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# Femtosecond laser applications in corneal surgery

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**Abstract:**

Femtosecond laser (FSL) applications in corneal surgery have increased since its inception. Corneal surgery has undergone a tremendous transformation thanks to the introduction of FSL technology. This laser makes precise, three-dimensional incisions while causing minimal damage to surrounding tissue. This review updates and summarizes current and upcoming FSL applications in corneal surgery, current commercially available FSL, and its respective applications. Refractive surgery applications include laser *in-situ* keratomileusis flaps, refractive corneal lenticule extraction such as small incision lenticule extraction, astigmatic keratotomy, intracorneal ring segments tunnels for keratoconus including corneal allogenic intrastromal ring segments, and presbyopia treatments with intrastromal pockets for corneal inlays and intrastromal incisions (INTRACOR). Keratoplasty applications include penetrating keratoplasty trephination; superficial and deep anterior lamellar keratoplasty trephination, lamellar dissection, and tunnel creation; posterior lamellar keratoplasty donor and recipient preparation; Bowman layer transplantation donor, and recipient preparation; and stromal keratophakia. Other applications include conjunctival graft preparation in pterygium surgery, and keratopigmentation (corneal tattooing). FSL is a surgical instrument widely used in corneal surgery because it improves reproducibility and safety in many procedures.

**Keywords:**

Anterior lamellar keratoplasty, astigmatic keratotomy, bowman layer transplantation, cornea, corneal pockets, descemet stripping automated endothelial keratoplasty, femtosecond laser, intracorneal ring segments, laser in-situ keratomileusis, penetrating keratoplasty, refractive corneal lenticule extraction, small incision lenticule extraction, stromal keratophakia

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## Introduction

This is a narrative review of the current applications of femtosecond laser (FSL) in corneal surgery. Advantages of using an FSL over a manual blade to create corneal incisions include increased reproducibility, predictability, and safety.[1] Limitations include new complications, a learning curve, and higher costs. The first ophthalmic FSL application was the creation of flaps in laser *in-situ* keratomileusis (LASIK), approved in 2001.[2] Multiple applications and improvements have been developed to date: LASIK flaps, refractive corneal lenticule extraction (RCLE), intracorneal ring segments (ICRS) tunnels, astigmatic keratotomy (AK), intrastromal pockets, intrastromal incisions, penetrating and lamellar keratoplasties, stromal keratophakia, Bowman layer transplantation (BLT), pterygium and conjunctiva surgery, and others [Figure 1 and Table 1].[1-5]

## Femtosecond Laser Concepts

The FSL is a neodymium glass solid-state photo-disruptor infrared laser (wavelength: 1053 nm) that safely passes unaffected through the cornea. The FSL uses ultrafast pulses of short duration (200–600 fs), high repetition rate (150–20,000 kHz), and low energy (0.05–2.5 μJ). It produces small spots of a few microns that separate and



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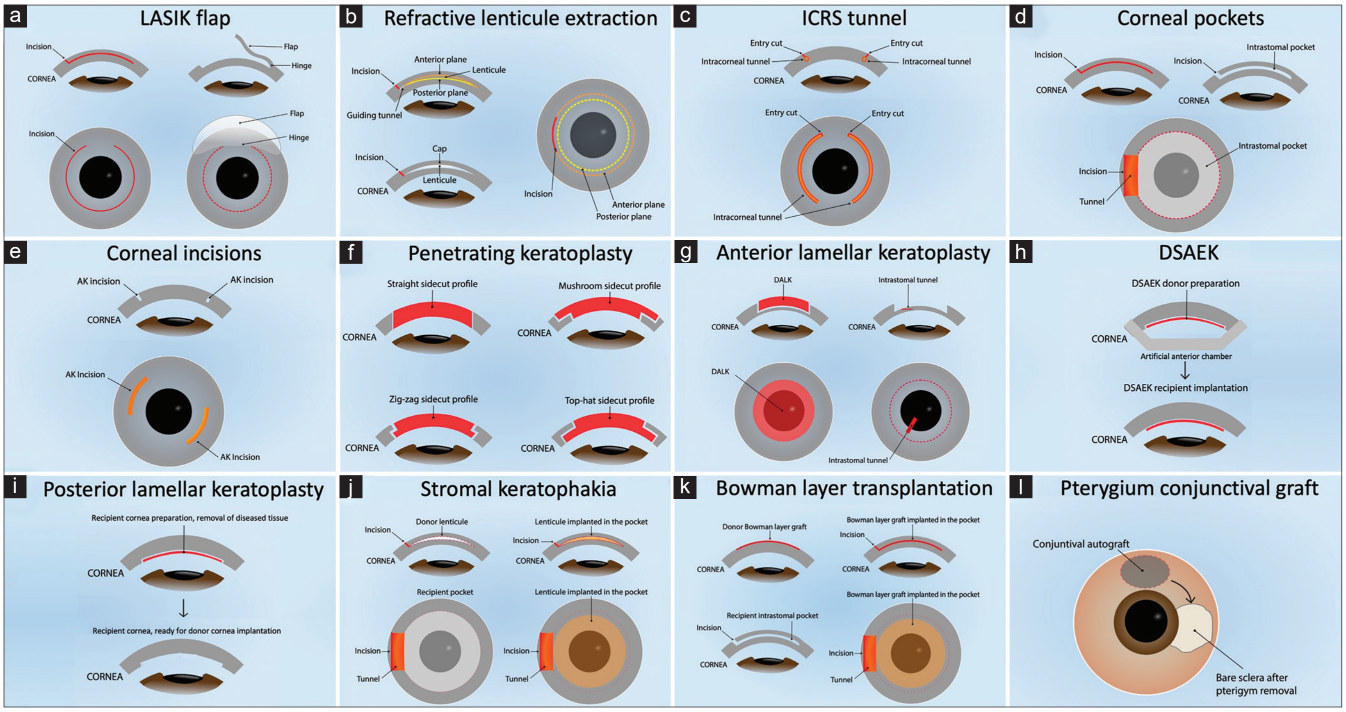


**Figure 1:** Femtosecond Laser Applications in Corneal Surgery. (a) Laser *in-situ* keratomileusis flap. (b) Refractive corneal lenticule extraction. (c) Intracorneal ring segments tunnel. (d) Intrastromal corneal pockets. (e) Corneal incisions, such as astigmatic keratotomy, intrastromal incisions, and clear cornea incisions. (f) Penetrating keratoplasty donor and recipient trephination. (g) Anterior lamellar keratoplasty, such as deep anterior lamellar keratoplasty and superficial anterior lamellar keratoplasty donor and recipient trephination and dissection. (h) Descemet's stripping automated endothelial keratoplasty donor preparation and recipient implantation. (i) Posterior lamellar keratoplasty recipient preparation and implantation. (j) Bowman layer transplantation donor bowman graft and recipient pocket preparation. (k) Stromal keratophakia donor lenticule and recipient pocket preparation. (l) Pterygium conjunctival autograft preparation

cut the corneal tissue. It is sharply focused on the targeted tissue allowing tridimensional incisions of precise and reproducible depth, length, and shape with very little tissue damage and a smooth surface.[1-4] The FSL creates a laser-induced optical breakdown when the focused laser energy in a small spot area exceeds the electron-to-nucleus bonding energy in the tissue. This results in ionization, release of free electrons, and creation of plasma that vaporizes the focused tissue and creates cavitations of gas bubbles in the tissue. These cavitation bubbles separate and cut the tissue, and when they are in place, one after the other forms lines of cavitations that lead to incisions in the tissues [Figure 2].[1,4] An interface device is in contact with the cornea; this interface surface can be flat, curved, or noncontact liquid. The latter could help to improve cut geometry by avoiding the deformation of the cornea. Some platforms have real-time optic coherence tomography to improve visualization, precision, and incision customization. FSL specifications and availability of applications are shown in Table 2 and vary between model and brand.

## Laser *in-situ* Keratomileusis

Over the years, LASIK has become an increasingly popular method to reduce or eliminate glasses

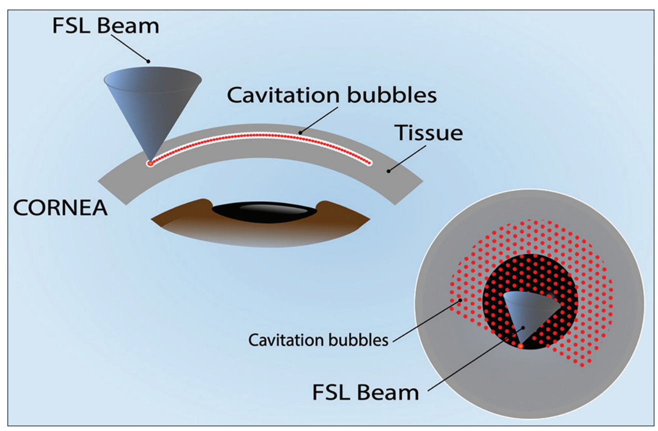


**Figure 2:** Illustration of Femtosecond Laser (FSL) Photo-disruption of Corneal Tissue. The FSL beam is sharply focused on the tissue and generates cavitation bubbles, arranged one next to the other to form lines of cavitations that separate and cut the tissue, forming incisions in the tissue

dependency.[6] The most frequently performed FSL application in corneal surgery is the creation of the LASIK flap, known as FSL-assisted LASIK (FS-LASIK). Flap creation is a fundamental step during LASIK; the consistency and predictability of the flap thickness and diameter are crucial.[7] FSL has the advantage of creating consistent flaps with better thickness accuracy than mechanical microkeratome (MK).[7] In FS-LASIK, the flap thickness is constant across its center and periphery. In contrast, in MK-LASIK, the flap is

**Table 1: Femtosecond laser applications in corneal surgery**

| Surgical procedure | Use and advantages |
|---|---|
| Refractive surgery | |
| LASIK | Refractive procedure. Precise flap depth, side cut, diameter, and shape |
| RCLE | Refractive procedure. Precise refractive lenticule shape, thickness, and depth. Small incision, flap-free procedure less dry eye |
| AK | Astigmatic management. Incision of precise depth, curvature, and location. Reliable outcomes and fewer complications |
| ICRS | Keratoconus treatment. Precise tunnel depth, length, width, radius of curvature, and location. Fewer complications. Can be used with CAIRS |
| Intrastromal pocket for corneal inlay | Presbyopia management. An intrastromal pocket of precise diameter, and depth for corneal inlay implantation, for |
| INTRACOR | Presbyopia management. INTRACOR with intrastromal circular incisions to make the cornea multifocal |
| Keratoplasty | |
| PKP | Donor and host precise trephination cuts in multiple shapes (straight, zig-zag, hat, mushroom) and good donor-host apposition |
| ALK: DALK and SALK | Partial trephination, precise lamellar dissection<br>Debulking, manual DALK, tunnel for big bubble DALK |
| PLK | DSAEK donor preparation<br>PLK recipient preparation: Removes host posterior stroma and endothelium, followed by a DSAEK/DMEK donor cornea implantation |
| BLT | Keratoconus treatment. Donor of precise diameter and fewer tears, but slightly thicker. Recipient pocket is safe and reliable in depth and size |
| Stromal keratophakia | Keratoconus and hyperopia treatment. Precise and safe donor lenticule and recipient intrastromal pocket creation |
| Others | |
| Conjunctival graft for pterygium surgery | Ultrathin conjunctival autograft, more predictable size and depth |
| Other applications | Case reports and small series have demonstrated the feasibility of keratopigmentation (corneal tattooing), corneal biopsy, stromal drug delivery, Boston keratoplasty donor preparation, and intrastromal implantation of biopolymers and an artificial cornea |

LASIK=Laser *in situ*-keratomileusis, RCLE=Refractive corneal lenticule extraction, ICRS=Intracorneal ring segments, CAIRS=Corneal allogenic intrastromal ring segments, INTRACOR=Intrastromal correction of presbyopia, AK=Astigmatic Keratotomy, PKP=Penetrating keratoplasty, ALK=Anterior lamellar keratoplasty, DALK=Deep ALK, SALK=Superficial ALK, EK=Endothelial keratoplasty, DSAEK=Descemet stripping automated EK, PLK=Posterior lamellar keratoplasty, BLT=Bowman layer transplantation, DMEK=Descemet's membrane EK

thinnest at the center and gradually thicker toward the periphery, resulting in a meniscus shape.[8] The peripheral edge of the flap differs between MK and FSL. A study reported that the MK-LASIK flap edge had an oblique configuration, while the FS-LASIK flap edge was perpendicular to the corneal surface.[9] The FSL flap size, shape, depth, and side cut orientation can be adjusted by the surgeon by controlling its parameters. The flap is typically 8–10 mm in diameter and 90–120 μm thick [Figure 1a].[10]

Compared to MK-LASIK, the FS-LASIK has similar visual, refractive, and safety outcomes, such as mean refractive spherical equivalent (MRSE) and uncorrected visual acuity (UCVA).[11] According to a metanalysis in 2020, FS-LASIK is similar to MK-LASIK in the early and midterm follow-up and does not have a clear advantage in efficacy, accuracy, and safety profile.[12] A recent systematic review found no clear superiority of one technique regarding complications and safety between FS-LASIK and MK-LASIK.[7] However, FS-LASIK has greater flap customization (thickness, diameter, and side-cut angle) and increased predictability, accuracy, and precision of flap creation.[7,13]

A retrospective study found that the flap complication rate was similar in MK-LASIK and FS-LASIK (14.2% vs. 15.2%).[14] Two of the most reported unique intraoperative complications associated with FSL flap creation are forming an opaque bubble layer (OBL) and vertical gas breakthrough (VGB). OBL is the accumulation of gas bubbles temporarily detained in the intrastromal interface, creating transient corneal opacity. Excessive OBL may interfere with eye tracker pupil recognition and generate difficulties in flap lifting.[15] No severe complications have been reported after OBL.[15] VGB can occur when cavitation bubbles dissect superiorly toward Bowman's layer and through the epithelium. Risk factors include a thin flap, corneal scar, previous radial keratotomy, and microscopic breaks in the Bowman layer (BL).[16] Intraoperative complications were more frequent with earlier FSL generations. Two unique postoperative complications of FS-LASIK are transient light sensitivity syndrome (TLSS) and rainbow glare. TLSS occurs 2–6 weeks after uneventful LASIK. It is characterized by sudden and severe episodes of light sensitivity and eye discomfort that occur spontaneously or in response to bright lights despite having good UCVA and minimal slit lamp findings. TLSS improves with topical steroids, which is believed to be related to the changes in the corneal nerves following surgery.[16] Rainbow glare is characterized by the appearance of colored rings or halos around point light sources (headlights or streetlamps), particularly in low-light conditions. It is a self-limiting condition, lasting up to several months after surgery. Even with the latest advances in FSL technology, rainbow glare remains a mild optical side effect, although it does not appear to interfere with visual acuity.[7]

**Table 2: Current commercially available femtosecond lasers for cornea surgery***

| Model and (Brand) | Laser specifications | | | | | | | | Corneal procedures | | | | | | | | | Cataract |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Wave length (nm) | Pulse repetition rate (kHz) | Pulse duration (fs) | Pulse energy (μJ) | Interface surface | Centration | Visuali-zation | Mobile | LASIK | RCLE | AK | ICRS | ISP | PKP | ALK | PLK | Other | |
| Femto LDV Z8 and NEO (Ziemer, CH) | 1045 | 100–10,000 | 250 | 0.050–2.5 | Flat and curved applanation, and liquid | Semi automatic | OCT and virtual | Yes | • | CLEAR | • | • | • | • | • | • | FLAP, BLT, SKP | • |
| Femto LDV Z6 (Ziemer, CH) | 1045 | 100–10,000 | 250 | <1 | Flat applanation | Manual | Virtual | Yes | • | | • | • | • | • | • | • | BLT, SKP | |
| Femto LDV Z4 (Ziemer, CH) | 1045 | 100–10,000 | 250 | <1 | Flat applanation | Manual | Virtual | Yes | • | | | • | • | | | | | |
| Visumax 800 (Carl Zeiss, DE) | 1043 | 2000 | 220–580 | 0.110–0.150 | Curved applanation | Semi automatic | Virtual and visual | No | • | SMILE | | • | | • | • | • | BLT, SKP | |
| Visumax 500 (Carl Zeiss, DE) | 1043 | 500 | 220–580 | <1 | Curved applanation | Manual | Virtual and visual | No | • | SMILE | | • | | • | • | • | BLT, SKP | |
| Wavelight FS200 (Alcon, USA) | 1030 | 200 | 350 | <2.4 | Flat applanation | Computer | Virtual and visual | No | • | | | • | • | • | • | | | |
| LenSx (Alcon, USA) | 1030 | 60 | 600–800 | >15 | Curved soft fit | Computer | OCT | No | • | | • | • | • | | | | | • |
| ELITA (J&J, USA) | 1053 | - | 150 | 0.06 | - | Computer | Virtual | No | • | SILK | • | | | | | | | |
| iFS Intralase 150 (J&J, USA) | 1053 | 150 | 600–800 | 0.3–2.5 | Flat applanation | Computer | Virtual | No | • | | • | • | • | • | | | | • |
| Catalys (J&J, USA) | 1030 | 120 | <600 | 3–10 | Liquid | Computer | OCT and virtual | No | | | • | | | | | | | • |
| ATOS (Schwind, DE) | 1030 | Up to 4000 | <295 | 0.075–0.135 | Curved applanation | Semi automatic | Virtual | No | • | Smart-sight | | | | | | | | |
| Victus (B&L, DE) | 1040 | 80–160 | 290–550 | 6–10 | Curved applanation | Computer | OCT and virtual | No | • | | • | • | • | • | • | • | | • |
| LensAR (LENSAR, USA) | 1030 | 80 | 500 | 7–15 | Fluid filled | Computer | OCT and virtual | No | • | | • | • | • | | | | | • |
| 520F (Technolas Perfect Vision, DE) | 1053 | - | - | - | Curved applanation | Manual | Visual | No | • | | • | | | | | | INTRACOR | |

*Public information, according to the specifications and description by the manufacturer. CH: Switzerland, DE: Germany, LASIK: Flap creation, RCLE: SMILE, CLEAR, SILK and smart-sight, ICRS: Tunnel creation, ISP: Multiple uses such as presbyopia corneal inlay implantation, stromal keratophakia, bowman transplantation and drug delivery, PKP: Trephination using multiple shapes for donor and recipient, mushroom, zig-zag, Christmas tree, top hat, ALK: SALK and DALK. Donor and recipient trephination and stromal bed incisions; and big-bubble air needle tunnel creation, EK: DSAEK and PLK, AK: Partial thickness or intrastromal arcuate incisions, FLAPS: FLAPS; conjunctival autograft preparation, BLT: BLT; donor preparation and recipient pocket creation, SKP: SKP, donor lenticule and recipient stromal pocket creation. LASIK=Laser *in situ*-keratomileusis, RCLE=Refractive corneal lenticule extraction, SMILE=Small incision lenticule extraction, CLEAR=Cornea lenticule extraction for advanced refractive correction, SILK=Sutureless intrastromal lamellar keratoplasty, ICRS=Intracorneal ring segment, ISP=Intrastromal pocket, PKP=Penetrating keratoplasty, ALK=Anterior lamellar keratoplasty, SALK=Superficial ALK, DALK=Deep ALK, EK=Endothelial keratoplasty, DSAEK=Descemet stripping automated EK, PLK=Posterior lamellar keratoplasty, AK=Astigmatic keratotomy, FLAPS=Femtosecond laser-assisted pterygium surgery, BLT=Bowman layer transplantation, SKP=Stromal keratophakia, INTRACOR=Intrastromal correction of presbyopia, OCT=Optic coherence tomography, •=Corneal procedures that can be performed with this FSL model

## Refractive Corneal Lenticule Extraction

RCLE is a minimally invasive new technique to correct refractive errors that require only the FSL. It creates a small incision in the cornea and a refractive lens-shaped lenticule of stromal tissue removed through the incision, eliminating the need for a corneal flap [Figures 1b and 3].[5] Small incision lenticule extraction (SMILE) was the first technique and has gained popularity among ophthalmologists worldwide. RCLE with FSL and flap (ReLEx FLEx) was the precursor to SMILE, which involves creating a flap in the cornea using an FSL to access and remove a lenticule. While ReLEx FLEx is still used in some centers, SMILE has become the preferred technique due to its advantages in visual recovery, patient comfort, and the potential for fewer complications.[5,17] One of the main advantages of SMILE is that it preserves more of the anterior corneal tissue and does not require a flap, preventing flap-related complications and quicker recovery of dry eye.[5,18] It is theoretically speculated that SMILE retains more corneal biomechanical strength; however, conflicting results are favoring either SMILE[19] and FS-LASIK.[20]

SMILE treats myopia with and without astigmatism[21,22] and hyperopia with and without astigmatism.[23,24] Most of the SMILE publications have been on myopia. The excellent results of current corneal laser refractive surgery make it difficult to find clear superiority between LASIK, PRK, or SMILE, and the results are generally comparable. Myopic SMILE has achieved similar outcomes to FS-LASIK concerning visual acuity, refractive error, and proportion of cases with loss of lines of best-corrected visual acuity in many studies.[5,21,22,25] SMILE could induce less dry eye and less damage to the corneal nerves in myopia and high myopia.[22]

In a systematic review and meta-analysis of 18 studies that included 3,466 eyes, the postoperative MRSE was -0.02 D, and the postoperative UDVA was 20/20 or better in 94.5% of eyes.[22] A 2016 systematic review and meta-analysis found similar outcomes in safety and efficacy.[22] Another more recent systematic review and meta-analysis of 11 randomized clinical trials published in 2023 also found that SMILE and FS-LASIK were comparable concerning the safety and efficacy as shown as follows: residual MRSE (mean difference (MD)-0.04, $P = 0.22$), the proportion of eyes losing one or more lines of corrected distance visual acuity (CDVA) (risk ratio [RR]: 1.14; $P = 0.70$), the proportion of eyes with UCVA of 20/20 or better (RR: 0.99; 95% confidence interval [CI], 0.94–1.05; $P = 0.71$), postoperative UCVA (MD: 0.01; $P = 0.13$), residual refraction within ± 1.0 D (RR: 1.00; $P = 0.60$), postoperative astigmatism within ± 0.25, 0.5 and 1.0 D (RR: 0.80, 0.99, 1.00; $P = 0.60, 0.86, 0.87$), and postoperative higher order aberrations (RR: 0.00; $P = 0.99$). However, FS-LASIK might be superior in predictability with a higher proportion of eyes within 0.5D, and SMILE might have fewer spherical aberrations.[21] Studies have confirmed the safety of SMILE as similar or better than FS-LASIK,[21,22] including a lower risk of dry eye disease,[22] and less corneal nerve damage.[26] Potential complications include suction loss, cap rupture, epithelial ingrowth, lenticule remnants, interface inflammation, epithelial defects, and delayed epithelialization.[27]

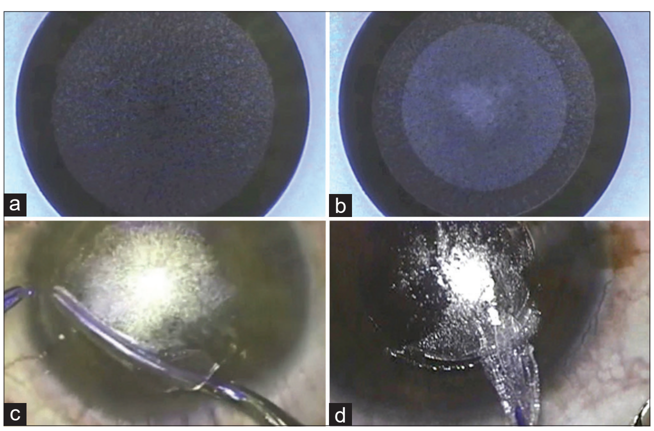

**Figure 3:** Small Incision Lenticule Extraction Procedure. (a) Posterior surface of lenticule cut, (b) Anterior surface of lenticule cut, (c) Lenticule dissection, (d) Lenticule extraction

In addition to SMILE, other new RCLE techniques use the same basic principles of SMILE to correct refractive errors. Cornea lenticule extraction for advanced refractive-correction (CLEAR) and SmartSight minimally invasive lenticule extraction. CLEAR uses a smaller incision (1.5 mm) than SMILE (2.5 mm) and can correct higher levels of myopia. SmartSight is a modified version of SMILE that leaves a portion of the lenticule in the cornea to improve corneal biomechanical stability.[5,28,29] Overall, RCLE is a promising advancement in refractive surgery.

## Astigmatic Keratotomy

A variety of corneal incisions can be performed. AK or arcuate incision to reduce corneal astigmatism has been used for many years. Peripheral corneal or limbal relaxing incisions are like AK but placed more peripherally. Cutting the cornea with a paired or single AK into a specific depth reduces astigmatism by flattening the corneal curvature in one axis.[30] Manual AK (MAK) is performed with a fixed or adjustable depth diamond blade. A limitation is that the depth, arc length, and regularity of corneal incisions during surgery may be unpredictable, leading to a higher risk of complications such as inadvertent perforation, wound dehiscence, epithelial downgrowth, infection, irregular astigmatism, or astigmatism under-correction.

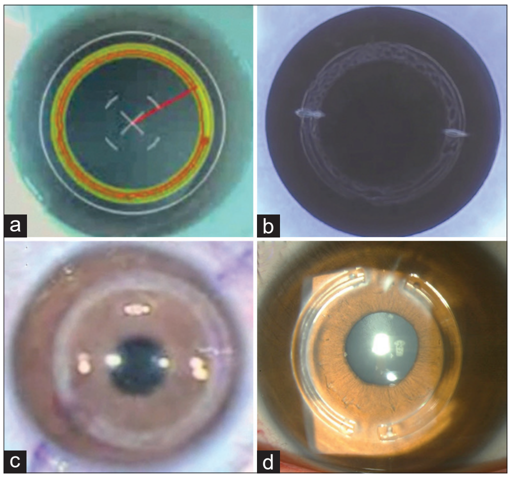


**Figure 4:** Intracorneal Ring Segments. (a) Femtosecond laser screen showing laser treatment plan, (b) Femtosecond laser pattern and incisions, (c) Femtosecond laser intrastromal tunnels, (d) Clinical picture after intrastromal ring segments implantation

FSL-assisted AK (FSAK) can create more controlled and symmetric arcuate incisions of precise depth, length arc, shape, and location [Figure 1e].[30-33] Thus, making FSAK safer, more effective, more predictable, and more reliable than MAK and with fewer complications.[30,31,34] FSAK can customize the incision characteristics, usually 75%–90% in-depth, but can also be intrastromal (IAK), avoiding the risk of infection. FSAK can correct naturally occurring or induced astigmatism after various types of surgeries, such as penetrating keratoplasty,[32,33,35] deep anterior lamellar keratoplasty (DALK),[35] cataract surgery,[36] and glaucoma surgery.[30,31] In addition, FSL-assisted wedge resection has been reported as an effective way to correct high astigmatism after PKP.[37] The amount of astigmatism that can be reduced with FSAK is significantly higher, up to 2.5–4.5D, compared to MAK, which typically reduces up to 1.5 D. FSAK can achieve more significant improvements than MAK in CDVA, UCVA, corneal and manifest astigmatism, success index, and correction index.[32,33,35,38]

## Intracorneal Ring Segments

A valuable application of FSL is the creation of intrastromal tunnels to insert ICRS in managing ectatic corneal disorders such as keratoconus.[1,39] Corneal ectatic diseases are characterized by progressive thinning and bulging of the cornea, resulting in irregular astigmatism, visual distortion, and reduced visual acuity.[39] The insertion of ICRS has been in use since the year 2000; it is a well-established treatment for these disorders, as it can help to reshape the cornea and improve visual function.[39-41] The ICRS are medical devices made of polymethyl methacrylate with variable thickness, geometries, and diameters. ICRS induces flattening of the cornea depending on the ICRS thickness and distance from the center of the cornea.[41]

Traditional ICRS insertion methods involve manual cornea dissection to create an intrastromal tunnel. Then the ICRS is inserted into the pocket or tunnel, where it exerts pressure on the cornea to reshape it and improve visual function. Associated complications include corneal perforation, infection, and implant displacement. In FSL-assisted ICRS implantation, the laser creates an intrastromal corneal pocket or tunnel of a desired depth, diameter, angle, and shape.[Figures 1c and 4].[41] The advantages of FSL are the precision, consistency, and reliability in creating the intrastromal corneal pocket or tunnel. FSL reduces the risk of complications and improves the accuracy of ICRS placement.[41] FSL can create a customized pocket or tunnel that fits the size and shape of the ICRS. This could help optimize visual outcomes and reduce the risk of infection and implant displacement, as the pocket or tunnel is created without direct contact with the cornea.[42]

Several studies have shown that FSL-assisted ICRS insertion is a safe and effective treatment for corneal ectatic disorders. There is a clear advantage of fewer intraoperative complications with FSL than traditional manual tunnel creation.[43,44] Complications include corneal perforation, infection, and implant displacement, although rare and significantly less frequent than mechanical techniques.[43,44] Regarding visual, refractive, and aberrometric outcomes, FSL and mechanical techniques offer similar outcomes.[40,41,43,44] A recent similar technique of FSL tunnel creation has been used in conjunction with corneal allogenic intrastromal ring segments as a potential treatment option for corneal ectasias.[45]

## Presbyopia Management with Femtosecond Laser

There are two FSL corneal applications for presbyopia, the intrastromal correction of presbyopia (INTRACOR) and an intrastromal pocket for corneal inlay implantation. The INTRACOR creates five intrastromal circular incisions 2–4 mm in diameter placed around the pupil of the nondominant eye. This induces topographic and aberrometric changes that make a multifocal cornea with a central steepening of 1–2 D.[46] It can be performed with the Technolas® FSL (Technolas Perfect Vision®, Germany). Patients showed improvement in binocular uncorrected near vision, with moderate patient satisfaction.[46-48] However, concerns about the loss of UCVA and CDVA and the irreversibility of the procedure limited its use. Further evaluation is needed.[47,48]

Several models of intrastromal corneal inlays for the management of presbyopia have been developed. Currently, only two are commercially available, Kamra and Flexivue. Kamra increases the depth of focus with a pinhole effect; it is a small aperture inlay of 3.8 mm made of polyvinylidene difluoride and pigmented with carbon nanoparticles. Flexivue is a bifocal transparent refractive inlay of 3.2 mm made of a biocompatible hydrophilic acrylic material, with a central plano refraction and a peripheral plus correction from +1.5 to +3.5 D.[49] The manufacturers recommend the use of FSL to create the intrastromal pocket and to implant the corneal inlay in the nondominant eye.[49] The FSL can create intrastromal pockets of a reliable and precise depth (200–300 µm), diameter (9.2–9.5 mm), and centration [Figure 1d].[49] The inlay must be centered in the pupillary center and the first Purkinje image.[49] In principle, it is a reversible procedure. A systematic review showed that all improved near UCVA, and patients were moderately satisfied.[49,50] There are concerns about long-term complications since many will lose one or more lines of CDVA.[49,50] Other complications are refractive instability, decentration of the inlay, corneal haze with a potential loss of CDVA, infectious keratitis, and epithelial ingrowth.[49] Recently, allograft corneal implants made of SMILE lenticules have been used to correct presbyopia and hyperopia with promising outcomes.[51]

## Penetrating Keratoplasty

Since the beginning of corneal transplantation in the year 1905, improvements have been made to achieve better outcomes. Lamellar keratoplasty is the preferred option for corneal transplantation. Full-thickness keratoplasty should be reserved for advanced-stage diseases that compromise all the layers of the cornea.[52] Conventional PKP with manual trephination achieves good results and vision improvement; however, induced astigmatism affects visual outcomes.[53,54] Induced astigmatism can be secondary to the sutures, scarring, and irregular corneal borders.

Manual trephination can cause irregular borders that affect the graft-host junction. An eccentric trephination is generated when the trephine is placed decentered, and the graft and host curvatures will not match. When the trephine is tilted, an oval opening can happen. Manual trephination is performed in the host cornea from the epithelial and donor cornea from the endothelial sides. Due to this, the posterior cornea of the recipient tends to have a larger diameter than the anterior cornea, while the donor cornea experiences the opposite effect; this is known as vertical tilt. A horizontal torsion occurs when the two first cardinal sutures are not placed symmetrically.[55] For these reasons, new technologies and instrumentation have been developed to make more precise cuts with better geometry.[56]

FSL-assisted PKP (femto-PKP) was first used in the year 2005 to trephine the host and donor corneas accurately.[57] FSL allows trephination to the donor and host corneas, improving incision geometry with more accurate angles and avoiding vertical tilt.[56] Different trephination shapes and patterns have been explored to enhance donor-host union adherence, such as straight cut, zig-zag, mushroom, top hat, and Christmas tree [Figure 1f].[58] These configurations increase the contact area between the graft and host, improving wound scarring and enhancing the strength of the donor-host union.[59] It is hypothesized that this reduces the risk of traumatic wound dehiscence, but no evidence supports it. This allows for earlier removal of stitches,[60] reducing the risks of suture-related infections and speeding up visual rehabilitation. An artificial anterior chamber is needed to perform FSL donor PKP trephination. It is performed from the epithelial side and prevents vertical tilt. In addition, FSL can create orientation marks in the donor and recipient cornea to enhance the placement of the cardinal sutures and reduce the risk of horizontal torsion.[61]

Femto-PKP achieves good visual outcomes with low degrees of postoperative astigmatism. However, two meta-analyses failed to show significant differences in induced astigmatism between femto-PKP and manual PKP.[62,63] This might be because postoperative astigmatism is multifactorial, depending on suturing and scarring process after PKP. An advantage of femto-PKP was founded in a meta-analysis that showed significantly lower endothelial cell loss.[62] Different platforms are used to perform femto-PKP, and there are variations in their interface with the cornea, which can be flat, curved, or noncontact liquid. The noncontact could help to improve cut geometry by avoiding the deformation of the cornea.[56] FSL with real-time ASOCT can have more customizable incisions.

## Deep anterior Lamellar Keratoplasty

It is indicated in corneal diseases affecting the anterior stroma with a healthy endothelium, such as keratoconus, stromal dystrophies, and scars.[52] DALK has some advantages compared to PKP, for example, less risk of rejection, less risk of glaucoma, and avoiding the risk of open sky surgery.[64] DALK is performed using techniques such as the manual, big bubble,[65] and viscoelastic dissection.[66] All are complex techniques, time-consuming, with a steep learning curve, and sometimes with unexpected outcomes.[67] FSL technology has allowed for more precise and predictable dissection during DALK.[68-70]

A primary advantage of FSL-assisted DALK (FSL DALK) is its ability to remove damaged stroma by creating a precise and reproducible predescemetic dissection at the recipient cornea. This allows for a better interface junction with the stromal donor cornea.[68,69,71] In addition, like PKP, the laser can be used to customize the shape and size of the corneal graft, resulting in a more accurate tight fit.[69] It can create different cutting patterns, including zig-zag, mushroom, and inverted mushroom. These interfaces reduce the risk of irregular astigmatism and allow early sutural removal.[58] Another advantage of FSL DALK is the reduced risk of intraoperative complications such as perforation.[71] The laser allows for a more controlled and less traumatic dissection of the corneal tissue. This reduces the risk of damage to the surrounding structures and creates a smooth stromal bed in the recipient cornea. Evidence has demonstrated that FSL DALK exhibits a lower incidence of corneal perforation and a reduced need for conversion to PKP compared to manual DALK.[71]

The FSL can be used to create an intrastromal guiding tunnel for the big bubble technique. Studies have described tunnel placement at a distance ranging from 50 to 130 μ away from Descemet's membrane (DM).[68,72,73] FSL improves the precision and predictability of the tunnel, reducing the risk of perforation or incomplete big-bubble formation [Figure 1g].[73] FSL DALK has shown promise in improving the success of big-bubble formation.

Multiple studies comparing the visual outcomes of FSL and manual DALK have demonstrated similar results.[69,70,74-76] Except for one study that found better visual outcomes at 1 year with FSL DALK using FSL only to trephine the cornea, the lamellar dissection was manually performed with a diamond knife.[77] One[77] study reported better CDVA 3 months after FSL DALK compared to manual DALK but similar outcomes after 1 year.[75] FSL DALK may contribute to faster visual recovery, leading to better CDVA in the early postoperative period. There[74] are no significant differences in the refractive outcomes between manual and FSL DALK.[69,75,76] The safety of FSL DALK has been supported by studies showing that the endothelial cell density remains stable from 1 month to 2 years after surgery.[76,77] Further research is needed to enhance the technique, maximize its benefits and ensure consistent outcomes.

## Posterior Lamellar Keratoplasty

Posterior lamellar keratoplasty (PLK) is an advanced surgical technique used to treat endothelial dysfunction of the cornea.[52] This procedure has gained popularity due to its numerous advantages over traditional PKP.[78] PLK offers improved visual and refractive outcomes, reduces the risk of rejection, and has become the preferred choice when the corneal stroma remains healthy.[78] The two main variants of PLK, Descemet's stripping automated endothelial keratoplasty (DSAEK), and DM endothelial keratoplasty (DMEK), have revolutionized the treatment of endothelial dysfunction, ensuring better patient outcomes and faster visual recovery.[79] FSL facilitates the precise formation of the descemetorhexis on the receptor cornea during DSAEK and DMEK procedures.[80,81] In addition, it is utilized to prepare the donor graft for DSAEK surgery, ensuring optimal fit and enhancing surgical outcomes.[82]

Traditional methods of preparing donor grafts for DSAEK involve using an MK, which carries a high risk of perforation and lacks predictability in graft thickness.[83] To address these limitations, FSL technology has been studied as an alternative approach. FSL allows for donor graft preparation using an artificial anterior chamber, starting the procedure from the epithelial side [Figure 1h].[84] After the creation of the lenticule with FSL, it is dissected, trephined, and prepared to be used with the conventional DSAEK technique. Conventional FSL preparation can result in a rough graft surface due to scattered laser energy in the posterior stroma or because of the posterior stromal collagen arrangement.[85,86] Studies have explored the feasibility of endothelial-side preparation using a viscoelastic coating for protection.[87] These studies have shown promising outcomes, including smoother graft surfaces and minimal loss of endothelial cells. One study has documented the utilization of FSL for DMEK graft preparation. In this study, FSL-assisted trephination was conducted before the peeling of the DM to mitigate the potential occurrence of peripheral tears caused by the manual trephination process and subsequent embedding of the DM into the stromal tissue.[88]

Recipient preparation during PLK consists of a circular peeling of DM, usually called descemetorhexis, commonly performed using inverse hooks. However, the diameter of the descemetorhexis tends to be unpredictable, and small fragments of DM remain attached to the stromal tissue. Such residual fragments can compromise the adherence of the PLK graft, increase the rates of rebubbling, and compromise the overall success of the graft.[89] FSL technology has been utilized in recipient preparation for descemetorhexis, enabling the creation of a posterior lenticule with a thickness ranging from 100 to 150 microns. The lenticule has the same in which endothelium, DM, and a thin layer of the posterior stroma are removed. The lenticule has a diameter like the graft.[80] This lenticule is removed to expose the stroma that will receive the graft [Figure 1i]. Comparative studies demonstrated that manual descemetorhexis had a higher incidence of graft detachment on the first postoperative day than FSL-assisted descemetorhexis. However, it is important to note that these studies reported similar visual outcomes and similar rates of endothelial cell loss across both groups.[80,90] In addition, the utilization of FSL for descemetorhexis enables the removal of the DM and endothelium and aids in removing posterior stromal scarring. Removing scar tissue is crucial as it can impact the visual outcomes of PLK procedures. The integration of FSL technology in PLK procedures has facilitated the precise formation of the descemetorhexis during DSAEK and DMEK, ensuring optimal graft fit and enhancing surgical outcomes. FSL-assisted graft preparation for DSAEK has shown reproducible lenticule creation avoiding de MK complications. Future research should focus on refining FSL-assisted techniques and exploring additional benefits in PLK procedures.

## Stromal Keratophakia

Stromal keratophakia is an additive refractive surgery; no tissue is removed from the cornea. Manual stromal keratophakia was almost abandoned because of the difficulties and limitations of shaping a donor stromal lenticule and creating a smooth and regular host stromal pocket to implant the donor lenticule.[91] FSL-assisted stromal keratophakia revolutionized the procedure by creating reliable lenticules and pockets. It can create intrastromal pockets with smooth and uniform surfaces, reliable depth, and diameter. It can shape donor stromal lenticules of specific thickness, diameter, and curvature to be further implanted into the host stromal pocket [Figure 1j].[91]

The donor lenticule can be obtained either from SMILE lenticules or donor corneas.[91] SMILE lenticules (~6–7 mm in diameter) can be frozen, stored, and decellularized. They can be reshaped to a precise thickness, diameter, and radius of curvature. These lenticules can be either convex or concave, plus, or minus lens-shaped. The intrastromal pocket is usually at 100–250 μm depth.[4,91,92] This procedure is particularly promising as an alternative treatment to avoid keratoplasty in keratoconus and can be combined with cross-linking. A recent meta-analysis found it safe, with no reported adverse events of persistent haze, perforation, or rejection. Meanwhile, significantly improving UCVA (2 lines) and CDVA (1.7 lines), reducing MRSE (-2.3D), flattening the cornea (-3D of Kmax), increasing corneal thickness, and improving corneal sphericity or Q-value.[92] Three options of SMILE lenticule have been studied in keratoconus treatment, doughnut-shaped (a lenticule with a central trephination), hyperopic, and myopic SMILE lenticules.[92] Stromal keratophakia has also been reported as a feasible option to treat high hyperopia,[93] aphakia, and presbyopia.[91] A variant of stromal keratophakia is lenticule addition keratoplasty,[91] where stored SMILE lenticules could be used in various procedures such as tectonic keratoplasty,[94-96] corneal or scleral thinning after pterygium,[97] or limbal dermoid excision.[49,98]

## Bowman's Layer Transplantation

Bowman's layer transplantation (BLT) is a new keratoconus treatment aimed to delay or avoid keratoplasty in corneas too thin or too advanced, not candidates for corneal cross-linking or ICRS.[99] This is an additive procedure because no tissue is removed from the host. The donor BL is implanted into an intrastromal host pocket in the mid-stroma. The limitations of manually peeling BL are less predictability, graft tearing, irregular surface, and irregular borders. Manual intrastromal pocket dissection limitations include the risk of perforation on the anterior or posterior corneal surface, unpredictable depth, and uneven surface.[100] FSL-assisted BLT is a newer and more promising procedure. The advantage is that it makes BL grafts more predictable and reproducible with no tears, regular borders, and even surfaces, although slightly thicker than manual dissection.[101] FSL-assisted mid-stromal pockets have more predictable depth and no perforations [Figure 1k].[101-103] A recent paper reported 97 and 100% successful BL grafting and pocket creation, respectively.[103] The FSL could be programmed using the anterior lamellar keratoplasty software to obtain BL graft and the intrastromal pocket standard software. The outcomes of BLT are encouraging for flattening the cornea, stabilizing the keratoconus, and stabilising the keratoconus while maintaining CDVA.[99,100,103]

## Pterygium Surgery

FSL-assisted pterygium surgery has been recently proposed as an alternative to achieve ultrathin conjunctival autograft (CAG) of more predictable size and thickness than the gold standard manual preparation [Figure 1l].[104,105] The CAG was prepared using the lamellar keratoplasty module to achieve a 7 mm × 10 mm diameter ellipsoidal shape and 60 μm depth.[105] One comparative study found that FSL-assisted CAG achieved thinner grafts and less thickness variability. No significant differences in CDVA, recurrence rate, astigmatism, or discomfort were noted.[105] Cosmetic outcomes were graded good-to-excellent in 93% of cases.[106]

## Other Procedures

Some studies have reported the feasibility of using the existing software to expand the FSL applications in corneal surgery. A case series on FSL-assisted keratopigmentation (corneal tattooing) uses the ICRS software to create intrastromal channels and corneal incisions of precise depth to safely place the pigments into the corneal stroma.[107] A long-term study reported keratopigmentation safety and efficacy, with all patients improving symptoms and cosmetics and 95% improving

CDVA.[108] A case report shows how to make a corneal biopsy using the anterior lamellar keratoplasty or the flap software.[109] A case report on Boston type 1 keratoprosthesis donor cornea preparation uses FSL to have precise centration of the peripheral and the inner 3-mm central trephination.[110] A case report used partial thickness corneal incisions with ICRS software as an alternative method for drug delivery in nonresponding intrastromal infectious keratitis.[111] Other case reports use FSL-assisted intrastromal pockets to implant intrastromal KeraKlear artificial cornea in congenital aniridia[112] or insert silicon oil as palliative management of bullous keratopathy in blind eyes.[113]

## The Future

Two nonablative laser procedures under development are worth mentioning,[4,29] the laser-induced refractive index change (LIRIC) and the nonlinear optical corneal cross-linking (NLO CXL). The LIRIC is a tissue-sparing procedure that uses low-pulse energy, below the damage threshold, to induce intrastromal changes, increase the refractive index and modify the aberrations of the cornea. LIRIC may be a promising alternative for those not candidates for LASIK or RCLE.[93,114] The NLO CXL is a promising alternative to cross-linking to halt keratoconus progression by creating intrastromal stiffening and flattening through low-energy intrastromal laser pulses and epithelial channels creation that improve riboflavin penetration into the stroma.[115,116] Finally, SMILE-derived stromal lenticules can be used as a scaffold for regenerative therapy.[117]

## Conclusions

The FSL has earned its place in contemporary corneal surgery as a versatile and valuable tool that enables the creation of three-dimensional corneal incisions of great precision, reproducibility, and safety. Its utility and advantages have been proven in corneal refractive surgery, keratoplasty, and other corneal and ocular surface diseases.

### Ethical approval and Declaration of patient consent

The institutional review board of hospital approved this study (Number: CE-2018-0032). Informed consent was waived by the IRB.

### Data availability statements

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.


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### Conflicts of interest

The authors declare that there are no conflicts of interests of this page.


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