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 myopia of less than or equal to -7.0 D with or without refractive astigmatism of less than or equal to -3.0 D, with a maximum MRSE of -7.00 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 Operator's 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.

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. Read and understand the MEL 80 Excimer Laser before operating this system.

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

High Pressure Gas Cylinders

In the MEL 80, 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 -7.0 D sphere, -3.0 D cylinder, and -8.0 D MRSE. Optical zones below 6.0 mm and above 7.0 mm are also locked out.

Laser Type:	Argon Fluoride
Laser Wavelength:	193 nanometers
Laser Pulse Duration:	4 to 6 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:	Up to 9 mm (optic zone of 6.0 to 7.0 mm, with a transition zone of 1.7 to 1.9 mm)
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 thyratron and HV 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 the flue gas 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 flue gas 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, PRECAUTIONS AND ADVERSE EVENTS

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 myopia of less than or equal to -7.0 D with or without refractive astigmatism of less than or equal to -3.0 D, with a maximum MRSE of -7.00 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

LASIK surgery is contraindicated in:

- Patients with diagnosed collagen vascular, autoimmune, or immunodeficiency diseases;
- Pregnant or nursing women;
- Patients with signs of keratoconus; and
- Patients who are taking one or both of the following medications: isotretinoin (Accutane®), or amiodarone hydrochloride (Cordarone®).

3.3 WARNINGS

LASIK surgery is not recommended in patients who have:

- Systemic diseases likely to affect wound healing, such as connective tissue disease, insulin dependent diabetes, severe atopic disease or an immunocompromised status;
- a history of *Herpes simplex* or *Herpes zoster* keratitis;
- a history of blepharitis;
- significant dry eye that is unresponsive to treatment; and
- severe allergies.

3.4 PRECAUTIONS

The safety and effectiveness of the MEL 80 Excimer Laser System have NOT been established for patients:

- with progressive myopia and/or astigmatism, ocular disease, previous corneal or intraocular surgery, or trauma to the intended ablation zone;
- with corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage;

- with residual corneal thickness after ablation of less than 250 microns due to an increased risk for corneal ectasia;
- with a history of glaucoma or ocular hypertension of > 23 mmHg;
- taking the medication sumatriptan succinate (Imitrex®);
- under 21 years of age;
- over the long term (more than 6 months after surgery);
- with media problems (corneal, lens, and/or vitreous opacities including, but not limited to, cataract);
- with iris problems including, but not limited to, coloboma and previous iris surgery compromising proper eyetracking;
- taking medications likely to affect wound healing including, but not limited to, antimetabolites;
- with a history of keloid formation;
- who are taking hormone replacement therapy or antihistamines who may experience delayed re-epithelialization of the cornea following surgery;
- with MRSE of -7.25 to -8.00 D, as insufficient safety and effectiveness data are available for eyes in this range;
- undergoing retreatment with the MEL 80 Excimer Laser System.

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. Visual performance possibly could be worsened by large pupil sizes.

The optical zone should be (a) at least as large as the scotopic 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. Patients should be advised of potential for worsening of symptoms associated with dry eye syndrome post-LASIK surgery.

3.5 ADVERSE EVENTS AND COMPLICATIONS

Tables 1A and 1B present the cumulative key safety and adverse events for all treated eyes reported in the study. The cumulative adverse event rate for all reported events was quite low, with no category of event exceeding 0.6% on a cumulative basis. Overall, the device was deemed to be reasonably safe.

TABLE 1.A
SUMMARY OF KEY SAFETY VARIABLES (ALL TREATED EYES)

Key Safety Variables	1 Week % (n/N) 95% CI*	1 Month % (n/N) 95% CI*	3 Months % (n/N) 95% CI*	6 Months % (n/N) 95% CI*
Loss of ≥ 2 lines BSCVA	2.2% (8/360) 1.0%, 4.3%	0.8% (3/356) 0.2%, 2.4%	0.6% (2/358) 0.1%, 2.0%	0.3% (1/354) 0.0%, 1.6%
Loss of > 2 lines BSCVA	0.6% (2/360) 0.1%, 2.0%	0.0% (0/356) 0.0%, 1.0%	0.0% (0/358) 0.0%, 1.0%	0.0% (0/354) 0.0%, 1.0%
BSCVA worse than 20/40	0.0% (0/360) 0.0%, 1.0%	0.0% (0/356) 0.0%, 1.0%	0.0% (0/358) 0.0%, 1.0%	0.0% (0/354) 0.0%, 1.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0% (0/360) 0.0%, 1.0%	0.0% (0/356) 0.0%, 1.0%	0.0% (0/358) 0.0%, 1.0%	0.0% (0/354) 0.0%, 1.0%
Haze ≥ trace with loss of BSCVA > 2 lines	0.0% (0/360) 0.0%, 1.0%	0.0% (0/356) 0.0%, 1.0%	0.0% (0/358) 0.0%, 1.0%	0.0% (0/354) 0.0%, 1.0%
Increased manifest refractive astigmatism > 2.0 D‡	0.0% (0/ 88) 0.0%, 4.1%	0.0% (0/ 87) 0.0%, 4.2%	0.0% (0/ 88) 0.0%, 4.1%	0.0% (0/ 88) 0.0%, 4.1%

N = Number of CRFs received with non-missing values at each visit.
†MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.
* The confidence interval was 95% and calculated based on Clopper-Pearson exact method.
‡ For eyes treated for spherical myopia only.

TABLE 1.B
ADVERSE EVENTS SUMMARY
ALL TREATED EYES

Adverse Event	1 Day N=360	1 Week N=360	1 Month N=356	3 Months N=358	6 Months N=354	Unsch.* N=20	Cum.* N=360
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Corneal infiltrate or ulcer	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Dry eye	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Epithelium in the interface	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Eye irritated	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Punctal plug inserted	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
VA blurry	0.0% (0)	0.0% (0)	0.6% (2)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)
VA decrease due to head trauma	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.3% (1)

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

* Unsch = Unscheduled visits. Cum (Cumulative) = any event during the course of the study.

Table 2 presents a summary of all complications reported for all treated eyes during the course of the study. The incidence rate for all reported categories was quite low, and at the 3-month visit the only complications reported were double/ghost images in the eye and epithelium in the interface. At the 6-month visit, the only complications reported were blepharitis, double/ghost images in the eye, and epithelium in the interface. On a cumulative basis, only epithelium in the interface (3.9%) and diffuse lamellar keratitis (5.3%) exceeded a 1% incidence rate.

TABLE 2
POSTOPERATIVE COMPLICATIONS SUMMARY
ALL TREATED EYES

Complications	1 Day N=360	1 Week N=360	1 Month N=356	3 Months N=358	6 Months N=354	Unsch.* N=20	Cum.* N=360
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Blepharitis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)	0.0% (0)	0.6% (2)
Conjunctivitis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	10.0% (2)	0.6% (2)
Diffuse lamellar keratitis†	4.7% (17)	0.8% (3)	0.0% (0)	0.0% (0)	0.0% (0)	10.0% (2)	5.3% (19)
Double/ghost images in the operative eye	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)	0.3% (1)	0.0% (0)	0.8% (3)
Epithelial defect	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Epithelial slide with bandage contact lens placed	0.6% (2)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (2)
Epithelial spots	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Epithelium Stained and rough	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Epithelium in the interface	0.0% (0)	0.3% (1)	2.2% (8)	2.2% (8)	1.4% (5)	15.0% (3)	3.9% (14)
Fibrosis at edge of epithelium	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Foreign body sensation	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Heaped epithelium	0.6% (2)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.8% (3)
Irregular astigmatism due to epithelial ingrowth	0.0% (0)	0.0% (0)	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Loose epithelium	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
SPK	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
SPK with bandage contact lens placed	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Sub-epithelial infiltrate	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)
Subconjunctival hemorrhage	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	5.0% (1)	0.3% (1)

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

* Unsch = Unscheduled visits. Cum (Cumulative) = any event during the course of the study.

† 18 of the 19 reports of DLK were associated with use of the Intralase Laser Keratome, 1 report was associated with the ACS keratome, and no reports were associated with the Hansatome keratome.

SECTION 4
CLINICAL RESULTS

4.1 STUDY OBJECTIVES

A prospective, non-randomized, multicenter clinical study of 360 eyes was conducted to evaluate the safety and effectiveness of the Carl Zeiss Meditec MEL 80 Excimer Laser System.

4.2 DATA ANALYSIS AND RESULTS

4.2.1 Demographics And Baseline Parameters

Demographic characteristics of the study population are presented in Table 3. The baseline refraction parameters are presented in Tables 4.A and 4.B for eyes treated for spherical myopia and astigmatic myopia, respectively. For eyes treated for spherical myopia, the mean sphere was -3.915 D (SD: 1.668 D); see Table 4.A. For eyes treated for astigmatic myopia (Table 4.B), the mean manifest sphere was -3.370 D (SD 1.716) and the mean cylinder was -0.975 D (SD: 0.684). The intended correction was the full manifest refraction spherical equivalent with the goal of achieving a plano refraction after the surgery. Preoperative refraction parameters for all eyes are also presented in Tables 4.C and 4.D.

TABLE 3
DEMOGRAPHICS
ALL TREATED EYES

Demographics	Treated for Spherical Myopia Only		Treated for Astigmatic Myopia		All Treated Eyes/Subjects*	
	Number	Percentage	Number	Percentage	Number	Percentage
NUMBER OF EYES & SUBJECTS	88 Eyes of 61 Enrolled Subjects		272 Eyes of 155 Enrolled Subjects		360 Eyes of 182 Enrolled Subjects	
	%	n	%	n	%	n
GENDER						
Male	47.5%	29	58.1%	90	55.5%	101
Female	52.5%	32	41.9%	65	44.5%	81
RACE						
White	85.2%	52	78.1%	121	79.7%	145
Black	4.9%	3	3.2%	5	3.3%	6
Asian	3.3%	2	5.8%	9	4.9%	9
Other	6.6%	4	12.9%	20	12.1%	22
SURGICAL EYE						
Right	51.1%	45	49.6%	135	50.0%	180
Left	48.9%	43	50.4%	137	50.0%	180
AGE (in years)						
Mean (SD)	33.0 (8.2)		33.6 (8.9)		33.5 (8.8)	
Minimum, Maximum	21.0, 51.0		21.0, 60.0		21.0, 60.0	

* Gender, Race, and Age were based on subjects, but Surgical Eye is based on eyes

TABLE 4.A
PREOPERATIVE REFRACTION PARAMETERS
EYES TREATED FOR SPHERICAL MYOPIA ONLY

Manifest Refraction	Primary Eyes %	n	Fellow Eyes %	n	Total Eyes %	n
Sphere						
-0.25 to -1.00 D	0.0	0	2.3	1	1.1	1
-1.01 to -2.00 D	11.1	5	7.0	3	9.1	8
-2.01 to -3.00 D	26.7	12	20.9	9	23.9	21
-3.01 to -4.00 D	26.7	12	32.6	14	29.5	26
-4.01 to -5.00 D	15.6	7	18.6	8	17.0	15
-5.01 to -6.00 D	11.1	5	4.7	2	8.0	7
-6.01 to -7.00 D	4.4	2	7.0	3	5.7	5
-7.01 to -8.00 D	2.2	1	4.7	2	3.4	3
-8.01 to -9.00 D	0.0	0	2.3	1	1.1	1
-9.01 to -10.00 D	2.2	1	0.0	0	1.1	1
Mean (SD)	*-3.800 (1.617)*		*-4.035 (1.731)*		*-3.915 (1.668)*	
Range	*-9.25 to -1.75*		*-9.00 to -1.00*		*-9.25 to -1.00*	
Total	100.0	45	100.0	43	100.0	88

TABLE 4.B
PREOPERATIVE REFRACTION PARAMETERS
STRATIFIED BY SPHERE AND CYLINDER COMPONENTS
EYES TREATED FOR ASTIGMATIC MYOPIA
(ATTEMPTED SPHERICAL AND CYLINDRICAL CORRECTIONS)

Manifest Sphere Mean: -3.370 SD: 1.716 Range: -10.00 to 0.00	**Manifest Cylinder Mean: -0.975, SD: 0.684, Range: -3.50 to -0.25**										**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**		**-3.01 to -3.50 D**			
	%	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**
-0.00 to -1.00 D	2.2	6/272	1.5	4/272	1.1	3/272	0.4	1/272	0.0	0/272	5.1	14/272
-1.01 to -2.00 D	8.8	24/272	6.3	17/272	4.8	13/272	1.1	3/272	0.0	0/272	21.0	57/272
-2.01 to -3.00 D	11.8	32/272	7.4	20/272	3.7	10/272	0.7	2/272	0.0	0/272	23.5	64/272
-3.01 to -4.00 D	9.9	27/272	5.9	16/272	4.0	11/272	1.8	5/272	0.0	0/272	21.7	59/272
-4.01 to -5.00 D	3.3	9/272	2.2	6/272	5.1	14/272	1.5	4/272	0.7	2/272	12.9	35/272
-5.01 to -6.00 D	3.3	9/272	0.7	2/272	3.7	10/272	1.1	3/272	0.0	0/272	8.8	24/272
-6.01 to -7.00 D	1.1	3/272	1.1	3/272	1.8	5/272	0.7	2/272	0.0	0/272	4.8	13/272
-7.01 to -8.00 D	0.4	1/272	0.4	1/272	0.4	1/272	0.0	0/272	0.0	0/272	1.1	3/272
-8.01 to -9.00 D	0.4	1/272	0.4	1/272	0.0	0/272	0.0	0/272	0.0	0/272	0.7	2/272
-9.01 to -10.00 D	0.4	1/272	0.0	0/272	0.0	0/272	0.0	0/272	0.0	0/272	0.4	1/272
Total	41.5	113/272	25.7	70/272	24.6	67/272	7.4	20/272	0.7	2/272	100.0	272/272

N = Total number of eyes treated for astigmatic myopia.

TABLE 4.C
PREOPERATIVE REFRACTION PARAMETERS
STRATIFIED BY MRSE AND CYLINDER COMPONENTS
ALL EYES TREATED

MRSE Mean: -3.872 SD: 1.769 Range: -10.250 to -0.625	Manifest Cylinder Mean: -0.737, SD: 0.727, Range: -3.500 to 0.000										Total	
	-0.00 to -0.50 D		-0.51 to -1.00 D		-1.01 to -2.00 D		-2.01 to -3.00 D		-3.01 to -3.50 D			
	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N
-0.00 to -1.00 D	0.6%	(2/360)	0.6%	(2/360)	0.8%	(3/360)	0.0%	(0/360)	0.0%	(0/360)	1.9%	(7/360)
-1.01 to -2.00 D	8.3%	(30/360)	2.5%	(9/360)	0.6%	(2/360)	0.0%	(0/360)	0.0%	(0/360)	11.4%	(41/360)
-2.01 to -3.00 D	13.9%	(50/360)	6.4%	(23/360)	3.6%	(13/360)	0.8%	(3/360)	0.0%	(0/360)	24.7%	(89/360)
-3.01 to -4.00 D	16.1%	(58/360)	5.3%	(19/360)	2.8%	(10/360)	0.8%	(3/360)	0.0%	(0/360)	25.0%	(90/360)
-4.01 to -5.00 D	7.2%	(26/360)	1.7%	(6/360)	3.3%	(12/360)	0.8%	(3/360)	0.0%	(0/360)	13.1%	(47/360)
-5.01 to -6.00 D	4.4%	(16/360)	1.4%	(5/360)	3.3%	(12/360)	1.4%	(5/360)	0.0%	(0/360)	10.6%	(38/360)
-6.01 to -7.00 D	3.1%	(11/360)	0.8%	(3/360)	2.8%	(10/360)	0.6%	(2/360)	0.6%	(2/360)	7.8%	(28/360)
-7.01 to -8.00 D	1.1%	(4/360)	0.3%	(1/360)	1.4%	(5/360)	0.8%	(3/360)	0.0%	(0/360)	3.6%	(13/360)
-8.01 to -9.00 D	0.6%	(2/360)	0.6%	(2/360)	0.0%	(0/360)	0.3%	(1/360)	0.0%	(0/360)	1.4%	(5/360)
-9.01 to -10.00 D	0.3%	(1/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.3%	(1/360)
-10.01 to -11.00 D	0.3%	(1/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.3%	(1/360)
Total	55.8%	(201/360)	19.4%	(70/360)	18.6%	(67/360)	5.6%	(20/360)	0.6%	(2/360)	100.0%	(360/360)

TABLE 4.D
PREOPERATIVE REFRACTION PARAMETERS
STRATIFIED BY SPHERE AND CYLINDER COMPONENTS
ALL EYES TREATED

Manifest Sphere Mean: -3.503 SD: 1.718 Range: -10.00 to 0.00	Manifest Cylinder Mean: -0.737, SD: 0.727, Range: -3.50 to 0.00										Total	
	-0.00 to -0.50 D		-0.51 to -1.00 D		-1.01 to -2.00 D		-2.01 to -3.00 D		-3.01 to -3.50 D			
	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N
-0.00 to -1.00 D	1.9%	(7/360)	1.1%	(4/360)	0.8%	(3/360)	0.3%	(1/360)	0.0%	(0/360)	4.2%	(15/360)
-1.01 to -2.00 D	8.9%	(32/360)	4.7%	(17/360)	3.6%	(13/360)	0.8%	(3/360)	0.0%	(0/360)	18.1%	(65/360)
-2.01 to -3.00 D	14.7%	(53/360)	5.6%	(20/360)	2.8%	(10/360)	0.6%	(2/360)	0.0%	(0/360)	23.6%	(85/360)
-3.01 to -4.00 D	14.7%	(53/360)	4.4%	(16/360)	3.1%	(11/360)	1.4%	(5/360)	0.0%	(0/360)	23.6%	(85/360)
-4.01 to -5.00 D	6.7%	(24/360)	1.7%	(6/360)	3.9%	(14/360)	1.1%	(4/360)	0.6%	(2/360)	13.9%	(50/360)
-5.01 to -6.00 D	4.4%	(16/360)	0.6%	(2/360)	2.8%	(10/360)	0.8%	(3/360)	0.0%	(0/360)	8.6%	(31/360)
-6.01 to -7.00 D	2.2%	(8/360)	0.8%	(3/360)	1.4%	(5/360)	0.6%	(2/360)	0.0%	(0/360)	5.0%	(18/360)
-7.01 to -8.00 D	1.1%	(4/360)	0.3%	(1/360)	0.3%	(1/360)	0.0%	(0/360)	0.0%	(0/360)	1.7%	(6/360)
-8.01 to -9.00 D	0.6%	(2/360)	0.3%	(1/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.8%	(3/360)
-9.01 to -10.00 D	0.6%	(2/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.0%	(0/360)	0.6%	(2/360)
Total	55.8%	(201/360)	19.4%	(70/360)	18.6%	(67/360)	5.6%	(20/360)	0.6%	(2/360)	100.0%	(360/360)

4.2.2 Accountability

Accountability was very good with only 6 eyes lost to follow-up and no eyes discontinued from the study. Accountability for all treated eyes across the study visit schedule is presented in Table 5.

TABLE 5
ACCOUNTABILITY
ALL TREATED EYES

Total Eyes (N) = 360		1 Day	1 Week	1 Month	3 Months	6 Months
Available for Analysis	% (n/N)	100.0% (360/360)	100.0% (360/360)	98.9% (356/360)	99.4% (358/360)	98.3% (354/360)
Discontinued*	% (n/N)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)
Deceased	% (n/N)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)
Retreatment	% (n/N)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)
Aborted	% (n/N)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)
Active (Not yet eligible for the interval)		0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)
Lost to Follow-up†	% (n/N)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	0.0% (0/360)	1.7% (6/360)
Missed Visit‡	% (n/N)	0.0% (0/360)	0.0% (0/360)	1.1% (4/360)	0.6% (2/360)	0.0% (0/360)
% Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible)		100.0% (360/360)	100.0% (360/360)	98.9% (356/360)	99.4% (358/360)	98.3% (354/360)

N = Total number of eyes enrolled.

* Discontinued = Exited due to retreatment (n = 0), aborted procedure (n = 0), or death (n = 0).

† Lost to follow-up: Eyes were not examined at the 6-month visit, and were not considered active or discontinued.

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

4.2.3 Key Effectiveness Parameters For All Treated Eyes

Table 6 presents the summary of the key effectiveness parameters for the 360 treated eyes at all available postoperative visits.

At 3 months, 92.5% of eyes had UCVA 20/20 or better, and 99.7% of eyes had UCVA 20/40 or better. At 6 months, 92.7% of eyes had UCVA 20/20 or better, and 99.4% of eyes had UCVA 20/40 or better. As shown in Table 6, 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 are all above the suggested minimum FDA Guidance document values for myopia.

TABLE 6
SUMMARY OF KEY EFFECTIVENESS VARIABLES (ALL TREATED EYES)

Key Effectiveness Variables	1 Week % (n/N) 95% CI*	1 Month % (n/N) 95% CI*	3 Months % (n/N) 95% CI*	6 Months % (n/N) 95% CI*
UCVA 20/20 or better	85.8% (309/360) 81.8%, 89.3%	91.6% (326/356) 88.2%, 94.2%	92.5% (331/358) 89.2%, 95.0%	92.7% (328/354) 89.4%, 95.1%
UCVA 20/40 or better	99.4% (358/360) 98.0%, 99.9%	99.7% (355/356) 98.4%, 100.0%	99.7% (357/358) 98.5%, 100.0%	99.4% (352/354) 98.0%, 99.9%
MRSE†, Attempted vs. Achieved, ± 0.50 D	75.3% (271/360) 70.5%, 79.6%	80.6% (287/356) 76.1%, 84.6%	84.9% (304/358) 80.8%, 88.5%	76.8% (272/354) 72.1%, 81.1%
MRSE†, Attempted vs. Achieved, ± 1.00 D	92.5% (333/360) 89.3%, 95.0%	96.3% (343/356) 93.8%, 98.0%	95.8% (343/358) 93.2%, 97.6%	95.5% (338/354) 92.8%, 97.4%
MRSE†, Attempted vs. Achieved, ± 2.00 D	100.0% (360/360) 99.0%, 100.0%	100.0% (356/356) 99.0%, 100.0%	99.7% (357/358) 98.5%, 100.0%	100.0% (354/354) 99.0%, 100.0%

N = Number of CRFs received with non-missing values at each visit.
†MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.
* The confidence interval was 95% and calculated based on Clopper-Pearson exact method.

4.2.3.1 Ablation Algorithm Adjustment Based on Effectiveness Outcomes

Based on regression analyses of the clinical trial data, the ablation algorithm was modified as follows:

- adjustment (reduction) to the sphere component of -0.25 D for both sphere and spherocylindrical eyes
- adjustment (reduction) to the cylinder component of -0.25 D for spherocylindrical eyes only

4.2.4 Key Effectiveness Parameters by Preoperative MRSE

Key effectiveness outcomes at 3 months stratified by each diopter of preoperative MRSE are presented in Tables 7.A, 7.B, and 7.C for all eyes, spherical myopia eyes, and astigmatic myopia eyes, respectively. As shown in Tables 7.A through 7.C, at 3 months postoperatively, between 85.7% and 100% of all eyes treated had uncorrected visual acuity of 20/40 or better, with the exception of astigmatic myopia eyes with a baseline MRSE of 0.0 D to -1.00 D (there were only 6 eyes in this group, and 5 eyes (83.3%) achieved UCVA of 20/40 or better). All other preoperative MRSE subgroups met the FDA target value of 85% of eyes with a UCVA of 20/40 or better.

The accuracy of the intended correction decreased somewhat with increasing preoperative MRSE. As can be seen in Table 7.A, efficacy data for the overall cohort stratified in one diopter increments of preoperative MRSE meet the outcomes recommended in the FDA guidance, with the exception of eyes with a preoperative MRSE of 0.0 D to -1.00 D and -9.01 to -10.00 D. Eyes with a preoperative MRSE of 0.0 D to -1.00 D had 71.4% of eyes (versus the recommended 75%) achieve MRSE within ± 1.00 D of the intended outcome, and eyes with a preoperative MRSE of -9.01 to -10.00 D had 0.0% of eyes (versus the recommended 50%) achieve MRSE within ± 0.50 D of the intended outcome. However, the sample size was small in both groups.

TABLE 7.A
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 3 MONTHS (POINT OF STABILITY)
STRATIFIED BY PREOPERATIVE MRSE
ALL TREATED EYES

Key Effectiveness Variables	Preoperative MRSE											Total	P-value†
	-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)	-7.01 to -8.00 D % (n/N)	-8.01 to -9.00 D % (n/N)	-9.01 to -10.00 D % (n/N)	-10.01 to -11.00 D % (n/N)	% (n/N)	
UCVA 20/20 or better	71.4% (5/7)	100.0% (41/41)	94.3% (82/87)	94.4% (85/90)	95.7% (45/47)	81.6% (31/38)	92.9% (26/28)	84.6% (11/13)	60.0% (3/5)	100.0% (1/1)	100.0% (1/1)	92.5% (331/358)	0.0381
UCVA 20/40 or better	85.7% (6/7)	100.0% (41/41)	100.0% (87/87)	100.0% (90/90)	100.0% (47/47)	100.0% (38/38)	100.0% (28/28)	100.0% (13/13)	100.0% (5/5)	100.0% (1/1)	100.0% (1/1)	99.7% (357/358)	0.3720
MRSE*, Attempted vs. Achieved, ± 0.50 D	71.4% (5/7)	92.7% (38/41)	92.0% (80/87)	82.2% (74/90)	83.0% (39/47)	71.1% (27/38)	92.9% (26/28)	76.9% (10/13)	80.0% (4/5)	0.0% (0/1)	100.0% (1/1)	84.9% (304/358)	0.0365
MRSE*, Attempted vs. Achieved, ± 1.00 D	71.4% (5/7)	100.0% (41/41)	97.7% (85/87)	93.3% (84/90)	97.9% (46/47)	94.7% (36/38)	100.0% (28/28)	92.3% (12/13)	80.0% (4/5)	100.0% (1/1)	100.0% (1/1)	95.8% (343/358)	0.4619
MRSE*, Attempted vs. Achieved, ± 2.00 D	100.0% (7/7)	100.0% (41/41)	100.0% (87/87)	100.0% (90/90)	97.9% (46/47)	100.0% (38/38)	100.0% (28/28)	100.0% (13/13)	100.0% (5/5)	100.0% (1/1)	100.0% (1/1)	99.7% (357/358)	0.3559

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

* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

† χ^2 test. Due to small sample sizes, baseline groups of MRSE -7.01 D or higher were combined and -2.00 D or lower were combined.

TABLE 7.B
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 3 MONTHS (POINT OF STABILITY)
STRATIFIED BY PREOPERATIVE MRSE
EYES TREATED FOR SPHERICAL MYOPIA ONLY

Key Effectiveness Variables	Preoperative MRSE										Total	P-value†
	-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)	-7.01 to -8.00 D % (n/N)	-8.01 to -9.00 D % (n/N)	-9.01 to -10.00 D % (n/N)	% (n/N)	
UCVA 20/20 or better	100.0% (1/1)	100.0% (8/8)	100.0% (21/21)	96.2% (25/26)	93.3% (14/15)	100.0% (7/7)	100.0% (5/5)	66.7% (2/3)	0.0% (0/1)	100.0% (1/1)	95.5% (84/88)	0.0106
UCVA 20/40 or better	100.0% (1/1)	100.0% (8/8)	100.0% (21/21)	100.0% (26/26)	100.0% (15/15)	100.0% (7/7)	100.0% (5/5)	100.0% (3/3)	100.0% (1/1)	100.0% (1/1)	100.0% (88/88)	NA
MRSE*, Attempted vs. Achieved, ± 0.50 D	100.0% (1/1)	100.0% (8/8)	100.0% (21/21)	96.2% (25/26)	100.0% (15/15)	85.7% (6/7)	80.0% (4/5)	66.7% (2/3)	100.0% (1/1)	0.0% (0/1)	94.3% (83/88)	0.0103
MRSE*, Attempted vs. Achieved, ± 1.00 D	100.0% (1/1)	100.0% (8/8)	100.0% (21/21)	100.0% (26/26)	100.0% (15/15)	100.0% (7/7)	100.0% (5/5)	66.7% (2/3)	100.0% (1/1)	100.0% (1/1)	98.9% (87/88)	0.0101
MRSE*, Attempted vs. Achieved, ± 2.00 D	100.0% (1/1)	100.0% (8/8)	100.0% (21/21)	100.0% (26/26)	100.0% (15/15)	100.0% (7/7)	100.0% (5/5)	100.0% (3/3)	100.0% (1/1)	100.0% (1/1)	100.0% (88/88)	NA

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

* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

† χ^2 test. Due to small sample sizes, baseline groups of MRSE -7.01 D or higher were combined and -2.00 D or lower were combined.

TABLE 7.C
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 3 MONTHS (POINT OF STABILITY)
STRATIFIED BY PREOPERATIVE MRSE
EYES TREATED FOR ASTIGMATIC MYOPIA

Key Effectiveness Variables	Preoperative MRSE											Total	P-value†
	-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)	-7.01 to -8.00 D % (n/N)	-8.01 to -9.00 D % (n/N)	-9.01 to -10.00 D % (n/N)	-10.01 to -11.00 D % (n/N)	% (n/N)	
UCVA 20/20 or better	66.7% (4/6)	100.0% (33/33)	92.4% (61/66)	93.8% (60/64)	96.9% (31/32)	77.4% (24/31)	91.3% (21/23)	90.0% (9/10)	75.0% (3/4)	NA NA	100.0% (1/1)	91.5% (247/270)	0.1022
UCVA 20/40 or better	83.3% (5/6)	100.0% (33/33)	100.0% (66/66)	100.0% (64/64)	100.0% (32/32)	100.0% (31/31)	100.0% (23/23)	100.0% (10/10)	100.0% (4/4)	NA NA	100.0% (1/1)	99.6% (269/270)	0.4294
MRSE*, Attempted vs. Achieved, ± 0.50 D	66.7% (4/6)	90.9% (30/33)	89.4% (59/66)	76.6% (49/64)	75.0% (24/32)	67.7% (21/31)	95.7% (22/23)	80.0% (8/10)	75.0% (3/4)	NA NA	100.0% (1/1)	81.9% (221/270)	0.0493
MRSE*, Attempted vs. Achieved, ± 1.00 D	66.7% (4/6)	100.0% (33/33)	97.0% (64/66)	90.6% (58/64)	96.9% (31/32)	93.5% (29/31)	100.0% (23/23)	100.0% (10/10)	75.0% (3/4)	NA NA	100.0% (1/1)	94.8% (256/270)	0.5946
MRSE*, Attempted vs. Achieved, ± 2.00 D	100.0% (6/6)	100.0% (33/33)	100.0% (66/66)	100.0% (64/64)	96.9% (31/32)	100.0% (31/31)	100.0% (23/23)	100.0% (10/10)	100.0% (4/4)	NA NA	100.0% (1/1)	99.6% (269/270)	0.2800

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

* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

† χ^2 test. Due to small sample sizes, baseline groups of MRSE -7.01 D or higher were combined and -2.00 D or lower were combined.

4.2.5 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 8. The analyses revealed that the optical zone size selected did not play a significant role in efficacy outcomes with regard to the proportion of eyes with UCVA of 20/40 or better and deviation from the intended correction within ± 0.50 D and within ± 1.00 D at 3 months postoperatively.

TABLE 8
SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 3 MONTHS
STRATIFIED BY OPTICAL ZONE
ALL TREATED EYES

Key Effectiveness Variables	Optical Zone			Total	P-value†
	< 6.5 mm % (n/N)	6.5 mm % (n/N)	7.0 mm % (n/N)	% (n/N)	
UCVA 20/20 or better	70.6% (12/17)	93.4% (310/332)	100.0% (9/9)	92.5% (331/358)	0.0127
UCVA 20/40 or better	100.0% (17/17)	99.7% (331/332)	100.0% (9/9)	99.7% (357/358)	1.0000
MRSE*, Attempted vs. Achieved, ± 0.50 D	88.2% (15/17)	84.6% (281/332)	88.9% (8/9)	84.9% (304/358)	1.0000
MRSE*, Attempted vs. Achieved, ± 1.00 D	100.0% (17/17)	95.5% (317/332)	100.0% (9/9)	95.8% (343/358)	1.0000
MRSE*, Attempted vs. Achieved, ± 2.00 D	100.0% (17/17)	99.7% (331/332)	100.0% (9/9)	99.7% (357/358)	1.0000

N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.
† Fisher's exact test.

4.2.6 Mean Manifest Spherical Equivalent

Mean manifest spherical equivalent (MRSE) results for the total study population over time is shown in Table 9. From 1 month to 3 months to 6 months, there was very little change in mean MRSE (0.29 D, 0.24 D, and 0.29 D, respectively).

TABLE 9
MEAN OF MANIFEST REFRACTIVE SPHERICAL EQUIVALENT
ALL TREATED EYES

	Preop	1 Month	3 Months	6 Months
N	360	356	358	354
Mean	-3.872	0.286	0.237	0.292
95% Confidence Interval	-4.055, -3.689	0.244, 0.328	0.196, 0.277	0.247, 0.336
Standard Deviation	1.769	0.401	0.388	0.423

N = Number of available CRFs received with non-missing values at each visit.

4.2.7 Stability Of The Manifest Refraction

Results for stability of the manifest refraction as determined by the manifest spherical equivalent refraction are presented for those eyes that had data at all scheduled follow-up visits during the study (the "consistent cohort"). An MRSE stability summary is presented in Table 10.A for all treated eyes, in Table 10.B in eyes treated for spherical myopia, and in Table 10.C for spherocylindrical eyes. Stability of the manifest refraction cylinder (MRCYL) is presented in Table 10.D.

As shown in Table 10.A, for the consistent cohort of study eyes, the mean change in MRSE between 1 and 3 months was -0.05 D with a standard deviation of 0.32 D, and the mean change in MRSE between 3 and 6 months was similar, i.e., 0.06 D, S.D. 0.38 D. Thus, there was essentially no change in mean MRSE across these study visits. Between 3 and 6 months, the mean change in MRSE per month was 0.02 D, well below the target value of 0.04 D. In addition, ≥ 98% of eyes were reported with a change of MRSE by ≤ 1.00 D at both intervals. The upper limit of the monthly 95% confidence interval (CI) was > -0.01 D for 1-3 months and the lower limit was < +0.01 D for 3-6 months. Thus, stability was demonstrated at 3-months postoperatively.

As shown in Table 10.D, for the consistent cohort of study eyes, the mean change in manifest refraction cylinder (MRCYL) between 1 and 3 months was -0.004 D with a standard deviation of 0.31 D, and the mean change in MRCYL between 3 and 6 months was similar, i.e., 0.014 D, S.D. 0.28 D. Thus, there was essentially no change in mean MRCYL across these study visits. Between 3 and 6 months, the mean change in MRCYL per month was 0.005 D, well below the target value of 0.04 D. In addition, ≥ 99% of eyes were reported with a change of MRSE by ≤ 1.00 D at both intervals. Thus, stability was demonstrated at 3-months postoperatively.

TABLE 10.A
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE)
ALL TREATED EYES

Change in MRSE	Between 1 and 3 Months	Between 3 and 6 Months
Pairwise Sequential Visits*		
Change of **MRSE** by ≤ 1.00 D		
% (n/N)	99.4% (354/356)	98.0% (345/352)
95% CI for %†	(98.0%, 99.9%)	(95.9%, 99.2%)
Change of **MRSE** (Paired-Differences) in Diopter		
Mean	-0.050	0.058
SD	0.317	0.380
95% CI for Mean	(-0.083, -0.016)	(0.018, 0.097)
Mean/month	-0.025	0.019
SD/month	0.159	0.127
95% CI for Mean/month	(-0.041, -0.008)	(0.006, 0.032)
Consistent Cohort*		
Change of **MRSE** by ≤ 1.00 D		
% (n/N)	99.4% (348/350)	98.0% (343/350)
95% CI for %†	(98.0%, 99.9%)	(95.9%, 99.2%)
Change of **MRSE** (Paired-Differences) in Diopter		
Mean	-0.046	0.059
SD	0.316	0.380
95% CI for Mean	(-0.079, -0.013)	(0.019, 0.099)
Mean/month	-0.023	0.020
SD/month	0.158	0.127
95% CI for Mean/month	(-0.040, -0.006)	(0.006, 0.033)

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

† It was calculated based on Clopper-Pearson exact method.

TABLE 10.B
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE)
EYES TREATED FOR SPHERICAL MYOPIA ONLY

Change in MRSE	Between 1 and 3 Months	Between 3 and 6 Months
Pairwise Sequential Visits*		
Change of **MRSE** by ≤ 1.00 D		
% (n/N)	100.0% (87/ 87)	100.0% (88/ 88)
95% CI for %†	(95.8%, 100.0%)	(95.9%, 100.0%)
Change of **MRSE** (Paired-Differences) in Diopter		
Mean	-0.001	-0.007
SD	0.244	0.276
95% CI for Mean	(-0.054, 0.051)	(-0.066, 0.051)
Mean/month	-0.001	-0.002
SD/month	0.122	0.092
95% CI for Mean/month	(-0.027, 0.025)	(-0.022, 0.017)
Consistent Cohort*		
Change of **MRSE** by ≤ 1.00 D		
% (n/N)	100.0% (87/ 87)	100.0% (87/ 87)
95% CI for %†	(95.8%, 100.0%)	(95.8%, 100.0%)
Change of **MRSE** (Paired-Differences) in Diopter		
Mean	-0.001	-0.004
SD	0.244	0.277
95% CI for Mean	(-0.054, 0.051)	(-0.063, 0.055)
Mean/month	-0.001	-0.001
SD/month	0.122	0.092
95% CI for Mean/month	(-0.027, 0.025)	(-0.021, 0.018)

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

† It was calculated based on Clopper-Pearson exact method.

TABLE 10.C
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE)
EYES TREATED FOR ASTIGMATIC MYOPIA

Change in MRSE	Between 1 and 3 Months	Between 3 and 6 Months
Pairwise Sequential Visits*		
Change of **MRSE** by ≤ 1.00 D		
% (n/N)	99.3% (267/269)	97.3% (257/264)
95% CI for %†	(97.3%, 99.9%)	(94.6%, 98.9%)
Change of **MRSE** (Paired-Differences) in Diopter		
Mean	-0.065	0.079
SD	0.336	0.407
95% CI for Mean	(-0.105, -0.025)	(0.030, 0.128)
Mean/month	-0.033	0.026
SD/month	0.168	0.136
95% CI for Mean/month	(-0.053, -0.012)	(0.010, 0.043)
Consistent Cohort*		
Change of **MRSE** by ≤ 1.00 D		
% (n/N)	99.2% (261/263)	97.3% (256/263)
95% CI for %†	(97.3%, 99.9%)	(94.6%, 98.9%)
Change of **MRSE** (Paired-Differences) in Diopter		
Mean	-0.061	0.080
SD	0.335	0.407
95% CI for Mean	(-0.102, -0.020)	(0.031, 0.130)
Mean/month	-0.030	0.027
SD/month	0.168	0.136
95% CI for Mean/month	(-0.051, -0.010)	(0.010, 0.043)

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

† It was calculated based on Clopper-Pearson exact method.

TABLE 10.D
STABILITY OF MANIFEST REFRACTION CYLINDER (MRCYL)
EYES TREATED FOR ASTIGMATIC MYOPIA

Change in MRCYL	Between 1 and 3 Months	Between 3 and 6 Months
Pairwise Sequential Visits*		
Change of **MRCYL** by ≤ 1.00 D		
% (n/N)	99.6% (268/269)	100.0% (264/264)
95% CI for %†	(97.9%, 100.0%)	(98.6%, 100.0%)
Change of **MRCYL** (Paired-Differences) in Diopter		
Mean	-0.004	0.014
SD	0.306	0.276
95% CI for Mean	(-0.040, 0.033)	(-0.019, 0.048)
Mean/month	-0.002	0.005
SD/month	0.153	0.092
95% CI for Mean/month	(-0.020, 0.017)	(-0.006, 0.016)
Consistent Cohort*		
Change of **MRCYL** by ≤ 1.00 D		
% (n/N)	99.6% (262/263)	100.0% (263/263)
95% CI for %†	(97.9%, 100.0%)	(98.6%, 100.0%)
Change of **MRCYL** (Paired-Differences) in Diopter		
Mean	-0.002	0.014
SD	0.308	0.276
95% CI for Mean	(-0.039, 0.036)	(-0.019, 0.048)
Mean/month	-0.001	0.005
SD/month	0.154	0.092
95% CI for Mean/month	(-0.020, 0.018)	(-0.006, 0.016)

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

† It was calculated based on Clopper-Pearson exact method.

4.2.8 Cylinder Correction/Vector Analysis

Table 11 presents the vector magnitude analysis of the cylinder correction at 1, 3, and 6 months. The vector magnitude ratio (SIRC/IRC) was 1.37 (S.D. 0.66) at 3 months, suggesting overcorrection of the baseline cylinder. A vector analysis summary is presented in Table 12 for astigmatic myopia eyes. At 3 months, a high Correction Ratio (CR) was observed in eyes with baseline cylinder of -0.25 to -0.50 D (CR = 1.78), and in eyes with baseline cylinder of -0.51 to -1.00 D (CR 1.26). Because nearly half of the study population had cylinder of -1.00 D or less, and even though the CR was close to 1.00 for the eyes with baseline cylinder of -1.01 to -3.50 D, this is not reflected in the overall mean CR of 1.42.

These data confirm that the overcorrections occurred primarily in the baseline cylinder groups of -0.25 to -0.50 D and -0.51 to -1.00 D, which had significantly higher CR values as compared to all other baseline cylinder groups at 3 months postoperatively. At 3 months, all other baseline cylinder groups had a CR value that was closer to the desired target value of 1.0. This was confirmed by the high levels of UCVA in the overall study population and in the eyes with low levels of preoperative cylinder.

TABLE 11
VECTOR MAGNITUDE ANALYSIS SUMMARY
EYES TREATED FOR ASTIGMATIC MYOPIA &
WITH COMPLETE PREOPERATIVE AND POSTOPERATIVE REFRACTION

Statistics	Preoperative	Postoperative	IRC	SIRC	SIRC/IRC
1 Month					
N	269	269	269	269	269
Mean	-0.982	-0.373	0.982	1.199	1.40
Standard Deviation	0.684	0.344	0.684	0.743	0.70
Minimum	-3.500	-1.500	0.250	0.051	0.18
Maximum	-0.250	0.000	3.500	3.999	4.94
3 Months					
N	270	270	270	270	270
Mean	-0.980	-0.377	0.980	1.185	1.37
Standard Deviation	0.684	0.356	0.684	0.747	0.66
Minimum	-3.500	-1.500	0.250	0.035	0.07
Maximum	-0.250	0.000	3.500	4.237	4.00
6 Months					
N	266	266	266	266	266
Mean	-0.986	-0.355	0.986	1.190	1.36
Standard Deviation	0.686	0.354	0.686	0.764	0.65
Minimum	-3.500	-2.000	0.250	0.169	0.24
Maximum	-0.250	0.000	3.500	4.740	5.80

N = Number of available CRFs received with non-missing values at each visit.

TABLE 12
VECTOR ANALYSIS SUMMARY AT 3 MONTHS (POINT OF STABILITY)
EYES TREATED FOR ASTIGMATIC MYOPIA

Preoperative Cylinder	|IRC|		|SIRC|		CR[1]		ER[2]	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
3 Months								
All	270	0.884 ± 0.600	270	1.095 ± 0.673	270	1.420 ± 0.722	270	0.606 ± 0.730
-0.25 to -0.50 D	111	0.385 ± 0.108	111	0.664 ± 0.354	111	1.784 ± 0.923	111	0.961 ± 0.951
-0.51 to -1.00 D	70	0.778 ± 0.112	70	0.978 ± 0.334	70	1.259 ± 0.405	70	0.412 ± 0.442
-1.01 to -2.00 D	67	1.343 ± 0.242	67	1.466 ± 0.503	67	1.095 ± 0.335	67	0.331 ± 0.281
-2.01 to -3.00 D	20	2.282 ± 0.239	20	2.513 ± 0.626	20	1.109 ± 0.288	20	0.270 ± 0.225
-3.01 to -3.50 D	2	2.892 ± 0.146	2	2.586 ± 0.783	2	0.888 ± 0.226	2	0.219 ± 0.074

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] CR = |SIRC|/|IRC|.

[2] ER = |EV|/|IRC|. EV = Error Vector = Vector difference between IRC and SIRC = IRC - SIRC.

4.2.9 CORRELATION TO PREOPERATIVE BEST CORRECTED VISUAL ACUITY

Change in BSCVA stratified by each diopter of preoperative MRSE for all treated eyes at 3 months is presented in Table 13. No eyes lost more than 2 lines, and only two eyes lost 2 lines of BSCVA.

TABLE 13
CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA) AT 3 MONTHS STRATIFIED BY PREOPERATIVE MRSE
ALL TREATED EYES

Change in BSCVA from Preop	-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)	-7.01 to -8.00 D % (n/N)	-8.01 to -9.00 D % (n/N)	-9.01 to -10.00 D % (n/N)	-10.01 to -11.00 D % (n/N)	Total % (n/N)
Decrease > 2 lines (Decrease > 10 letters)	0.0% (0/7)	0.0% (0/41)	0.0% (0/87)	0.0% (0/90)	0.0% (0/47)	0.0% (0/38)	0.0% (0/28)	0.0% (0/13)	0.0% (0/5)	0.0% (0/1)	0.0% (0/1)	0.0% (0/358)
Decrease 2 lines (Decrease 8 to 10 letters)	0.0% (0/7)	0.0% (0/41)	0.0% (0/87)	1.1% (1/90)	0.0% (0/47)	0.0% (0/38)	0.0% (0/28)	7.7% (1/13)	0.0% (0/5)	0.0% (0/1)	0.0% (0/1)	0.6% (2/358)
Decrease 1 line (Decrease 3 to 7 letters)	28.6% (2/7)	9.8% (4/41)	8.0% (7/87)	4.4% (4/90)	10.6% (5/47)	7.9% (3/38)	7.1% (2/28)	7.7% (1/13)	0.0% (0/5)	0.0% (0/1)	0.0% (0/1)	7.8% (28/358)
No change (Change within 2 letters)	42.9% (3/7)	36.6% (15/41)	51.7% (45/87)	48.9% (44/90)	48.9% (23/47)	50.0% (19/38)	35.7% (10/28)	38.5% (5/13)	40.0% (2/5)	0.0% (0/1)	100.0% (1/1)	46.6% (167/358)
Increase 1 line (Increase 3 to 7 letters)	28.6% (2/7)	39.0% (16/41)	36.8% (32/87)	43.3% (39/90)	31.9% (15/47)	36.8% (14/38)	46.4% (13/28)	30.8% (4/13)	40.0% (2/5)	0.0% (0/1)	0.0% (0/1)	38.3% (137/358)
Increase 2 lines (Increase 8 to 10 letters)	0.0% (0/7)	14.6% (6/41)	2.3% (2/87)	2.2% (2/90)	8.5% (4/47)	5.3% (2/38)	7.1% (2/28)	15.4% (2/13)	20.0% (1/5)	100.0% (1/1)	0.0% (0/1)	6.1% (22/358)
Increase > 2 lines (Increase > 10 letters)	0.0% (0/7)	0.0% (0/41)	1.1% (1/87)	0.0% (0/90)	0.0% (0/47)	0.0% (0/38)	3.6% (1/28)	0.0% (0/13)	0.0% (0/5)	0.0% (0/1)	0.0% (0/1)	0.6% (2/358)
Not reported*	0	0	0	0	0	0	0	0	0	0	0	0
Total†	7	41	87	90	47	38	28	13	5	1	1	358

N = Number of non-missing BSCVA change at 3 months for the corresponding sub-group.
* Number of available CRFs received with missing BSCVA change at 3 months.
† Number of available CRFs received at 3 months.

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Table 14 shows that at 3 months after surgery, 70.1% of the study patients saw as well *without* glasses after surgery as *with* glasses before surgery. At 6 months after surgery, the percentage increased to 72.9%.

TABLE 14
POSTOPERATIVE UNCORRECTED VISUAL ACUITY (UCVA) COMPARED TO PREOPERATIVE BEST SPECTACLE CORRECTED VISUAL ACUITY (BSCVA)
ALL TREATED EYES

Uncorrected Visual Acuity	1 Day % (n/N)	1 Week % (n/N)	1 Month % (n/N)	3 Months % (n/N)	6 Months % (n/N)
UCVA > 2 Lines Better Than Preop BSCVA	0.0% (0/360)	0.0% (0/360)	0.0% (0/356)	0.0% (0/358)	0.0% (0/354)
UCVA 2 Lines Better Than Preop BSCVA	0.6% (2/360)	0.3% (1/360)	2.2% (8/356)	2.5% (9/358)	4.0% (14/354)
UCVA 1 Line Better Than Preop BSCVA	8.1% (29/360)	11.9% (43/360)	20.2% (72/356)	21.5% (77/358)	29.4% (104/354)
UCVA Equal To Preop BSCVA	34.2% (123/360)	42.2% (152/360)	41.0% (146/356)	46.1% (165/358)	39.5% (140/354)
UCVA 1 Line Worse Than Preop BSCVA	31.1% (112/360)	27.2% (98/360)	25.8% (92/356)	21.5% (77/358)	17.5% (62/354)
UCVA 2 Lines Worse Than Preop BSCVA	16.7% (60/360)	9.4% (34/360)	5.9% (21/356)	4.2% (15/358)	7.3% (26/354)
UCVA > 2 Lines Worse Than Preop BSCVA	9.4% (34/360)	8.9% (32/360)	4.8% (17/356)	4.2% (15/358)	2.3% (8/354)
Not reported*	0	0	0	0	0
Total†	360	360	356	358	354

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.

4.2.10 Patient Symptoms and Satisfaction

Subjects filled out a subject questionnaire at the preoperative visit and at all follow-up visits. They graded their symptoms according to severity as either none, mild, moderate, marked, or severe. Table 15A provides all patient symptoms for all treated eyes both preoperatively and at 3 and 6 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 3 and 6 months fall predominantly into the "mild" category.

TABLE 15.A
PATIENT SYMPTOMS
ALL TREATED EYES
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Symptom	Preop		3 Months		6 Months	
Evaluation	N	%	n	%	n	%
Light sensitivity	N = 360		N = 356		N = 352	
Absent	244	67.8%	240	67.4%	256	72.7%
Mild	79	21.9%	92	25.8%	79	22.4%
Moderate	28	7.8%	17	4.8%	13	3.7%
Marked	7	1.9%	7	2.0%	4	1.1%
Severe	2	0.6%	0	0.0%	0	0.0%
Headaches	N = 360		N = 356		N = 352	
Absent	314	87.2%	319	89.6%	312	88.6%
Mild	33	9.2%	24	6.7%	32	9.1%
Moderate	10	2.8%	8	2.2%	6	1.7%
Marked	1	0.3%	3	0.8%	2	0.6%
Severe	2	0.6%	2	0.6%	0	0.0%
Pain/burning	N = 360		N = 356		N = 352	
Absent	332	92.2%	326	91.6%	330	93.8%
Mild	20	5.6%	23	6.5%	19	5.4%
Moderate	4	1.1%	4	1.1%	2	0.6%
Marked	3	0.8%	3	0.8%	1	0.3%
Severe	1	0.3%	0	0.0%	0	0.0%
Dryness	N = 360		N = 356		N = 352	
Absent	276	76.7%	163	45.8%	213	60.5%
Mild	64	17.8%	150	42.1%	104	29.5%
Moderate	14	3.9%	32	9.0%	34	9.7%
Marked	6	1.7%	11	3.1%	1	0.3%
Severe	0	0.0%	0	0.0%	0	0.0%
Excessive tearing	N = 360		N = 356		N = 352	
Absent	334	92.8%	339	95.2%	344	97.7%
Mild	18	5.0%	17	4.8%	6	1.7%
Moderate	4	1.1%	0	0.0%	2	0.6%
Marked	4	1.1%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	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 15.A *(CONTINUED)*
PATIENT SYMPTOMS
ALL TREATED EYES

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Symptom Evaluation	Preop		3 Months		6 Months	
	n	%	n	%	n	%
Gritty, scratchy	N = 360		N = 356		N = 352	
Absent	326	90.6%	316	88.8%	321	91.2%
Mild	28	7.8%	33	9.3%	30	8.5%
Moderate	6	1.7%	7	2.0%	1	0.3%
Marked	0	0.0%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	0	0.0%
Glare	N = 360		N = 356		N = 352	
Absent	281	78.1%	251	70.5%	261	74.1%
Mild	52	14.4%	85	23.9%	76	21.6%
Moderate	23	6.4%	15	4.2%	12	3.4%
Marked	4	1.1%	5	1.4%	1	0.3%
Severe	0	0.0%	0	0.0%	2	0.6%
Halos	N = 360		N = 356		N = 352	
Absent	303	84.2%	241	67.7%	271	77.0%
Mild	32	8.9%	94	26.4%	54	15.3%
Moderate	21	5.8%	6	1.7%	17	4.8%
Marked	4	1.1%	13	3.7%	8	2.3%
Severe	0	0.0%	2	0.6%	2	0.6%
Blurred vision	N = 360		N = 356		N = 352	
Absent	321	89.2%	286	80.3%	298	84.7%
Mild	32	8.9%	46	12.9%	29	8.2%
Moderate	5	1.4%	19	5.3%	23	6.5%
Marked	2	0.6%	5	1.4%	2	0.6%
Severe	0	0.0%	0	0.0%	0	0.0%
Double vision	N = 360		N = 356		N = 352	
Absent	354	98.3%	322	90.4%	334	94.9%
Mild	0	0.0%	24	6.7%	6	1.7%
Moderate	4	1.1%	6	1.7%	9	2.6%
Marked	2	0.6%	4	1.1%	3	0.9%
Severe	0	0.0%	0	0.0%	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 15.A *(CONTINUED)*
PATIENT SYMPTOMS
ALL TREATED EYES

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Symptom Evaluation	Preop		3 Months		6 Months	
	n	%	n	%	n	%
Fluctuation of vision	N = 360		N = 356		N = 352	
Absent	342	95.0%	273	76.7%	287	81.5%
Mild	16	4.4%	69	19.4%	52	14.8%
Moderate	2	0.6%	10	2.8%	11	3.1%
Marked	0	0.0%	4	1.1%	2	0.6%
Severe	0	0.0%	0	0.0%	0	0.0%
Variation - bright light	N = 360		N = 356		N = 352	
Absent	323	89.7%	315	88.5%	304	86.4%
Mild	29	8.1%	36	10.1%	42	11.9%
Moderate	5	1.4%	3	0.8%	5	1.4%
Marked	3	0.8%	2	0.6%	1	0.3%
Severe	0	0.0%	0	0.0%	0	0.0%
Variation - normal light	N = 360		N = 356		N = 352	
Absent	354	98.3%	328	92.1%	324	92.0%
Mild	4	1.1%	22	6.2%	22	6.3%
Moderate	2	0.6%	4	1.1%	5	1.4%
Marked	0	0.0%	2	0.6%	1	0.3%
Severe	0	0.0%	0	0.0%	0	0.0%
Variation - dim light	N = 360		N = 356		N = 352	
Absent	305	84.7%	273	76.7%	277	78.7%
Mild	41	11.4%	62	17.4%	61	17.3%
Moderate	10	2.8%	12	3.4%	8	2.3%
Marked	4	1.1%	9	2.5%	4	1.1%
Severe	0	0.0%	0	0.0%	2	0.6%
Night driving vision	N = 360		N = 356		N = 352	
Absent	253	70.3%	239	67.1%	257	73.0%
Mild	68	18.9%	81	22.8%	62	17.6%
Moderate	30	8.3%	23	6.5%	24	6.8%
Marked	9	2.5%	11	3.1%	7	2.0%
Severe	0	0.0%	2	0.6%	2	0.6%

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

TABLE 15.A *(CONTINUED)*
PATIENT SYMPTOMS
ALL TREATED EYES
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Symptom Evaluation	Preop		3 Months		6 Months	
	n	%	n	%	n	%
Other*	N = 360		N = 356		N = 352	
Absent	358	99.4%	354	99.4%	345	98.0%
Mild	2	0.6%	0	0.0%	3	0.9%
Moderate	0	0.0%	2	0.6%	4	1.1%
Marked	0	0.0%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	0	0.0%

N = Number of Self-evaluation Forms received with non-missing response for the corresponding symptom at each visit. % = n ÷ N × 100%.
*Other symptoms were pressure in eyes when tired or headaches (preop); trouble focusing on close objects (6 months); eyes jump when reading (6 months); floaters (6 months); itchiness (3 and 6 months).

Table 15.B presents the changes in patient symptoms from baseline to 3 and 6 months for all treated eyes. At 3 months, a greater percentage of patients experienced worsening of their symptoms than at 6 months. While most symptoms did not change or were better, as seen in Table 15.B, some of the symptoms that worsened at 3 months include the following: dryness, halos, blurred vision, and fluctuation of vision.

TABLE 15.B
PATIENT SYMPTOMS CHANGE FROM BASELINE
ALL TREATED EYES

Patient Symptom	3 Months % (n/N)			6 Months % (n/N)		
	Better	No Change	Worse	Better	No Change	Worse
Light sensitivity	18.5 (66/356)	64.9 (231/356)	16.6 (59/356)	22.7 (80/352)	63.4 (223/352)	13.9 (49/352)
Headaches	9.8 (35/356)	84.0 (299/356)	6.2 (22/356)	8.8 (31/352)	85.8 (302/352)	5.4 (19/352)
Pain/burning	5.9 (21/356)	88.8 (316/356)	5.3 (19/356)	7.4 (26/352)	88.4 (311/352)	4.3 (15/352)
Dryness	10.1 (36/356)	49.2 (175/356)	40.7 (145/356)	12.8 (45/352)	59.7 (210/352)	27.6 (97/352)
Excessive tearing	5.3 (19/356)	92.4 (329/356)	2.2 (8/356)	7.4 (26/352)	90.9 (320/352)	1.7 (6/352)
Gritty, scratchy	9.6 (34/356)	79.8 (284/356)	10.7 (38/356)	9.4 (33/352)	83.2 (293/352)	7.4 (26/352)
Glare	15.4 (55/356)	63.5 (226/356)	21.1 (75/356)	17.6 (62/352)	65.6 (231/352)	16.8 (59/352)
Halos	8.1 (29/356)	67.4 (240/356)	24.4 (87/356)	11.4 (40/352)	71.9 (253/352)	16.8 (59/352)
Blurred vision	7.6 (27/356)	75.0 (267/356)	17.4 (62/356)	8.8 (31/352)	77.3 (272/352)	13.9 (49/352)
Double vision	1.1 (4/356)	89.9 (320/356)	9.0 (32/356)	1.1 (4/352)	94.3 (332/352)	4.5 (16/352)
Fluctuation of vision	1.4 (5/356)	78.7 (280/356)	19.9 (71/356)	2.8 (10/352)	81.0 (285/352)	16.2 (57/352)
Variation - bright light	7.9 (28/356)	83.4 (297/356)	8.7 (31/356)	7.7 (27/352)	81.8 (288/352)	10.5 (37/352)
Variation - normal light	1.1 (4/356)	91.6 (326/356)	7.3 (26/356)	1.7 (6/352)	90.9 (320/352)	7.4 (26/352)
Variation - dim light	9.8 (35/356)	73.0 (260/356)	17.1 (61/356)	11.1 (39/352)	73.6 (259/352)	15.3 (54/352)
Night driving vision	23.0 (82/356)	55.9 (199/356)	21.1 (75/356)	20.7 (73/352)	64.2 (226/352)	15.1 (53/352)
Other	0.6 (2/356)	98.9 (352/356)	0.6 (2/356)	0.6 (2/352)	97.4 (343/352)	2.0 (7/352)

Clinically significant symptoms (those rated moderate to severe) with statistically significant change from baseline to month 3 are dryness (increased from 6% at baseline to 12% at 3 months), tearing (decreased 2% to 0%), blurred vision (increased 2% to 7%), and fluctuation of vision (increased 1% to 4%); see Table 15.C below.

TABLE 15.C
CLINICALLY SIGNIFICANT PATIENT SYMPTOMS
ALL TREATED EYES

Symptom	Preop. Versus 3 Months N = 356		Preop. Versus 6 Months N = 352	
	Preop (%)	3 Months (%)	Preop n (%)	6 Months n (%)
Light sensitivity	10.4%	6.7%	10.5%	4.8%
Headaches	3.7%	3.7%	3.7%	2.3%
Pain/burning	2.2%	2.0%	2.3%	0.9%
Dryness	5.6%	12.1%	5.7%	9.9%
Excessive tearing	2.2%	0.0%	2.3%	0.6%
Gritty, scratchy	1.7%	2.0%	1.7%	0.3%
Glare	7.0%	5.6%	7.7%	4.3%
Halos	7.0%	5.9%	7.1%	7.7%
Blurred vision	2.0%	6.7%	2.0%	7.1%
Double vision	1.7%	2.8%	1.7%	3.4%
Fluctuation of vision	0.6%	3.9%	0.6%	3.7%
Variation - bright light	2.2%	1.4%	2.3%	1.7%
Variation - normal light	0.6%	1.7%	0.6%	1.7%
Variation - dim light	3.9%	5.9%	4.0%	4.0%
Night driving vision	11.0%	10.1%	11.1%	9.4%
Other	0.0%	0.6%	0.0%	1.1%

Table 15.D shows the following problems were worse 3 months after LASIK for more than 1% of patients. 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 (7.6%), blurred vision (4.8%), variation in dim light (5.3%), and night driving (7.3%).

TABLE 15.D COMPARISON OF SYMPTOMS BEFORE AND AFTER SURGERY

(AT 3 MONTHS, N = 356)

SYMPTOM	WORSE % (n)	SIGNIFICANTLY WORSE % (n)
Light sensitivity	13.2% (47)	3.4% (12)
Headaches	3.7% (13)	2.5% (9)
Pain/burning	3.9% (14)	1.4% (5)
Dryness	33.1% (118)	7.6% (27)
Excessive tearing	2.2% (8)	0.0% (0)
Gritty, scratchy	8.7% (31)	2.0% (7)
Glare	17.7% (63)	3.4% (12)
Halos	20.8% (74)	3.7% (13)
Blurred vision	12.6% (45)	4.8% (17)
Double vision	6.7% (24)	2.2% (8)
Fluctuation of vision	16.3% (58)	3.7% (13)
Variation - bright light	7.9% (28)	0.8% (3)
Variation - normal light	5.6% (20)	1.7% (6)
Variation - dim light	11.8% (42)	5.3% (19)
Night driving vision	13.8% (49)	7.3% (26)
Other	0.0% (0)	0.6% (2)

Overall patient satisfaction with vision after surgery is shown in Table 16. At 3 months, 98% of patients reported marked or extreme improvement in overall vision quality. Only 1.1% report dissatisfaction with their surgery (4 eyes of 2 subjects, both with hyperopic MRSE at month 3: +1.0 D and +0.5 D for one subject, +1.12 D and +1.87 D for the other subject). Only 1.1% would not select refractive surgery again. Only 0.6% report no improvement in overall quality of vision (1 eye of one subject, whose 3-month uncorrected visual acuity (UCVA) was 20/80, best corrected visual acuity (BCVA) was 20/12, and MRSE was +1.87 D).

TABLE 16
PATIENT EVALUATION OF SATISFACTION AND VISION QUALITY IMPROVEMENT
ALL TREATED SUBJECTS (SUBJECT BASIS)

Self-evaluation	Response	3 Months % (n/N)	6 Months % (n/N)
Overall Vision Quality	No Improvement	0.6% (1/180)	0.6% (1/178)
	Slight Improvement	1.1% (2/180)	0.0% (0/178)
	Moderate Improvement	1.1% (2/180)	1.7% (3/178)
	Marked Improvement	14.4% (26/180)	16.3% (29/178)
	Extreme Improvement	82.8% (149/180)	81.5% (145/178)
	Not reported*	0	0
	Total†	180	178
Select Refractive Surgery Again	No	1.1% (2/180)	2.2% (4/178)
	Yes	94.4% (170/180)	94.4% (168/178)
	Unsure	4.4% (8/180)	3.4% (6/178)
	Not reported*	0	0
	Total†	180	178
Satisfaction	Very Satisfied	90.6% (163/180)	88.8% (158/178)
	Moderately Satisfied	7.8% (14/180)	8.4% (15/178)
	Neutral	0.6% (1/180)	1.7% (3/178)
	Dissatisfied	1.1% (2/180)	0.6% (1/178)
	Very Dissatisfied	0.0% (0/180)	0.6% (1/178)
	Not reported*	0	0
	Total†	180	178

Summaries were per subject basis. The worse response of the two eyes of a subject was used as the response of the subject. N = Number of available subjects with non-missing values at each visit. % = n ÷ N × 100%.

* Number of available subjects with missing values at the visit.

† Number of available eyes at the visit.

4.2.11 Factors Associated with Outcomes

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

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 four investigational sites at 3 and 6 months. At 3 months, 77% of eyes were within 0.50 D of intended MRSE at site #2, compared with 83%, 87%, and 92% at the other three study sites. At 6 months, 67% of eyes were within 0.50 D of intended MRSE at site #1, compared with 76%, 80%, and 86% at the other three study sites. This difference at 6 months, attributable to a change in manifest refraction technique during the study at one site, was statistically significant with respect to deviation from intended correction within ± 0.50 D for all eyes treated, with a significantly lower proportion of eyes achieving MRSE within ± 0.50 D at 6 months postoperatively ($p=0.0263$) at Site 1. 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 3 or 6 months.

With regard to effect of age, the requirements for deviation from emmetropia within ± 0.50 D and within ± 1.00 D were met for each age group in all cohorts of eyes, i.e., all treated eyes, spherical myopia eyes and astigmatic myopia eyes, at 3 months postoperatively. At 6 months, the only age subgroup that did not meet the minimum requirements of 50% of eyes within ± 0.50 D of emmetropia was the age group ≥ 50 years. All subgroups met the minimum target value of 75% of eyes within ± 1.00 D of emmetropia at 3 and 6 months.

With respect to the effect of baseline MRSE on refractive predictability, eyes with a baseline MRSE of higher than -7.00 D were reported with a lower proportion of eyes achieving refractive predictability within ± 0.50 D of the intended outcome at 6 months (note: this difference was not observed at 3 months). That is, at 6 months, eyes with baseline MRSE up to -7.00 D had statistically higher MRSE accuracy outcome (79% were within 0.50 D of intended MRSE), than eyes with baseline MRSE greater than -7.00 D (45% within 0.50 D of intended MRSE). Baseline MRSE did not have a significant statistical association with UCVA outcomes of 20/40 or better at 3 or 6 months. However, eyes with baseline MRSE -7.00 D or lower demonstrated a greater proportion of eyes achieving UCVA better than 20/40 (i.e., 20/12.5 to 20/16 at 3 months, and 20/16 to 20/32 at 6 months) than eyes with baseline MRSE higher than -7.00 D. In addition, subjects 50 years of age and older were reported with a lower proportion of eyes achieving 20/40 or better UCVA at 6 months as compared to subjects less than 50 years old (this difference was not observed at 3 months).

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. Myopic patients will have a higher incidence of retinal pathology, and 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 myopic 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 myopia including, but not limited to, spectacles, contact lenses, and other refractive surgeries.

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 pre operatively.

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 Operator's 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 post operative 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, and 6 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

Refer to the Operator's 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.).

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. Check room conditions (see technical data, ambient conditions for intended use in the MEL 80 Operator's Manual).
11. Starting 30 minutes before surgery, it is advisable to put a drop of a non-toxic antibiotic in the eye every 10 minutes.
12. Prepare the microkeratome.
13. Enter and verify patient data.
14. Microscope setting: magnification 1.0x.
15. Run the fluence test and confirm it with <Energy Ok>.

16. Switch off the aiming beam to avoid coverage of the fixation light. Move joystick aside, if necessary.
17. Bring patient in.
18. 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.
19. Position the patient on the bed so that the patient's eye is effortless in the position required.
20. 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.
21. Cover the operation area with a fenestrated adhesive drape and drape it in such a way that the lashes are folded back over the margin of the eyelid.
22. Microscope setting: magnification 0.6x.
23. Coarsely adjust the patient bed using the focusing beams.
24. Use an eyelid retractor.
25. Apply a drop of an anesthetic (e.g. Oxybuprocain-HCl) (not yet in the other eye if you plan bilateral treatment).
26. 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.
27. Using gentian violet, mark the cornea non-symmetrically.
28. Rinse excessive dye away.
29. Perform the keratome cut following the instructions for use of the keratome. Do not open the flap yet.
30. Microscope setting: magnification 1.0x.
31. Again, accurately position the patient's eye with the patient bed.
32. Swing in the CCA+ unit taking care that the position of the patient's eye remains stable.
33. 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 looses 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 post operative 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.