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# Femtosecond laser in refractive corneal surgery

Sarah Moussa, * Marie Dietrich, Markus Lenzhofer, Josef Ruckhofer and Herbert A. Reitsamer

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The introduction of the femtosecond (fs) laser has revolutionized ophthalmic surgery. With the worldwide application of fs-lasers, clinical outcomes and safety in corneal procedures have improved significantly and they have become an ideal tool for ultra-precise corneal refractive surgery. Flap creation in laser *in situ* keratomileusis (LASIK) is the most common use of this laser. It can also be used for other corneal refractive procedures including channel creation for the insertion of intrastromal corneal ring segments (ICRS), performing astigmatic keratotomies (AK), femtosecond lenticule extraction including small incision lenticule extraction (SMILE), and the insertion of corneal inlays. This article summarizes recent advanced applications of fs laser technology in corneal refractive surgery.

## Introduction

The fs laser has become a rapidly and widely adopted technology for surgeons performing refractive surgery. With the worldwide application of fs lasers, clinical outcomes and safety in corneal procedures have improved significantly. The history of laser surgery in ophthalmology began about 50 years ago. It was T. H. Maiman who developed the ruby laser and this opened a range of new therapeutic possibilities in ophthalmology. This resulted in a flood of practical clinical applications of lasers in eye surgery.[1] The development of clinical argon, krypton, carbon dioxide, neodymium-doped yttrium aluminum garnet (Nd:YAG), and excimer laser systems in ophthalmology allowed treating multiple eye diseases and disorders.[2]

## Near infrared lasers and the development of the femtosecond laser

The optically transparent anatomical structures of the eye, like cornea or lens, do not easily absorb electromagnetic radiation in the visible or near-infrared spectrum. Using higher power densities, these structures do absorb the light energy followed by tissue disruption and plasma degeneration.[2] This concept is used in near infrared lasers *e.g.* Nd:YAG laser for opening opacified posterior lens capsules after cataract surgery, iridotomy in pupillary-block glaucoma, and the lysis of vitreous membranes or tags. The use of near infrared lasers is highly prevalent nowadays. The Nd:YAG laser has a pulse duration in the nanosecond ($10^{-9}$ seconds) range. It produces photodisruption at a focal point in tissues. This results in a rapidly expanding cloud of free electrons and ionized molecules ("plasma") which creates an acoustic shock wave that disrupts the treated tissue. This process is also known as photoionization or laser-induced optical breakdown. Small volumes of tissue vaporize with the formation of cavitation gas bubbles consisting of carbon dioxide and water, which eventually dissipate into the surrounding tissue.[2] This zone of collateral damage exceeds more than 100 μm, and it is therefore not so suitable for precise corneal laser surgery. To reduce the undesirable zone of collateral damage the pulse duration of the near-infrared laser was shortened from the nanosecond to the picosecond ($10^{-12}$ seconds) domain and then to the femtosecond ($10^{-15}$ seconds) domain.[3] The fs laser is similar to the Nd:YAG laser, but with an ultra-short pulse duration that is capable of producing smaller shock waves and cavitation bubbles that affect a tissue volume about $10^3$ times less than picosecond-duration pulses.[4]

The first ophthalmic surgical fs laser system was developed at the University of Michigan College of Engineering Center for Ultra-fast Optical Sciences (CUOS) in the early 1990s. Dr Juhasz developed it through a $14.3 million endowment fund from the National Science Foundation. The design, development, and analyses of the clinical laser parameters for use in corneal surgery were done in collaboration with Dr Kurtz and associates from the W. K. Kellogg Eye Center, University of Michigan Medical School.

It was Dr Gerard Mourou who introduced a new technique – the chirped pulse amplification, a technique where laser pulses are stretched in duration from 200 fs to 50 picoseconds,

*Paracelsus Medical University Salzburg, Department of Ophthalmology and Optometry, Müllner Hauptstr. 48, 5020 Salzburg, Austria. E-mail: s.moussa@salk.at; Fax: +43 (662) 4482-3703; Tel: +43 (662) 4482-58371*

amplified, and recompressed to 500 fs, whereupon they are delivered at a repetition rate of 1 to 10 kHz *via* a complex system of mirrors.[4] The high peak intensity of the fs laser translates into smaller cavitation bubble size (microcavitation) and less collateral tissue damage compared to that of nanosecond or picosecond lasers.[5] The advantage of the near-infrared fs laser is that it is able to focus in or behind the cornea even through optically hazy media in contrast to the far-ultraviolet excimer laser which is absorbed at the anterior surface of the cornea.[2] In 2000, the IntraLase Pulsion fs laser was approved by the U.S. Food and Drug Administration (FDA). The first commercial laser producing laser *in situ* keratomileusis (LASIK) flaps was introduced to the market in 2001. Due to its advantages it has been widely adopted for the creation of laser *in situ* keratomileusis (LASIK) flaps. The fs laser offers improved safety, reproducibility, planar flap thickness and versatility. An important advantage of the femtosecond laser is the greater biomechanical flap stability compared to the microkeratome flap.[6]

Further applications of the fs laser include channel creation for the insertion of intrastromal corneal ring segments (ICRS), performing astigmatic keratotomies (AK), femtosecond lenticule extraction including small incision lenticule extraction (SMILE), the insertion of corneal inlays, intrastromal presbyopia correction (Intra-COR), and Femtosecond Laser Assisted Cataract Surgery (FLACS).

## Laser *in situ* keratomileusis (LASIK)

The most crucial step in the LASIK procedure is the creation of the flap. Before 2000, refractive surgeons used a microkeratome to create the flap. Microkeratome-induced complications were not common but studies have proven that since the introduction of the fs laser, flap creation has improved in safety and precision.[6]

One of the most convincing arguments for the fs LASIK is the possibility to create a "customized" flap. Surgeons have control over the flap diameter, thickness, hinge position and width.[7]

The microkeratome creates meniscus-shaped flaps, and these flaps are thinner at the centre than at the periphery, while the fs laser creates flaps of uniform (planar) thickness. The planarity of the flap is a clear advantage in precision, as the risk of flap complications such as epithelial defects, irregular and partial flaps and buttonholes is reduced. Finally, this results in less surgically induced refractive errors.[8–12]

Moreover the fs laser created flaps have shown stronger adhesion at the flap edge and interface compared with microkeratome flaps making them more resilient to trauma.

Another advantage is that fs created flaps are thinner than microkeratome created flaps, which is beneficial for patients with thin corneas and high refractive errors as it allows greater residual stromal thickness.[11,12]

Concerning the precision of targeted and achieved flap thickness the fs laser is superior to the microkeratome. Zhou *et al.* have shown that flaps created with the fs laser are found to be uniform with a smaller standard deviation.[13]

Of course, the fs laser also shows side effects such as opaque bubble layer (OBL) formation that may cause problems with iris registration and pupil tracking during excimer laser ablation. Due to a possible inflammatory response, temporarily symptoms, such as diffuse lamellar keratitis and transient light-sensitivity syndrome, might occur.

In summary, the fs laser and microkeratome are able to create accurate LASIK flaps. Fs LASIK flaps show significant improvement in morphology and predictability with implications for safety.[13] The advantages of fs LASIK are high patient satisfaction and excellent refractive results.[14,15]

## Small incision lenticule extraction (SMILE)

As we mentioned above fs LASIK is a well-established and commonly used refractive technique although small incision lenticule extraction (SMILE) has become more popular since its introduction in 2011.

In 2011, SMILE has been introduced as a kind of refinement of the LASIK technique. In SMILE an intrastromal lenticule is created with a fs laser and removed through a minor incision.[16,17]

Studies have shown that both fs SMILE and fs LASIK are effective, predictable and safe.[18,19] It is discussed that SMILE has the advantages of better ocular surface stability and biomechanical strength compared to fs LASIK.[20] Despite the promising long-term results, there are still questions about this minimally invasive technique which are not fully clarified yet. The possibility of eliminating a residual refractive error is not as easy with SMILE as with LASIK because after SMILE you might have to perform a photorefractive keratotomy to correct the residual refractive error whereas after LASIK you simply re-lift the pre-existing flap, which is far more comfortable for the patient. To our knowledge hyperopic SMILE has not yet been approved but research is ongoing.

Looking into the future, this might open fascinating possibilities of corneal refractive surgery.

## Intrastromal corneal ring segments (ICRSs)

Keratoconus is a progressive corneal ectatic disease, which leads to the impairment of the patient's visual function and optical quality.[21]

There are several therapeutic choices such as contact lens, corneal collagen crosslinking, lamellar and penetrating keratoplasty and intracorneal ring segment (ICRS) implantation.[22–26]

Since 1997, ICRSs have been used to treat keratectasia in keratoconus. The aim of this procedure is to achieve visual improvement by normalizing the corneal geometry and reduce astigmatism.

 

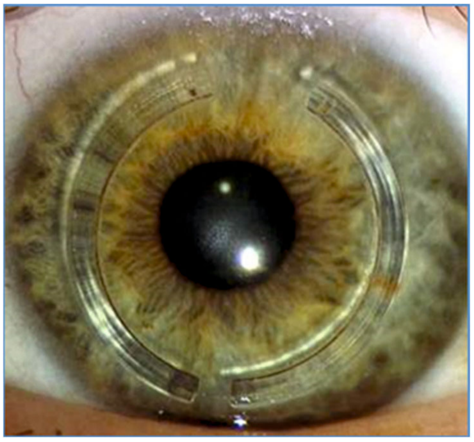

**Fig. 1** Slit lamp photograph of intracorneal ring segments in a fs laser created tunnel.

The types of ICRSs available for use include Intacs (Addition Technologies Inc., Fremont, California, USA), Keraring (Mediphacos, Belo Horizonte, Brazil) and Ferrara rings (Ferrara Ophthalmics, Belo Horizonte, Brazil). They are crescent-shaped polymethyl methacrylate implants with differences in design in terms of size (inner and outer diameters), range of available thicknesses, arc length and cross-sectional shape. They all have the following in common: they have an arc-shortening effect and change the distribution of corneal peripheral lamellae resulting in flattening of the central cornea.[27,28]

In most cases, they result in improvements in UCVA and BCVA as well as corneal topography.

The ICRS is intrastromally implanted (Fig. 1). The microkeratome or the femtosecond laser might create the tunnel for the ICRS. The fs laser makes tunnel creation faster, easier and more reproducible and allows precise tunnel dimensions (width, diameter and depth) compared with manual techniques.[29]

Complications occur more often with the mechanical technique. They include epithelial defects, anterior or posterior perforation with the mechanical spreader, shallow or uneven placement of the ICRSs, decentration, extension of the incision towards the central cornea or limbus and corneal stromal edema around the incision and channel from surgical manipulation.[30,31]

The last few decades have shown that fs ICRSs are safe and effective as well as minimally invasive and reversible.[32]

## Femtosecond laser-assisted astigmatic keratotomy

Astigmatic keratotomy (AK) or arcuate keratotomy to correct corneal astigmatism has a long history in ophthalmology. Since the introduction of the fs laser technology in 2000, AK has been performed using this method. It is simpler and has the advantage of greater precision in the arc depth, length and curvature than performing AK mechanically or manually with a free-hand diamond knife.[33]

Surgeons are able to customize incisions pre-operatively with a reduced risk of corneal perforation.[34]

fs AK has proven to be effective and safe in reducing corneal astigmatism especially in highly astigmatic eyes following penetrating keratoplasty.

The main goal of fs AK is to reduce postoperative astigmatism to a level that allows the patient to wear contact lens or spectacles.

Three variables are important:

1. the optical zone diameter,
2. the AK depth and
3. the arc length.

The optical zone is set within the graft–host junction at a fixed distance from 0.4 mm to 1 mm.[34–38]

The depth of penetrating fs AK ranges from 75% to 90% at the thinnest pachymetry at the optical zone.[39,40]

In penetrating fs AK, the cuts are performed from the anterior surface. The wounds are initially closed. If at a later follow-up the astigmatism correction is insufficient – the wound can be opened. However, differential healing can cause significant overcorrection.[41]

Studies have shown that the preoperative keratometric astigmatic levels ranged from 4.4 diopters[41] to 9.8 diopters,[42] while postoperatively they ranged from 0.67 diopters to 5.2 diopters.

Intrastromal fs AK is performed 60 to 90 μm from the epithelium and 10 to 20% from the posterior cornea. The cuts do not reach Bowman's layer, so we do not create an open wound, which might lead to infection, wound gape or epithelial ingrowth.

Studies have shown that the changes in keratometric astigmatism ranged from 6.66 diopters[43] to 9.28 diopters,[44] with the percentages of astigmatic reduction ranging from 23.53% to 89.42%.[44–46]

The arc length ranged from 50 to 120 degrees, and most of them are paired symmetrically along the steep axis.

It has been proven that arc length, depth and location precision can be better achieved in fs AK compared to manual and mechanized AK.[47,48]

fs AK is associated with reduced risk of wound dehiscence, epithelial ingrowth, infection and full-thickness corneal perforation.[48]

fs AK in native eyes is possible but the astigmatic correction is limited to 0.5 to 1.5 diopters and most of the cuts are performed at an optical zone of 7.5 mm or more to prevent dysphotopsia.

It is also possible to perform intrastromal or penetrating fs-AK in native eyes, nowadays *e.g.* for native eyes undergoing femtosecond laser-assisted cataract surgery.[49]

fs AK during cataract surgery should be intrastromal. Until better nomograms become available, intrastromal fs AK should be reserved to treat low level astigmatism (<1.5 D).

The effectiveness of intrastromal fs AK seems to be comparable to that of penetrating AK. Due to the superior safety profile of intrastromal AK, more attention should be paid to this corrective procedure (Fig. 2).[34,49]

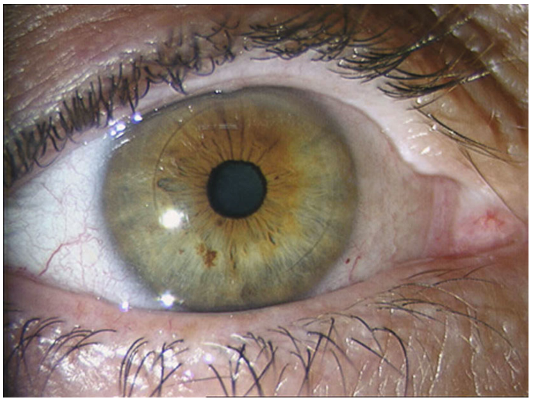

**Fig. 2** Slit lamp photograph with fs laser created intrastromal arcuate incisions.

## Corneal inlays

In 2020 we expect 2.1 billion presbyopes worldwide. Due to this demographic development and the growing expectations of prespyobic patients the interest in refractive surgeries for presbyopia compensation is steadily increasing. There are many methods available for presbyopia compensation. In addition to conservative methods such as reading glasses or multifocal contact lenses, there are a number of surgical methods. These include the well-established Lasik with monovision, multifocal laser ablation or intracorneal inlays and the refractive lens exchange with trifocal and multifocal lenses (IOL).

With the potential limitations of the above-mentioned methods, the reduction of distance vision, stereopsis, contrast vision and visual quality should be mentioned.

The Kamra Inlay (AcuFocus, Inc., Irvine, Calif., USA) is an opaque, microperforated polyvinyl fluoride inlay with carbon nanoparticles. It is based on the principle of the stenopeic pinhole to increase the depth of field. The diameter is 3.8 mm with a 1.6 mm large central opening. It is 5 µm thick, and it should be implanted either in a fs pocket or under a 200 µm thick laser flap (Fig. 3). The KAMRA inlay improves near and intermediate visual acuity without a barely noticeable change in distance vision.[49] However it has to be mentioned that the results of corneal inlay implantation are mixed, and long-term patient satisfaction will likely depend on subjective expectations about the capabilities of the inlays.[50]

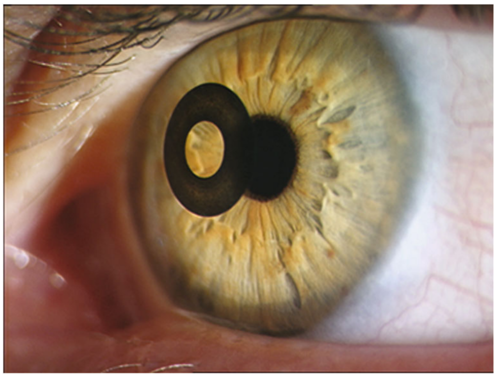

**Fig. 3** Slit lamp photograph of an implanted Kamra Inlay in a fs laser created pocket.

## Conclusion

The introduction of the fs laser has been a turning point in ophthalmology especially in corneal refractive surgery. The biggest strengths are its precision, safety and reproducibility.

Another great advantage of the fs laser is that it is applied successfully in refractive and corneal surgeries and recently in cataract surgery.

We will see further improvements and innovations in laser technology and software capabilities, which will lead to even better outcomes, safety and efficiency, and we will also see that femtosecond laser technology continues its progress in ophthalmology.

## Conflicts of interest

The authors have no proprietary or commercial interest in the medical devices that are used in this study.

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