Chapter 16

Excimer Laser and Femtosecond Laser in Ophthalmology

Liang Hu, Yiqing Huang and Meng Lin

Additional information is available at the end of the chapter

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Abstract

Laser technology is used in many basic and clinical disciplines and specialties, and it has played an important role in promoting the development of ophthalmology, especially corneal refractive surgery. We provide an overview of the evolution of laser technology for use in refractive and other ophthalmologic surgeries, mainly focusing on two types of lasers and their applications. First, we discuss the characteristics of the excimer laser and its application in corneal refractive surgery treating ametropia (e.g., photorefractive keratectomy (PRK), laser epithelial keratomileusis (LASEK), epipolis laser in situ keratomileusis (Epi-LASIK), and transepithelial photorefractive keratectomy (Trans-PRK) and presbyopia surgery). Second, we discuss the characteristics of the femtosecond laser and its application in corneal refractive surgery (e.g., femtosecond laser in situ keratomileusis (FS-LASIK), insertion of intracorneal ring segments, small-incision lenticule extraction (SMILE), and femtosecond lenticule extraction (FLEx)) and other ophthalmologic surgeries (e.g., penetrating keratoplasty (PKP), deep anterior lamellar keratoplasty, Descemet's stripping endothelial keratoplasty (DSEK), and cataract surgery). The patients studied received many benefits from the excimer laser and femtosecond laser technologies and were satisfied with their clinical outcomes.

Keywords: excimer laser, femtosecond laser, corneal refractive surgery, ophthalmology

1. Introduction

In the field of ophthalmology, laser technology is used in many basic and clinical disciplines and specialties. It has played an important role in promoting the development of ophthalmology. Advancements in technology have allowed measurable improvements in the surgical safety, efficacy, speed, and versatility of the laser, creating more operation methods to treat eye diseases, especially corneal refractive surgery. Because myopia is one of the most prevalent ocular disorders, and high myopia may result in comorbidities associated with significantly increased risks of severe and irreversible loss of vision, it is always an important topic of research worldwide. Laser technology, including the excimer laser and the femtosecond laser, has brought an era of laser corneal refractive surgery. According to the location of ablation, corneal refractive surgery can be divided into two types: laser corneal surface refractive surgery and laser corneal lamellar refractive surgery. Because of the increasing numbers of applications in ophthalmology and their successful implementations, ophthalmic use of laser technology is expected to continue flourishing.

The aim of this chapter is to review the evolution of laser technology in refractive and other ophthalmologic surgeries, mainly focusing on the characteristics of two types of lasers and their applications: the excimer laser applied in laser corneal surface refractive surgery and presbyopia surgery and the femtosecond laser applied in laser corneal lamellar refractive surgery and other ophthalmologic surgeries.

2. Excimer laser in ophthalmology

2.1. Characteristics of the excimer laser

The *excimer* (comprising the terms *excited* and *dimer*) was named by the Russian, Nikolay Basov, in 1970, based on his work with a xenon dimer gas [1]. An *excimer* is a short-lived dimeric or heterodimeric molecule formed from two species (a noble gas and a halide), at least one of which has completely filled the valence shell by electrons. Excimers are only formed when one of the dimer components is in the excited state. When the excimer returns to the ground state, its components dissociate. The wavelength of an excimer's emission depends on the noble gas, such as ArF (193 nm), KrF (248 nm), XeCl (308 nm), or XeF (351 nm). The ultraviolet laser (193 nm) is commonly used to ablate tissue through ablative photodecomposition. The process of ablative photodecomposition involves three main components: absorption, bond breaking, and ablation. A large number of experiments have shown that the ArF excimer laser (193 nm) is the most optimal for corneal absorption and ablation because of its sufficient photon energy (6.4 eV) and precision (only penetrating the superficial layer; 0.3 μm). The tissue-ablation depth is positively correlated with the logarithm of laser density; 1-J/cm^2 energy can ablate approximately 1-μm corneal tissue. In addition, as a cold laser, the excimer laser can ablate the tissue accurately without thermal damage.

2.2. Photorefractive keratectomy (PRK)

Professor Jose I. Barraquer described his coined technique of "keratomileusis" to correct myopia in 1949, and this could be the original form of photorefractive keratectomy (PRK). A few years later, many researchers designed similar surgical procedures. In 1983, Stephen Trokel first started using the ArF (193 nm) excimer laser as a precise and safe tool of corneal shaping in calf eyes. He found that the excimer laser not only accurately ablated central corneal tissues but also did not do excessive damage to the peripheral corneal tissues. After a large number of animal experiments, in 1989, Marguerite McDonald, who first applied the technology to human eyes, presented the first patency of using the excimer laser as a corneal refractive tool, and it was accepted. Since then, PRK has become the classic refractive surgery, and its safety and efficacy have been proven by abundant studies. China introduced this surgery in 1993, but the presence of postoperative complications has influenced its development [1].

Compared with the current, more popular lamellar corneal refractive surgery, PRK has shown similar postoperative visual quality but more intraoperative and postoperative complications, such as haze. Nevertheless, Wagoner et al. [2] proposed that PRK had better visual results compared with lamellar corneal refractive surgery. O'Brart [3] also thought PRK showed better cornea curvature and excellent visual quality compared with those of lamellar corneal refractive surgery.

2.3. Laser epithelial keratomileusis (LASEK)

Laser epithelial keratomileusis (LASEK), also called laser sub-epithelial keratectomy, was first proposed and named by Italian doctor Massimo Camellin in 1998. The first case of LASEK was performed by Azar at Massachusetts Eye and Ear Infirmary in 1996. It is a modified operation based on the PRK, which enabled the epithelium to be preserved as a flap (about 50–70 μm) using 20% ethanol to infiltrate and release the connection between the corneal epithelium and Bowman layer and then overturn the flap. The flap is then reset after ablating the stroma using the excimer laser.

Therefore, LASEK can be considered a kind of PRK that is "wearing flap." The key to success throughout the surgical procedure is the activity and good adhesion of the flap. Owing to the viable flap, it combines the advantages of laser in situ keratomileusis (LASIK) and PRK. Because LASEK is essentially a kind of surface ablation evolved from PRK; consequently, it reserves the features of safety, validity, simplicity, and stability in low to moderate ametropia and presbyopia correction. Moreover, its flap design, which is similar to that of LASIK, has several merits: postoperative discomfort can reduce within 2–8 h after the procedure; the epithelium of the optical region in the slit lamp after surgery is as complete and clear as it is before surgery within 12–24 h; there is no edema or postoperative haze; and early complications, such as corneal epithelium necrosis, are less common compared with PRK. These outstanding characteristics are likely to have provided the inspiration for the advent of LASIK.

Furthermore, LASEK preserves the corneal biomechanical integrity and results in good clinical outcomes. Scholars have indicated that LASEK shows better postoperative outcomes including postoperative corneal topography and contrast sensitivity, and faster postoperative recovery rate in low to moderate myopia correction compared with PRK. In addition, LASEK has a unique advantage for patients with retinal diseases, high myopia, or blepharophimosis. Lu Xiong conducted a study on the clinical outcomes in low to moderate myopia after LASEK treatment, and the results showed that LASEK has a good effect and better postoperative experience compared with PRK.

According to the principles of LASEK, it not only optimizes PRK but also avoids some disadvantages of laser lamellar corneal refractive surgery such as LASIK. First, it avoids the risk associated with the corneal flap (e.g., free flap, broken flap, and button flap) made by microkeratome in LASIK. Second, it has less effect on the corneal nerve and less serious dry eye syndrome than LASIK. Third, LASEK creates less surgically induced wavefront aberration because of its thinner flap. In addition, it saves the cost of the microkeratome or femtosecond laser used in LASIK.

Nevertheless, LASEK has some common risks of surface ablation in high myopia correction, such as postoperative haze and side effects of corticosteroid eye drops required after surgery. What is more, LASEK is a complex surgical procedure that requires high surgical skill with a long learning curve for beginners.

2.4. Epipolis laser in situ keratomileusis (Epi-LASIK)

Epipolis laser in situ keratomileusis (Epi-LASIK) was first reported by the Greek doctor Pallikaris in 2003. Different from LASEK, Epi-LASIK uses a microkeratome instead of ethyl alcohol to bluntly separate the corneal epithelial from the Bowman layer. Therefore, Epi-LASIK avoids direct stimulation of alcohol and reserves the intact epithelial basement membrane, which results in good subjective feelings in patients as well as quick recovery and haze reduction.

Epi-LASIK surgery takes the activity of the flap as the core, which is crucial to the therapy effect. Compared with PRK, Epi-LASIK has an extra flap covering the corneal stromal bed, which can effectively protect the stroma below and also promotes corneal tissue healing. Epi-LASIK has different methods of flap creation than those of LASEK. Its flap basement membrane is intact, continuous integrity segments of stratum lucidum and a longer compact layer. The postoperative healing time of Epi-LASIK is shorter without alcohol stimulation or chemical damage to the corneal epithelium. Even though the flap of Epi-LASIK is closer to corneal natural state, the postoperative biomechanical change of the corneal flap and the effect on corneal healing are yet to be determined [4].

2.5. Transepithelial photorefractive keratectomy (Trans-PRK)

Transepithelial photorefractive keratectomy (Trans-PRK), where both the epithelium and stroma are removed in a single step, is a relatively new procedure of laser refractive error correction. It has become the focus in the refractive surgery field recently and the first choice to treat ametropia with or without an irregular cornea. The excimer laser has been developed to the sixth-generation lasers, targeting the goal of minimally invasive laser refractive surgery during the past 30 years. The latest laser system delivers more laser spots per second so as to reduce the treatment time [5]. Tran-PRK has brought a new revolution to excimer laser techniques for its bladeless surgery process [6] and superiority in efficiency and safety. Hence, it has been considered as the representative operation of the laser corneal surface refractive surgery, and it is a step closer to the perfect refractive surgery. Trans-PRK has been indicated in low to moderate myopia patients and a small number of high myopia patients (−8D below), but not in patients with a very low-degree myopia. Trans-PRK is currently regarded as an optimal safety choice for patients with a thin cornea. In addition, it is also the best choice for combat athletes, high-risk workers, and patients with ocular surgical history. For the second operation and patients with irregular corneas, who need synergistic or customized surgery, Trans-PRK may be the only choice.

2.5.1. Advantages and disadvantages

Compared with other corneal refractive surgeries, Trans-PRK has the advantages of no chemical toxicity or mechanical damage, no corneal incision, no negative pressure suction, and less risk of infection, and it avoids the potential damage caused by negative pressure suction.

Trans-PRK was considered as a kind of minimally invasive surgery for its optimal safety. Without creating a corneal flap, Trans-PRK significantly reduces the postoperative corneal biomechanical change, and it has little effect on the structure of the cornea, without corneal flap mark and flap-related complications. In addition, Tran-PRK offers faster epithelial healing, lower postoperative pain, and significantly less haze formation. Kaluzny et al. [7] used optical coherence tomography to supervise the epithelial recovery time and found that Trans-PRK (3 days) has a significantly shorter recovery time than PRK does (4 days). Aslanides et al. randomly selected 60 eyes of 30 myopic patients who had undergone conventional alcohol-assisted PRK in one eye and Trans-PRK in the other eye. The postoperative follow-up showed that Trans-PRK offers faster epithelial healing and 64% lower average pain scores. The haze level was consistently lower after Trans-PRK from 1 to 6 months [8].

Trans-PRK is considered a minimal complication, maximum security single-laser surgery at present. There is no significant different between Trans-PRK and other laser surgery in final visual acuity [9, 10]. Patient satisfaction is not as high with Trans-PRK compared with the femtosecond laser-assisted laser in situ keratomileusis (FS-LASIK) and small-incision lenticule extraction (SMILE) soon after surgery because of the slightly higher incidence of haze, pain, and slower recovery of visual acuity. However, Trans-PRK has good long-term postoperative satisfaction.

2.5.2. Visual outcomes and visual quality

Many studies have shown that [8, 9, 11] Trans-PRK has high-precision visual outcomes and good stability in ametropia correction. A large retrospective comparison of transepithelial PRK with LASEK, Epi-LASIK, and LASIK detected better visual outcomes with Trans-PRK for high myopia [12]. In hyperopia correction, the effectiveness showed a substantial increase over the previous study, but there are still difficulties, such as the relatively high rate of secondary operation, residual refractive error, surgically induced negative spherical aberration, and astigmatism. In astigmatism correction, static cyclorotation component and dynamic cyclorotation component techniques greatly improve the effectiveness.

With the development of refractive surgery technology, its safety is high. Increasingly, researchers have focused on improving postoperative visual quality. The assessment of the visual quality is divided into two main aspects. The subjective part includes vision acuity (near, intermediate, and distance) and contrast sensitivity, whereas the objective part includes the objective wavefront aberration, point spread function, modulation transfer function, visual quality scale, and so on. Research shows that topography-guided Trans-PRK can effectively correct the irregular astigmatism and improve the postoperative contrast sensitivity in patients. On the contrary, Trans-PRK simplifies the process, which reduces the potential higher order wavefront aberration caused by irregular ablation and decreases postoperative glare and night vision loss. Therefore, increasingly ophthalmologists choose Trans-PRK to improve postoperative visual quality.

Trans-PRK is the easiest laser refractive surgery for refractive surgeons to learn, and it is stable in techniques and cost-effective. As a result, it is considered an ideal corneal refractive operation for patients.

2.6. Excimer laser in presbyopia correction

Presbyopia is an age-related condition in which accommodation gradually decreases and the eyes are unable to focus and obtain clear near vision. There is one approach to correct presbyopia through laser refractive surgery commonly called PresbyLASIK. Synonymous with LASIK, PresbyLASIK contains the process of making a special ablation profile to either perform a multifocal cornea procedure or increase the depth of field.

PresbyLASIK has been described in three different approaches: central PresbyLASIK, peripheral PresbyLASIK, and transitional multifocality. In central PresbyLASIK, the central area is shaped for near vision and the mid-peripheral cornea is shaped for distant vision. On the contrary, in peripheral PresbyLASIK, the central area is shaped for distant vision and the mid-peripheral corneal area for near vision. Both central and peripheral techniques reportedly obtained adequate spectacle independence in both myopia and hyperopia. In addition, a neuroadaptation process is needed in peripheral techniques. The third approach combines depth of field increase and micro-monovision, which induces a certain degree of spherical aberration to each eye to increase the depth of field while making the nondominant eye slightly myopic [13].

Presbyopia remains the biggest challenge to be corrected: the mechanism of accommodation and the cause of presbyopia are complex to understand fully. Therefore, the efficacy of presbyopia correction even with the latest platform is still in dispute. However, there is enough scientific evidence to consider PresbyLASIK as a useful tool in presbyopia correction [14]. Epstein and Gurgos [15] reported that 89% hyperopia (25/28) patients and 91.3% myopia (94/103) patients who underwent peripheral PresbyLASIK were completely spectacle independent and with distance unaided visual acuity of 20/20 in 67.9% (19/28) in hyperopia patients and 70.7% (53/75) in myopia patients.

3. Femtosecond laser in ophthalmology

3.1. Characteristic of femtosecond laser

Femtosecond laser technology was first introduced by Dr. Kurtz in the early 1990s, and it has developed rapidly over the past two decades. "Laser power" is defined as energy delivered per unit time. The laser-related damage will reduce with the decrease of pulse duration. The

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femtosecond laser for ophthalmology works at 1053-nm wavelength with a very short pulse duration of 10^{-15} s, minimizing the collateral damage [16]. The accuracy is 5 μm, allowing high precision in ophthalmic operations [17]. The use of the femtosecond laser has revolutionized the modern ophthalmic surgery.

3.2. Femtosecond laser in situ keratomileusis (FS-LASIK)

The concept of the lamellar refractive procedure was first introduced by Barraquer in the early 1960s. In the 1990s, an excimer laser ablation-assisted lamellar procedure was developed, as the foundation of modern laser in situ keratomileusis (LASIK). Compared with photorefractive keratectomy (PRK), visual recovery is faster and visual outcome is rapidly stable after LASIK. Flap-associated complications and increased incidence of dry eye after surgery, however, affect the quality of life. The safety, precision, and predictability of the femtosecond laser have changed LASIK over recent years.

Flap formation is critical to a successful LASIK surgery. Improper flap geometry, decentration, irregular cut, and epithelial damage lead to a large number of complications. Over the past decades, mechanical microkeratome has been performed in LASIK because of its reliability and safety. However, complications such as incomplete flap, free flap, and buttonhole continue to plague surgeons. Furthermore, because of the instability of mechanical microkeratome, corneas may be too steep, too flat, or too thin even after a successful operation [18].

The femtosecond laser became available for LASIK flap formation approximately 10 years ago. It reduced the risk of the above-mentioned complications. With mechanical microkeratome, the flap is thinner centrally and thicker peripherally (meniscus-shaped flap), which increases the incidence of buttonhole perforation. The femtosecond laser allows thin and uniform flaps, which improves the stability, safety, and precision of the flaps. It can also create thinner flaps with minimum effects on stromal architecture. Flap centration, diameter, and thickness are also more precise in femtosecond-created flaps. Another advantage of the femtosecond laser is that it allows the surgeon to select the cutting angle, position, and diameter of the hinge, as well as the flap diameter and flap thickness, which may provide better flap stability and reduce clinical epithelial ingrowth.

Though femtosecond lasers reduce the incidence of complications such as buttonhole perforation, incomplete flap, free cap, and irregular cuts, there are still some specific limitations in FS-LASIK. FS-LASIK requires two laser platforms—one for flap creation (femtosecond laser) and another for stromal bed ablation (excimer laser)—which increases the time and cost of the laser procedure. Because of the response of corneal keratocytes to the energy and inflammatory responses of adjacent tissues to gas bubbles, patients may encounter photophobia, called transient light-sensitivity syndrome (TLSS), early after FS-LASIK. With the development of the femtosecond laser, it needs less energy for flap formation, and thus reduces the incidence of TLSS [19]. The presence of cavitation gas bubbles during FS-LASIK, which originate from stray laser pulses into the aqueous humor, can impede the eye tracker of the excimer laser. An increased rate of diffuse lamellar keratitis, a sterile inflammatory reaction, was also observed in FS-LASIK because of the higher flap interface inflammatory response to laser energy and gas bubbles. Revolution in femtosecond laser energy is expected to reduce the specific complications.

In our previous study, patients treated with a femtosecond laser showed better corneal regeneration than those with a microkeratome did. Because of its precision and predictability, the femtosecond laser makes a smoother flap and causes less damage to the corneal nerve [20]. However, different from others' opinions, our data showed that there were no significant differences in the tear meniscus parameters between the microkeratome and femtosecond laser [21].

3.3. Femtosecond lenticule extraction (FLEx)

A new approach called femtosecond lenticule extraction (FLEx) was introduced to correct myopia and astigmatism. FLEx does not require a microkeratome or an excimer laser. It uses only the femtosecond laser, which is more convenient than other procedures that require both excimer and femtosecond lasers. Two cuts (posterior and anterior) in the cornea are involved in the procedure, which thus create a lenticule that is ultimately removed. There is no significant difference between FLEx and conventional LASIK, both in efficacy and safety, which promotes FLEx to be a promising new corneal refractive procedure to correct refractive errors.

However, it has been reported that the visual outcome after FLEx was stable early after surgery, but visual recovery was slow [22]. As a corneal flap is necessary before lenticule extraction, associated complications such as dry eye and compromise of corneal biomechanical strength are inevitable. Therefore, the technique evolved into SMILE.

3.4. Small-incision lenticule extraction (SMILE)

SMILE, passing the Conformite Europeenne (CE) certification in 2009, is a novel technique to correct refractive errors. The procedure involves passing a dissector through a small incision to separate the lenticular interfaces and allow the lenticule to be removed, thus eliminating the need to create a flap [23]. Early or late complications associated with flaps, such as dislocations and buttonholes are avoided; therefore, patients' experience and visual outcomes improve.

The absence of flap creation minimizes the disruption of the stromal architecture because the corneal lenticule is extracted from the mid-stroma [24]. Fewer corneal nerve branches are disrupted compared with FS-LASIK, which preserves corneal biomechanical strength and maintains sensitivity. Thus, the risk of dry eye and patients' discomfort is reduced after surgery [25]. The minimal disruption of the anterior corneal surface epithelium, Bowman's layer, and anterior stroma is also associated with less risk of dry eye [26]. Laser fluence and difference in stromal hydration, which may affect stromal ablation, are avoidable in SMILE. Prospective and retrospective studies of SMILE have shown that in the terms of efficacy, predictability, and safety SMILE is similar to FS-LASIK.

However, there are still some difficulties in SMILE. Similar to a flap in FS-LASIK, a cap whose uniform regularity is essential to optimal visual outcome is created using a femtosecond laser.

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In addition, the surface quality of the corneal lenticule can be irregular, causing tissue bridges, cavitation bubbles, scratches, or incomplete extraction of stromal lenticules [27]. At present, SMILE is mainly applied in mild myopia. It still needs more attempts and experience to be used in hyperopic eyes.

Complications such as epithelial erosion, suction loss, cap perforation, and lenticule extraction difficulty can all occur. Corneal haze, dry eye syndrome, keratitis, and interface inflammation have also been reported.

SMILE is a promising new technique for refractive error correction. With further development of the femtosecond laser, SMILE may gain greater acceptance in the future. However, we still have to pay more attention to its complications to verify its safety.

3.5. Femtosecond laser in presbyopia correction

3.5.1. Corneal inlay implantation

Corneal inlay implantation is performed for presbyopic correction. It changes the anterior corneal surface curvature, cornea refractive index, and depth of focus by placing a small inlay of suitable biocompatible material within the stroma. The benefits of inlays are the reversibility of the procedure by removal of the implant, implantation simplicity, and implant repositioning. The ability to perform ad hoc refractive procedures allows the simultaneous correction of ametropia. The most common complications after the surgery are glare and dry eye. The femtosecond laser advances flaps and tunnel creation to implant the inlays accurately on the line of sight, and thus result in remarkable improvements in uncorrected visual acuity (near and intermediate) and minimal change in uncorrected distance visual acuity. This procedure also provides good nonspectacle-corrected near vision for average daily activities [18, 28].

3.5.2. IntraCor surgery

IntraCor surgery is a new technique applicable for ametropic or low-degree hyperopic eyes (+0.5 to +1.5 D). It changes the topographic and refractive characteristics of the central portion of the cornea selectively with femtosecond laser. The procedure involves concentric intrastromal ring creation in the central portion of the cornea at different corneal depths (between the Bowman's and Descemet's boundaries). Other than the treatment failure in presbyopic correction, no major complications have been reported. IntraCor surgery is promising in the field of presbyopia correction [18].

3.6. Astigmatic keratotomy (AK)

To correct low to high astigmatism, astigmatic keratotomy (AK) is performed. The accuracy of length, optical zone, and incision depth are crucial in visual outcomes. However, the limitation of AK is the unpredictability of manual corneal incision. The application of femtosecond laser in AK provides accuracy and precision in corneal incision manufacturing and thus improves significantly in uncorrected and best-corrected visual acuity. The femtosecond laser can also be applied in case of high degrees of post-keratoplasty astigmatism. The incisions within the graft button present precise geometry and reliable depth of incision. Specific complications associated with femtosecond laser-assisted AK such as self-healing micro-corneal perforations and low-grade inflammation at the incision site appeared [18, 29].

3.7. Intracorneal ring segments

Intracorneal ring segments were small and curved when first proposed in 1978. Clear ring segments made of polymethylmethacrylate are implanted in the deep corneal stroma with the aim of generating modifications of corneal curvature and refractive changes. Peripheral intracorneal implantation has been permitted to correct low to moderate astigmatism and myopia and keratoconus by Food and Drug Administration (FDA). Complications such as incomplete tunnel formation, corneal perforation, endothelial perforation, corneal melting, and uneven implant placement may occur with the traditional technique. The femtosecond laser can be programmed to create corneal channels at a specific depth and orientation with high predictability and precision to allow safer insertion of Intacs segments. In patients with keratoconus, the femtosecond laser can be programmed to cut tunnels for the implantation of intracorneal ring segments, and it results in better safety owing to greater consistency of depth and uniformity [29, 30].

3.8. Penetrating keratoplasty (PKP)

Penetrating keratoplasty (PKP) developed rapidly after first being introduced in the early 1900s. The surgical outcomes rely on a centered and perpendicular cut of cornea, a well-matched donor button, and a recipient bed [18]. Manual PKP requires a long learning curve and a lengthy procedure time, which can be optimize using the femtosecond laser. The femtosecond laser can also achieve a higher precision in surgical steps, such as the donor cornea cutting. Moreover, the choice of shapes and diameters in femtosecond laser-assisted PKP is dependent on individualized clinical requirement. It enables advanced shaped corneal cuts creation, eliminates manual dissection, thus minimizing misalignments, and increases the stability of the wound. Some pattern of incisions that are not compassable with conventional technique can be achieved by femtosecond laser. However, postoperative regular and irregular astigmatism remain a major challenge in full-thickness keratoplasty.

3.9. Anterior lamellar keratoplasty (ALK)

Anterior lamellar keratoplasty (ALK) is a partial thickness corneal transplantation indicated for management of anterior corneal dystrophies degenerations, ulcers, and scars. The advantages of ALK over PKP include being less invasive and having a decreased rate of rejection. Femtosecond laser-assisted suture less anterior lamellar keratoplasty (FALK), first described in 2008, has been reported to be safe, effective, and stable. The femtosecond laser has reduced irregular astigmatism and accelerated visual recovery by its precision of pre-programmed corneal dissections at a variety of depths and orientations. As the corneal incision is well shaped, it can be converted to full-thickness keratoplasty in case of Descemet membrane perforation. The donor and recipient tissue are better positioned because of highly precise cuts assisted by the femtosecond laser, and thus sutures are typically removed earlier.

Limitations of ALK include the high cost and the slow growth of the epithelium over the graft [18, 30].

3.10. Femtosecond laser-assisted endothelial keratoplasty

3.10.1. Descemet's stripping endothelial keratoplasty (DSEK)

DSEK has been the preferred approach for treating corneal endothelial diseases, such as bullous keratopathy, Fuchs dystrophy, congenital hereditary endothelial dystrophy, and endothelium failure in previous penetrating keratoplasty. It removes the diseased endothelium and leaves the posterior cornea intact. However, technical challenges always afflict corneal surgeons. The application of the femtosecond laser alleviates certain difficulties. Significant advantages over manual dissection are that the femtosecond laser allows for increased automation and standardization in donor tissue preparation. In addition, lamellar interface preparation can be performed up to 3 weeks before the surgery, making it feasible for conversion to PKP owing to complications during preparation of the donor disk. It also creates a smoother donor-recipient interface to minimize induced refractive astigmatism. However, whether the femtosecond laser has an effect on endothelial cell loss and visual acuity after donor tissue preparation has yet to be determined [18, 30].

3.10.2. Descemet's membrane endothelial keratoplasty (DMEK)

Descemet's membrane endothelial keratoplasty (DMEK) has been proven to result in faster visual recovery, fewer higher order aberrations, and lower rejection rates by abundant evidence. The crucial technique is selective endothelial transplantation. The femtosecond laser offers a precise and predictable means to create the uniform thickness of the posterior stromal rim and control big bubble expansion that cannot be achieved by manual operation. The femtosecond laser not only avoids energy-associated damage but also results in smooth stromal interface by closer spots, line separations, and a low energy level. Thus, the femtosecond laser can be a novel approach for the donor grafts preparation of DMEK, which may reduce intraoperative graft manipulation and postoperative detachments [29, 31].

3.11. Cataract surgery

At 2008, the femtosecond laser was first performed in Europe in cataract surgery and was approved by the FDA in 2010. It was applied in the steps of corneal incision, arcuate corneal incisions, capsulorhexis, lens fragmentation, and liquefaction. The short pulses duration (10^{-15} s) make it a promising tool in cataract surgery [32].

3.11.1. Corneal incisions

Clear self-sealing corneal incision is of most importance in cataract surgery. In terms of length and tunnel structure, manual incision is difficult to control. In addition, bacteria have a chance to enter at low intraocular pressure because of the instability of manual incision and thus lead to endophthalmitis. Compared with manual incisions, corneal incisions made using the femtosecond laser are more precise in width, depth, and length. More consistency in the architecture is also achieved, which leads to better incision sealing without stromal hydration at the end of the surgery. The stability of the wound makes it more resistant to deformation and leakage. The femtosecond laser is used to create a clear corneal incision according to pre-programming, which requires a large amount of patient data to confirm, and definitive results. In cases of corneal astigmatism, an arcuate or a relaxing incision can be created, which has been reported to provide more stable and accurate long-term outcomes compared with toric intraocular lenses (IOLs). The femtosecond laser shows less damage by virtue of its construction and reduced mechanical stress during surgery, which may decrease corneal swelling after surgery.

3.11.2. Capsulotomy

A precise size and centration capsulorhexis are essential to optimize the IOL position. The IOL's longitudinal displacement per millimeter will lead to approximately 1.25-D refractive change, inducing myopia for an anterior shift and hyperopia for a posterior displacement. Capsulorhexis size is correlated with effective lens position. An insufficient overlap of the IOL, results in decentration, oblique astigmatism, and increased higher order aberration. A small capsulorhexis has been associated with anterior capsule fibrosis. Manual continuous curvilinear capsulorhexis (CCC) relies on the technique and proficiency of the surgeon. The femtosecond laser can be used to create a more precise, better-sized, and centered opening of the anterior capsule compared with the conventional CCC by dissecting it with a spiral laser pattern. Compared with the manual CCC group, the laser CCC group showed more accuracy and stability in anteroposterior and central IOL positioning. It is also more predictable in the refractive outcome, which is more important to patients with high expectation [33, 34].

3.11.3. Lens fragmentation and liquefaction

The increased energy for lens fragmentation and liquefaction delivered from the phacoemulsification probe to the eye can result in energy-associated capsule complications and corneal endothelial cell injury in manual phacoemulsification. The reduction in ultrasound energy can decrease the risk of such complications. It is reported that the femtosecond laser reduced the ultrasonic energy delivered during phacoemulsification significantly. However, its effect on endothelial damage is still unknown.

3.11.4. Limitation and complications

Although the femtosecond laser showed excellent advantages over manual operation in cataract surgery, there are still some inevitable limitations and complications.

1. Additional operating room shifting time

   Patients need to be shifted under the operating microscope after application of laser treatment. This logistical issue results in increased time spent with each patient, which could lead to overall delay.

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2. Applicability

   The femtosecond laser relies on good anterior chamber imaging. Patients with poor eyelid opening, nystagmus, poor pupillary dilatation, corneal opacities, and ocular surface disease are poor candidates. It is also not suitable for patients with tremors or dementia in the initial docking system. The femtosecond laser is not available for grade 4 cataract according to the Lens Opacities Classification System III (LOCS III).

3. Complications

   Capsular blockage syndrome: Large diameter hydrodissection cannula with high-speed fluid may inhibit a gas bubble that is formed from leaving the nucleus. Pressure elevation between the capsule leads to the rupture of the posterior capsule, and the lens may drop into the vitreous cavity. This is a learning curve-related complication, which can be avoided by a more cautious and skilled surgeon

   Pupillary constriction: Bubble formation and suction force can trigger pupillary constriction by releasing small amounts of free radicals. In addition, a delay between femtolaser pretreatment and cataract surgery may result in pupil diameter changes (5–10 min is recommended).

   Corneal incision sizing and positioning the initial docking of the laser ring is crucial to the accuracy of the intended femtolaser-created incision. Imperfect interface positioning causes inaccuracy of corneal incision sizing and positioning, which results in surgically induced astigmatism and complication in the manual final procedure [18, 35].

4. Summary

The surgery has gradually matured with the development of the modern excimer laser equipment and technology. Upgrading thermal control and ablation centration will achieve better corneal biomechanical results. We have reason to believe that a single excimer laser surgery would be the next breakthrough in refractive surgery, the next step toward the "perfection" of refractive surgery. Femtosecond laser advancements over the past two decades have brought revolutionary change in ophthalmic practice. It not only improves the safety and efficacy in corneal refractive surgery but also achieves remarkable advancement in the field of cataract surgery. Despite having certain limitations and complications, femtosecond lasers are promising in ophthalmology. Both excimer and femtosecond laser technology will serve for better human health as long as we apply it appropriately.

Author details

Liang Hu*, Yiqing Huang and Meng Lin

*Address all correspondence to: liang_hu@live.cn

School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, China

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