Professional Use Information

VISX STAR S2™ Excimer Laser System

Laser Assisted In Situ Keratomileusis (LASIK)

Photorefractive Keratectomy (PRK)

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

This document provides information concerning the intended clinical use of the STAR S2 Excimer Laser System. For complete information concerning system components, safety instructions, installation, maintenance, and troubleshooting, refer to the STAR S2 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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2.0 Indications, Contraindications, Warnings, Precautions, and Adverse Events

2.1 Indications for Use

Laser Assisted In Situ Keratomileusis (LASIK) procedure using the STAR S2™ System is intended for use:

- in patients with documented evidence of a change in manifest refraction of no more than 0.5 D (in both cylinder and sphere components) for at least one year prior to the date of pre-operative examination; and
- in patients 18 years of age or older in treatments for the reduction or elimination of myopia (nearsightedness) of no more than -14.0 D with or without refractive astigmatism from 0.5 to 5.0 D*; or
- in patients 21 years of age or older in treatments for the reduction or elimination of naturally occurring hyperopia between +0.5 and +5.0 D sphere at the spectacle plane with or without refractive astigmatism up to +3.0 D, with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D.
- in patients 21 years of age or older in treatments for the reduction or elimination of naturally occurring mixed astigmatism where the magnitude of cylinder (≤6.0 D at the spectacle plane) is greater than the magnitude of sphere and the cylinder and sphere have opposite signs.

Photorefractive Keratectomy (PRK) procedure using the STAR S2 System is intended for use:

- in patients with documented evidence of a change in manifest refraction of no more than 0.5 D (in both cylinder and sphere components) for at least one year prior to the date of pre-operative examination; and
- in patients 18 years of age or older in treatments for the reduction or elimination of myopia (nearsightedness) of no more than -6.0 D spherical equivalent at the corneal plane, with no more than 1.0 D of refractive astigmatism; or
- in patients 21 years of age or older in treatments for the reduction or elimination of myopia (nearsightedness) of no more than -12.0 D spherical myopia at the spectacle plane with no more than 4.0 D of refractive astigmatism*; or
- in patients 21 years of age or older in treatments for the reduction or elimination of naturally occurring hyperopia between +1.0 and +6.0 D sphere at the spectacle plane with no more than 1.0 D of refractive astigmatism; or

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* Caution must be used to calculate treatment in MINUS CYLINDER at the spectacle plane (vertex distance 12.5 mm) before entering the refraction into the laser in order to conform with the Indications for Use.

- in patients 21 years of age or older in treatments for the reduction or elimination of naturally occurring hyperopia between +0.5 and +5.0 D sphere at the spectacle plane with refractive astigmatism from 0.5 to 4.0 D, with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D.

Refer to the preceding General Warnings section of this Professional Use Information Manual, in addition to the warnings and precautions found in this section.

2.2 Contraindications

Laser refractive surgery is contraindicated:

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

2.3 Warnings

- The decision to perform laser refractive surgery in patients with systemic disease likely to affect wound healing, such as connective tissue disease, diabetes, severe atopic disease, or an immunocompromised status, should be approached cautiously. The safety and effectiveness of the STAR S2™ System has not been established in patients with these conditions.
- Laser refractive surgery is not recommended in patients with a history of ophthalmic *Herpes simplex* or *Herpes zoster*.
- Lower uncorrected visual acuity rates of 20/20 and 20/40 may be anticipated with higher degrees of correction of myopia and astigmatism.

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* Accutane is a registered trademark of Hoffmann-La Roche Inc.

† Cordarone is a registered trademark of Sanofi.

2.4 Precautions

A. General

There is no safety and effectiveness information for PRK refractive treatments greater than -12.0 D of myopia, greater than +6.0 D of hyperopia, or greater than 4.0 D of refractive astigmatism.

There is no safety and effectiveness information for LASIK refractive treatments greater than -14.0 D of myopia or greater than 5.0 D of refractive astigmatism.

There is not sufficient safety and effectiveness information for LASIK refractive treatments greater than +5.0 D of hyperopia or greater than +3.0 D of refractive astigmatism.

There is no safety and effectiveness information for LASIK refractive treatments in patients with mixed astigmatism where the magnitude of cylinder is greater than 6.0 D.

To avoid corneal ectasia, the posterior 250 microns (μm) of corneal stroma should not be violated by the laser or the microkeratome.

Of the eyes treated in the PRK trials, only 21/200 (10.5%) of highly myopic eyes had myopia between -10 and -12 diopters and only 13/275 (4.7%) of hyperopic eyes had hyperopia between +4 and +6 diopters. These populations were not sufficient to determine the level of effectiveness or the complication rates for this refractive error range with the same reliability as for eyes with less severe refractive errors.

PRK patients with **+4.0 to +6.0 D of spherical hyperopia** may be at a greater risk of regression of correction.

2.1% of hyperopic PRK patients with pre-operative Best Spectacle-Corrected Visual Acuity (BSCVA) of 20/20 or better, had post-operative BSCVA of worse than 20/25, but not worse than 20/32.

PRK patients treated for hyperopic astigmatism greater than or equal to 5 diopters spherical equivalent pre-operatively are less stable and have lower predictability with a greater probability of undercorrection.

LASIK treatment for astigmatism at or below +1.0 D may not be effective for some patients. Because of limitations in measurements of accuracy, there may be a greater incidence of large axis shifts with little or no reduction of cylinder magnitude. In this study, 45% of eyes with pre-operative astigmatism at or below +1 D had as much or more astigmatism after surgery than before. This type of result may cause visual distortions that are more disturbing to the patient than the original condition.

LASIK treatment of cylinder >3 D may result in a greater incidence of significant residual astigmatism (>1 D) and axis shift.

LASIK patients treated for mixed astigmatism demonstrated a small amount of hyperopic spherical equivalent at 6 months post-operatively (average of 0.3 D) as a consequence of systematic undercorrection of the hyperopic cylinder component of the treatment. A component analysis of undercorrections and overcorrections showed that in 14% of the eyes the hyperopic cylinder component was undercorrected by ≥1.0 D.

Sufficient data were provided to evaluate LASIK treatment to -14.0 diopters of sphere and -5.0 diopters of cylinder; however, there were insufficient eyes treated with a combination of -12.0 diopters of sphere and -3.5 or higher diopters of myopic cylinder to determine the level of effectiveness or the complication rates for this refractive error range with the same reliability as for eyes with less severe refractive errors.

The effects of laser refractive surgery on visual performance under poor lighting conditions have not been determined. It is possible, following laser refractive surgery, that patients will find it more difficult than usual 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 by large pupil sizes or decentered pupils.

Astigmatic patients between the ages of 21 and 30 should be reminded that, due to larger pupils, they are more likely than the over-30-year-old population to experience a degradation in visual performance under these conditions.

The safety and effectiveness of the STAR S2™ System have **NOT** been established:

- for PRK treatment of astigmatism in patients with refractive cylinder of less than 0.75 D.
- for PRK hyperopia treatment of patients with refractions less than +1.0 D.
- for LASIK and PRK treatment in patients with progressive myopia, progressive astigmatism, ocular disease, corneal abnormality, previous corneal surgery, or trauma in the ablation zone.
- for LASIK and PRK surgery in patients with corneal neovascularization within 1.0 mm of the ablation zone.
- for PRK in patients under 21 years of age with myopia greater than -6.0 D, with no more than 1.0 D of refractive astigmatism.
- for PRK in patients under 21 years of age with hyperopia between +1.0 and +6.0 D spherical equivalent, with no more than 1.0 D of refractive astigmatism.
- for PRK in patients under 21 years of age with hyperopia between +0.5 and +5.0 D spherical equivalent, with refractive astigmatism between +0.5 and +4.0 D.
- for LASIK in patients under 21 years of age with hyperopia between +0.5 and +5.0 D, with or without refractive astigmatism up to +3.0 D, with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D.

- for LASIK or PRK surgery in patients under 18 years of age.
- for LASIK in patients under 21 years of age with mixed astigmatism where the magnitude of cylinder (≤6.0 D) exceeds the magnitude of sphere and the cylinder and sphere have opposite signs.
- over the long term: more than 3 years after PRK surgery for low myopia; more than 1 year after PRK surgery for high myopia with astigmatism or hyperopia with or without astigmatism; or more than 6 months after LASIK surgery for myopia with or without astigmatism, hyperopia with or without astigmatism, or mixed astigmatism.
- for PRK in patients with a history of keloid formation.
- for LASIK and PRK surgery in patients who are taking sumatriptan (Imitrex®*).
- for PRK in patients taking hormone replacement therapy or antihistamines who may have delayed re-epithelialization of the cornea following surgery.
- for LASIK in patients who have had prior incisional refractive surgery.
- for LASIK in patients with myopia greater than -14.0 D or refractive astigmatism greater than 5.0 D.
- for LASIK in patients with hyperopia greater than +5.0 D sphere, refractive astigmatism greater than +3.0 D, or a maximum manifest refraction spherical equivalent (MRSE) of greater than +6.0 D.
- for LASIK in patients with mixed astigmatism where the magnitude of cylinder is greater than 6.0 D.
- for PRK in patients with hyperopic astigmatism greater than +5.0 D sphere or greater than +6.0 D of manifest refraction spherical equivalent.
- for LASIK and PRK retreatment of hyperopic astigmatism.

B. Patient Selection

Consideration should be given to the following in determining the appropriate patients for laser refractive surgery:

- Complete examination, including but not limited to, cycloplegic 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 is essential.

*Imitrex is a registered trademark of Glaxo Group Ltd.

- To obtain accurate refractive information, contact lens wearers must be examined after abstaining from contact lens use for at least 2 weeks for soft lenses and at least 3 weeks for hard lenses. Prior to treatment and after at least 3 weeks of contact lens abstinence, patients who wear rigid gas permeable or hard (PMMA) lenses must have 3 central keratometry readings and manifest refractions taken at 1 week intervals, the last 2 of which must not differ by more than 0.50 diopter in either meridian. All mires must be regular. Any patient with keratometry or a clinical picture that is suggestive of keratoconus is specifically contraindicated as described above.
- Glaucoma is more common in myopic patients than in the general population. Evaluation of the optic nerve and measurement of the intraocular pressure are necessary. If there are any concerns regarding the appearance of the optic nerve, a Humphrey 24-2 Fastpac or equivalent threshold test of the visual field should be performed. If elevated intraocular pressure and/or evidence of glaucomatous damage are found, topical steroids should be used only with careful medical supervision or the patient should not undergo laser refractive surgery.
- Pre-operative corneal mapping is essential on all patients to exclude topographical abnormalities. This is especially important when astigmatism or steep keratometry readings are present, which may indicate the presence of keratoconus or other irregularities.
- Baseline evaluation of patients requesting refractive surgery should be performed within 30 days of the laser refractive surgery.
- The patient should have the ability to tolerate local or topical anesthesia.
- 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 laser refractive procedure.
- The patient must be able to understand and give an informed consent.
- Patients must be clearly informed of all alternatives for the correction of myopia, hyperopia, and astigmatism. These alternative corrections include but are not limited to spectacles, contact lenses, and other refractive surgeries such as radial keratotomy or automated lamellar keratoplasty.

C. 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 the crystalline lens. The area of potential hazard (Nominal Hazard Zone) for 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 farther 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.

D. Post-Procedure

1) LASIK

The following post-operative examinations are recommended on day 1 or day 2, and at 1, 3, and 6 months:

- Uncorrected Visual Acuity (UCVA or VA-sc).
- Best Spectacle-Corrected Visual Acuity (BSCVA or VA-cc).
- Manifest refraction.
- Intraocular pressure (Goldmann applanation) at 3 months.
- Slit-lamp examination.
- Keratometry and videokeratography at 3 and 6 months.

2) PRK

A slit-lamp examination should be performed on a daily basis until re-epithelialization is complete. After re-epithelialization, the following examinations are recommended on a schedule of at least 1, 3, 6, and 12 months:

- Uncorrected Visual Acuity (UCVA or VA-sc).
- Manifest refraction with the Best Spectacle-Corrected Visual Acuity (BSCVA or VA-cc).
- Intraocular pressure (IOP).
- Slit-lamp examination, including corneal clarity evaluation.
- Videokeratography at 6 months (sooner only if unanticipated events occur during the healing process).
- If topical steroids are used post-operatively, patients should be monitored for development of possible steroid side-effects, including but not limited to ocular hypertension, glaucoma, and/or cataract.

2.5 LASIK and PRK Adverse Events

There was no patient death related to the use of the STAR S2™ System.

The following transient complications might be expected with patients undergoing the PRK procedure: moderate pain (1 to 4 days), foreign body sensation, tearing, photophobia, redness, itching/scratchiness, burning, dryness, headache, blurred vision, corneal swelling, and pupil enlargement.

Other adverse events that might be expected with patients undergoing the PRK procedure but have not been observed in the VISX® clinical studies are corneal perforations, intraocular infections, hyphemas, hypopyon, post-treatment lens abnormalities with vision loss, significant overcorrections, persistent corneal decompensation/edema, or cystoid macular edema.

Adverse events that might be expected with patients undergoing the LASIK procedure are glare, halos, monocular diplopia/polyopia, surface irregularity associated with cap healing, irregular ablations, decentered ablations, foreign body sensation, corneal scarring, keratitis (infectious or sterile) with the possible sequelae of corneal ulceration or perforation, dellen formation, foreign bodies in the interlamellar interface, vitreoretinal hemorrhage, cataract, corneal decompensation, and tenderness to touch.

Excimer laser energy has the potential to induce micromechanical damage to endothelial cells, induce cataracts, and cause mutations. These effects have not been observed in any clinical use, nor have they been reproducible in various animal and *in vitro* test systems.

2.5.1 LASIK Adverse Events and Complications

A. Myopia with or without Astigmatism

Twelve hundred and seventy-six (1276) eyes were used for safety analyses. Eight hundred and sixty-seven (867) eyes were followed for at least 6 months. The following Adverse Events (AEs) occurred at a rate of less than 1% at 6 months: Loss of 2 or more lines of BSCVA; BSCVA less than 20/40; increase of 2 D or more of cylinder; BSCVA less than 20/25 when the pre-operative eye was 20/20 or better; flap edema; interface epithelium; persistent staining; stromal edema; uncontrolled IOP; and wrinkling of the cap.

The following Adverse Events (AEs) did not occur: corneal infiltrate or ulcer; melting of the flap; late onset of haze; retinal detachment; retinal vascular accidents.

Intra-operative complications are presented in Table 2-1.

Table 2-1 — Myopia with or without Astigmatism Intra-Operative Complications (LASIK) (n = 1276)

Damage to Epithelium	7 (0.5%)
Epithelial Defect	8 (0.6%)
Free Cap	54 (4.2%)
Oval Keratectomy	9 (0.7%)
Small Flap	2 (0.2%)
Small Flap with Thin Flap	1 (0.1%)
Surgery Aborted: Inadequate Flap	2 (0.2%)
Thin Flap	4 (0.3%)

Patient Findings

Patients graded their glare, halo, and visual fluctuations complaints before and at 3 months post-operatively. Severe glare was reported in 9% of subjects pre-operatively while 6% of subjects complained of severe glare at 3 months post-operatively. Severe halos were reported in 9% of subjects pre-operatively while 4% of subjects complained of severe halos at 3 months post-operatively. Four percent of subjects reported severe fluctuations pre-operatively while 2% of subjects complained of severe fluctuations at 3 months post-operatively.

B. Hyperopia with or without Astigmatism

One hundred and sixty-nine (169) eyes were used for safety analyses. One hundred and fifty-eight (158) eyes were followed for at least 6 months. At the 3 and 6-month visits, no eye lost more than 2 lines of BSCVA. At the final visit, only 1 eye (0.6%) had a BSCVA worse than 20/40 and no eye with a pre-operative BSCVA of 20/20 or better had a post-operative BSCVA of worse than 20/40 at any visit.

The following Adverse Events (AEs) did not occur: corneal infiltrate or ulcer; melting of the flap; late onset of haze; retinal detachment; retinal vascular accidents. Adverse Events for 1 month and later are presented in Table 2-2. Complications for 1 month and later are presented in Table 2-3.

Table 2-2 — Hyperopia with or without Astigmatism Adverse Events (LASIK)

Adverse Event Description	1 M (n = 169)		3 M (n = 163)		6 M (n = 158)	
	n	%	n	%	n	%
Corneal Infiltrate/Ulcer	0*	0.0	0	0.0	0	0.0
Corneal epithelial defect involving the keratectomy at 1 month or later	0	0.0	0	0.0	0	0.0
Corneal edema at 1 month or later (specify "flap" or "bed" or both)	0	0.0	0	0.0	0	0.0
Epithelium in the interface with loss of 2 or more lines of BSCVA	0	0.0	0	0.0	0	0.0
Lost, misplaced or misaligned flap	0	0.0	0	0.0	0	0.0
Melting of the flap (LASIK only)	0	0.0	0	0.0	0	0.0
Uncontrolled IOP >10mm Hg or Any reading > 25 mm Hg	0	0.0	0	0.0	0	0.0
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more of BSCVA					0	0.0
Decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later					0	0.0
Retinal Detachment	0	0.0	0	0.0	0	0.0
Retinal Vascular Accidents	0	0.0	0	0.0	0	0.0

* Two cases of ILK (intrastromal lamellar keratitis) were reported in the immediate post-operative period. Both cases resolved without sequelae within 1 week of onset.

Table 2-3 — Hyperopia with or without Astigmatism Complications (LASIK)

Complication Description	1 M (n = 169)		3 M (n = 163)		6 M (n = 158)	
	n	%	n	%	n	%
Corneal edema between 1 week and 1 month after procedure	0	0.0	0	0.0	0	0.0
Peripheral corneal epithelial defect at 1 month or later	1	0.6	0	0.0	0	0.0
Epithelium in the interface	5	3.0	1	0.6	0	0.0
Foreign body sensation at 1 month or later	0	0.0	0	0.0	0	0.0
Pain at 1 month or later	0	0.0	0	0.0	0	0.0
Ghost/double images in the operative eye	0	0.0	3	1.8	0	0.0
Flap is not of the size and shape as initially intended or microkeratome stopped in mid-cut	0	0.0	0	0.0	0	0.0

Table 2-4 — Hyperopia with or without Astigmatism Patient Symptoms (LASIK): Comparison of Vision After Surgery (All Eyes with a Treatment Sphere ≤ 5.0 and Questionnaire, n = 156)

Patient Symptom Description	Worsen (-≥2)* 3 M (n = 147)		Worsen (-≥2)* 6 M (n = 144)	
	n	%	n	%
Sharpness and Clarity	7	4.8	10	6.9
Consistency of Vision	6	4.1	10	6.9
Sustained Close Work	5	3.4	4	2.8
Daylight Driving	6	4.1	6	4.2
Night Driving	6	4.1	7	4.9
Night Vision with Glare	8	5.4	6	4.2
Reading in Dim Light	10	6.8	9	6.3
General Vision in Dim Light	10	6.8	9	6.3
Overall Visual Comfort	8	5.4	3	2.1

* This table reflects the responses to a patient questionnaire on a scale of 1 (poor) to 5 (excellent). Responses at 3 and 6 months were compared to the pre-operative responses. The results presented reflect changes in response from baseline.

C. Mixed Astigmatism

One hundred and fifteen (115) eyes were used for safety analyses. One hundred and ten (110) eyes were followed for 6 months. At the 1, 3, and 6-month visits, no eye lost more than 2 lines of BSCVA and no eye had a BSCVA worse than 20/40.

The following Adverse Events (AEs) did not occur: corneal infiltrate or ulcer, melting of the flap, late onset of haze, retinal detachment, retinal vascular accidents. Adverse Events for 1 month and later are provided in Table 2-5. Complications for 1 month and later are presented in Table 2-6. Patient symptoms for 3 and 6 months are presented in Table 2-7.

Table 2-5 — Mixed Astigmatism Adverse Events (LASIK)

Adverse Event Description	1 M (n = 110)		3 M (n = 115)		6 M (n = 110)	
	n	%	n	%	n	%
Corneal Infiltrate/Ulcer	0	0.0	0	0.0	0	0.0
Corneal epithelial defect involving the keratectomy at 1 month or later	0	0.0	0	0.0	0	0.0
Corneal edema at 1 month or later (specify "flap" or "bed" or both)	0	0.0	0	0.0	0	0.0
Epithelium in the interface with loss of 2 or more lines of BSCVA	0	0.0	0	0.0	0	0.0
Lost, misplaced or misaligned flap	0	0.0	0	0.0	0	0.0
Melting of the flap (LASIK only)	0	0.0	0	0.0	0	0.0
Uncontrolled IOP >10mm Hg or Any reading > 25 mm Hg	0	0.0	0	0.0	0	0.0
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more of BSCVA					0	0.0
Decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later					0	0.0
Retinal Detachment	0	0.0	0	0.0	0	0.0
Retinal Vascular Accidents	0	0.0	0	0.0	0	0.0

Other: Two eyes of one patient developed diffuse lamellar keratitis (DLK) on post-operative day 1 (resolved within 3 days) and 2 eyes of another patient formed a bullous epithelium reaction during the microkeratome pass of each treatment (resolved within 3 months).

Table 2-6 — Mixed Astigmatism Complications (LASIK)

Complication Description	1 M (n = 110)		3 M (n = 115)		6 M (n = 110)	
	n	%	n	%	n	%
Corneal edema between 1 week and 1 month after procedure	0	0.0	0	0.0	0	0.0
Peripheral corneal epithelial defect at 1 month or later	0	0.0	0	0.0	0	0.0
Epithelium in the interface	1	0.9	0	0.0	0	0.0
Foreign body sensation at 1 month or later	3	2.7	1	0.9	0	0.0
Pain at 1 month or later	1	0.9	1	0.9	0	0.0
Ghost/double images in the operative eye	0	0.0	2	1.7	0	0.0
Flap is not of the size and shape as initially intended or microkeratome stopped in mid-cut	0	0.0	0	0.0	0	0.0

Table 2-7 — Mixed Astigmatism Patient Symptoms (LASIK): Comparison of Vision After Surgery (n = 115)

Patient Symptom Description	Worsen (-≥2)* 3 M (n = 115)		Worsen (-≥2)* 6 M (n = 110)	
	n	%	n	%
Sharpness and Clarity	7	6.2	6	5.5
Consistency of Vision	6	5.3	9	8.2
Daylight Driving	6	5.3	5	4.5
Night Driving	10	8.8	3	2.7
Night Vision with Glare	8	7.1	3	2.7
General Vision in Dim Light	6	5.3	5	4.5
Overall Visual Comfort	9	8.0	9	8.2

* This table reflects the responses to a patient questionnaire on a scale of 1 (poor) to 5 (excellent). Responses at 3 and 6 months were compared to the pre-operative responses. The results presented reflect changes in response from baseline.

2.5.2 PRK Adverse Events

A. Low Myopia

Nine hundred and nine (909) eyes of 676 subjects were used for safety analyses. Five hundred and forty-two (542) eyes were followed for at least 24 months.

Adverse events for 1 month and later are presented in Table 2-8.

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Table 2-8 — Low Myopia Adverse Events (PRK)
Eyes Treated with 6.0 mm Ablation Zone (n = 909)*

Adverse Event Description	3 to 6 M (n = 846)**		12 M (n = 520)**		≥ 24 M (n = 542)**	
	n	%	n	%	n	%
Loss ≥ 2 Lines of BSCVA	50	6.0♦	11	2.2	1	0.2
Pre-treatment BSCVA 20/20 or Better With Post-treatment BSCVA Worse than 20/25	52	6.4♦	10	2.1♦	7	1.3
With Post-treatment BSCVA Worse than 20/40	7	0.9	1	0.2	0	0
Overcorrection:						
> 1 D	44	5.2	6	1.2	7	1.3
> 2 D	9	1.1	1	0.2	3	0.6
Increase in Refractive Cylinder:						
≥ 1 D	46	5.5	16	3.1	16	3.0
≥ 2 D	3	0.4	0	0	0	0
Glare Testing: Abnormal (≥ 2 line loss in BSCVA with glare)	1	1.0♦	1	1.7♦	0	0
IOP Increase:						
> 5 to 10 mm Hg	61	7.3	9	1.8♦	19	3.6♦
> 10 mm Hg	7	0.8	0	0	0	0
Corneal Haze ≥ Grade 2	11	1.3	3	0.6	1	0.2
Corneal Infection/Ulcer/Infiltrate	0	0	0	0	0	0
Corneal Decompensation/Edema	0	0	0	0	0	0
Lens Abnormality Post-treatment †	2	0.2	1	0.2	3	0.6
Secondary Surgical Intervention:						
Single Retreatments	1	0.1	22	4.2	2	0.4
Double Retreatments	0	0	0	0	0	0
Other Refractive Procedures	4	0.5	14	2.7	9	1.7
Subjective Patient Responses††:						
"Double/Ghost Images" ††						
Somewhat Worse	14	1.7	3	0.6	4	0.7
Much Worse	9	1.1	5	1.0	3	0.6
"Sensitivity to Bright Lights" ‡,††						
Somewhat Worse	30	3.5	19	3.7	14	2.6
Much Worse	5	0.6	6	1.6	2	0.4
"Difficulty with Night Vision" ‡,††						
Somewhat Worse	29	3.4	14	2.7	11	2.0
Much Worse	12	1.4	13	2.5	10	1.8

* Last Observation - Post-retreatment data not included.

** For all adverse events, percentages are given as:

$$\frac{\text{number of eyes with at least one occurrence observed at the specified study visit}}{\text{number of eyes examined at the specified study visit}}$$

♦ These values were calculated using an (n) value slightly smaller than the (n) shown in the column heading due to missing measurements.

† Adverse Event #10: lens abnormality post-treatment counted by first occurrence.

†† Reflects patient responses obtained from subjective questionnaires.

‡ Results of questionnaire responses were not validated by glare testing in a clinical setting.

B. High Myopia

Two hundred (200) eyes of 157 subjects were used for safety analyses. One hundred and fifty-six (156) eyes were followed for at least 12 months.

During clinical trials, no new issues of patient safety or effectiveness were identified in the greater than 10 diopter range of pre-operative myopia. Because of the low numbers of patients (10.5%, 21/200) with myopia between the -10 and -12 diopters treated in these trials, there may not have been a sufficient population to determine the level of effectiveness or the complication rates for this refractive error range.

Adverse events for visits 6 months and later are presented in Table 2-9.

Table 2-9 — High Myopia Adverse Events* (PRK) (n = 200)

Adverse Event Description	6 M (n = 199)		12 M (n = 156)	
	n	%	n	%
Loss of ≥ 2 lines BSCVA due to				
All Causes	17	8.5	9	5.8
Corneal Causes	15	7.5	8	5.1
Pre-treatment BSCVA 20/20 or Better with a				
Post-treatment BSCVA Worse than 20/25	14	7.0	7	4.5
Post-treatment BSCVA Worse than 20/40	0	0	2	1.3
IOP Increase**				
> 5 mm Hg from baseline	5	2.7	1	0.7
> 10 mm Hg from baseline	2	1.1	0	0
> 25 mm Hg	1	0.5	0	0
Corneal Haze†				
With loss of ≥ 2 lines BSCVA	7	3.5	2	1.3
With loss of > 2 lines BSCVA	4	2.0	2	1.3
Retreatments not for primary undercorrection	0	0	3	1.5

* Patient survey not conducted for subjective evaluations of vision after surgery.

** There is a lower "n" for IOP data due to missing values (6 M n = 185 and 12 M n = 148).

† There is a lower "n" for haze data due to missing values (12 M n = 153).

C. Myopia with Astigmatism

One hundred and sixteen (116) eyes of 71 subjects, treated at five U.S. centers, were used for safety analyses. Eighty-two (82) of these eyes were followed for at least 2 years.

Adverse events for visits 6 months and later are presented in Table 2-10. They are ordered by frequency at final visit.

Table 2-10 — Myopia with Astigmatism Adverse Events (PRK) (n = 116)

Adverse Event Description	6 M (n = 108)		12 M (n = 92)		Final Visit ‡ (n = 82)	
	n	%	n	%	n	%
Loss of ≥ 2 lines BSCVA						
Due to Any Cause	5	4.6	6	6.5	7	8.5*
Due to Corneal Causes	4	3.7	4	4.3	4	4.9*
Pre-treatment BSCVA 20/20 or Better With Post-treatment BSCVA Worse than 20/25	5	4.8	4	4.3	5	6.1
With Post-treatment BSCVA Worse than 20/40	0	0	2	2.2	0	0
Secondary Surgical Intervention Retreatments	0	0	4	4.3	5	6.1
IOP Increase						
> 5 to 10 mm Hg	8	7.4	2	2.2	2	2.4
>10 mm Hg	0	0	0	0	0	0
Corneal Haze ≥ Grade 2	2	1.9	4	4.3	1	1.2
Secondary Surgical Intervention Other Refractive Procedures	0	0	1	1.1	0	0
Subjective Patient Responses ††:						
"Double/Ghost Images"††						
Somewhat Worse	5	4.6	1	1.1	5	6.1
Much Worse	1	0.9	4	4.3	0	0
"Sensitivity to Bright Lights"††						
Somewhat Worse	13	12.0	6	6.5	6	7.3
Much Worse	5	4.6	6	6.5	7	8.5
"Difficulty with Night Vision" ††						
Somewhat Worse	16	14.8	9	9.8	13	15.9
Much Worse	12	11.1	8	8.7	6	7.3

Percentages of safety outcomes are reported as:

$$\frac{\text{number of eyes with at least one occurrence observed/reported at the specified study visit}}{\text{number of eyes examined at the specified study visit}}$$

* Includes two eyes in one patient who had cataract formation upon enrollment and one eye of one patient who had a stroke; these losses of BSCVA were not attributed to corneal wound healing. **At no time did any eye lose BSCVA beyond 20/50 and at the Final Visit no eye was worse than 20/40-1.**

‡ The final visit occurred at 24 ± 3 months after treatment.

†† Reflects patient responses obtained from subjective questionnaires.

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D. Hyperopia

One hundred and twenty-four (124) subjects, treated at eight U.S. centers were used for safety analyses. The subjects were followed for at least 12 months.

Adverse events are presented in Table 2-11.

Table 2-11 — Hyperopia Adverse Events (PRK)

Adverse Event Description*	6 M (n = 201)		12 M (n = 115)	
	n	%	n	%
Decrease in BSCVA:				
> 2 Lines	2	1.0	1	0.9
2 Lines	0	0	3	2.6
Worse than 20/40	0	0	1	0.9
Pre-treatment BSCVA 20/20 or Better with a				
Post-treatment BSCVA Worse than 20/25	0	0	2	2.1*
Post-treatment Worse than 20/40	0	0	0	0
Increase >2.0 D Cylinder	0	0	1	0.9
Corneal Haze ≥ Grade 2	0	0	1	0.9
IOP Increase				
> 5 to 10 mm Hg	1	0.5*	1	0.9*
> 10 mm Hg	0	0	0	0
Overcorrection >1.0 D	4	2.0	3	2.6
Subjective Patient Responses††				
"Double/Ghost Images"††				
Somewhat Worse	6	3.0	6	5.2
Much Worse	4	2.0	1	0.9
"Sensitivity to Bright Lights",††**				
Somewhat Worse	11	5.5	7	6.1
Much Worse	1	0.5	1	0.9
"Difficulty with Night Vision",††**				
Somewhat Worse	8	4.0	5	4.3
Much Worse	2	1.0	2	1.7

* The percentage of adverse events reported reflects the actual number of occurrences reported divided by the number of data points available for each visit. Therefore, the percent reported may differ from the apparent value due to missing data points.

** Extensive contrast sensitivity and glare testing under mesopic and photopic conditions did not yield any statistically significant losses, nor any losses that could be interpreted as clinically significant.

†† Reflects patient responses obtained from subjective questionnaires.

E. Hyperopia with Astigmatism

Two hundred and seventy-six (276) eyes of 172 subjects, treated at seven U.S. centers were used for safety analyses.

Adverse events are presented in Table 2-12.

Table 2-12 — Hyperopia with Astigmatism Adverse Events (PRK)

Adverse Event Description	1 M (n = 275)		3 M (n = 272)		6 M (n = 272)		9 M (n = 255)		12 M (n = 237)	
	n	%	n	%	n	%	n	%	n	%
Corneal Infiltrate/ Ulcer	3*	1.1	0	0.0	0	0.0	0	0.0	0	0.0
Persistent Epithelial Defect at 1 Month or Later	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Uncontrolled IOP >5mm Hg or any reading >25 mm Hg	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Late Onset of Haze Beyond 6 Months with Loss of ≥2 Lines of BSCVA					0	0.0	0	0.0	0†	0.0
Decrease in BSCVA of >10 Letters not due to Irregular Astigmatism as Shown by Hard Contact Lens Refraction, at 6 Months or Later					0	0.0	0	0.0	0	0.0
Retinal Detachment	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Vascular Accidents	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

*Three eyes developed corneal infiltrates that were associated with the immediate post-operative period with a contact lens in place and all resolved without clinically significant sequelae.

†While there was 1 eye that had a 2 line loss of BSCVA at the 12-month visit, this was not considered an adverse event because it was noted to resolve after discontinuation of serzone medication.

Table 2-13 — Hyperopia with Astigmatism Patient Symptoms: Comparison of Vision After Surgery (All Eyes with a Pre-Operative Sphere ≤ 5.0 and Questionnaire, n = 206)

Patient Symptom Description	Worsen (-≥2)* 6 M (n = 203)		Worsen (-≥2)* 12 M (n = 180)	
	n	%	n	%
Sharpness and Clarity	7	3.4	11	6.1
Consistency of Vision	4	2.0	3	1.7
Sustained Close Work	13	6.5	19	10.6
Daylight Driving	6	3.0	9	5.0
Night Driving	6	3.0	6	3.4
Night Vision with Glare	5	2.5	7	3.9
Reading in Dim Light	8	4.0	16	9.0
General Vision in Dim Light	17	8.5	25	14.0
Overall Visual Comfort	0	0.0	0	0.0

* This table reflects the responses to a patient questionnaire on a scale of 1 (poor) to 5 (excellent). Responses at 6 and 12 months were compared to the pre-operative responses. The results presented reflect changes in response from baseline.

The following post-operative complications were noted at a frequency of less than 1% at any visit: corneal edema, recurrent corneal erosion, foreign body sensation, ghost/double images.

3.0 Clinical Results

3.1 LASIK Clinical Results

3.1.1 Myopia with or without Astigmatism

A prospective, non-randomized, unmasked, multicenter clinical study was conducted. The refractive inclusion criteria specified that the patient have myopia of between 0 and -14.0 diopters (D) with or without astigmatism of -0.25 to -6.00 D. A total of 1276 eyes were treated. Patients who exhibited any of the following conditions were excluded: anterior segment pathology; residual, recurrent, or active ocular disease; previous intraocular or corneal surgery in the operative eye; history of herpes keratitis; or autoimmune disease, systemic connective tissue diseases, or atopic syndrome.

A. About the Study

Treated eyes were followed for at least 3 months. Analyses of results were performed at 1, 3, and 6 months post-treatment. Effectiveness analyses included uncorrected visual acuity, accuracy of manifest refraction, stability, effectiveness of astigmatic correction, and vector analysis. Safety analyses included loss of 2 or more lines of best spectacle-corrected visual acuity (BSCVA); BSCVA of 20/40 or worse; haze with loss of BSCVA; or induced manifest astigmatism.

B. Patient Accountability

Twelve hundred and seventy-six (1276) eyes were treated at 11 centers.

Table 3-1 — Myopia (LASIK): Patient Accountability (n = 1276)

1 Day		3 M		6 M or Later	
%	n/N	%	n/N	%	n/N
99.0	1263/1276	81.5	1000/1227	89.3	1028/1151

C. Data Analysis and Results

1) Pre-Operative Characteristics

The mean age of the patients participating in this trial was 42.0 ± 9.8 years. Gender distribution was 43.2% male and 56.8% female. Mean amount of myopic sphere was 5.85 ± 2.8. Mean amount of myopic cylinder was 1.54 ± 0.77.

2) Uncorrected Visual Acuity (UCVA)

Table 3-2 shows that the UCVA target is exceeded at 6 months post-operative interval for all eyes ≤ -7 D. At 6 months, 97.0% (550/567) had a UCVA of 20/40 or better. For all eyes > -7 D, UCVA was 20/40 or better at 6 months in 91.7% (221/241).

Table 3-2 — Myopia (LASIK): UCVA in Eyes Intended to be Fully Corrected (Plano Target)

All Eyes	≤ -7D % n/N	> -7 D % n/N
Efficacy Variables		
UCVA 20/20 or better	58.6 332/567	43.6 105/241
UCVA 20/40 or better	97.0 550/567	91.7 221/241
MRSE +/- 0.50 D	77.8 455/585	60.6 157/259
MRSE +/- 1.00 D	94.4 552/585	82.2 213/259
MRSE +/- 2.00 D	99.8 584/585	96.9 251/259
Safety Variables		
Loss of ≥ 2 Lines BSCVA	0.5 3/590	0.4 1/260
BSCVA Worse than 20/40	0.2 1/590	0.8 2/260
Increase > 2 D Cylinder	0.0 0/131	0.0 0/53
BSCVA Worse than 20/25 if 20/20 or Better Pre-operatively	0.0 0/544	1.5 3/201

Table 3-3 — Myopia (LASIK): 6-Month Post-Operative Results (≤ -7 D) for Spheres

Spheres	0 to <-1.00 D	>-1.00 to -2.00 D	>-2.00 to -3.00 D	>-3.00 to -4.00 D	>-4.00 to -5.00 D	>-5.00 to -6.00 D	>-6.00 to -7.00 D	Cum. Total ≤ -7.00 D
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Efficacy Variables								
UCVA 20/20 or better*	1/1 (100)	7/8 (87.5)	15/18 (83.3)	11/16 (68.8)	15/27 (55.6)	16/26 (61.5)	12/17 (70.6)	77/113 (68.1)
UCVA 20/40 or better*	1/1 (100)	8/8 (100)	18/18 (100)	16/16 (100)	27/27 (100)	26/26 (100)	16/17 (94.1)	112/113 (99.1)
MRSE +/- 0.50 D	1/1 (100)	7/8 (87.5)	17/17 (100)	14/18 (77.8)	18/27 (66.7)	20/28 (71.4)	13/18 (72.2)	90/117 (76.9)
MRSE +/- 1.00 D	1/1 (100)	8/8 (100)	17/17 (100)	17/18 (94.4)	26/27 (96.3)	25/28 (89.3)	17/18 (94.4)	111/117 (94.9)
MRSE +/- 2.00 D	1/1 (100)	8/8 (100)	17/17 (100)	18/18 (100)	27/27 (100)	27/28 (96.4)	18/18 (100)	116/117 (99.1)
Safety Variables								
Loss of ≥ 2 Lines BSCVA	0/1 (0.0)	0/8 (0.0)	0/17 (0.0)	1/18 (5.6)	0/27 (0.0)	0/31 (0.0)	0/18 (0.0)	1/120 (0.8)
BSCVA Worse than 20/40	0/1 (0.0)	0/8 (0.0)	0/17 (0.0)	0/18 (0.0)	0/27 (0.0)	0/31 (0.0)	0/18 (0.0)	0/120 (0.0)
Increase > 2 D Cylinder †	0/1 (0.0)	0/9 (0.0)	0/20 (0.0)	0/19 (0.0)	0/29 (0.0)	0/35 (0.0)	0/18 (0.0)	0/131 (0.0)
BSCVA Worse than 20/25 if 20/20 or Better Pre-operatively	0/1 (0.0)	0/8 (0.0)	0/17 (0.0)	0/18 (0.0)	0/26 (0.0)	0/28 (0.0)	0/17 (0.0)	0/115 (0.0)

* For all eyes minus those intentionally undercorrected.

† For eyes treated for spherical corrections only.

Table 3-4 — Myopia (LASIK): 6-Month Post-Operative Results (≤ -7 D) for Spherocylinders

Spherocylinders	0 to <-1.00 D	>-1.00 to -2.00 D	>-2.00 to -3.00 D	>-3.00 to -4.00 D	>-4.00 to -5.00 D	>-5.00 to -6.00 D	>-6.00 to -7.00 D	Cum. Total ≤ -7.00 D
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Efficacy Variables								
UCVA 20/20 or better*	5/8 (62.5)	23/39 (59.0)	30/58 (51.7)	58/89 (65.2)	54/84 (64.3)	37/82 (45.1)	48/94 (51.1)	255/454 (56.2)
UCVA 20/40 or better*	8/8 (100)	38/39 (97.4)	56/58 (96.6)	88/89 (98.9)	80/84 (95.2)	79/82 (96.3)	89/94 (94.7)	438/454 (96.5)
MRSE +/- 0.50 D	6/6 (100)	29/33 (87.9)	51/61 (83.6)	79/91 (86.8)	71/89 (79.8)	60/91 (65.9)	69/97 (71.1)	365/468 (78.0)
MRSE +/- 1.00 D	6/6 (100)	31/33 (93.9)	57/61 (93.4)	90/91 (98.9)	84/89 (94.4)	84/91 (92.3)	89/97 (91.8)	441/468 (94.2)
MRSE +/- 2.00 D	6/6 (100)	33/33 (100)	61/61 (100)	91/91 (100)	89/89 (100)	91/91 (100)	97/97 (100)	468/468 (100)
Safety Variables								
Loss of ≥ 2 Lines BSCVA	0/7 (0.0)	0/34 (0.0)	1/61 (1.6)	0/93 (0.0)	0/88 (0.0)	1/91 (1.1)	0/96 (0.0)	2/470 (0.4)
BSCVA Worse than 20/40	0/7 (0.0)	0/34 (0.0)	0/61 (0.0)	0/93 (0.0)	0/88 (0.0)	1/91 (1.1)	0/96 (0.0)	1/470 (0.2)
Increase > 2 D Cylinder†	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)
BSCVA Worse than 20/25 if 20/20 or Better Pre-operatively	0/7 (0.0)	0/33 (0.0)	0/57 (0.0)	0/88 (0.0)	0/78 (0.0)	0/79 (0.0)	0/87 (0.0)	0/429 (0.0)

* For all eyes minus those intentionally undercorrected.

† For eyes treated for spherical corrections only

Table 3-5 — Myopia (LASIK): 6-Month Post-Operative Results (> -7 D) for Spheres

Spheres	>-7.00 to -8.00 D n/N (%)	>-8.00 to -9.00 D n/N (%)	>-9.00 to -10.00 D n/N (%)	>-10.00 to -11.00 D n/N (%)	>-11.00 to -12.00 D n/N (%)	>-12.00 to -13.00 D n/N (%)	>-13.00 to -14.00 D n/N (%)	Cum. Total >-7.00 D n/N (%)
Efficacy Variables								
UCVA 20/20 or better*	6/10 (60.0)	5/7 (71.4)	5/10 (50.0)	1/5 (20.0)	0/2 (0.0)	1/3 (33.3)	1/4 (25.0)	19/41 (46.3)
UCVA 20/40 or better*	10/10 (100)	5/7 (71.4)	10/10 (100)	4/5 (80.0)	2/2 (100)	3/3 (100)	4/4 (100)	38/41 (92.7)
MRSE +/- 0.50 D	12/15 (80.0)	3/7 (42.9)	6/9 (66.7)	0/6 (0.0)	1/2 (50.0)	2/3 (66.7)	2/5 (40.0)	26/47 (55.3)
MRSE +/- 1.00 D	13/15 (86.7)	5/7 (71.4)	8/9 (88.9)	5/6 (83.3)	1/2 (50.0)	3/3 (100)	5/5 (100)	40/47 (85.1)
MRSE +/- 2.00 D	15/15 (100)	7/7 (100)	9/9 (100)	5/6 (83.3)	2/2 (100)	3/3 (100)	5/5 (100)	46/47 (97.9)
Safety Variables								
Loss of ≥ 2 Lines BSCVA	0/15 (0.0)	0/7 (0.0)	0/9 (0.0)	0/6 (0.0)	0/2 (0.0)	0/3 (0.0)	0/5 (0.0)	0/47 (0.0)
BSCVA Worse than 20/40	0/15 (0.0)	1/7 (14.3)	0/9 (0.0)	1/6 (16.7)	0/2 (0.0)	0/3 (0.0)	0/5 (0.0)	2/47 (4.3)
Increase > 2 D Cylinder†	0/17 (0.0)	0/10 (0.0)	0/10 (0.0)	0/6 (0.0)	0/2 (0.0)	0/3 (0.0)	0/5 (0.0)	0/53 (0.0)
BSCVA Worse than 20/25 if 20/20 or Better Pre-operatively	0/12 (0.0)	0/5 (0.0)	0/6 (0.0)	0/5 (0.0)	0/1 (0.0)	0/2 (0.0)	0/1 (0.0)	0/32 (0.0)

* For all eyes minus those intentionally undercorrected.

† For eyes treated for spherical corrections only.

Table 3-6 — Myopia (LASIK): 6-Month Post-Operative Results (> -7 D) for Spherocylinders

Spherocylinders	>-7.00 to -8.00 D n/N (%)	>-8.00 to -9.00 D n/N (%)	>-9.00 to -10.00 D n/N (%)	>-10.00 to -11.00 D n/N (%)	>-11.00 to -12.00 D n/N (%)	>-12.00 to -13.00 D n/N (%)	>-13.00 to -14.00 D n/N (%)	>-14.00 to -15.00 D n/N (%)	Cum. Total > -7.00 D n/N (%)
Efficacy Variables									
UCVA 20/20 or better*	23/57 (40.4)	24/60 (40.0)	18/41 (43.9)	12/25 (48.0)	2/4 (50.0)	3/5 (60.0)	4/7 (57.1)	0/1 (0.0)	86/200 (43.0)
UCVA 20/40 or better*	51/57 (89.5)	56/60 (93.3)	39/41 (95.1)	21/25 (84.0)	4/4 (100)	4/5 (80.0)	7/7 (100)	1/1 (100)	183/200 (91.5)
MRSE +/- 0.50 D	43/63 (68.3)	39/66 (59.1)	24/40 (60.0)	15/24 (62.5)	3/5 (60.0)	2/6 (33.3)	5/7 (71.4)	0/1 (0.0)	131/212 (61.8)
MRSE +/- 1.00 D	52/63 (82.5)	53/66 (80.3)	34/40 (85.0)	19/24 (79.2)	5/5 (100)	4/6 (66.7)	6/7 (85.7)	0/1 (0.0)	173/212 (81.6)
MRSE +/- 2.00 D	60/63 (95.2)	65/66 (98.5)	39/40 (97.5)	22/24 (91.7)	5/5 (100)	6/6 (100)	7/7 (100)	1/1 (100)	205/212 (96.7)
Safety Variables									
Loss of ≥ 2 Lines BSCVA	0/63 (0.0)	0/66 (0.0)	0/40 (0.0)	1/25 (4.0)	0/5 (0.0)	0/6 (0.0)	0/7 (0.0)	0/1 (0.0)	1/213 (0.5)
BSCVA Worse than 20/40	0/63 (0.0)	0/66 (0.0)	0/40 (0.0)	0/25 (0.0)	0/5 (0.0)	0/6 (0.0)	0/7 (0.0)	0/1 (0.0)	0/213 (0.0)
Increase > 2 D Cylinder†	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)
BSCVA Worse than 20/25 if 20/20 or Better Pre-operatively	1/52 (1.9)	1/51 (2.0)	1/34 (2.9)	0/21 (0.0)	0/5 (0.0)	0/2 (0.0)	0/3 (0.0)	0/1 (0.0)	3/169 (1.8)

* For all eyes minus those intentionally undercorrected.

† For eyes treated for spherical corrections only.

3) Accuracy of Manifest Refraction

As shown in Table 3-7, for all eyes ≤ -7 D, at 3 months 93.1% (605/650) had an MRSE within ± 1.0 D of the attempted, while at 6 months 94.4% (552/585) had this result. Table 3-8 shows that for spheres, the rate is 92.5% (136/147) at 3 months, and 94.9% (111/117) at 6 months. Table 3-9 shows that for spherocylinders, the rate is 93.2% (469/503) at 3 months, and 94.2% (441/468) at 6 months.

Table 3-7 — Myopia (LASIK): Accuracy of Manifest Refraction (Attempted vs. Achieved, All Eyes)

All Eyes	3 M				6 M			
	≤ -7 D		> -7 D		≤ -7 D		> -7 D	
	n/N	%	n/N	%	n/N	%	n/N	%
MRSE +/- 0.50 D	478/650	73.5	167/319	52.4	455/585	77.8	157/259	60.6
MRSE +/- 1.00 D	605/650	93.1	240/319	75.2	552/585	94.4	213/259	82.2
MRSE +/- 2.00 D	648/650	99.7	299/319	93.7	584/585	99.8	251/259	96.9
Not Reported	28/678	4.1	3/322	0.9	65/650	10.0	14/273	5.1
Total	678	100	322	100	650	100	273	100
Overcorrected >+ 1 D	12/650	1.8	13/319	4.1	8/585	1.4	15/259	5.8
Overcorrected >+ 2 D	0/650	0.0	0/319	0.0	0/585	0.0	3/259	1.2
Undercorrected < - 1 D	33/650	5.1	66/319	20.7	25/585	4.3	31/259	12.0
Undercorrected < - 2 D	2/650	0.3	20/319	6.3	1/585	0.2	5/259	1.9
Not Reported	28/678	4.1	3/322	0.9	65/650	10.0	14/273	5.1
Total	678	100	322	100	650	100	273	100

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Table 3-8 — Myopia (LASIK): Accuracy of Manifest Refraction (Attempted vs. Achieved, Spheres)

Spheres	3 M				6 M			
	≤ -7 D		> -7 D		≤ -7 D		> -7 D	
	n/N	%	n/N	%	n/N	%	n/N	%
MRSE +/- 0.50 D	115/147	78.2	36/68	52.9	90/117	76.9	26/47	55.3
MRSE +/- 1.00 D	136/147	92.5	52/68	76.5	111/117	94.9	40/47	85.1
MRSE +/- 2.00 D	146/147	99.3	63/68	92.6	116/117	99.1	46/47	97.9
Not Reported	5/152	3.3	1/69	1.4	14/131	10.7	6/53	11.3
Total	152	100	69	100	131	100	53	100
Overcorrected >+ 1 D	3/147	2.0	2/68	2.9	1/117	0.9	1/47	2.1
Overcorrected >+ 2 D	0/147	0.0	0/68	0.0	0/117	0.0	0/47	0.0
Undercorrected < - 1 D	8/147	5.4	14/68	20.6	5/117	4.3	6/47	12.8
Undercorrected < - 2 D	1/147	0.7	5/68	7.4	1/117	0.9	1/47	2.1
Not Reported	5/152	3.3	1/69	1.4	14/131	10.7	6/53	11.3
Total	152	100	69	100	131	100	53	100

Table 3-9 — Myopia (LASIK): Accuracy of Manifest Refraction (Attempted vs. Achieved, Spherocylinders)

Spherocylinders	3 M				6 M			
	≤ -7 D		> 7 D		≤ -7 D		>7 D	
	n/N	%	n/N	%	n/N	%	n/N	%
MRSE +/- 0.50 D	363/503	72.2	131/251	52.2	365/468	78.0	131/212	61.8
MRSE +/- 1.00 D	469/503	93.2	188/251	74.9	441/468	94.2	173/212	81.6
MRSE +/- 2.00 D	502/503	99.8	236/251	94.0	468/468	100	205/212	96.7
Not Reported	23/526	4.4	2/253	0.8	51/519	9.8	8/220	3.6
Total	526	100	253	100	519	100	220	100
Overcorrected >+ 1 D	9/503	1.8	11/251	4.4	7/468	1.5	14/212	6.6
Overcorrected >+ 2 D	0/503	0.0	0/251	0.0	0/468	0.0	3/212	1.4
Undercorrected < - 1 D	25/503	5.0	52/251	20.7	20/468	4.3	25/212	11.8
Undercorrected < - 2 D	1/503	0.2	15/251	6.0	0/468	0.0	4/212	1.9
Not Reported	23/526	4.4	2/253	0.8	51/519	9.8	8/220	3.6
Total	526	100	253	100	519	100	220	100

4) Astigmatic Correction

Table 3-10 shows that 95.9% (462/482) of the eyes with pre-operative cylinder less than -3.0 D had -1.0 D or less of cylinder at 3 months. For the eyes with greater than -3.0 D of cylinder pre-operatively, 88.9% (8/9) had -1.0 D or less of cylinder at 3 months. 96.5% (357/370) of the eyes with pre-operative cylinder less than -3.0 D had -1.0 D or less of cylinder at 6 months. For eyes with greater than -3.0 D of cylinder present pre-operatively, 100% (3/3) had -1.0 D of cylinder at 6 months.

Table 3-10 — Myopia (LASIK): Cylinder Efficacy

Cylinder Range	± 1.00 D at 3 M	± 1.00 D at 6 M
0 to -3 D	95.9%	96.5%
> 3 D	88.9%	100%

5) Vector Analysis

Table 3-11 is a summary of the vector analysis results for all eyes undergoing cylinder correction. The ratio of surgically induced refractive vector change (SIRC) to intended refractive vector change (IRC) indicates the ratio of the vector cylinder change induced compared with the targeted amount. A ratio of 1.0 would indicate that the surgical correction exactly matched the targeted correction. Smaller ratios indicate that the cylinder correction was less than planned, and ratios > 1.0 indicate a cylinder overcorrection. At 6 months, the mean ratio of SIRC/IRC was 1.03 ± 0.32 D. The minimum was 0.00 and the maximum was 2.81 D.

Table 3-11 — Myopia (LASIK): Vector Analysis for All Eyes Undergoing Cylinder Correction; Results Reported at 6 Months (n = 510)

	6 M Results (n = 510)				
	Pre-operative	Post-operative	IRC	SIRC	SIRC/IRC
Mean	-1.54	-0.33	-1.47	-1.48	1.03
SD	0.77	0.43	0.71	0.75	0.32
Min	-4.75	-3.00	-4.50	-4.48	0.00
Max	-0.75	0.00	-0.56	0.00	2.81

6) Stability of Outcome

As shown in Table 3-12, using eyes seen at all follow-up exams (1, 3, and 6 months) shows that between 1 and 3 months, 93.6% (424/453) of all eyes experienced a change in MRSE of ≤ 1.00 D. In the ≤ -7 D group, the rate was 95.1% (294/309), and in the > -7 D group, the rate was 90.3% (130/144). For spheres ≤ -7 D, the rate was 95.8% (69/72), and for spherocylinders, the rate was 94.9% (225/237). For spheres > -7 D, the rate was 79.3% (23/29), and for spherocylinders, 93.0% (107/115). Table 3-13 shows that between 3 and 6 months, for spheres in the ≤ -7 D group, the rate was 97.2% (70/72), and for spherocylinders, 95.8% (227/237). For spheres >-7 D, the rate was 93.1% (27/29), and for spherocylinders, 88.7% (102/115).

Table 3-12 — Myopia (LASIK): Stability of Manifest Refraction with +/- 1.00 D (1 to 3 M)

	From 1 to 3 M					
	All Eyes		≤ -7 D		> -7 D	
	n/N	%	n/N	%	n/N	%
Full Cohort						
MRSE Change ≤ 1.00 D	424/453	93.6	294/309	95.1	130/144	90.3
Mean Difference	-0.05 D		-0.09 D		0.03 D	
SD	0.55 D		0.50 D		0.65 D	
95% CI	91.3 to 95.9		92.7 to 97.5		85.4 to 95.1	
Spheres						
MRSE Change ≤ 1.00 D	92/101	91.1	69/72	95.8	23/29	79.3
Mean Difference	-0.02 D		-0.11 D		0.20 D	
SD	0.71 D		0.58 D		0.94 D	
95% CI	85.5 to 96.6		91.2 to 100.4		64.6 to 94.1	
Spherocylinders						
MRSE Change ≤ 1.00 D	332/352	94.3	225/237	94.9	107/115	93.0
Mean Difference	-0.06 D		-0.08 D		-0.02 D	
SD	0.50 D		0.47 D		0.56 D	
95% CI	91.9 to 96.7		92.1 to 97.7		88.4 to 97.7	

Table 3-13 — Myopia (LASIK): Stability of Manifest Refraction with +/- 1.00 D (3 to 6 M)

	From 3 to 6 M					
	All Eyes		≤ -7 D		> -7 D	
	n/N	%	n/N	%	n/N	%
Full Cohort						
MRSE Change ≤ 1.00 D	426/453	94.0	297/309	96.1	129/144	89.6
Mean Difference	-0.05 D		-0.04 D		-0.05 D	
SD	0.51 D		0.43 D		0.64 D	
95% CI	91.9 to 96.2		94.0 to 98.3		84.6 to 94.6	
Spheres						
MRSE Change ≤ 1.00 D	97/101	96.0	70/72	97.2	27/29	93.1
Mean Difference	-0.08 D		-0.09 D		-0.06 D	
SD	0.44 D		0.39 D		0.55 D	
95% CI	92.2 to 99.8		93.4 to 101.0		83.9 to 102.3	
Spherocylinders						
MRSE Change ≤ 1.00 D	329/352	93.5	227/237	95.8	102/115	88.7
Mean Difference	-0.04 D		-0.03 D		-0.05 D	
SD	0.53 D		0.45 D		0.67 D	
95% CI	90.9 to 96.0		93.2 to 98.3		82.9 to 94.5	

7) Retreatments

One hundred and three eyes were retreated (103/1276 or 8.1%) for undercorrections.

8) Adverse Events and Complications

Refer to Table 2-1 in Section 2.5.1.

3.1.2 Hyperopia with or without Astigmatism

A prospective, non-randomized, unmasked, multicenter clinical study was conducted. The refractive inclusion criteria specified that the patient have hyperopia from +0.5 to +6.0 diopters (D) with or without astigmatism ≤+6.0 D. One hundred and sixty-nine (169) eyes comprised the cohort of eyes used for safety evaluations. Of these 169 eyes, 12 eyes were excluded from effectiveness analyses due to a spherical treatment magnitude of > 5 D and one eye was excluded due to failure to establish pre-operative refractive stability. Effectiveness evaluations were done on 156 eyes from the 169-eye cohort. Patients who exhibited any of the following conditions were excluded: anterior segment pathology; residual, recurrent, or active ocular disease; previous intraocular or corneal surgery in the operative eye; history of herpes keratitis; or autoimmune disease, systemic connective tissue diseases, or atopic syndrome.

A. About the Study

Treated eyes were followed for at least 3 months. Analyses of results were performed at 1, 3, and 6 months post-treatment. Effectiveness analyses included uncorrected visual acuity, accuracy of manifest refraction, stability, and vector analysis. Safety analyses included loss of 2 or more lines of best spectacle-corrected visual acuity (BSCVA), BSCVA of 20/40 or worse, haze with loss of BSCVA, intraocular pressure, adverse events, and complications. The post-operative spectacle/contact lens wear frequency was not assessed.

B. Patient Accountability

One hundred and sixty-nine (169) eyes of 89 subjects treated at six centers in the United States were evaluated for safety. One hundred and fifty-six (156) eyes were evaluated for effectiveness. More than 93% of the 169 eyes were available for analysis at 1, 3, and 6 months visits. Table 3-14 presents the accountability for all eyes treated in the study.

Table 3-14 — Hyperopia with or without Astigmatism (LASIK): Patient Accountability (n = 169)

1 M		3 M		6 M	
%	n/N	%	n/N	%	n/N
100	169/169	96.4	163/169	98.8	158/160

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C. Data Analysis and Results

1) Pre-Operative Characteristics

The mean age of the 89 patients participating in this trial was 50.6 ± 10.7 years. There were 45 women and 44 men. Table 3-15 presents refractive treatment stratified by sphere and cylinder.

Table 3-15 — Hyperopia with or without Astigmatism (LASIK): Refractive Treatment Stratified by Sphere and Cylinder (n = 169)

Sphere	Cylinder															
	0 D		>0 to ≤1 D		>1 to ≤2 D		>2 to ≤ 3 D		>3 to ≤4 D		>4 to ≤5 D		>5 to ≤6 D		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
>0 to ≤1 D	0	0.0	4	5.7	5	11.6	5	21.7	4	36.4	0	0.0	1	25.0	19	11.2
>1 to ≤2 D	5	33.3	25	35.7	6	14.0	4	17.4	1	9.1	0	0.0	3	75.0	44	26.0
>2 to ≤3 D	4	26.7	10	14.3	5	11.6	3	13.0	0	0.0	2	66.7	0	0.0	24	14.2
>3 to ≤4 D	5	33.3	16	22.9	11	25.6	2	8.7	4	36.4	1	33.3	0	0.0	39	23.1
>4 to ≤5 D	1	6.7	10	14.3	12	27.9	7	30.4	1	9.1	0	0.0	0	0.0	31	18.3
>5 to ≤6 D	0	0.0	5	7.1	4	9.3	2	8.7	1	9.1	0	0.0	0	0.0	12	7.1
Total	15	8.9	70	41.4	43	25.4	23	13.6	11	6.5	3	1.8	4	2.4	169	100

2) Uncorrected Visual Acuity (UCVA)

Pre-operatively 9.2% (13/141) of eyes targeted for emmetropia had an uncorrected visual acuity (UCVA) of 20/40 or better; at the 3 and 6-month visits, 97.0% (131/135 and 129/133) of these eyes had UCVA of 20/40 or better. Table 3-16 presents the UCVA of eyes targeted for emmetropia over time.

Table 3-16 — Hyperopia with or without Astigmatism (LASIK): UCVA Over Time (All Eyes Targeted for Emmetropia, n = 141)

	Pre-Op (n = 141)	1 M (n = 141)	3 M (n = 135)	6 M (n = 133)
	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
20/20 or better	0 0.0 (0.0, 8.3)	61 43.3 (35.1, 51.4)	62 45.9 (37.5, 54.3)	64 48.1 (39.6, 56.6)
20/25 or better	1 0.7 (0.0, 2.1)	93 66.0 (58.1, 73.8)	95 70.4 (62.7, 78.1)	89 66.9 (58.9, 74.9)
20/32 or better	6 4.3 (0.9, 7.6)	116 82.3 (76.0, 88.6)	119 88.1 (82.7, 93.6)	116 87.2 (81.5, 92.9)
20/40 or better	13 9.2 (4.4, 14.0)	128 90.8 (86.0, 95.6)	131 97.0 (94.2, 99.9)	129 97.0 (94.1, 99.9)
20/80 or better	68 48.2 (40.0, 56.5)	141 100 (91.7, 100)	135 100 (91.6, 100)	133 100 (91.5, 100)
20/200 or better	128 90.8 (86.0, 95.6)	141 100 (91.7, 100)	135 100 (91.6, 100)	133 100 (91.5, 100)
Worse than 20/200	13 9.2 (4.4, 14.0)	0 0.0 (0.0, 8.3)	0 0.0 (0.0, 8.4)	0 0.0 (0.0, 8.5)
Not Reported	0	0	0	0
Total	141 100	141 100	135 100	133 100

Analysis of UCVA as a measure of effectiveness is most meaningful for eyes with the ability to achieve BSCVA of at least 20/20 pre-operatively. These eyes have the capacity to achieve UCVA of 20/20 post-operatively. Of the eyes targeted for emmetropia, 115/141 met this criteria. At 3 months 99.1% (112/113) and at 6 months 100% (108/108) of these eyes had UCVA of 20/40 or better.

While pre-operatively, no eye had UCVA of 20/20 or better; at 3 months 54.0% (61/113) of eyes had UCVA of 20/20 or better and this increased to 56.5% at 6 months. Table 3-17 presents the distance UCVA of eyes targeted for emmetropia over time with a pre-operative BSCVA of 20/20 or better.

Table 3-17 — Hyperopia with or without Astigmatism (LASIK): UCVA Over Time (Eyes Targeted for Emmetropia, with a Pre-Op BSCVA of 20/20 or Better, n = 115)

	Pre-Op (n = 115)	1 M (n = 115)	3 M (n = 113)	6 M (n = 108)
	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
20/20 or better	0 0.0 (0.0, 9.1)	58 50.4 (41.3, 59.6)	61 54.0 (44.8, 63.2)	61 56.5 (47.1, 65.8)
20/25 or better	1 0.9 (0.0, 2.6)	87 75.7 (67.8, 83.5)	87 77.0 (69.2, 84.8)	81 75.0 (66.8, 83.2)
20/32 or better	5 4.3 (0.6, 8.1)	103 89.6 (84.0, 95.2)	104 92.0 (87.0, 97.0)	101 93.5 (88.9, 98.2)
20/40 or better	12 10.4 (4.8, 16.0)	108 93.9 (89.5, 98.3)	112 99.1 (97.4, 100)	108 100 (90.6, 100)
20/80 or better	62 53.9 (44.8, 63.0)	115 100 (90.9, 100)	113 100 (90.8, 100)	108 100 (90.6, 100)
20/200 or better	106 92.2 (87.3, 97.1)	115 100 (90.9, 100)	113 100 (90.8, 100)	108 100 (90.6, 100)
Worse than 20/200	9 7.8 (2.9, 12.7)	0 0.0 (0.0, 9.1)	0 0.0 (0.0, 9.2)	0 0.0 (0.0, 9.4)
Not Reported	0	0	0	0
Total	115 100	115 100	113 100	108 100

3) Best Spectacle-Corrected Visual Acuity (BSCVA)

Loss of BSCVA can be anticipated due to a surgical or healing effect and the optical effect of minification (approximately 7.0 D of corneal correction accounts for a 1 line loss of resolving power). At both the 3 and 6-month visits, 6 eyes (less than 4%) lost 2 lines of BSCVA, but no eye lost more than 2 lines of BSCVA. Table 3-18 presents the change in lines of BSCVA.

Table 3-18 — Hyperopia with or without Astigmatism (LASIK): Change in BSCVA Over Time (All Eyes, n = 169)

	1 M (n = 169)	3 M (n = 163)	6 M (n = 156)
	n % (95% CI)	n % (95% CI)	n % (95% CI)
Decrease > 2 Lines	2 1.2 (0.0, 2.8)	0 0.0 (0.0, 7.7)	0 0.0 (0.0, 7.8)
Decrease > 1 to ≤ 2 Lines*	20 11.8 (7.0, 16.7)	12 7.4 (3.4, 11.4)	14 9.0 (4.5, 13.5)
Decrease > 0 to ≤ 1 Line	67 39.6 (32.3, 47.0)	69 42.3 (34.7, 49.9)	56 35.9 (28.4, 43.4)
No Change	58 34.3 (27.2, 41.5)	54 33.1 (25.9, 40.4)	53 34.0 (26.5, 41.4)
Increase >0 to ≤1 Line	19 11.2 (6.5, 16.0)	27 16.6 (10.9, 22.3)	33 21.2 (14.7, 27.6)
Increase > 1 to ≤ 2 Lines	3 1.8 (0.0, 3.8)	1 0.6 (0.0, 1.8)	0 0.0 (0.0, 7.8)
Increase > 2 Lines	0 0.0 (0.0, 7.5)	0 0.0 (0.0, 7.7)	0 0.0 (0.0, 7.8)
Not Reported	0	0	2
Total	169 100	163 100	156 100

*Loss of 2 lines of BSCVA: 1 M = 6 (3.6%), 3 M = 6 (3.7%), and 6 M = 6 (3.8%).

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4) Accuracy of Outcome

Accuracy of outcome was evaluated by analysis of attempted versus achieved manifest refractive cylinder and sphere. At 3 months post-operatively, 74% (111/150) of eyes were within 0.50 D and 93% (140/150) were within 1.00 D of attempted sphere correction, and 65% (97/150) of eyes were within 0.50 D and 90% (135/150) were within 1.00 D of attempted cylinder correction. These results were maintained through 6 months. Table 3-19 presents the accuracy of sphere and cylinder over time.

Table 3-19 — Hyperopia with or without Astigmatism (LASIK): Accuracy of Sphere (to Target) and Cylinder (to Zero) Component (n = 156)

	1 M (n = 156)	3 M (n = 150)	6 M (n = 144)
	n % (95% CI)	n % (95% CI)	n % (95% CI)
Sphere			
± 0.50 D	113 72.4 (65.4, 79.4)	111 74.0 (67.0, 81.0)	109 75.7 (68.7, 82.7)
± 1.00 D	144 92.3 (88.1, 96.5)	140 93.3 (89.3, 97.3)	137 95.1 (91.6, 98.7)
Cylinder			
± 0.50 D	102 65.4 (57.9, 72.9)	97 64.7 (57.0, 72.3)	102 70.8 (63.4, 78.3)
± 1.00 D	144 92.3 (88.1, 96.5)	135 90.0 (85.2, 94.8)	133 92.4 (88.0, 96.7)

LASIK treatment of cylinder >3 D may result in a greater incidence of significant residual astigmatism (>1 D) and axis shift.

5) Accuracy of MRSE Over Time

At 3 months post-operatively, 70.7% (106/150) of eyes were within 0.50 D and 94.7% (142/150) were within 1 D of attempted MRSE. At 6 months, 76.4% (110/144) and 91% (131/144) were within 0.50 D and 1.0 D, respectively. Over the course of the follow-up period, no eye was overcorrected by more than 2 D and approximately 1% of eyes were undercorrected by more than 2 D. Table 3-20 presents the accuracy of MRSE over time.

Table 3-20 — Hyperopia with or without Astigmatism (LASIK): Accuracy of MRSE: Attempted versus Achieved (All Eyes, n = 156)

MRSE	Pre-Op (n = 156)	1 M (n = 156)	3 M (n = 150)	6 M (n = 144)
	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
± 0.50 D	0 0.0 (0.0, 7.8)	113 72.4 (65.4, 79.4)	106 70.7 (63.4, 78.0)	110 76.4 (69.5, 83.3)
± 1.00 D	2 1.3 (0.0, 3.0)	144 92.3 (88.1, 96.5)	142 94.7 (91.1, 98.3)	131 91.0 (86.3, 95.7)
± 2.00 D	34 21.8 (15.3, 28.3)	156 100 (92.2, 100)	148 98.7 (96.8, 100)	143 99.3 (97.9, 100)
Not Reported	0	0	0	2
Overcorrected	**(Myopic)**			
< -1.00 D		2 1.3 (0.0, 3.0)	1 0.7 (0.0, 2.0)	1 0.7 (0.0, 2.1)
< -2.00 D		0 0.0 (0.0, 7.8)	0 0.0 (0.0, 8.0)	0 0.0 (0.0, 8.2)
Undercorrected	**(Hyperopic)**			
> +1.00 D		10 6.4 (2.6, 10.3)	7 4.7 (1.3, 8.0)	12 8.3 (3.8, 12.8)
> +2.00 D		0 0.0 (0.0, 7.8)	2 1.3 (0.0, 3.2)	1 0.7 (0.0, 2.1)

6) Stability of Outcome

Stability of outcome is evaluated by the cohort of eyes with a refraction at each visit. The number of available eyes in the effectiveness cohort with every visit is the limiting factor of stability analysis. This cohort contains 140 eyes.

Between the 1 and 3-month visits, 97.9% (137/140) of eyes experienced a change of 1 D or less. Between the 3 and 6-month visits, 95.7% (134/140) of eyes experienced a change of 1 D or less. Refractive stability is reached at 3 months and confirmed at the 6-month visit. The difference in the percentage of eyes with a change of ≤1 D between 1-and 3-months and 3-and 6-months is not statistically significantly different from zero. Table 3-21 presents refractive stability over time.

Table 3-21 — Hyperopia with or without Astigmatism (LASIK): Refractive Stability (Eyes with 1, 3, and 6-month visits, n = 140)

Change in MRSE	1 and 3 M	3 and 6 M
	n % (95% CI)	n % (95% CI)
≤ 1.00 D	137 97.9	134 95.7
95% CI for %	(95.5, 100)	(92.4, 99.1)
MRSE (D)		
Mean	0.07	0.06
SD	0.46	0.45
95% CI for Mean	(0.14, -0.01)	(0.14, -0.01)

7) MRSE

At the 1-month visit, the mean refractive spherical equivalent is 0.08 D. From the point of defined stability (3 months) to the next visit (6 months) the mean MRSE changed 0.09 D, or 0.03 D per month. There is no statistically significant difference between the mean presented at 3 and 6 months. Table 3-22 presents the mean MRSE over time.

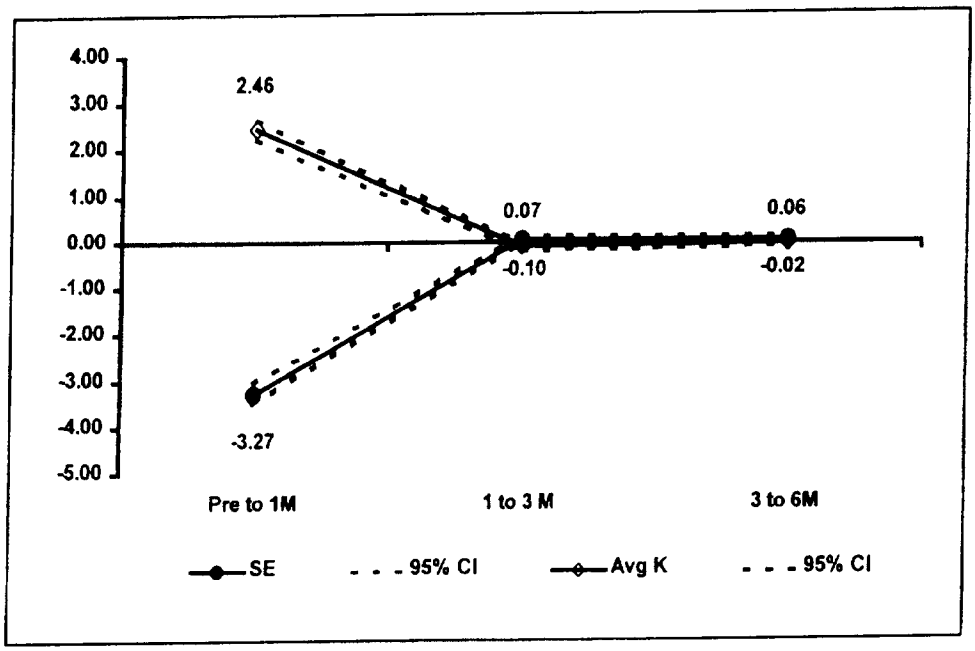
Table 3-22 — Hyperopia with or without Astigmatism (LASIK): Mean MRSE Over Time (Eyes Targeted for Emmetropia, n = 141)

	1 M (n = 141)	3 M (n = 135)	6 M (n = 131)
MRSE (D)			
Mean	0.08	0.12	0.21
SD	0.55	0.51	0.52
95% CI	0.17 to -0.01	0.21 to 0.04	0.30 to 0.12

8) Keratometry

From the point of defined stability (3 months) to the next visit (6 months), the mean keratometry changed 0.01 D. When plotted over time, the mean of the differences in manifest refraction spherical equivalent (MRSE) and average keratometry (Avg K) illustrates that stability is achieved by the 3-month visit. This trend is further supported by almost no change between the 3 and 6-month visits. Figure 3-Figure 3-1 presents the mean of the differences in MRSE and Avg K.

Figure 3-1: Mean of the Differences in MRSE and Avg K (Eyes with Visits at 1, 3, and 6 Months, n = 140)



9) Refractive Cylinder

Stability of refractive cylinder is achieved at 3 months post-operatively and confirmed at 6 months. There is no statistically significant difference between the data before 1-and 3-months and the data at 3-and 6-months. Table 3-23 presents stability of refractive cylinder.

Table 3-23 — Hyperopia with or without Astigmatism (LASIK): Stability of Refractive Cylinder (Eyes with 1, 3 and 6-month visits, n = 140)

Change in Cylinder	1 and 3 M	3 and 6 M
	n % (95% CI)	n % (95% CI)
≤ 1.00 D	136 97.1	136 97.1
95% CI for %	(94.4, 99.9)	(94.4, 99.9)
Cyl (D)		
Mean	0.03	-0.01
SD	0.46	0.43
95% CI for Mean	(-0.05, 0.10)	(-0.08, 0.06)

10) Vector Analysis

The vector magnitude ratio (SIRC/IRC) is an indicator of procedure effectiveness. Vector analysis was performed on the 136 eyes that had their 3-month visit (point of stability) and had an astigmatic procedure (no spherical treatments were included). At 3 months, the spherical SIRC/IRC is 98% and the cylindrical SIRC/IRC is 110% indicating a greater incidence of overcorrection among eyes with lower amounts of astigmatism (<1 D).

Table 3-24 — Hyperopia with or without Astigmatism (LASIK): Vector Magnitude (n = 136)

	Sphere					Cylinder				
	Pre	Post	IRC	SIRC	SIRC/IRC*	Pre	Post	IRC	SIRC	SIRC/IRC
Mean	2.5	-0.2	4.4	4.3	0.98	1.5	0.5	-1.7	-1.8	1.1
Median	2.3	0.0	4.0	4.0	1.00	1.3	0.5	-1.3	-1.5	1.2
SD	1.2	0.7	1.8	1.8		1.2	0.5	1.3	1.3	
Min	0.0	-2.8	1.3	1.2		0.3	0.0	-6.8	-7.2	
Max	4.8	1.3	8.6	8.5		6.0	2.3	0.0	-0.1	

* SIRC = Surgically Induced Refractive Change. IRC = Intended Refractive Change.

11) Retreatments

Procedures performed to improve refractive outcome:

Four eyes underwent LASIK retreatments (4/169 or 2.4%) during the study, mostly due to initial overcorrection. Post-operatively, 2 of these eyes had significant residual refractive error and the other 2 had no residual refractive error (plano). The small number of retreatments is insufficient to yield clinically useful information, however caution should be taken to assure refractive stability before performing additional procedures.

12) Patient Symptoms

Patient questionnaires reflected the following patient symptoms after treatment.

Table 3-25 — Hyperopia with or without Astigmatism (LASIK): Patient Symptoms: Comparison of Vision after Surgery (All Eyes with a Treatment Sphere ≤5.00 D, N = 156)*

	3 M (N = 147)							6 M (N = 144)						
	Improve (+ ≥ 2)		No Change (0 ± 1)		Worsen (− ≥ 2)		NR	Improve (+ ≥ 2)		No Change (0 ± 1)		Worsen (− ≥ 2)		NR
	n	%	n	%	n	%	n	n	%	n	%	n	%	n
Sharpness and Clarity	24	16.3	116	78.9	7	4.8	0	22	15.3	112	77.8	10	6.9	0
Consistency of Vision	19	12.9	122	83.0	6	4.1	0	19	13.2	115	79.9	10	6.9	0
Sustained Close Work	21	14.3	121	82.3	5	3.4	0	22	15.3	118	81.9	4	2.8	0
Daylight Driving	18	12.2	123	83.7	6	4.1	0	18	12.5	120	83.3	6	4.2	0
Night Driving	18	12.2	123	83.7	6	4.1	0	23	16.0	114	79.2	7	4.9	0
Night Vision with Glare	22	15.0	117	79.6	8	5.4	0	26	18.1	112	77.8	6	4.2	0
Reading in Dim Light	14	9.5	123	83.7	10	6.8	0	15	10.5	119	83.2	9	6.3	1
General Vision in Dim Light	19	12.9	118	80.3	10	6.8	0	19	13.2	116	80.6	9	6.3	0
Overall Visual Comfort	23	15.6	116	78.9	8	5.4	0	24	16.8	116	81.1	3	2.1	1

* This table reflects responses to a patient questionnaire on a scale of 1 (poor) to 5 (excellent). Responses at 3 and 6 months were compared to pre-operative responses. The results presented reflect changes in uncorrected vision compared to baseline.

In this study, at the point of stability, patients were asked a series of questions about their vision, including clarity, consistency, sustained close work, driving in day and night lighting, reading and vision in dim light, and visual comfort. For subjects with a pre-operative MRSE > 2.00 D, an average of 3.7% responded that they preferred their vision prior to the LASIK treatment (range 0 – 7.1%). This average was higher (11.5%) among subjects with a pre-operative MRSE < 2.00 D (range 0 – 21.2%). VISX® recommends that all patients be counseled carefully to establish realistic expectations before they proceed with the surgical correction of refractive error.

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13) Adverse Events and Complications

Refer to Tables 2-2, 2-3, and 2-4 in Section 2.5.1.

14) Summary of Key Safety and Effectiveness Variables

They key safety and effectiveness variables for all eyes are presented in Table 3-26. The key safety and effectiveness variables stratified by treatment MRSE are presented in Table 3-27.

Table 3-26 — Hyperopia with or without Astigmatism (LASIK): Summary of Key Safety and Effectiveness Variables (All Eyes, n = 169)

Criteria	1 M n % (95% CI)	3 M n % (95% CI)	6 M n % (95% CI)
Effectiveness Variables			
n =115*, †	n = 115	n = 113	n = 108
UCVA 20/20 or better	58 50.4 (41.3, 59.6)	61 54.0 (44.8, 63.2)	61 56.5 (47.1, 65.8)
UCVA 20/40 or better	108 93.9 (89.5, 98.3)	112 99.1 (97.4, 100)	108 100 (90.6, 100)
n = 141 *, ‡	n = 141	n = 135	n = 133
UCVA 20/20 or better	61 43.3 (35.1, 51.4)	62 45.9 (37.5, 54.3)	64 48.1 (39.6, 56.6)
UCVA 20/40 or better	128 90.8 (86.0, 95.6)	131 97.0 (94.2, 99.9)	129 97.0 (94.1, 99.9)
n = 156	n = 156	n = 150	n = 144
MRSE ± 0.50 D	113 72.4 (65.4, 79.4)	106 70.7 (63.4, 78.0)	110 76.4 (69.5, 83.3)
MRSE ± 1.00 D	144 92.3 (88.1, 96.5)	142 94.7 (91.1, 98.3)	131 91.0 (86.3, 95.7)
MRSE ± 2.00 D	156 100 (92.2, 100)	148 98.7 (96.8, 100)	143 99.3 (97.9, 100)
Stability			
n = 140**		n = 140	n = 140
Change ≤ 1.00 D		137 97.9 (95.5,100)	134 95.7 (92.4, 99.1)
Mean Change in MRSE		0.07 ± 0.46 (0.14, -0.01)	0.06 ± 0.45 (0.14, -0.01)
Safety Variables			
n = 169	n = 169	n = 163	n = 156
Loss of ≥ 2 lines BSCVA	8 4.7 (1.5, 7.9)	6 3.7 (0.8, 6.6)	6 3.8 (0.8, 6.8)
Loss of > 2 lines BSCVA	2 1.2 (0.0, 2.8)	0 0.0 (0.0, 7.7)	0 0.0 (0.0, 7.8)
BSCVA worse than 20/40	3 1.8 (0.0, 3.8)	2 1.2 (0.0, 2.9)	1 0.6 (0.0, 1.9)
Increase > 2 D cylinder	0 0.0 (0.0, 7.5)	0 0.0 (0.0, 7.7)	0 0.0 (0.0, 7.8)
n = 134†	n = 134	n = 132	n = 124
BSCVA worse than 20/40	0 0.0 (0.0, 8.5)	0 0.0 (0.0, 8.5)	0 0.0 (0.0, 8.8)

* Excluding eyes intentionally overcorrected for monovision.

† BSCVA 20/20 or better pre-operatively.

‡ Includes eyes with a pre-operative BSCVA worse than 20/20.

** Includes only eyes with all visits.

Table 3-27 — Hyperopia with or without Astigmatism (LASIK): Summary of Key Safety and Effectiveness Variables at Stability Endpoint at 3 Months (Stratified by Treatment MRSE)

Criteria	Up to 2.00 n/N, % (% CI)	>2 to 3.00 n/N, % (% CI)	>3 to 4.00 n/N, % (% CI)	>4 to 5.00 n/N, % (% CI)	>5 to 6.00 n/N, % (% CI)	>6 to 7.00 n/N, % (% CI)	>7 to 8.00 n/N, % (% CI)	Cum Total n/N, % (% CI)
Effectiveness Variables								
n = 113*,†	**n = 29**	**n = 31**	**n = 21**	**n = 15**	**n = 17**	**n = 0**		**n = 113**
UCVA 20/20 or better	18 62.1 (44.4, 79.7)	20 64.5 (47.7, 83.4)	11 52.4 (31.0, 73.7)	8 53.3 (28.1, 78.6)	4 23.5 (3.4, 43.7)	n/a		61 54.0 (44.8, 63.2)
UCVA 20/40 or better	29 100 (81.8, 100)	31 100 (82.4, 100)	20 95.2 (86.1, 100)	15 100 (74.7, 100)	17 100 (76.2, 100)	n/a		112 99.1 (97.4, 100)
n = 135*,‡	**n = 29**	**n = 38**	**n = 26**	**n = 17**	**n = 24**	**n = 1**		**n = 135**
UCVA 20/20 or better	18 62.1 (44.4, 79.7)	21 55.3 (39.5, 71.1)	11 42.3 (23.3, 61.3)	8 47.1 (23.3, 70.8)	4 16.7 (1.8, 31.6)	0 0.0 (0.0, 98.0)		62 45.9 (37.5, 54.3)
UCVA 20/40 or better	29 100 (81.8, 100)	38 100 (84.1, 100)	23 88.5 (76.2, 100)	17 100 (76.2, 100)	23 95.8 (87.8, 100)	1 100 (2.0, 100)		131 97.0 (94.2, 99.9)
n = 150	**n = 30**	**n = 39**	**n = 34**	**n = 20**	**n = 26**	**n = 1**		**n = 150**
MRSE ± 0.50 D	23 76.7 (61.5, 91.8)	31 79.5 (66.8, 92.2)	22 64.7 (48.6, 80.8)	13 65.0 (44.1, 85.9)	16 61.5 (42.8, 80.2)	1 100 (2.0, 100)		106 70.7 (63.4, 78.0)
MRSE ± 1.00 D	29 96.7 (90.2, 100)	38 97.4 (92.5, 100)	31 91.2 (81.6, 100)	18 90.0 (76.9, 100)	25 96.2 (88.8, 100)	1 100 (2.0, 100)		142 94.7 (91.1, 98.3)
MRSE ± 2.00 D	30 100 (82.1, 100)	39 100 (84.3, 100)	32 94.1 (86.2, 100)	20 100 (78.1, 100)	26 100 (80.8, 100)	1 100 (2.0, 100)		148 98.7 (96.8, 100)
n = 140	**n = 26**	**n = 36**	**n = 32**	**n = 19**	**n = 26**	**n = 1**		**n = 140**
Stability ± 1.00 D	26 100 (80.8, 100)	36 100 (83.7, 100)	31 96.9 (90.8, 100)	17 89.5 (75.7, 100)	26 100 (80.8, 100)	1 100 (2.0, 100)		137 97.9 (95.5, 100)
Mean Change in MRSE	0.01 ± 0.37 (-0.13, 0.15)	0.06 ± 0.32 (-0.04, 0.17)	0.17 ± 0.50 (0.00, 0.34)	-0.01 ± 0.64 (-0.30, 0.28)	0.04 ± 0.51 (-0.15, 0.24)	0.25**		0.07 ± 0.46 (-0.01, 0.14)
Safety Variables								
n = 163	**n = 30**	**n = 39**	**n = 34**	**n = 21**	**n = 29**	**n = 7**	**n = 3**	**n = 163**
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 17.9)	0 0.0 (0.0, 15.7)	0 0.0 (0.0, 16.8)	3 14.3 (0.0, 29.3)	2 6.9 (0.0, 16.1)	0 0.0 (0.0, 37.0)	1 33.3 (0.0, 86.7)	6 3.7 (0.8, 6.6)
Loss of > 2 lines BSCVA	0 0.0 (0.0, 17.9)	0 0.0 (0.0, 15.7)	0 0.0 (0.0, 16.8)	0 0.0 (0.0, 21.4)	0 0.0 (0.0, 18.2)	0 0.0 (0.0, 37.0)	0 0.0 (0.0,56.6)	0 0.0 (0.0, 7.7)
Increase > 2 D cylinder	0 0.0 (0.0, 17.9)	0 0.0 (0.0, 15.7)	0 0.0 (0.0, 16.8)	0 0.0 (0.0, 21.4)	0 0.0 (0.0, 18.2)	0 0.0 (0.0, 37.0)	0 0.0 (0.0, 56.6)	0 0.0 (0.0, 7.7)
n = 132†	**n = 30**	**n = 32**	**n = 28**	**n = 16**	**n = 21**	**n = 3**	**n = 2**	**n = 132**
BSCVA worse than 20/40	0 0.0 (0.0, 17.9)	0 0.0 (0.0, 17.3)	0 0.0 (0.0, 18.5)	0 0.0 (0.0, 24.5)	0 0.0 (0.0, 21.4)	0 0.0 (0.0, 56.6)	0 0.0 (0.0, 69.3)	0 0.0 (0.0, 8.5)

* Excluding eyes intentionally overcorrected for monovision.

† BSCVA 20/20 or better pre-operatively.

‡ Includes eyes with a pre-operative BSCVA worse than 20/20.

** It is not possible to calculate standard deviation and confidence intervals with an "n" of one.

3.1.3 Mixed Astigmatism

A prospective, non-randomized, unmasked, multicenter clinical study was conducted. The refractive inclusion criteria specified that the patient have mixed astigmatism ≤6.0 D (at the spectacle plane) where the magnitude of cylinder was greater than the magnitude of sphere and the cylinder and sphere have opposite signs. One hundred and fifteen (115) eyes comprised the cohort of eyes used for both safety and effectiveness evaluations. Patients who exhibited any of the following conditions were excluded: anterior segment pathology; residual, recurrent, or active ocular disease; previous intraocular or corneal surgery in the operative eye; history of herpes keratitis; or autoimmune disease, systemic connective tissue diseases, or atopic syndrome.

A. About the Study

Treated eyes were followed for at least 3 months. Analyses of results were performed at 1, 3, and 6 months post-treatment. Effectiveness analyses included uncorrected visual acuity, accuracy of manifest refraction, stability, and vector analysis. Safety analyses included loss of 2 or more lines of best spectacle-corrected visual acuity (BSCVA), BSCVA of 20/40 or worse, haze with loss of BSCVA, intraocular pressure, adverse events, and complications. The post-operative spectacle/contact lens wear frequency was not assessed.

B. Patient Accountability

One hundred and fifteen (115) eyes of 66 subjects treated at six centers in the United States were evaluated for safety and effectivness. More than 95% of the 115 eyes were available for analysis at 1, 3, and 6 months visits. Table 3-28 presents the accountability for all eyes treated in the study.

Table 3-28 — Mixed Astigmatism (LASIK): Patient Accountability (n = 115)

1 M		3 M		6 M	
%	n/N	%	n/N	%	n/N
95.7	110/115	100	115/115	97.3	110/113

C. Data Analysis and Results

1) Pre-Operative Characteristics

The mean age of the 66 patients participating in this trial was 41.3 ± 11.3 years. There were 41 women and 74 men. Table 3-29 presents refractive treatment stratified by sphere and cylinder.

Table 3-29 — Mixed Astigmatism (LASIK): Pre-Operative Refractive Error Stratified by Sphere and Cylinder (n = 115)

Sphere	Cylinder													
	0 to ≤1 D		>1 to ≤2 D		>2 to ≤ 3 D		>3 to ≤4 D		>4 to ≤5 D		>5 to ≤6 D		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
0 to ≥-1 D	4	3.5	21	18.3	7	6.1	1	0.9	9	7.8	2	1.7	44	38.3
<-1 to ≥-2 D	0	0.0	6	5.2	25	21.7	3	2.6	5	4.3	2	1.7	41	35.7
<-2 to ≥-3 D	0	0.0	0	0.0	5	4.3	6	5.2	8	7.0	0	0.0	19	16.5
<-3 to ≥-4 D	0	0.0	0	0.0	0	0.0	2	1.7	5	4.3	1	0.9	8	7.0
<-4 to ≥-5 D	0	0.0	0	0.0	0	0.0	0	0.0	1	0.9	2	1.7	3	2.6
Total	4	3.5	27	23.5	37	32.2	12	10.4	28	24.3	7	6.1	115	100

2) Uncorrected Visual Acuity (UCVA)

All eyes were targeted for emmetropia. Pre-operatively 20% (23/115) of eyes had an uncorrected visual acuity (UCVA) of 20/40 or better; at the 3 and 6-month visits, 98% and 99% (113/115 and 109/110) of these eyes had UCVA of 20/40 or better. Table 3-30 presents UCVA over time.

Table 3-30 — Mixed Astigmatism (LASIK): UCVA Over Time, n = 115

	Pre-Op (n = 115)	1 M (n = 110)	3 M (n = 115)	6 M (n = 110)
	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
20/20 or better	0 0.0 (0.0, 2.6)	60 54.5 (44.8, 64.1)	67 58.3 (48.7, 67.4)	68 61.8 (52.1, 70.9)
20/25 or better	5 4.3 (1.4, 9.9)	84 76.4 (67.3, 83.9)	96 83.5 (75.4, 89.7)	92 83.6 (75.4, 90.0)
20/32 or better	15 13.0 (7.5, 20.6)	102 92.7 (86.2, 96.8)	112 97.4 (92.6, 99.5)	106 96.4 (91.0, 99.0)
20/40 or better	23 20.0 (13.1, 28.5)	106 96.4 (91.0, 99.0)	113 98.3 (93.9, 99.8)	109 99.1 (95.0, 100)
20/80 or better	78 67.8 (58.5, 76.2)	109 99.1 (95.0, 100)	115 100 (97.4, 100)	110 100 (97.3, 100)
20/200 or better	115 100 (97.4, 100)	110 100 (97.3, 100)	115 100 (97.4, 100)	110 100 (97.3, 100)
Total	115 100	110 100	115 100	110 100

Analysis of UCVA as a measure of effectiveness is most meaningful for eyes with the ability to achieve BSCVA of at least 20/20 pre-operatively. These eyes have the capacity to achieve UCVA of 20/20 post-operatively. Ninety-four (94) out of 115 eyes met this criteria. At 3 months 99% (93/94) and at 6 months 100% (90/90) of these eyes had UCVA of 20/40 or better.

While pre-operatively, no eye had UCVA of 20/20 or better; at 3 months 69% (65/94) of eyes had UCVA of 20/20 or better and this increased to 70% (63/90) at 6 months. Table 3-31 presents distance UCVA over time of eyes with a pre-operative BSCVA of 20/20 or better.

Table 3-31 — Mixed Astigmatism (LASIK): UCVA Over Time (Eyes with a Pre-Op BSCVA of 20/20 or Better, n = 94)

	Pre-Op (n = 94)	1 M (n = 90)	3 M (n = 94)	6 M (n = 90)
	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
20/20 or better	0 0.0 (0.0, 3.1)	59 65.6 (54.8, 75.3)	65 69.1 (58.8, 78.3)	63 70.0 (59.4, 79.2)
20/25 or better	5 5.3 (1.7, 12.0)	74 82.2 (72.7, 89.5)	84 89.4 (81.3, 94.8)	84 93.3 (86.1, 97.5)
20/32 or better	14 14.9 (8.4, 23.7)	86 95.6 (89.0, 98.8)	93 98.9 (94.2, 100)	89 98.9 (94.0, 100)
20/40 or better	22 23.4 (15.3, 33.3)	89 98.9 (94.0, 100)	93 98.9 (94.2, 100)	90 100 (96.7, 100)
20/80 or better	68 72.3 (62.2, 81.1)	89 98.9 (94.0, 100)	94 100 (96.9, 100)	90 100 (96.7, 100)
20/200 or better	94 100 (96.9, 100)	90 100 (96.7, 100)	94 100 (96.9, 100)	90 100 (96.7, 100)
Not Reported	0	0	0	0
Total	94 100	90 100	94 100	90 100

3) Best Spectacle-Corrected Visual Acuity (BSCVA)

At the 3-month visit, 1 eye (less than 1%) lost 2 lines of BSCVA, but no eye at the 1, 3, or 6-month visits lost more than 2 lines of BSCVA. Table 3-32 presents the change in lines of BSCVA.

Table 3-32 — Mixed Astigmatism (LASIK): Change in BSCVA Over Time (n = 115)

	1 M (n = 110)	3 M (n = 115)	6 M (n = 110)
	n % (95% CI)	n % (95% CI)	n % (95% CI)
Decrease > 2 Lines	0 0.0 (0.0, 2.7)	0 0.0 (0.0, 2.6)	0 0.0 (0.0, 2.7)
Decrease > 1 to ≤ 2 Lines*	2 1.8 (0.2, 6.4)	1 0.9 (0.0, 4.7)	0 0.0 (0.0, 2.7)
Decrease > 0 to ≤ 1 Line	25 22.7 (15.3, 31.7)	17 14.8 (8.9, 22.6)	17 15.5 (9.3, 23.6)
No Change	41 37.3 (28.2, 47.0)	47 40.9 (31.8, 50.4)	47 42.7 (33.3, 52.5)
Increase >0 to ≤1 Line	39 35.5 (26.6, 45.1)	42 36.5 (27.7, 46.0)	39 35.5 (26.6, 45.1)
Increase > 1 to ≤ 2 Lines	3 2.7 (0.6, 7.8)	7 6.1 (2.5, 12.1)	6 5.5 (2.0, 11.5)
Increase > 2 Lines	0 0.0 (0.0, 2.7)	1 0.9 (0.0, 4.7)	1 0.9 (0.0, 5.0)
Not Reported	0	0	2
Total	110 100	115 100	110 100

*Loss of 2 lines of BSCVA: 1 M = 1 (0.9%), and 3 M = 1 (0.9%).

At the 1-month visit, 3 eyes experienced an improvement in BSCVA of more than 1 line. This increased to 7 and 8 eyes at the 3 and 6-month visits, respectively.

4) Accuracy of Manifest Refraction

Table 3-33 — Mixed Astigmatism (LASIK): Manifest Refractive Cylinder and Axis Change from Baseline

	1 M		3 M		6 M	
	n	%	n	%	n	%
Number of Eyes with ≤15° Axis Change from Baseline	55	50.0	67	58.3	64	58.2
Number of Eyes with >15° Axis Change from Baseline	55*	50.0	48†	41.7	46‡	41.8
Available for Analysis	N = 110		N = 115		N = 110	

*Thirty-four (34) of these eyes (61.8%) had a post-op cylinder of 0.50 D or less.

†Twenty-four (24) of these eyes (50.0%) had a post-op cylinder of 0.50 D or less.

‡Twenty (20) of these eyes (43.5%) had a post-op cylinder of 0.50 D or less.

Table 3-34 — Mixed Astigmatism (LASIK): Accuracy of Manifest Refraction in Pre-Op Hyperopic Meridian (For Eyes with ≤15° Axis Change from Baseline

Correction Error	1 M		3 M		6 M	
	n	%	n	%	n	%
0.00 to ± 0.50 D	38	69.1	53	79.1	48	75.0
Undercorrected	(Hyperopic)					
>0.50 to 0.99 D	8	14.5	4	6.0	7	10.9
1.00 to 1.99 D	8	14.5	9	13.4	9	14.1
≥2.00	1	1.8	1	1.5	0	0.0
Overcorrected	(Myopic)					
>0.50 to 0.99 D	0	0.0	0	0.0	0	0.0
1.00 to 1.99 D	0	0.0	0	0.0	0	0.0
≥2.00 D	0	0.0	0	0.0	0	0.0
Total	N = 55		N = 67		N = 64	

Table 3-35 — Mixed Astigmatism (LASIK): Accuracy of Manifest Refraction in Pre-Op Myopic Meridian (For Eyes with ≤15° Axis Change from Baseline)

Correction Error	1 M		3 M		6 M	
	n	%	n	%	n	%
0.00 to ± 0.50 D	49	89.1	59	88.1	61	95.3
Undercorrected	(Myopic)					
>0.50 to 0.99 D	2	3.6	2	3.0	0	0.0
1.00 to 1.99 D	1	1.8	3	4.5	2	3.1
≥2.00 D	0	0.0	0	0.0	0	0.0
Overcorrected	(Hyperopic)					
>0.50 to 0.99 D	2	3.6	1	1.5	0	0.0
1.00 to 1.99 D	1	1.8	2	3.0	1	1.6
≥2.00 D	0	0.0	0	0.0	0	0.0
Total	N = 55		N = 67		N = 64	

5) Accuracy of MRSE Over Time

At 3 months post-operatively, 79% (91/115) of eyes were within 0.50 D and 97% (112/115) were within 1 D of attempted MRSE. At 6 months, 77% (85/110) and 96% (105/110) were within 0.50 D and 1 D, respectively. At the 3 and 6-month visits, no eye was overcorrected by more than 1 D and no eye was undercorrected by more than 2 D. Table 3-36 presents the accuracy of MRSE over time.

Table 3-36 — Mixed Astigmatism (LASIK): Accuracy of MRSE: Attempted versus Achieved (n = 115)

MRSE	Pre-Op (n = 115)	1 M (n = 110)	3 M (n = 115)	6 M (n = 110)
	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
± 0.50 D	61 53.0 (43.5, 62.4)	84 76.4 (67.3, 83.9)	91 79.1 (70.6, 86.1)	85 77.3 (68.3, 84.7)
± 1.00 D	87 75.7 (66.8, 83.2)	107 97.3 (92.2, 99.4)	112 97.4 (92.6, 99.5)	105 95.5 (89.7, 98.5)
± 2.00 D	113 98.3 (93.9, 99.8)	109 99.1 (95.0, 100)	115 100 (97.4, 100)	110 100 (97.3, 100)
Not Reported	0	0	0	2
Overcorrected	**(Myopic)**			
< -1.00 D		0 0.0 (0.0, 2.7)	0 0.0 (0.0, 2.6)	0 0.0 (0.0, 2.7)
< -2.00 D		0 0.0 (0.0, 2.7)	0 0.0 (0.0, 2.6)	0 0.0 (0.0,2.7)
Undercorrected	**(Hyperopic)**			
> +1.00 D		3 2.7 (0.6, 7.8)	3 2.6 (0.5, 7.4)	5 4.5 (1.5, 10.3)
> +2.00 D		1 0.9 (0.0, 5.0)	0 0.0 (0.0, 2.6)	0 0.0 (0.0, 2.7)

6) Stability of Outcome

Stability of outcome is evaluated by the cohort of eyes with a refraction at each visit. This cohort contains 105 eyes.

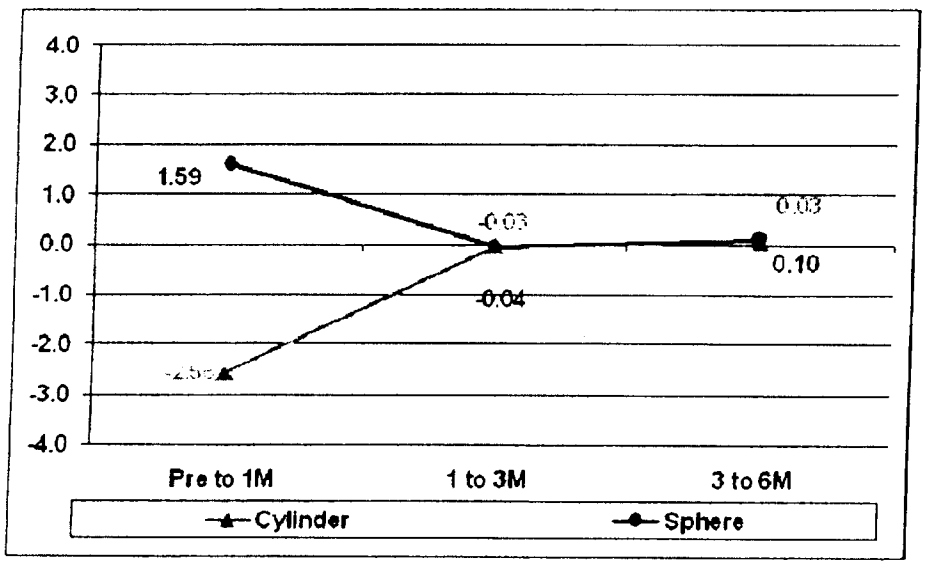
Between the 1 and 3-month visits, 100% (105/105) of eyes experienced a change of 1 D or less. Between the 3 and 6-month visits, 99% (104/105) of eyes experienced a change of 1 D or less. Refractive stability is reached at 3 months and confirmed at the 6-month visit. Table 3-37 presents refractive stability over time.

Table 3-37 — Mixed Astigmatism (LASIK): Refractive Stability (Eyes with 1, 3, and 6-month visits, n = 105)

Change in MRSE	1 and 3 M n % (95% CI)	3 and 6 M n % (95% CI)
≤ 1.00 D	105 100	104 99.0
95% CI for %	(97.2, 100)	(94.8, 100)
MRSE (D)		
Mean	-0.05	0.11
SD	0.32	0.33
95% CI for Mean	(-0.12, 0.01)	(0.05, 0.18)

When plotted over time, the mean of the differences in cylinder and sphere illustrate that stability is achieved by the 3-month visit. This trend is further supported by almost no change between the 3 and 6-month visits.

Figure 3-2: Mean of the Differences —Cylinder and Sphere (Eyes with Visits at 1, 3, and 6 Months, n = 105)



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7) MRSE and Cylinder

At the 1-month visit, the mean manifest refractive spherical equivalent is 0.28 D, representing a change of +0.33 D from the pre-operative refraction. From the point of defined stability (3 months) to the next visit (6 months) the mean MRSE changed 0.08 D, or 0.02 D per month. Table 3-38 presents the mean MRSE and cylinder over time.

Table 3-38 — Mixed Astigmatism (LASIK): Mean MRSE and Cylinder Over Time (n = 115)

	Pre-Op (n = 115)	1 M (n = 110)	3 M (n = 115)	6 M (n = 110)
MRSE (D)				
Mean	-0.05	0.28	0.22	0.30
SD	0.91	0.42	0.42	0.38
95% CI	(-0.22, 0.11)	(0.20, 0.36)	(0.15, 0.30)	(0.23, 0.37)
Cylinder (D)				
Mean	3.10	0.53	0.52	0.51
SD	1.35	0.47	0.52	0.45
95% CI	(2.85, 3.35)	(0.44, 0.62)	(0.43, 0.62)	(0.43, 0.59)

8) Keratometry

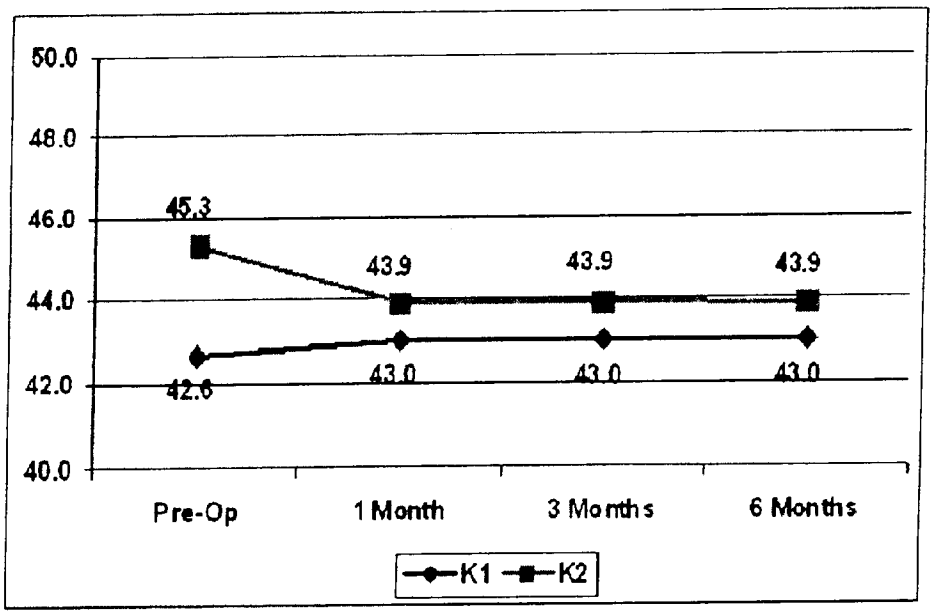
Since the treatment of refractive errors was achieved by an alteration of the anterior corneal curvature, an important method to evaluate treatment stability is through keratometry. From the point of defined stability (3 months) to the next visit (6 months), the mean keratometry changed 0.02 D.

Table 3-39 — Mixed Astigmatism (LASIK): Stability of Keratometry (Eyes with 1, 3, and 6-month visits, n = 105)

Change In Avg K	1 and 3 M		3 and 6 M	
	n	% (95% CI)	n	% (95% CI)
≤ 1.00 D	102	97.1	104	99.0
95% CI for %	(91.9, 99.4)		(94.8, 100)	
Avg K (D)				
Mean	-0.01		0.02	
SD	0.44		0.36	
95% CI for Mean	(-0.09, 0.08)		(-0.05, 0.09)	

The average power in the flat meridian (K1) increased from pre-op (42.6) to 1-month (43.0) and the power in the steep meridian (K2) decreased from pre-op (45.3) to 1-month (43.9).

Figure 3-3: Mean Keratometry (K1 and K2) Over Time



9) Refractive Cylinder

Stability of refractive cylinder is achieved at 3 months post-operatively and confirmed at 6 months. Table 3-40 presents stability of refractive cylinder.

Table 3-40 — Mixed Astigmatism (LASIK): Stability of Refractive Cylinder (Eyes with 1, 3 and 6-month visits, n = 105)

Change in Cylinder	1 and 3 M	3 and 6 M
	n % (95% CI)	n % (95% CI)
≤ 1.00 D	105 100	103 98.1
95% CI for %	(97.2, 100)	(93.3, 99.8)
Cylinder (D)		
Mean	-0.03	0.03
SD	0.34	0.36
95% CI for Mean	(-0.09, 0.04)	(-0.04, 0.10)

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10) Vector Analysis

The vector magnitude ratio (SIRC/IRC) is an indicator of procedure effectiveness. Vector analysis was performed at the point of stability (3 months). The cylindrical SIRC/IRC is >94%.

Table 3-41 — Mixed Astigmatism (LASIK): Vector Magnitude (n = 115)

	Cylinder				
	Pre	**Post**	**IRC**	**SIRC**	**SIRC/IRC***
Mean	-3.1	-0.5	-3.1	-2.9	0.9
Median	-2.8	-0.5	-2.8	-2.7	1.0
SD	1.3	0.5	1.4	1.4	
Min	-0.8	0.0	-0.8	-0.7	
Max	-6.0	-2.8	-6.3	-6.8	

* SIRC = Surgically Induced Refractive Change. IRC = Intended Refractive Change.

11) Retreatments

Procedures performed to improve refractive outcome:

One eye underwent LASIK retreatment (1/115 or 0.9%) during the study. One retreatment is insufficient to yield clinically useful information, however caution should be taken to assure refractive stability before performing additional procedures.

12) Patient Symptoms

Patient questionnaires reflected the following patient symptoms after treatment.

Table 3-42 — Mixed Astigmatism (LASIK): Patient Symptoms: Comparison of Pre-Operative Best-Corrected Vision to Post-Operative Uncorrected Vision, n = 115*

	3 M (N = 115)							6 M (N = 110)						
	Improve (+ ≥ 2)		No Change (0 ± 1)		Worsen (− ≥ 2)		NR	Improve (+ ≥ 2)		No Change (0 ± 1)		Worsen (− ≥ 2)		NR
	n	%	n	%	n	%	n	n	%	n	%	n	%	n
Sharpness and Clarity	2	1.8	104	92.0	7	6.2	2	3	2.7	101	91.8	6	5.5	0
Consistency of Vision	4	3.5	103	91.2	6	5.3	2	1	0.9	100	90.9	9	8.2	0
Daylight Driving	2	1.8	105	92.9	6	5.3	2	3	2.7	102	92.7	5	4.5	0
Night Driving	9	8.0	94	83.2	10	8.8	2	15	13.6	92	83.6	3	2.7	0
Night Vision with Glare	11	9.7	94	83.2	8	7.1	2	13	11.8	94	85.5	3	2.7	0
General Vision in Dim Light	6	5.3	101	89.4	6	5.3	2	6	5.5	99	90.0	5	4.5	0
Overall Visual Comfort	12	10.6	92	81.4	9	8.0	2	7	6.4	94	85.5	9	8.2	0

* This table reflects responses to a patient questionnaire on a scale of 1 (poor) to 5 (excellent). Responses at 3 and 6 months were compared to pre-operative responses. The results presented reflect changes in uncorrected vision compared to baseline.

13) Adverse Events and Complications

Refer to Tables 2-5, 2-6, and 2-7 in Section 2.5.1.

14) Summary of Key Safety and Effectiveness Variables

The key safety and effectiveness variables for all eyes are presented in Tables 3-43 and 3-44. The key safety and effectiveness variables stratified by pre-operative cylinder are presented in Table 3-45.

Table 3-43 — Mixed Astigmatism (LASIK): Summary of Key Safety Variables (n = 115)

Safety Variables			
	1 M	3 M	6 M
Criteria	n % (95% CI)	n % (95% CI)	n % (95% CI)
n = 115	n = 110	n = 115	n = 110
Loss of ≥ 2 lines BSCVA	1 0.9 (0.0,5.0)	1 0.9 (0.0, 4.7)	0 0.0 (0.0, 2.7)
Loss of > 2 lines BSCVA	0 0.0 (0.0, 2.7)	0 0.0 (0.0, 2.6)	0 0.0 (0.0, 2.7)
Increase > 2 D cylinder	0 0.0 (0.0, 2.7)	0 0.0 (0.0, 2.6)	0 0.0 (0.0, 2.7)
n = 94*	n = 90	n = 94	n = 90
BSCVA worse than 20/40	0 0.0 (0.0, 3.3)	0 0.0 (0.0, 3.1)	0 0.0 (0.0, 3.3)

* BSCVA 20/20 or better pre-operatively.

Table 3-44 — Mixed Astigmatism (LASIK): Summary of Key Effectiveness Variables (n = 115)

Criteria	1 M n % (95% CI)	3 M n % (95% CI)	6 M n % (95% CI)
Effectiveness Variables			
n = 94 *	n = 90	n = 94	n = 90
UCVA 20/20 or better	59 65.6 (54.8, 75.3)	65 69.1 (58.8, 78.3)	63 70.0 (59.4, 79.2)
UCVA 20/25 or better	74 82.2 (72.7, 89.5)	84 89.4 (81.3, 94.8)	84 93.3 (86.1, 97.5)
UCVA 20/40 or better	89 98.9 (94.0, 100)	93 98.9 (94.2, 100)	90 100 (96.7, 100)
n = 115 †	n = 110	n = 115	n = 110
UCVA 20/20 or better	60 54.5 (44.8, 64.1)	67 58.3 (48.7, 67.4)	68 61.8 (52.1, 70.9)
UCVA 20/25 or better	84 76.4 (67.3, 83.9)	96 83.5 (75.4, 89.7)	92 83.6 (75.4, 90)
UCVA 20/40 or better	106 96.4 (91.0, 99.0)	113 98.3 (93.9, 99.8)	109 99.1 (95.0, 100)
n = 115	n = 110	n = 115	n = 110
MRSE ± 0.50 D	84 76.4 (67.3, 83.9)	91 79.1 (70.6, 86.1)	85 77.3 (68.3, 84.7)
MRSE ± 1.00 D	107 97.3 (92.2, 99.4)	112 97.4 (92.6, 99.5)	105 95.5 (89.7, 98.5)
MRSE ± 2.00 D	109 99.1 (95.0, 100)	115 100 (97.4, 100)	110 100 (97.3, 100)
Cylinder ± 0.50 D	71 64.5 (54.9, 73.4)	76 66.1 (56.7, 74.7)	70 63.6 (53.9, 72.6)
Cylinder ± 1.00 D	99 90.0 (82.8, 94.9)	97 84.3 (76.4, 90.5)	98 89.1 (81.7, 94.2)
Cylinder ± 2.00 D	108 98.2 (93.6, 99.8)	114 99.1 (95.3, 100)	110 100 (97.3, 100)
Stability			
n = 105		n = 105	n = 105
Change in MRSE ≤ 1.00 D		105 100 (97.2,100)	104 99.0 (94.8, 100)
Mean Change in MRSE		-0.05 ± 0.32 (-0.12, 0.01)	0.11 ± 0.33 (0.05, 0.18)
Change in Cylinder ≤ 1.00 D		105 100 (97.2,100)	103 98.1 (93.3, 99.8)
Mean Change in Cylinder		-0.03 ± 0.34 (-0.09, 0.04)	0.03 ± 0.36 (-0.04, 0.10)

* BSCVA 20/20 or better pre-operatively.

† Includes eyes with a pre-operative BSCVA worse than 20/20.

Table 3-45 — Mixed Astigmatism (LASIK): Summary of Key Safety and Effectiveness Variables at Stability Endpoint at 3 Months (Stratified by Pre-Operative Cylinder)

Criteria	0 to 1.00 n/N, % (% CI)	>1 to 2.00 n/N, % (% CI)	>2 to 3.00 n/N, % (% CI)	>3 to 4.00 n/N, % (% CI)	>4 to 5.00 n/N, % (% CI)	>5 to 6.00 n/N, % (% CI)	Cum Total n/N, % (% CI)
Effectiveness Variables							
n = 94*	**n = 4**	**n = 26**	**n = 32**	**n = 9**	**n = 17**	**n = 6**	**n = 94**
UCVA 20/20 or better	3 75.0 (19.4, 99.4)	22 84.6 (65.1, 95.6)	24 75.0 (56.6, 88.5)	6 66.7 (29.9, 92.5)	9 52.9 (27.8, 77.0)	1 16.7 (0.4, 64.1)	65 69.1 (58.8, 78.3)
UCVA 20/40 or better	4 100 (47.3, 100)	26 100 (89.1, 100)	31 96.9 (83.8, 99.9)	9 100 (71.7, 100)	17 100 (83.8, 100)	6 100 (60.7, 100)	93 98.9 (94.2, 100)
n = 115†	**n = 4**	**n = 27**	**n = 37**	**n = 12**	**n = 28**	**n = 7**	**n = 115**
UCVA 20/20 or better	3 75.0 (19.4, 99.4)	23 85.2 (66.3, 95.8)	24 64.9 (47.5, 79.8)	7 58.3 (27.7, 84.8)	9 32.1 (15.9, 52.4)	1 14.3 (0.4, 57.9)	67 58.3 (48.7, 67.4)
UCVA 20/40 or better	4 100 (47.3, 100)	27 100 (89.5, 100)	36 97.3 (85.8, 99.9)	12 100 (77.9, 100)	27 96.4 (81.7, 99.9)	7 100 (65.2, 100)	113 98.3 (93.9, 99.8)
n = 115	**n = 4**	**n = 27**	**n = 37**	**n = 12**	**n = 28**	**n = 7**	**n = 115**
MRSE ± 0.50 D	3 75.0 (19.4, 99.4)	23 85.2 (66.3, 95.8)	29 78.4 (61.8, 90.2)	9 75.0 (42.8, 94.5)	20 71.4 (51.3, 86.8)	7 100 (65.2, 100)	91 79.1 (70.6, 86.1)
MRSE ± 1.00 D	4 100 (47.3, 100)	27 100 (89.5, 100)	35 94.6 (81.8, 99.3)	12 100 (77.9, 100)	27 96.4 (81.7, 99.9)	7 100 (65.2, 100)	112 97.4 (92.6, 99.5)
MRSE ± 2.00 D	4 100 (47.3, 100)	27 100 (89.5, 100)	37 100 (92.2, 100)	12 100 (77.9, 100)	28 100 (89.9, 100)	7 100 (65.2, 100)	115 100 (97.4, 100)
Cylinder ± 0.50 D	4 100 (47.3, 100)	27 100 (89.5, 100)	21 56.8 (39.5, 72.9)	6 50.0 (21.1, 78.9)	15 53.6 (33.9, 72.5)	3 42.9 (9.9, 81.6)	76 66.1 (56.7, 74.7)
Cylinder ± 1.00 D	4 100 (47.3, 100)	27 100 (89.5, 100)	33 89.2 (74.6, 97.0)	10 83.3 (51.6, 97.9)	19 67.9 (47.6, 84.1)	4 57.1 (18.4, 90.1)	97 84.3 (76.4, 90.5)
Cylinder ± 2.00 D	4 100 (47.3, 100)	27 100 (89.5, 100)	37 100 (92.2, 100)	12 100 (77.9, 100)	27 96.4 (81.7, 99.9)	7 100 (65.2, 100)	114 99.1 (95.3, 100)
Safety Variables							
n = 115	**n = 4**	**n = 27**	**n = 37**	**n = 12**	**n = 28**	**n = 7**	**n = 115**
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 10.5)	0 0.0 (0.0, 7.8)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 10.1)	1 14.3 (0.4, 57.9)	1 0.9 (0.8, 4.7)
Loss of > 2 lines BSCVA	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 10.5)	0 0.0 (0.0, 7.8)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 10.1)	0 0.0 (0.0, 34.8)	0 0.0 (0.0, 2.6)
Increase > 2 D cylinder	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 10.5)	0 0.0 (0.0, 7.8)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 10.1)	0 0.0 (0.0, 34.8)	0 0.0 (0.0, 2.6)
n = 94*	**n = 4**	**n = 26**	**n = 32**	**n = 9**	**n = 17**	**n = 6**	**n = 94**
BSCVA worse than 20/40	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 10.9)	0 0.0 (0.0, 8.9)	0 0.0 (0.0, 28.3)	0 0.0 (0.0, 16.2)	0 0.0 (0.0, 39.3)	0 0.0 (0.0, 3.1)

* BSCVA 20/20 or better pre-operatively.

† Includes eyes with a pre-operative BSCVA worse than 20/20.