

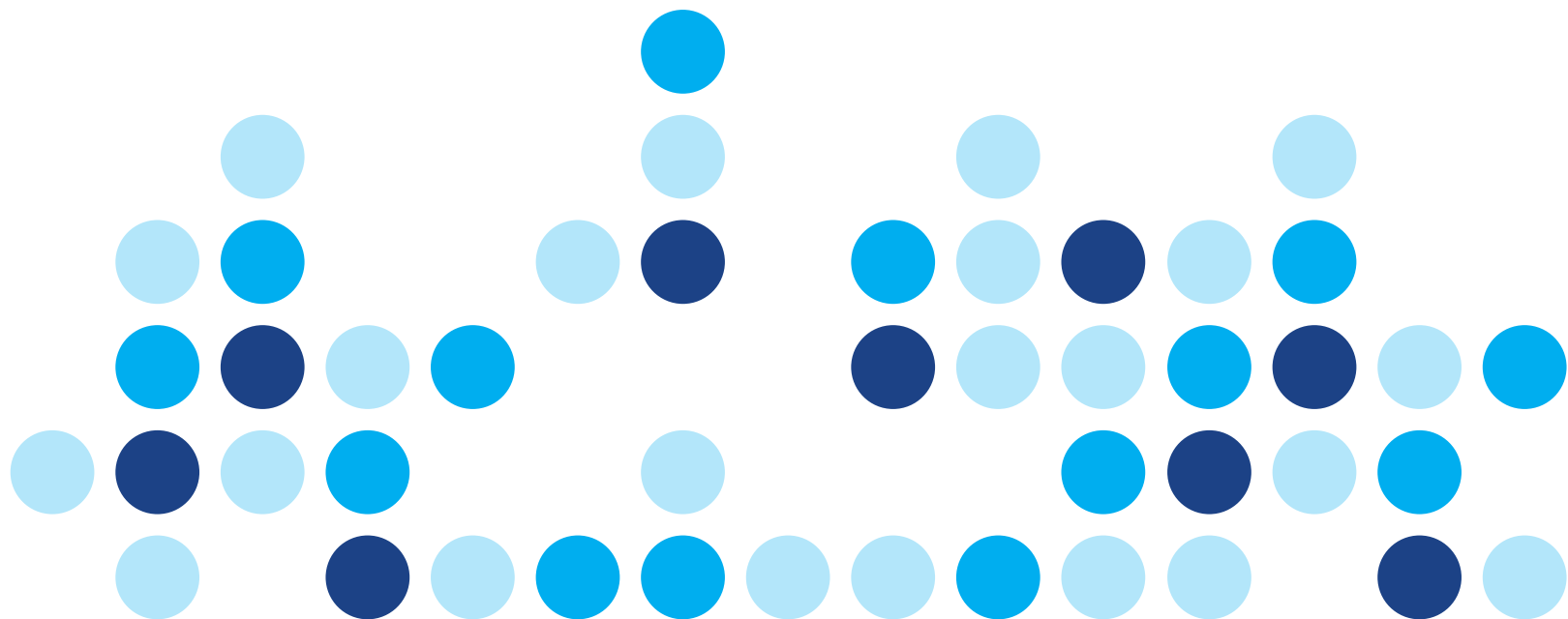
Femtosecond-assisted LASIK flap versus microkeratome-assisted LASIK flap creation

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Key Take-aways:

- Two fundamentally different principles of flap creation: the microkeratome mechanically separates the corneal tissue with the blade to create a flap, while in femtosecond LASIK a spatula is required to separate the stromal tissue bridges to create a flap
- Microkeratome and femtosecond LASIK provide overall a similar safety and visual outcome profile
- Age-related differences may exist, with femtosecond LASIK being more predictable and safe in patients older than 40 years compared to microkeratome LASIK
- Femtosecond laser created flaps allow for higher accuracy, a more uniform thickness across the flap diameter, produce smoother stromal bed surfaces and allow for quicker recovery

Introduction

Laser in-situ keratomileusis (LASIK) is a surgical procedure that reshapes the corneal surface to correct refractive error. There are two approaches to create a LASIK corneal flap: using a mechanical microkeratome or a femtosecond laser. About 53.1% and 28.7% of worldwide LASIK procedures in 2018 were performed using femtosecond lasers and blade based microkeratomes, respectively.¹

Microkeratome and femtosecond flap creation are two fundamentally different procedures. The microkeratome generates a corneal flap using a blade in a single mechanical cut. The femtosecond laser vaporizes small amounts of intrastromal tissue via photodisruption. This process generates small gas cavitation bubbles that expand and separate the stromal tissue (Figure 1).² With femtosecond LASIK, the flap is not separated from the stromal bed unless a spatula is used to separate the stromal tissue bridges.

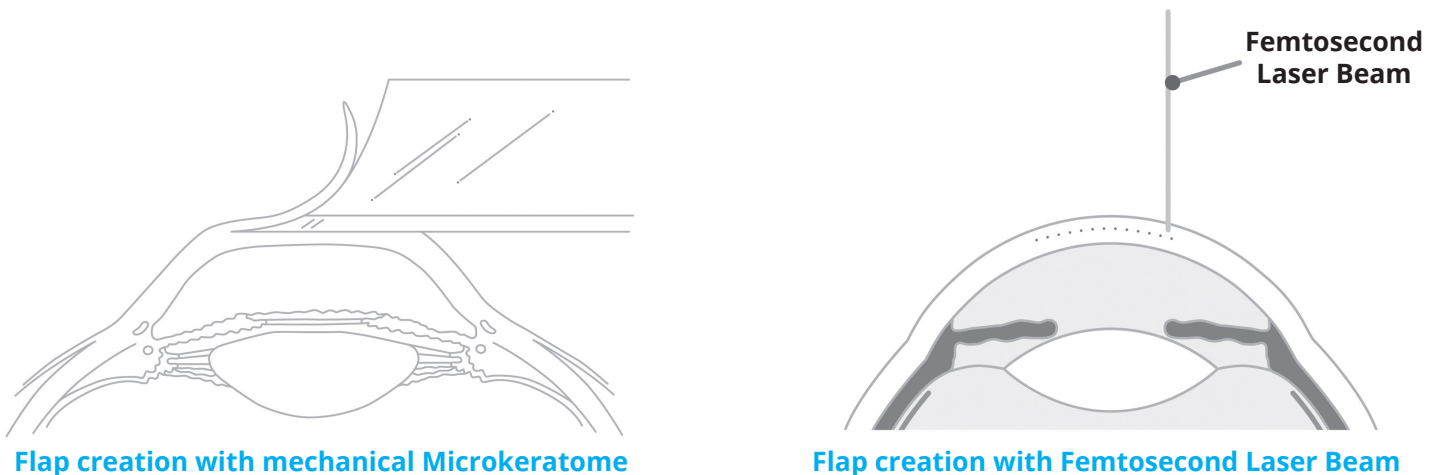
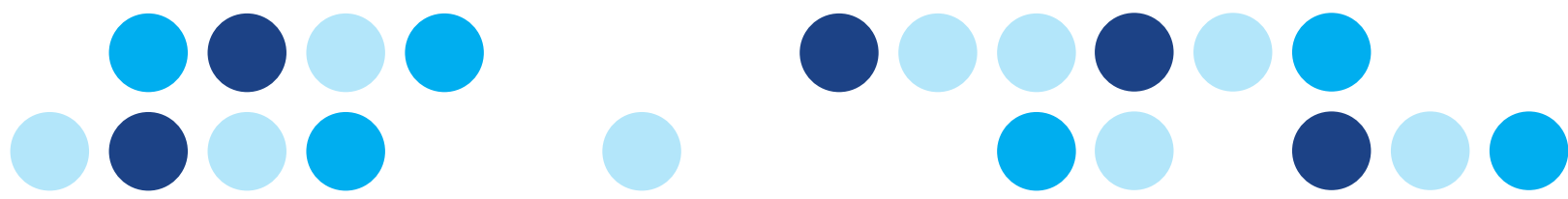


Figure 1. Microkeratome and Femtosecond Laser flap creation.

Other basic differences include the individual eye-level customization capabilities of the flap parameters. Unlike microkeratomes, femtosecond lasers generally allow for visualization of the stroma throughout the procedure and customization of the following flap parameters after suction has been applied to the cornea:

- Individualization of side cut angle
- Selection of the flap thickness, flap diameter and centration
- Selection of hinge and flap orientation independent of the suction ring location



With a microkeratome, some of the above mentioned parameters are related with a hardware change (e.g. change of cutting head for flap thickness), while the side cut angle can never be customized. Also the flap centration, hinge location and orientation can no longer be adjusted once the suction ring is docked and suction is applied to the cornea.

This white paper provides a clinical perspective on the differences between corneal flaps created with a microkeratome or femtosecond laser.

Predictability, Effectiveness, and Safety

Two meta-analyses comprising 7 articles³ and 15 articles⁴ examined differences between microkeratome and femtosecond LASIK. Meta-analyses are generally helpful when assessing the efficacy and safety profiles of treatments, particularly in the pharmacological realm. In regard to technology, however, meta-analyses may not be able to assess the evolution of the technology and how technology becomes more efficient over time. For example, the introduction of higher frequency lasers enable tighter spot/line separations that allow for smoother stromal bed surfaces which may positively impact safety and predictability. These developments have not been considered in these systematic reviews.^{3,4}

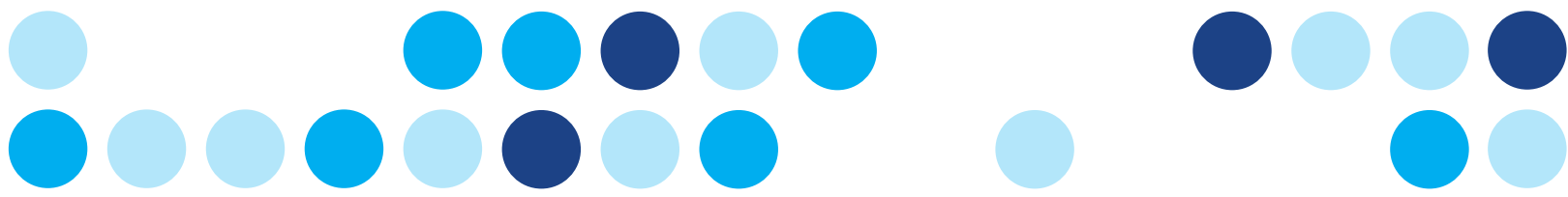
The analyses indicated that both, microkeratome and femtosecond LASIK, are equally safe and effective.^{3,4} Specifically, the studies found the following:

- **Visual outcome** - There were no differences in the uncorrected distance visual acuity of $\geq 20/20$.^{3,4}
- **Loss of vision** - There were no differences in the loss corrected distance visual acuity ≥ 2 lines were identified.^{3,4}

The study analyses were not in agreement for several parameters tested:

- **Predictability** - While Chen et al.⁴ reported on a greater proportion of eyes with a mean spherical equivalent of ± 0.50 D in femtosecond LASIK, Zhang et al.³ did not find an improved refractive predictability with femtosecond LASIK.
- **Higher order aberrations (HOA)** - Chen et al.⁴ reported that there was no difference in HOAs between both flap creating techniques. In contrast, Zhang et al.³ described that the total HOAs and spherical aberrations were significantly higher in microkeratome LASIK. A higher level of aberrations with microkeratome LASIK may likely be a consequence of the meniscus-shaped flap that allows for more profound biomechanical changes of the anterior cornea.³ Femtosecond LASIK flaps, on the other hand, are more uniform and have constant hinge angles that may reduce coma.⁴ In line with Zhang et al.,³ a recent study reported that the microkeratome induced significantly higher levels of trefoil and horizontal coma.⁵ However, none of these studies investigated the diameter and centration of the flap as well as the orientation of the ablation profile relative to the hinge. If the hinge location and ablation profile are not aligned, the stromal bed and the flap hinge may be ablated and consequently HOA may be induced (Figure 2).

A significant impact of age on visual and refractive results have been documented after LASIK. Garcia-Gonzalez et al.⁶ described a study including 3,826 eyes treated with either microkeratome or femtosecond LASIK for the correction of myopia (1,725 treated with microkeratome LASIK and 2,101 eyes treated with femtosecond LASIK). In patients over 40 years of age, predictability improved and the efficacy and safety indices were significantly better with femtosecond LASIK than with microkeratome LASIK.⁶ The authors offered possible explanations for these findings, such as age-related structural changes in the corneal biomechanical properties (i.e. reduced viscoelastic properties with age) and more severe wound healing responses in younger patients.⁶



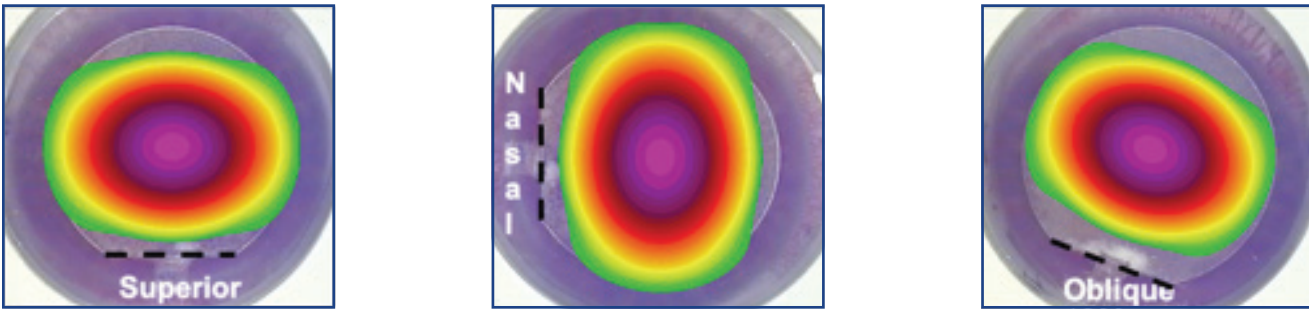
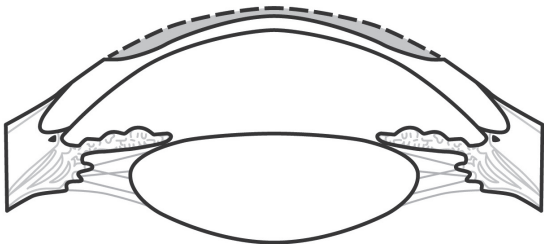


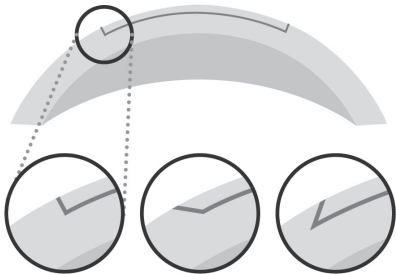
Figure 2. Depending on the ablation profile, the hinge can be placed in superior, nasal or oblique positions to avoid accidental ablation of the hinge and induction of HOAs. The customization of the hinge location is possible with the femtosecond laser, but not with a microkeratome. (Screenshots from the WaveLight® Refractive Suite)

Flap accuracy, uniformity and surface roughness

Fundamentally, the corneal flaps created by the microkeratome are meniscus-shaped, with the flap being thicker in the periphery. In contrast, the femtosecond laser creates a flap in a surface-parallel fashion which results in a planar-shaped corneal flap (Figure 3). One of the major concerns for the refractive surgeon is the accuracy of the corneal flap thickness. Several comparative studies have examined the accuracy of the cut depth and uniformity of the flap thickness.



Meniscus-shaped corneal flap with mechanical Microkeratome



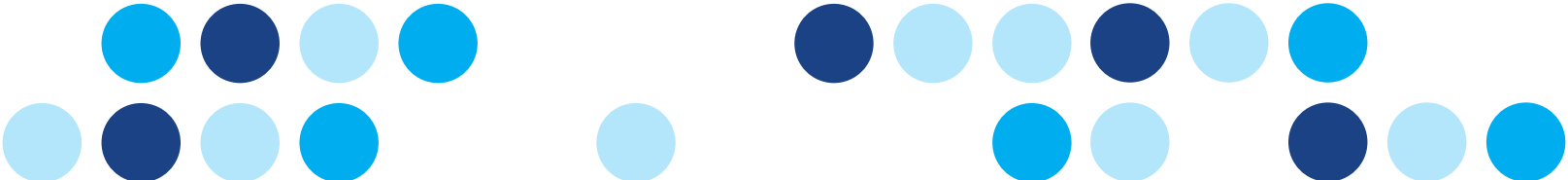
Planar-shaped corneal flap with customization of hinge angle/length and side cut angle with Femtosecond Laser

Figure 3. Microkeratome and Femtosecond laser created flaps have a different shape.

The two meta-analyses^{3,4} found that femtosecond-created flaps deviate less from the target thickness. Recent publications confirmed this result and although technical improvements were made to microkeratomes, the femtosecond laser-created flaps have smaller flap thickness variability and are more uniform across the flap diameter.⁷⁻⁹ In-vitro studies also determined that the stromal bed surface quality is smoother in corneal flaps created by a femtosecond laser.^{7,10}

Ocular surface changes

Ocular surgery interferes with the delicate balance of the ocular surface system. The creation of a corneal flap severs the corneal nerves of the richly innervated cornea, thereby reducing corneal sensitivity and inducing dry eye symptoms in the short term.¹¹ Long term, severed corneal nerve fibers regenerate. Earlier work described a reduction in the tear menisci height using spectral domain optical coherence tomograph (SD-OCT), but no differences between microkeratome and femtosecond laser-created flaps were identified.¹² Later, similar methodology using SD-OCT showed a significantly higher tear meniscus height and larger tear meniscus area at each post-op visit up to 6 months with femtosecond LASIK as compared to microkeratome LASIK.¹³ Femtosecond



LASIK also allowed for a full recovery of the tear menisci, while microkeratome LASIK failed to reach pre-operative levels.¹³ Further work in this area showed similar corneal and conjunctival scores between both techniques and significantly greater tear film break-up time with femtosecond LASIK.¹⁴

Complications

Intra-operative complications with a mechanical microkeratome are rare, but may be more severe. The microkeratome creates an immediate irreversible mechanical cut and it is possible that the microkeratome creates a completely detached flap instead of a hinged flap. This occurrence is not possible with femtosecond laser technology as a manual separation of the flap and stroma with a blunt spatula is needed.

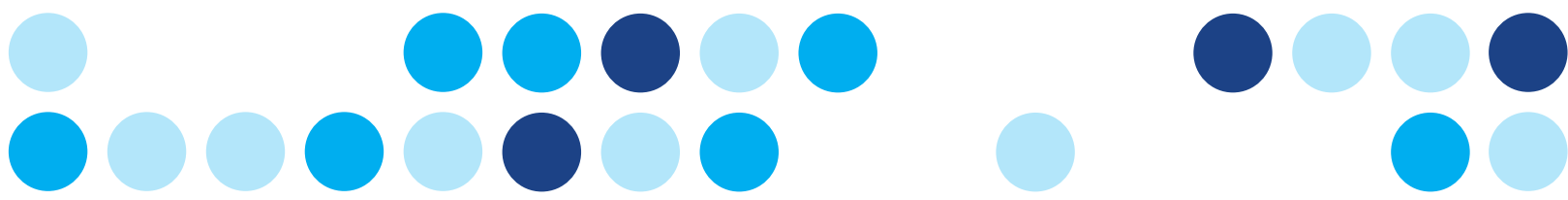
Overall, intra- and post-operative complication rates of both flap creating techniques are low but there are some differences:

- **Suction loss** is a possible intra-operative complication that needs to be addressed differently for each flap-creating technique. With microkeratome LASIK, postponing of the surgery is the most likely scenario, as the treatment may need to be converted to a surface ablation. If a suction loss occurs with a femtosecond laser, the surgery may proceed and a new laser cut can be performed without sacrificing outcomes.
- Microkeratomes most commonly, although rarely, may produce **buttonholes** in the central cornea. Other complications include incomplete cut, free cap or very thin/thick flaps. In the femtosecond procedure a **vertical gas breakthrough** may occur, particularly when a very thin flap is desired or a focal break in the Bowman's layer exists.¹⁵ Other rare complications that are unique to femtosecond LASIK are transient light-sensitivity syndrome* and rainbow glare**.^{17,23}
- The meta-analysis by Chen et al.⁴ reported on a higher incidence of **intraoperative epithelial defects** with microkeratome use. This was also corroborated by more recent studies in which epithelial defects were detected in 0.3%¹⁶ to 0.6%¹⁷ of eyes treated with femtosecond LASIK and 2.6%¹⁷ of eyes treated with microkeratome LASIK.
- **Diffuse lamellar keratitis** (DLK) is an early post-operative complication associated with the inflammatory response to the LASIK treatment that can cause scarring and impact the visual outcome.¹⁸ A higher tendency towards postoperative DLK was reported with femtosecond LASIK.^{3,4} It has been hypothesized that the higher incidence rate of DLK post-operatively is associated with lower frequency lasers applying higher energy, but this has not been conclusively confirmed.¹⁹ A recent review summarized the incidence of DLK as ranging from 0.2% to 19.4% after femtosecond LASIK and 0.1% to 7.7% after microkeratome LASIK.¹⁸ The review did not include most recent publications reporting on the incidence rate of DLK in femtosecond LASIK, which was as low as 0.68% and no higher than 5.7%.²⁰⁻²²
- It was speculated that the rates of **epithelial ingrowth** may be improved with femtosecond LASIK due to flap angulation in the periphery. However, this hypothesis has not been confirmed.^{4,17}
- Femtosecond laser flaps create a stronger adhesion of the flap to the stromal bed as compared to microkeratomes. This difference was attributed to a greater inflammatory response of the cornea without an increase in apoptosis.^{24,25} In line with this finding, Clare et al. reported on a significantly lower risk of early flap displacements with femtosecond created flaps post-operatively.²⁶ When planning LASIK retreatment, one should consider this fact as flap lifting can cause epithelial ingrowth. Alternative ways to perform LASIK retreatment are available and include making a side cut with the laser or surface ablation.²⁷

Footnotes:

*Unusual photosensitivity despite normal visual acuity.

**Rainbow glare is a rare complication thought to be associated with the spot and line pattern created by the femtosecond laser in the corneal stroma that allows for separation of the tissue. These patterns create diffraction of light and subsequent visualization of multicolored light fringes around white light sources.



Femtosecond Lasers

Many different femtosecond lasers exist today. Current platforms utilize different pulse energy and frequency, docking mechanisms (flat or curved appplanation surfaces), laser delivery (raster or spiral patterns), gas bubble management techniques and laser mobility.¹⁰

The WaveLight® FS200 Femtosecond Laser is part of the WaveLight® Refractive Suite and is one example of a femtosecond laser. The laser emits laser pulses with durations of 350 fs at a wavelength of 1050 nm and a pulse repetition rate of 200 kHz. The intra-operative gas-venting technique reduces the risk for gas build up (opaque bubble layer, OBL). Prior to flap creation, a canal is generated to allow the gas to escape (Figure 4).^{28,29}

The WaveLight® FS200 Femtosecond Laser is highly versatile and creates standard or customized flaps (round or oval), corneal ring tunnels, pockets or arcuate incisions and has keratoplasty applications (penetrating keratoplasty, anterior lamellar keratoplasty, posterior lamellar keratoplasty).

To allow for an optimal centration of the treatment, the WaveLight® FS200 Femtosecond Laser automatically centers the flap in accordance to the pupil within the large 10mm appplanation area (Figure 5). If required, the surgeon can adjust the centration.

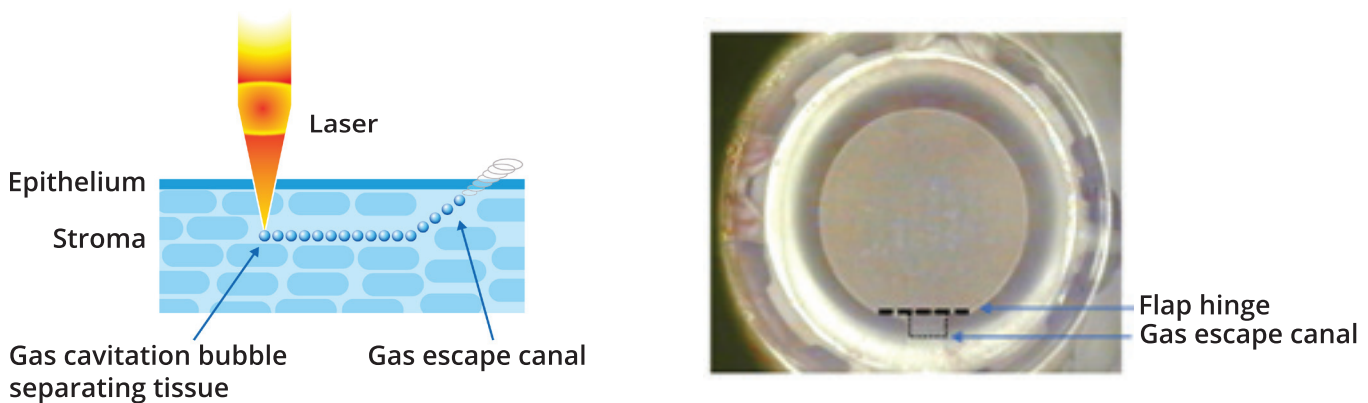


Figure 4. Gas-venting technique for the WaveLight® FS200 Femtosecond Laser to prevent OBL.

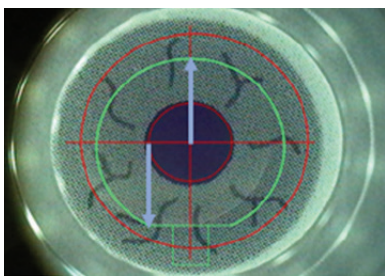


Figure 5. In the WaveLight® FS200 Femtosecond Laser, the flap is automatically positioned to the patient's pupil to allow for an optimally centered treatment. Surgeon adjustment of the flap centration can be performed, if required. This feature is not available when using a microkeratome.

Summary

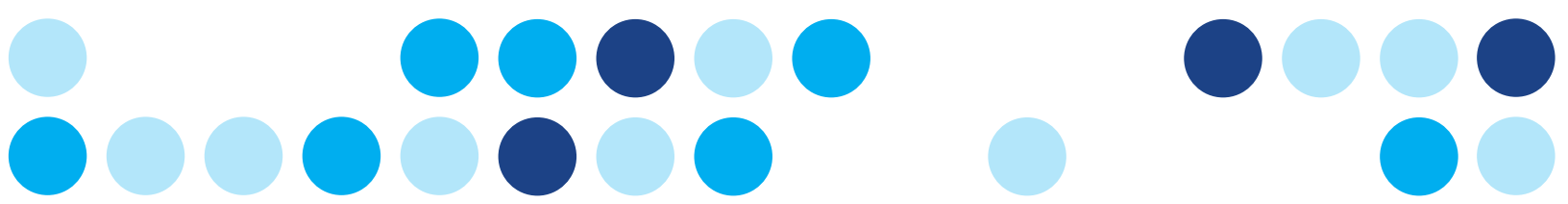
In summary, the published literature suggests that microkeratome and femtosecond LASIK provide a similar safety and effectiveness profile. However, age-related differences may exist between the two methods for flap creation and femtosecond LASIK may be more predictable and safe in a population older than 40 years. Femtosecond laser-created flaps have a higher accuracy, are more uniform, produce smoother stromal bed surfaces and allow



for a quicker recovery of the ocular surface than microkeratome created flaps. Each technique has its unique set of complications and may be more severe with a microkeratome due to the mechanical nature of the cut, but the occurrence of complications is generally rare.

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Important Product Information about the WaveLight® FS200 Laser System

CAUTION: Federal (USA) law restricts this device to sale by, or on the order of, a physician.

INDICATIONS: The WaveLight® FS200 Laser System is indicated for use in the creation of a corneal flap in patients undergoing LASIK surgery or other surgery or treatment requiring initial lamellar resection of the cornea; in patients undergoing surgery or other treatment requiring initial lamellar resection of the cornea to create tunnels for placement of corneal ring segments; in the creation of a lamellar cut/resection of the cornea for lamellar keratoplasty; and in the creation of a penetrating cut/incision for penetrating keratoplasty and for corneal harvesting.

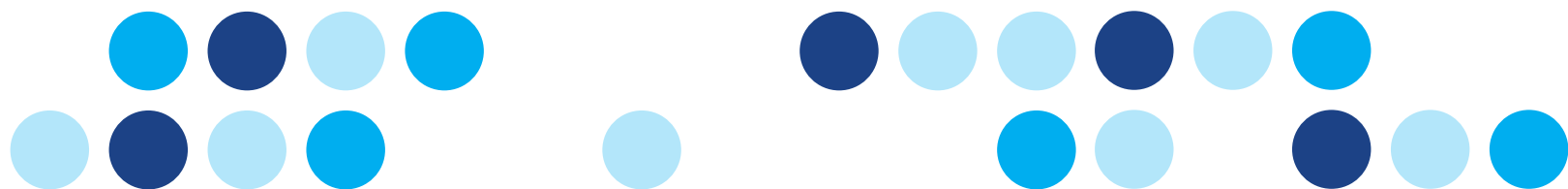
The WaveLight® FS200 delivery system is used in conjunction with a sterile disposable Patient Interface, consisting of pre-sterilized suction ring assemblies and pre-sterilized applanation cones, intended for single use.

The WaveLight® FS200 Laser System should only be operated by, or under the direct supervision of, a trained physician with certification in laser safety and in the use of the WaveLight® FS200 Laser.

CONTRAINDICATIONS: LASIK treatments are contraindicated in: Pregnant or nursing women; patients with a diagnosed collagen vascular, autoimmune or immunodeficiency disease; and patients who are taking one or both of the following medications: isotretinoin (Accutane*), amiodarone hydrochloride (Cordarone*).

Flap Contraindications: Lamellar resection for the creation of a corneal flap using the WaveLight® FS200 laser is contraindicated if any of the following conditions exist. Potential contraindications are not limited to those included in this list: corneal edema; corneal lesions; hypotony; glaucoma; existing corneal implant; and keratoconus.

Keratoplasty Contraindications: Penetrating cut/incision (for penetrating keratoplasty) is contraindicated in: any corneal opacity adequately dense to obscure visualization of the iris; descemetocoele with impending corneal rupture; previous corneal incisions that might provide a potential space into which the gas produced by the procedure can escape; and corneal thickness requirements that are beyond the range of the System.



Other Considerations: The following conditions should also be considered: severe corneal thinning; subjects with pre-existing glaucoma; a history of steroid responsive rise in intraocular pressure; preoperative intraocular pressure greater than 21 mmHg in the operative eye; subjects with more than 1000 µm corneal thickness at the 9 mm peripheral zone; active intraocular inflammation; and active ocular infection.

WARNINGS: Any treatment with the WaveLight® FS200 is not recommended in 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; and a history of glaucoma or ocular hypertension.

COMPLICATIONS: Possible complications which may result from flap cutting include (potential complications are not limited to those included in this list): corneal edema; corneal pain; epithelial ingrowth; epithelial infection; flap de-centration; incomplete flap creation; flap tearing or incomplete lift-off; free cap; photophobia; corneal inflammation, such as diffuse lamellar keratitis (DLK), corneal infiltrates and iritis; thin- or thick flaps; flap striae; and corneal ectasia (secondary keratoconus).

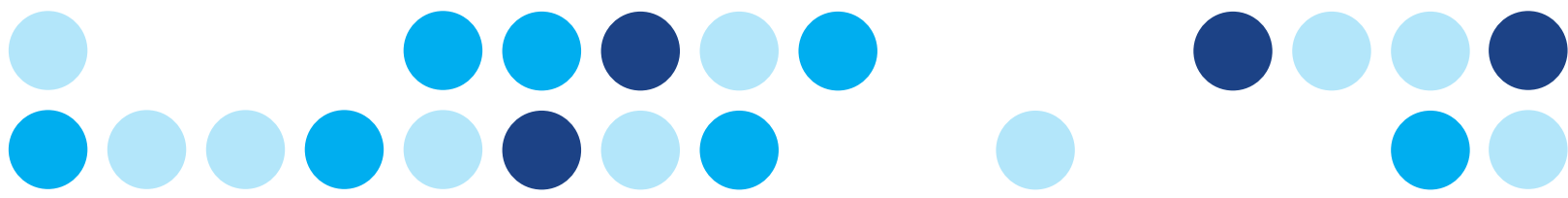
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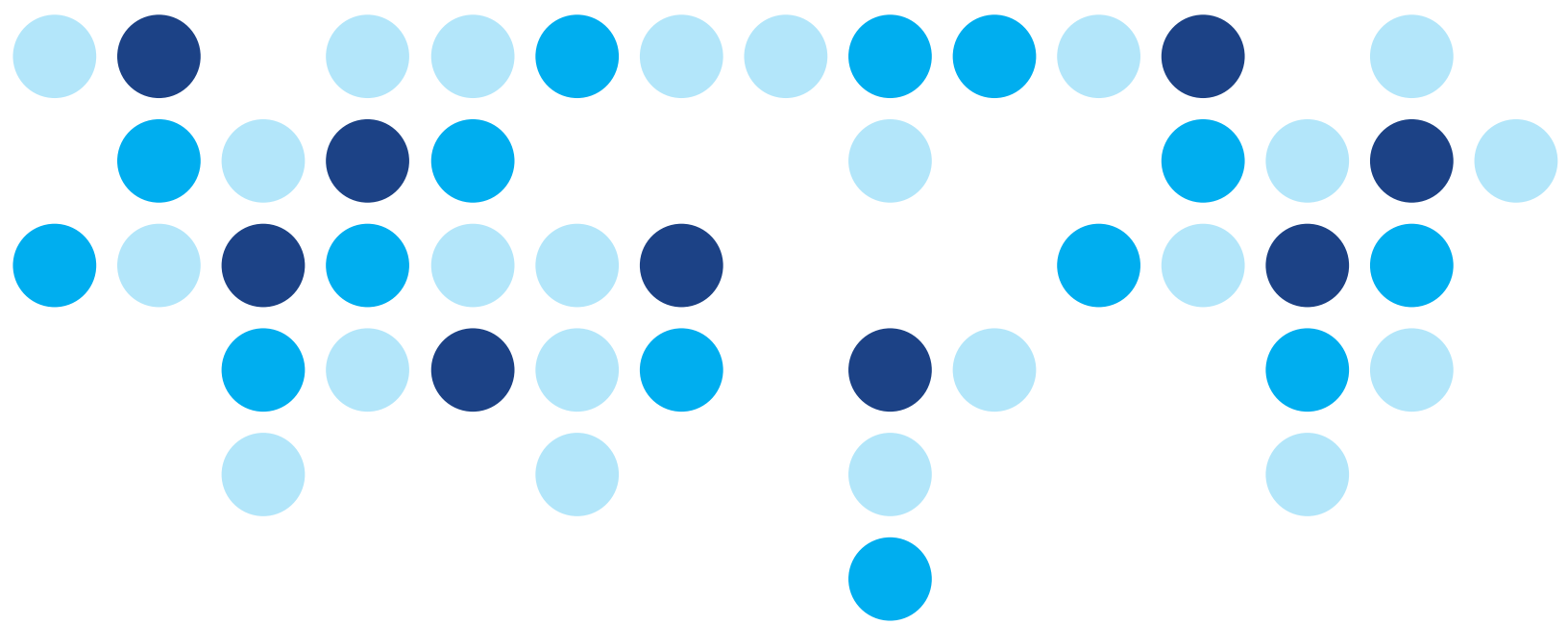
Transient Light Sensitivity Syndrome (TLSS): Transient Light Sensitivity Syndrome is characterized by symptoms of mild to severe light sensitivity which manifests between two and six weeks postoperatively. Patients experience no decrease in uncorrected or best spectacle-corrected visual acuity. The incidence of this sensitivity was observed in approximately 1% of patients who undergo flap creation with a femtosecond laser.* Patients respond to the use of hourly topical steroids such as prednisolone acetate, and most report improvement within one week of treatment.

Peripheral Light Spectrum (PLS): Peripheral Light Spectrum is a temporary phenomenon whereby patients report the perception of a spoke-like spectrum of light in the periphery of their vision. PLS has no clinical examination findings and no effect on visual acuity; however the potential diffractive effects may be bothersome to some patients. Reported in only a small amount of cases, the onset of symptoms occurs during the immediate postoperative period, and typically resolves within three months but may be slightly persistent in rare cases. The visual impact of PLS is clinically inconsequential for the vast majority of patients.

ATTENTION: Please refer to a current WaveLight® FS200 Laser System Procedure Manual for a complete listing of the indications, complications, warnings, precautions, and side effects.

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Alcon Medical Affairs