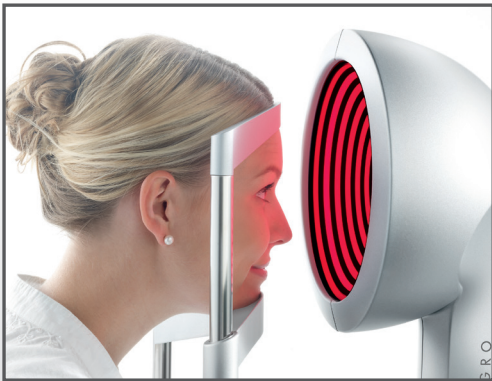


Introducing

TOPOGRAPHY-GUIDED REFRACTIVE SURGERY

Results of the T-CAT Phase III Clinical Trial



The Alcon WaveLight ALLEGRETTO WAVE Eye-Q Excimer Laser System gained FDA approval in October 2013 for the application of topography-guided corneal ablation treatments—a procedure called T-CAT. Topography is able to map corneal irregularities with such precision that it captures data that wavefront might miss. Thus, T-CAT treatments make it possible to normalize corneas that previously were more difficult to treat with an excimer laser.

This article is the first in a series about the T-CAT procedure that Cataract & Refractive Surgery Today is producing in partnership with Alcon in 2015. For more information about the T-CAT technology, visit www.eyetube.net or www.mylalcon.com.

Results of the T-CAT Phase III Clinical Trial

BY DAVID W. FRIESS, OD, FAAO, AND R. DOYLE STULTING, MD, PhD

Topography-guided custom ablation treatments (T-CAT) using the WaveLight ALLEGRETTO WAVE platform (Alcon Laboratories, Inc.; Figures 1 and 2) have been performed outside the US since 2003. Although the software has been available outside the US for use with primary eyes, international surgeons have used T-CAT mostly for previously operated symptomatic eyes with decentered ablations, or small optical zones and residual or induced corneal irregularities.¹⁻⁴ However, FDA approval of the T-CAT procedure was not for symptomatic or therapeutic eyes.

Alcon and study management contractor (CRC, Inc.) developed the T-CAT LASIK protocol for the treatment of primary eyes with no abnormalities other than refractive error. When the study began, only unilateral treatments were allowed. Bilateral treatments were performed after initial interim data analysis.

On September 27, 2013, the FDA approved T-CAT LASIK for the treatment of eyes with myopia and myopic astigmatism.⁵ T-CAT LASIK's Indications for Use states:

- The WaveLight ALLEGRETTO WAVE Eye-Q Excimer Laser System used in conjunction with the WaveLight ALLEGRO Topolyzer (topographer) and T-CAT treatment planning software is indicated for performing topography-guided laser assisted in situ keratomileusis (T-CAT LASIK):
 - for the reduction or elimination of up to -9.00 diopters (D) of spherical equivalent myopia or myopia with astigmatism, with up to -8.00 D of spherical component and up to -3.00 D of astigmatic component at the spectacle plane;
 - in patients who are 18 years of age or older; and,
 - in patients with documentation of a stable manifest refraction defined as 0.50 D or less of preoperative spherical equivalent shift over one year prior to surgery.



Figure 1. The ALLEGRO Topolyzer.



Figure 2. The ALLEGRETTO WAVE Eye-Q 400-Hz laser.

The US T-CAT Phase III clinical study involved topography-based customized LASIK treatments of healthy myopic eyes with or without astigmatism.⁵

The three devices used to plan and perform the topography-guided LASIK treatments were the ALLEGRETTO WAVE EYE-Q 400 Hz Laser System, the

ALLEGRO Topolyzer topography system, and the T-CAT software for treatment planning.

STUDY PARAMETERS

This was a prospective, IRB-approved, nonrandomized, multicenter study completed with nine investigational sites for FDA PMA Supplement submission. Refractive treatment planning was based upon preoperative manifest refraction and corneal topography data. All LASIK flaps were created using an approved femtosecond laser or a microkeratome. Study objectives included standard measures of safety and effectiveness for refractive pre-market studies. No retreatments were performed during the course of the study.

The FDA clinical trial for topography-guided LASIK using the ALLEGRETTO WAVE Eye-Q Excimer Laser included 249 eyes of 212 subjects that had not undergone previous refractive surgery and did not display ocular pathology, such as keratoconus or forme fruste keratoconus, with up to -9.00 D of myopic sphere with and without astigmatic refractive errors of up to 6.00 D that was stable for at least 1 year. By gender, 56% of enrolled subjects were female and 44% male. By race, 74% of subjects were Caucasian, 17.5% Hispanic, 4% Asian, and 2% black. Mean subject age was 34.0 years (range, 18 to 65). Patient accountability was excellent at each study visit, ranging from 95% to 100%. Accountability at 12 months was 95%.

Overall, this was a large enrollment of eyes across a broadly located number of investigational sites, including a broad range of myopia with astigmatism, with excellent accountability at all time periods over a long range of 12 months follow-up.

Corneal topographies for T-CAT LASIK planning were obtained using the ALLEGRO Topolyzer topography system. Multiple images were obtained and then submitted for review by three members of the study clinical regulatory team. Criteria for acceptance of images were developed, including coverage area, percent of data obtained within the measurement area, quality of mires, correct recognition of mire edges by the software, correct recognition of the pupil by the software, lack of evidence of keratoconus or forme fruste keratoconus, lack of other topographic abnormalities, and consistency among topographic measurements.

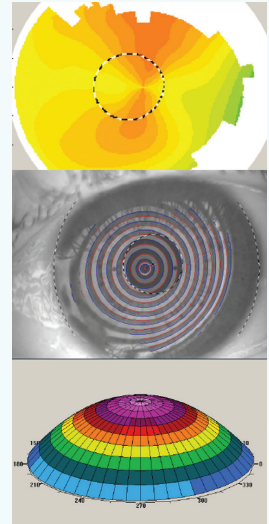
During the clinical trial, the investigators recognized that acquiring at least four corneal topographic images that met the above criteria was critical to the outstanding clinical outcomes that were obtained during the clinical trial.

SAFETY PROFILE

All safety endpoints were met, with only five single reports of loss of best spectacle-corrected visual acuity

ALLEGRO TOPOLYZER DIAGNOSTIC DEVICE WITHIN THE T-CAT TREATMENT SYSTEM

- Placido disc corneal topographer
- Detects mire edges
- Detects pupil margins
- Calculates the location of the pupil area centroid
- Calculates the location of the corneal apex
- Calculates height data for areas where mire images are available
 - No interpolated data
 - No extrapolated data



(BSCVA) of 2 or more lines at 1 month or later. All of these were transient, unrelated to the T-CAT LASIK treatment, and resolved by the next postoperative follow-up visit. At 3 months, the time point of refractive stability, none of the eyes lost 2 or more lines of BSCVA, and at 12 months, 1 eye lost 2 or more lines of BSCVA that resolved 1 month later. There were no cumulative adverse events at 3 months.

Certain visual symptoms improved at 3 months after T-CAT compared to preoperative levels with habitual correction, reaching statistical significance for light sensitivity, difficult driving at night, reading difficulty, and glare. Only double vision and foreign body sensation were reported as worse after 3 months, with minimal increases of 0.8% and 0.4%, respectively. The incidence and severity of visual symptoms continued to improve during the 12-month course of the investigation.

OUTCOMES

Subjects in the clinical trial reported an improvement in parameters measured by the Refractive Status and Vision Profile (RSVP) including physical/social functioning, driving, visual symptoms, optical problems, and problems with corrective lenses that were evident at 3 months and continued to improve through 12 months postoperatively, compared to their habitual refractive correction method (glasses or contact lenses) preoperatively. Finally, 98.4% of patients in the clinical study stated that they were satisfied with their outcomes and would have T-CAT LASIK treatment again.

Efficacy of T-CAT LASIK was excellent. At 3 months postoperatively, 31.6% of eyes achieved a UCVA of

TOPOGRAPHY-GUIDED REFRACTIVE SURGERY

Topography-Guided Custom Ablation Treatments (T-CAT) with the WaveLight ALLEGRETTO WAVE Eye-Q Excimer Laser

20/12.5 or better; 68.9% of the eyes had a UCVA of 20/16 or better; and 92.7% of eyes had a UCVA of 20/20 or better (Figure 3). Over time, there was a slight improvement in UCVA through the 12-month examination after T-CAT LASIK. At 12 months, 34.4% of eyes saw 20/12.5 or better; 64.8% of eyes saw 20/16 or better; and 92.6% of eyes saw 20/20 or better. At 3 months, 91.9% of eyes had an MRSE within 0.5 diopters (D) of the intended treatment, and 98.8% had an MRSE within 1.00 D of the intended treatment. At 12 months, 94.8% of eyes achieved MRSE within 0.50 D of the intended treatment, and 99.6% of eyes achieved an MRSE within 1.00 D of the intended treatment.

Eyes treated with T-CAT demonstrated a shift toward an improvement in UCVA compared to preoperative BSCVA, with 29.6% of eyes gaining 1 or more lines of UCVA at 3 months compared with preoperative BSCVA. At 12 months, 30.9% of eyes gained 1 or more lines of UCVA compared to preoperative BSCVA. In total, 89.9% of eyes were seeing at least as well without correction

postoperatively as they did with best spectacle correction preoperatively. In comparing preoperative BSCVA to postoperative BSCVA, 39.3% of eyes gained 1 or more lines at 3 months and 40.4% of eyes gained 1 or more lines at 12 months (Figure 4). One eye lost more than 2 lines of BSCVA compared to preoperatively, but none were recorded at 12 months.

Contrast sensitivity testing demonstrated that the number of T-CAT LASIK-treated eyes with a clinically significant increase in contrast sensitivity was two- to three-folds higher than those eyes with clinically significant decreases, both with and without glare under mesopic and photopic testing conditions at 3 and 6 months postoperatively.

In summary, the data derived from the FDA clinical trial demonstrated that T-CAT LASIK is a safe and effective treatment for myopia and myopic astigmatism, with an increase in UCVA postoperatively compared to BSCVA preoperatively, an increase in BSCVA compared to preoperatively, and an improvement in visual symptoms. ■

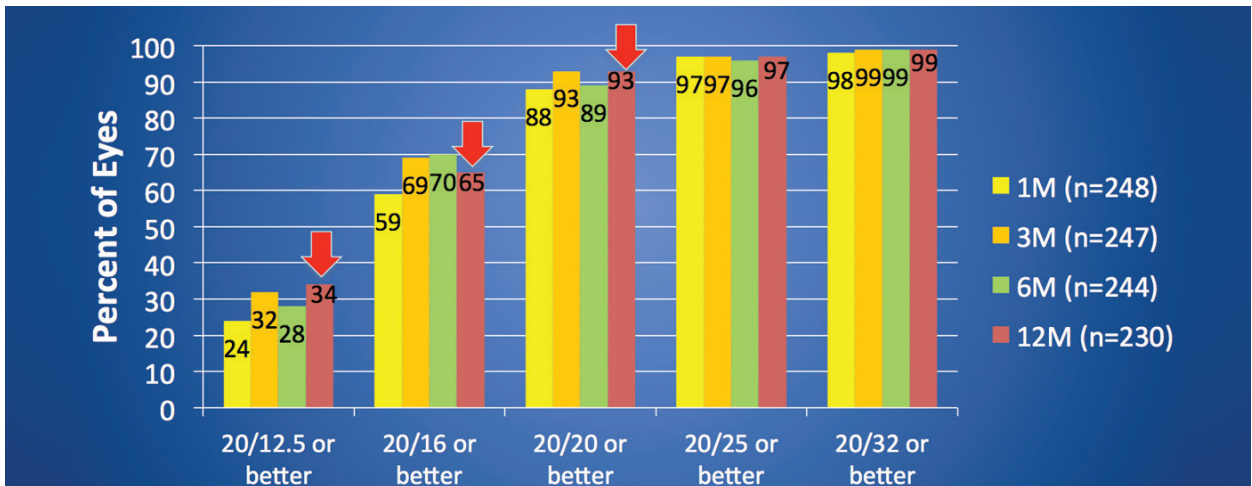


Figure 3. Cumulative postoperative UCVA (ETDRS) in the T-CAT LASIK FDA clinical trial.

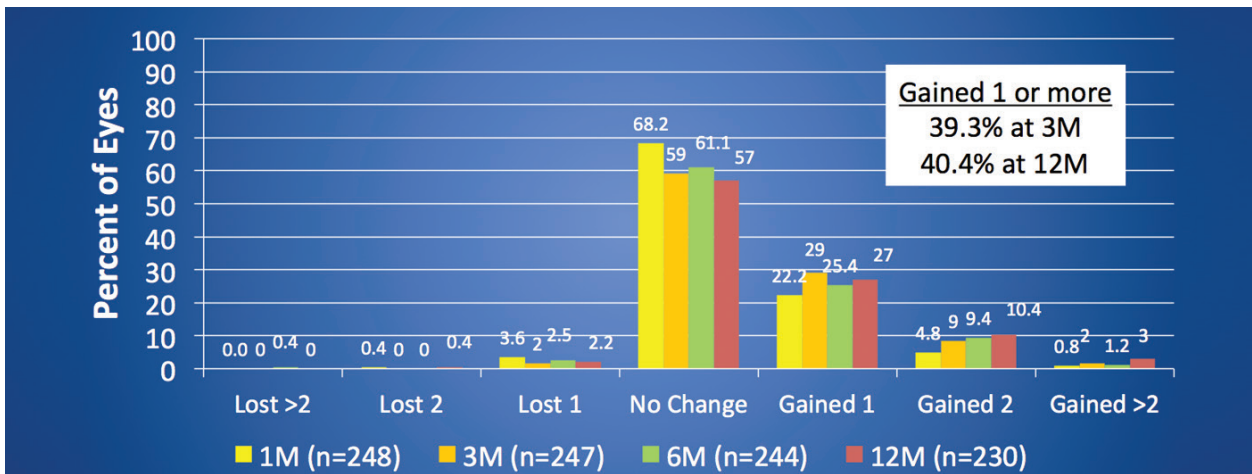


Figure 4. Postoperative BSCVA compared to preoperative BSCVA (change in lines) in the T-CAT LASIK FDA clinical trial.

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- FDA device approvals website: Topography-guided Custom Ablation Treatment, or T-CAT Summary of Safety and Effectiveness Data (SSED), available at: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm3372964.htm>.

Important Product Information about the WaveLight® Excimer Laser Systems

This information pertains to all WaveLight® Excimer Laser Systems, including the WaveLight® ALLEGRETTO WAVE®, the ALLEGRETTO WAVE® Eye-Q, and the WaveLight® EX500.

Caution: Federal (U.S.) law restricts the WaveLight® Excimer Laser Systems to sale by or on the order of a physician. Only practitioners who are experienced in the medical management and surgical treatment of the cornea, who have been trained in laser refractive surgery (including laser calibration and operation) should use a WaveLight® Excimer Laser System.

Indications: FDA has approved the WaveLight® Excimer Laser systems for use in laser-assisted in situ keratomileusis (LASIK) treatments for:

- the reduction or elimination of myopia of up to - 12.00 D and up to 6.00 D of astigmatism at the spectacle plane;
- the reduction or elimination of hyperopia up to + 6.00 D with and without astigmatic refractive errors up to 5.00 D at the spectacle plane, with a maximum manifest refraction spherical equivalent of + 6.00 D;
- the reduction or elimination of naturally occurring mixed astigmatism of up to 6.00 D at the spectacle plane; and
- the wavefront-guided reduction or elimination of myopia of up to -7.00 D and up to 3.00 D of astigmatism at the spectacle plane.

In addition, FDA has approved the WaveLight® ALLEGRETTO WAVE® Eye-Q Excimer Laser System, when used with the WaveLight® ALLEGRO Topolyzer® and topography-guided treatment planning software for topography-guided LASIK treatments for the reduction or elimination of up to -9.00 D of myopia, or for the reduction or elimination of myopia with astigmatism, with up to -8.00 D of myopia and up to 3.00 D of astigmatism.

The WaveLight® Excimer Laser Systems are only indicated for use in patients who are 18 years of age or older (21 years of age or older for mixed astigmatism) with documentation of a stable manifest refraction defined as ≤ 0.50 D of preoperative spherical equivalent shift over one year prior to surgery, exclusive of changes due to unmasking latent hyperopia.

Contraindications: The WaveLight® Excimer Laser Systems are contraindicated for use with patients who:

- are pregnant or nursing;
- have a diagnosed collagen vascular, autoimmune or immunodeficiency disease;
- have been diagnosed keratoconus or if there are any clinical pictures suggestive of keratoconus;
- are taking isotretinoin (Accutane®) and/or amiodarone hydrochloride (Cordarone®);
- have severe dry eye;
- have corneas too thin for LASIK;
- have recurrent corneal erosion;
- have advanced glaucoma; or
- have uncontrolled diabetes.

Warnings: The WaveLight® Excimer Laser Systems are not recommended for use with patients who have:

- systemic diseases likely to affect wound healing, such as connective tissue disease, insulin dependent diabetes, severe atopic disease or an immunocompromised status;
- a history of Herpes simplex or Herpes zoster keratitis;
- significant dry eye that is unresponsive to treatment;
- severe allergies;
- a history of glaucoma;
- an unreliable preoperative wavefront examination that precludes wavefront-guided treatment; or
- a poor quality preoperative topography map that precludes topography-guided LASIK treatment.

The wavefront-guided LASIK procedure requires accurate and reliable data from the wavefront examination. Every step of every wavefront measurement that may be used as the basis for a wavefront-guided LASIK procedure must be validated by the user. Inaccurate or unreliable data from the wavefront examination will lead to an inaccurate treatment.

Topography-guided LASIK requires preoperative topography maps of sufficient quality to use for planning a topography-guided LASIK treatment. Poor quality topography maps may affect the accuracy of the topography-guided LASIK treatment and may result in poor vision after topography-guided LASIK.

Precautions: The safety and effectiveness of the WaveLight® Excimer Laser Systems have not been established for patients with:

- progressive myopia, hyperopia, astigmatism and/or mixed astigmatism, ocular disease, previous corneal or intraocular surgery, or trauma in the ablation zone;
- corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage;
- residual corneal thickness after ablation of less than 250 microns due to the increased risk for corneal ectasia;
- pupil size below 7.0 mm after mydriatics where applied for wavefront-guided ablation planning;
- history of glaucoma or ocular hypertension of > 23 mmHg;
- taking the medications sumatriptan succinate (Imitrex®);
- corneal, lens and/or vitreous opacities including, but not limited to cataract;
- iris problems including, but not limited to, coloboma and previous iris surgery compromising proper eye tracking; or
- taking medications likely to affect wound healing including (but not limited to) antimetabolites.

In addition, safety and effectiveness of the WaveLight® Excimer Laser Systems have not been established for:

- treatments with an optical zone < 6.0 mm or > 6.5 mm in diameter, or an ablation zone > 9.0 mm in diameter; or
- wavefront-guided treatment targets different from emmetropia (plano) in which the wavefront calculated defocus (spherical term) has been adjusted;

In the WaveLight® Excimer Laser System clinical studies, there were few subjects with cylinder amounts > 4 D and ≤ 6 D. Not all complications, adverse events, and levels of effectiveness may have been determined for this population.

Pupil sizes should be evaluated under mesopic illumination conditions. Effects of treatment on vision under poor illumination cannot be predicted prior to surgery.

Adverse Events and Complications

Myopia: In the myopia clinical study, 0.2% (2/876) of the eyes had a lost, misplaced, or misaligned flap reported at the 1 month examination.

The following complications were reported 6 months after LASIK: 0.9% (7/818) had ghosting or double images in the operative eye; 0.1% (1/818) of the eyes had a corneal epithelial defect.

Hyperopia: In the hyperopia clinical study, 0.4% (1/276) of the eyes had a retinal detachment or retinal vascular accident reported at the 3 month examination.

The following complications were reported 6 months after LASIK: 0.8% (2/262) of the eyes had a corneal epithelial defect and 0.8% (2/262) had any epithelium in the interface.

Mixed Astigmatism: In the mixed astigmatism clinical study, two adverse events were reported. The first event involved a patient who post-operatively was subject to blunt trauma to the treatment eye 6 days after surgery. The patient was found to have an intact globe with no rupture, inflammation or any dislodgement of the flap. UCVA was decreased due to this event. The second event involved the treatment of an incorrect axis of astigmatism. The axis was treated at 60 degrees instead of 160 degrees.

The following complications were reported 6 months after LASIK: 1.8% (2/111) of the eyes had ghosting or double images in the operative eye.

Wavefront-Guided Myopia: The wavefront-guided myopia clinical study included 374 eyes treated; 188 with wavefront-guided LASIK (Study Cohort) and 186 with Wavefront Optimized® LASIK (Control Cohort). No adverse events occurred during the postoperative period of the wavefront-guided LASIK procedures. In the Control Cohort, one subject undergoing traditional LASIK had the axis of astigmatism programmed as 115 degrees instead of the actual 155 degree axis. This led to cylinder in the left eye.

The following complications were reported 6 months after wavefront-guided LASIK in the Study Cohort: 1.2% (2/166) of the eyes had a corneal epithelial defect; 1.2% (2/166) had foreign body sensation; and 0.6% (1/166) had pain. No complications were reported in the Control Cohort.

Topography-Guided Myopia: There were six adverse events reported in the topography-guided myopia study. Four of the eyes experienced transient or temporary decreases in vision prior to the final 12 month follow-up visit, all of which were resolved by the final follow-up visit. One subject suffered from decreased vision in the treated eye, following blunt force trauma 4 days after surgery. One subject experienced retinal detachment, which was concluded to be unrelated to the surgical procedure.

Clinical Data

Myopia: The myopia clinical study included 901 eyes treated, of which 813 of 866 eligible eyes were followed for 12 months. Accountability at 3 months was 93.8%, at 6 months was 91.9%, and at 12 months was 93.9%. Of the 782 eyes that were eligible for the uncorrected visual

acuity (UCVA) analysis of effectiveness at the 6-month stability time point, 98.3% were corrected to 20/40 or better, and 87.7% were corrected to 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms at a “moderate” or “severe” level at least 1% higher at 3 months post-treatment than at baseline: visual fluctuations (28.6% vs. 12.8% at baseline).

Long term risks of LASIK for myopia with and without astigmatism have not been studied beyond 12 months.

Hyperopia: The hyperopia clinical study included 290 eyes treated, of which 100 of 290 eligible eyes were followed for 12 months. Accountability at 3 months was 95.2%, at 6 months was 93.9%, and at 12 months was 69.9%. Of the 212 eyes that were eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 95.3% were corrected to 20/40 or better, and 69.4% were corrected to 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms as “much worse” at 6 months post-treatment: halos (6.4%); visual fluctuations (6.1%); light sensitivity (4.9%); night driving glare (4.2%); and glare from bright lights (3.0%).

Long term risks of LASIK for hyperopia with and without astigmatism have not been studied beyond 12 months.

Mixed Astigmatism: The mixed astigmatism clinical study included 162 eyes treated, of which 111 were eligible to be followed for 6 months. Accountability at 1 month was 99.4%, at 3 months was 96.0%, and at 6 months was 100.0%. Of the 142 eyes that were eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 97.3% achieved acuity of 20/40 or better, and 69.4% achieved acuity of 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms at a “moderate” or “severe” level at least 1% higher at 3 months post-treatment than at baseline: sensitivity to light (52.9% vs. 43.3% at baseline); visual fluctuations (43.0% vs. 32.1% at baseline); and halos (42.3% vs. 37.0% at baseline).

Long term risks of LASIK for mixed astigmatism have not been studied beyond 6 months.

Wavefront-Guided Myopia: The wavefront-guided myopia clinical study included 374 eyes treated; 188 with wavefront-guided LASIK (Study Cohort) and 186 with Wavefront Optimized® LASIK (Control Cohort). 166 of the Study Cohort and 166 of the Control Cohort were eligible to be followed at 6 months. In the Study Cohort, accountability at 1 month was 96.8%, at 3 months was 96.8%, and at 6 months was 93.3%. In the Control Cohort, accountability at 1 month was 94.6%, at 3 months was 94.6%, and at 6 months was 92.2%.

Of the 166 eyes in the Study Cohort that were eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 99.4% were corrected to 20/40 or better, and 93.4% were corrected to 20/20 or better. Of the 166 eyes in the Control Cohort eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 99.4% were corrected to 20/40 or better, and 92.8% were corrected to 20/20.

In the Study Cohort, subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms at a “moderate” or “severe” level at least 1% higher at 3 months post-treatment than at baseline: light sensitivity (47.8% vs. 37.2% at baseline) and visual fluctuations (20.0% vs. 13.8% at baseline). In the Control Cohort, the following visual symptoms were reported at a “moderate” or “severe” level at least 1% higher at 3 months post-treatment than at baseline: halos (45.4% vs. 36.6% at baseline) and visual fluctuations (21.9% vs. 18.3% at baseline).

Long term risks of wavefront-guided LASIK for myopia with and without astigmatism have not been studied beyond 6 months.

Topography-Guided Myopia: The topography-guided myopia clinical study included 249 eyes treated, of which 230 eyes were followed for 12 months. Accountability at 3 months was 99.2%, at 6 months was 98.0%, and at 12 months was 92.4%. Of the 247 eyes that were eligible for the UCVA analysis at the 3-month stability time point, 99.2% were corrected to 20/40 or better, and 92.7% were corrected to 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms as “marked” or “severe” at an incidence greater than 5% at 1 month after surgery: dryness (7% vs. 4% at baseline) and light sensitivity (7% vs. 5% at baseline). Visual symptoms continued to improve with time, and none of the visual symptoms were rated as being “marked” or “severe” with an incidence of at least 5% at 3 months or later after surgery.

Long term risks of topography-guided LASIK for myopia with and without astigmatism have not been studied beyond 12 months.

Information for Patients: Prior to undergoing LASIK surgery with a WaveLight® Excimer Laser System, prospective patients must receive a copy of the relevant Patient Information Booklet, and must be informed of the alternatives for correcting their vision, including (but not limited to) eyeglasses, contact lenses, photorefractive keratectomy, and other refractive surgeries.

Attention: Please refer to a current WaveLight® Excimer Laser System Procedure Manual for a complete listing of the indications, complications, warnings, precautions, and side effects.

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