SUMMARY OF SAFETY AND EFFECTIVENESS DATA
FOR A SUPPLEMENTAL PREMARKET APPROVAL APPLICATION

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Medical Laser System (193 nanometer wavelength)
Device Trade Name:	WaveLight ALLEGRETTO WAVE™ Excimer Laser System and the ALLEGRO Analyzer
Applicant's Name and Address:	SurgiVision® Regulatory Consultants, Inc. 5 Timber Lane North Reading, MA 01864
Panel Recommendation:	None (see Section XII.)
Premarket Approval (PMA) Application Number:	P020050/S004
Date of Notice of Approval to Applicant:	July 26, 2006

The WaveLight ALLEGRETTO WAVE Excimer Laser System was approved on October 7, 2003 for the indication of reduction or elimination of myopia of up to -12.0 diopters (D) of sphere and of up to -6.0 D of astigmatism at the spectacle plane; in patients who are 18 years of age or older with a documentation of a stable manifest refraction defined as ≤0.50 D of preoperative spherical equivalent shift over one year prior to surgery (P020050). On October 10, 2003, the device was approved for the reduction or elimination of hyperopic refractive errors up to +6.0 D of sphere with and without astigmatic refractive errors up to 5.0 D at the spectacle plane, with a maximum manifest refraction spherical equivalent (MRSE) of +6.O D; in patients who are 18 years of age or older with documentation of a stable manifest refraction defined as ≤0.50 D of preoperative spherical equivalent shift over one year prior to surgery, exclusive of changes due to unmasking latent hyperopia (P030008). On April 19, 2006, the device was approved for the reduction or elimination of naturally occurring mixed astigmatism of up to 6.00 D at the spectacle plane; in patients who are 21 years of age or older with documentation of a stable manifest refraction defined as ≤0.50 D of preoperative spherical equivalent shift over one year prior to surgery (P030008/S004).

The sponsor submitted this supplement to further expand the clinical indications to include wavefront-guided LASIK for myopia with astigmatism. The updated clinical data to support the expanded indication is provided in this summary. For

more information on the data which supported the approved indications, the summaries of safety and effectiveness data (SSED) for P020050 and P030008 should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20857 under Docket # 03M-0491 (P020050), Docket # 03M-0492 (P030008), and Docket # 06M-0199 (P030008/S004) or you may download these files from the internet sites http://www.fda.gov/cdrh/pdf/p020050/.pdf and http://www.fda.gov/cdrh/pdf/p030008.pdf.

II. INDICATIONS FOR USE

The WaveLight Allegretto Wave Excimer Laser System used in conjunction with the WaveLight ALLEGRO Analyzer (Aberrometer) is indicated for wavefront-guided (WFG) laser assisted in situ keratomileusis (LASIK):

- for the reduction or elimination of up to -7.00 diopters (D) of spherical equivalent myopia or myopia with astigmatism, with up to -7.00 D of spherical component and up to 3.00 D of astigmatic component at the spectacle plane;
- in patients who are 18 years of age or older; and
- in patients with documentation of a stable manifest refraction defined as ≤0.50 D of preoperative spherical equivalent shift over one year prior to surgery.

III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

LASIK surgery is contraindicated in:

- pregnant or nursing women;
- patients with a diagnosed collagen vascular, autoimmune or immunodeficiency disease;
- patients with diagnosed keratoconus or any clinical pictures suggestive of keratoconus; and
- patients who are taking one or both of the following medications: isotretinoin (Accutane®[1]); amiodarone hydrochlorid (Cordarone®[2]).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the device labeling.

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

V. DEVICE DESCRIPTION

A. ALLEGRO Analyzer

The first step in performing Wavefront-guided LASIK or A-CAT (Aberroscopy-based Custom Ablation Treatment) involves measuring the eye with the ALLEGRO Analyzer. The ALLEGRO Analyzer diagnostic system is an optical wavefront measuring system for the quantitative evaluation of the aberrations of the human eye.

The technology of the ALLEGRO Analyzer is based on the approach of Tscherning. His principle is applied as follows: a set of 168 well-defined rays enter the eye. Each ray passes the interfaces within the eye and is individually refracted. As a result, a spot pattern is generated on the retina which will differ from the pattern created in an aberration free eye by individual and local errors of the imaged eye. Using optics, this pattern is captured by a highly sensitive camera. For each measurement, four images are created which can be overlaid onto one image. This digital image is transferred to the analyzer's computer for image processing. The Analyzer software compares the positions of each point of the pattern with the calculated ideal position. Using polynomial equations the wavefront maps and corresponding Zernike coefficients are calculated for the exit plane of the eye. The ALLEGRO Analyzer can display aberrations in various formats such as wavefront error map, power map or point-spread function. All quantitative representations of the wavefront error depend upon the reference optical zone which in this study was 6.0 mm.

1. Head Rest and Fixation
   The patient sits in front of the ALLEGRO Analyzer. The head is placed in a head rest. A fixation target will help the patient keep their eye steady during image capture.

2. Pupil Camera
   The Analyzer is equipped with a camera providing a live image of the pupil on the monitor. The image aids proper centration and focusing. Tolerances are +/- 100 microns for centration and +/-200 microns for focus distance.

3. Projector
   Up to 168 red light rays are projected through the pupil onto the retina while the examination is performed. The rays create a spot pattern of lit areas on the retina. Aberrations of the eye refract the rays and create a distorted grid pattern which can be imaged by a second camera. This distorted pattern can also be seen by the patient.

4. Retina Camera
   The second camera captures a synchronized retinal image while the pupil camera indicates the focused and centered position of the device.

5. Analysis Software
   Determination of the wavefront image of the retinal spot pattern is analyzed by image processing software. The wavefront information is retrieved from the distortion of the spot pattern. Graphical and numerical representations (Zernike polynomials) of the wavefront errors up to the 6th order are calculated and saved.

6. Data Export
   The patient's demographic data and the numerical representation of the measured aberrations can be exported via electronic media for use with the ALLEGRETTO Wave. Export files are protected against manipulation and tampering by proprietary encryption of the electronic file.

B. Microkeratome

The LASIK procedure requires the use of a commercially available microkeratome that has been cleared for marketing via premarket notification. Treatments in this study were conducted with a laser microkeratome.

Laser keratomes include a transparent applanation plate used to flatten the cornea and establish a known reference plane. The laser is a femtosecond laser that is operated through a software interface and is activated by use of a foot pedal. The laser keratome used in this series was operated at a 15 kHz repetition rate.

C. Notebook Portal Software A-CAT Module

The Notebook Portal Software allows import, selection and processing of wavefront data from the ALLEGRO Analyzer as well as input of additional personal patient and clinical data. Individual ablation profiles and treatment shot lists are generated and transferred to the ALLEGRETTO WAVE for wavefront-guided treatments.

D. ALLEGRETTO WAVE™ Excimer Laser System

Features and components of the ALLEGRETTO WAVE™ Excimer Laser System include:

The WaveLight ALLEGRETTO WAVE™ Excimer Laser System is a scanning-spot excimer laser system which includes an excimer laser with high pulse repetition rate, beam delivery optics and a pair of galvanometer scanners for positioning the laser pulses. The integrated eye-tracker permits the system to track fast eye movements or to interrupt the treatment when the eye moves out of a predetermined range.

The specially shaped profile of the treatment beam and the small spot diameter provide the accuracy to achieve the desired contour of the treated surface. The ablation contours are based on sophisticated numerical algorithms. Since the small spot diameter allows for a low pulse energy, a compact excimer laser source with a small gas volume and low gas consumption is integrated into the laser console.

The operative laser parameters are summarized as follows:

Pulse repetition rate:	200 Hz
Fluence:	200 mJ/cm^2 (average) 400 m J/cm^2 (peak)
Optical zone:	6.5 mm
Ablation zone:	9.0 mm
Ablation spot diameter:	0.95 + 0.10 mm

The software versions in the laser system during the clinical trial were as follows:

a. Notebook Software	1.208
b. Firmware Software	PR034901
c. Treatment Lists	NG-041301
d. Eyetracker	4.08
e. Laser Head Firmware	H4.2 / G3.6 / E3.8 / M3.3 / P3.7

The software versions in the laser system at approval are as follows:

a. Notebook Software	NB-PSW 2.0xx
b. Firmware Software	PR-V2-1.00
c. Treatment Lists	NG-051701
d. Eyetracker	4.10
e. Laser Head Firmware	H4.2 / G3.6 / E3.8 / M3.3 / P3.7

The ALLEGRETTO WAVE™ Excimer Laser System for wavefront-guided LASIK myopia plus astigmatism ablations is locked out for spherical treatments greater than -7.00 D spherical equivalent and greater than -3.00 D cylinder, and for optical zones (OZ) different from the approved OZ of 6.5 mm or treatment zones (TZ) different from the approved TZ of 9.0 mm. A surgeon refractive offset is present which allows the surgeon to adjust the spherical component of the refraction by +1.00 D to -3.00 D and the cylindrical component by -3.00 D. Surgeon refractive offsets are not allowed to exceed the range as approved in the

indications for use and no cylinder may be added to the treatment. A flag warning will appear when surgeon refractive off-sets are invoked.

1. Optical transmission system

   The excimer laser passes through a beam homogenizing optic, followed by a series of mirrors and lenses. Two mirrors are driven by galvanometer scanner motors for precise positioning the excimer laser pulses at the correct locations on the treated surface.

2. Energy monitoring and control

   The laser pulse energy is monitored at several locations of the beam path inside and outside the laser console. Measured energy values are used to control and maintain required energy output levels.

3. Gas handling system

   The ALLEGRETTO WAVE incorporates two gas supply devices; one for the premix ArF gas used for laser light formation and one for nitrogen gas, used to rinse the beam path and optics during treatment.

4. Eye Tracking System

   Active eye tracking is applied to ensure that laser pulses are positioned exactly on the eye, even when the eye is moving. An infrared high speed camera images the eye with a capture rate of 200 Hz. Each image is processed to determine the current position and size of the pupil. Pupil position information is then used to actively align mirrors for correct placement of the next laser pulse on the eye. The whole process takes ≤ 10 milliseconds.

5. Operating microscope

   The laser system is equipped with a binocular stereo operating microscope. The laser beam is located in the center of the converging oculars of the microscope. A five fold magnification changer allows for image size adjustment.

6. Fixation target

   A green blinking fixation light, which is coaxial to the laser beam is visible for the patient and.aids steady fixation of the patient.

7. Illumination System

   Two different light sources can be used to illuminate the surgical field: a top light full field illumination is provded by white light emitting diodes. A slit lamp can be used to visualize corneal structures by means of a light slit. The slit lamp utilizes a cold light source with high color temperature.

8. Patient bed

   The patient's eye has to be focused and centered with regards to the laser beam focus point. For this purpose the patient bed can be moved in three directions with various speeds.

9. System Software Control
   Two different types of software are used to run the laser system: the laser firmware controls functions and interaction of all components inside the laser console. The notebook portal software is used to prepare treatment plans and to program the laser with such treatment plans and is located on the notebook computer which is separate from the laser console.

10. Plume Removal System

    For convenience and safety of surgeon and patient, ablated corneal debris or plume is removed by a plume evacuation system immediately after formation.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional methods in correcting myopia and myopic astigmatism are: spectacles, contact lenses, photorefractive keratectomy (PRK), traditional LASIK or other types of refractive surgery.

VII. MARKETING HISTORY

The device has been commercially distributed in approximately 53 countries (Austria, Australia, Bahrain, Belgium, Brazil, Canada, China, France, Germany, Great Britain, Greece, Hong Kong, India, Ireland, Israel, Italy, Japan, Korea, Lebanon, Mexico, Netherlands, Norway, Russia, Saudi Arabia, Singapore, Slovenia, Spain, Sri Lanka, Sweden, Switzerland, United States, Egypt, Algeria, Argentina, Chile, Columbia, Curacao, Finland, Iran, Jordan, Kenya, La Reunion, Malaysia, New Zealand, Poland, Serbia, Slovakia, South Africa, Sweden, Taiwan, Thailand, Czech Republic, Dubai). The WaveLight ALLEGRETTO WAVE™ has not been withdrawn from any country or market for reasons of safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects associated with LASIK include: loss of best spectacle corrected visual acuity, overcorrection, increase in refractive cylinder, worsening of patient complaints such as double vision and glare, sensitivity to bright lights, increased difficulty with night vision, fluctuation in vision, increase in intraocular pressure, corneal haze, corneal infection/ulcer/infiltrate, corneal decompensation/edema, problems associated with the flap including a lost,

misplaced or misaligned flap, retinal detachment, and retinal vascular accidents. The occurrence of many of these events may involve the necessity of secondary (additional) surgical intervention.

Please refer to the complete list of adverse events and complications observed during the clinical study, which are presented in the clinical study section.

IX. SUMMARY OF PRECLINICAL STUDIES

Please refer to the SSED for PMA P020050 for the preclinical studies conducted on the ALLEGRETTO WAVE Laser System. The in vitro and animal studies provided evidence to support the conclusion that the device did not present an unreasonable risk to subjects and could proceed to clinical trials under an approved investigational device exemption (IDE).

In addition, preclinical testing of the measurement device required for wavefront-guided treatments was performed to ensure reliable and precise measurement results. Tests involved correlation tests between wavefront and manifest refraction values of human eyes as well as validation of wavefront calculation results using well defined artificial retinal images.

Testing of the whole device chain consisting of the ALLEGRO Analyzer, the treatment planning software and the ALLEGRETTO WAVE laser system was performed to ensure the reliability and precision of the treatment properties. The chain was validated using wavefront measurements of well defined artificial eyes and succeeding ablation of the resulting wavefront treatment profiles on plastic material. The resulting ablation profiles were measured and checked against their target profiles resulting from the parameters of the artificial eyes.
All tests showed excellent agreement with specification and target values.

X. SUMMARY OF CLINICAL STUDIES

The sponsor performed a clinical study of the WaveLight ALLEGRETTO WAVE™ Excimer Laser System in conjunction with the ALLEGRO Analyzer at five U.S. clinical sites under the auspices of an Investigational Device Exemption (IDE) G040112. The data from this study served as the basis for the approval decision. Specifically, safety and effectiveness outcomes at 3 months postoperatively were assessed, as stability was reached at that time. Outcomes at 6 months postoperatively were also evaluated for confirmation of stability. The IDE study is described in detail as follows.

A. Study Objective

The objective of the study was to determine the safety and effectiveness of the WaveLight ALLEGRETTO WAVE™ Excimer Laser System used in conjunction with the ALLEGRO Analyzer for Wavefront-Guided LASIK treatment of up to -7.00 D of manifest refractive myopic spheroequivalent with or without 0 to 3.00 D of astigmatism.

B. Study Design

The study was a prospective, controlled, randomized, non-blinded consecutive enrollment study conducted at 5 centers with 7 surgeons. Subjects were enrolled in order to evaluate safety and effectiveness targets across the refractive range considered in the study. Two main cohorts were identified: Study Cohort and Control Cohort.

- Study Cohort: The Study Cohort underwent bilateral LASIK treatments based on aberrometry measurements.

- Control Cohort: The Control Cohort underwent bilateral LASIK treatments based on clinical refractions, without regard to aberrometry.

C. Inclusion and Exclusion Criteria

Enrollment in the WaveLight Wavefront-Guided LASIK study for myopia and myopic astigmatism was limited to:

- Subjects must be undergoing LASIK surgery for the correction of myopia
- Intended treatment from 0 to 7 D of spherical equivalent myopia or myopia with astigmatism, with up to 7 D of spherical component and up to 3 D of astigmatic component. (All refractions measured at the spectacle plane in minus cylinder notation).
- Subjects must have bilateral physiologic myopia with intended treatment in the study for both eyes.
- BSCVA of 20/25 or better in each eye.
- Subjects must have had a stable refraction (0.5 D or less change in spheroequivalent) for the last twelve (12) months, objectively documented (by previous clinical records, eyeglass prescriptions, etc.). Serial topographies shall not be required.
- Subjects who are contact lens wearers must have hard or gas permeable lenses discontinued for 3 weeks and soft lenses discontinued for 3 days prior to the preoperative evaluation.
- Subjects must be at least eighteen (18) years of age.
- Corneal topography must be normal, as judged by the operating investigator.

- Maximum distance of 1.5 mm angle kappa at the corneal surface, as documented as either (1) the distance between the visual axis and pupillary center measured on topography; or (2) measured using a penlight test.
- Subjects must sign a written Informed Consent form acknowledging their awareness of their participation in this study, the alternative treatments available, the risks involved, and the investigative nature of LASIK, and other issues which conform to the standard of care for Informed Consent practices.
- Subjects must be able to return for scheduled follow-up examinations for 12 months after surgery.
- Must be able to successfully perform preoperative aberrometry.
- Pupil must be able to dilate to at least 7.0 mm diameter.

Subjects with the following conditions were not eligible for enrollment in the Wavefront-Guided LASIK study:

- Subjects with corneal dystrophies or guttata.
- Subjects with anterior segment pathology.
- Subjects with residual, recurrent or active ocular disease.
- Subjects who have undergone previous intraocular or corneal surgery involving the stroma in the eye to be operated.
- Subjects who have a history of herpes keratitis.
- Subjects with diagnosed autoimmune disease, systemic connective tissue diseases or atopic syndrome, diabetes mellitus, or taking systemic medications (i.e., corticosteroids or antimetabolites) likely to affect wound healing.
- Subjects with unstable central keratometry/topography readings with irregular topography patterns or keratometry mires, including signs of keratoconus.
- Subjects with known sensitivity to study medications.
- Subjects with intraocular pressure of > 23 mm Hg by Goldmann applanation tonometry, a history of glaucoma, or glaucoma suspect.
- Women who are pregnant or nursing or who plan to become pregnant over the course of their participation in this investigation.
- Participation in other ophthalmic clinical trials during this clinical investigation.
- Subjects with colobomas of the iris or other irregularities of the pupil margin.
- Inability to successfully perform preoperative aberrometry.

D. Study Plan, Patient Assessments, and Efficacy Criteria

Subjects were evaluated preoperatively and postoperatively at 1 day, 1 month, 3 months, 6 months, and 12 months. Preoperative objective measurements

included: uncorrected distance and near visual acuity, manifest refraction, distance best spectacle corrected visual acuity, low contrast visual acuity, contrast sensitivity, cycloplegic refraction, applanation tonometry, slit lamp examination, pupil size measurement in photopic and scotopic conditions, central keratometry, computerized corneal topography, aberrometry, pachymetry, dilated fundus examination, measurement of angle kappa, and patient questionnaire.

Postoperatively, objective measurements included: uncorrected distance and near visual acuity, manifest refraction, distance best spectacle corrected visual acuity, low contrast acuity, contrast sensitivity, cycloplegic refraction, applanation tonometry, slit lamp examination, central keratometry, computerized corneal topography, aberrometry, dilated fundus examination, and patient questionnaire.

All subjects in this study were planned for bilateral treatments and all subjects actually underwent bilateral treatment. Subjects were eligible for retreatment no sooner than 3 months after surgery. Subjects were eligible for retreatment if the manifest refractive spherical equivalent was 0.5 D or greater (myopic or hyperopic), the manifest astigmatism was 0.5 D or more, the distance visual acuity was 20/30 or less, or due to any subjective complaints by the patient with treatable cause as determined by the investigator.

Effectiveness was evaluated based on improvement in uncorrected visual acuity and predictability of the manifest refraction spherical equivalent (MRSE).

E. Study Period, Investigational Sites and Demographic Data

1. Study Period

A total of 374 eyes were treated; 188 in the Study Cohort and 186 in the Control Cohort between September 14, 2004 and September 7, 2005. All follow-up received by SurgiVision prior to December 8, 2005 was included in this PMA Supplement.

2. Demographics

In the Study Cohort, more males than females were treated with 55.3% (104/188) of the cases being male and 44.7% (84/188) being female. Overall, 93.6% (176/188) of eyes treated were in Caucasian subjects, 3.2% (6/188) in Blacks, 2.1% (4/188) in Asians, and 1.1% (2/188) in Hispanics. The mean age of the patients treated was 33.5±7.7 years with a range from 21 to 52.

Table 1-Study Cohort Demographic Characteristics (N=188)			
Category	**Classification**	**%**	**n**
Gender	Female	44.7	84
	Male	55.3	104
Race	Caucasian	93.6	176
	Black	3.2	6
	Asian	2.1	4
	Hispanic	1.1	2
	Other	0.0	0
	Not Reported	0.0	0
Eyes	OD	50.0	94
	OS	50.0	94
CL History	Soft	66.0	124
	RGP	5.3	10
	PMMA	0.0	0
	Glasses	28.7	54
	Unknown	0.0	0
Age (in Years)	Average	33.5	
	Standard Deviation	7.7	
	Minimum	21.0	
	Maximum	52.0	

In the Control Cohort, more females than males were treated with 53.8% (100/186) of the cases being female and 46.2% (86/186) being male. Overall, 92.5% (172/186) of eyes treated were in Caucasian subjects, 4.3% (8/186) in Blacks, 2.1% (4/186) in Asians, and 1.1% (2/186) in Hispanics. The mean age of the patients treated was 34.2±8.3 years with a range from 19 to 58.

Table 1-Control Cohort Demographic Characteristics (N=186)			
Category	**Classification**	**%**	**n**
Gender	Female	53.8	100
	Male	46.2	86
Race	Caucasian	92.5	172
	Black	4.3	8
	Asian	2.1	4
	Hispanic	1.1	2
	Other	0.0	0
	Not Reported	0.0	0
Eyes	OD	50.0	93
	OS	50.0	93
CL History	Soft	67.7	126
	RGP	7.5	14
	PMMA	0.0	0
	Glasses	23.7	44
	Unknown	1.1	2
Age (in Years)	Average	34.2	
	Standard Deviation	8.3	
	Minimum	19.0	
	Maximum	58.0	

F. Data Analysis and Results

1. Baseline characteristics

Tables 2-Study Cohort and 2-Control Cohort contain a summary of the preoperative sphere and cylinder for the entire Study Cohort and Control Cohort while Table 3 provides the preoperative spherical equivalent for both Cohorts.

Table 2-Study Cohort
Preoperative Refractive Error Stratified by Sphere and Cylinder
(N=188)

Sphere	Cylinder (Minus Cylinder Notation)													
	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	3.2	6	2.1	4	0.5	1	0.0	0	0.0	0	0.0	0	5.9	11
>1 to ≤2 D	20.7	39	3.7	7	0.0	0	0.0	0	0.0	0	0.0	0	24.5	46
>2 to ≤3 D	16.5	31	1.1	2	1.1	2	0.0	0	0.0	0	0.0	0	18.6	35
>3 to ≤4 D	17.6	33	2.1	4	2.1	4	0.0	0	0.0	0	0.0	0	21.8	41
>4 to ≤5 D	14.4	27	2.1	4	1.1	2	0.0	0	0.0	0	0.0	0	17.6	33
>5 to ≤6 D	4.8	9	2.1	4	0.0	0	0.0	0	0.0	0	0.0	0	6.9	13
>6 to ≤7 D	4.3	8	0.5	1	0.0	0	0.0	0	0.0	0	0.0	0	4.8	9
>7 to ≤8 D	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
Total	81.5	153	13.7	26	4.8	9	0.0	0	0.0	0	0.0	0	100	188

Table 2-Control Cohort
Preoperative Refractive Error Stratified by Sphere and Cylinder
(N=186)

Sphere	Cylinder (Minus Cylinder Notation)													
	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	8.6	16	4.8	9	0.0	0	0.0	0	0.0	0	0.0	0	13.4	25
>1 to ≤2 D	17.2	32	3.8	7	1.1	2	0.0	0	0.0	0	0.0	0	22.1	41
>2 to ≤3 D	19.9	37	2.2	4	0.0	0	0.0	0	0.0	0	0.0	0	22.1	41
>3 to ≤4 D	15.6	29	3.8	7	0.5	1	0.0	0	0.0	0	0.0	0	19.9	37
>4 to ≤5 D	11.8	22	1.6	3	0.0	0	0.0	0	0.0	0	0.0	0	13.4	25
>5 to ≤6 D	2.7	5	2.2	4	0.0	0	0.0	0	0.0	0	0.0	0	4.9	9
>6 to ≤7 D	3.8	7	0.5	1	0.0	0	0.0	0	0.0	0	0.0	0	4.3	8
>7 to ≤8 D	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
Total	79.6	148	18.9	35	1.6	3	0.0	0	0.0	0	0.0	0	100	186

Table 3 Preoperative Spherical Equivalent				
	Study Cohort (N=188)		Control Cohort (N=186)	
Spherical Equivalent	**%**	**n**	**%**	**n**
0 to ≤1 D	1.6	3	5.9	11
>1 to ≤2 D	23.4	44	23.1	43
>2 to ≤3 D	21.3	40	26.3	49
>3 to ≤4 D	17.6	33	15.1	28
>4 to ≤5 D	19.7	37	17.2	32
>5 to ≤6 D	9.6	18	5.9	11
>6 to ≤7 D	6.9	13	5.9	11
>7 to ≤8 D	0.0	0	0.5	1
Total	100	188	100	186

2. Postoperative Characteristics and Results

a. Patient Accountability

There were 188 eyes treated in the Study Cohort and 186 in the Control Cohort. Accountability information is provided in Tables 4-Study Cohort and 4-Control Cohort. Accountability in the Study Cohort was 96.8% (182/188) at 1–month, 96.8% (180/186) at 3-months, and 93.3% (166/178) at 6-months. Accountability in the Control Cohort was 94.6% (176/186) at 1–month, 94.6% (176/186) at 3-months, and 92.2% (166/180) at 6-months. The following cohorts were used for analysis:

- Safety-all eyes (188 in the Study Cohort and 186 in the Control Cohort)
- Effectiveness- all eyes (188 in the Study Cohort and 186 in the Control Cohort)
- Stability-subset of all eyes seen at any two consecutive visits, and subset of all eyes seen at 1, 3 and 6-months (156 and 174 for the Study Cohort and 148 and 166 for the Control Cohort)

Table 4-Study Cohort Subject Accountability (N=188)					
		1 Day	1 Month	3 Months	6 Months
Available for Analysis	%	100	96.8	95.7	88.3
	n	188	182	180	166
Discontinued-Deceased	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Discontinued-Retreated	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Discontinued-Total (Cumulative)	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Not Yet Eligible for Interval	%	0.0	0.0	1.1	5.3
	n	0	0	2	10
Expected	%	100	100	98.9	94.7
	n	188	188	186	178
Lost to Follow-Up (Cumulative)	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Missed Visit	%	0.0	3.2	3.2	6.4
	n	0	6	6	12
% Accountability	%	100	96.8	96.8	93.3
	n	188	182	180	166

Table 4-Control Cohort Subject Accountability (N=186)					
		1 Day	1 Month	3 Months	6 Months
Available for Analysis	%	100	94.6	94.6	89.3
	n	186	176	176	166
Discontinued-Deceased	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Discontinued-Retreated	%	0.0	0.0	0.0	1.1
	n	0	0	0	2
Discontinued-Total (Cumulative)	%	0.0	0.0	0.0	1.1
	n	0	0	0	2
Not Yet Eligible for Interval	%	0.0	0.0	0.0	3.2
	n	0	0	0	6
Expected	%	100	100	100	96.8
	n	186	186	186	180
Lost to Follow-Up (Cumulative)	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Missed Visit	%	0.0	5.4	5.4	7.5
	n	0	10	10	14
% Accountability	%	100	94.6	94.6	92.2
	n	186	176	176	166

b. Stability of Outcome

In the 1-3 and 3-6 month windows, greater than 98% of eyes in the Study Cohort and 100% of eyes in the Control Cohort experienced a change of MRSE not exceeding 1.0 D. Furthermore, the mean of the paired difference of MRSE was -0.02 D in the 1 to 3-month time period and -0.01 D in the 3 to 6-month time period for the Study Cohort and was -0.06 D in the 1 to 3-month time period and 0.00 D in the 3 to 6-month time period for the Control Cohort. Thus, stability was demonstrated at 3-months postoperatively for both Cohorts.

Table 5-Study Cohort
Refractive Stability
(Eyes with 1, 3 and 6 Month Visits (n=156)

Change in MRSE	1 and 3 Months	3 and 6 Months
	% n 95% CI	% n 95% CI
≤1.00 D 95% CI for %	98.7 154 97.8%, 99.6%	100 156 100%, 100%
MRSE (D)		
Mean	-0.02 D	-0.01 D
SD	0.28	0.22
95% CI for Mean	-0.07, +0.02	-0.04, +0.03

Table 5-Control Cohort
Refractive Stability
(Eyes with 1, 3 and 6 Month Visits (n=148)

Change in MRSE	1 and 3 Months	3 and 6 Months
	% n 95% CI	% n 95% CI
≤1.00 D 95% CI for %	100 148 100%, 100%	100 148 100%, 100%
MRSE (D)		
Mean	-0.06 D	0.00 D
SD	0.24	0.22
95% CI for Mean	-0.10, -0.02	-0.03, +0.04

c. Effectiveness Outcomes

The analysis of effectiveness was based on the 180 eyes available at the 3-month stability time point in the Study Cohort and 176 eyes in the Control Cohort. Key efficacy outcomes over the course of the study and at the point of stability stratified by diopter of MRSE are presented in Tables 6-Study Cohort and 6-Control Cohort and 7-Study Cohort and 7-Control Cohort. At 3-months, the UCVA was 20/20 or better in 95.0%

(171/180) of the Study Cohort and 93.8% (165/176) in the Control Cohort. UCVA was 20/16 or better in 62.8% (113/180) of the Study Cohort and 69.3% (122/176) in the Control Cohort at 3 months. UCVA was 20/12.5 or better in 24.4% (44/180) of the Study Cohort and 19.3% (34/176) in the Control Cohort at 3 months.

Table 6-Study Cohort
Summary of Key Efficacy Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
Efficacy Variables	**N=182**	**N=180**	**N=166**
UCVA 20/12.5 or better	20.9 38 17.9%, 23.9%	24.4 44 21.2%, 27.6%	25.3 42 21.9%, 28.7%
UCVA 20/16 or better	63.2 115 59.6%, 66.8%	62.8 113 59.2%, 66.4%	63.9 106 60.1%, 67.6%
UCVA 20/20 or better*	94.5 172 92.8%, 96.2%	95.0 171 93.4%, 96.6%	93.4 155 91.4%, 95.3%
UCVA 20/40 or better*	99.5 181 98.9%, 100%	100 180 100%, 100%	99.4 165 98.8%, 100%
MRSE ± 0.50 D	93.4 170 91.6%, 95.3%	94.4 170 92.7%, 96.2%	94.6 166 92.8%, 96.3%
MRSE ± 1.00 D	97.3 177 96.0%, 98.5%	97.8 176 96.7%, 98.9%	98.2 163 97.2%, 99.2%
MRSE ± 2.00 D	100 182 100%, 100%	99.4 179 98.9%, 100%	100 166 100%, 100%

*For all eyes minus those intentionally treated for monovision.

Table 6-Control Cohort
Summary of Key Efficacy Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
Efficacy Variables	**N=176**	**N=176**	**N=166**
UCVA 20/12.5 or better	18.8 33 15.8%, 21.7%	19.3% 34 16.3%, 22.3%	21.7 36 18.5%, 24.9%
UCVA 20/16 or better	68.8 121 65.3%, 72.2%	69.3 122 65.8%, 72.8%	75.9 126 72.6%, 79.2%
UCVA 20/20 or better*	94.3 166 92.6%, 96.1%	93.8 165 91.9%, 95.6%	92.8 154 90.8%, 94.8%
UCVA 20/40 or better*	100 176 100%, 100%	100 176 100%, 100%	99.4 165 98.8%, 100%
MRSE ± 0.50 D	97.7 172 96.6%, 98.9%	96.6 170 95.2%, 98.0%	95.2 158 93.5%, 96.8%
MRSE ± 1.00 D	99.4 175 98.9%, 100%	100 176 100%, 100%	100 166 100%, 100%
MRSE ± 2.00 D	100 176 100%, 100%	100 176 100%, 100%	100 166 100%, 100%

*For all eyes minus those intentionally treated for monovision.

Table 7-Study Cohort
Summary of Key Efficacy Variables
at 3 Months (Stratified by Preoperative MRSE)

	0 to 1.0 D % n 95% CI	>1.0 to 2.0 D % n 95% CI	>2.0 to 3.0 D % n 95% CI	>3.0 to 4.0 D % n 95% CI	>4.0 to 5.0 D % n 95% CI	>5.0 to 6.0 D % n 95% CI	>6.0 to 7.0 D % n 95% CI	Total ≤7 D % n 95% CI
Efficacy Variables	**N=3**	**N=42**	**N=38**	**N=29**	**N=37**	**N=18**	**N=13**	**N=180**
UCVA 20/20 or better*	100 3 100%,100%	95.2 40 92.0%,98.5%	100 38 100%,100%	96.6 28 93.2%, 99.4%	94.6 35 90.9%, 98.3%	88.9 16 81.5%, 96.3%	84.6 11 74.6%, 94.6%	95.0 171 93.4%,96.6%
UCVA 20/40 or better*	100 3 100%,100%	100 42 100%,100%	100 38 100%,100%	100 29 100%,100%	100 37 100%,100%	100 18 100%,100%	100 13 100%,100%	100 180 100%,100%
MRSE ± 0.50 D	100 3 100%,100%	97.6 41 95.3%,100%	100 38 100%,100%	100 29 100%,100%	91.9 34 87.4%,96.4%	77.8 14 68.0%, 87.6%	84.6 11 74.6%, 94.6%	94.4 170 92.7%,96.2%
MRSE ± 1.00 D	100 3 100%,100%	100 42 100%, 100%	100 38 100%,100%	100 29 100%,100%	94.6 35 90.9%, 98.3%	88.9 16 81.5%, 96.3%	100 13 100%, 100%	97.8 176 96.7%, 98.9%
MRSE ± 2.00 D	100 3 100%,100%	100 42 100%, 100%	100 38 100%,100%	100 29 100%,100%	100 37 100%,100%	94.4 17 89.1%, 99.8%	100 13 100%, 100%	99.4 179 98.9%, 100%

*For all eyes minus those intentionally treated for monovision.

Table 7-Control Cohort
Summary of Key Efficacy Variables
at 3 Months (Stratified by Preoperative MRSE)

	0 to 1.0 D % n 95% CI	>1.0 to 2.0 D % n 95% CI	>2.0 to 3.0 D % n 95% CI	>3.0 to 4.0 D % n 95% CI	>4.0 to 5.0 D % n 95% CI	>5.0 to 6.0 D % n 95% CI	>6.0 to 7.0 D % n 95% CI	Total ≤7 D % n 95% CI
Efficacy Variables	**N=11**	**N=39**	**N=47**	**N=26**	**N=32**	**N=10**	**N=10**	**N=175**
UCVA 20/20 or better*	100 11 100%, 100%	97.4 38 94.9%, 100%	91.5 43 87.4%, 95.6%	96.2 25 92.4%, 99.9%	90.6 29 85.5%, 95.8%	80.0 8 67.4%, 92.7%	100 10 100%, 100%	93.7 164 91.9%,95.6%
UCVA 20/40 or better*	100 11 100%, 100%	100 39 100%,100%	100 47 100%,100%	100 26 100%,100%	100 32 100%,100%	100 10 100%,100%	100 10 100%,100%	100 175 100%,100%
MRSE ± 0.50 D	100 11 100%, 100%	97.4 38 94.9%,100%	95.7 45 92.8%,98.7%	100 26 100%,100%	93.8 30 89.5%,98.0%	90.0 9 80.5%, 99.5%	100 10 100%, 100%	96.6 169 95.2%,98.0%
MRSE ± 1.00 D	100 11 100%, 100%	100 39 100%, 100%	100 47 100%,100%	100 26 100%,100%	100 32 100%, 100%	100 10 100%, 100%	100 10 100%, 100%	100 175 100%, 100%
MRSE ± 2.00 D	100 11 100%, 100%	100 39 100%, 100%	100 47 100%,100%	100 26 100%,100%	100 32 100%,100%	100 10 100%, 100%	100 10 100%, 100%	100 175 100%, 100%

*For all eyes minus those intentionally treated for monovision.

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Analysis of the correction of the cylindrical component of the astigmatic eyes is presented in Tables 8-Study Cohort and 8-Control Cohort and 9-Study Cohort and 9-Control Cohort. The Ophthalmic Devices Panel (the Panel), at the January 14, 1997 meeting, assessed outcomes from a myopic astigmatic treatment and provided FDA with recommendations as to acceptable effectiveness rates. The Panel considered 64% as an acceptable mean reduction in absolute cylinder at the point of stability. Therefore, the 80.7% reduction in the Study Cohort and 83.3% in the Control Cohort at 3 months achieved with this device is acceptable.

Table 8-Study Cohort
Cylinder Correction Efficacy Stratified by Preoperative Cylinder
(N=69)

	3 Months
Preoperative Cylinder	**% Reduction of Absolute Cylinder**
0 to 0.50 D	-
> 0.50 to ≤ 1.00 D	81.0%
> 1.00 to ≤ 2.00 D	77.4%
> 2.00 to ≤ 3.00 D	88.2%
Total	80.7%

Table 8-Control Cohort
Cylinder Correction Efficacy Stratified by Preoperative Cylinder
(N=80)

	3 Months
Preoperative Cylinder	**% Reduction of Absolute Cylinder**
0 to 0.50 D	-
> 0.50 to ≤ 1.00 D	83.5%
> 1.00 to ≤ 2.00 D	81.6%
> 2.00 to ≤ 3.00 D	100%
Total	83.3%

Looking at the intended versus achieved vector magnitude cylinder, in the Study Cohort, the Intended Refractive Correction ("IRC") had a mean of -1.11 ± 0.50 D. The Surgically Induced Refractive Correction ("SIRC") had a mean of -1.26 ± 0.58 D. The vector magnitude ratio (SIRC/IRC) was 1.15 at 3-months. In the Control Cohort, the IRC had a mean of -1.11 ± 0.45 D. The SIRC had a mean of -1.17 ± 0.59 D. The vector magnitude ratio (SIRC/IRC) was 1.03 at 3-months. The Panel has found 0.82 acceptable for correction efficacy (SIRC/IRC) at stability.

Table 9-Study Cohort Cylinder Correction Efficacy Stratified by Preoperative Cylinder	
	3 Months
Preoperative Cylinder	Achieved vs. Intended Vector Magnitude Ratio (Achieved/Intended) Mean
ALL	1.15
0 to 0.50 D	NA
>0.50 to ≤ 1.00 D	1.16
>1.00 to ≤ 2.00 D	1.17
>2.00 to ≤ 3.00 D	1.01
>3.00 to ≤ 4.00 D	NA
>4.00 to ≤ 5.00 D	NA
>5.00 to ≤ 6.00 D	NA

Table 9-Control Cohort Cylinder Correction Efficacy Stratified by Preoperative Cylinder	
	3 Months
Preoperative Cylinder	Achieved vs. Intended Vector Magnitude Ratio (Achieved/Intended) Mean
ALL	1.03
0 to 0.50 D	NA
>0.50 to ≤ 1.00 D	0.95
>1.00 to ≤ 2.00 D	1.14
>2.00 to ≤ 3.00 D	1.00
>3.00 to ≤ 4.00 D	NA
>4.00 to ≤ 5.00 D	NA
>5.00 to ≤ 6.00 D	NA

Tables 10-Study Cohort and 10-Control Cohort present the accuracy of the sphere and cylinder components in a non-vector analysis, for each postoperative interval. Sphere accuracy is rated against the target sphere while cylinder accuracy is rated against zero.

Table 10-Study Cohort Accuracy of Sphere (To Target) and Cylinder (To Zero) Component (For Eyes Treated for Astigmatic Myopia)			
	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
CYLINDER	N=70	N=69	N=67
<= 0.50 D	91.4 64 88.1%, 94.8%	91.3 63 87.9%, 94.7%	94.0 63 91.1%, 96.9%
<=1.00 D	98.6 69 97.2%, 100%	98.6 68 97.1%, 100%	98.5 66 97.0%, 100%
SPHERE			
± 0.50 D	87.1 61 83.1%, 91.1%	88.4 61 84.6%, 92.3%	91.0 61 87.6%, 94.5%
± 1.00 D	94.3 66 91.5%, 97.1%	94.2 65 91.4%, 97.0%	95.5 64 93.0%, 98.1%

Table 10-Control Cohort Accuracy of Sphere (To Target) and Cylinder (To Zero) Component (For Eyes Treated for Astigmatic Myopia)			
	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
CYLINDER	N=79	N=80	N=73
<= 0.50 D	96.2 76 94.1%, 98.4%	93.8 75 91.0%, 96.5%	97.3 71 95.4%, 99.2%
<=1.00 D	97.5 77 95.7%, 99.2%	96.3 77 94.1%, 98.4%	98.6 72 97.3%, 100%
SPHERE			
± 0.50 D	96.2 76 94.1%, 98.4%	93.8 75 91.0%, 96.5%	94.5 69 87.6%, 94.5%
± 1.00 D	98.7 78 97.5%, 100%	100 80 100%, 100%	100 73 100%, 100%

An analysis of the **postoperative** uncorrected visual acuity (UCVA) to **preoperative** best spectacle corrected visual acuity (BSCVA) after Wavefront-Guided and Standard LASIK is presented in Table 11-Study Cohort and Table 11-Control Cohort. At 3 months, postoperative UCVA was equal to or better than preoperative BSCVA in 81.1% of eyes in the Study Cohort and 83.6% of eyes in the Control Cohort.

Table 11-Study Cohort Postoperative UCVA Compared to Preoperative BSCVA			
	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
	N=182	N=180	N=166
> 2 lines better	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.6 1 0.0%, 1.2%
2 lines better	4.4 8 2.9%, 5.9%	8.9 16 6.8%, 11.0%	9.0 15 6.8%, 11.3%
1 line better	29.7 54 26.3%, 33.1%	29.4 53 26.1%, 32.8%	30.7 51 27.1%, 34.3%
No change	50.6 92 46.8%, 54.3%	42.8 77 39.1%, 46.5%	45.8 76 41.9%, 49.7%
1 line worse	13.2 24 10.7%, 15.7%	17.2 31 14.4%, 20.0%	9.0 15 6.8%, 11.3%
2 lines worse	1.7 3 0.7%, 2.6%	0.6 1[1] 0.0%, 1.1%	3.6 6 2.2%, 5.1%
> 2 lines worse	0.6 1 0.0%, 1.1%	1.1% 2[1] 0.3%, 1.9%	1.2% 2 0.4%, 2.1%

[1] At 3 Months postop, 3 eyes had UCVA that was 2 or more lines worse than the preoperative BSCVA. They are as follows:

1 case	Preoperative BSCVA	20/20	3 Month UCVA	20/40
1 case	Preoperative BSCVA	20/16	3 Month UCVA	20/32
1 case	Preoperative BSCVA	20/20	3 Month UCVA	20/32

Table 11-Control Cohort Postoperative UCVA Compared to Preoperative BSCVA			
	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
	N=176	N=176	N=168
> 2 lines better	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
2 lines better	4.0 7 2.5%, 5.5%	4.0 7 2.5%, 5.5%	6.0 10 4.1%, 7.8%
1 line better	31.8 56 28.3%, 35.3%	32.4 57 28.9%, 35.9%	36.9 62 33.2%, 40.6%
No change	48.9 86 45.1%, 52.6%	47.2 83 43.4%, 50.9%	42.3 71 38.5%, 46.1%
1 line worse	9.1 16 6.9%, 11.3%	11.4 20 9.0%, 13.8%	9.5 16 7.3%, 11.8%
2 lines worse	4.6 8 3.0%, 6.1%	3.4 6[1] 2.0%, 4.8%	2.4 4 1.2%, 3.6%
> 2 lines worse	1.7 3 0.7%, 2.7%	1.7% 3[1] 0.7%, 2.7%	3.0% 5 1.7%, 4.3%

[1] At 3 Months postop, 9 eyes had UCVA that was 2 or more lines worse than the preoperative BSCVA. They are as follows:

1 case	Preoperative BSCVA	20/12.5	3 Month UCVA	20/32
2 cases	Preoperative BSCVA	20/16	3 Month UCVA	20/32
2 cases	Preoperative BSCVA	20/20	3 Month UCVA	20/32
4 cases	Preoperative BSCVA	20/16	3 Month UCVA	20/25

d. Safety Outcomes

The analysis of safety was based on the 180 eyes in the Study Cohort and 176 in the Control Cohort that have had the 3-month examination. The key safety results for this study are presented in Tables 12-Study Cohort and 12-Control Cohort and 13-Study Cohort and 13-Control Cohort, with all adverse events reported in Tables 14-Study Cohort and 14-Control Cohort. Overall the device was deemed reasonably safe.

Table 12-Study Cohort
Summary of Key Safety Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
Safety Variables	N=182	N=180	N=166
Loss of ≥ 2 lines BSCVA	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/40	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=112	N=111	N=99
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%
	N=181	N=179	N=165
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

#For eyes treated for spherical correction

Table 12-Control Cohort Summary of Key Safety Variables Over Time			
	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
Safety Variables	**N=176**	**N=176**	**N=166**
Loss of ≥ 2 lines BSCVA	1.7 3 0.7%, 2.7%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/40	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=97	**N=96**	**N=93**
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%
	N=174	**N=174**	**N=164**
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

#For eyes treated for spherical correction

Table 13-Study Cohort
Summary of Key Safety Variables
at 3 Months (Stratified by Preoperative MRSE)

	0 to 1.0 D % n 95% CI	>1.0 to 2.0 D % n 95% CI	>2.0 to 3.0 D % n 95% CI	>3.0 to 4.0 D % n 95% CI	>4.0 to 5.0 D % n 95% CI	>5.0 to 6.0 D % n 95% CI	>6.0 to 7.0 D % n 95% CI	Cum Total ≤7 D % n 95% CI
Safety Variables	**N=3**	**N=42**	**N=38**	**N=29**	**N=37**	**N=18**	**N=13**	**N=180**
Loss of ≥ 2 lines BSCVA	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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
BSCVA worse than 20/40	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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=3	**N=27**	**N=25**	**N=22**	**N=20**	**N=7**	**N=7**	**N=111**
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%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=3	**N=42**	**N=38**	**N=29**	**N=36**	**N=18**	**N=13**	**N=179**
BSCVA worse than 20/25 if 20/20 or better preoperatively	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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%

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Table 13-Control Cohort Summary of Key Safety Variables at 3 Months (Stratified by Preoperative MRSE)								
	0 to 1.0 D % n 95% CI	>1.0 to 2.0 D % n 95% CI	>2.0 to 3.0 D % n 95% CI	>3.0 to 4.0 D % n 95% CI	>4.0 to 5.0 D % n 95% CI	>5.0 to 6.0 D % n 95% CI	>6.0 to 7.0 D % n 95% CI	Cum Total ≤7 D % n 95% CI
Safety Variables	**N=11**	**N=39**	**N=47**	**N=26**	**N=32**	**N=10**	**N=10**	**N=175**
Loss of ≥ 2 lines BSCVA	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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
BSCVA worse than 20/40	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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=5	**N=22**	**N=25**	**N=20**	**N=15**	**N=3**	**N=6**	**N=96**
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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=11	**N=39**	**N=45**	**N=26**	**N=32**	**N=10**	**N=10**	**N=173**
BSCVA worse than 20/25 if 20/20 or better preoperatively	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%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%

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Tables 14-Study Cohort and 14-Control Cohort present a summary of adverse events. The benchmark for each adverse event is a rate of less than 1% per event.

Table 14-Study Cohort Adverse Events						
Adverse Event	**1 Month**		**3 Months**		**6 Months**	
	%	**n**	**%**	**n**	**%**	**n**
		N=182		**N=180**		**N=166**
Corneal infiltrate or ulcer requiring treatment	0.0	0	0.0	0	0.0	0
Lost, misplaced, or misaligned flap, or any flap/cap problems requiring surgical intervention beyond 1 month	0.0	0	0.0	0	0.0	0
Corneal edema at 1 month or later visible in the slit lamp exam	0.0	0	0.0	0	0.0	0
Any complication leading to intraocular surgery	0.0	0	0.0	0	0.0	0
Melting of the flap of >1 mm sq	0.0	0	0.0	0	0.0	0
Epithelium of > 1 mm2 in the interface with loss of 2 lines or more of BSCVA	0.0	0	0.0	0	0.0	0
Uncontrolled IOP rise with increase of > 5 mm Hg or any reading above 25 mm Hg	0.0	0	0.0	0	0.0	0
Retinal detachment or retinal vascular accident	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	0.0	0	0.0	0	0.0	0

Table 14-Control Cohort Adverse Events						
Adverse Event	1 Month %	n N=176	3 Months %	n N=176	6 Months %	n N=166
Corneal infiltrate or ulcer requiring treatment	0.0	0	0.0	0	0.0	0
Lost, misplaced, or misaligned flap, or any flap/cap problems requiring surgical intervention beyond 1 month	0.0	0	0.0	0	0.0	0
Corneal edema at 1 month or later visible in the slit lamp exam	0.0	0	0.0	0	0.0	0
Any complication leading to intraocular surgery	0.0	0	0.0	0	0.0	0
Melting of the flap of >1 mm sq	0.0	0	0.0	0	0.0	0
Epithelium of > 1 mm2 in the interface with loss of 2 lines or more of BSCVA	0.0	0	0.0	0	0.0	0
Uncontrolled IOP rise with increase of > 5 mm Hg or any reading above 25 mm Hg	0.0	0	0.0	0	0.0	0
Retinal detachment or retinal vascular accident	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	0.0	0	0.0	0	0.0	0

No protocol-defined adverse events occurred during this clinical trial.
One event was reported to FDA and the IRB as adverse events during the follow-up period of this clinical trial. A subject enrolled in the Control Cohort and undergoing traditional LASIK had the axis of astigmatism programmed as 115 degrees instead of the actual 155 degree axis. This led to significant cylinder in

the left eye. Due to the presence of mixed astigmatism, this subject was retreated with another manufacturer's laser system and as a result was discontinued from the clinical investigation.

Table 15-Study Cohort Complications Summary Table Cumulative						
Complications	**1 Month**		**3 Months**		**6 Months**	
	%	**n**	**%**	**n**	**%**	**n**
	(N=182)		**(N=180).**		**(N=166)**	
Corneal edema between 1 week and 1 month after the procedure	0.0	0	0.0	0	0.0	0
Corneal epithelial defect at 1 month or later	0.0	0	0.6	1	1.2	2
Any epithelium in the interface	0.0	0	0.0	0	0.0	0
Foreign body sensations at 1 month or later	0.0	0	0.6	1	1.2	2
Pain at 1 month or later	0.0	0	0.6	1	0.6	1
Ghosting or double images in the operative eye at stability or beyond			0.0	0	0.0	0
Need for lifting and/or reseating of the flap/cap prior to 1 month	0.0	0	0.0	0	0.0	0

Table 15-Control Cohort Complications Summary Table Cumulative						
Complications	**1 Month**		**3 Months**		**6 Months**	
	%	**n (N=176)**	**%**	**n (N=176)**	**%**	**n (N=166)**
Corneal edema between 1 week and 1 month after the procedure	0.0	0	0.0	0	0.0	0
Corneal epithelial defect at 1 month or later	0.0	0	0.0	0	0.0	0
Any epithelium in the interface	0.0	0	0.0	0	0.0	0
Foreign body sensations 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
Ghosting or double images in the operative eye at stability or beyond			0.0	0	0.0	0
Need for lifting and/or reseating of the flap/cap prior to 1 month	0.0	0	0.0	0	0.0	0

Table 16 details changes in patient's responses to survey questions regarding symptoms. As can be seen in the table, in the majority of cases, there was no change in the patient's report of symptoms. Patients completed a questionnaire in which they rated symptoms on a 10 point scale. Results were considered to be "much worse" than preop if the response changed by 7 or more points on the 10 point scale and were considered to be "somewhat worse" if the response changed by 3 to 6 points. Results were considered to be "much better" than preop if the response improved by 7 or more points on the 10 point scale and were considered to be "somewhat better" if the response changed by 3 to 6 points.

Table 16-Study Cohort
Change in Patient Symptoms at 3 Months

	Much Worse %	n	Somewhat Worse %	n	No Change %	n	Somewhat Better %	n	Much Better %	n
	N=180		N=180		N=180		N=180		N=180	
Glare from Bright Lights	0.0	0	7.8	14	67.8	122	22.2	40	2.2	4
Halos	4.4	8	14.4	26	66.7	120	14.4	26	0.0	0
Light Sensitivity	2.2	4	24.4	44	61.1	110	12.2	22	0.0	0
Visual Fluctuations	0.0	0	14.4	26	76.7	138	8.9	16	0.0	0
Night Driving Glare	0.0	0	8.9	16	70.6	127	20.6	37	0.0	0

Table 16-Control Cohort
Change in Patient Symptoms at 3 Months

	Much Worse %	n	Somewhat Worse %	n	No Change %	n	Somewhat Better %	n	Much Better %	n
	N=174		N=174		N=174		N=174		N=174	
Glare from Bright Lights	0.0	0	9.2	16	66.7	116	20.7	36	3.4	6
Halos	3.4	6	17.8	31	60.3	105	17.2	30	1.1	2
Light Sensitivity	0.0	0	14.9	26	64.4	112	19.5	34	1.1	2
Visual Fluctuations	2.3	4	13.8	24	71.3	124	12.6	22	0.0	0
Night Driving Glare	0.0	0	9.2	16	63.2	110	23.0	40	4.6	8

e. Retreatments

A total of 5 eyes (2.7%) in the Study Cohort were retreated with the study laser for overcorrection. No eyes (0.0%) were retreated in the

Control Cohort. Table 17-Study Cohort contains the outcomes for retreated eyes in the Study Cohort.

Table 17-Study Cohort
Summary of Key Safety and Efficacy Variables Over Time for Retreated Eyes

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
Efficacy Variables	**N=4**	**N=3**	**N=1**
UCVA 20/20 or better*	50.0 2 25.0%, 75.0%	100 3 100%, 100%	·0 0 0%, 0%
UCVA 20/40 or better*	100 4 100%, 100%	100 3 100%, 100%	100 1 100%, 100%
	N=3	**N=3**	**N=1**
MRSE ± 0.50 D	100 3 100%, 100%	100 3 100%, 100%	100 1 100%, 100%
MRSE ± 1.00 D	100 3 100%, 100%	100 3 100%, 100%	100 1 100%, 100%
MRSE ± 2.00 D	100 3 100%, 100%	100 3 100%, 100%	100 1 100%, 100%
Safety Variables	**N=3**	**N=3**	**N=1**
Loss of ≥ 2 lines BSCVA	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/40	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=2	**N=2**	**N=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%

*For all eyes minus those intentionally treated for monovision.
#For eyes treated for spherical myopia

f. Wavefront Outcomes

This study prospectively evaluated changes in wavefront (aberrometry) measurements between the two cohorts. Subjects were randomized upon enrollment to the Study (wavefront-guided, aberrometer-based treatment) or Control (wavefront-optimized, phoropter refraction-based treatment) Cohort. Analysis showed that the randomization process successfully resulted in statistically equivalent cohorts for demographics (age, sex), refractive characteristics, BSCVA and wavefront characteristics.

No significant differences were found between the two cohorts for UCVA, MRSE or BSCVA changes. Differences between the Cohorts were found for aberrometry results.

Table 18 shows the mean change in aberrations for the two cohorts. In the Study Cohort, overall higher-order RMS (RMS_H) was unchanged. Trefoil was slightly but significantly reduced. Increases were seen only for secondary astigmatism and 5th and 6th order aberrations. In the Control Cohort, overall RMS_H increased by 12%, and spherical aberration increased by approximately 33%. Increased aberrations were seen for the 4th – 6th order, coma, spherical aberration and secondary astigmatism.

Table 18 (Both Cohorts): Change in aberrations from preoperative values for each cohort at the M6 visit in a paired-eye analysis. Pupil size for wavefront analysis was 6.00 mm.

All Eyes	**6-Month Mean Value**					
Study Cohort: N = 146	**Study Cohort**			**Control Cohort**		
Control Cohort: N = 149	**µm**	**%**	**p****	**µm**	**%**	**p****
Total RMS	0.640	-86%	<0.01	0.775	-82%	<0.01
Higher Order RMS	0.322	3%	NS	0.362	12%	<0.01
2nd Order	0.536	-88%	<0.01	0.662	-84%	<0.01
3rd Order	0.241	-3%	NS	0.275	8%	NS
4th Order	0.167	9%	NS	0.188	20%	<0.01
5th Order	0.085	34%	<0.01	0.086	19%	<0.01
6th Order	0.067	22%	<0.01	0.069	18%	0.01
Coma	0.140	6%	NS	0.150	16%	<0.05
Trefoil	0.083	-17%	<0.01	0.108	-2%	NS
Quatrefoil	0.047	5%	NS	0.047	-10%	NS
Spherical Aberration (C12)	0.119	5%	NS	0.147	35%	<0.01
Spherical Aberration (C12 + C24)	0.088	6%	NS	0.107	33%	<0.01
Secondary Astigmatism	0.051	37%	<0.01	0.047	17%	<0.05

*p value refers to change in mean from preoperative level (Student's t-test).

Changes in RMS_H were dependent on the preoperative RMS_H amounts. Table 19 presents the change in RMS_H stratified by the preoperative RMS_H amounts. Mean preoperative RMS_H of ≤ 0.3 μm was associated with a slight increase in postoperative RMS_H in both Cohorts. Higher levels of preoperative RMS_H (>0.3 μm) experienced a mean decrease in RMS_H in the Study Cohort, but not the Control Cohort. Table 20 shows the rates of increase, no change and decreased RMS_H for each cohort. Differences between the cohorts become larger as the preoperative RMS_H level increases.

Table 19-Study Cohort: Mean (SD) values of preoperative and postoperative RMS_H values, stratified by the preoperative RMS_H amount. The Delta RMS_H columns show the mean and SD change in RMS_H from a paired-analysis, where the preoperative value is subtracted from the postoperative value for each eye, and then the results averaged. The probability compares the mean preoperative and postoperative values using a Student's t-test. Note the significant change in RMS_H values for most groups, with the first two groups tending to increase the mean RMS_H values and the bottom two tending to show improved (lower) RMS_H values.

Study Cohort		Preop RMSH		Postop RMSH		Delta RMSH (Paired)		
Range	N	Mean	SD	Mean	SD	Mean	SD	P*
<=0.2 μ	14	0.18	0.01	0.27	0.09	0.06	0.10	<0.01
>0.2 to 0.3 μ	70	0.25	0.03	0.33	0.13	0.07	0.13	<0.01
>0.3 to 0.4 μ	49	0.35	0.03	0.32	0.12	-0.04	0.14	NS
>0.4 to 0.5 μ	15	0.44	0.02	0.32	0.12	-0.12	0.14	<0.01
>0.5 μ	10	0.55	0.05	0.33	0.11	-0.22	0.16	<0.01

*Comparison of postoperative mean value to preoperative mean value, using a Student's T-Test.

Table 19-Control Cohort: Same data as shown in Table 19 but for the Control Cohort. As with the Study Cohort, the mean postoperative RMS_H tended to increase for the two groups with the lowest preoperative RMS_H values. However, unlike the Study Cohort, the mean values for the Control Cohort did not significantly improve for the three groups with higher preop RMS_H values. Notably, they were not increased in this range, either.

Control Cohort		Preop RMSH		Postop RMSH		Delta RMSH (Paired)		
Range	N	Mean	SD	Mean	SD	Mean	SD	P*
<=0.2 μ	21	0.17	0.03	0.27	0.09	0.07	0.13	<0.01
>0.2 to 0.3 μ	65	0.26	0.03	0.33	0.09	0.05	0.13	<0.01
>0.3 to 0.4 μ	46	0.35	0.03	0.39	0.10	0.03	0.11	<0.05
>0.4 to 0.5 μ	20	0.46	0.02	0.43	0.10	-0.01	0.11	NS
>0.5 μ	11	0.57	0.08	0.53	0.07	-0.03	0.12	NS

*Comparison of postoperative mean value to preoperative mean value, using a Student's T-Test.

Table 20 (Both Cohorts): Rates of Decrease, No Change and Increase of RMS_H from preoperative to postoperative, in a paired-eye analysis. The All Eyes row shows similar results for both Cohorts for increases in RMS_H, and show that 23% in the Study Cohort and 7% of the Control Cohort have decreased higher-order aberrations after surgery. However the stratified analysis shows that eyes with higher amounts of preoperative RMS_H tend to have decreased RMS_H values in the Study Cohort, but not in the Control Cohort, after surgery.

	Study Cohort				Control Cohort			
Range	N	Decrease	No Change	Increase	N	Decrease	No Change	Increase
<=0.2 μ	14	0%	57%	43%	21	0%	67%	33%
>0.2 to 0.3 μ	70	6%	57%	37%	65	0%	65%	35%
>0.3 to 0.4 μ	49	29%	57%	14%	46	4%	76%	20%
>0.4 to 0.5 μ	15	67%	27%	7%	20	35%	50%	15%
>0.5 μ	10	90%	10%	0%	11	18%	73%	9%
All Eyes	158	23%	51%	25%	163	7%	67%	26%

*No Change indicates a delta RMS_H of 0.1 μm or less

Changes in RMS_H were also dependent on the treatment amounts. Correlation of preoperative spheroequivalent with postoperative RMS_H was 0.63 in the Study Cohort and 0.35 in the Control Cohort, using the M6 RMS_H data. As seen in Table 21, the higher correlation in the Study Cohort was due to the ability of Wavefront-Guided LASIK to reduce RMS_H in lower myopes, while RMS_H was increased in eyes undergoing treatment for higher spheroequivalent errors in both Cohorts.

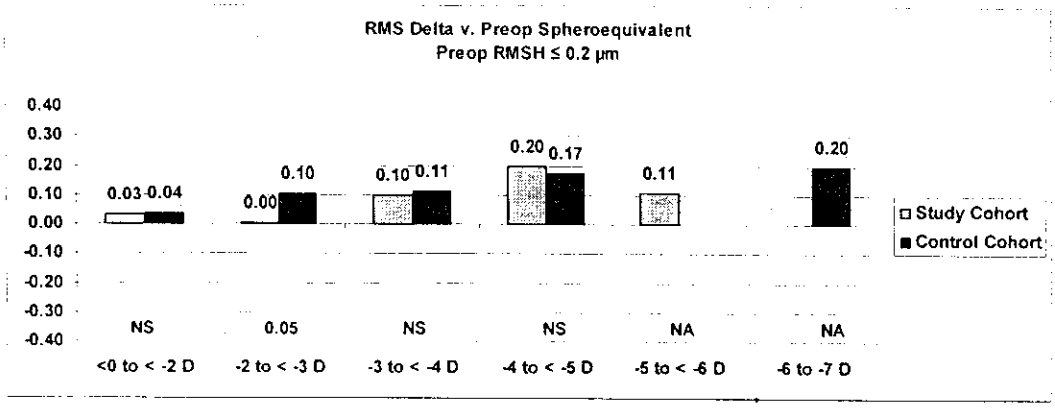
Table 21: Delta RMS_H v. Preoperative Spheroequivalent (Paired-Eye Analysis)

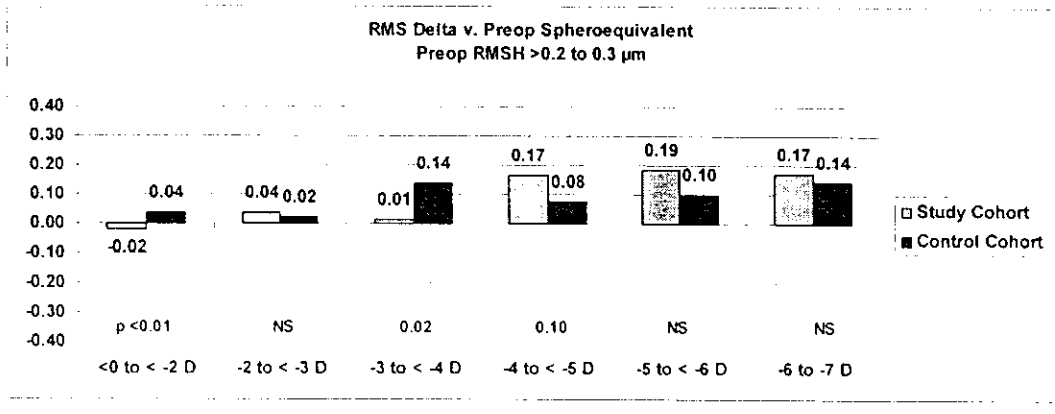
	Study Cohort Delta RMSH Preop to M6			Control Cohort Delta RMSH Preop to M6		
Preop S.E. Range	N	Mean	SD	N	Mean	SD
<0 to < -2 D	37	-0.06	0.09	44	0.03	0.08
-2 to < -3 D	32	-0.03	0.11	39	0.00	0.08
-3 to < -4 D	22	-0.06	0.13	29	0.10	0.11
-4 to < -5 D	34	0.07	0.19	29	0.04	0.11
-5 to < -6 D	19	0.10	0.14	10	0.07	0.14
-6 to -7 D	14	0.08	0.13	12	0.04	0.10

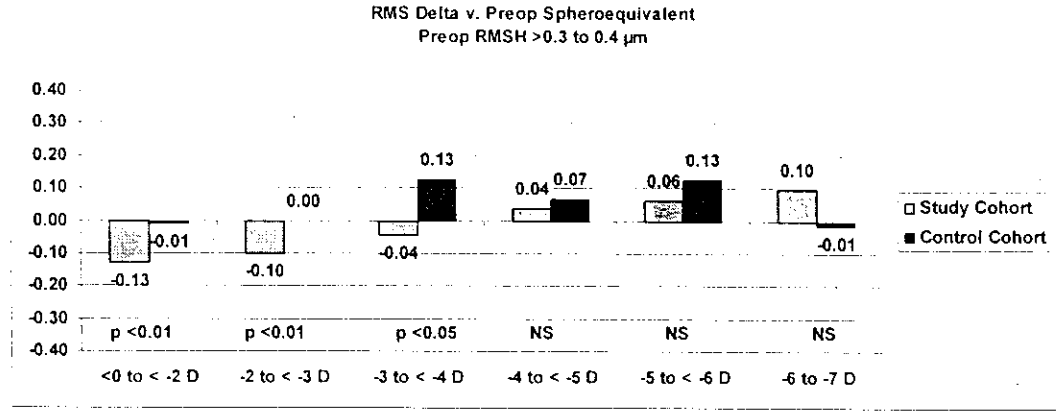
Analysis of the combined effects of preoperative RMS_H and preoperative spheroequivalent (Figure 1) showed that eyes with very low preoperative RMS_H ($\leq$0.3 μm) had equivalent postoperative RMS_H values in both Cohorts. Eyes in the Study Cohort had lower postoperative RMS_H than eyes in the Control Cohort if the preoperative RMS_H was >0.3 μm to $\leq$ 0.4 μm in spheroequivalent treatments up to 4 D. Postoperative RMS_H results were the same for the two Cohorts with higher treatment amounts.

Eyes in the Study Cohort had lower postoperative RMS_H values than in the Control Cohort if the preoperative RMS_H value was >0.4 μm throughout the 7 D spheroequivalent treatment range.

Figure 1: Combined effect of preoperative RMSH and preoperative spheroequivalent on aberrometry changes.


RMS Delta v. Preop Spheroequivalent
Preop RMSH ≤ 0.2 µm
0.40
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
-0.40
0.03 0.04
0.00 0.10
0.10 0.11
0.20 0.17
0.11
0.20
Study Cohort
Control Cohort
NS
0.05
NS
NS
NA
NA
<0 to < -2 D
-2 to < -3 D
-3 to < -4 D
-4 to < -5 D
-5 to < -6 D
-6 to -7 D


RMS Delta v. Preop Spheroequivalent
Preop RMSH >0.2 to 0.3 µm
0.40
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
-0.40
-0.02 0.04
0.04 0.02
0.01 0.14
0.17 0.08
0.19 0.10
0.17 0.14
Study Cohort
Control Cohort
p <0.01
NS
0.02
0.10
NS
NS
<0 to < -2 D
-2 to < -3 D
-3 to < -4 D
-4 to < -5 D
-5 to < -6 D
-6 to -7 D


RMS Delta v. Preop Spheroequivalent
Preop RMSH >0.3 to 0.4 µm
0.40
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
-0.40
-0.13 -0.01
-0.10 0.00
-0.04 0.13
0.04 0.07
0.06 0.13
0.10 -0.01
Study Cohort
Control Cohort
p <0.01
p <0.01
p <0.05
NS
NS
NS
<0 to < -2 D
-2 to < -3 D
-3 to < -4 D
-4 to < -5 D
-5 to < -6 D
-6 to -7 D

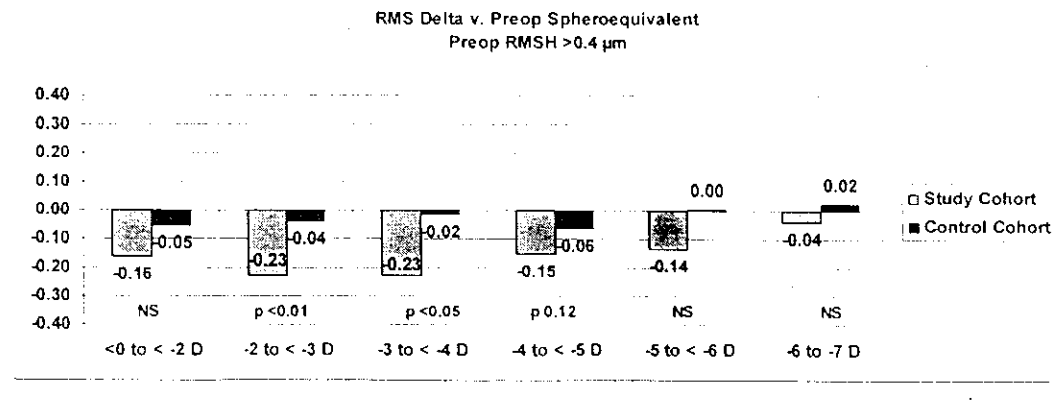

RMS Delta v. Preop Spheroequivalent
Preop RMSH >0.4 µm
0.40
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
-0.40
-0.16 -0.05
-0.23 -0.04
-0.23 -0.02
-0.15 -0.06
-0.14 0.00
-0.04 0.02
Study Cohort
Control Cohort
NS
p <0.01
p <0.05
p 0.12
NS
NS
<0 to < -2 D
-2 to < -3 D
-3 to < -4 D
-4 to < -5 D
-5 to < -6 D
-6 to -7 D

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Table 22 presents the treatment recommendations based on these findings. In general, lower treatments with lower RMS_H values are recommended to have Wavefront-Optimized LASIK, while higher RMS_H values are recommended for Wavefront-Guided LASIK. Mid-range RMS_H values may benefit from with Wavefront-Optimized LASIK or Wavefront-Guided LASIK, depending on the spheroequivalent treatment amount.

Table 22: Treatment recommendation based on preoperative spheroequivalent and RMS_H values. (WG = Wavefront-Guided LASIK, WO = Wavefront-Optimized LASIK, WG/WO = both equally safe and effective)

	Spheroequivalent Treatment Range					
Preop RMS_H	**-1 to < -2 D**	**-2 to < -3 D**	**-3 to < -4 D**	**-4 to < -5 D**	**-5 to < -6 D**	**-6 to < -7 D**
<=0_2 μ	WG/WO	WG/WO	WG/WO	WG/WO	WG/WO	WG/WO
>0_2 to 0_3 μ	WG/WO	WG/WO	WG/WO	WG/WO	WG/WO	WG/WO
>0_3 to 0_4 μ	WG	WG	WG	WG/WO	WG/WO	WG/WO
>0_4 μ	WG	WG	WG	WG	WG	WG

Additional Findings:

- Agreement of the preoperative manifest spheroequivalent and preoperative aberrometer spheroequivalent within ± 0.50 D was 97.6%
- Postoperative RMS_H was found to have a significant effect on postoperative UCVA, especially at the 20/12.5 level in both cohorts (Figure 2).
- Agreement of the preoperative manifest spheroequivalent and preoperative aberrometer spheroequivalent within ± 0.50 D was 84.1%
- Contrast sensitivity tests, low-contrast visual acuity and scores for subjective patient symptoms were similar for the two cohorts overall. No significant differences were seen for these tests based on pre- or postoperative RMS_H amounts. The only difference was seen for the subjective question about glare with night driving, where the Study Cohort outperformed the Control Cohort at both the pre- and postoperative intervals.
- The proportional contribution of the various aberrations (coma, trefoil, spherical aberration) was similar preoperatively and postoperative for both Cohorts. Neither treatment modality resulted in disproportionate increases in any single aberration, nor was spherical aberration disproportionately increased in the Control Cohort with Wavefront-Optimized LASIK.
- Spherical Aberration (Figure 3)

- For the Control Cohort, postoperative spherical aberration (C12) was strongly correlated with preoperative amounts (R = 0.71 using the M6 data). This indicates that Wavefront-Optimized LASIK had little effect on spherical aberration. The mean preoperative amount for C12 in the Control Cohort was 0.09 ± 0.11 μm, the mean postoperative amount was 0.14 ± 0.10 μm.
- For the Study Cohort, postoperative spherical aberration was weakly correlated with the preoperative amounts (R = 0.36). Mean preoperative C12 for the Study Cohort was 0.09 ± 0.11 μm, mean postoperative amount was 0.11 ± 0.8 μm.

Figure 2 (Both Cohorts): Postoperative UCVA 20/12.5 stratified by postoperative RMS_H levels in eyes with refractive errors within 0.25 D of plano. No significant differences were seen at the 20/20 or 20/16 levels (not shown). At the 20/12.5 level, UCVA in the both cohorts is significantly worse in eyes that had higher amounts of postoperative RMS_H, indicating that postoperative aberrations may affect UCVA, even in eyes with plano outcomes.

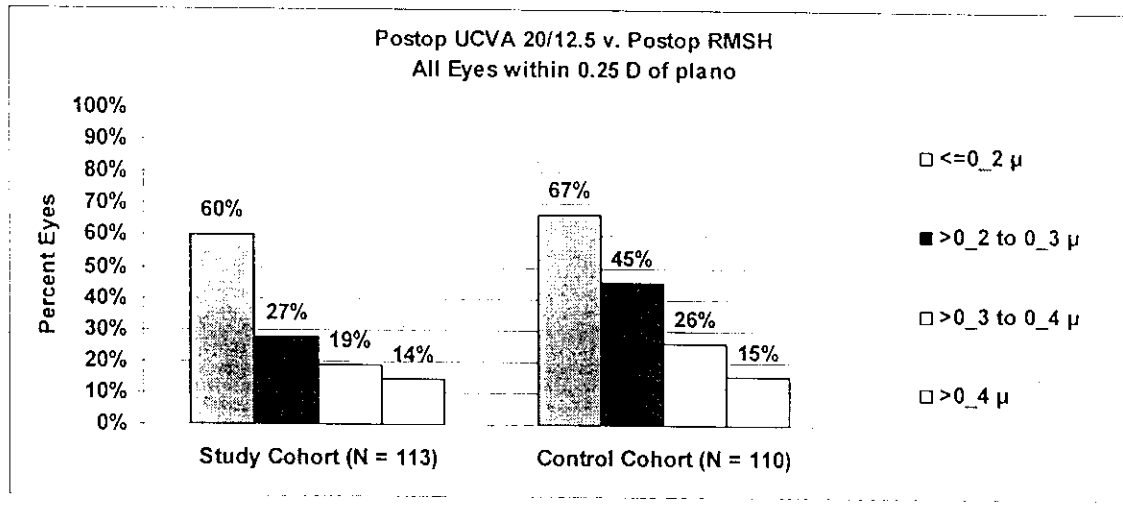
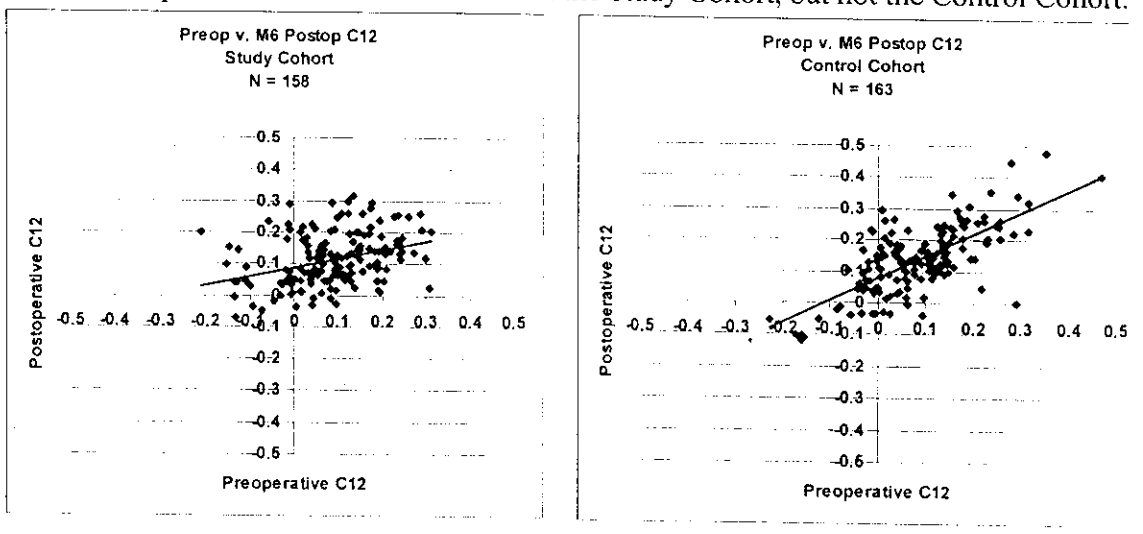


Figure 3: Pre- v. M6 Postoperative Spherical Aberration (C12). Reductions of higher amounts of spherical aberration were seen in the Study Cohort, but not the Control Cohort.



g. Contrast Sensitivity and Low Contrast Acuity

Low contrast acuity (LCA) was measured using the Vector Vision CSV 1000 ETDRS 10% charts, with the best-corrected refraction in place. Results are shown in Table 23. No significant mean differences were seen in either overall cohort from pre- to postoperative.

Table 23 (Both Cohorts): Low Contrast Acuity for all eyes

		Study Cohort				Control Cohort		
	N	Mean	SD	p	N	Mean	SD	p
PREOP	188	20/29.6	0.9 Lines	-	186	20/30.3	1.1 Lines	-
M3	180	20/27	1.1 Lines	NS	176	20/27.6	1.1 Lines	NS
M6	166	20/27.6	1.1 Lines	NS	166	20/28.3	1.2 Lines	NS

Table 24 shows the change in LCA scores stratified by the preoperative RMS_H levels. All groups improved slightly. Significant changes were seen in the mid-level RMS_H group for the Control Cohort, and the highest level RMS_H group in the Study Cohort.

Table 24-Study Cohort: Low Contrast Acuity at preoperative and M6 intervals, stratified by preoperative RMS_H levels (paired-eye analysis).

Study Cohort		Preoperative		M6 Visit		
Preop RMSH	N	Mean	SD	Mean	SD	p
<=0.2 μ	23	20/28.5	1 Line(s)	20/26.7	1.1 Line(s)	NS
>0.2 to 0.4 μ	111	20/29	0.9 Line(s)	20/27.8	1.1 Line(s)	NS
>0.4 μ	24	20/32.6	0.7 Line(s)	20/29.1	1.1 Line(s)	<0.03

Table 24-Control Cohort: Low Contrast Acuity at preoperative and M6 intervals, stratified by preoperative RMS_H levels (paired-eye analysis).

Control Cohort		Preoperative		M6 Visit		
Preop RMSH	N	Mean	SD	Mean	SD	p
<=0.2 μ	25	20/28.5	0.7 Line(s)	20/26.9	1.2 Line(s)	NS
>0.2 to 0.4 μ	106	20/29.7	1.1 Line(s)	20/27	1.1 Line(s)	<0.05
>0.4 μ	32	20/33.8	1.2 Line(s)	20/32.4	1.3 Line(s)	NS

Contrast Sensitivity was measured using the Vector Vision CSV 1000E at 3, 6, 12 and 18 cycles per degree. Changes of 0.3 log units or more at 2 or more spatial frequencies are interpreted as significant. Rates were similar in the two cohorts and neither cohort experienced a mean decrease in Contrast Sensitivity.

With the Allegretto Laser for spherical and spherocylindrical myopia up to 7 D sphere and 3 D cylinder, no symptomatic increases in aberrations were seen with either Wavefront-Guided LASIK or Wavefront-Optimized LASIK.

h. Factors Associated with Outcomes

An extensive analysis was performed to determine what influences, if any, affected outcomes in this series. Potential influences examined include gender, race, age, history of contact lens wear, effect of the preoperative refraction, preoperative keratometry, pupil diameter, laser room temperature and humidity, and the keratome used to make the flap. Because this was a LASIK-only study, epithelial factors applicable to surface procedures were not considered. As all eyes in this series were targeted for distance outcomes, monovision analysis could not be performed.

The results of the analysis mirrored prior studies (PMA 020050 and PMA 030008) with the device used in this study, the WaveLight Allegretto Wave Excimer Laser. No detectable effect was found for any potential influence (sex, age, prior contact lens history, preoperative refraction, preoperative keratometry, pupil diameter, laser room temperature and humidity or keratome) on major outcomes targets.

It is worthwhile to note that some of these influences were controlled within relatively narrow tolerances – e.g., laser room temperature and humidity. The conclusion should not be drawn that these potential influences cannot affect outcomes, nor should it be said that the major targets completely describe outcomes.

As noted above, eyes the Study Cohort were more likely to experience decreases in RMS_H values than in the Control Cohort. Eyes with higher preoperative RMS_H were most likely to experience decreased postoperative RMS_H values.

i. Patient Satisfaction

Subjects were asked to complete a patient questionnaire preoperatively and at 3-months, 6-months, and 1-year postoperatively. Responses were made by placing a mark or an "x" through the provided line. Each end of the line was marked with opposing answers such as "Never" versus "All the Time". A mark on either end of the bar represented an extreme answer (never on one end, all the time on the other end) and a mark in the middle indicated a scaled response between the extremes.

In the Study Cohort, patient reports of glare from bright lights and night driving glare improved after LASIK and in the Control Cohort patient reports of glare from bright driving, light sensitivity and night driving glare improved after LASIK.

Table 26-Study Cohort Patient Symptoms												
	Preoperative						3 Months					
	None-Mild		Moderate		Marked-Severe		None-Mild		Moderate		Marked-Severe	
	%	n	%	n	%	n	%	n	%	n	%	n
	N=188		N=188		N=188		N=180		N=180		N=180	
Glare from Bright Lights	52.1	98	27.7	52	20.2	38	60.0	108	31.1	56	8.9	16
Halos	63.8	120	23.4	44	12.8	24	66.7	120	17.8	32	15.6	28
Light Sensitivity	62.8	118	26.6	50	10.6	20	52.2	94	30.0	54	17.8	32
Visual Fluctuations	86.2	162	11.7	22	2.1	4	80.0	144	14.4	26	5.6	10
Night Driving Glare	56.9	107	25.0	47	18.1	34	68.9	124	22.2	40	8.9	16

Table 26-Control Cohort Patient Symptoms												
	Preoperative						3 Months					
	None-Mild		Moderate		Marked-Severe		None-Mild		Moderate		Marked-Severe	
	%	n	%	n	%	n	%	n	%	n	%	n
	N=186		N=186		N=186		N=174		N=174		N=174	
Glare from Bright Lights	47.3	88	31.2	58	21.5	40	60.9	106	29.9	52	9.2	16
Halos	63.4	118	18.3	34	18.3	34	54.6	95	31.0	54	14.4	25
Light Sensitivity	59.1	110	23.7	44	17.2	32	64.4	112	26.4	46	9.2	16
Visual Fluctuations	81.7	152	11.8	22	6.5	12	78.2	136	18.4	32	3.5	6
Night Driving Glare	46.2	86	28.0	52	25.8	48	60.9	106	32.2	56	6.9	12

Subjects were also asked how often they wear glasses or contact lenses to see far away. In the Study Cohort 96.8% (182/188) said that they "always" wear correction preoperatively while this decreased to 5.6% (10/180) at 3 months and 1.8% (3/163) at 6 months. In the Control Cohort 95.7% (178/186) said that they "always" wear correction preoperatively while this decreased to 2.3% (4/174) at 3 months and 0.0% (0/165) at 6 months.

Subjects were also asked to rate the quality of their vision without correction. In the Study Cohort, preoperatively 2.1% (4/188) rated their vision quality as good or excellent and postoperatively this improved to 94.5% (170/180) at 3-months. In the Control Cohort, preoperatively 2.2% (4/186) rated their vision quality as good or excellent and postoperatively this improved to 92.0% (160/174) at 3-months.

Subjects were asked if they would recommend the surgery to a friend or relative and at 3-months 88.9% (160/180) in the Study Cohort and 87.4% (152.174) in the Control Cohort said they would highly recommend it.

Subjects were asked to rate the quality of their distance vision now without glasses compared with their vision before surgery with their glasses. In the Study Cohort, 90.0% (162/180) said their vision was somewhat or much better without glasses after surgery than with glasses before surgery while in the Control Cohort 87.4% (152/174) had this response.

j. Device Failures

There were no device failures reported during this study.

XI. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The data in this application support reasonable assurance of the safety and effectiveness of these devices when used in accordance with the approved indications for use.

XII. PANEL RECOMMENDATIONS

In accordance with the provision of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

FDA issued an approval order on July 26, 2006.

The applicant's manufacturing facility was inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

- Directions for use: See the labeling.
- Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.
- Postapproval Requirements and Restrictions: See approval order.