (183)	26.0% (87)	8.1% (27)
Excessive tearing	334	3.3% (11)	3.0% (10)	90.7% (303)	3.0% (10)	0.0% (0)
Gritty, scratchy	335	0.6% (2)	6.9% (23)	78.8% (264)	9.0% (30)	4.8% (16)
Glare	335	2.7% (9)	7.2% (24)	69.6% (233)	18.5% (62)	2.1% (7)
Halos	335	1.2% (4)	2.7% (9)	78.5% (263)	14.6% (49)	3.0% (10)
Blurred vision	335	6.3% (21)	4.2% (14)	67.2% (225)	15.2% (51)	7.2% (24)
Double vision	335	0.0% (0)	0.9% (3)	90.7% (304)	6.3% (21)	2.1% (7)
Fluctuation of vision	335	2.7% (9)	4.8% (16)	67.5% (226)	19.4% (65)	5.7% (19)
Variation - bright light	335	3.6% (12)	4.5% (15)	79.1% (265)	11.6% (39)	1.2% (4)
Variation - normal light	333	0.6% (2)	6.6% (22)	81.1% (270)	7.2% (24)	4.5% (15)
Variation - dim light	335	5.1% (17)	4.8% (16)	67.2% (225)	13.1% (44)	9.9% (33)
Night driving vision	335	5.4% (18)	13.1% (44)	62.7% (210)	14.6% (49)	4.2% (14)
Other	335	1.5% (5)	0.6% (2)	94.6% (317)	1.2% (4)	2.1% (7)

N = Number of eyes with nonmissing preoperative and postoperative responses. % = n ÷ N × 100%.
Better (worse) is one grade better (worse). Significantly better (worse) is ≥ 2 grades better (worse).

Responses provided by the study subjects at 6, 9, and 12 months to three questions regarding their experiences with the laser surgery are provided in Table 17. These three questions related to: 1) the perceived overall quality of vision following surgery; 2) the subject's willingness to have the surgery again if he/she could make the choice over; and 3) the subject's overall satisfaction with the results of the surgical procedure.

At 9 months, the overall quality of vision was rated highly, with 97.9% of patients indicating that there was an improvement, while only 2.1% indicated that there was no improvement; 88.5% would elect to have the surgery again; 95.8% reported being satisfied, while 3.1% were neutral and 1.0% were dissatisfied.

TABLE 17
PATIENT EVALUATION OF SATISFACTION AND VISION QUALITY IMPROVEMENT EFFECTIVENESS COHORT SUBJECTS (SUBJECT BASIS)

Response	6 Months % (n/N)	9 Months % (n/N)	12 Months % (n/N)
Overall Vision Quality			
Extreme Improvement	52.5% (53/101)	51.0% (49/96)	60.8% (59/97)
Marked Improvement	29.7% (30/101)	35.4% (34/96)	23.7% (23/97)
Moderate Improvement	10.9% (11/101)	6.3% (6/96)	8.2% (8/97)
Slight Improvement	5.9% (6/101)	5.2% (5/96)	6.2% (6/97)
No Improvement	1.0% (1/101)	2.1% (2/96)	1.0% (1/97)
Not reported*	0	0	0
Total†	101	96	97
Select Refractive Surgery Again			
Yes	85.1% (86/101)	88.5% (85/96)	89.7% (87/97)
No	4.0% (4/101)	5.2% (5/96)	3.1% (3/97)
Unsure	10.9% (11/101)	6.3% (6/96)	7.2% (7/97)
Not reported*	0	0	0
Total†	101	96	97
Satisfaction			
Very Satisfied	71.3% (72/101)	76.0% (73/96)	75.3% (73/97)
Moderately Satisfied	19.8% (20/101)	19.8% (19/96)	17.5% (17/97)
Neutral	6.9% (7/101)	3.1% (3/96)	4.1% (4/97)
Dissatisfied	1.0% (1/101)	1.0% (1/96)	3.1% (3/97)
Very Dissatisfied	1.0% (1/101)	0.0% (0/96)	0.0% (0/97)
Not reported*	0	0	0
Total†	101	96	97

Effectiveness Cohort: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available eyes with non-missing values at each visit. % = n ÷ N × 100%.
* Number of available eyes with missing values at the visit.
† Number of available eyes at the visit.

4.2.5 Factors Associated with Outcomes

Gender, preoperative refraction, age, baseline MRSE, primary vs. fellow eye, study site, and use of an ablation algorithm adjustment were evaluated as statistically significant predictors of the UCVA and refractive outcome for the LASIK procedure. These analyses identified a site effect, an ablation algorithm adjustment effect, an effect of baseline MRSE, a small cylinder cyclotorsional effect, and an effect of keratome use.

Statistical analysis of the study data by site revealed that the percentage of eyes reported with a MRSE within ± 0.50 D of the attempted correction was significantly different among the six investigational sites at 9 months. At 9 months, 93% of eyes were within 0.50 D of intended MRSE at site #5, compared with 81%, 67%, 63%, 62%, and 65% at the other five study sites. There were no statistically significant differences observed between the study sites with respect to attempted versus achieved MRSE within ± 1.00 D of the intended correction at 9 months.

Statistical analysis of the study data by site revealed that the percentage of eyes reported with UCVA outcomes of 20/40 or better and 20/20 or better were not significantly different among the six investigational sites at 9 months. At 9 months, 100% of eyes had 20/32 or better UCVA at site #1 and site #2, compared with 99%, 92%, 96%, and 86% at the other four study sites. Similar findings were observed for UCVA outcomes of 20/25 or better, 20/16 or better, and 20/12.5 or better. The clinical significance, if any, of this difference is uncertain.

Analyses of the effect of the use of an ablation algorithm adjustment revealed that eyes treated with the ablation algorithm adjustment had significantly better predictability outcomes for the proportion of eyes within ± 0.50 D of attempted versus achieved MRSE at 9 months ($p= 0.0006$). Other key effectiveness endpoints were shown to be significantly better as a result of the algorithm adjustment.

Eyes with preoperative MRSE > 5.0 D were significantly less likely to achieve refractive predictability within ± 0.50 D of the intended outcome at 9 months. In contrast, at 9 months, eyes with baseline MRSE up to +5.00 D had significantly better MRSE accuracy outcomes (> 61% within ± 0.50 D of intended MRSE) than eyes with baseline MRSE greater than +5.00 D (ranging from 33% to 40% for both groups within 0.50 D of intended MRSE). Baseline MRSE did not have a significant association with UCVA outcomes of 20/40 or better at 9 months. However, a greater proportion of eyes with baseline MRSE ≤ +5.00 D achieved UCVA better than 20/40 (i.e., 20/16 to 20/25 at 9 months) than eyes with baseline MRSE higher than +5.00 D.

Analysis of the cylinder treatment revealed a small amount of cyclorotation. This may have been the result of cyclotorsional movement of the patient's eye that occurs when moving from the sitting position to the position under the laser. It is recommended that a mark be made on the patient's corneal limbus using a sterile single use marker for alignment with the reticle of the laser surgical microscope to be certain that no

cyclorotation is present. The marking should be made with the patient in the sitting position behind a slit lamp. Once the patient is lying down, if necessary, the patient's head can be repositioned to properly align the reticle with the mark(s) during the treatment to reduce or eliminate any rotational misalignment.

An analysis of the keratome used in the study procedures revealed a possible effect on UCVA outcomes and MRSE predictability. Site 5, which used the Moria keratome, showed better efficacy outcomes with regard to the proportion of eyes with deviation from the intended correction within ± 0.50 D at 9 months postoperatively (92.9%, $p<0.0001$). In addition, the IntraLase keratome and the Hansatome keratome were associated with a significantly lower proportion of eyes achieving UCVA of 20/20 or better (62.1% and 62.9%, respectively) as compared to the other keratomes. However, this analysis of outcomes by keratome type is confounded by other factors that may have contributed to this difference in outcomes, including site and introduction of the algorithm adjustment. Since the key effectiveness outcomes for the total cohort of eyes were not affected by the type of keratome used, the differences observed with different keratomes for the sphere only and the astigmatic hyperopia eyes in the study may reflect other, non-keratome factors.

In addition, the complications were reported with a significantly higher proportion of eyes for the IntraLase keratome as compared to the various mechanical microkeratomes included diffuse lamellar keratitis (8.3%), dry eye (8.3%), epithelium at flap edge (4.9%), epithelium in the interface (13.9%), foreign body sensation (5.6%), punctal plug insertion (30.6%), superficial punctate keratitis (16.0%), steroid induced IOP increase (5.6%), and transient light sensitivity syndrome (8.3%).

SECTION 5

SURGICAL PLANNING AND PROCEDURES

5.1 INTRODUCTION

LASIK is a procedure that combines the use of a microkeratome to create a lamellar corneal flap and the energy of the excimer laser to create a keratectomy in the corneal stroma of a shape designed to correct or reduce a specific refractive error. The intent is to properly focus visible light entering the eye to provide improved vision. It is essential that the refractive information upon which this surgical procedure is based is accurate and correctly transmitted to the laser. It is the sole responsibility of the surgeon to ensure that the information for each individual patient is accurate.

5.2 PATIENT SELECTION

Consideration should be given to the following in determining the appropriate patients for LASIK:

- Complete examination, including, but not limited to, manifest and cycloplegic refraction evaluation, must be performed. The lens must be evaluated, especially in the older patient, to assure that nuclear sclerosis or any other lens opacity is not present prior to laser surgery. Indirect ophthalmoscopy through a dilated pupil and a clear crystalline lens is essential.
- To obtain accurate refractive information, contact lens wearers must be examined after a period of not wearing contact lenses for at least 2 weeks for soft lenses and at least 3 weeks for hard (PMMA) and gas-permeable lenses. Prior to treatment and after at least 3 weeks of not wearing contact lenses, patients who wear rigid gas permeable or hard lenses must have 3 central keratometry readings and manifest refraction taken at one-week intervals, the last 2 of which must not differ by more than 0.50 diopter in either meridian. All mires must be regular.
- Glaucoma is more common in hyperopic patients than in the general population. Evaluation of the optic nerve and measurement of intraocular pressure 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 intraocular pressure and/or evidence of glaucomatous damage are found, topical steroids should only be used with careful medical supervision or the patient should not undergo LASIK surgery.

- Pachymetry must be performed to obtain a baseline central corneal thickness measurement to assure that the combination of the planned corneal flap thickness and the planned laser ablation will not approach closer than 250 microns to the corneal endothelium.
- Baseline evaluation of patients requesting refractive surgery should be performed within 30 days of the LASIK surgery.
- 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 LASIK procedure.
- The patient must be able to understand the surgery and give informed consent.
- The patient must be able to tolerate eye drops to numb the eye.
- The patient should be clearly informed of all alternatives for the correction of his/her hyperopia including, but not limited to, spectacles, contact lenses, and other refractive surgeries.
- Due to the importance of managing a patient's expectations in elective refractive surgery, it is recommended that the physician also complete an assessment of the patient's expectations and psychological state, which would include:
    - conveying realistic expectations to the prospective patient;
    - attempting to ensure patient comprehension of the risks and benefits at the of the informed consent process;
    - providing a patient information card that has eye measurements from before the LASIK surgery. Patients can keep this card to help their doctor calculate the lens implant power should they need to have future cataract surgery; a form for the necessary information is available on the internet at: http://www.geteyesmart.org/eyesmart/upload/kcard.pdf;
    - discussing with patients how having LASIK may affect the future interpretation of intraocular pressure measurements; patients should be instructed to inform future eye care providers that they have had LASIK.

5.3 PROCEDURE

The output of the laser is potentially hazardous only to the skin and the surface layers of the cornea. This radiation has not been shown to pose a threat to retinal structures or to the crystalline lens. The area of potential hazard (Nominal Hazard Zone) for the production of a photochemical keratitis has been determined to be less than 40 cm from the primary beam. All healthcare personnel should avoid direct exposure to the skin or eye by the primary beam. While no hazard may exist further than 40 cm from the beam, the use of protective eyewear is recommended if the possibility exists that healthcare personnel will approach closer than this distance to the primary beam.

Prior to initiating the lamellar keratectomy portion of the surgery with the microkeratome, the physician should perform the fluence test to ensure that the laser is ready to deliver laser energy.

5.4 PERI-OPERATIVE PROCEDURES

5.4.1 Anesthesia

Extensive clinical experience has shown that LASIK excimer surgery is well tolerated and rarely causes significant pain. For this reason, systemic sedatives and injected local anesthetics are not required. Topical anesthesia applied just before insertion of the lid speculum should provide adequate control of pain during surgery. For those patients with a high degree of anxiety, appropriate medication may be given preoperatively.

5.5 INTRA-OPERATIVE PROCEDURES

5.5.1 Creating the Lamellar Flap with the Microkeratome

The LASIK procedure requires the creation of a hinged corneal flap using a microkeratome prior to the laser ablation procedure. The microkeratome used to perform the LASIK procedure should be a legally marketed device in the United States. The physician should follow the specific procedures recommended in the Operator's Manual supplied with the particular brand of microkeratome to be used. Once the corneal flap has been created, the laser ablation step may be performed.

5.5.2 Performing the Laser Ablation

Following creation of the corneal flap, the laser ablation is then performed. The physician should refer to the User Manual supplied with the MEL 80 Excimer Laser System for proper operation and maintenance instructions. The physician also must have completed the appropriate technical and medical in-service training provided by the manufacturer prior to using the laser for actual surgery.

5.6 POST OPERATIVE PROCEDURES

5.6.1 Patching and Medications

Following completion of the excimer laser surgery, appropriate topical medications and a corneal shield or firm patch should be applied to the eye. A combination steroid-antibiotic medication should be included at the time of patching. Some physicians may wish to omit steroids until the edge of the lamellar keratectomy has healed completely. The patient should be seen one day postoperatively to ensure that the corneal flap is properly in place.

5.6.2 Analgesia

The physician may wish to administer appropriate postoperative medications for the management of ocular pain. These may include the use of topical ophthalmic non-steroidal anti-inflammatory drugs (NSAIDs), as well as systemically administered medications for pain management.

5.6.3 Handling Complications

Following the LASIK procedure, the physician should carefully monitor the condition of the patient's cornea on a periodic basis with regard to the condition of the corneal flap and its location. Special attention should be given to the presence of any debris or epithelial cells in the interface between the flap and the underlying corneal stroma. The presence of such foreign material may require lifting of the flap to remove such debris and/or cells using appropriate surgical techniques. The use of topical ophthalmic steroid medications may be required to suppress any associated inflammation caused by debris or cells in the interface.

5.7 POST PROCEDURE

A slit-lamp examination should be performed on postoperative day one and as needed thereafter to ensure that healing of the cornea is complete. After the one-day examination, the following examinations are recommended at a schedule of at least 1, 3, 6, and 9 months:

- Uncorrected visual acuity (UCVA or VA-sc)
- Manifest refraction with best spectacle-corrected visual acuity (BSCVA or VA-cc)
- Intraocular pressure (IOP)
- Slip-lamp examination, including evaluation of corneal clarity and the condition of the flap.

SECTION 6
CARL ZEISS MEDITEC MEL 80 EXCIMER LASER SURGICAL PROCEDURE STEP BY-STEP PROCEDURE

6.1 Prior to Surgery

1. Refer to the User Manual for the complete step-by-step procedure to be followed prior to commencement of the actual surgical procedure (laser set-up, fluence test, etc.).
2. Provide instructions to the patient explaining what to expect during (i.e. where to look during the procedure) and after the procedure (i.e. the eyes will feel irritated and the vision will be blurry). In addition, provide patient with the device labeling "Patient Information Booklet" for additional information.

6.2 Preparing Device and Patient for Treatment

1. Fully examine the patient's eye(s) including the retina (inquire also about the patient's working conditions, e.g. night driving).
2. Two weeks before surgery, the patient should stop wearing hard contact lenses. Soft lenses should be removed one week before surgery.
3. Check refraction yourself or have it done by an appropriately qualified person. Use subjective manifest refraction.
4. Check pupil size in the dark (e.g. with a Colvard pupillometer or WASCA Analyzer).
5. Determine corneal thickness at the thinnest point.
6. Calculate the ablation depth with the adequate treatment diameter (0.5 mm > mesopic pupil size) and check for a sufficient residual stroma (250 µm).
7. Never perform LASIK in a patient who is presumed to have a residual stroma thickness of less than 250 µm. Always consider the inaccuracy of the microkeratome.
8. Check the national legislation and all contraindications specified in relevant literature (e.g. keratoconus, irregular topography, etc.), before you decide on the surgery.
9. Recheck refraction and topography (3 pictures minimum) immediately before surgery (possibly the topography has changed by contact lens effects since the first measurement).
10. The clinical study showed small amounts of cylcorotation present. It is recommended to mark the cylinder axis on the corneal limbus using a sterile single use marker behind the slit lamp prior to entering the operating room. The cylinder

marking can be used to align the reticle during the treatment to reduce or eliminate any rotational misalignment.

11. Check room conditions (see technical data, ambient conditions for intended use in the MEL 80 User Manual).
12. Starting 30 minutes before surgery, it is advisable to put a drop of a non-toxic antibiotic in the eye every 10 minutes.
13. Prepare the microkeratome.
14. Enter and verify patient data.
15. Microscope setting: magnification 1.0x.
16. Run the fluence test and confirm it with <Energy Ok>.
17. Switch off the aiming beam to avoid coverage of the fixation light. Move joystick aside, if necessary.
18. Bring patient in.
19. Check patient data and the eye to be operated. If you use OPASS, you may correct patient data, if necessary. If patient data is correct, click on <Calculate> to have the correction program calculated.
20. Position the patient on the bed so that the patient's eye is effortless in the position required.
21. It may be favorable to wipe the inner side of the lids with a triangular swab soaked with anesthetics (1% Xylocaine, no preservatives) in order to reduce irritation and thus avoid increased production of tear fluid.
22. Cover the operation area with a fenestrated adhesive drape and arrange it in such a way that the lashes are folded back over the margin of the eyelid.
23. Microscope setting: magnification 0.6x.
24. Coarsely adjust the patient bed using the focusing beams.
25. Use an eyelid retractor.
26. Apply a drop of an anesthetic (e.g. Oxybuprocain-HCl) (not yet in the other eye if you plan bilateral treatment).
27. Open the lid retractor as wide as the patient can just tolerate. Fine align the patient bed so that the iris is in the center of the palpebral fissure.
28. Using gentian violet, mark the cornea non-symmetrically.
29. Rinse excessive dye away.
30. Perform the keratome cut following the instructions for use of the keratome. Do not open the flap yet.
31. Microscope setting: magnification 1.0x.
32. Again, accurately position the patient's eye with the patient bed.

33. Swing in the CCA+ unit taking care that the position of the patient's eye remains stable.

34. Have the patient look at the green, blinking LED (Note: The patient's eye must be in the center of the field of view; microscope setting: magnification 1.0x.) Tell the patient that the aiming beam will outshine the LED.

6.3 Microkeratome Surgery

The physician should perform the lamellar keratectomy to create the corneal flap according to the instructions provided with the microkeratome. Once the corneal flap has been created, the laser ablation portion of the procedure may be started.

6.4 Laser Treatment

1. Activate the eyetracker.

2. The eyetracker automatically sets the aiming beam to the center of the entrance pupil ("line of sight"). To choose another centration point, use the offset keys. Turn on the satellite illumination, if necessary.

   Note: Since the fixation light is central, it is advisable to center the patient's right eye with the surgeon's left eye and vice versa to avoid parallax errors.

3. Open the flap and settle it on a sterile LASIK shield soaked in BSS; the inside of the flap must not be touched throughout the treatment.

4. Click on the <Ready> button.

5. Start ablation by depressing the footswitch.

6. Stop every 15 seconds to verify proper centration.

7. After the last shot, move the CCA+ unit out of the surgical field.

   Note: The treatment progress is indicated by a progress display. By a click on the <Cancel> button, you can abort the treatment after releasing the footswitch.

   The control computer will automatically stop lasing after the correction program is finished. If you aborted the treatment by releasing the footswitch, you can continue it by depressing the footswitch again.

   Note: If the eyetracker loses track of the pupil during the treatment or the pupil leaves the hot zone, the control computer will interrupt the treatment.

   You can then continue the treatment with the <Continue> button, when the pupil has been detected again or the eyetracker has been deactivated.

8. Immediately after ablation, clean the stromal bed very carefully with a new moist triangular swab moved clockwise and with another new moist swab moved

counterclockwise to remove debris and epithelial cells. Continue until the bed looks dry.

9. Fold back the flap by means of a bent cannula. If folds have formed, use the cannula to unfold them. Then, rinse with BSS to clean the site and remove any wrinkles.

   Note: Rinse briefly at high pressure to avoid hydration of the flap and thus canalization -greater ingrowth of epithelium.

10. Make sure the flap is properly positioned (marks, symmetry of the duct). If not, use the cannula again. Then, using a wet triangular swab, wipe the flap away from the hinge to fix its position.

    Note: Use the segmenting facility of the ring lamp, if necessary, to check the correct position of the flap.

11. Apply a few drops of an antibiotic.
12. Wait one minute while keeping the central epithelium moist.
13. Carefully remove the eyelid retractor and the drapes. Ask the patient to blink repeatedly and observe the behavior of the flap.
14. Microscope setting: Magnification 0.6x.
15. Contact lenses may be inserted only if the epithelium is injured.
16. Tell the patient to keep the eye closed until the next morning. For one week, have him or her wear an eyepatch at night and sunglasses during the day when being in the open air.
17. When checking the position of the flap on the first postoperative day, you can reposition the flap, if necessary.
18. The treatment with antibiotics and anti-inflammatory drops should be continued for four days.

SECTION 7
EMERGENCY STOP

If a system emergency situation arises, press the Emergency Stop button. This switch turns off the complete laser system. It is located on the front side below the computer monitor in the Carl Zeiss Meditec MEL 80 Excimer Laser. Pressing the Emergency Stop button is the fastest possible way to completely switch off the laser system.

FACTS YOU NEED TO KNOW ABOUT LASER IN SITU KERATOMILEUSIS (LASIK)

A SURGERY TO REDUCE OR ELIMINATE NATURALLY OCCURING HYPEROPIA
WITH OR WITHOUT ASTIGMATISM USING THE
CARL ZEISS MEDITEC MEL 80 EXCIMER LASER SYSTEM

PATIENT INFORMATION BOOKLET

Please read this entire booklet. If you have any questions about it, discuss them with your doctor before you agree to the surgery.

The MEL 80 Excimer Laser is indicated for use in primary Laser Assisted *in situ* Keratomileusis (LASIK) treatments for the reduction or elimination of naturally occurring hyperopia of less than or equal to +5.0 D with or without refractive astigmatism of > +0.5 D and ≤ +3.0 D, with a maximum MRSE of +5.0 D, in patients who are 21 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by change in sphere and cylinder of ≤ 0.5 D.

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CARL ZEISS MEDITEC, INC.
MEL 80 EXCIMER LASER SYSTEM
PATIENT INFORMATION BOOKLET

TABLE OF CONTENTS

GLOSSARY OF TERMS

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

Astigmatism: A type of refractive error in which light rays from horizontal and vertical lines cannot both be in focus on the **retina** at the same time.

Cataract: Cloudiness of the natural lens of the eye.

Cornea: Transparent front portion of the eye. It covers the iris and the **pupil**. It provides most of the eye's focusing power.

Device Treatment: The pattern of laser pulses which the laser applies to the cornea to treat your hyperopia.

Diopter: Unit of measure for refractive power of lenses.

Ectasia: Bulging region of the cornea due to a thinning of the corneal tissue.

Excimer Laser: A medical device used to remove tissue from the **cornea** with short pulses of ultraviolet light. It re-shapes the cornea to correct refractive errors. This allows light rays to better focus on the retina.

Farsightedness or Hyperopia: A type of refractive error in which both distant and near objects appear blurred because the light rays are focused behind the retina.

Glare: A light within the field of vision that is bright enough to interfere with the ability to see other lights or objects.

Glaucoma: Group of diseases marked by increased pressure in the eye. It results in damage to the optic nerve and retinal nerve fibers.

Halo: Hazy ring around a bright light. Some patients with refractive errors or optical defects (e.g., cataracts or corneal swelling) see halos.

Keratoconus: An inherited disease of the cornea. It is progressive. It is marked by thinning and cone-shaped bulging of the central cornea.

LASIK: An acronym for "Laser *in situ* Keratomileusis." LASIK is a type of surgery to treat nearsightedness, farsightedness, and astigmatism. A device called a microkeratome, which is like a carpenter's plane, cuts a thin flap of tissue from the front of the cornea (clear part on the front of the eye). The doctor then folds the flap out of the way. Next, an excimer laser removes tissue

from the front surface of the cornea to make it more curved in hyperopic treatments. After the laser treatment, the doctor replaces the corneal flap.

Lens: A clear structure located behind the iris of the eye. It adds optical power to the eye to sharpen the image on the retina.

MRSE: Abbreviation for Manifest Refraction Spherical Equivalent, which is the average refractive power in diopters needed to correct the refractive error of the eye.

Nearsightedness or Myopia: A type of refractive error in which distant objects appear blurred because light rays from them are focused in front of the retina.

Ocular Hypertension: Pressure inside the eye of more than 21 mm Hg with no other signs of glaucoma.

Pellucid Marginal Degeneration: Thinning of the lower outer edge of your cornea, where adjacent cornea may protrude

Pupil: The dark circular opening in the center of the iris that allows light into the eye. It shrinks in bright light and enlarges in dim light. (It is like a camera aperture.)

PRK: An acronym for "photorefractive keratectomy." In this surgery, an excimer laser removes tissue from the front part of the cornea. The goal is to re-shape the cornea to correct refractive errors of the eye.

Refractive Surgery: Surgery to change how the eye bends light. The goal is to repair the eye's focusing errors.

Retina: The thin layer of nerve cells, or "film," at the back of the eye. It converts light images into nerve signals sent to the brain.

RK: An acronym for "radial keratotomy." In this surgery, radial cuts are made near the edge of the cornea. This flattens the central cornea to reduce nearsightedness.

Vitreous: A clear, jelly-like substance that fills the middle of the eye.

INTRODUCTION

This booklet is written to help you decide whether to have **LASIK** surgery to correct your **farsightedness** (LASIK stands for Laser *in situ* Keratomileusis). Glasses and contact lenses also correct farsightedness, as do the surgeries known as **PRK** (PRK stands for photorefractive keratectomy). This booklet refers to LASIK using the Carl Zeiss Meditec MEL 80 Excimer Laser System. It is somewhat similar to PRK.

If you are farsighted in both eyes, you may want to treat both eyes with LASIK. Sometimes, it is better to treat only one eye with LASIK. Talk with your doctor about whether it would be better to treat one eye or both eyes.

Please read this whole booklet. Discuss your questions with your doctor. Your doctor can determine whether or not you are medically suitable for LASIK, but only you can decide whether the expected benefits are worth the risks. Some jobs have vision requirements that **RK** (Radial Keratotomy), PRK, or LASIK do not meet (for example, military pilots).

Please note that words in **bold** print indicate that they can be found in the glossary.

HOW THE EYE FUNCTIONS

Your eye focuses light to form images or "pictures" much like a camera. Your eye changes the images into nerve signals. Then it sends them to the brain. If your eye is out of focus, what you see is blurred.

The **cornea** (clear front portion of the eye) bends the light toward your retina. The clear tissue of the cornea provides two-thirds of the focusing power of the eye. The **lens** (a clear organ found in the front third of the eyeball, and it adds optical power to the eye) finishes the job of focusing the light onto your retina.

FOCUSING WITH YOUR EYE

The eye focuses light by bending all light rays to meet at a single point. If it works perfectly, a sharp image of the object you look at will be focused on the retina (Fig. 1). You will see a clear image. But, if the light focuses in front of or behind the retina, the image you see will be blurred. Whether you are farsighted or astigmatic (Fig.2, Fig.3) depends on where the image focuses.

The shape of the cornea determines the focusing power of the eye. The more curved the cornea, the more the light rays are bent. If the cornea is too flat, the image focuses behind the retina. The eye then is farsighted (Fig. 2). If the cornea shape is irregular (like a football rather than a basketball), it is called astigmatic (Fig. 3).

Figure 1
Normal Eye

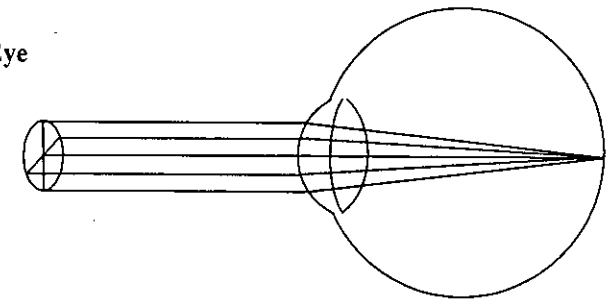


Figure 2
Farsighted Eye

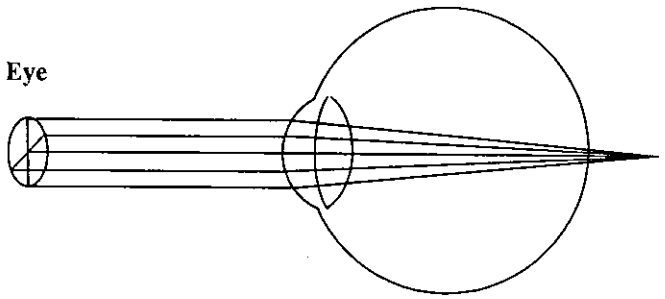
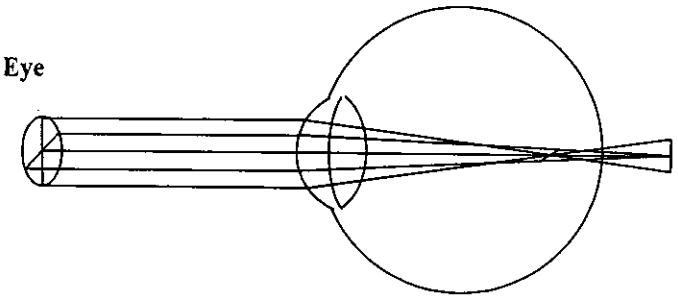


Figure 3
Astigmatic Eye



CHECKING YOUR FOCUS

Your doctor checks where your eye focuses light. When he/she corrects your vision, he/she adds one or more lenses to move the focal point so that the focal point strikes your retina perfectly. Good focus depends on the shape and size of your eyeball, the shape of your cornea, and the power of your natural lens.

THE FARSIGHTED EYE

Hyperopia (i.e. farsightedness) is less common than **myopia (nearsightedness)** or emmetropia (i.e., ideal correction). Farsightedness occurs when the eye does not have enough refractive power to focus distant objects on the retina, while nearsightedness occurs when the eye has too much refractive power to focus distant objects on the retina. Hyperopia is typically in the +1.00 to +4.00 **diopter** (a unit of measure for refractive power

of lenses; abbreviated D) range, and rarely can be as high as +8.00 D. In contrast to myopia, hyperopia occurs when the eye is too short for the power of its optical components. In hyperopia, the cornea is not steep enough and light rays hit the retina before they come into focus. Distant objects appear blurred, and nearby objects are even more fuzzy. Most farsighted individuals need corrective eyewear to see clearly at all distances. Glasses, contact lenses or **refractive surgery** (surgery to change how the eye bends light) can correct farsightedness.

If your vision changes over time, you can change glasses or contact lenses. Changes due to refractive surgery cannot be reversed. Sometimes the first surgery doesn't correct your vision enough or corrects it too much. Sometimes your vision changes as time passes. In either case, your doctor can try to improve it with added treatments.

WHAT IS LASIK?

LASIK is a surgical treatment for farsightedness. A device called a microkeratome, which is like a carpenter's plane, cuts a thin flap of tissue from the front of the cornea. The doctor then folds the flap out of the way. Next, an **excimer laser** (a medical device used to remove tissue from the cornea) removes some tissue from the front surface of the cornea to make it more curved. After the laser treatment, the doctor replaces the corneal flap back in place.

An excimer laser is a laser that aims a strong beam of UV (ultraviolet) light at your eye. The laser creates a brief, intense pulse that lasts just a few billionths of a second. Each pulse removes a tiny amount of tissue from the surface of the cornea. It makes little heat and does not change the tissue beneath.

Doctors perform LASIK surgery on one eye at a time. If all goes well with the first eye, he/she can treat the second eye. Often the doctor does the second eye on the same day. The doctor can also do it later; it depends on his/her judgment of your particular case.

LASIK corrects your vision so you can see distant objects better. It does not take away the need for reading glasses. You may need reading glasses after laser surgery even if you did NOT wear them before.

INDICATIONS FOR USE

The MEL 80 Excimer Laser is indicated for use in primary LASIK treatments for the reduction or elimination of naturally occurring hyperopia of less than or equal to +5.0 D with or without refractive astigmatism of > 0.5 D and ≤ 3.0 D, with a maximum MRSE of +5.0 D, in patients who are 21 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by change in sphere and cylinder of ≤ 0.5 D.

CONTRAINDICATIONS – WHEN YOU SHOULD NOT HAVE LASIK

You should **NOT** have LASIK if any of the things below apply. In these cases, the risk is greater than the benefit.

- You have severe dry eye; this problem may become worse after LASIK and may put you at risk for infection.
- You have an active infection or inflammation of the eye. These may increase the risk of complications and should be cleared up before LASIK treatment.
- You have advanced glaucoma, because the increased eye pressure associated with cutting the LASIK flap might cause further damage to your vision, as might increased eye pressure associated with response to steroid eye drops in some patients.
- Your cornea is too thin to perform LASIK without increasing the risk of causing a bulging cornea (ectasia).
- You have an active connective tissue disease or autoimmune disease which may be associated with corneal melting, such as rheumatoid arthritis, Wegener's granulomatosis, relapsing polychondritis, systemic lupus erythematosus, or polyarteritis nodosa. If you have LASIK, there is risk of severe damage to your cornea.
- You have a significantly weakened immune system due to medications (such as high dose steroids) or disease (such as AIDS). These conditions make you more prone to infection after surgery.
- You are pregnant or nursing, which can cause short-term changes in your cornea. Such changes cannot be predicted. In such cases, LASIK might improperly change the shape of your cornea in a way that would harm your vision.
- You have a history of, or show any signs of, keratoconus (thinning and cone-shaped bulging of your cornea), pellucid marginal degeneration (thinning of the lower outer edge of your cornea, where adjacent cornea may protrude), or any other condition that causes thinning or bulging of your cornea. These conditions can lead to further distortion and thinning of the cornea, and permanently reduced vision after LASIK surgery. This may result in the need for additional surgery (such as a corneal transplant) after LASIK.
- You have recently had or now have a herpes eye infection (simplex or zoster), or have significant corneal damage (poor sensation, scarring, blood vessels growing into the cornea) from a past herpes infection. These may put you at high risk for further corneal damage.
- You have uncontrolled diabetes or you have visually significant diabetic complications. If your blood sugar is uncontrolled, your spectacle prescription will be changing and your doctor will not be able to accurately determine what treatment is appropriate. If you have vision problems related to diabetes, the LASIK procedure may make them worse.

WARNINGS

If you have any of the following conditions, you should talk to your doctor before you decide to have LASIK, because you may be at greater risk for poor outcomes or injury related to LASIK. You should discuss your level of risk with your doctor. You and your doctor should determine whether the benefits of LASIK outweigh the risks for you, <u>based on the nature and severity of</u>

your condition. There is risk of serious adverse outcomes if LASIK surgery is performed in patients with the following conditions:

- Remote history of herpes (simplex or zoster) infection that affected your eyes. It is possible that LASIK surgery might lead to reactivation of the dormant herpes virus. (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)
- Symptoms of dry eye. If you have dry eyes, LASIK may increase the dryness, with accompanying discomfort and visual problems. This may or may not go away. (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)
- You are taking isotretinoin (Accutane®)[1], for acne treatment. This medication may cause increased dryness and result in increased complications after LASIK.
- Diabetes. Even if you have well controlled diabetes, LASIK may be risky for you because your diabetes may interfere with the healing of your eyes. (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)
- Glaucoma, elevated eye pressure (ocular hypertension), or being followed for possible glaucoma (glaucoma suspect). These conditions may be associated with increased risk with LASIK. There is greater difficulty in accurately monitoring eye pressure after LASIK. You may also be at greater risk for damage to your vision associated with increased eye pressure when cutting the LASIK flap. You may also be at greater risk for increased eye pressure related to medication given after surgery (steroid eye drops). (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)
- Severe allergies. If you rub your eyes a lot after LASIK, you may be at risk for dislodging the corneal "flap" that was cut for the procedure. The strength of the flap attachment to the underlying cornea is significantly and permanently reduced after surgery. Additionally, if you have severe allergies and take medicines for them, LASIK may be more risky for you, because symptoms of dryness, often associated with anti-allergy medication, may increase after LASIK.
- Connective tissue diseases or autoimmune diseases (such as rheumatoid arthritis, lupus erythematosus), even if well controlled and stable. You may have slower healing and less predictable outcomes. Depending upon your disease, its severity, and the medication you are taking, there may be additional risks. These may include an increased risk of severe dry eye, infection, inflammation, or corneal melting. Discuss your additional risks with your surgeon, after he or she has consulted with the other doctors who are treating you. (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)
- A condition (such as HIV) or a medication (such as steroids) that affects your immune system. You may be at increased risk for infection. (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)

1 Accutane (isotretinoin) is the registered trademark of Hoffman La Roche Inc.

- Glasses or contact lens prescription has changed in the last 12 months. If your prescription is not stable, the right amount of treatment may not be determined accurately enough. This may result in poor vision after LASIK.
- Blepharitis, or prior history of blepharitis. Blepharitis is redness on the line of the eyelash. It includes crusting of the lashes, often with burning, itching and irritation of the eyes. It can increase the risk of infection of the flap after LASIK. It also can increase the risk of inflammation of the flap.
- You have a history of rubbing your eyes. The LASIK flap never completely heals, and it can be dislodged by eye rubbing. If you are not sure you can keep from rubbing your eyes after LASIK, you may not be a good LASIK candidate.

PRECAUTIONS

It is not known whether LASIK is safe and effective for the following conditions or situations. If you have any of the conditions below, tell your doctor. You should discuss possible risks with your doctor before you decide whether to have LASIK.

- You have 0.75 D or more of difference between refractions of your eye taken with and without eye drops that prevent your lens from adjusting.
- Your cornea, lens, or the **vitreous** (a clear, jelly-like substance that fills the middle of the eye) are not normal due to disease or other factors (such as a scar or cataract). Things like corneal scars may affect the accuracy of LASIK or the way your eye heals. This may result in poor vision after LASIK.
- You have or had uveitis/iritis (inflammation of the iris or other structures within the eye). In such cases, it is not known whether LASIK is safe and effective. Such diseases are often treated with steroids, which can affect wound healing. While these diseases are active or resolving, they could affect the accuracy of LASIK. They also could affect the healing process.
- You have had prior eye surgery (including refractive surgery such as RK, PRK, LASIK, or other surgery) or eye injury. You should tell your doctor about any such history, as it may affect your risk with LASIK.
- You are less than 21 years of age. It is not known whether LASIK is safe and effective for you. The safety and effectiveness of LASIK has not been evaluated in people in this age group.
- You take medicines that may affect wound healing. One such medicine is Imitrex[2], used for migraine headaches, and others which include hormone replacement therapy and antihistamines. It is not known whether LASIK is safe and effective for you.
- You are taking any medicines. Tell your doctor all medicines you are taking, with or without a prescription. It is possible that medications you are taking might have some effect on surgical outcome or healing. Tell your doctor if you are taking any

2 Imitrex (sumatriptan succinate) is a registered trademark of Glaxo Group Limited

prescription medicines, any medications you bought without a prescription, or any vitamins or supplements.

- You have a history of keloid formation.
- You have a **MRSE** of > +5.0 D, sphere > +5.0 D, cylinder +0.5 D or less, or cylinder greater than +3.0 D, as insufficient safety and effectiveness data are available for eyes in this range.
- **You are older than 50 years of age.** Compared to younger patients, it is harder to predict outcomes for those 50 years and older.
- You are taking amiodarone hydrochloride (e.g., Cordarone®[3]), used to treat irregular heartbeats (ventricular arrhythmias). This medication can cause opacities in the cornea and might cause problems with healing after LASIK.
- You have a close family member with keratoconus, pellucid marginal degeneration or another disorder which may cause thinning or bulging of the cornea. These conditions may run in families. If you have one of these conditions and it has not been diagnosed, LASIK may cause more rapid progression of the disease. You should tell your doctor about any family history of these problems. (See CONTRAINDICATIONS: **Conditions When You Should Not Have LASIK** for related information.)
- You have a history of any eye disease or abnormality. If you are aware of any eye disease or abnormality, you should discuss this with your doctor, as it might increase risks associated with LASIK.
- You have large pupils. You should discuss with your doctor whether your pupil size may have negative effects on your vision after LASIK, such as glare, halos, and night driving difficulty. Regardless of how large your pupils appear to you, your doctor should measure your pupil size under dim lighting conditions before surgery.
- You are having LASIK for farsightedness and have a history of "crossed eyes". You should tell your doctor if you have this condition as you might have an increased risk of increased problems with "misaligned eyes" after surgery.
- You have any other medical conditions (other than those already mentioned). It is possible that your medical condition might have some effect on surgical outcomes or healing. Let your doctor know all your medical conditions.

For the following additional conditions, it is not known whether LASIK is safe and effective:

- Over the long term, more than 24 months after LASIK, it is not known whether LASIK is safe and effective.
- LASIK retreatment with the MEL 80. The clinical study provided insufficient data to determine the safety or effectiveness of LASIK retreatment with the MEL 80 laser. The

3 Cordarone (amiodarone hydrochloride) is the registered trademark of Sanofi-Synthlabo.

risk and accuracy of LASIK retreatment, or LASIK with another surgery to correct vision, has not been evaluated.

- Under conditions of dim lighting, rain, snow, fog or bright glare. Under these conditions, you might have problems seeing after LASIK. Whether you may have poor vision under these conditions is hard to predict because it has been studied so little. You should discuss with your doctor the effects of LASIK on vision in dim lighting, rain, snow, fog, or bright glare, since these conditions have not been fully evaluated.
- It is harder to predict outcomes for those 50 years and older.

Your doctor should evaluate you for dry eyes before surgery. Be sure you tell your eye doctor if you have ever had symptoms of eye dryness or difficulty wearing contact lenses because of dryness. You may have dry eyes after LASIK surgery even if you did not have dry eyes before surgery.

You should be aware that the thinning of the cornea due to LASIK surgery may affect the accuracy of eye pressure measurements after LASIK, for instance when evaluating your eyes for glaucoma, and make them more difficult to interpret. For this reason, you should inform future eye care providers that you have had LASIK, so that they may be better able to interpret your eye pressure measurements.

LASIK surgery may make it more difficult for a surgeon to determine the correct artificial lens power for cataract surgery implantation. For this reason, you should ask for a patient information card that has your eye measurements from before the LASIK surgery. You should keep this card to help the cataract surgeon accurately calculate the lens implant power should you need to have cataract surgery in the future.

If you have one eye that cannot see clearly even with glasses (e.g., if you have amblyopia or "lazy eye", or bad vision from injury or disease), you should discuss this with your doctor. The risk of LASIK-related vision loss in your "good eye" might mean a lot more to you, since you cannot see well with your other eye.

WHAT ARE THE RISKS OF LASIK SURGERY?

- Sometimes LASIK does not give you the best vision the first time. To get the best vision you can, you may need to have LASIK surgery again.
- LASIK can sometimes leave your vision worse than before, even with glasses or contacts.
- After LASIK, you may need to wear glasses or contacts to see clearly up close, even if you did not need to wear them before. Starting around 40 years of age, people usually need glasses for close work such as reading, even if they did not need them before surgery.
- LASIK can give you vision problems or symptoms that you did not have before. It can also cause vision problems or symptoms that you had before to become worse (for

example, dry eye, halos, glare, difficulty with night driving, ghost images, and fluctuating vision) with symptoms that may range from mild and annoying to severe and affecting ability to perform tasks.

- Permanent loss of vision; some complications may lead to vision loss that cannot be corrected by glasses, contact lenses, or further surgical treatment.

Some associated risks of the LASIK procedure are listed below:

- The cornea or other parts of the eye can become infected because the cornea has been cut and tissue has been removed from it.
- The blade that is used to make the corneal flap can cut all the way through the front part of the eye. This is called perforation of the eye, which can lead to loss of fluid from inside the eye, **cataract** (cloudiness of the natural lens of the eye) formation, and infection of the eye.

Other flap complications include:

- The corneal flap can come loose, or can be torn or cut off the eye completely and be lost, making your vision much worse.

The following possibilities are also considered risk factors:

- Retreatment with the MEL 80. It is not known whether LASIK is safe and effective to repeat on the same eye.
- Undiagnosed dry eyes. Your doctor should test you for dry eyes before you have LASIK. LASIK can make dry eyes worse, and it can give you dry eyes even if you did not have them before. Symptoms may include burning, feeling as though something is in the eye, excessive tearing, pain, redness, and blurred vision. In some cases, the symptoms interfere with the ability to do daily tasks.
- Allergic reactions. Your eye may have an allergic reaction such as itching, swelling, irritation, tearing or redness.
- Large pupils. Before LASIK, your doctor should measure your **pupil** (the dark circular opening in the center of the iris that allows light into the eye; it shrinks in bright light and enlarges in dim light) size under dim light. Pupils too large under dim light can lead to bad effects from LASIK. "Too large" means more than 7 mm. These effects include **glare** (a light within the field of vision that is bright enough to interfere with the ability to see other lights or objects), **halo** (hazy ring around a bright light), and problems driving at night. If your pupils are too large, talk with your doctor about the risks.
- Ectasia- Bulging of the cornea due to remaining tissue being too thin after LASIK.
- Inflammation- Swelling of the eye often associated with redness and pain. Sometimes swelling can occur without any associated pain, but vision is often blurred. Inflammation

is the body's response to harmful stimuli or injury, achieved by movement of white blood cells into the injured tissues. Prolonged inflammation can lead to destruction of the tissue. Some inflammation of the cornea after LASIK surgery is normal. But if it is uncontrolled, it can interfere with healing and cause vision loss. It often responds to therapies such as antibiotics and topical steroids, but the flap also might need to be lifted and rinsed for removal of inflammatory cells and to prevent tissue damage.

During the First Week Following Surgery

- You may have pain and discomfort for up to 7 days after surgery.
- You can expect to have blurred vision and tearing as the cornea heals.
- You may be sensitive to bright lights, or you may have a feeling of a foreign body sensation on the surface of your eye.
- You may have short-term swelling of the front surface of your eye or eyelids.
- The pressure in your eye may increase. This is often due to the use of eye drops to control inflammation. To control this, your doctor may prescribe another kind of eye drop, or stop giving you such drops. An increase in eye pressure does not usually cause any symptoms. But to make sure, you must see your doctor as directed to check for an increase in eye pressure. A severe increase in eye pressure could cause eye pain or nausea. If you have these symptoms, you should contact your doctor.
- You must never rub your eyes. This can cause a shift of the flap, which leads to bad effects. These can include blurred vision, risk of infection, inflammation, edema, loss of cornea cells or cells to start growing under the LASIK flap, which can cause bumps in the flap.

During the First Week to One Month Following Surgery

- The pressure in your eye may increase. This is often due to the use of eye drops to control inflammation. When you stop the drug therapy, the pressure goes back to normal.
- Your cornea may become so hazy or cloudy that it affects your vision. This haze disappears over time, and may be related to cells being introduced between the corneal flap and underlying tissue. Some patients see haze up to 6 months after LASIK.

3 months or Longer After Surgery

- You may have periodic loss of the outer layer of the cornea. This can happen following PRK, and does not usually occur following LASIK. Treatment for loss of the cells may include medication or surgical intervention.
- You may have a wrinkle in the inner layer of the cornea. This layer is made up of strong collagen fibers and helps the cornea maintain its shape. A wrinkle in the flap may be

caused by external pressure after surgery (rubbing the eye, eye squeezing) or due to a high amount of tissue removal from the refractive procedure. A procedure of re-lifting the LASIK flap is performed to remove the wrinkle. Re-lifting of the flap may cause a decrease in best corrected visual acuity, which should return as the eye heals.

- Some patients have vision complaints and experience a loss of best corrected vision (with glasses).

Research has not shown what effects LASIK has on vision performance in poor lighting. After LASIK, some patients may find it harder than before to see in dim light, rain, snow, fog, or glare from lights at night. Vision performance could be worsened by large pupil size.

Speak with your doctor about the risk that LASIK may cause bad effects on your vision. These include glare, halos, and problems driving at night.

Your doctor should test you for dry eyes before LASIK. LASIK may make dry eyes worse. You may have dry eyes after LASIK even if you did not before.

Compared to younger patients, it is harder to predict outcomes for those 50 years and older.

WHAT ARE THE BENEFITS OF LASIK SURGERY?

The MEL 80 is intended to reduce or eliminate your farsightedness. It may reduce or end your need to use contact lenses or glasses. Doctors can use it on farsighted patients up to these limits:

- Patients who are farsighted up to +5.0 D, with astigmatism > +0.50 and ≤ +3.0 D, with a maximum manifest refraction spherical equivalent (MRSE) of +5.0 D.

The clinical study described at the end of this booklet found that LASIK surgery with the MEL 80 Excimer Laser System is a reasonably safe and effective way to correct farsightedness.

ARE YOU A GOOD CANDIDATE FOR LASIK?

To have LASIK, you must:

- Be 21 years of age or older.
- Have healthy eyes free from retinal problems, corneal scars, and any eye disease.
- Have farsightedness within the range of treatment. The range is up to +5.0 D of sphere with > +0.50 and ≤ +3.0 D of astigmatism. (The maximum manifest refraction spherical equivalent (MRSE) is +5.0 D.)
- Have proof your vision has not changed more than one half diopter for at least one year before your pre-surgery exam.

- Be fully informed about the risks and benefits of LASIK as compared to other treatments for farsightedness.
- Be able to lie flat without difficulty.
- Be able to keep your eye on the blinking fixation light during the whole LASIK process.
- Be willing to sign an Informed Consent Form provided by your doctor.
- Be able to tolerate eye drops to numb your eye.

WHAT YOU NEED TO KNOW ABOUT THE SURGERY

Unrealistic Expectations about Surgery

Before LASIK, talk to your doctor about your expectations for LASIK surgery. Unrealistic expectations may lead you to be disappointed or cause you to make the wrong decision about whether to have surgery. You should discuss with your doctor whether your expectations are realistic, particularly about how LASIK will change your quality of life.

If you expect "perfect vision" and believe that you will never need to wear glasses again, then this is an unrealistic expectation. It is realistic for most patients to expect to be able to perform most distance tasks without glasses. However, a significant number of people will not achieve 20/20 vision without glasses. Patients should consider whether they will be happy with less than "perfect vision" or will be able to do their work. Patients should consider whether they would be willing to wear glasses for certain activities such as driving at night, or for reading.

As people age, everyone loses the ability to focus their eyes from far to near. This usually becomes a significant problem by the time a person is in his or her forties. If patients have their eyes fully corrected for distance vision, they will need reading glasses in middle age. This is true, even if before surgery they could read clearly without glasses. In some cases, the LASIK surgery may cause the need for reading glasses sooner than if they had not had the surgery.

Before the Surgery

If you think you want LASIK, you will need an exam first to assess your eyes. This is to make sure your eyes are healthy and suitable for LASIK. This would include a medical exam and eye history. Both eyes will be checked.

WARNING: If you wear contact lenses, the doctor will ask you to stop wearing them before your exam. You must stop two weeks before for hard contact lenses, or one week before for soft contact lenses. This is so the doctor can get a stable eye measurement. Failure to do this may lead to poor results from LASIK.

Before LASIK, talk to your doctor if you take any medications or if you have any allergies. These may cause healing problems. Also discuss whether you should eat and drink just before surgery. You should arrange to have someone drive you home after surgery. Also have them drive you to your next doctor's visit. You should not drive after surgery until your doctor gives you permission.

The Day of Surgery

Before the day of surgery, you will be given the chance to hear the sounds the laser makes. Thus you will be prepared for the noise. On the actual day of surgery, you will be given some numbing drops in the eye that will be treated. If necessary, the surgeon may also place a reference mark on your cornea to aid in alignment prior to the surgical procedure. This is a temporary dot made on your cornea with an instrument similar to a felt tipped marker. You will not feel any pain with this additional procedure. You will be shown into the surgery room. There you will see a large machine with a computer screen, a surgeon's chair and a patient bed. You will be asked to lie down on the bed. You will lay face up toward the laser's microscope and the ceiling. Your eye may be numbed with more drops. The eye not having surgery may be covered with a temporary shield.

The surgery takes 10 to 20 minutes in total, but the laser is used only about 30 to 60 seconds. The doctor will place a small spring-like device between your eyelids to hold them open.

When the surgery begins, the doctor will put a suction ring onto your eye. This will serve as a track for a small device called a microkeratome. This device will create a thin flap of corneal tissue. While this is done, your vision will become blurry. This is due to the suction ring, which can cause extreme, temporary increase in eye pressure. After the flap is made, the suction will be switched off. Then the doctor will fold the flap away from the cornea. The doctor will then reposition your head under the microscope. You will be asked to look directly at the blinking light. Try to keep both eyes open without squinting. Try even though a drape or a patch may cover the eye not having LASIK. This makes it easier to keep looking at the blinking light. You will then hear the noise the laser makes when it does its work.

WARNING: It is vital to keep looking right at the blinking light, even if the light fades or dims. Your results depend on how well you keep focus on this blinking light throughout the treatment.

Immediately After the Surgery

After it's done, your doctor will put medicine drops or ointment into your eye. Your doctor may apply a patch or shield to your eye for protection and comfort.

Numbing drops make the surgery painless. When these drops wear off, your eye will probably hurt for a day or two. Most patients describe the pain as moderate to severe.

Your doctor may prescribe pain medicine to make you more comfortable. Do not remove the patch or shield until instructed to do so.

WARNING: You should never rub or touch your treated eye after surgery. This can cause a shift of the flap, which leads to bad effects. These can include blurred vision, risk of infection, inflammation, edema or epithelial in-growth (a condition where epithelial cells grow in between the undersurface of the flap and the front surface of the cornea, which can decrease the quality of vision).

First Days After Surgery

The patch or shield is usually removed the next day. You may be mildly sensitive to light and glare. Wear sunglasses to ease your discomfort. You may also have the feeling that something is in your eye. This happens while the outer layer of your cornea is healing.

Your vision should stabilize within a few weeks. Some patients report small changes in vision. These could be better or worse. These may occur up to six months or more after LASIK.

You may see a haze or cloudiness in the cornea after LASIK. It usually will not affect your vision. This haze tends to decrease over time. Most often it ends by 12 to 24 months after LASIK. However, some patients continue to see haze.

Use as directed any drops and lubricants your doctor prescribes. Your results depend on you following your doctor's orders. If you use topical steroids, your doctor should watch you for side effects of long-term use. One side effect may be increased eye pressure or **ocular hypertension** (pressure inside the eye of more than 21 mm Hg with no other signs of glaucoma). This condition is often linked to bad effects. One such effect is **glaucoma,** which is a group of diseases often marked by increased pressure in the eye. It is marked by damage to the nerve fiber layer. It can cause loss of vision. Another bad effect of high eye pressure could be cataract formation. It also can cause a loss of vision.

WARNING: You should contact your doctor if you notice any pain or change or loss of vision in the eye. These may be signs of a serious medical condition.

QUESTIONS TO ASK YOUR DOCTOR

You may want to ask the questions below to help you decide if LASIK with the MEL 80 Excimer Laser is right for you.

- What are the other options to correct farsightedness?
- Will I have to limit what I do after LASIK? If yes, for how long?
- What are the benefits of LASIK for my level of farsightedness?
- What vision can I expect in the first few months after LASIK?

- If LASIK does not correct my vision, could my vision be worse than before? Could my need for glasses increase over time?
- Will I be able to wear contact lenses if I still need them after LASIK?
- How is LASIK likely to affect my need to use glasses or contact lenses as I get older?
- Will my cornea heal differently if I injure it after LASIK?
- Should I have LASIK surgery on my other eye?
- How long will I have to wait before I can have LASIK surgery on my other eye?
- What vision problems will I have if I have LASIK in only one eye?

Discuss the cost of surgery and follow-up care with your doctor. Most health insurance does not cover LASIK for vision correction.

SUMMARY OF IMPORTANT INFORMATION

- LASIK is permanent. Once done, it cannot be reversed.
- LASIK does NOT end the need for reading glasses, even if you have never worn them.
- LASIK is used to treat farsightedness.
- Your vision must be stable for at least one year before LASIK. You will need written proof that it has not changed by more than 0.50 D.
- Pregnant and nursing women should wait to have LASIK. For these women, it may cause over- or under-correction as well as regression (reduction or loss of the correction over time).
- You should not have LASIK if you have a medical condition that impairs wound healing. (For example, corneal scars, uveitis, diabetes, dry eyes etc.)
- The LASIK treatment may cause you discomfort.
- LASIK is not risk-free. Please read this whole booklet before you agree to the treatment. Pay special attention to the sections on Risks and Benefits.
- LASIK is not a laser version of RK. (RK stands for radial keratotomy.) LASIK and RK are completely different from each other.
- Some alternatives to LASIK are glasses, contact lenses, RK and PRK. (PRK stands for photorefractive keratectomy.)
- Some jobs have vision requirements that RK, PRK, and LASIK do not meet (for example, military pilots).
- Before you decide to have LASIK you should do as follows:

- Have a complete eye exam.
- Talk with one or more doctors about LASIK. Discuss its benefits, complications, risks and time required to heal.

CLINICAL STUDY TO EVALUATE RISKS AND BENEFITS

Researchers did a study to evaluate the safety and effectiveness of LASIK with the MEL 80 Excimer Laser. The safety summaries presented in this section were based on the entire study eye population while the effectiveness analyses were based on study subjects treated in the refractive range and with the **device treatment** consistent with the marketed indication for use. The study included 369 eyes.

DEMOGRAPHICS

- 94.7% of study subjects were Caucasian
- Subjects ages ranged from 22 to 69 years

SAFETY OUTCOMES: ADVERSE EVENTS, COMPLICATIONS, AND MODERATE-SEVERE SYMPTOMS

The study also reports adverse events after LASIK. This is to assess risks, including worse vision. Some of the more common adverse events and complications are also described in the previous section of this document titled "What Are The Risks Of LASIK Surgery?"

1. POSTOPERATIVE BEST-CORRECTED VISION WITH GLASSES COMPARED TO PREOPERATIVE BEST-CORRECTED VISION WITH GLASSES

Some people still needed glasses or contact lenses after LASIK. The study measured vision with glasses at 6, 9, and 12 months after LASIK. (See Table 1 on the following page)

- At 9 months, the vision with glasses did not change or was improved in 79% of eyes compared with best vision with glasses before LASIK.
- At 9 months, 16.4% of eyes lost 1 line, and 4.7% lost 2 or more lines of vision; however, only 0.3% of eyes were reported with a decrease of 2 lines or more at the last available visit.
- At 9 months, 0.3% of eyes had best vision with glasses worse than 20/40.
- At 9 months, 0.3% of eyes had best vision with glasses worse than 20/25 when they were 20/20 or better with glasses before surgery

TABLE 1
SUMMARY OF BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA)
ALL TREATED EYES

Change in BSCVA from before surgery	6 Months (%)	9 Months (%)	12 Months (%)	Last Available Visit (%)
Decrease of more than 2 lines	1.9%	1.5%	1.1%	0%
Decrease of 2 or more lines	4.5%	4.7%	3.4%	0.3%
Decrease of 1 line	19.2%	16.4%	17.8%	20.7%
No loss	76.3%	78.9%	78.8%	79.0%
BCVA worse than 20/40	0.3%	0.3%	0.3%	0%
BCVA worse than 20/25 if 20/20 or better at baseline	1.5%	0.3%	0.3%	0%

2. ADVERSE EVENTS

Adverse events that occurred during the study for all eyes treated were as follows:

- Corneal epithelial defect involving the keratectomy (flap) in 1 eye (0.3%)
- Decrease in best-corrected vision of more than (10 letters) 2 lines in 1 eye (0.3%), when considering last available visits for the study participants
- Diabetes in 2 subjects (4 eyes, 1.1%)
- Melting of the corneal flap in 1 eye (0.3%)
- Miscreated (i.e. irregular) flaps in 2 eyes (0.5%)
- Ocular migraine in 1 subject (2 eyes, 0.5%)
- Vitreous floaters in 1 eye (0.3%)

3. COMPLICATIONS

Complications that occurred at any visit for all eyes treated at a 1% or greater incidence after LASIK in the study are as follows:.

- Conjunctivitis in 4 eyes (1.1%)
- Corneal edema between 1 week to less than 1 month after the procedure in 4 eyes (1.1%)
- Diffuse lamellar keratitis (DLK) in 17 eyes (4.6%)
- Double/ghost images in the operative eye in 9 eyes (2.4%)
- Dry eye in 15 eyes (4.1%)
- Epithelium at flap edge in 7 eyes (1.9%)
- Epithelium in the interface in 29 eyes (7.9%)
- Foreign body sensation at 1 month or later in 9 eyes (2.4%)
- Punctal plug inserted in 49 eyes (13.3%)

- Superficial punctuate keratitis in 25 eyes (6.8%)
- Steroid induced IOP increase in 8 eyes (2.2%)
- Transient light sensitivity syndrome in 12 eyes (3.3%)

In addition, the following complications were reported with a higher proportion of eyes for the IntraLase keratome (a device used to make the corneal flap without a blade) as compared to the various mechanical microkeratomes (devices used to make a flap with a blade):

- DLK (Diffuse Lamellar Keratitis, a noninfectious inflammation that arises between the corneal flap and the underlying tissue)
- Dry eye
- Cells at flap edge
- Cells under the flap
- Foreign body sensation
- Silicone plug insertion into tear drainage opening
- Superficial corneal lesions
- Medication induced increase in eye pressure
- Transient light sensitivity syndrome

4. MODERATE TO SEVERE PATIENT SYMPTOMS

Symptoms were rated by patients 9 months after LASIK and compared to their ratings before surgery. Any symptom for which there is a one grade increase from before surgery is considered "worse" and at least a two grade increase is considered "significantly worse". Table 2 shows the symptoms that were worse 9 months after LASIK.

Table 2
Comparison of Symptoms Before and After Surgery at 9 Months
ALL TREATED EYES

Symptom	Worse % (n/N)	Significantly Worse % (n/N)
Light sensitivity	17.9% (60/335)	3.3% (11/335)
Headaches	7.5% (25/335)	1.5% (5/335)
Pain/burning	6.9% (23/335)	1.8% (6/335)
Dryness	26.0% (87/335)	8.1% (27/335)
Excessive tearing	3.0% (10/334)	0.0% (0/334)
Gritty, scratchy	9.0% (30/335)	4.8% (16/335)
Glare	18.5% (62/335)	2.1% (7/335)
Halos	14.6% (49/335)	3.0% (10/335)
Blurred vision	15.2% (51/335)	7.2% (24/335)
Double vision	6.3% (21/335)	2.1% (7/335)
Fluctuation of vision	19.4% (65/335)	5.7% (19/335)
Variation - bright light	11.6% (39/335)	1.2% (4/335)
Variation - normal light	7.2% (24/333)	4.5% (15/333)
Variation - dim light	13.1% (44/335)	9.9% (33/335)
Night driving vision	14.6% (49/335)	4.2% (14/335)
Other	1.2% (4/335)	2.1% (7/335)

Symptoms that had the highest percentage of "significantly worse" grading are listed below:

- Dryness: 8.1%
- Gritty/scratchy: 4.8%
- Blurred vision: 7.2%
- Fluctuation of vision: 5.7%
- Variation of vision in normal light: 4.5%
- Variation of vision in dim light: 9.9%
- Night driving vision difficulty: 4.2%

Symptoms were rated by patients 9 months after LASIK. Clinically significant symptoms were those rated as moderate to severe at the 9-month visit. The percentage of patients with moderate to severe symptoms rated significantly worse after surgery are as follows:

- Dryness: 11% at 9 Months (versus 5% before surgery)
- Gritty/scratchy: 5% at 9 Months (versus 1% before surgery)
- Fluctuation of vision: 8% at 9 Months (versus 5% before surgery)
- Variation of vision in normal light: 6% at 9 Months (versus 1% before surgery)
- Variation of vision in dim light: 11% at 9 Months (versus 7% before surgery)

EFFECTIVENESS OUTCOMES

The research study included 369 eyes, of which 259 eyes were treated with an algorithm adjustment of +0.75 D added to the sphere component. However, after analysis of these 259 eyes, it was found that insufficient effectiveness data existed to approve the following range of treatment: sphere > +5.0 D, cylinder ≤ +0.50 D and > +3.00 D, and MRSE > +5.0 D. Thus, after excluding eyes outside of these parameters, the effectiveness cohort consisted of a total of 160 eyes, of which 149 eyes were available at the 9 month point of stability and 153 eyes were available at 12 months for the effectiveness analysis.

1. UNCORRECTED VISUAL ACUITY (UCVA)

In the study, doctors gave each eye one LASIK treatment with the Carl Zeiss Meditec MEL 80 Excimer Laser. Then the doctors measured the vision of each eye without glasses after 1, 3, 6, 9, and 12 months. After 3, 6, 9, and 12 months, more than 59% of eyes had 20/20 vision or better without correction. More than 96% had 20/40 vision or better without correction after 3, 6, 9, and 12 months. Most states require your vision to be 20/40 or better for you to drive without correction (such as glasses or contacts). In the study on LASIK using the Carl Zeiss MEL 80 Excimer Laser System, vision without glasses improved for all eyes.

- At 9 months, 66% of eyes treated for hyperopia with a laser setting adjustment in the approved range had 20/20 or better vision without glasses.
    - 77.2% of the eyes treated for sphere only had 20/20 or better vision without glasses
    - 59.8% of the eyes treated for sphere + cylinder had 20/20 or better vision without glasses
- After 3, 6, 9, and 12 months, more than 59% of all eyes had 20/20 vision or better without correction.

2. UNCORRECTED VISUAL ACUITY (VISION WITHOUT GLASSES) AFTER SURGERY COMPARED TO BEST-CORRECTED VISION (VISION WITH GLASSES) BEFORE SURGERY

The study compared the vision of each eye treated with a laser setting adjustment in the approved range with glasses before LASIK and without glasses 9 and 12 months after LASIK. At 9 months, 49.7% saw as well ***without*** glasses as they did before ***with*** glasses. At 12 months, it was 51.3%. This was measured in terms of a gain of lines on the eye chart (the eye chart is the visual acuity chart). A gain of lines means a patient could read lines of smaller letters after LASIK than they could read before.

- At 9 months, 49.7% saw as well without glasses as they did before surgery with their glasses.

- At 12 months, 51.3% saw as well without glasses as they did before surgery with their glasses.

3. PATIENT SELF-EVALUATION BEFORE AND AFTER LASIK

At each scheduled visit after LASIK, patients were asked to complete a survey. Through it they could report on their vision and eye comfort in each eye. Patients were asked to grade their symptoms compared to the same symptoms before LASIK according to their severity as either none, mild, moderate, marked, or severe. Patients graded symptoms at 9 months after LASIK. Patients described some symptoms as better, while some symptoms were worse. Any symptom for which there is at least a one grade increase from before surgery is considered "worse", and at least a one grade decrease is considered "better".

At 9 months for all eyes treated, a higher percentage of patients reported the following symptoms as "worse" than reported them as "better" after LASIK.

- Light sensitivity
- Headaches
- Pain
- Dryness
- Gritty feeling
- Glare
- Halos
- Blurred vision
- Double vision
- Fluctuation of vision
- Variation of vision in bright, normal, and dim light
- Night driving vision

As part of the study, patients were asked to assess their vision quality after LASIK. They were asked to assess it in these terms:

- Quality of vision
- Whether they would choose to have LASIK done again
- How satisfied they are with the results

At 9 months for eyes treated with a laser setting adjustment in the approved range, the overall quality of vision was rated highly, with:

- 97.9% of patients indicating that there was an improvement, while only 2.1% indicated that there was no improvement;
- 88.4% would elect to have the surgery again, while 6.3% were unsure and 5.3% would not have the surgery again;
- 96.8% reported being satisfied, while 2.1% were neutral and 1.1% were dissatisfied.

PATIENT ASSISTANCE INFORMATION

PRIMARY DOCTOR

Name:
Address:

Telephone Number:

LASIK DOCTOR

Name:
Address:

Telephone Number:

LOCATION WHERE TREATMENT WAS DONE

Name:
Address:

Telephone Number:

LASER MANUFACTURER

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