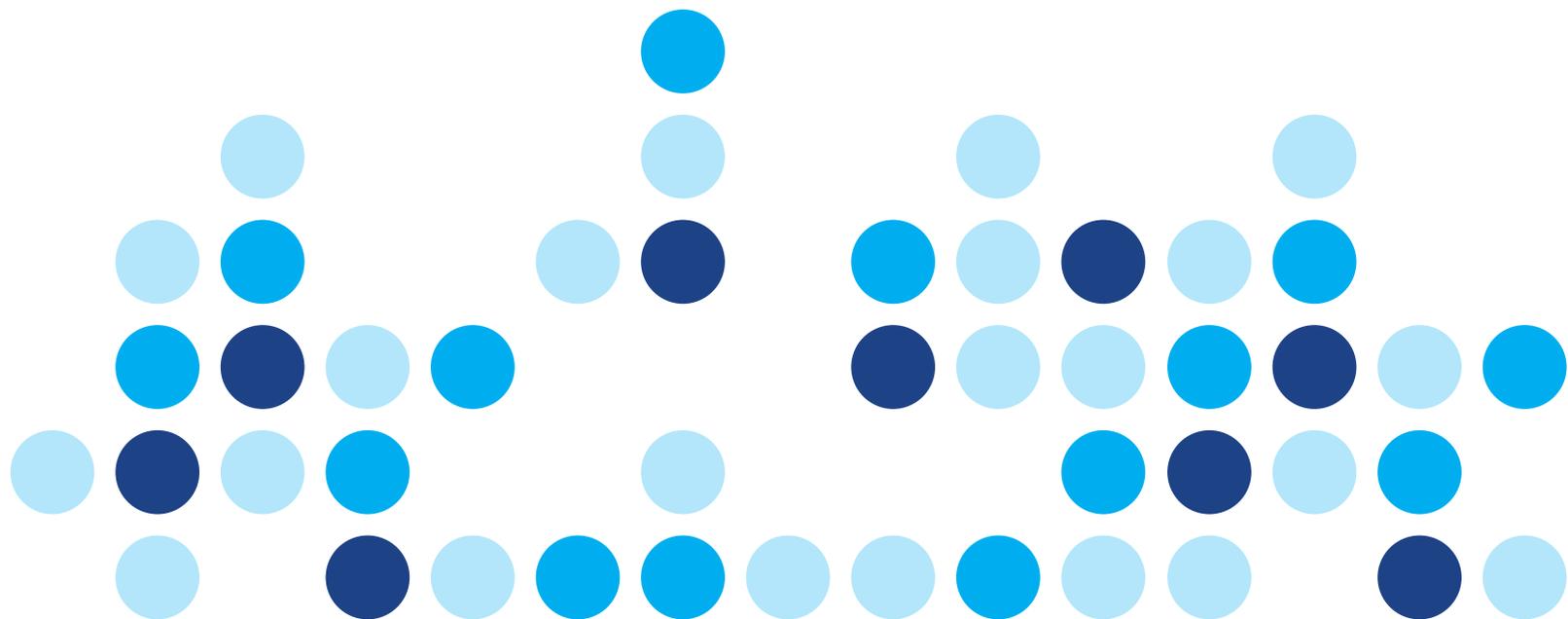


## Topography-Guided Laser Assisted In-Situ Keratomileusis vs Small-Incision Lenticule Extraction Refractive Surgery — A Summary of Clinical Outcomes

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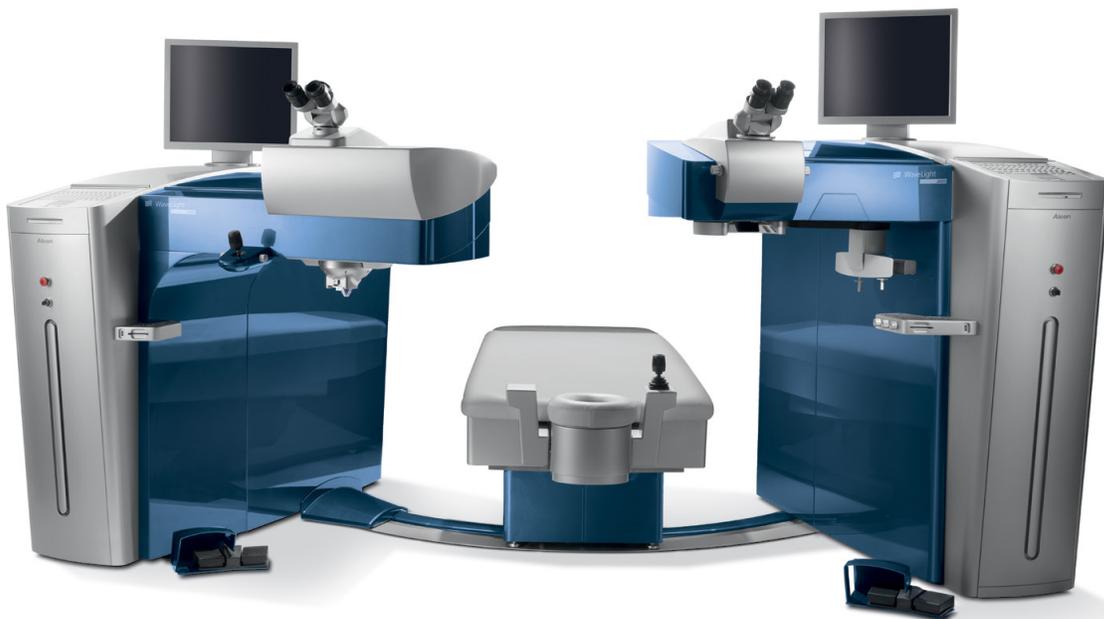


# Introduction

The global procedure volume for refractive surgery was approximately 4.3 million in 2018. Of those procedures, 774,000 were performed in the US market.<sup>1</sup> Modern refractive surgery has evolved significantly since the era of Radial Keratotomy, and with a projected growth of up to 5.5 million procedures globally in 2023<sup>1</sup>, it is important to provide a clinical perspective of the latest available refractive surgery modalities.

## Key Take-aways:

- Alcon WaveLight® Topography-Guided platform outperforms small-incision lenticule extraction (SMILE\*)
- When compared to LASIK, SMILE has not conclusively shown that the procedure has greater biomechanical stability and results in reduced post-operative dry eye symptoms as a short-term consequence of higher nerve fiber preservation
- Alcon WaveLight® Topography-Guided platform improves quality of vision and results in a high patient satisfaction

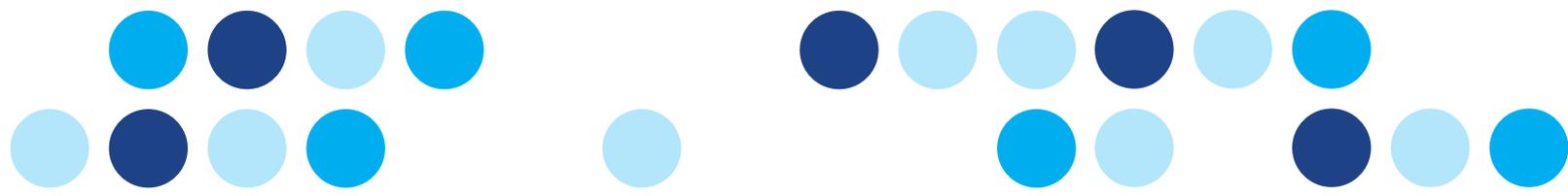


## Clinical challenge: Maintaining the natural shape of the cornea

Refractive Surgery reduces refractive error by reshaping the corneal surface. The ultimate goal of refractive surgery is to eliminate patient's dependency on glasses or contact lenses. Since refractive surgery is an elective surgery, there are many options for the surgeon to recommend and the patient to choose from, including but not limited to, Photorefractive Keratectomy (PRK), Laser Assisted In-situ Keratomileusis (LASIK) or Small Incision Lenticule Extraction (SMILE) to name a few. Ideally, these procedures should provide the patient with (1) excellent visual acuity and quality of vision within a short period after surgery, and (2) as little disturbance or impact on ocular health as possible.

This white paper describes two advanced technologies in refractive surgery in detail, namely Topography-Guided LASIK and SMILE and will provide the reader with a comprehensive summary of clinical benefits of each approach.

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# Topography-Guided LASIK and SMILE

Both Topography-Guided LASIK and SMILE are refractive procedures that remove corneal tissue to correct refractive error. However, there are fundamental differences between these two approaches, some of which are listed in Table 1. The indications for use in the United States are further detailed in Figure 1. The approved range for SMILE does not include cylinder treatments of less than 0.75D, which is important to note considering that more than one third of the US population have a cylinder of less than 1.0D.<sup>1</sup>

	Topography-guided LASIK	SMILE
<b>Procedural Technique</b>	<ul style="list-style-type: none"> <li>• A thin hinged corneal flap is created using a femtosecond laser. The flap is opened to expose the underlying stroma.</li> <li>• An excimer laser treatment is applied to reshape the stromal tissue, neutralizing irregularities of the corneal surface using the patient's manifest refraction and corneal topography data.</li> <li>• The corneal flap is repositioned.</li> </ul>	<ul style="list-style-type: none"> <li>• A femtosecond laser creates both an intrastromal lenticule that corresponds to the patient's spherical equivalent from the manifest refraction and a small site cut incision to allow for access to the lenticule. In low myopia, a refraction neutral corneal tissue base may be added to create a lenticule with a minimum thickness of 40 <math>\mu\text{m}</math>.<sup>2</sup></li> <li>• After dissection of residual tissue bridges, the intrastromal lenticule is manually removed through the small incision.</li> </ul>
<b>Customization of the Treatment Profile</b>	The treatment profile is customized based on the patient's specific corneal topography. A more uniform anterior corneal surface is created that corrects corneal irregularities causing HOAs.	The correction of HOAs is not possible. Small cylinder amounts of less than 0.75D are not treated.  Corneal topography data is <b>not</b> being used in the treatment.
<b>Retreatments/Enhancements</b>	The corneal flap can be re-lifted and the residual refractive error corrected using an excimer laser.	No new lenticule can be created. The SMILE procedure effectively needs to be converted into either of the 2 options below to correct residual refractive error with an excimer laser: <ol style="list-style-type: none"> <li>1. The pocket could be converted into corneal flap (if pocket parameters are known).</li> <li>2. Convert into PRK to allow for surface ablation with an excimer laser.</li> </ol>

**Table 1. Overview of topography-guided LASIK and SMILE Procedures.**

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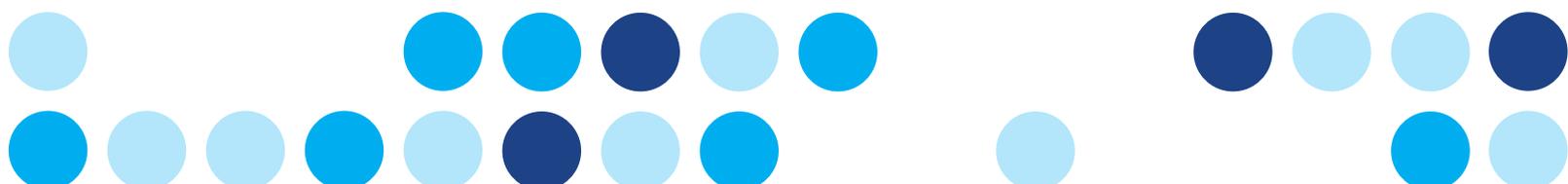




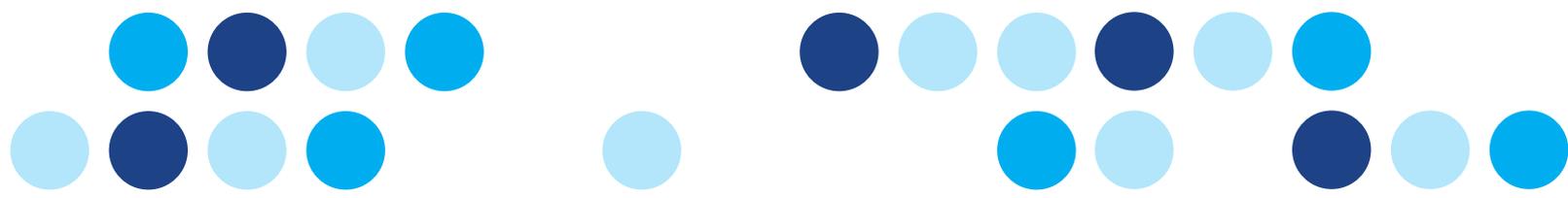
Figure 1. Maximum indicated treatment ranges available for topography-guided LASIK and SMILE Procedures in the US.<sup>3,4</sup> LASIK: Laser Assisted In-situ Keratomileusis; SMILE: Small Incision Lenticule Extraction; MRSE: Manifest Refraction Spherical Equivalent.

## Comparison of Topography-Guided LASIK and SMILE outcomes

Important measures for the evaluation of a refractive surgery procedure include visual outcomes, refractive stability, patient reported post-operative dry eye symptoms, complications and safety. The following section aims to provide the reader with an overview of each of these measures.

Several Topography-assisted or -guided systems are available in the US. However, only the Alcon WaveLight® Topography-Guided platform incorporates the topography of the patient fully in the treatment profile. Table 2 outlines the **visual outcomes** of available LASIK and SMILE procedures for myopia and myopic astigmatism as described in the Summary of Safety and Effectiveness Data Sheets of the US-approved devices. Overall, the visual acuity of each procedure is well within the required FDA efficacy criterion of 85% of eyes with 20/40 or better. A direct comparison of the data detailed in this table is not possible as these are three separate clinical trial datasets with differences in laser technology, laser indications, and/or patient populations. A comparative study by Kanellopoulos described significantly better visual performance in eyes that underwent Topography-Guided LASIK at 3 months<sup>5</sup> and 12 months<sup>6</sup> than in eyes that were treated with SMILE (see Figure 2).

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		Topography-guided LASIK	SMILE
Percentage of eyes with		Alcon CONTOURA® Vision (n = 230 eyes)	Zeiss VisuMax SMILE (n = 345 eyes)
UCVA of 20/20 or better		92.6%	89.4%
UCVA of 20/15 - 20/16 or better		64.8%	59.3%
UCVA of 20/12.5 or better		34.4%	NR
UCVA of 20/10 or better		15.7%	NR
Attempted vs Achieved	MRSE ± 0.50D	94.8%	94.8%
	MRSE ± 1.00D	99.6%	99.1%
	MRSE ± 2.00D	100%	100%
Post-op UCVA compared to pre-op BCVA	more than 2 lines better	3%	0.3%
	2 lines better	8.3%	6.6%
	1 line better	19.6%	32.1%
	equal	58.3%	42.1%
	1 line worse	7.8%	12.0%
	2 line worse	1.3%	3.7%
	more than 2 lines worse	1.7%	3.2%

UCVA – uncorrected visual acuity; MRSE – manifest refraction spherical equivalent; BCVA – best corrected visual acuity; NR – not reported.

Table 2. Visual Outcomes for Topography-Guided LASIK and SMILE Procedures at 12 months after surgery per the respective FDA Summary of Safety and Effectiveness Data (SSED) Sheet of three different clinical data sets.<sup>3,4</sup>

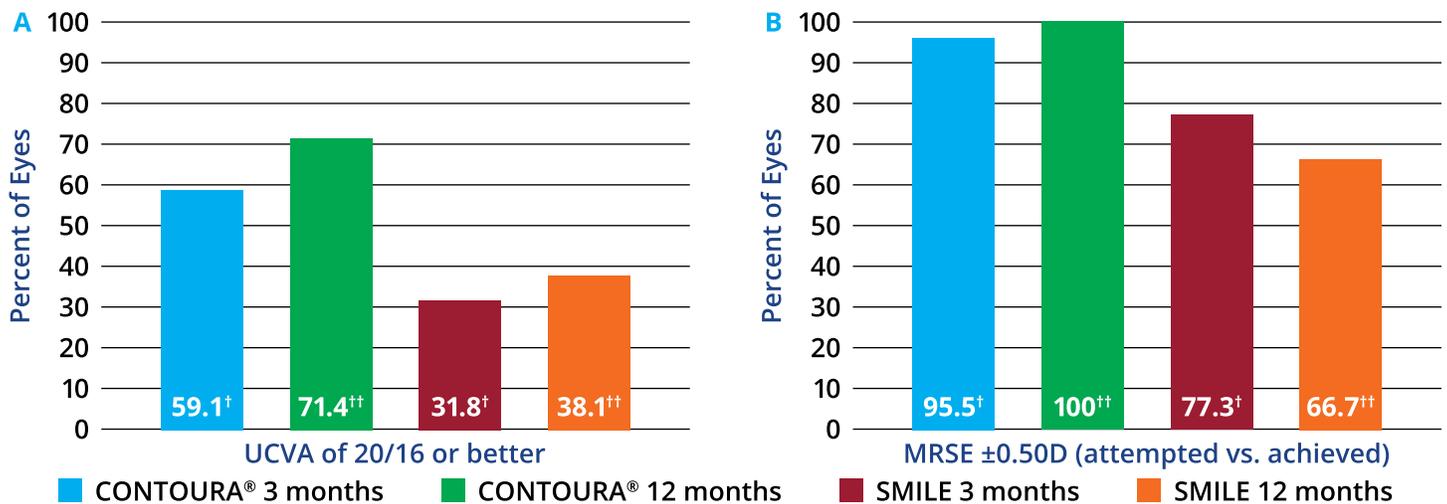
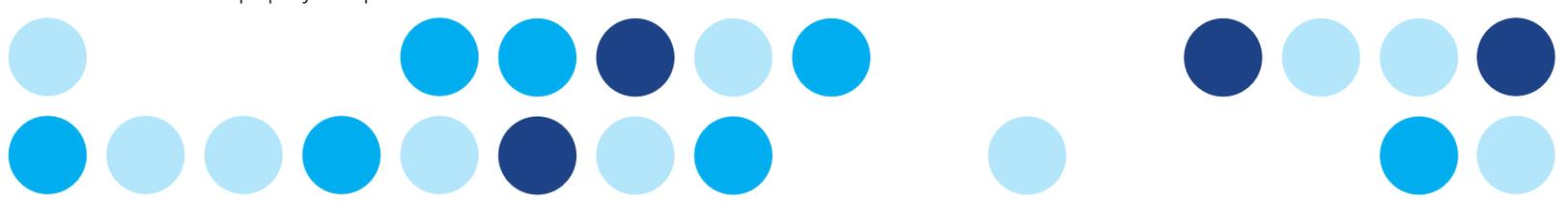


Figure 2. Visual performance parameters (A: UCVA of 20/16 or better; B: MRSE ± 0.50 D) at 3 months and 12 months after surgery in eyes undergoing myopic and myopic astigmatism treatment as described in a prospective, randomized contralateral study by Kanellopoulos.<sup>5,6</sup>

† significant difference between CONTOURA® Vision and SMILE group at 3 months (p < 0.01);  
 †† significant difference between CONTOURA® Vision and SMILE group at 12 months (p < 0.01)  
 UCVA – uncorrected visual acuity; MRSE – manifest spherical equivalent.

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**Refractive stability** is a crucial factor when assessing options for refractive error correction. It has been speculated that eyes undergoing the SMILE procedure would require a longer time to remodel and adjust to the removed intrastromal corneal tissue to achieve refractive stability after surgery. Similar to Topography-Guided LASIK, there are only minimal fluctuations in the manifest refractive spherical equivalent (MRSE) noted for SMILE from 1 month to 12 months post-surgery.<sup>3,4</sup>

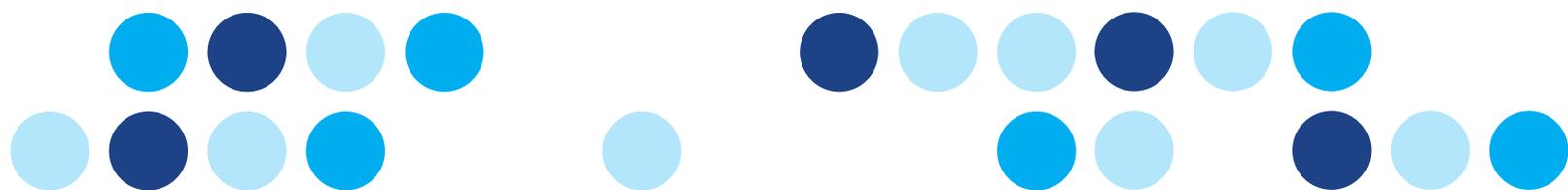
Other factors that may affect refractive stability have been considered as potential advantages of SMILE procedures, including (1) reduced severance of corneal nerves and therefore a lower incidence of **patient reported** dry eye symptoms and (2) a greater biomechanical stability. The following paragraphs examine these potential advantages in comparison to general LASIK in more detail.

Any ocular surgery interferes with the delicate balance of the ocular surface system. In corneal refractive surgery, creating a corneal flap or an intrastromal lenticule severs the corneal nerves of the richly innervated cornea, thereby reducing corneal sensitivity in the short term. Long term, severed corneal nerve fibers regenerate. SMILE procedures seem to be better at preserving the sub-basal nerve fiber density in the early post-operative period (up to 3 months) compared to Femtosecond LASIK (FS-LASIK) created flaps.<sup>7</sup> However, 6 months after surgery no differences between FS-LASIK and SMILE created flaps were identified and the sub-basal nerve density recovered to similar levels in both groups.<sup>7</sup> The question whether the preservation of nerve fibers results in a lower incidence, frequency and severity of dry eye symptoms has not yet been conclusively answered. A meta-analysis described significantly better corneal sensation, longer tear film break up times (TBUT) and patient reported Ocular Surface Disease Index (OSDI) scores in the early post-operative period in SMILE treated eyes.<sup>8</sup> Nevertheless, these differences did not translate into greater tear secretion in SMILE compared to FS-LASIK.<sup>8</sup> In a recent prospective, randomized, paired-eye study with 70 patients undergoing SMILE in one eye and LASIK, no differences in dry eye symptoms, specifically eye discomfort, eye dryness, excessive tearing and gritty sensation, at 1 and 3 months post-operatively were identified.<sup>9</sup>

It has been hypothesized that the flapless nature of the SMILE procedure may have less impact on the **biomechanical characteristics** of the cornea than femtosecond laser created flaps because the most anterior stromal lamellae remain intact during the SMILE procedure. Clinical investigations into corneal refractive surgeries specifically studied corneal hysteresis and corneal resistance, parameters that assess the viscoelasticity of the cornea in ocular diseases such as glaucoma.<sup>10</sup> The majority of studies showed that the biomechanical strength between FS-LASIK and SMILE was equivalent<sup>11-14</sup> or a very small difference in favor of SMILE.<sup>15</sup> Another study conducted in an ex-vivo setting evaluated the corneal tensile strength of human donor corneas that were subjected to both surgical procedures and demonstrated that the level of myopic correction was the determining factor of post-procedure corneal tensile strength.<sup>16</sup> Both groups revealed similar tensile strength reductions for higher myopic corrections.<sup>16</sup> Contrary to previous findings, SMILE showed a greater reduction in tensile strength in lower myopic corrections compared to LASIK.<sup>16</sup> The authors noted that SMILE implements an additional refraction neutral corneal tissue base to maintain a minimum thickness of the lenticule, which may explain this finding. Future paired-eye studies should be conducted to reach a consistent conclusion on any differences in biomechanical characteristics.

FS-LASIK and SMILE, because of their different approach to correct refractive errors, encounter procedure-specific complications. Table 3 lists unique intra- and post-operative complications that are flap or lenticule related for each procedure.

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Flap-related complications <sup>17</sup>	Lenticule-related complications <sup>18</sup>
<ul style="list-style-type: none"> <li>• Buttonhole flaps as a result of vertical gas breakthrough for thin flap or conditions, such as previous radial keratotomy, corneal scars or microscopic breaks in the Bowman's membrane</li> <li>• Flap tears during lifting of the flap (a free flap may occur if the tear is at the hinge)</li> <li>• Interface debris</li> <li>• Dislocated flaps post-operatively</li> </ul>	<ul style="list-style-type: none"> <li>• Incisional abrasion due to excessive manipulation</li> <li>• Inadvertent dissection of the posterior plane with resulting cap-lenticule adhesion and very challenging to impossible extraction of the lenticule</li> <li>• Cap perforation/ incisional tear during plane dissection</li> <li>• Lenticule tear with lenticule remnants remaining in the interface (can generate topographic irregularities, irregular astigmatism and vision loss)</li> </ul>

**Table 3. FS-LASIK and SMILE related intra- and post-operative complications.**

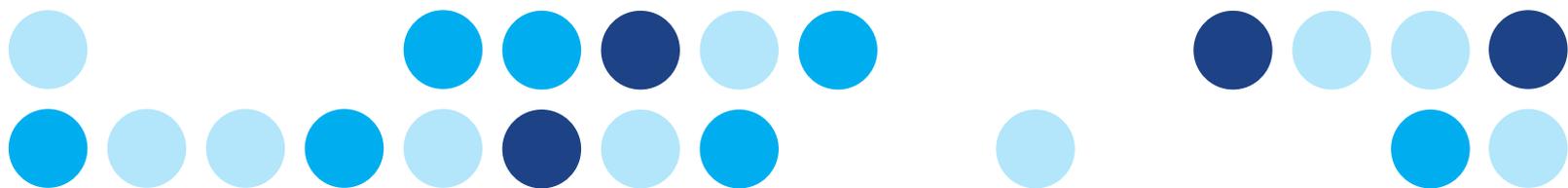
In terms of **safety**, both procedures have an acceptable safety profile based on loss of BCVA at 12 months (see Table 4). However, Alcon CONTOURA® Vision may have a higher percentage of patients that gained 2 or more lines of BCVA as shown in Table 4.

	Topography-guided LASIK	SMILE
Percentage of eyes with	Alcon CONTOURA® Vision (n = 230 eyes)	Zeiss VisuMax SMILE (n = 349 eyes)
Loss of more than 2 lines BCVA	0%	0%
Loss of 2 lines BCVA	0.4%	0%
Loss of 1 line BCVA	2.2%	2.3%
Equal BCVA	57%	73.6%
Gain of 1 line BCVA	27%	22.3%
Gain of 2 lines BCVA	10.4%	1.4%
Gain of more than 2 lines BCVA	3%	0.3%
BCVA worse than 20/40	0%	0%

**Table 4. Best corrected visual acuity (BCVA) for Topography-Guided LASIK and SMILE Procedures at 12 months after surgery per the respective FDA Summary of Safety and Effectiveness Data (SSED) Sheet of three different clinical data sets.<sup>3,4</sup>**

In summary, the Topography-Guided LASIK and SMILE platforms provide acceptable effectiveness and safety profiles. The Alcon WaveLight® Topography-Guided LASIK platform outperforms the SMILE procedure in visual performance as demonstrated by the comparative study conducted by Kanellopoulos.<sup>5,6</sup> SMILE may not provide a reduced dry eye benefit and did not better preserve the biomechanical characteristics as compared to FS-LASIK. Both platforms have unique intraoperative and post-operative complications that surgeons should consider.

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# Alcon WaveLight® Topography-Guided Treatment

Alcon WaveLight® Topography-Guided platform uses the individual corneal topography of the patient to customize the ablation profile. Adjusted laser pulse placement also neutralizes corneal surface irregularities and preserves the aspheric shape of the cornea.

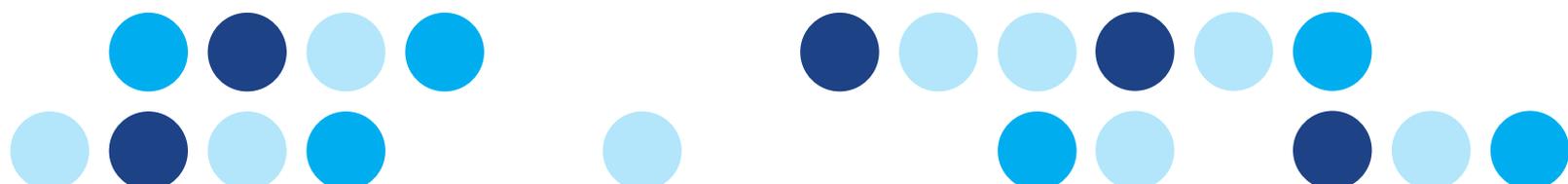
The WaveLight® TOPOLYZER® Vario system measures up to 22,000 unique elevation data points to capture the distinct characteristics of the patient's anterior cornea and creates a complete topography map (Figure 3). The Topography-Guided treatment planning software uses this information to guide the EX500 excimer laser and applies a smoothing ablation profile that flattens elevations and steepens flatter areas by ablating around them. The treatment is centered on the corneal apex and as opposed to the pupil center, thereby minimizing concerns related to the effect of angle Kappa in a pupil centered ablation treatment. In addition, planning refractive surgery using corneal topography is more consistent as it is less affected by pupil size, pupil centroid shift, accommodation and internal ocular pathologies associated with aging.<sup>19</sup>

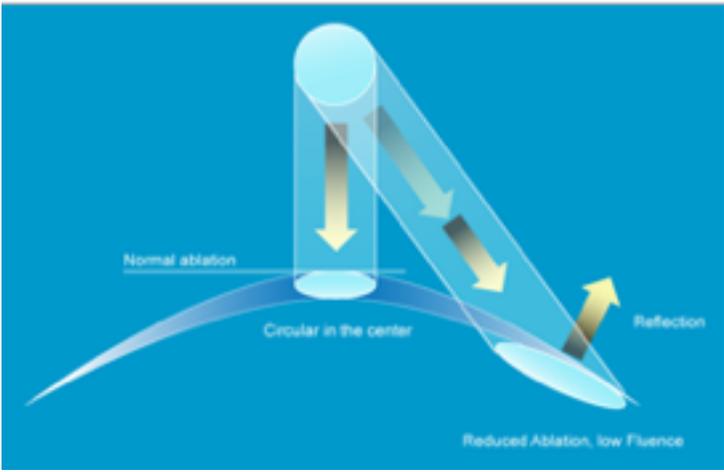


**Figure 3. Alcon WaveLight® Topography-Guided platform incorporates the elevation map from the WaveLight® TOPOLYZER® Vario system to individualize the ablation profile.**

The Alcon WaveLight® Topography-Guided platform builds on *Wavefront Optimized®* fundamentals. The ablation profile compensates for the cosine effect by fine-tuning the energy delivery profile in the periphery of the treatment zone, which preserves the aspheric shape of the cornea (see Figure 4). Without such compensation, the energy per unit area would be lower in the periphery and the effectiveness of the laser would be reduced. Reasons for the cosine effect are: 1) the shape of the laser beam ovalizes towards the periphery of the treatment resulting in a larger energy distribution for the same amount of energy; 2) the angle of incidence between the laser beam relative to the cornea is increased which subsequently increases beam reflectivity; 3) the likelihood of beam interference is increased by the plume created from earlier tissue ablation due to the longer path length. Overall, the compensation for the cosine effect helps to minimize the induction of spherical aberrations.<sup>20</sup>

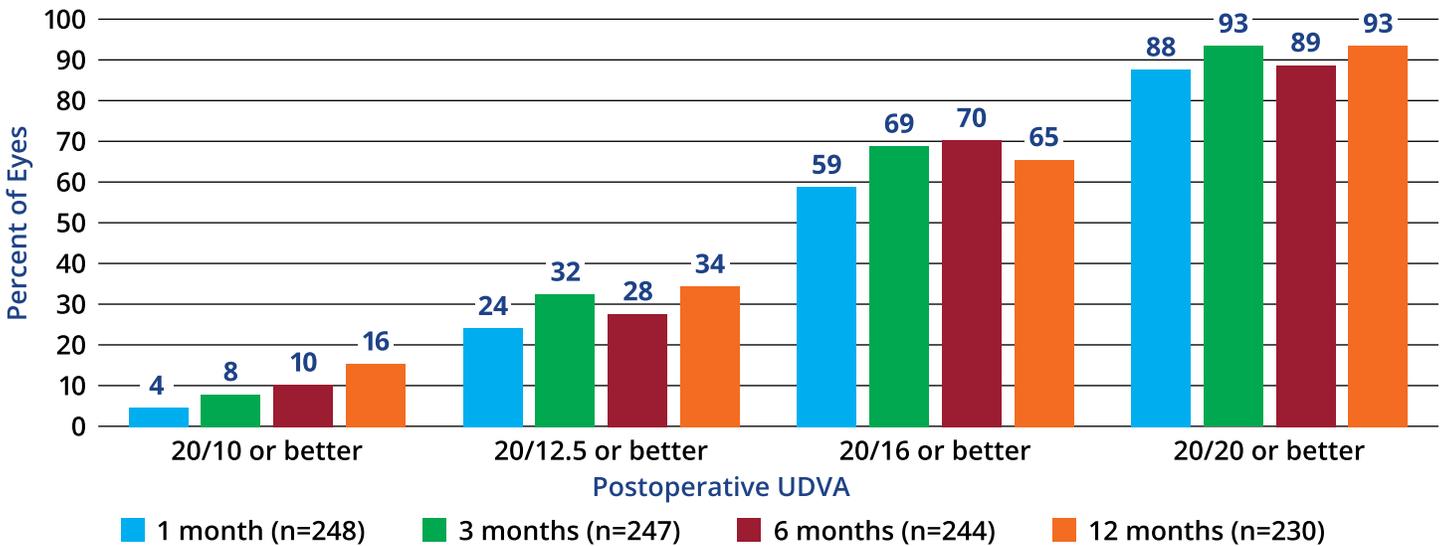
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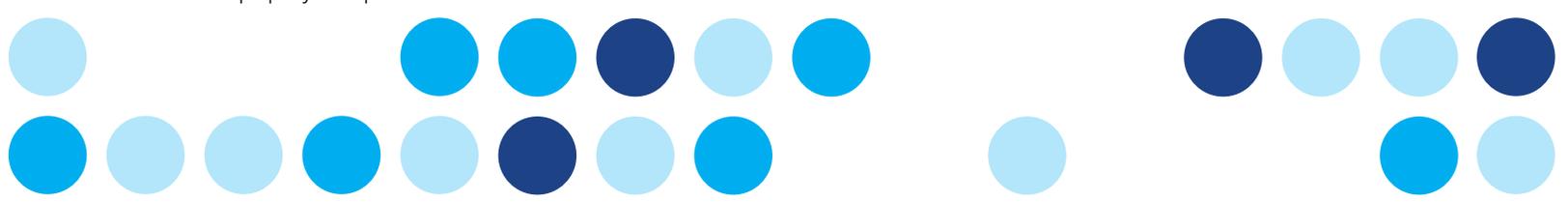
**Figure 4. The Alcon WaveLight® Topography-Guided platform compensates for the cosine effect by applying additional laser pulses in the periphery of the treatment zone.**

The cornea accounts for almost 70% of the overall refracting power of the eye. A uniform shape of the cornea is therefore a prerequisite to good vision and the WaveLight® Topography-Guided system excels in providing uniform corneal shape by removing corneal irregularities. Stulting et al.<sup>19</sup> described excellent visual outcomes of eyes treated with the WaveLight® Topography-Guided platform, with 92.6% of eyes achieving 20/20 or better (see Figure 5). Other authors have also reported excellent visual acuity outcomes with 94% to 100% of eyes treated achieving 20/20 or better.<sup>20-22</sup> A recent post-hoc analysis of the WaveLight® Topography-Guided FDA clinical trial data also showed improvement of vision over time. At 12 months post-operatively, the number of eyes achieving uncorrected distance visual acuity (UCVA) of 20/10 was 2.2 times greater compared to 3 months post-operatively.<sup>23</sup> Furthermore, smoothing of the corneal surface improved vision and studies have shown that 7% to 55.6% of eyes gain 1 line or more of BVCA.<sup>19,20,22,24</sup>



**Figure 5. Uncorrected distance visual acuity (UDVA) at each post-operative visit following Alcon WaveLight® Topography-Guided treatment.**

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A more uniform corneal shape improves the quality of vision. The WaveLight® Topography-Guided treatment showed reduced induction of higher and lower order aberrations<sup>20,22</sup> as well as better mesopic contrast sensitivity post-operatively<sup>22,25</sup> in comparison to traditional LASIK procedures. In addition, patients that underwent WaveLight® Topography-Guided treatment surgery were happier and had fewer visual complaints. Patient satisfaction with WaveLight® Topography-Guided treatment is exceptionally high, with 98.4% of 124 patients willing to undergo the procedure again.<sup>19</sup> The severity of patient reported visual symptoms, such as light sensitivity, difficulty driving at night, reading difficulty, problems with glare and halos, were significantly reduced (Table 5).<sup>19</sup> In 30% of patients, visual acuity improvement surpassed the vision they had with their glasses or contact lenses before surgery.<sup>19</sup>

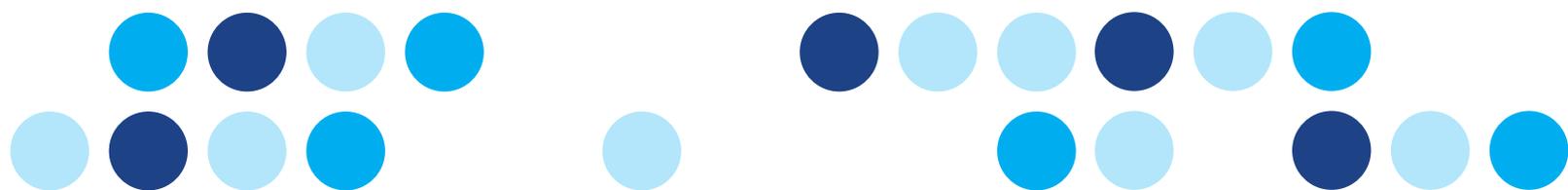
In conclusion, Alcon WaveLight® Topography-Guided treatment offers patients a personalized treatment plan that improves the quantity and quality of vision and surpasses the vision they had known with glasses and contact lenses.

Patient reported outcome	Prior Surgery (n=249 eyes)		12 months after surgery (n=230 eyes)		Difference prior surgery to 12 months after surgery (in marked to severe)
	% of eyes with no to moderate symptoms	% of eyes with marked to severe symptoms	% of eyes with none to moderate symptoms	% of eyes with marked to severe symptoms	
Light sensitivity	94.8	5.2	100	0	p<0.0005*
Difficulty driving at night	91.6	8.4	99.6	0.4	p<0.0001*
Reading difficulty	90.0	10.0	98.7	1.3	p<0.0001*
Glare	95.2	4.8	100	0	p<0.001*
Halos	96.8	3.2	100	0	p<0.01*
Starbursts	96.8	3.2	99.6	0.4	p<0.03*

\* Significantly different

**Table 5. Patient reported outcomes prior to and 12 months after surgery with Alcon WaveLight® Topography-Guided treatment.<sup>19</sup>**

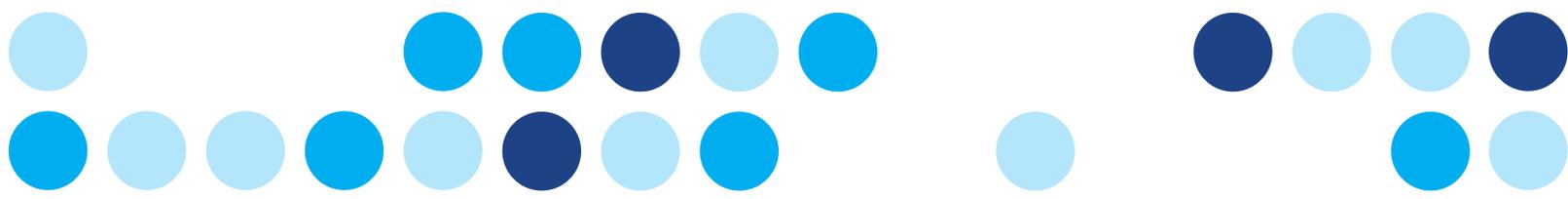
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# Important Product Information about the WaveLight® Excimer Laser Systems

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 for use in laser-assisted in situ keratomileusis (LASIK) treatments for:

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

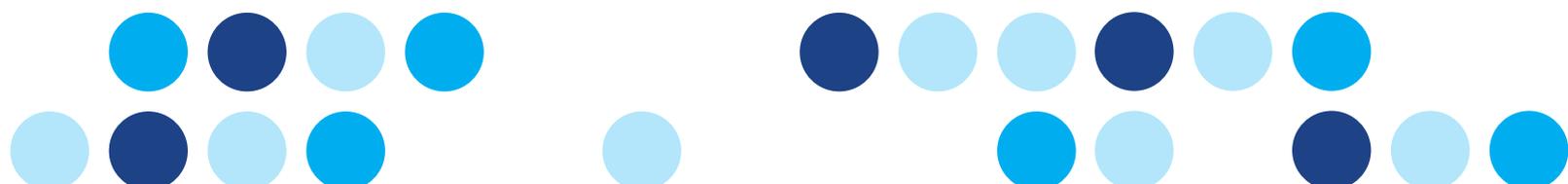
In addition, FDA has approved the WaveLight® ALLEGRETTO WAVE® Eye-Q Excimer Laser System, when used with the WaveLight® ALLEGRO Topolyzer® and topography-guided treatment planning software for topography-guided LASIK treatments for the reduction or elimination of up to -9.00D of myopia, or for the reduction or elimination of myopia with astigmatism, with up to -8.00D of myopia and up to 3.00D 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  $\leq 0.50D$  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.

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**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 7.0mm after mydriatics where applied for wavefront-guided ablation planning;
- history of glaucoma or ocular hypertension of > 23mmHg;
- 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

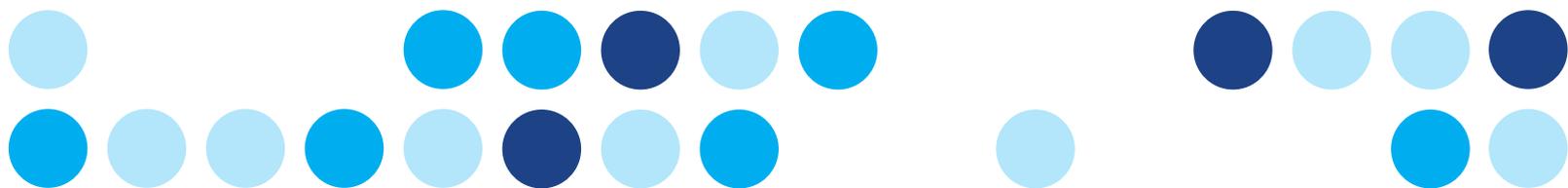
- taking medications likely to affect wound healing including (but not limited to) antimetabolites.

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

- treatments with an optical zone < 6.0mm or > 6.5mm in diameter, or an ablation zone > 9.0mm 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 > 4D and ≤ 6D. 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.

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## 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 postoperatively 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.

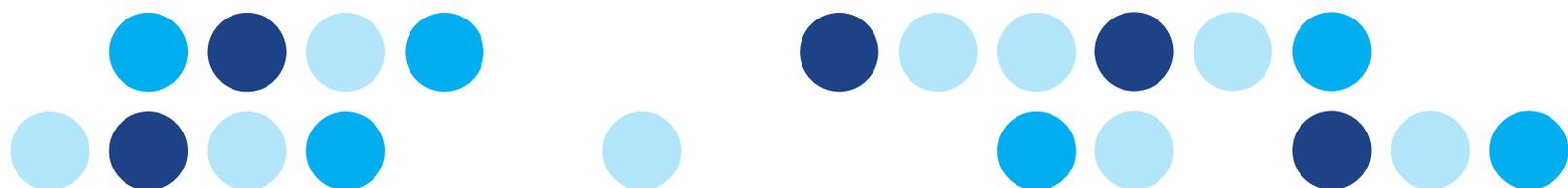
The following complications were reported 6 months after LASIK: 1.8% (2/111) of the eyes had ghosting or double images in the operative eye.

**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.

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## 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.

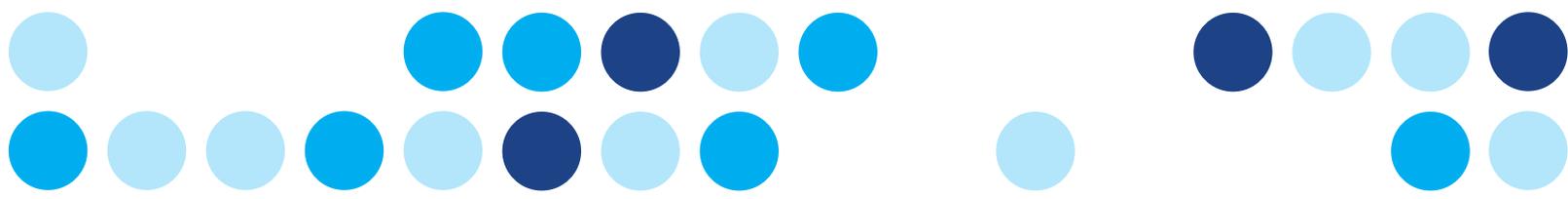
**Wavefront-Guided Myopia:** : The wavefront-guided myopia clinical study included 374 eyes treated; 188 with wavefront-guided LASIK (Study Cohort) and 186 with Wavefront Optimized® LASIK (Control Cohort). 166 of the Study Cohort and 166 of the Control Cohort were eligible to be followed at 6 months. 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.

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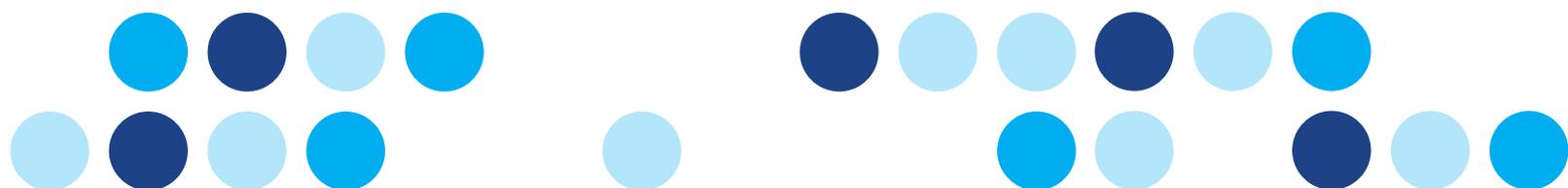
**Topography-Guided Myopia:** The topography-guided myopia clinical study included 249 eyes treated, of which 230 eyes were followed for 12 months. Accountability at 3 months was 99.2%, at 6 months was 98.0%, and at 12 months was 92.4%. Of the 247 eyes that were eligible for the UCVA analysis at the 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.

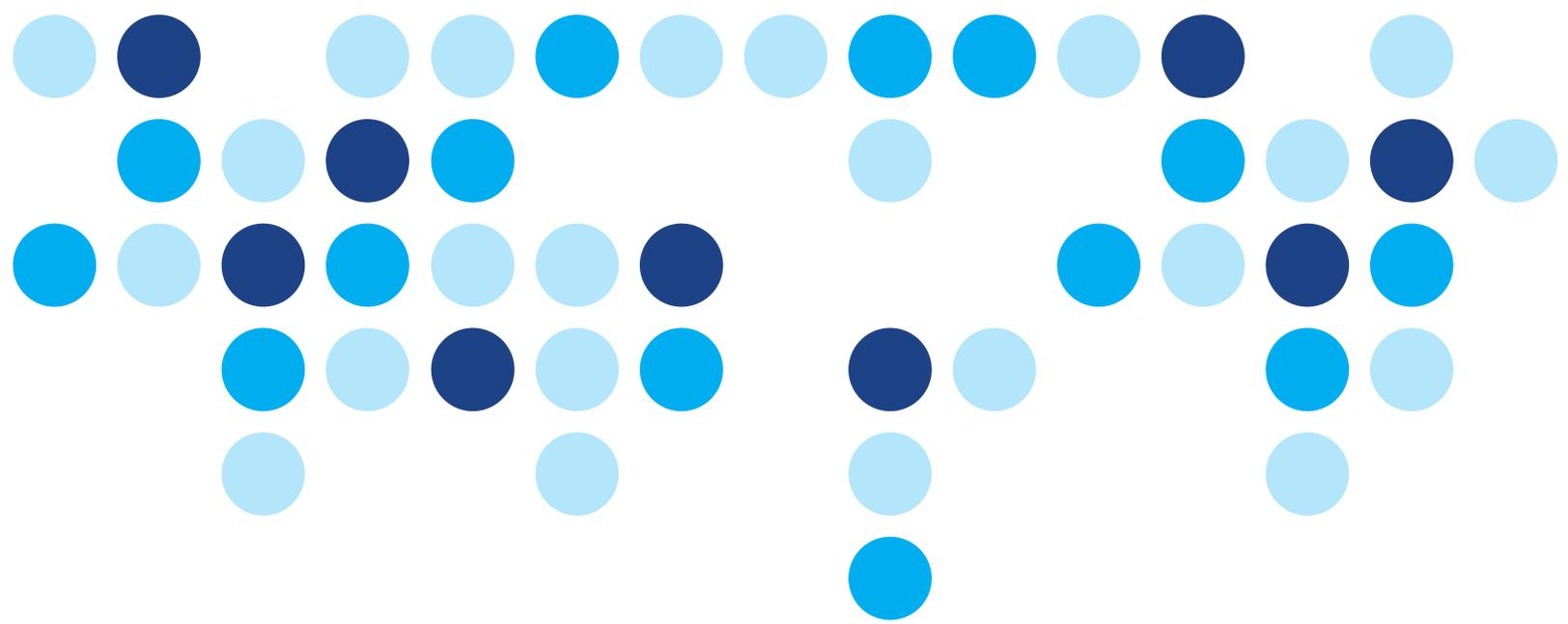
Long term risks of topography-guided LASIK for myopia with and without astigmatism have not been studied beyond 12 months.

**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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# Alcon Medical Affairs