We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

6,500
Open access books available

177,000
International authors and editors

195M
Downloads

154
Countries delivered to

TOP 1%
Our authors are among the most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chapter

Fundamentals of Femtosecond Laser and Its Application in Ophthalmology

Sana Niazi and Farideh Doroodgar

Abstract

Modern advancement in lithographic technology, injection molding, and nano-imprinting has improved the patterning of small structures, resolution, productivity, and materials. Ultrafast laser micro/nano-manufacturing technologies, including nano- and femtosecond lasers, have the advantage of high precision as a result of suppressed heat diffusion to the surroundings. This precision imposes strict requirements on the temporal characteristics of laser pulses. Ultrafast lasers also have advantages in terms of technique, application, and processing. Femtosecond laser (FSL) uses photo disruption to form micro-cavitation bubbles within the cutting plane. The controllable spatiotemporal properties of FSL make it applicable for the three-dimensional fabrication of transparent materials. Using smart materials to create 3D microactuators and microrobots is a newfound application of FSL processing, which enables the integration of optical devices with other components and is practiced in new applications, such as 3D microfluidic, optofluidic, and electro-optic devices. We discuss mechanisms and methods of FSL (including digital micromirror devices, different processes, and interferences). Microlens arrays, micro/nanocrystals, photonic crystals, and optical fibers all have applications in the production of optical devices. Using FSLs, one may create scalable metamaterials with multiscale diameters from tens of nanometers to centimeters. The huge potential of FSL processing in various fields, such as machinery, electronics, biosensors and biomotors, physics, and chemistry, requires more research.

Keywords: lasers, lasers, solid-state, corneal surgery, laser, ophthalmology, cornea, optics and photonics

1. Introduction

Ophthalmology has faced substantial changes by the advances in medical technology. These advances include developments in diagnostic and therapeutic strategies. One of the important advances of recent years, which has changed the field of ophthalmology, is the laser. After the development of the early solid-state lasers, FSL was developed as a near-infrared laser with ultra-short pulse duration, which enabled safety, precision, and predictability of ophthalmic surgeries and improved the postoperative outcome of
patients. It has also been used for the fabrication of several optic devices, which helped to improve the precision of diagnosis and treatment in the field of ophthalmology. The ongoing advances in FSL technology since its introduction are making the newer machines with better quality, stability, and fewer complications. Therefore, it is suggested that researchers and clinicians keep themselves updated about the advances in FSL technology and make use of the updated technologies to benefit from its advantages.

Nano/micro-devices have diverse applications in optics, nanophotonics, Opto-electronics, and biomedical engineering. As the transparent layers of the eye do not absorb electromagnetic radiation, light does not alter them, but the light energy is absorbed by them, causing focal tissue disruption. Laser systems with different wavelengths have been developed based on these principles with several applications in ophthalmology. The femtosecond laser (FSL) is a near-infrared laser with a wavelength of 1053 nm and a diameter of 0.001 mm. The term “femtosecond” refers to the pulse duration of one billionth of a second, fired in the nanosecond domain. This ultra-short pulse duration allows for smaller shock waves, focus to a 3-μm spot, no heat development, and less damage to the adjacent and superficial tissue (collateral damage) [1].

FSL works by the production of a different tissue interaction, known as photodisruption. Within the cutting plane, micro-cavitation bubbles are formed discretely. Non-linear absorption of laser energy is obtained by using many photons at the same place and time. This multiphoton effect causes the tissue to absorb energy as high as it results in optical breakdown. This process of photodisruption creates plasma, acoustic shockwave, thermal energy, and cavitation bubble, which expands at supersonic speed, slows down, and then implodes and eventually forms a gas bubble composed of carbon dioxide, water, nitrogen, and other elements. This will break the limitations of traditional fabrication methods, which results in two–threefold better precision than cell surgery using continuous-wave irradiation [2]. In addition, the quality of fabrication is also improved in FSL, due to the non-equilibrium and non-thermal absorption phase transitions, resulting in reduced heat-affected zones, cracks, and recast layers. Furthermore, FSL requires no mask, vacuum, or reactive gas environment. The non-linear and material-independent absorption of femtosecond lasers makes them ideal for creating complex 3D structures in composite substrates with nanometer-scale precision [3].

Modern laser technology is rapidly improving in terms of resolution, productivity, and materials. Using smart materials to create three-dimensional (3D) microactuators and microrobots is a newfound application. With femtosecond laser processing, optical devices can be seamlessly integrated with other components, enabling new applications such as 3D microfluidic, optofluidic, and electro-optic devices.

We discuss mechanisms and methods for femtosecond laser, including digital micromirror devices, different processes, and interferences. Microlens arrays, micro/nanocrystals, photonic crystals, and optical fibers all have applications in the production of optical devices. Using femtosecond lasers, one may create scalable metamaterials with multiscale diameters from tens of nanometers to centimeters. Improved methods may result from the availability of effective femtosecond laser surgical equipment for any refractive surgery processes, Photo disruptive ultrasonic lens surgery as a combo approach in any medium to altering the power of the intraocular lens (IOL) postoperatively. The huge potential of femtosecond laser processing in fields such as machinery, electronics, biosensors and biomotors, physics, and chemistry requires more research.
2. Historical background for development of femtosecond laser systems in ophthalmology

Various laser sources were developed and pioneered by solid-state and organic dye lasers in the 1960s and early 1970s. In 1979, short-pulse lasers at near-infrared wavelengths were used in ophthalmology for the treatment of posterior capsule opacification after surgery (by Aron-Rosa). In the 1980s, research continued on non-linear effects in optical fibers and near-infrared spectral region; in 1982, the first Titane (Ti): sapphire laser was built by Moutan, which had a wide tuning range (680–1130 nm), which was based the tunable FSL source. Following the use of the coupled-cavity mode-locking technique with a Ti: sapphire laser to constitute the generation of sub-100 fs pulses, a new generation of FSL was generated, which matched the cavity containing the ‘non-linear element’ with interferometric precision to the master cavity of the color-center laser oscillator. With peak optical pulse powers of >5 MW from a Ti: sapphire laser, compared with the dye-laser pulse peak powers, oscillator-amplifier combinations were no longer required, but for using the optical Kerr effect, cavity-design parameters were required (Figure 1). In 1984, FS dye laser was used in oscillator-amplifier configurations, and in 1989, Stern and colleagues found that reducing the pulse duration of near-infrared laser from the nanosecond to the picosecond ($10^{-12}$) and then FS ($10^{-15}$) resulted in higher precision ablation profiles and less collateral damage. FS belongs to ultra-fast or ultra-short pulse lasers with a beam diameter of <8 microns in the near-infrared spectral region and is capable of producing smaller shock waves and cavitation bubbles that affect a tissue volume about $10^3$ times less than picosecond-duration pulses [1].

The first prototype of the ophthalmic surgical FSL system was developed by Dr. Jujasz and colleagues and was clinically used by Dr. Kurtz at the University of Michigan in the early 1990s. The IntraLase Pulsion FSL was approved by the U.S. Food and Drug Administration (FDA) for lamellar corneal surgery in Jan. 2000, and the first commercial laser was introduced to the market in 2001 for the creation of the corneal flap in
refractive surgery, i.e. laser in situ keratomileuses (LASIK). The advantages of this system caused FSL to replace the mechanical cutting devices shortly. In 2002, Advanced Medical Optics (IntraLase FS, Irvine, California, USA) fired a 10–kHz laser. In 2007, Ziemer FEMTO LDV™ introduced new low pulse energy with high frequency. The current IntraLase system has a pulse rate of 60 kHz, which enables shorter flap-cutting times, less energy to cut the flap, and closer separation of the spots and lines. The fifth generation of the IntraLase FS system fires at 150 kHz with high-precision computer control of the parameters, which enables cutting flaps in less than 10 seconds with a variety of geometric shapes, depths, diameters, wound configurations, energy, spot sizes, and spot separation, allowing for precise corneal cutting.

FSL has also been used for cataract surgery since 2008; the LensX™ system, approved for this procedure by FDA in 2009, opened another sector of ophthalmic FS-laser application. The early version operated at 33 kHz pulse frequency and 6–15 μJ energies. LensX was then integrated with Alcon, and similar products were launched by multiple manufacturers. In 2014, the first low pulse energy FSL system was introduced for cataract and cornea surgery, the Ziemer FEMTO LDV Z8™ [4].

Simultaneous with the development of FSL, optical coherence tomography (OCT) was also described (1988), which provided non-invasive 3D in vivo imaging with fine resolution (microscopic resolution of 5–20 μm) in both lateral and axial dimensions at a micrometer level. Several variations have been developed for OCT since its introduction and are currently used with FSL systems in most modern cataract procedures after docking the laser interface to the eye.

Fourier Domain Optical Coherence Tomography (FD-OCT) employed a fixed reference arm length but a spectrometer with a linear detector array instead of a single detector. In this scenario, optical path length variations between interferometer arms cause periodic interference modulation. By Fourier transformation, the measured spectrum can yield an A-scan. “Sweep-source” (SS) OCT is an improved frequency-domain OCT variant. A tunable light source with a “sawtooth” frequency profile over time is used with a fast single-pixel detector instead of a spectrometer. After docking the laser interface to the eye, most current cataract fs-lasers do three-dimensional OCT scans.

Also, a 3D confocal structured illumination is used with the Scheimpflug camera, which was first described by Theodor Scheimpflug in 1904, and is currently used in LENSAR™ system. Therefore, the integration of FSL processing with optical devices enabled new applications in ophthalmology [5]. Considering the day-to-day advancements of FSL, in this chapter, we describe the latest micromachining advancements in optical systems and devices.

3. Characteristics of femtosecond laser

Before we describe the processing methods, we need to know about the characteristics of FSL. Compared with the conventional laser microfabrication techniques, which use continuous-wave lasers or long-pulse lasers, the processing of ultrafast lasers, including nano- and femtosecond lasers, has several advantages. The short laser pulse (< electron–phonon coupling time of the laser-matter interactions) makes the laser energy absorbed by electrons and rapidly transferred, which reduces the thermal effect of ultrafast laser. This characteristic of ultrafast lasers is one of the fundamental advantages, which results in higher precision that enables the
fabrication of fine structures. This characteristic is especially important when the peak intensity of the laser has to be controlled near the ablation threshold with a low repetition rate.

The second important advantage of ultrafast lasers is related to the non-linear electron excitation mechanism that is unique to these lasers and results in the induction of strong absorption, even in transparent materials. In the conventional linear single-photon, absorption (long-pulsed or CW lasers) requires photon energies greater than the material’s band gap for excitation of an electron from the valence band to the conduction band by absorbing a single photon. Because of the surface absorption, the transparent materials cannot be internally modified. In ultrafast lasers, absorption of the extremely high density of photons (multiphoton) enables the interaction between the laser pulse and a transparent material only near the focal point (Figure 2). Therefore, no out-of-focus absorption occurs by focusing FSL beam on transparent bulk material. In the next subtitle, we describe the mechanism of non-linear and multiphoton absorption processes of FSL in detail.

The combination of the two above-mentioned characteristics (heat-affected zones suppression and non-linear multiphoton absorption) shapes the third advantage of ultrafast laser processing, i.e. a resolution far beyond the diffraction limit. This factor is related to the Gaussian spatial profile of the laser beam intensity, which makes the effective absorption coefficient for \(n\)-photon absorption proportional to the \(n^{th}\) power of the laser intensity that causes a narrower absorbed energy distribution for multiphoton absorption. The fabrication resolution can be additionally improved by adjusting the laser intensity at a threshold above which a reaction occurs on absorption.

The last important characteristic of FSL to be mentioned here is the spatially selective manner of tuning or altering the physical and chemical properties of a material. This characteristic, along with the multiphoton effect, is used in 3D femtosecond laser direct writing for the integration of multiple functions on a single substrate [6].
4. Mechanisms of femtosecond processing

Understanding the physical mechanisms and processes of FSL is important, as they differ between FSL fabrication (including phase change and material removal) and traditional manufacturing methods, which are essentially determined by laser-electron interactions. Hence, the regulation of laser-electron interactions or electrons dynamics is critical to the future development of femtosecond laser manufacturing, which poses a challenge for measuring and controlling at the electron level during fabrication processes. Hence, the development of theory and observation systems must be synchronized with the development of laser fabrication methods and applications. In ophthalmic surgery, laser energy is channeled as efficiently as possible. The flap thickness is determined by placing a sterile plastic foil between the laser and the cornea. The computer keeps all corneal cuts suctioned up in a total vacuum time of <40 seconds. Laser cuts the tissue by two mechanisms; some laser pulses vaporize small amounts of tissue by photodisruption process. Vaporized tissue causes multiple intrastromal cavitation bubbles of microplasma, composed of water and carbon dioxide. The bubbles disrupt the tissue at a larger radius than the plasma created at the laser focus, which dissociates the tissue and creates a lamellar corneal dissection plane. Other lasers create a dissection plane using the desired pattern (e.g., a raster or spiral pattern), controlled by the surgeon using laser software. The nature of the cutting processes differs based on the laser-tissue interaction parameters, which include (1) Pulse energy, (2) Pulse repetition rate, (3) Pulse duration, (4) Wavelength, (5) Focusing power, (6) Focus spot shape, and (7) Spatial pulse spacing.

The laser energy used may be a high or low pulse. Lasers with high pulse energy and low frequency (with pulse energies in J and repetition rates in kHz) were used earlier (Figure 3). Low repetition rate and pulse overlap reduce tissue bridging. In the high pulse energy laser group, the mechanical forces drive the cutting process by the expanding bubbles, which disrupt the tissue at a larger radius than the plasma created at the laser focus. Modern FSLs use low pulse energy by shortening the pulse duration.

Figure 3.
High pulse low-frequency energy.
or reducing the focal spot size to reduce the side effects at a given wavelength. In the low pulse energy group, high pulse frequencies are applied (MHz range), which helps achieve a cutting speed as effective as in the high energy laser group. Tissue evaporation inside the plasma effectively separates tissue without a need for secondary mechanical tearing effects [5].

Several parameters play a role in the interaction between the laser and the material, including chemical, thermal, and mechanical effects via free-electron generation. Ablation of material is caused by thermal damage resulting from impurities and defects in the samples. FSL intensities \( \geq 10^{14} \text{ W/cm}^2 \) are anticipated to have the same ablation mechanisms for metals and dielectric materials. Gamaly et al. also verified the ablation threshold value and ablation velocity formula of the metal and dielectric material. This interaction also differs between metallic and non-metallic materials, as metallic materials have a large number of free electrons while non-metallic materials do not. The absorbed FSL by free photons of metallic materials results in heated photons and their collision with other electrons that transfer energy to each other and increase the interaction with the lattice. The heated lattice results in the phase transition of the material, at picosecond \((10^{-12} \text{ s})\) to tens of nanoseconds \((10^{-8} \text{ s})\), resulting in micro- to millisecond-scale plasma. Conversely, in non-metallic materials, electrons are bound in the valence band. The processing of FSL in non-metallic materials includes ionization and phase change. Ionization involves photoionization (which includes tunnel ionization and multiphoton ionization) and impacts ionization mechanisms. Photoionization is the main mechanism of seed-electron generation. The super-strong electromagnetic field generated by FSL reduces the Coulomb potential barrier of valence-band electrons by the tunneling effect, which results in the transfer of electrons into the conduction band and become free electrons. Multiphoton ionization refers to the absorption of multiple photon energies by the valence-band electrons, which obtain higher levels of kinetic energy, collide with other valence electrons, and transfer into the conduction band, causing a chain reaction similar to avalanche, resulting in free electrons. In other words, avalanche ionization involves free carrier absorption followed by impact ionization. As the electron’s energy exceeds the conduction band minimum (more than the band-gap energy), it can ionize another electron from the valence band, which results in two excited electrons that can be heated by the laser field through free carrier absorption. This process repeats as long as the laser field is present and intense enough, leading to an electronic avalanche.

The phase change follows the first part of ionization and electron heating. In this part, the accumulation of a large number of free electrons inside the non-metallic material and the lattice-electron interaction results in the exhibition of transient metallic characteristics. In the temporal scale of picosecond \((10^{-12} \text{ s})\) to tens of nanoseconds \((10^{-8} \text{ s})\) and the spatial scale of tens-of-nanometers-to-tens-of-micrometers, the phase change includes thermal phase transitions (melting and gasification; when the lattice temperature rises above the melting point of the material) and non-thermal phase transitions (Coulomb explosions and electrostatic ablation; based on plasma expansion). The pump-probe technique can be used to observe the ablation processes on this temporal and spatial scale. The thermal damage depends on the pulse width and intrinsic parameters of the material (like melting point, thermal expansion coefficient, thermal conductivity coefficient, and tensile strength). As a general rule, only the fraction of energy within a laser pulse, absorbed inside the tissue, is responsible for interactions with tissue. The emitted laser energy is redistributed from a surgical laser device at the end of the tissue dissection process (Figure 4), and only non-linear
absorbed energy, which constitutes only 10–15% of FS pulses, contributes to the tissue dissection process. Similarly, in transparent dielectric materials, the laser creates free carriers inside materials by non-linear absorption processes. For transparent materials, similar models have been described (as for non-metallic materials), including multi-photon, tunnel ionization, and avalanche.

It has to be noted that the material-laser interaction is complex, and different theoretical models have been suggested for its description, including time-dependent density function theory, molecular dynamics model, plasma model, and improved two-temperature model. But, each of these has its own limitations in special and temporal scales. For example, molecular dynamics combines the thermal and non-thermal phase transition mechanisms to explain material ablation due to lattice phase transition. However, some aspects have been described simply in this model, such as the alteration of the interaction force between atoms during the ablation process and approximate simplifications in the first-principles model, such as a time-dependent exchange-correlation, which influence the accuracy of theoretical predictions. The plasma model is used to describe photon absorption, plasma generation, and recombination of electronic systems before lattice phase transitions and offers a good explanation for the non-metallic ionization process. However, the phase transition process is not discussed in this model. Two-temperature model, described by Anisimov and colleagues for the interaction between ultrafast laser pulses and solids, is widely used for the prediction of the electron and phonon temperature distributions in laser processing. However, in this model, the electron density is set to a constant value; therefore, it is only applicable in metallic materials [3].

The models were extended by other researchers for more accurate calculations, such as the multiscale theoretical model and observation system, applicable for problems associated with each temporal scale to cover the overall scope of laser fabrication. The imaging system, such as sequentially time all-optical mapping photography, can be integrated with FSL fabrication system to realize real-time continuous observation and feedback of the fabrication process. Other theoretical models, based
on simplified rate equations or a kinetic approach to Boltzmann’s equations, have also been described. Models considered for the multiphoton non-linear optical process include two-photon absorption (which occurs when two photons are absorbed simultaneously by material) and two-photon polymerization (TPP; which occurs when two photons are absorbed on photosensitive material). This process changes the material and leads to polymerization by activating the photoinitiator-activated free radicals in the resist. Fabrication resolution of true 3D micro/nanostructures by TPP varies based on the laser energy, exposure duration, and concentration of the free radical [7].

Micro/nanostructures induced in transparent materials have been classified by Qiu et al. into four types based on optical coloration, refractive index modification, micro-hole creation, and micro-crack creation. FS pump-probe interferometry technique, with 100 fs temporal resolution, allows measuring the modification of refractive index induced by ultra-short intense laser pulses. When a dielectric material is subject to intense FSL, a large number of excited electrons may be generated by laser pulses, which produce intrinsic defects that make FSL an ideal tool for high-precision material processing. A complex secondary process of high-temperature and high-pressure plasma at the tightly focused laser point would induce a phase or structural modification of the material. The splitting and self-(de)focusing of FSL pulses inside dielectrics are the topics that researchers have used for the calculation of the excitation and relaxation channels of FS-induced carriers. Despite various models and explanations for laser-material interactions, the dynamics of specific phenomena are realized only partially. To quantify dynamics of laser-excited carriers, direct visualization of FSL dynamics using ultrafast imaging and spectral interferometry techniques has been designed and implemented successfully [8].

5. Systems and methods of femtosecond laser fabrication

Two important types of FSL micromachining include direct writing, parallel method, laser pulse shaping in the temporal and spatial domain, laser frequency modulation, and laser-pulse-coordinated shaping in temporal/spatial/frequency domain based on electrons dynamics control. The direct writing processing method, the commonly used basic processing method, is a serial fabrication process, and the increased numerical aperture results in achieving augmented resolution. The high resolution, excellent flexibility, and quality make this method suitable for fabricating 3D microstructures within transparent materials, while in the parallel method, a slit-oriented parallel is placed in the scanning direction before the objective lens, and the slit’s orientation should be adjusted along with the scanning direction; therefore, the aspect ratio of the hollow microchannel and the laser efficiency is low. This method can only fabricate periodic structures. Another difference between the two methods is the throughputs; parallel microprocessing can realize high throughputs and is appropriate for large-scale FSL micromachining. But direct writing method has the limitation of low throughputs, which has been improved by the use of high-average-power and high-repetition-rate FSLs in recent years [3, 6, 9].

The choice of method to be used depends on what is required in that particular application. For each specific application, we have to consider the relation between working distance and fabrication resolution, as well. The fabrication resolution depends on their numerical aperture (NA). The focal spot diameter is inversely proportional to the NA (in the lateral direction, $1.22 \lambda / NA$). Consequently, we require an objective lens with NA of ~0.5 for 3D machining. Then, a high-NA objective
lens (e.g., oil immersion objectives), which usually has a short working distance, is applicable for surface nanostructuring or TPP (which involves surfaces and thin samples); while they are not appropriate for the fabrication of 3D microstructures deep in a substrate [6].

If the spatial and temporal aspects of laser pulses are simultaneously focused, the laser components will be separated spatially in space before they enter the objective lens and then overlap at the spatial focal point focus of the objective lens. For processing a symmetric spherical light intensity distribution and improved axial resolution, the shortest pulse duration should be confined to the spatial focus; this approach increases the resolution. In contrast, for application in microfluidics, we require an improved aspect ratio of a hollow microchannel, achieved by combining temporally- and spatially-shaped laser pulses to enhance the etching depth of the microchannel by a factor of 13, enabling high-throughput fabrication of ultra-high-aspect-ratio hollow microchannel [9]. In the following, we explain the FSL processing systems in detail.

6. Direct writing

A typical FSL direct writing system is composed of a laser source, a beam control/shaping system, a microscope objective, or an aspherical lens (Figure 5). A tightly focused spot and a high-precision XYZ translation stage are produced by the lens (which determines the fabrication resolution) and controlled by a computer for 3D translation of the sample. As FSL pulses possess broad spectra, objective microscope lenses are frequently used for minimizing both spherical and chromatic aberrations. For controlling the repetition rate, an electro-optic or acoustic-optic device is employed in the beam control/shaping system, which can also be used for creating burst mode, a spatial or temporal pulse shaper, a tunable attenuator, and a mechanical shutter. For real-time monitoring of the fabrication process, a charge-coupled device camera connected to a computer can be installed above the focusing lens. A tunable

Figure 5.
Schematic image of femtosecond laser direct writing system.
attenuator is another component of the direct writing system, which controls the power and ensures stable operation of laser parameters such as the pulse width, pulse energy, and pointing direction. Autocorrelator devices have also been developed for characterizing the spatiotemporal profiles, including temporal duration or structure of ultrashort pulses [6].

Direct writing has two methods, depending on scanning directions (geometries): horizontal (where the sample is moved perpendicularly to the laser beam, commonly used to fabricate surface structures) and vertical (where the sample is moved along the direction of laser beam irradiation; it can be performed from the upper or lower surface). The greater longitudinal depth of the focal spot intensity distribution than its transverse dimension results in an asymmetric cross-section of the laser modification zone. An objective lens with a larger NA can reduce this difference, resulting in tight focusing and adjust the spatial distribution of pulse intensity. When direct longitudinal writing is processed from top to bottom, the laser beam is affected by the scattering of ablated materials, which reduces fabrication quality [3].

Horizontal direct writing is appropriate for the fabrication of ultra-slip surface porous network structures with excellent performance in liquid repellency and cell proliferation resistance, hierarchical structures, nano grooves, nanoholes, and 3D resonant optical cavities, widely used in applications such as hydrophilic and hydrophobic treatments, optical communication and sensors and biomedicine. Direct writing is also applicable for the fabrication of two-dimensional (2D) and 3D microstructures, either through moving the 3D transform stage (applicable to array machining and applications not requiring high precision) or through a galvanometer combined with the transform stage. In the former method, even by using Bessel Beam, which improves efficiency, rapid and flexible micromachining of complex microstructures cannot be achieved at a large scale. On the contrary, the latter method, scanning galvanometers and piezo has highly-developed high power, high repetition frequency, and miniaturized FSL, which makes it appropriate for high throughput and high-resolution micromachining both axially and laterally; this method is beneficial for the commercialization of FSL micromachining. TPP technique can be used for the construction of complex mesoscale 3D microstructures with nanoscale precision, like entire hollow devices and spiral phase plates. Direct writing also has another great potential, such as large-scale multifunctional smart materials with 3D gradient densities that can be widely employed in the processing of four-dimensional (4D) smart sensors and reconfigurable micromachines, actuators, and soft robots applicable in biomedicines (which use hydrogels: soft materials with high biocompatibility and deformability).

Besides the advantages of FSL direct writing, it also has some limitations, which makes it inappropriate for oil-working conditions used for biomaterials (e.g., cells and tissues). The serial process nature of this method also results in low throughput, although we can increase the scanning speed by replacing the XYZ motion stage with a galvo scanner. The recent ultrafast laser systems have high power and high repetition rate and their pulses are much broader than the pulses generated by the Ti:sapphire systems [9].

6.1 Parallel systems

Parallel FS microprocessing has three typical systems: multifocus laser writing, processing based on multiple-beam interference, and using a hologram. The first system, the most straightforward technique, is based on a microlens array that splits the single focal spot into multiple foci, uniformly distributed in the focal plane. By the
combination of a relay lens and an objective lens, a fabrication resolution comparable with that of the objective lens can be realized. This method can be used for the fabrication of structures with arbitrary 3D geometries in each unit cell. In earlier models, multifocus parallel laser fabrication could only be used for microstructures arranged in periodic arrays. Implementation of multifocus TPP technique, based on individually-controlled phase modulation, enabled rapid prototyping of symmetric and asymmetric complex 2D and 3D structures. The second technique, parallel processing using multiple-beam interference, is potentially faster than the first method and can be used for the fabrication of periodic 2D/3D structures with a wide variety of interference patterns by only a single laser shot. In this technique, an optical diffraction element splits the incident beam into five diverging beamlets, which are collimated by a lens. The phase and amplitude of each beamlet can be tuned, and the beamlets are refocused into the sample by a second lens to create the interference patterns [6].

Various methods have been developed for efficient and flexible fabrication of complex microstructures, including multi-focus parallel processing through optical modulation and diffraction, structured light, photolithography based on a digital micromirror device (DMD), and a liquid crystal spatial light modulator (LC-SLM). The two latter methods, DMD and LC-SLM based FSL processing, can modulate the graphic fabrication of arbitrary structures dynamically with high speed and flexibility, which makes them applicable in various structures. Cross-scale high throughput processing with submicron resolution can also be achieved through a spatiotemporal synchronization focusing approach.

DMD technique is high-throughput, high-contrast, rapid-response, and easy-to-use, appropriate for modulating spatially homogenized flat-headed light sheets into arbitrary 2D patterns, high throughput processing of large-scale microstructural arrays, and single-pulse fabrication of the complex microstructure arrays. It can also be used in combination with digital holography technology for printing various arbitrarily complex 3D structures with high resolution. A larger field of view and patterned area can also be obtained by an objective lens with moderate magnification in applications where super-resolution is not required. A maximum of 44% of laser energy is irradiated on the sample, considering reflection from the DMD surface and energy loss in the gaps between the micromirrors [9].

The second most widely used technique for direct writing is LC-LSM, which modulates the light field phase by a variable distribution of liquid crystals and produces a higher utilization rate of the light energy. This flexible micro-patterning approach was first introduced by researchers from Tokushima University and gained interest in recent years. The accuracy, efficiency, and resolution of LC-SLM-based FSL processing have been improved by achieving the desired patterned beam through holographic algorithm and fabrication approaches. Special microstructures have also been built using structured laser micromachining. It generates Matthew beam, appropriate for fabrication of complex microcages, by regular intensity distribution and the diversification of controllable parameters, as well as Bessel beams, appropriate for fabrication of high aspect ratio microtubes, hollow microhelical structures, and chiral rotating microstructures using the non-diffracting high-quality beam. Both approaches, DMD and LC-SLM based FSL processing, have limitations in achieving high precision and large size simultaneously, for instance, in TPP applications. This limitation has been improved by the spatiotemporal synchronization focusing technology proposed by Cheng et al., which can realize the shortest laser pulse width with the highest laser intensity and improves the efficiency, volume, resolution, and flexibility of FSL fabrication [9].
6.2 Micromachining via interference

FSL has enabled the imprinting of large-scale periodic micro/nanostructures directly on the surface of hard materials or within transparent materials. By adjusting the laser energy, angle of incidence, the number of interference beams, the focal length of the focusing lens, exposure time, laser wavelength, and other parameters, we can modify the period, morphology, and dimension of the structures. Stable and applicable coaxial multi-beam interference can be produced by splitting lenses with a beam splitter and gratings and used for the fabrication of 3D spiral optical fields and chiral microstructures. Michelson interferometer-based FSL spatiotemporal interference approach was proposed for efficient and flexible surface patterning, which can produce a custom-designed gray-scale patterning on a bulk material with a single laser SLM pulse. Direct interference patterning has also been used for nanoparticles size distribution tailoring and multifunctional metal surface modification. This technique, FSL interference, enables the fabrication of periodic functional micro/nanostructures, used in information storage, biomedical engineering, and metamaterials, owing to the invaluable features of this laser technique, including single-step processing, high efficiency, and controllable period [9].

The advantages of FSL have made it appropriate for the fabrication of various optical devices. In the following, we provide a summary of its applications:

- **Subtractive fabrication, additive fabrication, and laser-induced modification of microlens arrays.** Microlens arrays are used in light modulation, optical sensors, integration of optical systems, parallel micromachining, optical imaging, illumination, and complex quasi-3D surface structures owing to their advantages, including small volume, low cost, and distinctive optical performance. High repetition FSL direct writing enables super-wide-angle imaging, used in completely enclosed cavity concave and convex micro ball lens arrays, embedded in transparent bulk polymer, applicable for aligning with other optical devices.

- **Micro/nano gratings, including shape-shifted fiber gratings, highly refractive negative-index gratings, and highly birefringent fiber Bragg gratings.** FSL-induced photoreduction of silver ions inside hydrogel can also be used for the fabrication of shrinkable silver diffraction grating.

- **Photonic crystals that generate a band gap to prevent the propagation of electromagnetic waves of specific frequencies can be manufactured by FSL, owing to its high precision, high efficiency, special 3D dielectric structure, and non-polluting nature, which enables the fabrication of waveguides, communications, lasers, and exciting molecular chemical reactions.** Integration of photonic crystals with all-optical and micro-nanotechnology enables nanotechnology, quantum dot, fiber, and dirac cone. Challenges remain for the fabrication of 3D photonic crystals with bandages.

- **Optical fibers:** FS direct writing has high efficiency, zero pollution, and 3D precision that makes it appropriate for the processing of small diameter of optic fibers with a transparent material in bulk volume. Multifunctional micro/nanomaterials and devices can also be integrated within a single optical fiber (lab-on-fiber), which has potential for applications in multifunctional sensing and actuating. Both dielectric ad metallic nanostructures can be fabricated on the fiber tip. Direct writing has also been used for the fabrication of multi-core fiber...
for multiplexing. Multi-components fiber sensors, 3D waveguides, X-couplers, Bragg gratings, microholes, mirrors, optofluidic components, and microfluidic structures can also be processed within a single-mode fiber. Optical fiber using FSL can be used for on-surface and sub-surface fabrication of optical devices and microfluidic devices, which can be integrated onto an optical platform for various materials with diverse physical, chemical, mechanical, and biological properties.

7. Docking

For the fs lasers to be docked with the eyes, head must be in the fixed laser housing, the articulated arm holding handpiece be on the eye, and there should be a distance between eye surface and laser optics. Sterile, single-use components, referred to as “patient interfaces,” are used to actually make contact with the eye. There are two types of interfaces in use: an applanating interface, which has a curved or flat surface that touches the cornea directly; and a liquid-filled interface, which has a vacuum ring that makes contact with the sclera or the outer cornea and a liquid-filled center. The liquid-filled interface maintains the cornea’s natural shape while enabling laser energy transmission. Despite the fact that contact surfaces momentarily alter the curvature of the cornea [10], mechanical contact significantly stabilizes the cornea during surgery. This is especially crucial in refractive surgery, where micrometer-level tissue movement must be prevented and precise incisions are necessary. Because refractive surgery has no obvious clinical downsides [11–13], contact interfaces will predominate in corneal surgery in the future (Figure 6). Liquid-filled interfaces that cause minimum disruption to the eye may end up being the best option for cataract surgery. Vacuum docking contact stability during laser emission is crucial. Loss of touch can lead to wrong-plane cuts. All lasers are designed to automatically monitor vacuum levels and halt laser emission upon loss of contact. Eye surgeons watch their patients during the process and might manually interrupt or pause it if difficulties arise. In laser systems with an articulated arm, surgeons can use their manual abilities to actively stabilize the laser handpiece. With a vacuum loss, treatment can be restarted after a new docking.

Figure 6. Docking by femtosecond laser.
8. Applications in ophthalmology

As described above, FSL has several advantages, such as minimum collateral damage, which enables bladeless high-precision incisions within the tissue by different patterns and depths. Accordingly, FSL has been implemented in several ophthalmologic surgical procedures, which has substantially revolutionized the safety, precision, and predictability of surgeries (Figure 7). The ongoing advances in FSL technology since its introduction are making the newer machines with improved postsurgical outcomes in terms of visual quality, stability of treatments, and complications [14]. Fs-laser cuts can be used to produce “pockets” in the cornea, from which either material can be extracted or implanted, in a variety of refractive surgeries (Figure 8). The cornea’s refracting power is altered in both scenarios.

8.1 Refractive surgery

8.1.1 Ablative procedure

FSLs are used in various refractive surgery procedures such as FSL-assisted laser in LASIK, refractive lenticular extraction (RELEX), and small-incision lenticule extraction (SMILE) (Figure 9). During LASIK procedure, first, a corneal flap is created by FSL; for this purpose, the laser spot moves inside the cornea at a programmed thickness, and by a perfect cut, the lamella is created. Then, the FS bundle continues along the flap circumference, and the flap is lifted; then, excimer- or solid-state UV-laser energy is used to change the cornea’s refractive power by flattening or steepening the stromal bed. Later, the flap is repositioned.

Advances in FS laser technology, including the availability of fast-firing rates, enabled smaller spot sizes and tighter spot separation, which made sweeping and lifting of the flap easier. A well-fitting manhole is also enabled by the vertical side cuts of FSL. Compared with the traditional photo-refractive keratectomy, LASIK...
(using IntraLase™) showed to have a shorter rehabilitation period, more predictable flap thickness, better astigmatic neutrality, less epithelial injury, and faster stabilization of visual outcome; but is associated with a higher risk of dry eye and flap-related complications, such as transient light-sensitivity syndrome after surgery and diffuse lamellar keratitis in the flap interface. Nonetheless, the risk of dry eye and visual loss (related to intraocular pressure) in FS-LASIK is less than the conventional microkeratome-assisted LASIK. In lenticule extraction, FSL system is used for cutting a small lenticule in corneal tissue, and similar to the flap created in LASIK, the flap is lifted, the lenticule is removed, and then the flap is repositioned. Also, in the SMILE
procedure (Carl Zeiss Meditec AG), the intrastromal lenticule is sculpted for correction of myopic or astigmatic refractive error; during this procedure, FSL is used for the anterior and posterior dissection of both faces of the refractive lenticule in addition to the small incision in the mid-periphery of the cornea for safe extraction of the intrastromal lenticule. Other companies introduced their own laser systems later, such as SmartSight by Schwind and corneal lenticule extraction for advanced refractive correction by Ziemer Ophthalmic Systems AG. Research is continued to determine the superiority of FS-LASIK over RELEX and SMILE [4, 5, 14, 15].

When corneal incisions are used to treat astigmatism, Fs-technology allows for exceptional precision and control over all aspects of the keratotomy procedure. Fs-specific intrastromal keratotomies, on the other hand, reduce the risk of infection by avoiding open wounds.

8.1.2 Additive procedure (keratophakia in the stroma)

Since 1949, Barraquer has been studying keratophakia as a technique of sculpting corneal curvature by adding tissue. As a result of inconsistencies in the quality of the cuts and reactive wound healing at the borders of the cut, the procedure was often abandoned. New steps toward keratophakia are being taken as a result of advances in femtosecond technology. For starters, an intrastromal pocket or stromal bed can now be prepared with better precision. A second development is the creation of novel inlay materials. Decellularization and preservation of extracted lenticules following lenticule extraction procedures are the subject of current research [16]. Anterior OCT should be examined pre and postoperative together with topography and slit photo for the changes that have been resulted from process (Figure 10).
8.2 Keratoplasty (penetrating, femtosecond laser-assisted, anterior and posterior lamellar keratoplasty)

Penetrating keratoplasty (PKP) has evolved substantially over the years, and various alternative surgical procedures have been introduced to improve patients’ outcomes. The introduction of FS laser into PKP (full-thickness keratoplasty) has improved postoperative outcomes in different keratoplasty procedures, owing to the reduced misalignment, higher precision, and wound stability. Tension-free incisions and waterproof-adapting incision margins can be achieved with the use of a perfect trephination device [17]. Trephination systems include hand-held, motorized, excimer-laser, and fs-laser. Graft alignment is better with motor-trephine and excimer-based trephination [18]. Treatment of the eye that receives trephination frequently lacks appropriate centering. Another challenge with trephination is how the recipient eye and donor button are fixed and stabilized; any mechanical stress on the tissue produces compression and distortion, reducing recipient and donor fit. Vacuum and applanation are common fixing methods (vacuum suction with applanation). fs- and excimer-assisted trephination demonstrated superior alignment in all sutures-out keratoplasty patients in the excimer group. Patterned trephination increases the strength and structural integrity of the graft-host junction and reduces the number of requisite sutures, which results in reduced astigmatism, and possibly the time of visual recovery. FS laser has also improved the shaped corneal cuts with various patterns and angles of incisions, as well as different wound configurations, such as “top-hat”, “mushroom”, “zigzag” and “Christmas tree”, which improve wound healing and result in improved best spectacle-corrected visual acuity.

When only specific layers of the five corneal layers (such as anterior or posterior layers of the cornea), lamellar keratoplasty is performed, which has several modifications [19]. In deep anterior lamellar keratoplasty (DALK), the use of FS allows for precise trephination cuts for separation of corneal layers with desired depths, diameters, centration, shape, and size [20], which facilitates big bubble formation, which has several advantages over manual technique in terms of accelerated wound healing/stability (owing to the different side-cut profiles), precise sutureless cuts of both donor and recipient cornea (increased alignment), and preservation of healthy recipient corneal endothelium [21]. Also, conversion into full-thickness keratoplasty is feasible with FS-assisted lamellar keratoplasty. New big bubble formation approaches, such as the IntraBubble technique, creates a channel in the posterior stromal for the introduction of air injection, which results in cleavage of the corneal tissue. FSL has also been introduced into endothelial lamellar keratoplasty techniques such as deep lamellar endothelial keratoplasty (DLEK) and Descemet’s stripping automated endothelial keratoplasty (DSAEK). Posterior trephination cut prevents the intrastromal cavitation bubbles in the lamellar interface with a shorter applanation lens assembly used to create LASIK flaps. However, the effectiveness of FSL in DSAEK requires further studies on the eye banks, as scanning electron microscopic studies have shown occasional mild stucco-like texture of the lamellar surface caused by laser scatter and attenuation in deep stroma. Additionally, poorer visual outcomes are anticipated during the laser procedure, owing to the increased roughness at the deep intrastromal dissection surface and irregularities of the endothelial surface [4, 5, 14, 15].
8.3 Cataract surgery

In cataract surgery, the current FS systems allow imaging and measurement of the anterior segment of the eye, cutting the tissue at the desired location depth, pattern, and size, full-thickness corneal incisions for the introduction of instruments to the eye, partial thickness corneal incisions for treatment of corneal astigmatism, circular incision to the anterior lens capsule (capsulotomy), and fragmentation of the cataractous lens nucleus (Figure 11). Advantages of FSL-assisted cataract surgery include precision and repeatability of incisions, lower ultrasound energy used for lens nucleus emulsification/liquefication), perfect sizing, and predictability of corneal incisions and capsulotomy (Figure 12). Despite the numerous studies suggesting the superiority of different FSLs used for cataract surgery (Table 1) over the conventional phacoemulsification manual operation and emphasis of review studies on the advantages of FSL method, meta-analysis studies failed to prove its superiority considering the overall outcome of patients. The introduction of low-energy lasers may have improved outcomes compared with first-generation FSL [5, 14].

Despite the above-mentioned clear benefits and multiple studies indicating superiority of femto laser cataract surgery in completing the single surgical stages [22, 23]. Review papers stress fs-assisted cataract surgery in specific patient groups, i.e., those with low corneal endothelial cell numbers, but a clear advantage of the fs approach over manual phacoemulsification is not found in normal cases [24, 25]. Primary posterior capsulotomy assisted by fs laser, as well lens capsule labeling, altering the power of the intraocular lens (IOL) postoperatively using more mobile, and adaptable fs-laser systems will make the future of femtosecond laser brighter (Figure 13) [26].
Terahertz, Ultrafast Lasers and Their Medical and Industrial Applications

**Figure 12.** Femtosecond Laser Assisted Cataract Surgery (FLACS) vs. Micro Incision Cataract Surgery (MICS); Effects of Learning Curve.

<table>
<thead>
<tr>
<th>Femto-Laser</th>
<th>CATALYS</th>
<th>LenSx</th>
<th>LENSAR</th>
<th>VICTUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arcuate incisions</td>
<td>Surface and Intrastromal</td>
<td>Surface and Intrastromal</td>
<td>Surface and Intrastromal</td>
<td>Capable of surface or stromal</td>
</tr>
<tr>
<td>Pulse frequency (kHz)</td>
<td>120</td>
<td>50</td>
<td>80</td>
<td>Up to 160</td>
</tr>
<tr>
<td>FDA approvals</td>
<td>Corneal + arcuate incisions Ant capsulotomy Lens fragmentation</td>
<td>Corneal + arcuate incisions Ant capsulotomy Lens fragmentation</td>
<td>Corneal + arcuate incisions Ant capsulotomy Lens fragmentation</td>
<td>Corneal + arcuate incisions Ant capsulotomy Corneal flap</td>
</tr>
<tr>
<td>Patient interface design</td>
<td>Liquid optics Non-anplanating Liquid interface 2-piece Vacuum docking</td>
<td>Soft fit 2-piece Vacuum docking</td>
<td>Robocone Non-anplanating Fluid interface 2-pieces Vacuum docking</td>
<td>Dual modality Curve lens Applanating Spherical 2-pieces Vacuum docking Solid + Liquid</td>
</tr>
<tr>
<td>Docking</td>
<td>Ocular surface bathed in saline solution No corneal applanation No glaucoma contraindication</td>
<td>Curved applanation No glaucoma Intra indication (soft fit PI)</td>
<td>No corneal applanation</td>
<td>Soft docking for capsulotomy and lens fragmentation Regular docking for corneal incisions</td>
</tr>
<tr>
<td>IOP rise</td>
<td>10.3 mm Hg rise</td>
<td>16.4 mm Hg rise (cioni, ASCRS 2012 presentation)</td>
<td>Unknown (currently under evaluation)</td>
<td>Unknown (currently under evaluation)</td>
</tr>
</tbody>
</table>

**Table Notes:**
- **FDA approvals:** Corneal + arcuate incisions, Ant capsulotomy, Lens fragmentation
- **Patient interface design:** Liquid optics, Non-anplanating, Liquid interface, 2-piece, Vacuum docking
- **Docking:** Ocular surface bathed in saline solution, No corneal applanation, No glaucoma contraindication
- **IOP rise:** 10.3 mm Hg rise (cioni, ASCRS 2012 presentation), 16.4 mm Hg rise (currently under evaluation)
9. Conclusions

As a precise and reliable tool in the field of ophthalmic surgery, fs-laser technology has evolved over the past few decades. Fs-laser-assisted cataract and corneal surgery have reached a high standard worldwide, despite the fact that some applications are still in the early stages of development. These procedures have been made safer and more effective by the use of fs-laser technology, which has opened the door to new surgical approaches.

Conflict of interest

The authors declare no conflict of interest.
Author details

Sana Niazi¹ and Farideh Doroodgar²,³*

1 Medical Research center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2 Translational Ophthalmic Research Centre, Tehran University of Medical Science, Tehran, Iran
3 Negah Specialty Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Address all correspondence to: farinaz_144@yahoo.com

© 2022 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
References


[18] Seitz B et al. Reconsidering sequential double running suture


