WaveLight®

Addendum

ALLEGRETTO WAVE ™

Scanning Spot LASIK Laser System

Procedure Manual
Wavefront-Guided Treatments
Information for professional use

WaveLight AG
Am Wolfsmantel 5
91058 Erlangen, Germany

USING THE ADDENDUM ALLEGRETTO WAVE™ PROCEDURE MANUAL A-CAT (WAVEFRONT-GUIDED TREATMENTS)

This manual provides information for the intended clinical use of the ALLEGRETTO WAVE™ Laser System for wavefront guided treatments.

This manual provides only information that is specific for wavefront guided LASIK. Refer to the Operator's Manual of the Laser Console, to its addendums, its Procedure Manual and to the user's manuals of the approved accessories for further information.

Carefully read and understand this manual and all related documents and instructions before using the ALLEGRETTO WAVE Laser System for performing wavefront guided LASIK treatments.

Observe all warnings, precautions and contra-indications as described in these documents.

Do not perform adjustments and procedures other than those described in these documents. Failure to do so may result in harm to the patient and / or user.

Consult the Table of Contents, Appendices or Index for specific information.

If you have questions that are not addressed in the manuals, contact:

WaveLight Inc.
46040 Center Oak Plaza
Sterling, VA 20166,
USA

Contact
Toll Free: 1-866-WAVELIGHT
Phone: 571.434.8500
Fax: 571.434.8180

Email
sterling@wavelight-laser.com

Internet
www.wavelight-laser.com

TYPOGRAPHICAL CONVENTIONS

The following conventions are used in this manual for Warnings, Precautions and Notes:

WARNING

A Warning alerts the user to potential serious outcomes to the patient or the user.

CAUTION

Precautions alert the user to exercise special care necessary for the safe and effective use of the device.

NOTE

Notes provide user with helpful or supplementary information.

NOTICE TO USERS

RESTRICTIONS BY US FEDERAL LAW

CAUTION

US Federal law restricts this device to sale by or on the order by a physician or licensed eye care practitioner.

US Federal law restricts the use of this device to practitioners who have been trained in its operation, test and calibration and who have experience in the surgical management and treatment of refractive errors of the human eye.

RESTRICTIONS BY MANUFACTURER

There are no rightful claims to system upgrades in the event of the introduction of product improvements based on new technological developments.

CAUTION
Other Manuals

This addendum is only valid in conjunction with related manuals.
Read and understand this addendum and all related manuals of the Laser System and its approved accessories before starting to use the ALLEGRETTO WAVE Laser System!

CAUTION

The system user alone is responsible for having sufficient medical knowledge for carrying out all surgical procedures!

This page intentionally left blank.

TABLE OF CONTENT

page

62

page

This page intentionally left blank!

1. SAFETY OF WAVEFRONT-GUIDED TREATMENTS

The wavefront-guided LASIK procedure requires accurate and reliable data from the wavefront examination. Every step of every wavefront measurement that may be used as the basis for a wavefront-guided LASIK procedure must be validated by the user.

Inaccurate or unreliable data from the wavefront examination will lead to an inaccurate treatment.

2. SYSTEM DESCRIPTION

2.1. Device Description (A-CAT Option)

The ALLEGRETTO WAVE™ Laser System is able to perform customized LASIK treatment according to data provided by WaveLight's 'ALLEGRO Analyzer' if the 'A-CAT' option is enabled. These procedures are called 'wavefront-guided' or 'A-CAT' (Aberration-guided Custom Ablation Treatment) treatments.

The ALLEGRO Analyzer collects wavefront data from the eye. Collected data can be transferred to the notebook computer of the ALLEGRETTO WAVE™ Laser System via media, such as floppy, where it is used for planning and carrying out wavefront-guided treatments of the eye.

Note that the treatment planning function of the Notebook Portal Software for wavefront guided treatments (A-CAT option) requires specific licensing of this software. This involves authorization for specific ALLEGRO Analyzers and ALLEGRETTO WAVE™ laser devices. Devices that have not been authorized cannot be used for wavefront guided treatments.

2.2. Treatment Description A-CAT Option

A wavefront guided treatment uses a tissue ablation profile based upon the eye's individual optical errors. Errors are not limited to just spherical and astigmatic errors, they also include the eye's higher order aberrations as well as tilt. Therefore, a wavefront guided treatment represents a higher level of customization than a wavefront-optimized LASIK treatment, which is based on the eye's refraction, and K-readings. Such treatments are often called 'Standard', 'Classic' or 'Traditional' LASIK.

3. INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS AND ADVERSE EVENTS

3.1. Indications for Use

The ALLEGRETTO WAVE™ Laser System is indicated for use in wavefront-guided laser assisted in situ keratomileusis (LASIK) treatments:

- 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 ≤ 0.5 D preoperative spherical equivalent shift over one year prior to surgery.

3.2. Contraindications

Wavefront-guided LASIK treatments are contraindicated in:

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

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

3.3. Warnings

Wavefront-guided LASIK treatment is not recommended for persons who have any of the following:

- Systemic diseases likely to affect wound healing, such as connective tissue disease, insulin dependent diabetes, severe atopic disease or an immunocompromised status
- A history of herpes simplex or herpes zoster keratitis
- Significant dry eye that is unresponsive to treatment
- Severe allergies
- Unreliable preoperative wavefront examination that precludes wavefront-guided treatment.

3.4. Precautions

3.4.1. General

Safety and effectiveness of the ALLEGRETTO WAVE™ Laser System for wavefront guided treatments has not been established for patients:

- With progressive myopia and/or astigmatism, ocular disease, previous corneal or intraocular surgery, or trauma in the ablation zone
- With corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage
- With residual corneal thickness after ablation of less than 250 microns (due to an increased risk for corneal ectasia)
- With pupil sizes below 7.0 mm under mydriasis
- With history of glaucoma or ocular hypertension of > 23 mm Hg
- Taking the medication sumatriptan succinate (Imitrex®[3])
- Under 18 years of age

[3] Imitrex® is a registered trademark GlaxoSmithKline Inc.

68

- Over the long term (more than 12 months after surgery)
- With media problems, corneal, lens and/or vitreous opacities including, but not limited to cataract
- With iris problems including, but not limited to, coloboma and previous iris surgery compromising proper eyetracking
- Taking medications likely to affect wound healing including, but not limited to, antimetabolites
- For treatment targets different from emmetropia (plano) in which the wavefront-calculated defocus (spherical term) has been adjusted; additionally, physician adjustment of wavefront-calculated defocus may negate the potential benefits of the wavefront-guided procedure to reduce higher order aberrations. You should discuss with your patient the potential risks and benefits associated with treatment targets different from emmetropia.

Pupil sizes should be evaluated under mesopic illumination conditions. Effects of treatment on eyes under poor illumination cannot be predicted prior to surgery. Some patients may find it more difficult to see in such conditions as very dim light, rain, fog, snow and glare from bright lights. This has been shown to occur more frequently in the presence of residual refractive error and perhaps in patients with pupil sizes larger than the optical zone size.

Preoperative evaluation for dry eyes must be performed. Patients should additionally be advised of the potential risk for dry eyes after any LASIK treatment (including after wavefront guided treatments).

3.4.2. Patient Selection

In addition to previously described contraindications, warnings and general precautions, the following points must be considered to identify good candidates for wavefront guided treatments and to get sufficient information for the treatment plan.

The following examinations must have been performed prior to the treatment:

- A complete baseline exam including, but not limited to, cycloplegic refraction within 60 days prior to surgery is necessary.
- A slit lamp exam has to be performed. The status of the lens has to be evaluated to ensure that neither nuclear sclerosis nor other lens opacities are present. These opacities may adversely affect final result.
- Dilated fundus exam by indirect ophthalmoscopy has to be performed, as retinal pathology is more likely in patients with myopia.
- Optical nerve and intraocular pressure have to be examined, as glaucoma is more common in myopic than emmetropic patients. If elevated pressure or signs of glaucomatous damage are found, topical steroids should be used only under careful medical supervision or the patient should not be treated.
- In order to exclude corneal abnormalities, videokeratography (topography) is essential.
- Wavefront measurements have to be performed with the ALLEGRO Analyzer in order to provide necessary wavefront data for the treatment plan.

For contact lens wearers, the following must additionally be considered:

- Contact lens wearers must discontinue wearing hard or gas permeable lenses for at least 3 weeks and soft lenses for at least 3 days **prior to preoperative evaluation**.

- Contact lens wearers must also discontinue wearing hard or gas permeable lenses for at least 3 weeks and soft lenses for at least 3 days **prior to surgery**.

The patients must meet certain general requirements for the treatment:

- The patient must be able to lie flat in a supine position

- Topical or local anesthesia must be tolerated.

- The patient must be able to fixate steadily.

- The patient must be able to understand and give the informed consent and sign the consent form.

The patient must be informed about and understand all alternatives to the wavefront guided LASIK treatment for correcting myopia and/or astigmatism: with glasses or contact lenses, or other surgical procedures such as classic LASIK, radial keratotomy, automated lamellar keratoplasty or clear lens exchange.

Additionally patients should be instructed not to wear makeup at the day of surgery, because this poses risk for contamination of the stromal interface. Patients must not use perfumes, aftershave, Eau de Cologne or other substances applied to the skin containing alcohol at that day.

3.4.3. Wavefront Examination

The wavefront guided treatment is completely reliant on accurate and reliable wavefront examination data.
For this reason, all wavefront examinations have to be performed with great care. Only well-trained personnel shall perform, validate and export examinations, according to instructions given in the ALLEGRO Analyzer manuals and in this procedure manual.

Pay attention to the following during the wavefront examination with ALLEGRO Analyzer:

- Enter and check all patient data carefully.
- Enter the patient's manifest refraction and K-readings correctly, as they will be transferred to the laser and provided as default values. They will be used if a standard LASIK treatment will be performed after having started planned a wavefront guided treatment for the same eye.
- Make sure that the eye to be examined has not had applanation tonometry or contact pachymetry during 12 hours prior to the wavefront examination.
- The eye must be dilated to ensure that the pupil is sufficiently large. A proper tear film is essential for good image contrast. Use only artificial tears that are recommended by WaveLight.
- Instruct the patient about what she/he has to do, what she/he and should avoid and what she/he will notice during examination.

Perform wavefront examination as well as image and data validation according to the ALLEGRO Analyzer manuals and the validation checklist provided in the appendix of this manual. Examination procedure steps and validation checkpoints shall include, but are not limited to the following:

- Confirm the proper head alignment (0°-Axis) with the 'eye-to-eye test'
- Double-check the eye actually measured with the eye identifier shown on the device screens.
- Apply fogging to rule out possible accommodation capabilities
- Check the centering and focusing of the aberrometer on the pupil.
- Check the captured pupil image (the eyelid must not block the pupil and the pupil's margin must be marked properly).

- Check the obtained retinal images for good spot contrast and the image analysis for proper spot detection and marking. False spot detection leads to unreliable or wrong wavefront maps and treatment plans.

- Compare the simulated phoropter refraction of wavefront examination with patient's manifest refraction. Differences may indicate an unreliable wavefront map or accommodation during measurement.

Multiple wavefront examinations of each eye are recommended to ensure reproducibility and to identify possible examination outliers.

CAUTION
Wavefront Examination Use

All wavefront examinations have to pass validation checks for wavefront-guided procedures. Use of inaccurate or unreliable examinations will lead to unreliable or inaccurate treatments.
All data entered at the examination device (patient data, refraction data, keratometric data) must be accurate. This data will be transferred and used at the Notebook Portal Software for treatment plans and their validation.

3.4.4. Data Transfer

Use formatted, virus-free media, such as floppy disk to transfer treatment data from the ALLEGRO Analyzer to the ALLEGRETTO WAVE™ Laser System. Follow the instructions in the appropriate manuals and their addendums.

3.4.5. Laser Preparation

- Transfer treatment data and entered patient and eye data from the ALLEGRO Analyzer to the ALLEGRETTO WAVE™ Laser System.

- Verify the transferred examination data is correct and complete any additional entries.

- Double-check with the patient and assisting personnel to ensure that there are no possible restrictions for the treatment. It is the sole responsibility of the operating surgeon to ensure that all data is accurate and that the treatment can be safely carried out.

3.4.6. Patient Preparation

When preparing the patient for the treatment, pay attention to the following points:

- Ensure that the data on the laser matches the patient and eye to be treated. Patient and eye data will show on the laser LCD screen.
- Pupil size for treatment should be within 2 mm of the size during the wavefront examination. Medications likely to dilate the pupil should be administered with careful supervision prior to surgery, as the Analyzer's eyetracker will not be able to track pupils of more than 8.0 mm diameter.

3.4.7. Procedure

Ablation Depth and Ablation Zone
The area of the deepest ablation as well as shape and size of the Ablation Zone may differ from the general pattern of ALLEGRETTO WAVE™ standard myopic LASIK treatments.

The Notebook Portal Software provides a graphical display to check value and location of the highest ablation depth as well as shape and size of the overall ablation. 'Hotter' colors show areas of deeper ablation.

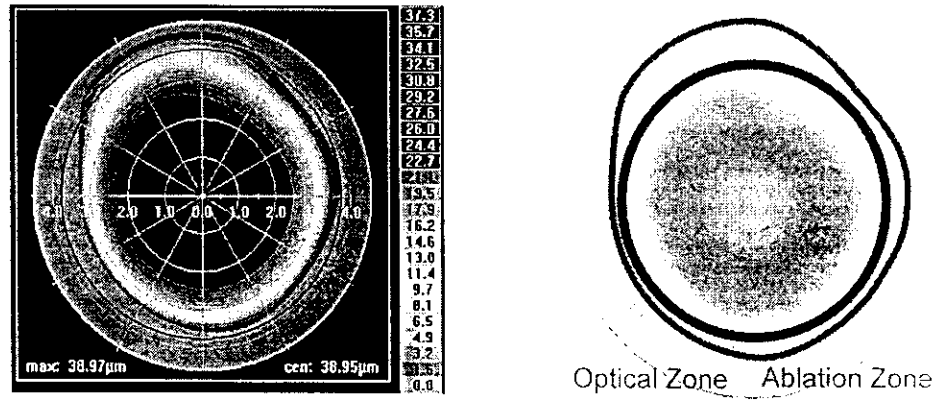

Figure 1: Examples Ablation Depth Display (left) and Optical / Ablation Zone borders (right)

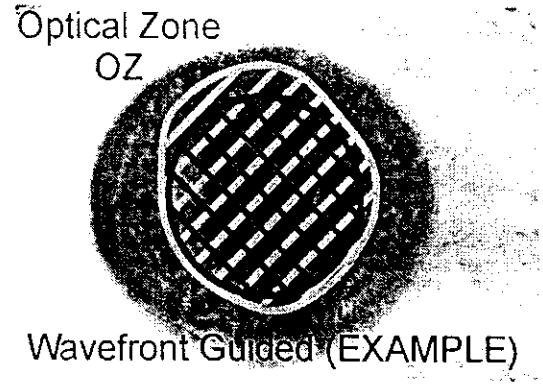

Figure 2: Example Optical and Ablation Zone over Pupil

The Ablation Zone has no specific shape. It is specific for the individual treatment

Optical Zone
Optical Zones are always circular. The Ablation Zone shape depends on the individual aberrations. Its diameter is determined by the size of the Transition Zone (width of blend zone) surrounding the Optical Zone. The laser LCD display of the Laser Console shows the Optical Zone diameter only.

Ablation Details

During wavefront guided myopic ablation, lower-order aberrations (including sphere and cylinder) and higher-order aberrations are treated simultaneously. During the course of the ablation, the zone already corrected will be enlarged to the programmed Optical Zone diameter. The currently achieved diameter is not indicated.

This evolution of ablation and zone may not apply if higher-order aberrations are relatively high compared to spherical and cylindrical errors.

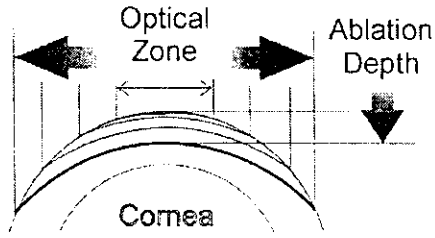

Figure 3: Evolution of Mainly Myopic Ablation Treatment

Ablation depth profiles for wavefront guided treatments are as individual as the aberrations of the specific eye. Mainly myopic spherical treatments flatten the cornea; mainly myopic astigmatism treatments flatten the axis of the positive cylinder.

The following figure shows an example of an ablation depth profile for a myopic wavefront guided treatment (the higher the profile or the 'hotter' the color, the deeper the ablation).

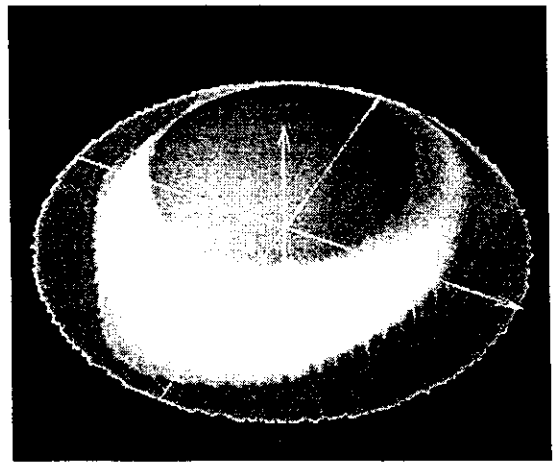

Figure 4: Example Wavefront Guided Ablation Depth Profile

3.5. Adverse Events

Certain adverse events and complications have been noticed after wavefront guided LASIK surgery. No adverse events occurred during the postoperative period of the wavefront-guided LASIK procedures. In the Control Cohort (traditional LASIK treatment) one subject undergoing traditional LASIK had the axis of astigmatism programmed as 115 degrees instead of the actual 155 degree axis. This led to cylinder in the left eye.

The following adverse events did **not** occur:

- Corneal infiltrate or ulcer requiring treatment
- Lost, misplaced, or misaligned flap, or any flap/cap problems requiring surgical intervention beyond 1 month
- Corneal edema at 1 month or later visible in the slit lamp exam
- Complications leading to intraocular surgery
- Melting of the flap of >1 mm sq
- Epithelium of > 1 mm^2 in the interface with loss of 2 lines or more of BSCVA
- Uncontrolled IOP rise with increase of > 5 mm Hg or any reading above 25 mm Hg
- Retinal detachment or retinal vascular accident
- Decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction

Table 1-Study Cohort and Table 1-Control Cohort list complications that occurred at the time of surgery. There were no operative complications in either Cohort.

Table 1-Study Cohort
Operative Complications

N=188

Complication	%	n
Epithelial Defect	0.0	0
Flap relift/irrigate debris	0.0	0
Other	0.0	0
Total Eyes Affected	0.0	0

Table 1-Control Cohort
Operative Complications

N=186

Complication	%	n
Epithelial Defect	0.0	0
Flap relift/irrigate debris	0.0	0
Other	0.0	0
Total Eyes Affected	0.0	0

77

Table 2-Study Cohort lists complications that occurred during the follow-up period for the wavefront guided treatments and **Table 2-Control Cohort** lists complications in the Control Cohort. All complications are reported cumulatively.

Table 2-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	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 2-Control Cohort
Complications Summary Table (Cumulative)

Complications	1 Month		3 Months		6 Months	
	%	n	%	n	%	n
	N=176		N=176		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	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

4. STUDY DATA

A clinical study was performed of the WaveLight ALLEGRETTO WAVE Excimer Laser System 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.

4.1. Study Objectives

The objectives of the study were to determine the safety and effectiveness of the WaveLight ALLEGRETTO WAVE Excimer Laser System for wavefront-guided LASIK treatment of myopic spherical equivalent refractive errors up to -7.0 D with and without astigmatic refractive errors up to 3.0 D.

4.2. Study Design

The study was a prospective, controlled, randomized, non-blinded consecutive enrollment 5-center, 7-surgeon 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.

4.3. Inclusion And Exclusion Criteria

Subjects in the LASIK for myopia and myopic astigmatism study must have met all of the following criteria to qualify for enrolment:

- 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.

80

- 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 enrolment in the LASIK for myopia and myopic astigmatism 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.

4.4. Study Plan, Patient Assessments And Efficacy Criteria Myopia

Subjects were evaluated preoperatively and then postoperatively at 1 day, 1 month, 3 months, 6 months, and 1 year.

Preoperative 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
- pupil size measurement in photopic and scotopic conditions
- central keratometry
- computerized corneal topography
- wavefront measurement
- pachymetry
- dilated fundus examination
- measurement of angle kappa
- 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
- wavefront measurement
- dilated fundus examination
- 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).

4.5. Study Period, Investigational Sites And Demographic Data

4.5.1. 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.

4.5.2. Demographics And Baseline Characteristics

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 3-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 3-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	

4.6. Data Analysis And Results

Table 4-Study Cohort and Table 4-Control Cohort contain a summary of the preoperative sphere and cylinder for the entire cohort while Table 5 shows the preoperative spherical equivalents for both cohorts.

Table 4-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 4-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 5
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

4.7. Postoperative Characteristics And Results

4.7.1. Patient Accountability

There were 188 eyes treated in the Study Cohort and 186 in the 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)

4.7.2. 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 6-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	%	n
	95% CI		95% CI	
≤1.00 D	98.7	154	100	156
95% CI for %	97.8%, 99.6%		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 6-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		
	%	95% CI	n	%	95% CI	n
≤1.00 D	100		148	100		148
95% CI for %		100%, 100%			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	

Please note that the confidence interval gives an estimated range of values that is likely to include an unknown population parameter, the estimated range being calculated from a given set of data. The width of the confidence interval gives us some idea about how uncertain we are about the parameter.

4.7.3. Effectiveness Outcomes

The analysis of effectiveness was based on the 180 eyes evaluable 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 7 and 8**.

Table 7-Study Cohort
Summary of Key Efficacy Variables Over Time

	1 Month		3 Months		6 Months	
	%	n	%	n	%	n
	95% CI		95% CI		95% CI	
Efficacy Variables						
UCVA 20/20 or better*	94.5	172	95.0	171	93.4	155
	92.8%, 96.2%		93.4%, 96.6%		91.4% 95.3%	
UCVA 20/40 or better*	99.5	181	100	180	99.4	165
	98.9%, 100%		100%, 100%		98.8%, 100%	
MRSE ± 0.50 D	93.4	170	94.4	170	94.6	166
	91.6%, 95.3%		92.7%, 96.2%		92.8%, 96.3%	
MRSE ± 1.00 D	97.3	177	97.8	176	98.2	163
	96.0%, 98.5%		96.7%, 98.9%		97.2%, 99.2%	
MRSE ± 2.00 D	100	182	99.4	179	100	166
	100%, 100%		98.9%, 100%		100%, 100%	

Table 7-Control Cohort
Summary of Key Efficacy Variables Over Time

	1 Month		3 Months		6 Months	
	%	n	%	n	%	n
	95% CI		95% CI		95% CI	
Efficacy Variables						
UCVA 20/20 or better*	94.3	166	93.8	165	92.8	154
	92.6%, 96.1%		91.9%, 95.6%		90.8%	94.8%
UCVA 20/40 or better*	100	176	100	176	99.4	165
	100%, 100%		100%, 100%		98.8%, 100%	
MRSE ± 0.50 D	97.7	172	96.6	170	95.2	158
	96.6%, 98.9%		95.2%, 98.0%		93.5%, 96.8%	
MRSE ± 1.00 D	99.4	175	100	176	100	166
	98.9%, 100%		100%, 100%		100%, 100%	
MRSE ± 2.00 D	100	176	100	176	100	166
	100%, 100%		100%, 100%		100%, 100%	

* For all eyes minus those intentionally treated for monovision.

Table 8-Study Cohort

Summary of Key Efficacy Variables at 3 Months (Stratified by Preoperative MRSE)

Efficacy Variables	0 to 1 D N=3	> 1 to 2 D N=42	> 2 to 3 D N=38	> 3 to 4 D N=29	> 4 to 5 D N=37	> 5 to 6 D N=18	> 6 to 7 D N=13	Total ≤ 7 D N=180
UCVA 20/20 or better*	% 100 95% CI 100%,100% n 3	% 95.2 95% CI 92.0%,98.5% n 40	% 100 95% CI 100%,100% n 38	% 96.6 95% CI 93.2%,99.9% n 28	% 94.6 95% CI 90.9%,98.3% n 35	% 88.9 95% CI 81.5%,96.3% n 16	% 84.6 95% CI 74.6%,94.6% n 11	% 95.0 95% CI 93.4%,96.6% n 171
UCVA 20/40 or better*	% 100 95% CI 100%,100% n 3	% 100 95% CI 100%,100% n 42	% 100 95% CI 100%,100% n 38	% 100 95% CI 100%,100% n 29	% 100 95% CI 100%,100% n 37	% 100 95% CI 100%,100% n 18	% 100 95% CI 100%,100% n 13	% 100 95% CI 100%,100% n 180
MRSE ± 0.50 D	% 100 95% CI 100%,100% n 3	% 97.6 95% CI 95.3%,100% n 41	% 100 95% CI 100%,100% n 38	% 100 95% CI 100%,100% n 29	% 91.9 95% CI 87.4%,96.4% n 34	% 77.8 95% CI 68.0%,87.6% n 14	% 84.6 95% CI 74.6%,94.6% n 11	% 94.4 95% CI 92.7%,96.2% n 170
MRSE ± 1.00 D	% 100 95% CI 100%,100% n 3	% 100 95% CI 100%,100% n 42	% 100 95% CI 100%,100% n 38	% 100 95% CI 100%,100% n 29	% 94.6 95% CI 90.9%,98.3% n 35	% 88.9 95% CI 81.5%,96.3% n 16	% 100 95% CI 100%,100% n 13	% 97.8 95% CI 96.7%,98.9% n 176
MRSE ± 2.00 D	% 100 95% CI 100%,100% n 3	% 100 95% CI 100%,100% n 42	% 100 95% CI 100%,100% n 38	% 100 95% CI 100%,100% n 29	% 100 95% CI 100%,100% n 37	% 94.4 95% CI 89.1%,99.8% n 17	% 100 95% CI 100%,100% n 13	% 99.4 95% CI 98.9%,100% n 179

* For all eyes minus those intentionally treated for monovision.

Table 8-Control Cohort

Summary of Key Efficacy Variables at 3 Months (Stratified by Preoperative MRSE)

Efficacy Variables	0 to 1 D N=11	> 1 to 2 D N=39	> 2 to 3 D N=47	> 3 to 4 D N=26	> 4 to 5 D N=32	> 5 to 6 D N=10	> 6 to 7 D N=10	Total ≤ 7 D N=175
UCVA 20/20 or better*	% 100 n 11 95% CI 100%,100%	% 97.4 n 38 95% CI 94.9%,100%	% 91.5 n 43 95% CI 87.4%,95.6%	% 96.2 n 25 95% CI 92.4%,99.9%	% 90.6 n 29 95% CI 85.5%,95.8%	% 80.0 n 8 95% CI 67.4%,92.7%	% 100 n 10 95% CI 100%,100%	% 93.7 n 164 95% CI 91.9%,95.6%
UCVA 20/40 or better*	% 100 n 11 95% CI 100%,100%	% 100 n 39 95% CI 100%,100%	% 100 n 47 95% CI 100%,100%	% 100 n 26 95% CI 100%,100%	% 100 n 32 95% CI 100%,100%	% 100 n 10 95% CI 100%,100%	% 100 n 10 95% CI 100%,100%	% 100 n 175 95% CI 100%,100%
MRSE ± 0.50 D	% 100 n 11 95% CI 100%,100%	% 97.4 n 38 95% CI 94.9%,100%	% 95.7 n 45 95% CI 92.8%,98.7%	% 100 n 26 95% CI 100%,100%	% 93.8 n 30 95% CI 89.5%,98.0%	% 90.0 n 9 95% CI 80.5%,99.5%	% 100 n 10 95% CI 100%,100%	% 96.6 n 169 95% CI 95.2%,98.0%
MRSE ± 1.00 D	% 100 n 11 95% CI 100%,100%	% 100 n 39 95% CI 100%,100%	% 100 n 47 95% CI 100%,100%	% 100 n 26 95% CI 100%,100%	% 100 n 32 95% CI 100%,100%	% 100 n 10 95% CI 100%,100%	% 100 n 10 95% CI 100%,100%	% 100 n 175 95% CI 100%,100%
MRSE ± 2.00 D	% 100 n 11 95% CI 100%,100%	% 100 n 39 95% CI 100%,100%	% 100 n 47 95% CI 100%,100%	% 100 n 26 95% CI 100%,100%	% 100 n 32 95% CI 100%,100%	% 100 n 10 95% CI 100%,100%	% 100 n 10 95% CI 100%,100%	% 100 n 175 95% CI 100%,100%

* For all eyes minus those intentionally treated for monovision.

Analysis of the correction of the cylindrical component of the astigmatic eyes is presented in **Table 9-Study Cohort and Table 9-Control Cohort and Table 10-Study Cohort and Table 10-Control Cohort.**

Table 9-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 9-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.

Table 10-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 10-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

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 10-Study Cohort and Table 10-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

4.7.4. Key Safety Results

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 **Table 12-Study Cohort and Table 12-Control Cohort** and **Table 13-Study Cohort and Table 13-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 only.

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 only.

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%

For eyes treated for spherical correction only.

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%

For eyes treated for spherical correction only.

4.7.5. Wavefront Outcomes

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

In the Study Cohort, overall higher-order RMS (RMS_H) was unchanged. In the Control Cohort, overall RMS_H increased by 12%

Changes in RMS_H were dependent on the preoperative RMS_H amounts. **Table 14** 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 15** 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 14-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 14-Control Cohort: Same data as shown in Table 14 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 Range	N	Preop RMSH Mean	Preop RMSH SD	Postop RMSH Mean	Postop RMSH SD	Delta RMSH (Paired) Mean	Delta RMSH (Paired) 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.

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 15 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 15: Delta RMS_H v. Preoperative Spheroequivalent (Paired-Eye Analysis)

Preop S.E. Range	Study Cohort Delta RMSH Preop to M6 N	Mean	SD	Control Cohort Delta RMSH Preop to M6 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 showed that eyes with very low preoperative RMS_H (≤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 ≤ 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.

Table 16 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 16: 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

4.7.6. Retreatment

A total of 5 eyes in the Study Cohort were retreated with the study laser for overcorrection. No eyes were retreated in the Control Cohort. **Table 17-Study Cohort** contains the outcomes for retreated eyes.

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 correction only.

4.7.7. Patient Questionnaire

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 along a 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 a severe answer ("Never" on one end, "All the Time" on the other end), a mark in the middle indicated a response scaled between the extremes.

Based on the answers, in the Study Cohort, patient complaints of glare from bright lights and night driving glare were reduced after the treatment. In the Control Cohort, patient complaints of glare from bright lights, light sensitivity and night driving glare were reduced after treatment. The percent of patients reporting "none" or "mild" for these symptoms improved after treatment. Using a 10 point scale, responses were rated as None-Mild if the patient marked 1 – 3; Moderate if the response was 4 – 6; and Marked-Severe if the response was 7 – 10.

Table 18-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 18-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

Table 19 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 19-Study Cohort Change in Patient Symptoms at 3 Months										
	Much Worse		Somewhat Worse		No Change		Somewhat Better		Much Better	
	%	n	%	n	%	n	%	n	%	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 19-Control Cohort Change in Patient Symptoms at 3 Months										
	Much Worse		Somewhat Worse		No Change		Somewhat Better		Much Better	
	%	n	%	n	%	n	%	n	%	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

5. WAVEFRONT EXAMINATION

5.1. General

Select only patients suitable for wavefront guided treatments. Patients must meet inclusion and exclusion criteria provided in this manual. See section 3.4, Precautions for details.

All wavefront examinations have to be performed with great care. Only well-trained personnel shall perform and validate wavefront examinations.

All steps have to be performed according to instructions given in the manuals of the ALLEGRO Analyzer. Additional notes related to measurements intended to be used for wavefront guided treatments are provided in the following sections.

5.2. Data Entry

Enter and check all patient data carefully. All data entered at the wavefront analyzer will be transferred to the treatment planning software and then to the Laser Console for treatment.

CAUTION

Manifest refraction as well as K-readings entered at the Analyzer will be default values for treatment if a 'Standard' LASIK shall be performed after the A-CAT procedure planning was started at the laser notebook.

For this reason, make sure that entered values are correct (even if they will not be required for the A-CAT treatment).