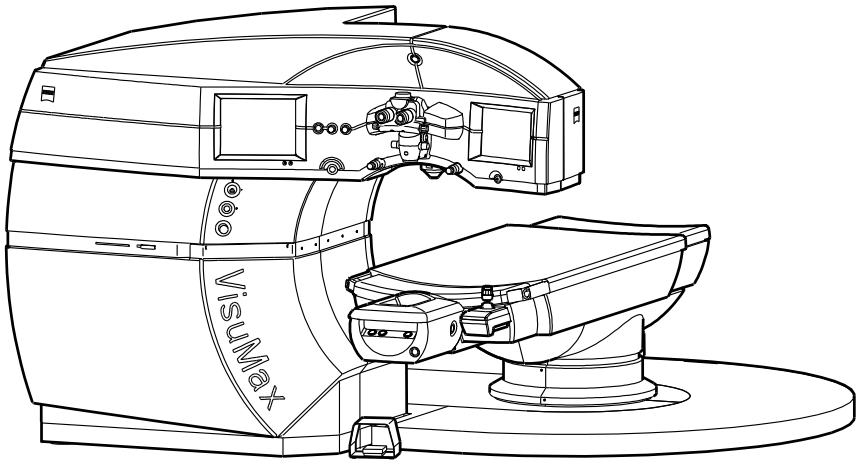
VisuMax Femtosecond Laser

Small Incision Lenticule Extraction (SMILE) procedure for the correction of myopia

PROFESSIONAL USE INFORMATION



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Notes on the Professional Use Information

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed practitioner.

Use of this device is restricted to practitioners who have been trained in its calibration and operation and who have knowledge of current therapy methods in refractive surgery and practical experience in corneal surgery .

This document (Professional Use Information) provides information concerning the intended clinical use of the Carl Zeiss Meditec VisuMax Femtosecond Laser. This manual must be used in conjunction with the VisuMax Femtosecond Laser user manual that provides general use information concerning system components, safety instructions, installation, maintenance, and troubleshooting for this device.

The Professional Use Information booklet is provided to all users that have purchased the required lenticule removal procedure license. The VisuMax Femtosecond Laser user manual is supplied with the device at the time of purchase.

CAUTION

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

Purpose and availability of documents

This Professional Use Information booklet and the online help information of this instrument explain the safety precautions, functions, usage and performance parameters of this option. In addition, the VisuMax Femtosecond Laser user manual should be observed which contains information on the operation of the device.

Correct operation of the device is imperative for its safe and successful function. You should therefore ensure that you are thoroughly familiar with this Professional Use Information booklet before setting up and using this option the first time.

The Professional Use Information booklet and other documents enclosed with this device should be kept accessible to users at all times to ensure that the information required for use of this product is readily available.

Questions and comments

If you have any questions or comments concerning this user manual or the device, please contact Carl Zeiss Meditec customer service or your local dealer (Contact details see reverse).

Explanation of symbols used

The symbols used in this user manual refer to important safety information which may warn against possible health risks or fatal injuries and contain useful notes. Whenever you see these symbols, read the accompanying information carefully and observe all safety notes and information in this user manual and on device labels.

WARNING

Indicates a hazardous situation which may result in fatal or serious injury if the appropriate safety precautions are not heeded.

CAUTION

Indicates a situation in which special care should be exercised for the safe and effective use of the device.

Information, hints and advice for a better understanding of the instructions to be observed in the operation of the device.

Package checklist

The following documents are supplied with the purchase of the VisuMax SMILE module:

- VisuMax Professional Use Information
- License Certificate for VisuMax SMILE Procedure

***Note:** The **License Certificate** serves as a proof of purchase for the VisuMax SMILE software module. The certificate informs Zeiss personnel that they can proceed with activation of the VisuMax SMILE module. Activation of this module is what allows Zeiss personnel to proceed with training.

Following successful completion of training, a **Treatment License** will be issued separately. This **Treatment License** contains the required codes which, upon being entered into the laser, enable the SMILE procedure to be performed.

Note: The following abbreviations are used on the License Certificate

- SW ReLEx – Software for the SMILE procedure on the VisuMax laser (SW = Software; ReLEx is the trademark name of the operating software).
- VisuMax S/N – refers to the serial number for the particular VisuMax Femtosecond Laser.

General Cautions

Reading this Professional Use Information document is not a substitute for the need to carefully study the VisuMax Femtosecond Laser user manual, or for the detailed training provided by Carl Zeiss Meditec, nor does it release you from the obligation to update your own expertise in keeping up with the latest results of general research in the field of refractive surgery on a regular basis.

This device may only be set up, operated and used for the specified purpose. Observe all warnings, precautions, and contraindications as described in the Professional Use Information booklet and the VisuMax Femtosecond Laser user manual.

This device may only be installed, operated, used and maintained by persons who have been properly trained or who have the required knowledge and experience to do so.

Only accessories, including software, conforming to the requirements stated in this user manual may be used.

Use of the controls or settings in a manner other than described herein may result in exposure to dangerous radiation.

The light dosage from the illumination system is a product of light intensity and exposure time. In order to minimize radiation exposure, limit one of these parameters to the medically required level for observing the patient's eye. The optical radiation safety of VisuMax has been demonstrated for a maximum observation and treatment time of 900 seconds.

Prior to use, examine the packaging of the Treatment Pack accessory to ensure there is no damage. Do not use a Treatment Pack if you are not certain that it is sterile. Ensure that the Treatment Pack accessory remains sterile during the procedure! Treatment Packs are single-use, disposable articles and re-sterilization is not permitted. Considerable risk of injury to the patient exists in re-sterilization.

Intended user profile

User profile for the approval of treatment planning and execution

The following training, knowledge and experience prerequisites must be fulfilled:

- Training as a physician or licensed practitioner specializing in the eye (ophthalmologist)
- Training on the calibration and operation of this device
- Experience with the Microsoft Windows operating system and applications based on it
- Knowledge of current ophthalmic diagnostic procedures and their measurement results for proper application in refractive surgery treatment planning
- Experience with the accurate interpretation of diagnostic measurements
- Knowledge of current therapy methods in refractive surgery
- Practical experience in corneal surgery

System description

VisuMax Femtosecond Laser

The VisuMax Femtosecond Laser system (Figure 1) is a precision ophthalmic surgical laser designed for the creation of incisions in the cornea. The action of the VisuMax and other femtosecond lasers mimics the cutting action of mechanical or blade-based keratomes. The VisuMax accomplishes this by scanning tightly focused patterns of femtosecond laser pulses in the cornea at precise and predefined positions and depths. Each laser pulse produces a micro-photodisruption in tissue of only a few microns in size. Patterns of contiguous, focused laser pulses results in the creation of continuous cut surfaces in the cornea.

Figure 1. VisuMax Femtosecond Laser

The VisuMax Femtosecond Laser System consists of the following major components:

Laser Console	The Laser Console houses the femtosecond laser source, the scanning delivery system, the computer and software-hardware control system, an uninterruptible electrical power supply, the power supply distribution electronics, a visualization system and surgical microscope, two slit illumination units, the interface hardware for the Treatment Pack, user controls and user interface.
Patient Supporting System	The Patient Supporting System (PSS) is used to support the patient in a supine position during corneal surgery with the VisuMax Femtosecond Laser. The PSS is also used to properly position the patient with respect to the Treatment Pack affixed to the treatment objective lens in the Laser Console. The joystick control on the PSS is manipulated by the user to position the patient with respect to the Treatment Pack, and to applanate and immobilize the eye of the patient in preparation for laser treatment.
Accessories - Treatment Pack	The VisuMax Treatment Pack is a commercially available, pre-sterilized, single-use disposable accessory to the VisuMax Femtosecond Laser. It consists of disposable elements that allow for the laser beam to be properly coupled onto a patient's cornea in a precise and controlled manner. No cleaning, disinfection or re-sterilization by the user is required or permitted. The Treatment Pack is contained in the blister pack that has been tested to maintain the sterility of the inner contents during the labeled shelf life using accepted international standards and accelerated test conditions accompanied by real life testing.

VisuMax SMILE Procedure

For the small incision lenticule extraction procedure, an intrastromal lenticule is created with the femtosecond laser in a shape corresponding to the desired refractive correction in the intact cornea. The femtosecond incisions for the SMILE procedure consist of four separate cuts (posterior cut, side cut for the lenticule, cap cut, side cut for the opening incision) which are completed in succession in the integrated procedure. The lenticule is subsequently accessed and removed by the surgeon through the opening incision.

The geometry of the lenticule resection procedure is depicted below in Figure 2, and a schematic of the procedure is provided in Figure 3. The VisuMax Femtosecond Laser is used to perform lenticule resection for myopia by creating a series of femtosecond laser cuts. An initial cut (Cut 1 on Fig. 3) defines the posterior surface of the lenticule. The first side cut (Cut 2 on Fig. 3) defines the diameter of the resected lenticule. A shallower and larger diameter second lamellar cut (Cut 3 on Fig. 3) defines both the anterior surface of the lenticule and the posterior surface of the attached cap. Finally, a second side cut (Cut 4 on Fig. 4) defines the opening incision. The opening incision arc is used to access and extract the resected lenticule (shown in dark grey on Fig. 2) from the stromal bed, without disturbing the attached cap overlying the resected lenticule. Standard surgical instruments for corneal refractive procedures (see *List of Recommended Instruments for Lenticule Extraction*, p. 49) are utilized to access the opening, then separate and remove the lenticule. The procedure is very similar to the keratoplasty and LASIK flap-cutting procedures. The principal difference is in the number and geometry of the laser cut patterns. Refer to the *Surgical planning and procedures section* (p. 38) for further details on the procedure.

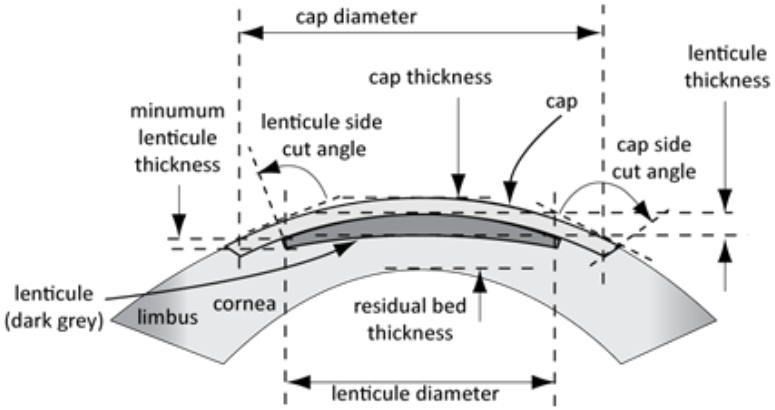

Figure 2. Schematic depiction of cut geometry for the SMILE procedure performed with the VisuMax Femtosecond Laser

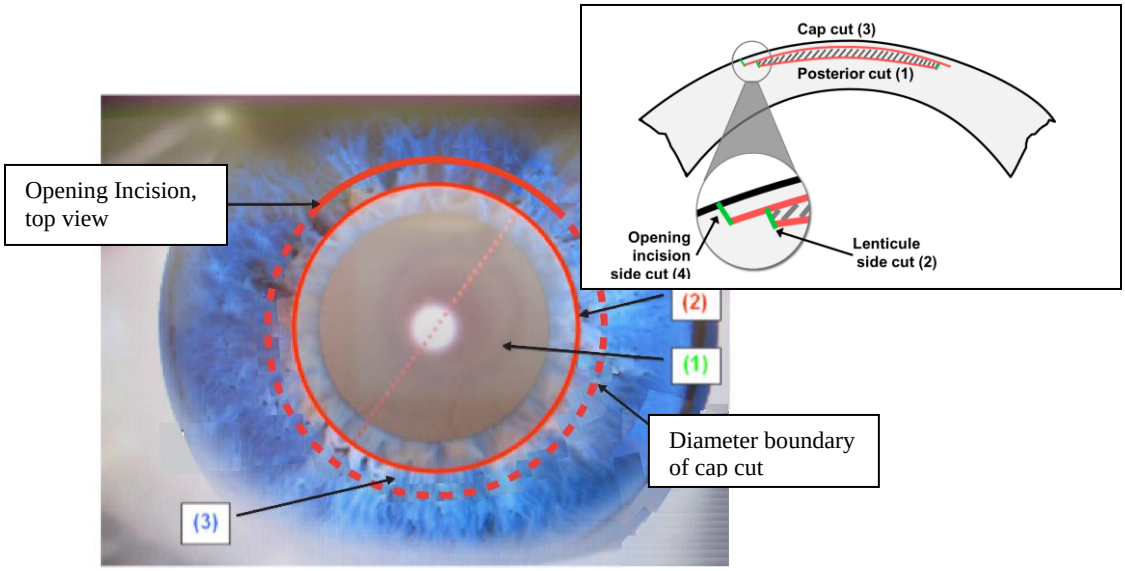

Figure 3. Planning view from VisuMax Femtosecond Laser graphical user interface (GUI) of a SMILE procedure (left graphic) and schematic of lenticule and attached cap cuts (top right graphic).
The number labels (1-4) depict the planned cuts. These cuts are:

(1) Lenticule posterior surface cut (horizontal plane)
(2) Lenticule side cut (vertical plane)
(3) Lenticule anterior surface cut/cap cut (horizontal plane)
(4) Opening incision side cut (vertical plane)

Indications, contraindications, warnings, precautions, and potential risks

Indication for use

The VisuMax Femtosecond Laser is indicated for use in small incision lenticule extraction (SMILE) for the reduction or elimination of myopia ≥ -1.00 D to ≤ -8.00 D, with ≤ -0.50 D cylinder and MRSE ≤ -8.25 D in the eye to be treated in patients who are 22 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by a change of ≤ 0.50 D MRSE.

Contraindications

VisuMax SMILE procedure for the correction of myopia is contraindicated in patients with:

- a residual stromal bed thickness that is less than 250 microns from the corneal endothelium;
- abnormal corneal topographic findings, e.g. keratoconus, pellucid marginal degeneration;
- ophthalmoscopic signs of progressive or unstable myopia or keratoconus (or keratoconus suspect);
- irregular or unstable (distorted/not clear) corneal mires on central keratometry images;
- severe dry eye ;
- active eye infection or inflammation;
- recent herpes eye infection or problems resulting from past infection;
- active autoimmune disease or connective tissue disease;
- uncontrolled diabetes;
- uncontrolled glaucoma.

Warnings

VisuMax SMILE procedure is not recommended for patients with:

- controlled autoimmune or connective tissue disease;
- controlled diabetes;
- immunocompromised status (weakened immune system) due to medication or a disease condition, e.g., immunosuppressive therapy, such as corticosteroids, or AIDS;
- a history of Herpes simplex or Herpes zoster keratitis;
- controlled glaucoma;
- a history of taking isotretinoin (Accutane®);
- epithelial basement membrane dystrophy;
- amblyopia;
- dry eyes;

- deep orbits, strong blink, anxiety, pterygium, or any other finding suggesting difficulty in achieving or maintaining suction;
- eyelid malposition (e.g. severe lagophthalmos)
- difficulty following directions or are unable to fixate.

Precautions

The safety and effectiveness of the VisuMax SMILE procedure have NOT been established for patients:

- with refractive error outside the range in the approved indications for use;
- a difference between cycloplegic and manifest refractions of greater than or equal to 0.75 D spherical equivalent in the eye to be treated;
- with central corneal thickness of less than 500 microns in the eye to be treated;
- with a family history of thinning of the cornea due to keratoconus, pellucid marginal degeneration, or other conditions that may cause ectasia;
- with uncorrected visual acuity (UCVA) better than or equal to 20/40 in the eye to be treated;
- with best spectacle-corrected visual acuity (BSCVA) worse than 20/20 in the eye to be treated;
- who wear contact lenses and did not discontinue use of contact lenses for at least 2 weeks (for hard lenses) or 3 days (for soft lenses) prior to the preoperative examination, and through the day of surgery;
- who wear contact lenses and did not demonstrate a stable refraction (within ±0.5 D), as determined by MRSE, on two consecutive examinations at least 1 week apart, in the eye to be treated;
- with mesopic pupil diameter >8.0 mm;
- with eye to be treated targeted for monovision;
- with BSCVA in the fellow eye worse than 20/40;
- with previous corneal or intraocular surgery, or trauma to the intended ablation zone;
- with corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage;
- with severe blepharitis (e.g. ocular rosacea)
- with elevated intraocular pressure (IOP), ocular hypertension or being followed for possible glaucoma (glaucoma suspect);
- with atopic syndrome;
- with severe allergies and eye rubbing;
- taking the medication sumatriptan succinate (Imitrex®);
- who are taking the medication Amiodarone hydrochloride (Cordarone®);
- under 22 years of age;

- more than 12 months after surgery;
- with media problems (corneal, lens, and/or vitreous opacities including, but not limited to, cataract);
- with a history of uveitis;
- who are pregnant or nursing.

Patient selection precautions

All patients must be given the opportunity to read and understand the Patient Information Booklet and to have all questions answered to their satisfaction prior to giving consent for the VisuMax SMILE procedure. Consideration should be given to the following in determining the appropriate patients for the procedure:

- Complete examination, including but not limited to cycloplegic evaluation, must be performed. Preoperative corneal mapping is essential to exclude any topographical abnormalities, such as keratoconus. The lens must be evaluated, especially in older patients, to assure that nuclear sclerosis or any other lens opacity is not present prior to laser surgery. Indirect ophthalmoscopy through a dilated pupil is essential to rule out any retinal pathology.
- To obtain accurate and stable refractive information, contact lens wearers must be examined after a sufficient period of not wearing contact lenses. Additional precautions should be taken for rigid gas permeable or hard contact lens wearers with respect to stable central keratometry readings. Refractive stability is considered to be a change of ≤ 0.50 D in both MRSE and keratometric meridian (either axis) as compared to the baseline measurements.
- Evaluation of the optic nerve and measurement of intraocular pressure are necessary to rule out glaucoma. If elevated intraocular pressure and/or evidence of glaucomatous damage are found, topical steroids should only be used with careful medical supervision or the patient should not undergo refractive surgery.
- Pachymetry must be performed to obtain a baseline central corneal thickness measurement to assure that the combination of the planned corneal cap thickness and the planned lenticule thickness will not approach closer than 250 microns to the corneal endothelium.
- The patient should have the ability to lie flat without difficulty and fixate steadily for the duration of the procedure.
- The patient should be clearly informed of all alternatives for the correction of his/her myopia including, but not limited to, spectacles, contact lenses, and other refractive surgeries, prior to consenting for the procedure.
- Due to the importance of managing patient expectations in elective refractive surgery, it is recommended that the physician:
  - convey realistic expectations to the prospective patient;
  - ensure patient comprehension of the risks and benefits at the start of the informed consent process;
  - discuss with patients how having the VisuMax SMILE procedure may affect the future interpretation of intraocular pressure measurements; patients should be instructed to inform future eye care providers that they have had a refractive procedure to correct their myopia;

- discuss the risk of decreased contrast sensitivity potentially affecting activities under low-light conditions;
- provide a patient information card that has eye measurements from before the procedure. Patients can keep this card to help their doctor calculate the lens implant power should they need to have future cataract surgery; a form for the necessary information is available on the internet.

Procedure-related precautions

The surgeon should share all expectations with the patient prior to initiating a procedure and to coach and encourage the patient to continue fixating throughout the short duration of the VisuMax SMILE procedure.

Surgeons should be vigilant for possible small eye movements through the operating microscope during the procedure. There can be a relative shift of the pupil center during the operation and this does not necessarily entail a shift of the cornea. Because the surgeon always retains direct control of the delivery of laser energy, in the unlikely event these findings are observed, treatment can be suspended or terminated by releasing the foot switch and disconnecting the suction. Follow the instructions provided in the section for Treatment Interruption.

The formation of bubbles at the periphery of the suction zone is an indication of imminent suction loss. In the event of a complete loss of suction, the VisuMax console detects the reduction in pressure of the eye and the procedure is automatically halted. In this case, users are directed to follow the instructions displayed on the graphic user interface (GUI) screen in accordance with instructions provided below in the section for Treatment Interruption.

To ensure adequate suction prior to and throughout the laser procedure:

- Do not use a contacting agent with the interface, as the desired result will not be achieved.
- Ensure that no liquid is allowed to enter the vacuum system.
- Take special care to ensure exact alignment of the patient's eye. Continuously optimize the eye position along the X and Y axes as the eye is brought closer to the contact glass.
- Total surgery time (centering, suction time) should be kept as short as possible.
- Ensure that conditions which may distract the patient (background noise, other activity in the surgery) are kept to a minimum while the eye is under suction.

Note: The energy settings for the VisuMax SMILE procedure are programmable and adjustable only by trained Zeiss personnel.

Potential risks

The potential risks associated with the VisuMax SMILE procedure include, but are not limited to:

- Loss of BSCVA or contrast sensitivity;
- Over-correction or under-correction;

- Increase in refractive cylinder;
- Difficulty with night driving;
- Headache or eyestrain due to imbalance between the eyes;
- Worsening of patient complaints such as glare, halos, starbursts, hazy or blurred vision, distortion, double or ghost images, fluctuation of vision, focusing difficulty, difficulty with depth perception, light sensitivity; grittiness, and ocular pain/soreness;
- Transient light sensitivity syndrome;
- Dry eye;
- Ptosis;
- Increase in IOP;
- Lens opacity;
- Conjunctivitis;
- Iritis;
- Corneal haze/scar/infection/inflammation/infiltrate/ulcer/epithelial defect/epithelium in the interface/ edema/decompensation/striae or microstriae/ectasia;
- Perforated, miscreated, or melting of the cap;
- Treatment interruption, difficult lenticule removal with tissue damage or retained lenticule; ocular penetration;
- Retinal detachment/posterior vitreous detachment/vascular accidents.

For further discussion of adverse events and complications that occurred during the course of the clinical trial, refer to the section on *Key Safety Outcomes* (p. 20).

Alternative Treatment Options

Alternatives to the small incision lenticule extraction (SMILE) available to a patient might include spectacle correction (glasses), contact lenses, surgery with another FDA approved laser using PRK (Photo Refractive Keratectomy) or LASIK (Laser-Assisted In Situ Keratomileusis), or a lens implant surgically placed inside the eye. You should discuss with your patient whether they are a candidate for these procedures as well as the risks/benefits of each alternative. Furthermore, for this discussion important information about these alternative procedures is available at the following websites (accessed August, 2016):

- ***FDA***:*http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/default.htm*
- ***NEI***: *https://nei.nih.gov/health/errors/myopia*
- ***AAO***: *http://www.aao.org/eye-health/treatments/lasik*
- ***FTC:*** *https://www.consumer.ftc.gov/articles/0062-basics-lasik-eye-surgery#lasikbasics*

Clinical results

Study objectives and methods

The objective of this study was to evaluate the safety and effectiveness of the Carl Zeiss Meditec VisuMax SMILE procedure for the reduction or elimination of myopia from ≥ -1.00 D to ≤ -10.00 D with ≤ -0.50 D cylinder and MRSE ≤ -10.25 D. Myopic spherical eyes and myopic eyes with ≤ 0.50 D of astigmatism were treated with a spherical treatment only.

Study design

This was a 12-month, prospective, multi-center, open-label, non-randomized clinical trial of up to 360 eyes of 360 consecutive subjects enrolled and treated with the VisuMax Femtosecond Laser. Retreatments were not allowed during the study.

Follow-up examinations were scheduled at 1 day, 1 week, 1 month, 3 months, 6 months, 9 months, and 12 months.

- Postop Day 1: Day 1
- Postop Week 1: Days 5 to 9
- Postop Month 1: Days 21 to 35 (Weeks 3 to 5)
- Postop Month 3: Days 70 to 98 (Weeks 10 to 14)
- Postop Month 6: Days 147 to 182 (Weeks 21 to 26)
- Postop Month 9: Days 245 to 301 (Weeks 35 to 43)
- Postop Month 12: Days 330 to 420 (Months 11 to 14)

The key effectiveness variables for the study were:

- Predictability: the percentage of eyes achieving MRSE within ± 1.00 D of the intended outcome, and within ± 0.50 D of the intended outcome at the point at which stability is first achieved
- Improvement in UCVA following treatment: the percentage of eyes that achieve uncorrected visual acuity (UCVA) of 20/40 or better at the postoperative interval at which stability has been established, as well as the percentage of eyes that achieve UCVA of 20/20 or better

Refractive stability was also evaluated:

Stability was considered to have been achieved at the latter of two postoperative refractions performed at least 3 months apart or at 3 months after surgery when compared with the 1-month interval, if at least three of the four stability criteria were met; these criteria were as follows:

1. At least 95% of the treated eyes should have a change ≤ 1.00 D of MRSE at the latter of two postoperative refractions performed at least 3 months apart or at 3 months after surgery when compared with the 1-month interval;
2. The mean rate of change in MRSE, as determined by paired analysis, is ≤ 0.5 D per year (0.04 D/month) over the same time period;

3. The mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging;
4. The 95% confidence interval for the mean rate of change includes zero or a rate of change attributable to normal aging;

Stability was confirmed at least 3 months after the stability time point by a statistically adequate subgroup.

The key safety variables for the study were:

- Preservation of Best-Spectacle Corrected Visual Acuity (BSCVA)
  - In eyes with preoperative BSCVA 20/20 or better, the percentage of eyes with BSCVA worse than 20/40 at the postoperative interval at which stability has been established
  - The percentage of eyes with ≥ 2 lines BSCVA loss
- Induced manifest refractive astigmatism:
  - the percentage of eyes with induced manifest refractive cylinder of >2.00 D at the postoperative interval at which stability has been established
- Loss of Contrast Sensitivity
  - Mean "within-eye" loss of contrast sensitivity from baseline to 12 months with the 1-sided 95 % confidence interval for each spatial frequency
  - The percentage of eyes showing ≥ 0.3 log units loss at two or more spatial frequencies
- Incidence of Adverse Events
  - The counts and percentages of eyes for each adverse event
- Patient Reported Symptoms
  - Patient reported symptoms were considered as a secondary safety variable and were stratified by pupil size and fellow eye status

Additional safety variables for the study were:

- Corneal Topography
- Wavefront Aberrometry

Inclusion and exclusion criteria

In order to be enrolled in the study, patients needed to meet these conditions:

- be 22 years of age and older;
- have spherical myopia from ≥ -1.00 D to ≤ -10.00 D, with ≤ -0.50 D cylinder and MRSE ≤ -10.25 D, in the eye to be treated;
- have a stable refraction for the past year, as demonstrated by a change in MRSE of ≤ 0.50 D in the eye to be treated;

- have a difference between cycloplegic and manifest refractions of < 0.75 D spherical equivalent (SE) in the eye to be treated. (SE is the difference between cycloplegic and manifest refractions);
- have UCVA worse than 20/40 in the eye to be treated;
- have BSCVA of at least 20/20 in the eye to be treated;
- discontinue use of contact lenses at least 2 weeks for hard contacts and 3 days for soft lenses prior to the preoperative examination; all contact wearers must have two manifest refractions taken at least one week apart that did not differ by more than 0.50 D;
- have central corneal thickness of at least 500 microns in the eye to be treated;
- be willing and able to return for scheduled follow-up examinations;
- and provide written informed consent.

Patients not meeting the above inclusion criteria were excluded from the study.

In addition, subjects who exhibited any of the following conditions were excluded:

- a mesopic pupil diameter > 8.0 mm;
- cylinder of greater than 0.50 D;
- treatment depth is less than 250 microns from the corneal endothelium;
- eye to be to be treated is targeted for monovision;
- fellow eye has BSCVA worse than 20/40;
- abnormal corneal topographic findings, e.g. keratoconus, pellucid marginal degeneration, in either eye;
- history of anterior segment pathology, including cataracts in the treated eye;
- clinically significant dry eye syndrome unresolved by treatment in either eye;
- residual, recurrent, active ocular or uncontrolled eyelid disease, corneal scars or other corneal abnormality such as recurrent corneal erosion or severe basement membrane disease in the eye to be treated;
- ophthalmoscopic signs of progressive or unstable myopia or keratoconus (or keratoconus suspect) in either eye;
- irregular or unstable (distorted/not clear) corneal mires on central keratometry images in either eye;
- history of ocular herpes zoster or herpes simplex keratitis;
- have deep orbits, strong blink, anxiety, pterygium, or any other finding suggesting difficulty in achieving or maintaining suction;
- have difficulty following directions or unable to fixate;
- have previous intraocular or corneal surgery of any kind in the eye to be treated, including any type of surgery for either refractive or therapeutic purposes;
- history of steroid-responsive rise in intraocular pressure, glaucoma, or preoperative IOP > 21 mm Hg in either eye;

- history of diabetes, diagnosed autoimmune disease, connective tissue disease or clinically significant atopic syndrome;
- be immunocompromised or requires chronic systemic corticosteroids or other immunosuppresive therapy that may affect wound healing;
- have a history of known sensitivity to planned study medications;
- participating in any other ophthalmic drug or device clinical trial during the time of this clinical investigation;
- and pregnant, lactating, or child-bearing potential and not practicing a medically approved method of birth control.

Results and data analysis

Demographics and baseline parameters

A total of 336 eyes were treated across five U.S. sites. Demographic information for all treated subjects is provided in Table 1. Subjects ranged in age from 22 to 58 years, with a mean age of 33.3 for all treated eyes. More females (58.3 %) than males (41.7 %) were enrolled and treated in the study, and the majority of subjects were Caucasian (92.0 %).

Table 1
Demographics
All Treated Eyes

Demographics	All Treated Eyes	
	Number	Percentage
NUMBER OF EYES & SUBJECTS	336 Eyes of 336 Subjects	
GENDER		
Male	140	41.7 %
Female	196	58.3 %
RACE		
White	309	92.0 %
Black	10	3.0 %
Asian	6	1.8 %
Other	11	3.3 %
SURGICAL EYE		
Right	152	45.2 %
Left	184	54.8 %
AGE (In Years)		
Mean (SD)	33.3 (7.9)	
Min., Max.	22.0, 58.0	
Fellow-eye Status		
Excimer Laser Refractive Surgery	333	99.1 %
Untreated	3	0.9 %

Preoperative refraction parameters are shown in Table 2**.** Mean manifest refraction sphere at baseline for all treated eyes was -4.762 D, with a range of -1.00 D to -10.00 D. The mean manifest refraction cylinder at baseline for all treated eyes was -0.194 D (SD = 0.20), with a range of 0.00 D to -0.50 D. As specified in the study protocol, cylinder was not treated in the study eyes. Among all treated eyes, the procedures were not completed for two subjects, due to intraoperative suction loss during the posterior lamellar cut. Additionally, one subject had treatment on the wrong eye. These three subjects were excluded from the effectiveness population, resulting in 333 total eyes.

Table 2
Preoperative Refraction Parameters

Manifest Refraction	All Treated Eyes		Effectiveness Population	
	Number	**%**	**Number**	**%**
Sphere				
0.00 to -1.00 D	4	1.2	4	1.2
-1.01 to -2.00 D	35	10.4	35	10.5
-2.01 to -3.00 D	54	16.1	53	15.9
-3.01 to -4.00 D	50	14.9	50	15.0
-4.01 to -5.00 D	50	14.9	49	14.7
-5.01 to -6.00 D	43	12.8	43	12.9
-6.01 to -7.00 D	44	13.1	44	13.2
-7.01 to -8.00 D	29	8.6	28	8.4
-8.01 to -9.00 D[1]	15	4.5	15	4.5
-9.01 D or higher[1]	12	3.6	12	3.6
Mean (SD)	*-4.762 (2.202)*		*-4.763 (2.202)*	
Range	*-10.00 to -1.00*		*-10.00 to -1.00*	
Total	336	100.0	333	100.0
Cylinder				
0.00 D	153	45.5	152	45.6
-0.25 D	105	31.3	105	31.5
-0.50 D	78	23.2	76	22.8
Mean (SD)	*-0.194 (0.200)*		*-0.193 (0.199)*	
Range	*-0.50 to 0.00*		*-0.50 to 0.00*	
Total	336	100.0	333	100.0

[1] Please note that treatment of these dioptric powers will present a flagged warning to the users so that the user understands that correction of these powers had not been substantiated by an adequate set of data.

Accountability

Accountability for all treated eyes through 12 months is presented in Table 3. Accountability over the course of the entire study was excellent with 98.5 % (329/336) of eyes treated in the study available for analysis at the 6-month visit, the point at which refractive stability was identified. The study results presented below include all available outcomes through database lock in March, 2015.

Table 3
Accountability
All Treated Eyes

Enrolled (N = 336)	**Day 1**	**Week 1**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12**
Available for analysis	335 (99.7 %)	334 (99.4 %)	335 (99.7 %)	333 (99.1 %)	329 (97.9 %)	320 (95.2 %)	311 (92.6 %)
Active	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	8 (2.4 %)	17 (5.1 %)
Missing	1 (0.3 %)	2 (0.6 %)	1 (0.3 %)	3 (0.9 %)	7 (2.1 %)	8 (2.4 %)	8 (2.4 %)
Discontinued	1 (0.3 %)	1 (0.3 %)	1 (0.3 %)	1 (0.3 %)	2 (0.6 %)	2 (0.6 %)	3 (0.9 %)
Death	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	1 (0.3 %)
Alternative treatment	1 (0.3 %)	1 (0.3 %)	1 (0.3 %)	1 (0.3 %)	2 (0.6 %)	2 (0.6 %)	2 (0.6 %)
Scheduled visit data outstanding	0 (0.0 %)	1 (0.3 %)	0 (0.0 %)	1 (0.3 %)	2 (0.6 %)	2 (0.6 %)	0 (0.0 %)
Lost to follow-up	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	1 (0.3 %)	3 (0.9 %)	4 (1.2 %)	5 (1.5 %)
% Accountability	335 (100.0 %)	334 (99.7 %)	335 (100.0 %)	333 (99.4 %)	329 (98.5 %)	320 (98.2 %)	311 (98.4 %)

Status categories were based on ANSI-Z80.11-2012.
% = n ÷ N × 100.
% Accountability = available ÷(enrolled - discontinued - active) ×100

Key safety outcomes

In Table 4, key safety variables are presented for all 329 available eyes at the point of stability, which was established at 6 months (details provided on p. 38, Stability of the manifest refraction). Additionally, key safety variables at the last available visits for each of the 336 treated eyes are summarized in Table 5. No study subject presented with a loss of ≥ 2 lines BSCVA, with BSCVA worse than 20/40, or with increased manifest refractive astigmatism > 2.00 D at 6 months or at the last available visits. With regard to loss of ≥ 2 lines BSCVA at any point during the study, there were 19 study eyes at Week 1, 5 eyes at Month 1, and 3 eyes at interim visits with this degree of loss. These are further presented and discussed below (Table 6).

Table 4
Summary of Key Safety Variables at 6-Month Point of Refractive Stability
All Treated Eyes

Key Safety Event	n/N	%	95 % CI[1]
Loss of ≥ 2 lines BSCVA	0/329	0.0 %	(0.0 %, 1.1 %)
BSCVA worse than 20/40 if 20/20 or better preoperatively	0/329	0.0 %	(0.0 %, 1.1 %)
Increased manifest refractive astigmatism > 2.0 D	0/329	0.0 %	(0.0 %, 1.1 %)

N = Number of case report forms received with non-missing values at each visit.
95 % CI was calculated based on Clopper-Pearson exact method.

Table 5
Summary of Key Safety Variables at Last Available Visit
All Treated Eyes

Key Safety Event	n/N	%	95 % CI[1]
Loss of ≥ 2 lines BSCVA	0/336	0.0 %	(0.0 %, 1.1 %)
BSCVA worse than 20/40 if 20/20 or better preoperatively	0/336	0.0 %	(0.0 %, 1.1 %)
Increased manifest refractive astigmatism > 2.0 D	0/336	0.0 %	(0.0 %, 1.1 %)

N = Number of case report forms received with non-missing values at each visit.
95 % CI was calculated based on Clopper-Pearson exact method.

The change in BSCVA postoperatively from baseline for all treated eyes is presented in Table 6. For all scheduled visits from Month 1 and on, there were no BSCVA losses greater than one line, with 3.3 % (11/329) of eyes at 6 months and 2.6 % (8/311) of eyes at 12 months, showing a one line decrement. With regard to loss of ≥ 2 lines BSCVA, 5.7% (19/334) of treated eyes at Week 1 and 1.5% (5/335) of treated eyes at Month 1 manifested this level of loss. Beyond Month 1, there were three other instances, involving three separate subjects, of BSCVA loss ≥ 2 lines, all during interim visits. Two of these occurred between Months 1 and 3, while one occurred between Months 6 and 9, and each case was resolved by the subsequent visit. Further, following the Month 1 time point when the proportions of eyes with losses versus gains in BSCVA were comparable, every subsequent visit demonstrated a consistently and increasingly higher proportion of eyes with gains in BSCVA, compared to losses.

Table 6
Change in Best Spectacle-Corrected Visual Acuity (BSCVA) from Preop
All Treated Eyes

BSCVA	Week 1		Month 1		Month 3		Month 6		Month 9		Month 12	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Available (N)	334		335		333		329		319		311	
Lost > 2 lines (>10 letters)	13	(3.9 %)	5	(1.5 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)
Lost 2 lines (10 letters)	6	(1.8 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)
Lost 1 line (5-9 letters)	75	(22.5 %)	36	(10.7 %)	21	(6.3 %)	11	(3.3 %)	10	(3.1 %)	8	(2.6 %)
Unchanged (< 5 letters)	222	(66.5 %)	255	(76.1 %)	246	(73.9 %)	243	(73.9 %)	239	(74.9 %)	224	(72.0 %)
Gained 1 line (5-9 letters)	15	(4.5 %)	38	(11.3 %)	59	(17.7 %)	66	(20.1 %)	64	(20.1 %)	71	(22.8 %)
Gained 2 lines (10 letters)	0	(0.0 %)	1	(0.3 %)	4	(1.2 %)	6	(1.8 %)	3	(0.9 %)	3	(1.0 %)
Gained > 2 lines (>10 letters)	3	(0.9 %)	0	(0.0 %)	3	(0.9 %)	3	(0.9 %)	3	(0.9 %)	5	(1.6 %)
Not reported	0		0		0		0		1		0	
Total	334		335		333		329		320		311	

N = Number of case report forms received with non-missing values at each visit.

Through the point of data lock, a total of 14 subjects were reported with 15 ocular adverse events (AEs) over the course of the study. The intraoperative AEs are summarized in Table 7, while all postoperative AEs are summarized in Table 8. In total, there were four intraoperative AEs: 2 cases of difficult lenticule removal with tissue, 1 case with a cap perforation, and 1 case of retained tissue following lenticule removal. With the exception of one subject, whose intraoperative AE was present through the 3-month visit, none of the reported cases persisted beyond the 1-week visit. Importantly, all four subjects completed the study with UCVA no worse than 20/16.

Table 7
Intraoperative Adverse Events

Intraoperative AE	n
Difficult lenticule removal with tissue damage	2 (0.6%)
Perforated cap	1 (0.3%)
Retained tissue, small	1 (0.3%)

The other 10 subjects experienced adverse events postoperatively which occurred at various time points throughout the study. These events included 1 case of conjunctival carcinoma in situ; 1 case of allergic conjunctivitis; 1 case of viral conjunctivitis; 1 case of decrease in BSCVA of greater than or equal to 2 lines (≥10 letters) not due to irregular astigmatism as shown by hard contact lens refraction at 3 months or later; 1 case of herpetic lid and corneal lesion; 2 cases of iritis (involving one subject); 1 case of posterior vitreous detachment (PVD); 1 case of pyogenic granuloma; 1 case of retinal vasculitis, and 2 cases of retained tissue following lenticule removal, one of which is accounted for in Table 7. With the exception of one subject whose UCVA at study exit was 20/25, the other 9 subjects completed and exited the study with UCVA no worse than 20/20.

Table 8
Postoperative Ophthalmic Adverse Events — All Treated Eyes

AE	D1 N=335	W1 N=334	M1 N=335	M3 N=333	M6 N=329	M9 N=320	M12 N=311	Uns N=24	Cum N=336
Diffuse lamellar keratitis (Stage 3 or above)	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Corneal infiltrate or ulcer	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Any persistent corneal epithelial defect at 1 month or later	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Corneal edema at 1 month or later	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Epithelium in the interface with loss of 2 lines (10 letters) or more of 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%
Melting of the cap	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
IOP increase of > 10 mmHg above baseline or IOP > 30 mmHg on 2 consecutive exams	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Haze beyond 6 months with loss of 2 lines or greater (≥10 letters) of 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%
Decrease in BSCVA of greater than or equal to 2 lines (≥10 letters) not due to irregular astigmatism as shown by hard contact lens refraction at 3 months or later	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
Retinal Detachment	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Retinal vascular accidents	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Ocular penetration	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Any other vision-threatening event									
Retinal vasculitis	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0	1 0.3%
Other									
Carcinoma in situ, conjunctival	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0	1 0.3%
Conjunctivitis, allergic	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0 0.0%	0	1 0.3%
Conjunctivitis, viral	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
Herpetic lid and corneal lesion	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
Iritis	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
PVD	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0 0.0%	0	1 0.3%
Pyogenic Granuloma	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0 0.0%	0 0.0%	1	1 0.3%
Retained tissue, small	2 0.6%	2 0.6%	1 0.3%	1 0.3%	0 0.0%	0 0.0%	0 0.0%	1	2* 0.6%

Multiple events could be reported for each subject.

Uns = interim visit, N is the number of eyes with interim visits, and incidence is the number of eyes with the reported events during the interim visits.

Cum = cumulative, N is the number of all treated eyes with postoperative visits, and incidence is the number of eyes with the reported events during the study.

*One of these subjects is also accounted for in Table 7, as the retained tissue was first observed intraoperatively.

In addition to the intraoperative and postoperative adverse events noted above, there were a total of 15 intraoperative events observed among the 336 procedures. These events, presented in Table 9 below, include 8 cases of difficult lenticule removal without tissue damage, 6 cases in which suction was lost during the procedure, and 1 case of decentered treatment which was identified by postoperative topography. It should be noted that none of these events led to clinically significant sequelae.

Table 9
Intraoperative Events
All Treated Eyes

N = 336	Number	Percent
Difficult lenticule removal without tissue damage	8	2.4 %
Loss of suction: completed treatment	4	1.2 %
Loss of suction: discontinued treatment	2	0.6 %
Decentered treatment*	1	0.3%
Any Events	15	4.5 %

Multiple events could be reported for each subject.
Percent = Number/N ×100.
* Identified by postoperative topography

Complications over the course of the study are summarized below in Table 10. The majority of these reports involved questionnaire responses of moderate or severe glare or halos, at 10.4 % (35/336) and 6.0 % (20/336), respectively. The peak incidence of these reports occurred at 3 and 6 months, with a significant reduction by the 9 and 12 month visits. At Month 12, in fact, there were four residual reports of moderate or severe glare and one report of moderate or severe halos. The definitions for glare and halo complications did not take into consideration whether the symptom was considered bothersome, whether it was present at baseline with the use of contact lens or spectacle correction, or whether it readily resolved when distance correction is worn.

Other findings included: clinical signs and/or subject symptoms consistent with dry eye (2.7 %, 9/336); diffuse lamellar keratitis (DLK) stage 2 or less (0.9 %, 3/336); epithelium in the interface (0.9 %, 3/336); foreign body sensation at 1 month or later (0.3 %, 1/336); interface debris (2.7 %, 9/336); pain at 1 month or later (0.3 %, 1/336); striae/microstriae (0.3 %, 1/336); and transient light sensitivity syndrome (0.3 %, 1/336).

Table 10
Complications
All Treated Eyes

Complications	D0 N=336	D1 N=335	W1 N=334	M1 N=335	M3 N=333	M6 N=329	M9 N=320	M12 N=311	Uns N=24	Cum N=336
Clinical signs and/or subject symptoms consistent with dry eye	0 0.0 %	0 0.0 %	5 1.5 %	1 0.3 %	4 1.2 %	0 0.0 %	0 0.0 %	0 0.0 %	3	9 2.7 %
Corneal edema between 1 week and 1 month after procedure	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Corneal scarring	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Crystalline lens opacity	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Diffuse lamellar keratitis (Stage 2 or less)	0 0.0 %	1 0.3 %	3 0.9 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	3 0.9 %
Epithelium in the interface	0 0.0 %	1 0.3 %	2 0.6 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	3 0.9 %
Foreign body sensation at 1 month or later	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	1 0.3 %	0 0.0 %	0	1 0.3 %
Ghost/double images in the operative eye	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Interface debris, such as lint, pigment, air bubbles, and meibomian gland secretions	0 0.0 %	5 1.5 %	5 1.5 %	2 0.6 %	2 0.6 %	0 0.0 %	0 0.0 %	0 0.0 %	1	9 2.7 %
Moderate or severe glare	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	21 6.3 %	15 4.6 %	7 2.2 %	4 1.3 %	0	35 10.4 %
Moderate or severe halos	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	10 3.0 %	11 3.3 %	4 1.3 %	1 0.3 %	0	20 6.0 %
Pain at 1 month or later	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	1 0.3 %	1 0.3 %	1 0.3 %	0	1 0.3 %
Striae/microstriae	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	1 0.3 %
Transient light sensitivity syndrome (TLSS)	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	1	1 0.3 %

Multiple events could be reported for each subject.
Uns = interim visit, N is the number of eyes with interim visits, and incidence is the number of eyes with the reported events during the interim visits.
Cum = cumulative, N is the number of all treated eyes with postoperative visits, and incidence is the number of eyes with the reported events during the study.
One subject did not complete VisuMax treatment and had an alternative treatment at the operative visit. Since the data after the alternative treatment were not included, the total number of subjects with postoperative visits was 335.

Secondary Surgical Interventions

Three secondary interventions for epithelial ingrowth or interface debris were performed at or before the 1-week time point, one involving an irrigation to remove interface debris and two involving irrigation with BSS to remove epithelial cells in the interface.

Contrast sensitivity outcomes

Mesopic (monocular) contrast sensitivity in the study eye was assessed at a calibrated luminance of 3 cd/m^2 with no glare, using sine wave gratings at spatial frequencies of 1.5, 3.0, 6.0, and 12.0 cycles per degree (cpd). Subjects were dark-adapted for 10 minutes prior to mesopic contrast sensitivity testing.

As shown in Table 11, the mean change in monocular mesopic contrast sensitivity (CS) were positive at all postoperative time points for 1.5, 3.0, and 6.0 cpd and at 12 months for 12 cpd, indicating a

consistent sensitivity gain for the cohort. At 12 months the proportion of subjects with clinically significant gains was 23.5%, compared to 1.6% with clinically significant losses. "Clinically significant" was defined as ≥ 0.3 log units of change at two or more spatial frequencies.

Table 11
Log Contrast Sensitivity Change from Preoperative Visit
All Treated Eyes

Frequency	Statistics	Preop	Month 3	Month 6	Month 9	Month 12
A (1.5 cpd)	N	335	333	329	320	311
	Mean (SD)	1.584 (0.226)	1.606 (0.230)	1.658 (0.212)	1.653 (0.222)	1.665 (0.224)
	Q1, Q2, Q3	1.40, 1.56, 1.70	1.40, 1.56, 1.85	1.56, 1.70, 1.85	1.48, 1.56, 1.85	1.56, 1.70, 1.85
	Min., Max.	0.95, 2.00	0.85, 2.00	0.95, 2.00	0.95, 2.00	0.95, 2.00
	< 0.85	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not Reported	1	0	0	0	0
B (3 cpd)	N	335	333	329	320	311
	Mean (SD)	1.800 (0.211)	1.839 (0.214)	1.882 (0.215)	1.886 (0.203)	1.907 (0.209)
	Q1, Q2, Q3	1.76, 1.76, 1.90	1.76, 1.90, 2.06	1.76, 1.90, 2.06	1.76, 1.90, 2.06	1.76, 1.90, 2.06
	Min., Max.	1.18, 2.20	1.00, 2.20	1.00, 2.20	1.00, 2.20	1.00, 2.20
	< 1.00	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not Reported	1	0	0	0	0
C (6 cpd)	N	335	333	329	320	311
	Mean (SD)[1]	< 1.749 (> 0.240)	< 1.785 (> 0.254)	< 1.826 (> 0.252)	< 1.846 (> 0.245)	< 1.883 (> 0.250)
	Q1, Q2, Q3	1.52, 1.81, 1.95	1.65, 1.81, 1.95	1.65, 1.81, 2.11	1.65, 1.81, 2.11	1.65, 1.95, 2.11
	Min., Max.[1]	< 1.08, 2.26	< 1.08, 2.26	< 1.08, 2.26	< 1.08, 2.26	< 1.08, 2.26
	< 1.08	5 (1.5%)	4 (1.2%)	1 (0.3%)	3 (0.9%)	1 (0.3%)
	Not Reported	1	0	0	0	0
D (12 cpd)	N	335	333	329	320	311
	Mean (SD)[1]	< 1.349 (> 0.305)	< 1.353 (> 0.303)	< 1.408 (> 0.323)	< 1.424 (> 0.335)	< 1.469 (> 0.339)
	Q1, Q2, Q3	1.18, 1.34, 1.63	1.18, 1.34, 1.48	1.18, 1.48, 1.63	1.18, 1.48, 1.63	1.18, 1.48, 1.78
	Min., Max.[1]	< 0.90, 2.08	< 0.90, 2.08	< 0.90, 2.08	< 0.90, 2.08	< 0.90, 2.08
	< 0.90	24 (7.2%)	35 (10.5%)	27 (8.2%)	23 (7.2%)	22 (7.1%)
	Not Reported	1	0	0	0	0
0 patch at one or more cpds		24 (7.2%)	35 (10.5%)	27 (8.2%)	23 (7.2%)	22 (7.1%)

One subject had an alternative treatment after the 3-month visit and one subject had an alternative treatment at the operative visit. Records after alternative treatment were excluded. Both were followed for safety after the alternative treatment.
One subject had the incorrect eye treated. The treated OS did not have the contrast sensitivity test preoperatively.
N = Number of case report forms received with non-missing values at each visit. Not Reported = Number of case report forms received with missing values at each visit. Q1 = first quartile, Q2 = second quartile (median), and Q3 = third quartile.

[1] Number of subjects that could not read any patch at the respective spatial frequency. 0.85, 1.00, 1.08, and 0.90 are the lowest measurable contrast sensitivity values at 1.5, 3, 6, and 12 cpd, respectively. **These lowest values were used for statistical calculation**. In case of no patches could be read, a "<" sign was included in the Mean and Minimum, and ">" sign was included in the SD.

Patient reported outcomes

The patient reported outcomes (PRO) instrument used in IDE clinical study consisted of the full Quality of Vision (QoV) questionnaire with accompanying photographs, and 2 of the 3 domains of the Ocular Surface Disease Index (OSDI). The QoV instrument had three domains (frequency, severity, and bothersome) each consisting of 10 items which evaluate glare, halos, starbursts, hazy vision, blurred vision, distortion, double or multiple images, fluctuation, focusing, and judging

distance or depth perception. The two domains of the OSDI included all questions related to ocular symptoms and all questions related to environmental triggers.

Table 12 provides the QoV score changes from baseline to each postoperative visit stratified by whether the score was "worse", "same", or "improved".

The data suggest that, on average, subjects noted less severity and were less bothered by symptoms at 12 months following the procedure compared to the preoperative visit, during which subjects were using spectacle and contact lens correction for myopia.

Table 12
QoV Score Change from Preoperative
All Treated Eyes

Sub-scale		Month 3	Month 6	Month 9	Month 12
Frequency	**N**	**332**	**328**	**319**	**309**
	Worse	176/332 (53%)	150/328 (46%)	133/319 (42%)	116/309 (38%)
	Same	70/332 (21%)	74/328 (23%)	74/319 (23%)	71/309 (23%)
	Improved	86/332 (26%)	104/328 (32%)	112/319 (35%)	122/309 (39%)
	Not Reported	1	1	1	2
Severity	**N**	**332**	**328**	**319**	**309**
	Worse	160/332 (48%)	131/328 (40%)	108/319 (34%)	93/309 (30%)
	Same	81/332 (24%)	97/328 (30%)	93/319 (29%)	95/309 (31%)
	Improved	91/332 (27%)	100/328 (30%)	118/319 (37%)	121/309 (39%)
	Not Reported	1	1	1	2
Bothersome	**N**	**332**	**328**	**319**	**309**
	Worse	138/332 (42%)	106/328 (32%)	95/319 (30%)	79/309 (26%)
	Same	102/332 (31%)	123/328 (38%)	119/319 (37%)	119/309 (39%)
	Improved	92/332 (28%)	99/328 (30%)	105/319 (33%)	111/309 (36%)
	Not Reported	1	1	1	2

Change = Postop - Preop (pairwise).
Worse: Change > 0. Same: Change = 0. Improved: Change < 0.
Not Reported = Number of eyes with missing values at each visit.

As shown in Table 13**,** the proportion of subjects at Month 12 with an improvement of at least two grades from baseline (with contact lenses and/or spectacle wear) was consistently the same or larger than the proportion of subjects with at least a two-grade worsening for the majority of QoV symptoms and their domains. In total, the overall proportion of subjects that experienced improvement in QoV symptoms from baseline at 12 months was greater than the proportion of subjects who experienced worsening of PRO symptoms, with 12.6% of subjects experiencing improvement versus 8.7% experiencing worsening.

Table 13 also highlights the QoV symptoms with the highest rate of worsening of 2-grades or more at 12 months, with respect to frequency, severity, and bothersomeness. Starbursts (1.6%) and blurred vision (2.6%) represented the symptoms with the highest proportion of subjects with a 2-grade or more worsening in frequency from baseline at 12 months. With respect to severity, double or multiple images and blurred vision, both at 1.3%, had the highest proportion of reported worsening by two grades or more at 12 months. Starbursts, blurred vision, and judging distance or depth perception, each with 1.3%, were the symptoms that had the highest proportion of subjects with a 2-grade or more worsening at 12 months in terms of bothersomeness.

Note: There were minor differences in instructions, method of choosing the response option formatting, and directions associated with choosing the responses for the QoV questionnaire used in this trial compared to the original QoV questionnaire. The impact of these differences on the reported frequency, bothersome-ness, and severity of symptoms is unknown.

Table 13
Changes of 2 or More Grades in QoV Symptoms at 12 Months

Symptom	Outcomes	Better n/N (%)	Worse n/N (%)
Glare	Frequency	5/309 (1.6%)	3/309 (1.0%)
	Severity	11/309 (3.6%)	3/309 (1.0%)
	Bothersome	7/309 (2.3%)	2/309 (0.6%)
	# of Subjects	17/309 (5.5%)	7/309 (2.3%)
Halos	Frequency	7/309 (2.3%)	4/309 (1.3%)
	Severity	4/309 (1.3%)	0/309 (0.0%)
	Bothersome	2/309 (0.6%)	0/309 (0.0%)
	# of Subjects	8/309 (2.6%)	4/309 (1.3%)
Starbursts	Frequency	1/309 (0.3%)	5/309 (1.6%)
	Severity	2/309 (0.6%)	3/309 (1.0%)
	Bothersome	0/309 (0.0%)	4/309 (1.3%)
	# of Subjects	3/309 (1.0%)	7/309 (2.3%)
Hazy Vision	Frequency	4/309 (1.3%)	1/309 (0.3%)
	Severity	2/309 (0.6%)	0/309 (0.0%)
	Bothersome	2/309 (0.6%)	0/309 (0.0%)
	# of Subjects	5/309 (1.6%)	1/309 (0.3%)
Blurred Vision	Frequency	3/309 (1.0%)	8/309 (2.6%)
	Severity	4/309 (1.3%)	4/309 (1.3%)
	Bothersome	5/309 (1.6%)	4/309 (1.3%)
	# of Subjects	5/309 (1.6%)	8/309 (2.6%)
Distortion	Frequency	1/309 (0.3%)	0/309 (0.0%)
	Severity	0/309 (0.0%)	0/309 (0.0%)
	Bothersome	1/309 (0.3%)	0/309 (0.0%)
	# of Subjects	1/309 (0.3%)	0/309 (0.0%)
Double or Multiple Images	Frequency	0/309 (0.0%)	4/309 (1.3%)
	Severity	0/309 (0.0%)	4/309 (1.3%)
	Bothersome	0/309 (0.0%)	3/309 (1.0%)
	# of Subjects	0/309 (0.0%)	5/309 (1.6%)
Fluctuation	Frequency	0/309 (0.0%)	2/309 (0.6%)
	Severity	2/309 (0.6%)	1/309 (0.3%)
	Bothersome	1/309 (0.3%)	1/309 (0.3%)
	# of Subjects	2/309 (0.6%)	2/309 (0.6%)
Focusing	Frequency	0/309 (0.0%)	2/309 (0.6%)
	Severity	7/309 (2.3%)	2/309 (0.6%)
	Bothersome	5/309 (1.6%)	2/309 (0.6%)
	# of Subjects	11/309 (3.6%)	3/309 (1.0%)
Judging Distance or Depth Perception	Frequency	6/309 (1.9%)	0/309 (0.0%)
	Severity	5/309 (1.6%)	1/309 (0.3%)
	Bothersome	4/309 (1.3%)	4/309 (1.3%)
	# of Subjects	9/309 (2.9%)	4/309 (1.3%)
	# of Subjects	39/309 (12.6%)	27/309 (8.7%)

N = Number of eyes with non-missing values the 12-Month visit. % = n/N ×100.
The symptoms with the two highest rates of 2-grades of worsening or more within each subscale are shaded.

Table 14 presents the two highest reported categories (i.e., symptoms reported as being "quite" or "very" bothersome, as well as those reported with severity of "moderate" or "severe") of bothersomeness and severity for each symptom at 12 months. The table does not, however, take into consideration the corresponding reports at baseline. As shown, there were very few reports overall, with the large majority being "quite" bothersome and of "moderate" severity. There was a single report each of "very" bothersome and "severe" involving the symptom of double or multiple images, and there was one report of "severe" for the symptom of difficulty focusing.

Table 14
Two Highest Categories of Bothersome and Severity for Each QoV Symptom at 12 Months

Visual Symptom	Number of patients out of 310 Total			
	Bothersome		Severity	
Glare	Quite	3 (1.0%)	Moderate	4 (1.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	3 (1.0%)	**Total**	4 (1.3%)
Halos	Quite	1 (0.3%)	Moderate	1 (0.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	1 (0.3%)	**Total**	1 (0.3%)
Starbursts	Quite	6 (1.9%)	Moderate	6 (1.9%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	6 (1.9%)	**Total**	6 (1.9%)
Hazy vision	Quite	0 (0.0%)	Moderate	0 (0.0%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	0 (0.0%)	**Total**	0 (0.0%)
Blurred vision	Quite	4 (1.3%)	Moderate	4 (1.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	4 (1.3%)	**Total**	4 (1.3%)
Distortion	Quite	0 (0.0%)	Moderate	0 (0.0%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	0 (0.0%)	**Total**	0 (0.0%)
Double or Multiple Images	Quite	2 (0.6%)	Moderate	3 (1.0%)
	Very	1 (0.3%)	Severe	1 (0.3%)
	Total	3 (1.0%)	**Total**	4 (1.3%)
Fluctuation	Quite	1 (0.3%)	Moderate	1 (0.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	1 (0.3%)	**Total**	1 (0.3%)
Focusing	Quite	3 (1.0%)	Moderate	2 (0.6%)
	Very	0 (0.0%)	Severe	1 (0.3%)
	Total	3 (1.0%)	**Total**	3 (1.0%)
Judging Distance or Depth Perception	Quite	5 (1.6%)	Moderate	2 (0.6%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	5 (1.6%)	**Total**	2 (0.6%)

Table 15 provides the OSDI score changes from baseline to each postoperative visit (during the last week) stratified by whether the score was "worse", "same", or "improved".

When looking at the OSDI score for symptoms (i.e. symptoms of light sensitivity, grittiness and ocular pain or soreness), a larger proportion of subjects reported improved symptoms compared to the proportion reporting worse symptoms at 12 months compared to the preoperative visit. However, the OSDI domain related to environmental triggers (i.e. windy conditions, low humidity and air conditioning) showed a slightly larger proportion of subjects reporting worse symptoms (30 %) compared to the proportion reporting improved symptoms (22 %) when subjects were queried about these specific environmental conditions.

Table 15
OSDI Score Change from Preoperative
All Treated Eyes

Sub-scale		Month 3	Month 6	Month 9	Month 12
Experienced Symptoms during the Last Week	**N**	**332**	**328**	**319**	**308**
	Worse	128/332 (39%)	92/328 (28%)	76/319 (24%)	73/308 (24%)
	Same	130/332 (39%)	145/328 (44%)	151/319 (47%)	144/308 (47%)
	Improved	74/332 (22%)	91/328 (28%)	92/319 (29%)	91/308 (30%)
	NA	0	0	0	0
	Not Reported	1	1	1	3
Felt Uncomfortable in Situations during the Last Week	**N**	**310**	**307**	**300**	**288**
	Worse	134/310 (43%)	119/307 (39%)	88/300 (29%)	87/288 (30%)
	Same	121/310 (39%)	127/307 (41%)	144/300 (48%)	138/288 (48%)
	Improved	55/310 (18%)	61/307 (20%)	68/300 (23%)	63/288 (22%)
	NA	22	21	19	20
	Not Reported	1	1	1	3

Change = Postop - Preop (pairwise).
Worse: Change > 0. Same: Change = 0. Improved: Change < 0.
NA = Number of subjects with "Not applicable" response to all questions of the sub-scale. The NA responses were not included in the OSDI score calculation. Subjects with NA to all questions of the sub-scale were excluded from the analyses.
Not Reported = Number of eyes with missing values at each visit.

Table 16 presents the frequency of moderate and severe dry eye symptoms classified by OSDI Scores preoperatively and at 6 months, and 12 months postoperatively. As shown, a total of 8% of subjects preoperatively had OSDI total scores ≥ 23, placing them in the “moderate” or “severe” categories. At 6 months, this remained consistent with baseline levels. However at 12 months, as well as the last available visits, there was a reduction (to 5% and 6%, respectively) in the proportion of subjects with total OSDI scores reflective of these two categories.

Table 16
Frequency of Moderate and Severe Dry Eye Symptoms Classified by OSDI Scores
All Treated Eyes

Severity of Dry Eye Symptoms	Preop	Month 6	Month 12	Last Available Visit
N	335	329	309	336
Moderate	16 (5%)	21 (6%)	7 (2%)	10 (3%)
Severe	10 (3%)	6 (2%)	8 (3%)	9 (3%)
Not Reported	1	0	2	0

OSDI score = (sum of scores) x 25/(# of questions answered). The responses of N/A were excluded.
"Moderate": OSDI score ≥ 23 to < 33. "Severe": OSDI score ≥ 33.
Scoring based on Miller et al. Minimal Clinically Important Difference for the Ocular Surface Disease Index *Arch Ophthalmol.* 2010;128(1):94-101.

Additional safety outcomes

Corneal topography

Computerized corneal topography was performed in all study subjects preoperatively and at the 3, 6, 9, and 12-month visits using the ATLAS 9000 system. A corneal axial curvature map was generated for each subject using the standard scale of 38.5 D to 49.5 D. Difference corneal power maps, i.e. 3 months minus baseline and 6 months minus 3 months, were also generated.

Other than the seven instances during the study, where topographies were mistakenly not performed, the remaining topographic scans were of high quality in terms of the interpretability of these topographic maps. As shown in Table 17, there were no postoperative findings suggesting the development of irregular astigmatism or ectasia or any "other" topographic findings outside of the specified categories, such as flattening over the superior opening incision, abnormal curvature changes over the peripheral treatment zone corresponding to the lenticule edge, or localized areas of steepening corresponding to retained lenticule fragments. Over the course of the study, there were 23 reports of tear film artifacts, involving 17 subjects. Each of these subjects had BSCVA of 20/25 or better at the respective visits. There were also seven reports of decentration greater than 1 mm, involving three subjects, but only one subject showed consistent decentration at all four scheduled postoperative visits indicating true decentration. All three subjects completed the study with BSCVA of 20/16 or better, but the subject with true decentration also experienced overcorrection of myopia, induced astigmatism, reduced contrast sensitivity, dry eye symptoms, and temporary loss of more than two lines of BSCVA. However, there is no definitive relationship of this subject's post-operative course to the finding of decentration on topography.

Table 17
Topography Findings
All Treated Eyes

	Preop n/N (%)	Month 3 n/N (%)	Month 6 n/N (%)	Month 9 n/N (%)	Month 12 n/N (%)
Evaluable	335	332	325	319	311
Irregular Astigmatism	0/335 (0.0%)	0/332 (0.0%)	0/325 (0.0%)	0/319 (0.0%)	0/311 (0.0%)
Ectasia	0/335 (0.0%)	0/332 (0.0%)	0/325 (0.0%)	0/319 (0.0%)	0/311 (0.0%)
Tear Film Artifacts	3/335 (0.9%)	3/332 (0.9%)	9/325 (2.8%)	3/319 (0.9%)	5/311 (1.6%)
Decentration	NA	1/332 (0.3%)	2/325 (0.6%)	2/319 (0.6%)	2/311 (0.6%)
Other	0/335 (0.0%)	0/332 (0.0%)	0/325 (0.0%)	0/319 (0.0%)	0/311 (0.0%)
Topography not performed	1	1	4	1	0
Total	336	333	329	320	311

N = Number of eyes with non-missing values at each visit. % = n/N ×100.

Wavefront outcomes

Wavefront aberrometry measurements were obtained at preoperatively, then at 3 and 12 months postoperatively, using the Tracey™ iTrace aberrometer, which has an infrared laser wavelength of 785 nm. A Zernike analysis was performed to evaluate the effect of the SMILE procedure on aberrations in the treated eyes. Calculations of the total higher order-order aberrations root mean square (HORMS) on the iTrace encompass the 6th order of Zernike polynomial terms. Since quantification of wavefront aberrations are dependent on pupil size, wavefront aberrometry was assessed at fixed pupil sizes. Depending on each subject's mesopic pupil size, wavefront images were obtained at 4.0 mm, 5.0 mm, and/or 6.0 mm, so that reliable data at the largest pupil size obtainable for each given subject could be compared preoperatively and postoperatively. If the pupil of any subject did not reach the minimum size necessary to obtain a reliable image at 4.0 mm, no comparisons of wavefront scans were performed.

Table 18 summarizes the change in wavefront aberrometry findings from baseline at the 3-month and 12-month visits, stratified by the largest scan size (i.e., 4.0, 5.0, or 6.0 mm) obtained preoperatively and postoperatively at these time points. These are specified in terms of the RMS changes of Zernike coefficients from baseline for the total HORMS, as well as for coma (microns) and spherical aberration (microns), specifically. Of the 311 eyes with 12-month visits at the time of the database lock, wavefront data for 250 eyes at the preoperative, 3-month, and 12-month visits were available for the comparison presented in Table 18.

Total HORMS for wavefront images obtained with an image size of 4.0 mm was essentially the same at baseline (0.175) and 12 months (0.173). Only a small increase in total HORMS was observed for 5.0 mm scan sizes (from 0.289 at baseline to 0.340), with slightly larger increases for 6.0 mm scan sizes (from 0.450 at baseline to 0.698), as expected. The mean changes in total HORMS from baseline to 12 months for scan sizes of 5.0 and 6.0 mm were 0.051 and 0.248, respectively.

With regard to postoperative changes in coma and spherical aberration for 4.0 mm scan sizes at 3 and 12 months, there was essentially no change. At the 5.0 mm scan size, the postoperative changes at both time points with respect to coma and spherical aberration were slightly more evident, with changes less than 0.07 microns for coma and less than 0.05 microns for spherical aberration. Not unexpected were the more pronounced corresponding changes at the 6.0 mm scan size, though only 16 scans were available for analysis.

Table 18
Change in Wavefront Aberrometry from Preoperative
Stratified by Largest Scan Size (mm)
Treated Eyes with Preoperative, 3-Month, and 12-Month Visits

Scan Size	Parameters	Statistics	Month 3	Month 12
4.0	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	106	106
		Mean (SD)	-0.001 (0.086)	-0.002 (0.079)
		Min, Max	-0.310, 0.234	-0.341, 0.142
	Coma	Mean (SD)	0.010 (0.087)	0.013 (0.079)
		Min, Max	-0.268, 0.258	-0.274, 0.199
	Spherical	Mean (SD)	-0.002 (0.047)	-0.002 (0.047)
		Min, Max	-0.201, 0.120	-0.180, 0.112
5.0	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	128	128
		Mean (SD)	0.049 (0.141)	0.051 (0.149)
		Min, Max	-0.293, 0.397	-0.311, 0.365
	Coma	Mean (SD)	0.070 (0.170)	0.064 (0.170)
		Min, Max	-0.288, 0.515	-0.420, 0.467
	Spherical	Mean (SD)	0.048 (0.100)	0.046 (0.101)
		Min, Max	-0.184, 0.400	-0.174, 0.339
6.0	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	16	16
		Mean (SD)	0.220 (0.268)	0.248 (0.314)
		Min, Max	-0.239, 0.766	-0.248, 0.806
	Coma	Mean (SD)	0.232 (0.289)	0.261 (0.326)
		Min, Max	-0.255, 0.793	-0.392, 0.874
	Spherical	Mean (SD)	0.129 (0.196)	0.149 (0.173)
		Min, Max	-0.285, 0.511	-0.255, 0.414
Overall	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	250	250
		Mean (SD)	0.039 (0.143)	0.041 (0.153)
		Min, Max	-0.310, 0.766	-0.341, 0.806
	Coma	Mean (SD)	0.055 (0.161)	0.055 (0.165)
		Min, Max	-0.288, 0.793	-0.420, 0.874
	Spherical	Mean (SD)	0.032 (0.098)	0.032 (0.097)
		Min, Max	-0.285, 0.511	-0.255, 0.414

N = Number of case report forms received with non-missing values at each visit.
The largest scan size was 4.0, 5.0, or 6.0 mm, depending on the largest scan size obtained at all the preoperative and postoperative visits

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Key effectiveness outcomes

A summary of the key effectiveness outcomes for all 333 eyes in the effectiveness population is shown in Table 19. While there were no eyes preoperatively with UCVA of 20/40 or better, at the 6-month visit, 99.7 % (327/328) and 87.5 % (287/328) of treated eyes achieved UCVA levels of 20/40 or better and 20/20 or better, respectively. With respect to MRSE predictability, 93.0% and 98.5% achieved MRSE within ±0.50D and ±1.00D, respectively, of the attempted correction.

Table 19
Summary of Key Effectiveness Variables
Effectiveness Cohort Eyes

Key Effectiveness Variables	Week 1 n/N (%) 95 % CI	Month 1 n/N (%) 95 % CI	Month 3 n/N (%) 95 % CI	Month 6 n/N (%) 95 % CI	Month 9 n/N (%) 95 % CI	Month 12 n/N (%) 95 % CI
Effectiveness Variables (Effectiveness Population)						
UCVA, 20/16 or better	95/332 (28.6 %) (23.8 %, 33.8 %)	155/333 (46.5 %) (41.1 %, 52.1 %)	192/331 (58.0 %) (52.5 %, 63.4 %)	197/328 (60.1 %) (54.5 %, 65.4 %)	196/319 (61.4 %) (55.9 %, 66.8 %)	198/310 (63.9 %) (58.2 %, 69.2 %)
UCVA, 20/20 or better	210/332 (63.3 %) (57.8 %, 68.5 %)	262/333 (78.7 %) (73.9 %, 83.0 %)	282/331 (85.2 %) (80.9 %, 88.8 %)	287/328 (87.5 %) (83.4 %, 90.9 %)	281/319 (88.1 %) (84.0 %, 91.4 %)	273/310 (88.1 %) (83.9 %, 91.5 %)
UCVA, 20/25 or better	286/332 (86.1 %) (82.0 %, 89.7 %)	308/333 (92.5 %) (89.1 %, 95.1 %)	317/331 (95.8 %) (93.0 %, 97.7 %)	313/328 (95.4 %) (92.6 %, 97.4 %)	309/319 (96.9 %) (94.3 %, 98.5 %)	301/310 (97.1 %) (94.6 %, 98.7 %)
UCVA, 20/32 or better	315/332 (94.9 %) (91.9 %, 97.0 %)	324/333 (97.3 %) (94.9 %, 98.8 %)	324/331 (97.9 %) (95.7 %, 99.1 %)	322/328 (98.2 %) (96.1 %, 99.3 %)	315/319 (98.7 %) (96.8 %, 99.7 %)	305/310 (98.4 %) (96.3 %, 99.5 %)
UCVA, 20/40 or better	325/332 (97.9 %) (95.7 %, 99.1 %)	333/333 (100.0 %) (98.9 %, 100.0 %)	329/331 (99.4 %) (97.8 %, 99.9 %)	327/328 (99.7 %) (98.3 %, 100.0 %)	318/319 (99.7 %) (98.3 %, 100.0 %)	309/310 (99.7 %) (98.2 %, 100.0 %)
MRSE, Attempted vs. Achieved, ±0.25D	262/331 (79.2 %) (74.4 %, 83.4 %)	264/333 (79.3 %) (74.5 %, 83.5 %)	262/331 (79.2 %) (74.4 %, 83.4 %)	261/328 (79.6 %) (74.8 %, 83.8 %)	258/319 (80.9 %) (76.1 %, 85.0 %)	250/310 (80.6 %) (75.8 %, 84.9 %)
MRSE, Attempted vs. Achieved, ±0.50D	308/331 (93.1 %) (89.8 %, 95.5 %)	310/333 (93.1 %) (89.8 %, 95.6 %)	304/331 (91.8 %) (88.4 %, 94.6 %)	305/328 (93.0 %) (89.7 %, 95.5 %)	303/319 (95.0 %) (92.0 %, 97.1 %)	291/310 (93.9 %) (90.6 %, 96.3 %)
MRSE, Attempted vs. Achieved, ±1.00D	328/331 (99.1 %) (97.4 %, 99.8 %)	331/333 (99.4 %) (97.8 %, 99.9 %)	328/331 (99.1 %) (97.4 %, 99.8 %)	323/328 (98.5 %) (96.5 %, 99.5 %)	316/319 (99.1 %) (97.3 %, 99.8 %)	306/310 (98.7 %) (96.7 %, 99.6 %)
MRSE, Attempted vs. Achieved, ±2.00D	331/331 (100.0 %) (98.9 %, 100.0 %)	333/333 (100.0 %) (98.9 %, 100.0 %)	331/331 (100.0 %) (98.9 %, 100.0 %)	328/328 (100.0 %) (98.9 %, 100.0 %)	319/319 (100.0 %) (98.9 %, 100.0 %)	310/310 (100.0 %) (98.8 %, 100.0 %)

N = Number of case report forms received with non-missing values at each visit.
95 % CI was calculated based on Clopper-Pearson exact method.

Stratification by age revealed differences in proportions of eyes achieving UCVA of 20/20 or better, with lower proportions of eyes in the 40 to 49 and 50+ age groups achieving UCVA of 20/20 or better at the point of stability (72.0% for the 40 to 49 years subgroup and 71.4% for the 50 years & above subgroup). Despite these slight differences, the older age groups still experienced a clinically significant visual benefit as 98.4% of the subjects in these age bins achieved UCVA of 20/40 or better postoperatively.

Key effectiveness outcomes stratified by preoperative manifest refraction sphere (MRSPH)

The key effectiveness variables at 6 months stratified by preoperative MRSPH are presented below in Table 20. As shown below, there was no obvious clinically significant impact of preoperative MRSPH on 6-month outcomes for UCVA of 20/40 or better or on outcomes for achieved MRSE within ± 0.50 D of attempted MRSPH.

Table 20
Summary of Key Effectiveness Variables at 6 Months
Stratified By Preoperative MRSPH
Effectiveness Population

Key Effectiveness Variables	Preop MRSPH					
	0.00 to -1.00 D n/N (%)	-1.01 to -2.00 D n/N (%)	-2.01 to -3.00 D n/N (%)	-3.01 to -4.00 D n/N (%)	-4.01 to -5.00 D n/N (%)	-5.01 to -6.00 D n/N (%)
UCVA, 20/16 or better	2/4 (50.0%)	20/35 (57.1%)	35/52 (67.3%)	37/50 (74.0%)	32/48 (66.7%)	23/42 (54.8%)
UCVA, 20/20 or better	3/4 (75.0%)	32/35 (91.4%)	48/52 (92.3%)	48/50 (96.0%)	44/48 (91.7%)	35/42 (83.3%)
UCVA, 20/25 or better	4/4 (100.0%)	33/35 (94.3%)	51/52 (98.1%)	48/50 (96.0%)	47/48 (97.9%)	40/42 (95.2%)
UCVA, 20/32 or better	4/4 (100.0%)	35/35 (100.0%)	51/52 (98.1%)	48/50 (96.0%)	48/48 (100.0%)	40/42 (95.2%)
UCVA, 20/40 or better	4/4 (100.0%)	35/35 (100.0%)	52/52 (100.0%)	49/50 (98.0%)	48/48 (100.0%)	42/42 (100.0%)
MRSE, Attempted vs. Achieved, ±0.25D	3/4 (75.0%)	29/35 (82.9%)	45/52 (86.5%)	46/50 (92.0%)	40/48 (83.3%)	34/42 (81.0%)
MRSE, Attempted vs. Achieved, ±0.50D	4/4 (100.0%)	34/35 (97.1%)	50/52 (96.2%)	48/50 (96.0%)	45/48 (93.8%)	38/42 (90.5%)
MRSE, Attempted vs. Achieved, ±1.00D	4/4 (100.0%)	35/35 (100.0%)	52/52 (100.0%)	49/50 (98.0%)	48/48 (100.0%)	41/42 (97.6%)
MRSE, Attempted vs. Achieved, ±2.00D	4/4 (100.0%)	35/35 (100.0%)	52/52 (100.0%)	50/50 (100.0%)	48/48 (100.0%)	42/42 (100.0%)

Key Effectiveness Variables	Preop MRSPH				Total
	-6.01 to -7.00 D n/N (%)	-7.01 to -8.00 D n/N (%)	-8.01 to -9.00 D[1] n/N (%)	> -9.01 D[1] n/N (%)	n/N (%)
UCVA, 20/16 or better	25/42 (59.5%)	16/28 (57.1%)	4/15 (26.7%)	3/12 (25.0%)	197/328 (60.1%)
UCVA, 20/20 or better	36/42 (85.7%)	24/28 (85.7%)	9/15 (60.0%)	8/12 (66.7%)	287/328 (87.5%)
UCVA, 20/25 or better	39/42 (92.9%)	27/28 (96.4%)	13/15 (86.7%)	11/12 (91.7%)	313/328 (95.4%)
UCVA, 20/32 or better	42/42 (100.0%)	28/28 (100.0%)	15/15 (100.0%)	11/12 (91.7%)	322/328 (98.2%)
UCVA, 20/40 or better	42/42 (100.0%)	28/28 (100.0%)	15/15 (100.0%)	12/12 (100.0%)	327/328 (99.7%)
MRSE, Attempted vs. Achieved, ±0.25D	31/42 (73.8%)	16/28 (57.1%)	11/15 (73.3%)	6/12 (50.0%)	261/328 (79.6%)
MRSE, Attempted vs. Achieved, ±0.50D	38/42 (90.5%)	24/28 (85.7%)	14/15 (93.3%)	10/12 (83.3%)	305/328 (93.0%)
MRSE, Attempted vs. Achieved, ±1.00D	41/42 (97.6%)	27/28 (96.4%)	15/15 (100.0%)	11/12 (91.7%)	323/328 (98.5%)
MRSE, Attempted vs. Achieved, ±2.00D	42/42 (100.0%)	28/28 (100.0%)	15/15 (100.0%)	12/12 (100.0%)	328/328 (100.0%)

N = Number of case report forms received with non-missing values for each group.

[1] Please note that treatment of -8.01 to -10.0 D will present a flagged warning to the users so that the user understands that correction of these powers had not been substantiated by an adequate set of data.

Postoperative UCVA versus preoperative BSCVA

Postoperative UCVA results, as compared to preoperative BSCVA at all scheduled visits, are presented in Table 21. Over the course of the study from Day 1 through Month 12, there was a steady increase in the proportion of eyes with UCVA equal to or better than preoperative BSCVA.

Table 21
Postoperative Uncorrected Visual Acuity (UCVA) Compared to Preoperative Best Spectacle Corrected Visual Acuity (BSCVA) Effectiveness Cohort Eyes

UCVA	Day 1 n	Day 1 (%)	Week 1 n	Week 1 (%)	Month 1 n	Month 1 (%)	Month 3 n	Month 3 (%)
Available (N)	333		332		333		331	
UCVA >2 Lines Better than Preop BSCVA	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)
UCVA 2 Lines Better than Preop BSCVA	1	(0.3 %)	1	(0.3 %)	5	(1.5 %)	12	(3.6 %)
UCVA 1 Line Better than Preop BSCVA	10	(3.0 %)	20	(6.0 %)	56	(16.8 %)	71	(21.5 %)
UCVA Equal to Preop BSCVA	51	(15.3 %)	106	(31.9 %)	125	(37.5 %)	137	(41.4 %)
UCVA 1 Line Worse than Preop BSCVA	111	(33.3 %)	109	(32.8 %)	94	(28.2 %)	73	(22.1 %)
UCVA 2 Lines Worse than Preop BSCVA	86	(25.8 %)	56	(16.9 %)	31	(9.3 %)	25	(7.6 %)
UCVA >2 Lines Worse than Preop BSCVA	74	(22.2 %)	40	(12.0 %)	22	(6.6 %)	13	(3.9 %)
UCVA Better than or Equal to Preop BSCVA	62	(18.6 %)	127	(38.3 %)	186	(55.9 %)	220	(66.5 %)
Not reported	0		0		0		0	
Total	333		332		333		331	

UCVA	Month 6 n	Month 6 (%)	Month 9 n	Month 9 (%)	Month 12 n	Month 12 (%)
Available (N)	328		319		310	
UCVA >2 Lines Better than Preop BSCVA	1	(0.3 %)	1	(0.3 %)	3	(1.0 %)
UCVA 2 Lines Better than Preop BSCVA	12	(3.7 %)	4	(1.3 %)	13	(4.2 %)
UCVA 1 Line Better than Preop BSCVA	83	(25.3 %)	93	(29.2 %)	93	(30.0 %)
UCVA Equal to Preop BSCVA	133	(40.5 %)	132	(41.4 %)	119	(38.4 %)
UCVA 1 Line Worse than Preop BSCVA	67	(20.4 %)	59	(18.5 %)	57	(18.4 %)
UCVA 2 Lines Worse than Preop BSCVA	19	(5.8 %)	20	(6.3 %)	18	(5.8 %)
UCVA >2 Lines Worse than Preop BSCVA	13	(4.0 %)	10	(3.1 %)	7	(2.3 %)
UCVA Better than or Equal to Preop BSCVA	229	(69.8 %)	230	(72.1 %)	228	(73.5 %)

Not reported	0	0	0
Total	328	319	310

N = Number of case report forms received with non-missing values at each visit.

Accuracy of MRSE

Accuracy of the intended refractive correction, with respect to MRSE, is shown in Table 22 for the 6-month consistent effectiveness cohort. This cohort consists of all eyes from the effectiveness cohort with every follow-up exam from 1 week onward to the 6-month point of stability. The deviation of MRSE is considered in terms of a refractive target that is not necessarily emmetropia, due to the astigmatic components of 0.25 D and 0.50 D that were not treated in the study.

The MRSE was within ±1.00 D of attempted correction in over 98 % of eyes at all study visits. No less than 79 % of eyes were within ±0.25 D, and no less than 92 % of eyes were within ±0.50 D of the targeted MRSE correction from the 1-week through 12-month visits. There were no reports of overcorrection > 1.00 D MRSE at any point in the study.

Table 22
Accuracy of MRSE — Attempted vs. Achieved
6-Month Consistent Effectiveness Cohort

MRSE Deviation	Week 1 n/N (%)	Month 1 n/N (%)	Month 3 n/N (%)
Available (N)	326	327	327
± 0.25 D	257/326 (78.8%)	259/327 (79.2%)	258/327 (78.9%)
± 0.50 D	303/326 (92.9%)	304/327 (93.0%)	300/327 (91.7%)
± 1.00 D	323/326 (99.1%)	325/327 (99.4%)	324/327 (99.1%)
± 2.00 D	326/326 (100.0%)	327/327 (100.0%)	327/327 (100.0%)
Overcorrected > 1.00 D	0/326 (0.0%)	0/327 (0.0%)	0/327 (0.0%)
Overcorrected > 2.00 D	0/326 (0.0%)	0/327 (0.0%)	0/327 (0.0%)
Undercorrected > 1.00 D	3/326 (0.9%)	2/327 (0.6%)	3/327 (0.9%)
Undercorrected > 2.00 D	0/326 (0.0%)	0/327 (0.0%)	0/327 (0.0%)
Mean (SD)	0.035 (0.311)	0.054 (0.301)	0.062 (0.328)
Range	-1.000, 1.375	-1.000, 1.375	-0.875, 1.875
Not reported	1	0	0
Total	327	327	327

MRSE Deviation	Month 6 n/N (%)	Month 9 n/N (%)	Month 12 n/N (%)
Available (N)	327	316	307
± 0.25 D	260/327 (79.5%)	256/316 (81.0%)	248/307 (80.8%)
± 0.50 D	304/327 (93.0%)	300/316 (94.9%)	288/307 (93.8%)
± 1.00 D	322/327 (98.5%)	313/316 (99.1%)	303/307 (98.7%)
± 2.00 D	327/327 (100.0%)	316/316 (100.0%)	307/307 (100.0%)
Overcorrected > 1.00 D	0/327 (0.0%)	0/316 (0.0%)	0/307 (0.0%)
Overcorrected > 2.00 D	0/327 (0.0%)	0/316 (0.0%)	0/307 (0.0%)
Undercorrected > 1.00 D	5/327 (1.5%)	3/316 (0.9%)	4/307 (1.3%)
Undercorrected > 2.00 D	0/327 (0.0%)	0/316 (0.0%)	0/307 (0.0%)
Mean (SD)	0.041 (0.325)	0.023 (0.292)	0.017 (0.309)
Range	-0.750, 1.750	-0.875, 1.250	-1.000, 1.750
Not reported	0	0	0
Total	327	316	307

N = Number of case report forms received with non-missing values at each visit.

Stability of MRSE

As presented in Table 23**,** MRSE stability was identified at the 3 to 6 month interval and confirmed at the 6 to 9 month interval.

Table 23
Stability of Manifest Refraction Spherical Equivalent (MRSE)
Effectiveness Population

Change in MRSE	Between 1 and 3 Months	Between 3 and 6 Months	Between 6 and 9 Months	Between 9 and 12 Months
Pairwise Sequential Visits				
Eyes within 0.50 D change (n/N, %, [% CI][1])	319/331 (96.4%) (93.8%, 98.1%)	317/327 (96.9%) (94.4%, 98.5%)	311/317 (98.1%) (95.9%, 99.3%)	301/308 (97.7%) (95.4%, 99.1%)
Eyes within 1.00 D change (n/N, %, [% CI][1])	331/331 (100.0%) (98.9%, 100.0%)	327/327 (100.0%) (98.9%, 100.0%)	316/317 (99.7%) (98.3%, 100.0%)	307/308 (99.7%) (98.2%, 100.0%)
Mean change between visits (D) SD 95% CI	-0.008 0.241 (-0.034, 0.018)	0.021 0.232 (-0.005, 0.046)	0.013 0.213 (-0.011, 0.037)	0.005 0.198 (-0.017, 0.027)
Mean change per month (D)	-0.004	0.007	0.004	0.002
Mean change per year (D) (change per month × 12)	-0.048	0.083	0.052	0.019
12-Month Consistent Cohort				
Eyes within 0.50 D change (n/N, %, [% CI][1])	296/305 (97.0%) (94.5%, 98.6%)	298/305 (97.7%) (95.3%, 99.1%)	301/305 (98.7%) (96.7%, 99.6%)	298/305 (97.7%) (95.3%, 99.1%)
Eyes within 1.00 D change (n/N, %, [% CI][1])	305/305 (100.0%) (98.8%, 100.0%)	305/305 (100.0%) (98.8%, 100.0%)	304/305 (99.7%) (98.2%, 100.0%)	304/305 (99.7%) (98.2%, 100.0%)
Mean change between visits (D) SD 95% CI	0.002 0.231 (-0.024, 0.028)	0.014 0.219 (-0.011, 0.039)	0.013 0.205 (-0.010, 0.036)	0.005 0.198 (-0.018, 0.027)
Mean change per month (D)	0.001	0.005	0.004	0.002
Mean change per year (D) (change per month × 12)	0.010	0.056	0.051	0.018

Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam.
Consistent Cohort = All eyes examined at 1, 3, 6, 9 and 12 months.
[1] 95% CI was calculated based on Clopper-Pearson method.

Surgical planning and procedures

Laser activation, calibration, and surgical room environmental control

☞ Detailed information on general operation of the VisuMax is provided in the VisuMax Femtosecond Laser user manual

☞ Detailed information on general operation of the VisuMax as well as the planning and execution of treatment is to be found in the VisuMax Femtosecond Laser user manual

☞ The stromal thickness shown is a theoretical anticipated value. If changes occur in the course of the operation the achieved residual stromal thickness may deviate from the value shown. Please take into account that the calculation of residual stromal thickness is based on the pachymetry value entered, which is subject to measurement uncertainty.

General VisuMax procedure overview

Note that the following procedure overview is general for all VisuMax procedures. See *Treatment Planning*, page 45 and following, for complete procedure instructions.

1. The surgeon or other suitably trained personnel switches on the VisuMax Femtosecond Laser and initiates the surgical start-up routine.
2. The monitor on the left-hand side in combination with the keyboard/trackball is used to enter patient data and patient related treatment parameters as part of the treatment planning process. Treatment parameters entered by the surgeon may include patient eye manifest refraction, pachymetry, lenticule diameter, cap diameter, etc. After the appropriate treatment parameters have been entered, the particular resection parameters for the procedure are displayed to the surgeon on the video display. The surgeon must review and verify the parameters (i.e. the residual stromal thickness for corneal caps, or the lenticule diameter for lenticule removal).
3. When the treatment planning is complete, the keyboard tray is pushed back into the VisuMax Femtosecond Laser console housing. This activates the surgery controls on the touch screen (located on the right hand side of the laser arm).
4. The patient is then positioned on the Patient Supporting System (PSS). The PSS is manually rotated into the observation position underneath the laser arm.
5. The PSS with the patient situated properly is then moved using the PSS translation control joystick to center the eye to be treated in the observation position under the surgical microscope.
6. Using the surgical microscope, the surgeon prepares the eye to be treated.
7. The touch screen display is used to start the surgical routine. The treatment parameters previously entered should be verified.

8. Instructions are displayed on the touch screen display by a treatment wizard, and should be followed by the surgeon.
9. The surgeon places the sterile contact glass of the Treatment Pack onto the treatment objective lens and connects the filter and vacuum connector to the Vacuum Connection fixture on the laser console when indicated by the treatment wizard on the touch screen display.
10. The treatment objective lens is then slightly lifted by the physician when indication is shown on the touchscreen display. The VisuMax Femtosecond Laser then automatically initiates a system test.
11. After the system test has been completed, the surgeon checks the preparation of the eye once again and moves the Patient Supporting System into the treatment position.
12. In the treatment position, the surgeon positions the eye to be treated against the contact glass so that the lens applanates the patient's cornea. Taking care to center the contact glass with respect to the optical axis of the patient's eye, the cornea is then completely pressed against the contact glass. The surgeon then presses the vacuum suction control which produces appropriate suction force to cause the eye to adhere to the contact glass.
13. When the suction pressure is sensed by the laser console hardware to reach the acceptable range, the READY mode indicator becomes active.
14. The laser surgery procedure is initiated by pressing and holding down the foot switch.

☞ Carefully monitor centration and suction throughout the laser treatment initiation.

15. Upon completion of the laser procedure, the vacuum is automatically released and the patient's eye is separated from the contact glass. The surgeon returns the PSS and patient to the observation position using the PSS joystick.
16. The physician uses the VisuMax Femtosecond Laser surgical microscope to complete the treatment under direct visualization, as required.
17. When the entire surgical procedure has been completed, the surgeon moves the PSS into the patient exit position.
18. Finally, the physician clears the surgery area and closes the treatment routine in the user interface/Touch Screen Display. The software returns the display to the main screen, and is now ready for a new surgical procedure.

Treatment license

The VisuMax SMILE procedure requires activation by a treatment license to carry out the surgery. The treatment license will be provided by Carl Zeiss Meditec or its authorized representatives based on the commercial agreement.

Treatment parameters

Treatment parameters available for the VisuMax lenticule procedure are provided in the **Technical Data section** of this document.

Treatment planning

☞ Treatment License - The VisuMax SMILE procedure requires activation by a treatment license for the specific procedure to carry out the surgery. The treatment license will be provided by Carl Zeiss Meditec or its authorized representatives based on the commercial agreement.

☞ For system start-up, patient record management, and general laser operating instructions, see the VisuMax Femtosecond Laser's user manual.

Treatment planning steps are provided in this section.

1. Switch the laser system on. The computer will execute several internal test routines and then automatically start the main menu.
2. Select the small incision lenticule extraction procedure.
3. To enter procedure parameters, use the two separate tabs displayed in the graphical user interface (GUI) window. The window shows two separate tabs: the **Lenticule** Tab and the **Cap** Tab.

The Lenticule tab contains procedure parameters associated with the refractive aspect of the procedure. The Cap tab contains parameters related to the creation of the opening and lenticule access cuts.

Parameters may be entered directly using the trackball and cursor, or by simply using the cursor to increment the up and down arrows. Some parameters are not adjustable.

NOTE: Laser parameters cannot be modified by the users.

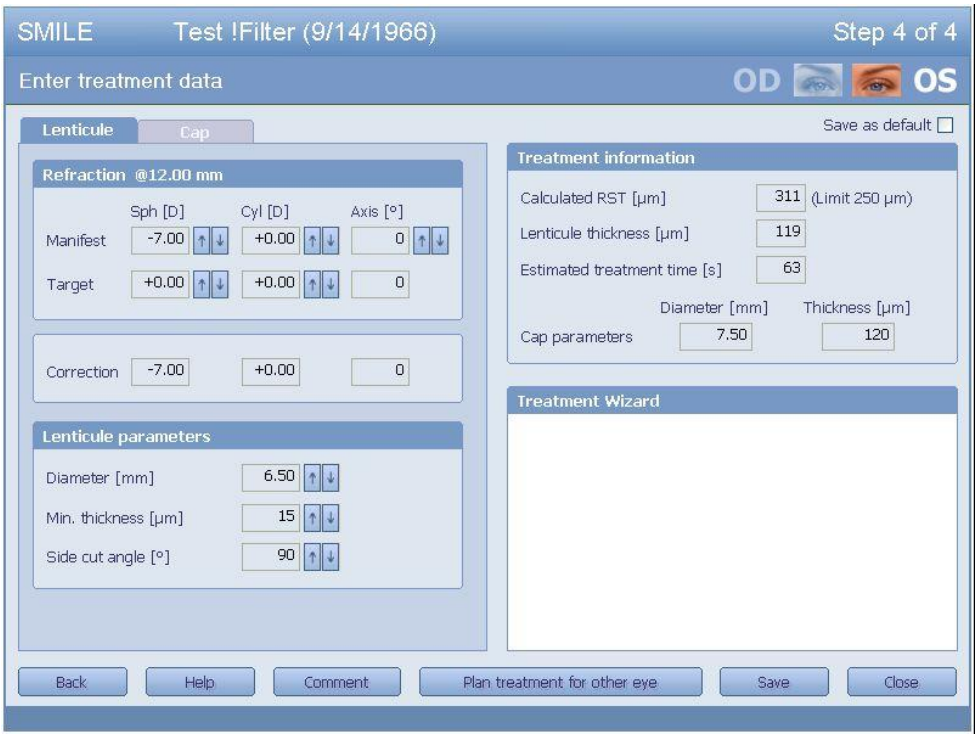

Figure 4. Lenticule Tab used for entering Procedure Parameters Associated with the Lenticule Cutting and Refractive Targets

Lenticule tab parameters are grouped into Refraction, Lenticule parameters, and Treatment Information (Figure 4).

In the Refractive parameter group, enter the patient's MRSPH in the **Manifest Sph [D]** box. The Correction fields represent the intended correction and are calculated by the VisuMax as the difference between the manifest and target refraction values. Corrections are restricted to sphere only, from ≥ -1.00 D to ≤ -8.00 D. A value of 0.00 D must be entered for both manifest cylinder and target cylinder to ensure that only a spherical correction is performed.

In the Lenticule Parameters group, the Minimum Edge Thickness and Side Cut Angle parameters are fixed (15 microns and 90 degrees, respectively). Enter the Lenticule Diameter in millimeters (allowed values are 6.0 or 6.5 mm). Enter a Lenticule Diameter of 6.5 mm unless doing so would result in a residual stromal thickness < 250 microns for the treatment eye. In that case, enter a Lenticule Diameter of 6.0 mm. If the residual stromal thickness is still < 250 microns, the eye cannot be treated. The residual stromal thickness is displayed in the Calculated RST field under Treatment Information.

Treatment Information parameters include pachymetry measurements and desired correction values. These displayed values include calculated residual stromal thickness, maximum or central lenticule thickness, and estimated treatment time. The minimum residual stromal thickness is fixed at 250 microns.

Cap tab parameters (Figure 5) are grouped into Anatomical Parameters, Treatment Pack size, Cap Parameters, Incision Parameters, and Treatment Information.

The Cap tab is used to select or indicate the eye to be treated. A graphic of both eyes with a designation is shown in the upper right part of the window. Use the cursor to select the appropriate eye. The graphic will highlight your choice.

In the Anatomical parameters group, biometric values are entered. Enter the pachymetry values in the appropriate box. The average corneal radius may be entered directly into the Corneal Radius field. Alternatively, K-readings may be entered. To enter K-readings, select the K-readings button and enter values for K min and K max. The corneal radius is calculated using the index of refraction stored in the Settings window and the formula:

$$1/Kmean(mm) = (1/Kmax(mm) + 1/Kmin(mm))/2.0$$

In the Treatment Pack size group, only the small size can be selected.

In the Cap Parameters group, enter a Cap Diameter of 7.5 mm (if a 6.5 mm lenticule diameter was specified) or 7.0 mm (if a 6.0 mm lenticule diameter was specified). Cap Thickness is fixed at 120 microns and Side Cut Angle is fixed at 90 degrees.

In the Incision Parameters group, only a single incision can be selected. The Position parameter refers to the opening incision clock position, and is fixed at the superior location. The Angle parameter refers to the angular width of the procedure, and is fixed at 90 degrees. The width parameter is calculated based on the Angle parameter and the Cap Diameter parameter and is not independently selected.

Treatment Information parameters are again summarized/displayed for convenience. The Treatment Wizard box indicates any problems associated with selected treatment parameters. If any parameters entered are incorrect or inconsistent, appropriate fields will be highlighted in red and the user can select and adjust the indicated fields to correct any errors.

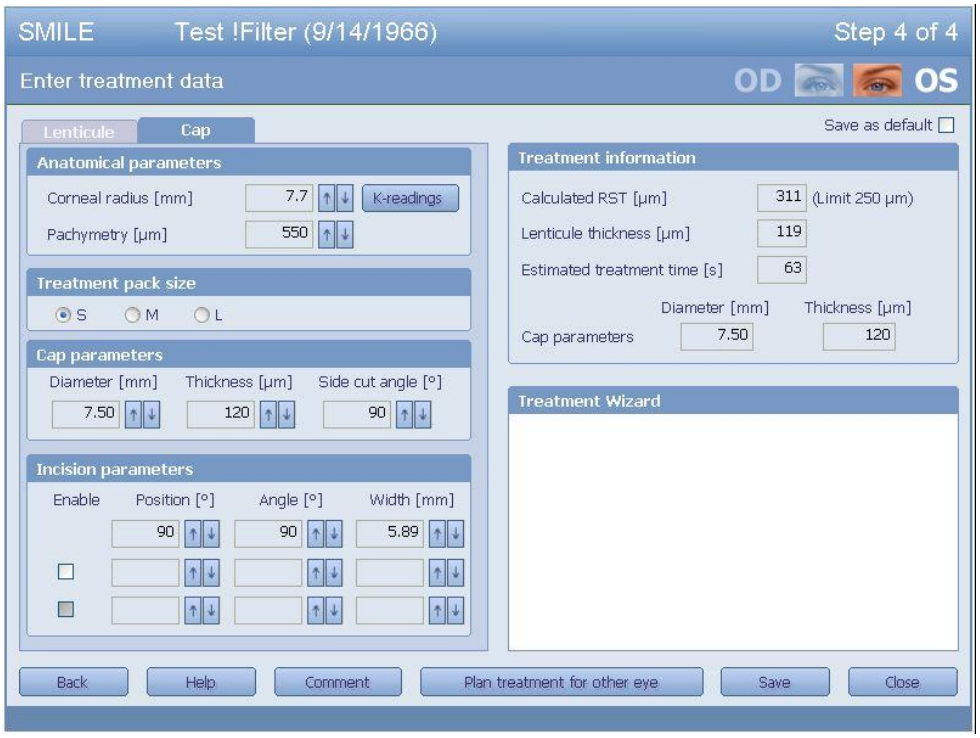

Figure 5. Cap Tab used for entering Procedure Parameters Associated with the Opening Cut and Cap Cut

The user is to proceed as per the following instructions:

- Click **Save** to store treatment data. Click **Close** to return to step 1 - Select patient.
- To cancel the treatment planning without storing the data, click on **Close** without previously saving.
- Once the planning is complete, click on **Close** to return to step 1. Click on **Cancel** to quit planning and return to the main dialog.
- Once the treatment planning has been completed, push the keyboard back into the VisuMax housing. This procedure activates the treatment check on the touchscreen on the right-hand side.

Laser treatment and SMILE procedure

WARNING

Upon connection of the Treatment Pack you will be asked via the graphical user interface to perform an excursion test. When testing the excursion by lifting the treatment objective, the treatment objective must travel smoothly. If you feel that the treatment objective does not move freely, shut down the laser and contact Carl Zeiss Meditec customer service. As soon as the treatment objective is moved, the system test will be started, a status bar on the display shows the progress and end of the test.

CAUTION

Use only Treatment Packs expressly approved by Carl Zeiss Meditec. If Treatment Packs not expressly approved by Carl Zeiss Meditec are used, there is a risk of treatment errors.

Examine the wrappings of the Treatment Pack to ensure there is no damage before removing the Treatment Pack. Do not use a Treatment Pack if you are not certain that it is sterile. In the subsequent procedure take steps to ensure that the Treatment Pack remains sterile! Treatment Packs are disposable articles. The re-sterilization of Treatment Packs is not permitted. Considerable risk of injury to the patient exists in re-sterilization.

Ensure sterility, especially of the contact glass!

Ensure that the filter is correctly attached.

Ensure that no liquid is allowed to enter the vacuum system to avoid suction loss with termination of treatment.

Do not use a contacting agent, as the desired result will otherwise not be achieved.

Take special care to ensure precise alignment of the patient's eye. Continuously optimize the eye position along the X and Y axes as the eye is brought closer to the contact glass.

Surgeons should be vigilant for possible small eye movements through the operating microscope during the procedure. There can be a relative shift of the pupil center during the operation, which does not necessarily entail a shift of the cornea. The process must be stopped immediately if the size and position of the incision deviate from the intended treatment.

Prior to and throughout treatment, ensure adequate suction. Total surgery time should be kept as short as possible, minimizing conditions which may distract the patient.

Observe the entire surgical procedure through the surgical microscope. The process must be stopped immediately if the size and position of the incision deviate from the intended treatment. This may otherwise result in treatment errors. Do not perform surgery if the incisions are incorrectly positioned!

The formation of bubbles at the periphery of the suction zone is an indication of imminent suction loss. In the event of a complete loss of suction, the VisuMax console detects the reduction in pressure of the eye and the procedure is automatically halted.

Preparation

1. Adjust the microscope positioning controls and adjust the microscope magnification as required.
2. Bring the patient into the operating room and have the patient lie comfortably supine on the patient supporting system (PSS) such that his/her eye is appropriately positioned.
3. Ready the Treatment Pack by first examining the packaging to verify that there is no damage. Remove the sterile Treatment Pack from the packaging. Do not use a Treatment Pack if you are not certain that it is sterile.
4. Connect the filter from the Treatment Pack to the vacuum connection on the laser console.
5. Place the sterile contact glass on the laser aperture. The contact glass will now be held to the treatment objective by suction pressure.
6. The GUI instructs the user to manually lift the treatment objective. If the treatment objective does not move freely, abort the procedure, shut down the VisuMax Femtosecond Laser and contact customer service.
7. Verify patient, eye, and prescription to be treated.
8. Approximately two minutes prior to the laser initiation, administer topical proparacaine or tetracaine anesthetic to the conjunctival sac of the operative eye. The patient is monitored as appropriate for the degree of anesthesia.
9. Swivel the PSS into the observation position.
10. Prep and drape the operating area for corneal refractive surgery.
11. Using the illumination controls, illuminate the eye and surgical field appropriately.
12. Insert a lid speculum to provide adequate corneal exposure.
13. Open the lid speculum to comfortably accommodate the contact glass using the PSS control joystick, fine align the PSS such that the iris is in the center of the palpebral fissure. Rotate the patient head as necessary to allow for contact glass to touch cornea without impinging on nose or other face structures.
14. Remove excess fluid from the cornea and area where the suction surface of the Treatment Pack will be applied. The target corneal surface should be moist but not wet.
15. Initiate the treatment routine by selecting patient/eye mode on the right hand touch screen monitor and follow the steps indicated by the treatment wizard. Selecting the Start button initiates the PSS to move the patient into the treatment position. The operator is able to stop the movement with the joystick at any time. The automatic motion will stop as the eye approaches the contact glass that has been affixed to the treatment objective by the system vacuum pressure.
16. Use the surgical microscope to visualize and inspect patient's eye and surgical field.
17. Instruct the patient to maintain a fixed gaze on the internal fixation light during the procedure.
18. Raise the operative eye into position by elevating the PSS through the use of the PSS joystick. Move the PSS laterally and vertically using the PSS joystick to properly center the cornea under the treatment objective. Observe all PSS movements and repeatedly check the positions of the eye and contact glass in the microscope or by direct visualization until initial contact is made with the contact glass. Use the concentric circles of the ocular reticule in the surgical microscope as an aid in aligning the pupil with respect to the contact glass center.

19. The visual axis of the cornea should be exactly in the center of the contact glass as the eye meets the contact glass. When the eye is approaching the contact glass the reflex of the ring-shaped treatment illumination should be in the center of the observation area. On the left-hand side monitor the reflection of the flashing green fixation light indicates the center of treatment. A symmetrical appearance of the tear meniscus on the contact glass is an indication of proper centering.
20. If lateral movement of the contact glass is noted during applanation, rotate the patient's head slightly (as necessary) to avoid contact or interference between the Treatment Pack, the patient’s nose and/or eyebrow.
21. The switch on the PSS joystick, or the "SUCTION ON/OFF" button on the laser console may now be activated to turn on suction pressure to engage the cornea and affix it to the contact glass. Proper suction will result in at least four of the blue LED segments on the vacuum display on the control panel to be illuminated and an audible acoustic signal. If the eye is not properly centered after engaging the suction switch, release the suction and correct the position. Once the suction has been engaged, laser emission is enabled.

Laser treatment

1. Carefully check centering and suction. Do not begin laser treatment until all parameters are correct. Total surgery time (centering, suction time) should be kept as short as possible, as there is otherwise a risk of suction loss. Conditions which may distract the patient (background noise, other activity in the surgery) should be controlled while the eye is under suction. After suction has been applied it is important to start the laser procedure immediately. The patient should be instructed not to talk or move during this time. The patient should be instructed that the green fixation light may appear to move and that they should not track it during the treatment.
2. When ready, press and hold the footswitch. The operation will be interrupted if the foot switch is released. Press the foot switch once again to resume the treatment. The parameters cannot be changed during treatment. If surgery is interrupted, a message will appear on the display.
3. Observe the entire laser procedure through the surgical microscope or on the video display. Halt the laser procedure immediately if the size and position of the incision deviate from the intended treatment.

   ☞ If the VisuMax Femtosecond Laser malfunctions, if incomplete or decentered cuts are created, or if any other difficulty occurs such that it would not be in the patient's best interest to continue, the procedure should be aborted.

4. Upon completion of laser treatment, switch off the suction (press "SUCTION ON/OFF" button on the control panel or toggle the button on the PSS joystick). The patient's eye will be immediately released from the contact glass. The PSS will move down automatically to a safe distance. A message will appear in the Treatment dialog box confirming completion of the laser procedure.

Lenticule removal

1. Move the patient from the femtosecond laser position to the observation position under the surgical microscope using the PSS controls. The VisuMax Femtosecond Laser surgical microscope position can be used for the extraction portion of the procedure.
2. Inspect the complete cap and lenticule cut. Confirm that there are no obvious abnormalities in the interface or sidecuts before attempting removal of the lenticule.
3. Insert a sterilized Sinsky hook into the small superior incision to open the incision and expose the superior portion of the stroma beneath it.
4. Once stroma has been exposed, the lenticule edge should be identified using the Sinsky hook and separating the anterior corneal layer from anterior surface of the lenticule (the cap cut) followed by separation of posterior layer of lenticule from posterior layer of cornea. This initial separation should be performed for approximately 1 to 1.5 mm from the edge of lenticule for the purpose of identification of lenticule.
5. Using sterilized hand held instruments, use a thin blunt corneal spatula or iris spatula to separate the anterior corneal layer from anterior surface of the lenticule (the cap cut). The tissue should be separated to the full extent of the Cap cut which is 0.5mm larger in the periphery than the refractive cut.

CAUTION

External perforation of the cap is possible even with the use of a blunt corneal spatula due to excessive pressure at the tip of the instrument or due to a sudden eye movement by the patient during tissue separation.

   a. The anterior surface of the lenticule cut should be addressed first, otherwise an overextension of the cap, striae or even penetration of the cap may result. It is more difficult to separate the lenticule from the cap than from the bed, which makes the superficial separation best performed initially followed by the deeper tissue separation. During the dissection of the cuts, it is important to avoid pulling on or distorting the lenticule.

   b. The lip of the opening incision should be gently reflected and the internal side cut visually identified and then separated superiorly with the Sinsky hook.

6. Separate the lenticule posterior surface from the stromal bed. This is best performed with a broad tipped rounded spatula which is blunt but thin of which there are many examples. Confirm that the tissue has been adequately separated from the entire lenticule and from the lenticule internal side cut.
7. Once the surfaces of the lenticule have been freed, grasp the resected tissue with sterilized forceps and carefully extract it through the small incision. This is best performed by grasping the lenticule with a smooth tipped non-toothed forceps and gently applying force in a circular direction similar to performing a capsulorhexis maneuver.
8. Once the lamellar tissue has been removed, it should be placed on the corneal surface under the microscope to be certain that the entire lenticule has been removed. The tissue is then discarded or saved with consideration to appropriate treatment of medical waste.

9. Inspect the surgical field and irrigate the interface with filtered BSS through a disposable blunt tipped 27 or 30 gauge cannula to allow the anterior cap to come into contact with the stroma without microstriae. The incision site should be well approximated, and can be swabbed closed with an ophthalmic surgical sponge, if necessary.
10. A final inspection of the surgical site completes the procedure with removal of the lid speculum.

Completion of procedure

1. Move the PSS to the exit position.
2. Allow the patient to stand up and exit the PSS.
3. Remove and dispose of the Treatment Pack. Remove surgical instruments from operating field.
4. Close the surgical management software by clicking the Finish button. The main dialog box will open again. The VisuMax Femtosecond Laser is ready for the next laser procedure or treatment planning activity.

List of Recommended Instruments for Lenticule Extraction:

1. Sinsky Hook
2. LASIK Flap “unzipper”
3. Cyclodialysis Spatula
4. Iris Spatula
5. LASIK Spatula
6. Platinum Spatula
7. LASIK Cannula blunt tipped irrigating 27G or 30G
8. LASIK Forceps
9. Capsulorhexis or other fine smooth tipped, non-toothed forceps
10. Weck-Cel sponge

Treatment interruption

WARNING

When resuming the laser treatment following treatment interruption, strict care must be taken to ensure that the centering of the initial treatment is reproduced as accurately as possible. Lack of caution during this step may result in misalignment of incisions and misaligned corneal cuts as a result.

If treatment is interrupted during laser incision generation, the user interface will automatically display the treatment approach offered by the system for resuming the laser procedure. The procedures automatically recommended by the system are based on progress information acquired from electronic process monitoring. This process monitoring does not substitute for monitoring by the physician and the automatic recommendation does not substitute for the physician's decision regarding the method of continuation of treatment. If the surgeon decides to proceed with continuation of treatment as recommended by the system, treatment should be resumed promptly after the treatment interruption has occurred.

For any treatment interruption, when resuming the laser treatment, centering of the initial treatment should be reproduced as accurately as possible.

In the event of an intraoperative treatment interruption, the following procedures are recommended:

Interruption of the lenticule cut in the first 10 %:

If laser treatment is interrupted during the first 10 % of lenticule cut (underside of lenticule), the entire procedure should be repeated.

Interruption of the lenticule cut between 10 % and 100 % or interruption of a lenticule side cut:

If laser treatment is interrupted between 10 % and 100 % of the lenticule cut or during the lenticule side cut, the case should be aborted.

Cap cut interruption

If treatment interruption occurs during the cap cut, this portion of the treatment should be repeated. The cap cut will default to the same thickness as originally programmed. Since the cap cut has no effect on the refractive correction, the diameter of the cap cut can be increased to ensure that the cap completely covers the lenticule.

Postoperative care

A regimen of postoperative topical ophthalmic medications (antibiotic and steroid) is recommended. Use of a clear shield is also recommended; the shield should not be disturbed except for lifting the shield to instill drops.

A slit-lamp examination should be performed on postoperative day one and as needed thereafter to ensure that healing of the cornea is complete.

User Manual

Please reference the *VisuMax Femtosecond Laser User Manual*.

Technical data

Limit values of adjustment ranges

PARAMETER	UNIT	RANGE
LASER PARAMETER		
Laser energy	nJ	125-170
Track distance	µm	2.0 – 3.0
Spot distance	µm	2.0 – 3.0
SURGICAL		
Cap diameter	mm	7.0 or 7.5
Cap thickness	um	120
Lenticule diameter	mm	6.0 or 6.5
Lenticule edge minimum thickness	µm	15
Residual bed minimum thickness	µm	250
Incision position – opening position	deg	90
Incision angle - cap opening size	deg	90
Side cut angle – opening cut	deg	90
Side cut angle – lenticule cut	deg	90
REFRACTIVE		
Intended spherical corrections	D	- 1.00 to -8.00*
Intended cylindrical corrections	D	- - -
Intended cylindrical axis	deg	- - -

* Please note that treatment of -8.01 through -10.00 D will present a flagged warning to the users so that the user understands that correction of these powers had not been substantiated by an adequate set of data.

Abbreviations

D	Diopter
Deg	Degree
µm	Micrometer
mm	Millimeter
MRSE	Manifest refractive spherical equivalent
nJ	nanojoule
OSDI	Ocular Surface Disease Index
PRO	Patient reported outcomes
QoV	Quality of Vision
HORMS	Higher-order aberrations root mean square
SMILE	Small Incision Lenticule Extraction

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